Development of Viable Synthetic Approaches to Highly Functionalized Small Ring Systems – Synthesis of Novel Cyclopropylacrylates as Monomers for Low-Shrinkage Polymer-Composites

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Dedicated to my Teachers

Knowledge may have its purposes, but guessing is always more fun than knowing.

W. H. Auden

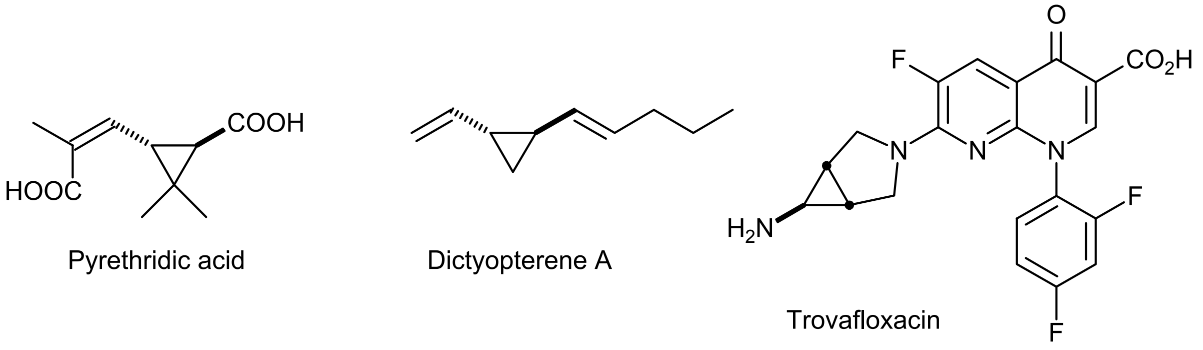
Abbreviations

Ac	acetyl
acac	acetylacetonato
BHT	2,6-di(*tert*-butyl)-4-methylphenol
Bn	benzyl
Bz	benzoyl
dba	dibenzalacetonato
DBU	1,8-diazabicyclo[5.4.0]undec-7-en
DCC	*N,N'*-dicyclohexylcarbodiimide
DECVCP	1,1-diethoxycarbonyl-2-vinylcyclopropane
DIC	*N,N'*-diisopropylcarbodiimide
DMAP	4-(dimethylamino)pyridine
DME	1,2-dimethoxyethane
DMF	dimethylformamide
DMSO	dimethylsulfoxide
LDA	lithium diisopropylamide
TDMPP	tris(2,6-dimethoxyphenyl)phosphane
TFA	trifluoroacetic acid
THF	tetrahydrofuran
THP	2-tetrahydropyranyl
TMEDA	tetramathylethylenediamine
Tris	2,4,6-triisopropylphenyl

A. INTRODUCTION

A manifold of unusual chemical properties and high reactivity makes cyclopropane units a fundamental class of functional group playing a key structural role as a fragment in a range of substances, both natural and synthetic.[1] Isolated or synthesized, such compounds due to their wide spectrum of biological activities, find more and more applications as commercial products. Examples of biologically active compounds are the pyrethroid insecticides,[2] dictyopterenes[3] or non-steroidal anti-inflammatory agents.[4] Manufacturing of such products obviously requires reliable preparative protocols, which can easily be scaled up to a necessary volume. Although during the last 45 years a significant number of novel cyclopropanations based on the addition of various carbenes, carbeniods or their ylide-like synthetic equivalents to double bonds have been discovered,[5] the classical reactions employing 1,3-eliminations in different variations constitute still the most useful methodology for the industrial production of cyclopropane derivatives. Therefore, there is still need for the development of novel cyclopropane forming methods applicable on a large preparative scale for the manufacturing of new products (Scheme 1).

Scheme 1



Pyrethridic acid

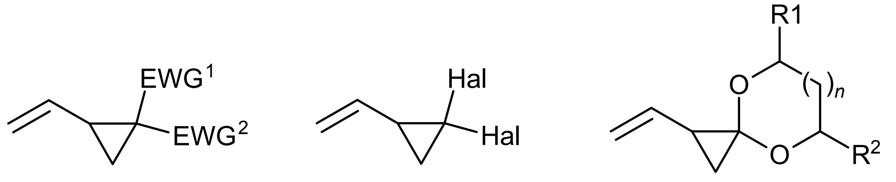
Dictyopterene A

Trovafloxacin

One of the latest achievements in this field is a large-scale adaptation of the aminocyclopropanation of alkenes as recently discovered by de Meijere et al.[6] towards the synthesis of 6-amino-3-azabicyclo[3.1.0]hexane,[7] a key structural fragment of the once commercialized antiinfective drug “Trovafloxacin”.[8]

Another potential industrial application of cyclopropane derivatives was triggered by the discovery that certain substituted vinylcyclopropanes readily undergo radical ring-opening polymerization to give polymers and copolymers with significantly lower shrinkage[9] than those from commonly applied methacrylates and therefore have been considered for use in photopolymerizable dental composites.[10] The monomers which showed promising results in this context,[11] can be divided into three groups: 1,1-disubstituted 2-vinylcyclopropanes with electron-withdrawing groups (EWG = CO_2Alk, CH_3CO, CN), *gem*-dihalovinylcyclopropanes and alkylideneacetals of vinylcyclopropanone (Scheme 2).

Scheme 2



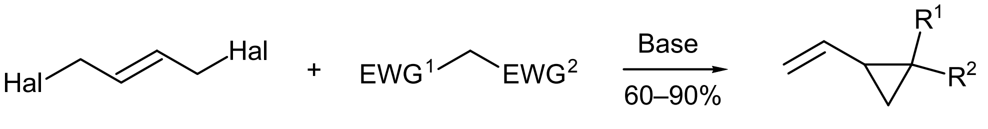
EWG^1, EWG^2 = CN, CO_2Alk, CH_3CO

Hal = Cl, Br

n = 0, 1, 2, $R^1 = R^2$ = H; n = 0, 1, R^1, R^2 = H, Ph; n = 0, R^1, R^2 = 1,2-$(CH_2)_2C_6H_4$

The EWG-substituted vinylcyclopropanes (VCPs) are readily accessible by 1,2-cycloalkylation of 1,3-dicarbonyl compounds with 1,4-dihalobut-2-enes.[12] This reaction provided the target VCPs in moderate to good yields as of *cis*- and *trans*-isomers mixtures (when $EWG^1 \neq EWG^2$) sometimes contaminated with the corresponding cyclopentene[13] or dihydrofurane[14] (EWG^1 or/and EWG^2 = CH_3CO) derivatives (Scheme 3).

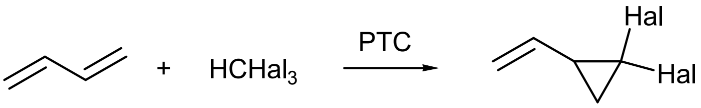
Scheme 3



Hal = Cl, Br; EWG^1, EWG^2 = CN, $COCH_3$, CO_2Alk

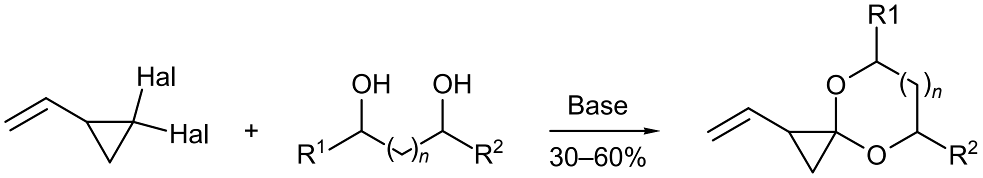
gem-Dihalovinylcyclopropanes are accessible on a multigram scale by addition of the corresponding dihalocarbene generated from the respective haloform under “Phase Transfer Catalysis” conditions (PTC). The main drawbacks of this approach are lack of chemo- and regio- (for substituted 1,3-butadienes) selectivity and difficulties connected with the isolation of the product from the reaction mixture. Thus, in spite of various attempts to optimize this reaction towards VCP synthesis, the yield of the desired products never exceeded 30%[15] (Scheme 4).

Scheme 4



Further derivatization of *gem*-dihalovinylcyclopropanes with substituted 1,ω-diols provided vinylcyclopropanes of the third group[16] (Scheme 5).

Scheme 5

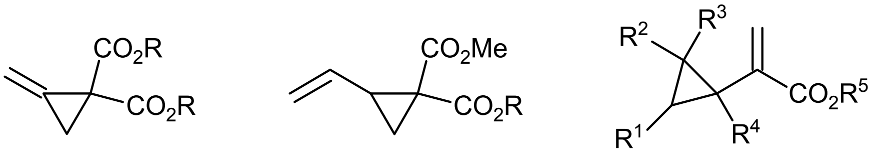


n = 0, 1, 2, $R^1 = R^2$ = H; n = 0, 1, R^1, R^2 = H, Ph

According to the screening of substances mentioned above, and concerning such criteria as degree of conversion of monomer to polymer (%), number-average molecular weight ($\overline{M}_n$), glass-transition temperature (T_g) and polymerization shrinkage (%), the best results were obtained for 1,1-diethoxycarbonyl-2-vinylcyclopropane (DECVCP). In contrast to other ring-opening polymerizable low-shrinkage monomers, such as spiro orthocarbonates or cyclic ketene acetals, the DEVCP is stable towards humidity, towards acidic and basic impurities as well as inorganic fillers. In addition, it shows a higher tendency to undergo radical copolymerization with other vinyl monomers. However, in comparison with methacrylates, DECVCP is less reactive in the radical copolymerization;[12] this fact restricts its practical application. Since the reactivity of vinylcylopropanes in the radical polymerization had been shown to depend on their structure[11] and can therefore be influenced by the kind and number of substituents, it was decided to synthesize novel cyclopropyl-containing monomers with various substitution patterns on the cyclopropane ring in order to investigate the dependence of polymer characteristics on monomer structure. Such knowledge might be an extremely important step towards the synthesis of "tailor-made" polymers.

As a field of investigation only such cyclopropane derivatives were chosen, which could be synthesized along reasonable reaction sequences on at least 5 g scales (Scheme 6).

Scheme 6



Thus, the goals of the present work can be summarized as follows:

- synthesis of various new monomers with functionalized cyclopropyl units,
- polymerization experiments, structural studies, investingation of the physical and chemical properties of the synthesized polymers to be performed by Ivoclar Vivadent AG,
- correlation between monomer structure and properties of the polymer formed and advanced search for a monomer able to excel the characteristics of the benchmark DECVCP,
- development of a protocol for the synthesis of this monomer on a large scale,
- toxicity tests for the new monomers (Ivoclar Vivadent AG).

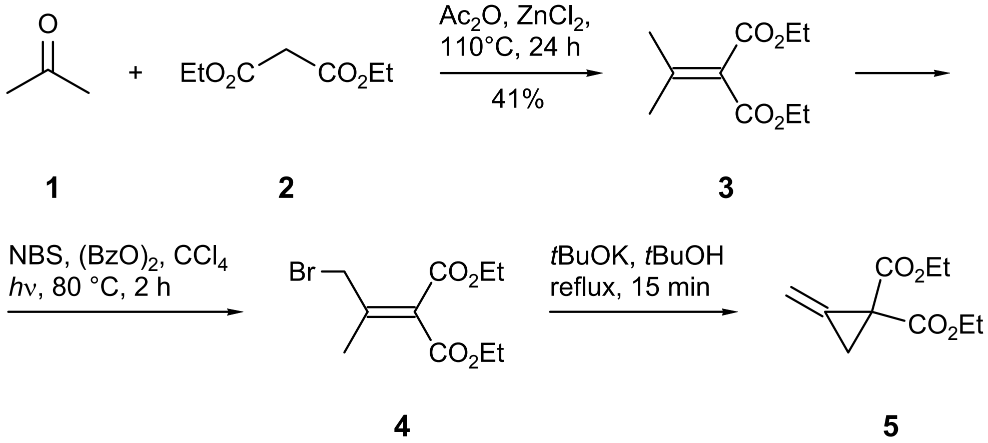
B. MAIN PART

1. Synthesis of Methylene- and Vinylcyclopropanes Bearing One or Two Electron-Withdrawing Substituents on the Cyclopropane Ring

1.1. Synthesis of diethyl 2-methylenecyclopropanedicarboxylate

Although diethyl 2-methylenecyclopropanedicarboxylate (**5**) has been known since 1959 and well described in the literature,[17] the synthesis of pure **5** on a preparative scale encounters some difficulties which have to be detailed.

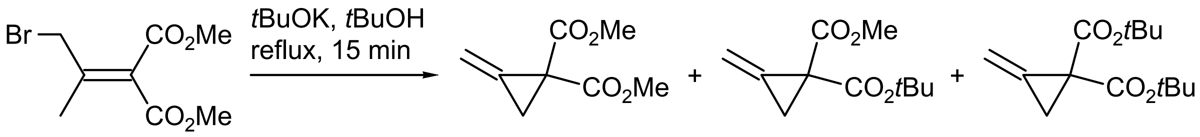
Scheme 7



The classical synthetic route starts from acetone (**1**) and diethyl malonate (**2**), by KNOEVENAGEL condensation, followed by WOHL-ZIEGLER allylic bromination of the resulting diethyl isopropylidenemalonate (**3**) with NBS in the presence of benzoyl peroxide as a radical initiator and under irradiation with 500 W lamp, and finally 1,3-dehydrobromination of the crude reaction mixture by heating under reflux with potassium *tert*-butoxide in *tert*-butyl alcohol. The resulting crude mixture contained the methylenecyclopropane **5** in a moderate yield. Pure **5** then could be isolated either by preparative GC,[17] or by "Spaltrohr" distillation[18] of the crude mixture containing also isopropylidenemalonate (**3**) and a small amount of the corresponding *tert*-butyl esters formed by transesterification. The boiling points of all these components were very close to each other; therefore the separation of pure **5** from the by-products is a main problem of this synthetic sequence. In order to avoid these difficulties, an attempt was made to isolate the pure bromoisopropylidenemalonate **4** by distillation of the crude reaction mixture under reduced pressure. Unfortunately, this turned to be impossible because the decomposition temperature of **4** was lower than its boiling point even at 10^{-3} Torr. Taking this fact into consideration, dimethyl isopropylidenemalonate[19] (**6**) was subjected to the bromination protocol mentioned above. In this case, sufficiently pure (~93%, according to ^{1}H NMR, 59% yield) dimethyl 2-(2-bromo-1-methylethylidene)malonate (**7**) was successfully separated from the starting material and overbrominated products by distillation of the crude reaction mixture under reduced pressure (b. p. 93– 95 °C/0.001 Torr, $T_{bath} \leq 130$ °C). However, the distillation under these conditions succeeded only when amount of mixture in the distillation flask did not exceed 20 g. Attempted distillation on a larger scale caused spontaneous decomposition in the distillation flask.

The pure bromide **7** (40 g, 159 mmol), when subjected to dehydrobromination under the same conditions as **4**, after distillation gave 18 g of a colorless oil, which was a mixture of approximately equal amounts of all possible esters of 2-methylene-1,1-dicarboxylic acid **8-10** (Scheme 8).

Scheme 8



7 **8** **9** **10**

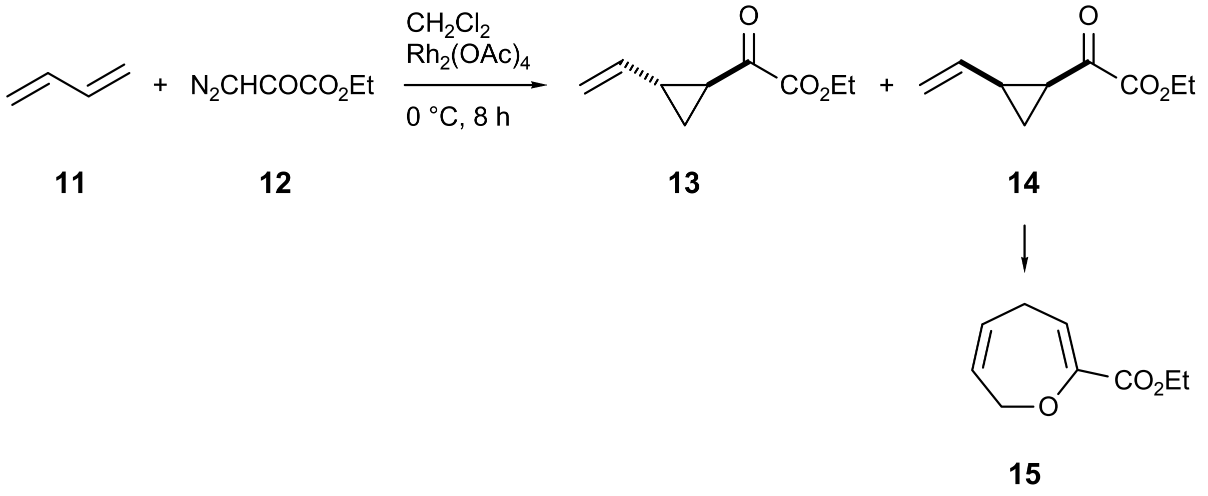
Since all attempts to dehydrobrominate **7** without transesterification failed (*tert*-BuOK/DMSO, *tert*-BuOK/THF and *iso*-Pr_2NEt/C_7H_8, DBU/C_6H_6 were tested), it was decided to return to the original synthetic sequence (Scheme 7). Thus, crude bromide **4 (**44.8 g) gave 18.8 g of crude reaction mixture (**5**:**3** ratio ~3:2 according to ^{1}H NMR), which was fractionated on a “Spaltrohr” column within 5 days to yield 8 g of pure **5**.

1.2. Synthesis of ethyl 2-vinylcyclopropyloxoacetate

Preparation of ethyl 2-vinylcyclopropyloxoacetate (**13**) was based on a protocol developed by WENKERT et al.[20] for $Rh_2(OAc)_4$-catalyzed addition of ethyl diazopyruvate (**12**) to 1,3-butadiene (**11**). The starting diazopyruvate **12** is accessible on about 0.2 mol scale via acylation of diazomethane by the commercially available ethyl chloroxalate according to Ratuský and Šorm.[21]

The $Rh_2(OAc)_4$-catalyzed addition of **12** to butadiene (**11**) was shown to be not a stereoselective one; it led to approximately equimolar mixture of isomers **13** and **14.** The second one under reaction conditions had readily undergone rearrangement to give the corresponding ethyl dihydrooxepinecarboxylate **15** (Scheme 9). Therefore, the yield of this reaction obviously could not exceed 50%, and a value of 37% obtained by Wenkert et al. seemed impossible to excel because there were no literature examples for the diazopyruvate addition to alkenes yielding more than 75% of corresponding cyclopropane.[22]

Scheme 9



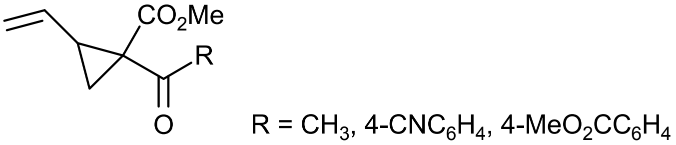
According to the original protocol, ethyl diazopyruvate dissolved in 400 mL of methylene chloride was added dropwise within 8 h into a stirred at 0 °C solution of the Rh-catalyst and an excess of butadiene in the same solvent to yield after column chromatography 2 g of pure product. Therefore, it would be difficult to reproduce this protocol in a five-fold scale as required. On the other hand, it turned to be problematic to use a syringe pump because of two reasons: due to diazopyruvate crystallization from a concentrated solution between agile surfaces of glass syringe, it was stopped; a plastic syringe usually used in laboratory practice, was unable to keep methylene chloride for more than 2 h. Attempted continuous addition of CH_2Cl_2 solution caused only the lost of syringe content. In order to avoid this problem, a simple trick was used, namely the *vertically* oriented plastic syringe. This excluded continuous contact of syringe piston with methylene chloride and was enough to keep it sealed during the time required. There was only one limitation: diazopyruvate applied must contain no trace of impurities which could cause decomposition of diazocompound in a syringe, followed by nitrogen evolution that could push the reagent into reaction media within a significantly shorter time than required. An improvement adopted from DOYLE's general procedure for Rh-catalyzed addition of diazoacetates to alkenes,[23] was the next: the needle immersed into reaction mixture was taken as thin as possible (Ø 0.9 mm usually was enough). It prevented nitrogen bubbles from returning back into the syringe, and provided the *continuous* reagent delivery into the reaction media.

Due to these improvements it became possible to add 178 mmol of ethyl diazopyruvate (**12**) to the excess of butadiene dissolved in 1 L of methylene chloride, that afforded 10.9 g (36%) of the target oxoester **13**.

1.3. Synthesis of 1,1-disubstituted 2-vinylcyclopropanes by alkylation of 1,3-dicarbonyl compounds

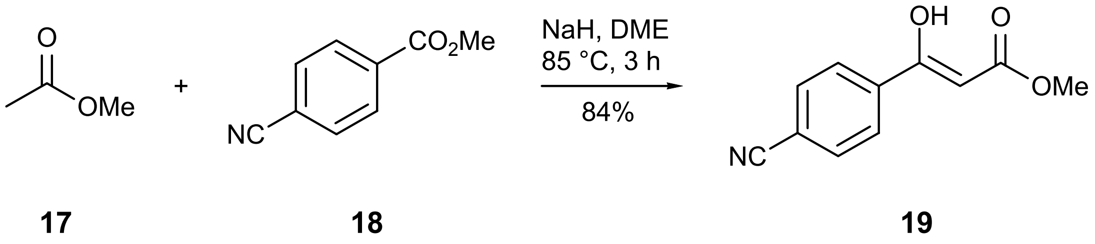
1,1-Disubstituted 2-vinylcyclopropanes are accessible via well-known double alkylation of CH-acids with 1,4-dihalobut-2-enes (Scheme 3). This approach is described in literature enough to choose an appropriate synthetic method for a preparation of the *gem*-EWG disubstituted vinylcyclopropanes currently ordered for polymerization experiments (Scheme 10).

Scheme 10



Among the required starting 1,3-dicarbonyl compounds, methyl acetoacetate (**16**) was commercially available, whereas 2-aroyl acetic acid methyl esters had to be prepared in some different ways. Thus, according to a modified CLAISEN condensation protocol,[24] refluxing of methyl acetate (**17**) with methyl 4-cyanobenzoate (**18**) in the presence of sodium hydride excess, gave methyl 3-(4-cyanophenyl)-3-oxyprop-2-enoate (**19**) in good yield (Scheme 11).

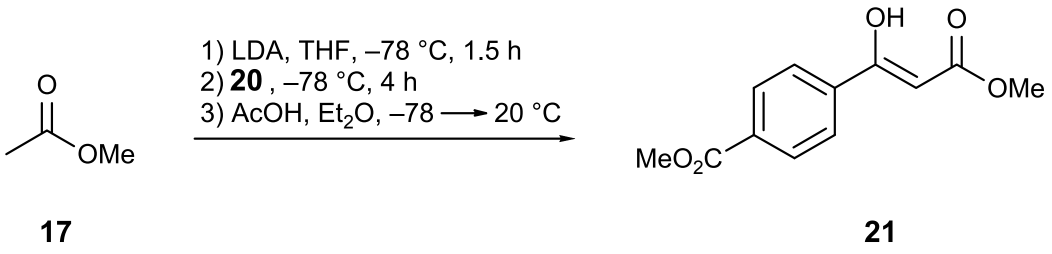
Scheme 11



Unfortunately, this method could not be applied for the condensation of methyl acetate (**17**) with dimethyl terephthalate, because its low solubility could not provide a sufficient excess of diester in respect to the slowly added into the reaction media methylene component **17**. It resulted in various self-condensation products instead of the desired cross-condensation product. On the other hand, previously described two-step procedure for the synthesis of ethyl [4-(methoxycarbonyl)benzoyl]acetate[25] starting from 4-methoxycarbonylbezoyl chloride (**20**) and ethyl acetoacetate, has no preparative value because of its low yield (25% after column chromatography).

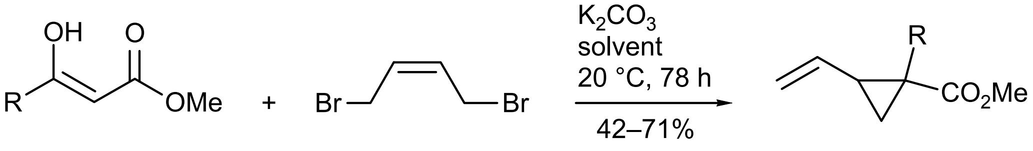
Therefore, an original protocol for the synthesis of **21** was developed. Lithium enolate generated from methyl acetate (**17**) and LDA at –78 °C, had been found to be acylated by a slow addition of 0.5 equivalents of 4-methoxycarbonylbezoyl chloride (**20**) at –78 °C, to give the target product **21** in satisfactory yield (40% after recrystallization) (Scheme 12).

Scheme 12



Thus prepared methyl 2-aroylacetates 19 and 21 were alkylated with *cis*-1,4-dibromobut-2-ene[26] (22) in the presence of potassium carbonate according to Jacobi et al. protocol,[27] which was successfully reproduced in the case of methyl acetoacetate (**16**) to give a sufficient amount of **23** in good yield (71%) (Scheme 13). This protocol was chosen because of mild reaction conditions that excluded, so far as possible, various side reactions. Thus, at relatively low temperature (about 20 °C) the formation of cyclopentenone, a major product at increased temperature (especially when *Z*-dihalide and the base with a hard counter-ion have been used[13]), was avoided. Protic solvent (MeOH) reduced the formation of O-alkylated products, because nucleophilic oxygen atom of the corresponding enolate had been solvated.

Scheme 13



16,19,21 **22** **23-25**

Table 1. Synthesis of vinylcyclopropanes **23-25**. Yields and reaction conditions.

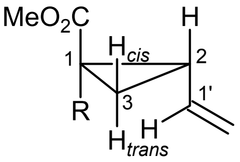
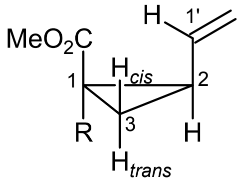
Entry	Starting material	R	Product	Solvent	Yield, % (*E/Z*-ratio)
1	**16**	CH_3	**23**	Methanol	71(~2:1)
2	**19**	4-CNC_6H_4	**24**	Methanol/THF	42[a]
3	**21**	4-$CO_2MeC_6H_4$	**25**	Methanol/THF	65 (~5:1)[b]

[a] Pure ***E*-24** was obtained; *E/Z*-ratio was not determined. – [b] Yield of crude product is given.

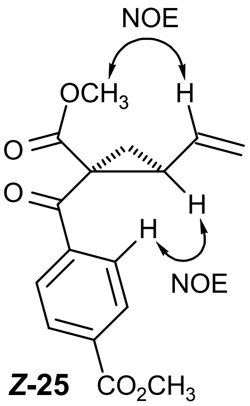
As can be seen from the Table 1, increasing of electron-withdrawing character of substituent attached to a carbonyl group decreases the yield of target product. Thus, in the case of **24** and **25**, some amounts of the corresponding 4-substituted benzoic acids and their methyl esters were found among the by-products. Their formation could be attributed to retro-CLAISEN reaction of the starting 1,3-dicarbonyl compounds **19** and **21**. Commonly, a formation of relatively high number of by-products drastically complicated the purification of target product. Thus, even in case of **16**, characterized by the highest yield in this series, purification of the product **23** by column chromatography had not been avoided. Fortunately, diastereomerically pure **24** appeared to be easily isolated just by recrystallization of a crude product from the mixture of hexane and *iso*-propanol, whereas a column chromatography of the crude **25** could reach only 90% purity.

Stereochemical assignment of the synthesized products **23-25** was conducted taking in consideration its ^1H NMR spectra. On the first look, they showed clear difference between signals of olefin proton 1'-H for major and minor isomers. Thus, $\delta_{maj}(1'\text{-H}) < \delta_{min}(1'\text{-H})$ and $(^3J_{2\text{-H}-1'\text{-H}})_{maj} < (^3J_{2\text{-H}-1'\text{-H}})_{min}$; this trend was maintained for all substances **23-25** (Table 2).

Table 2. Selected chemical shifts and coupling constants for the compounds **23-25**.

Compd.	*E*- 			*Z*- 		
	3-H_{cis}, $^3J_{cis}$	3-H_{trans}, $^3J_{trans}$	2-H 1'-H $^3J_{2\text{-}H\text{–}1'\text{-}H}$	3-H_{cis}, $^3J_{trans}$	3-H_{trans}, $^3J_{cis}$	2-H 1'-H $^3J_{2\text{-}H\text{–}1'\text{-}H}$
23	1.53, 8.9	1.84, 7.5	2.62 5.18 7.6	1.75, 7.8	1.58, 8.8	2.59 5.48 7.8
24	1.70, 9.0	1.98, 7.5	2.94 5.13 8.5	–	–	– –
25	1.65, 9.0	1.96, 7.3	2.93 5.14 8.5	1.96, 7.8	1.70, 9.0	2.72 5.77 8.8

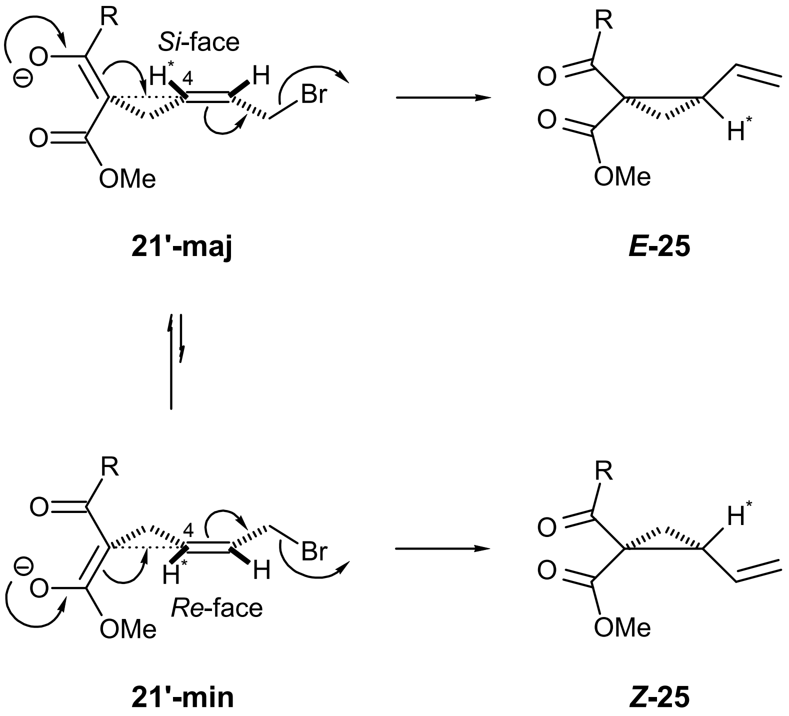
Then, the pure minor isomer of **25** was isolated and investigated by 1D NOE. Correlation obtained between 2-H – Ar-H_{ortho} as well as 1'-H – OCH_3 attached to a cyclopropane ring, clearly evidences that *minor* isomer of **25** adopts (*Z*)-configuration (Figure 1). Hence the presented double alkylation of β-ketoesters resulted in more sterically congested *E*-isomer as a major product. This outcome may be explained in terms of a concerted ring closure process. Enolic double bond was supposed to attack diastereotopic carbon atom (C-4) in tautomeric enolate **21'** only *suprafacially* because the conformation required for energetically more advantageous *antarafacial* ring-closure, is sterically impeded. Thus, growing of electron density towards C-4 position to be attacked in the enolate **21'-maj**, occured from the *Si*-face, whereas the C-4 position of enolate **21'-min**, was attacked from the *Re*-face (the direction of electron density redistribution is shown on Scheme 14). Since the only one concerted bond redistribution order has been assumed to be possible for each isomer, a stereochemical outcome of ring closure should depend on the ratio of tautomeric enolates in the reaction mixture.



***Z*-25**

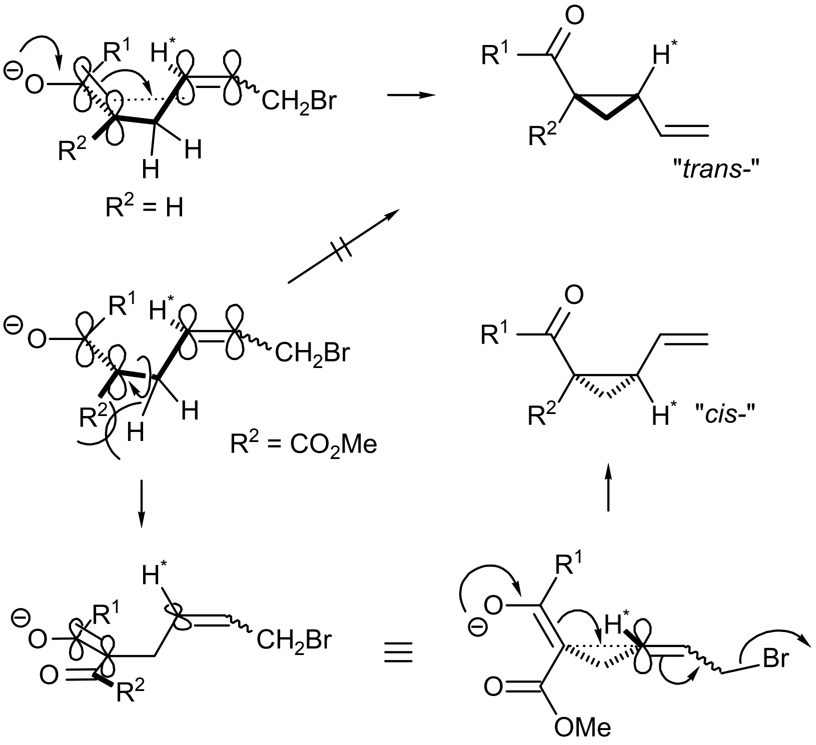
Figure 1

Scheme 14



This consideration is in a good accordance with experimental data. Thus, the cyclization of more thermodynamically stable enolate **21'-maj** resulted in less thermodynamically stable vinylcyclopropane ***E*-25** as a major isomer, whereas less thermodynamically stable enolate **21'-min** yielded after cyclization more thermodynamically stable vinylcyclopropane ***Z*-25** as the minor one. Moreover, in terms of this assumption, the increasing of electron-withdrawing character of substituent R (which obviously would increase the tautomeric excess of enolate mixture) should also increase diastereomeric excess of the reaction, what in fact has been observed (Table 1). However, it should be noted that these revelations, together with a spectroscopical trend (because of alkoxycarbonyl group influence on chemical shifts of cyclopropane protons) (Table 1) cannot be applied for the structure elucidation of monosubstituted vinyl cyclopropanes, which formation is featured by clear *trans*-diastereoselectivity.[28] That direction of monosubstituted enolate ring closure could be referred to an *antarafacial* process. Its realization becomes possible by removing one of the EWG substituent from α-position of enolate (Scheme 15). As it is shown on Scheme 15, coplanarity (and, correspondingly, the best overlapping) of the frontier orbitals forming cyclopropane bond, could be achieved by *antarafacial* process. It requires strain conformation, therefore such process is preferential only for R^2 = H. Otherwise, more bulky substituent (R^2 = CO_2Me) pushed the 4-bromobut-2-enylic fragment onto the plane perpendicular to that of 1,3-dicarbonyl fragment. That resulted in the less sterically strained conformation **21'**, though with less frontier orbital overlapping opportunity. Therefore, suprafacial ring closure mechanism was realized in this case.

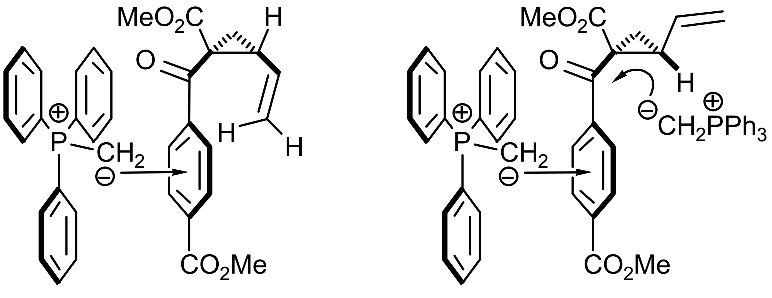
Scheme 15



1.4. Attempted methylenation of the methyl 1-aroyl-2-vinylcyclopropanecarboxylates

As an additional opportunity for further functionalization of the synthesized 1-aroyl-1-methoxycarbonyl-2-vinylcyclopropanes, WITTIG reaction was tested.

Compounds ***E*-24**, **25** were found unable to be olefinated by WITTIG reaction under various reaction conditions. Thus, no trace of olefinated product had been detected by treatment of the compound **24** either with pure methylene triphenylphosphonium ylide (prepared according to a previously described protocol[29]) in THF, or that generated in situ from methyl triphenylphosphonium bromide and the corresponding base under following conditions: *n*-butyl lithium in ether, sodium hydride in dimethylsufoxide, sodium hydride in THF, LDA in THF. It should be noted that observed in all the cases deep (usually, blue or green) and firm colorization of reaction mixture, disappeared only after work-up procedure (addition of at least one equivalent of 10% aqueous H_2SO_4) had been conducted. It may be attributed to an appearance of substrate-ylide electron donor-acceptor complex (EDA). Its formation consumed one equivalent of ylide and restricted addition of an excess of bulky ylide onto carbonyl group of complexed substrate in the case of *E*-configuration of starting material (Figure 2).


***E*-24,25**

***Z*-25**

Figure 2

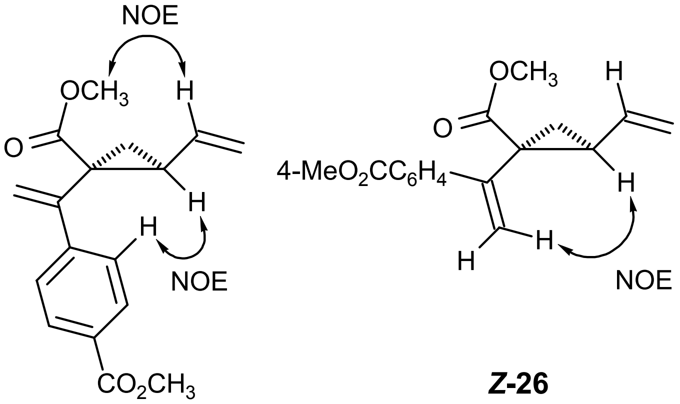

***Z*-26**

Figure 3

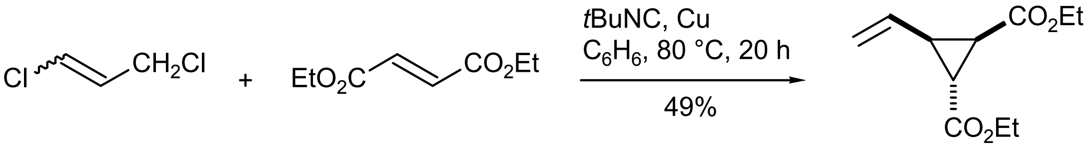
Nevertheless, a small amount of desired olefinated product **26** had been obtained after the 5:1 (*E*/*Z*)-isomeric mixture of **25** was methylenated with excess of ylide prepared from $MePh_3PBr$ and LDA in THF. After a corresponding work-up, a small amount of pure ***Z*-26** (7% yield) was isolated. Figure 2 shows a preferential direction for nucleophilic attack of the ylide onto carbonyl group in ***Z*-25**. Together with ***Z*-26**, 80% of starting compound enriched with ***E*-**

25 (in comparison to starting 5:1 isomeric mixture) was recovered. The relative configuration of **26** was ambiguously confirmed by 1D NOE experiments (Figure 3).

1.5. Synthesis of diethyl 3-ethenylcyclopropane-1,2-dicarboxylate

3-Ethenylcyclopropane-1,2-dicarboxylate (**29**) was for the first time obtained by addition of in situ generated vinyl carbene to diethyl fumarate (**28**). This reaction was discovered by Saegusa[30] and later developed in a preparative scale by Cluet.[31] A reactive carbenoid particle generated by continuous refluxing of 1,3-, 3,3-dichloroprop-1-ene or its crude mixture **27** in benzene in the presence of 400 mol % of copper and 800 mol% of *tert*-butyl isonitrile, reacted with electrophilic double bond to give a corresponding vinylcyclopropane in moderate yield (Scheme 16).

Scheme 16

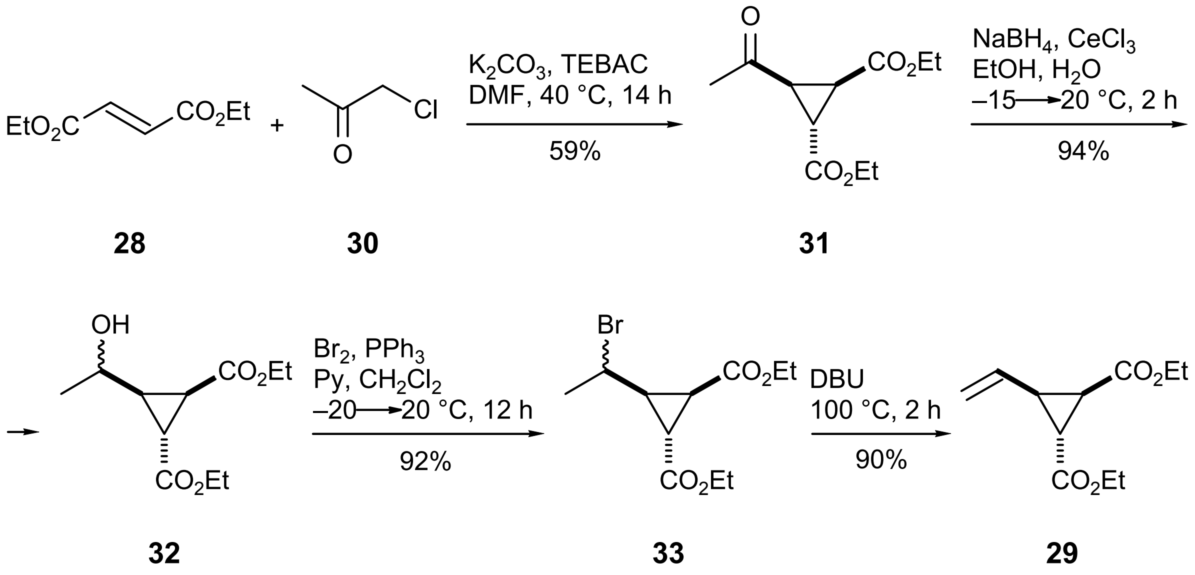


27 **28** **29**

Eight-fold excess of the expensive *tert*-butyl isonitrile was a serious drawback of this reaction. In addition, a reasonable yield could not be actually reached because the preparation of copper used was not outlined in the papers of the both authors although this information was important. Thus, active copper prepared according to Gore and Hughes[32] or Brewster and Groening[33] had not provided satisfactory yields of **28**. That's why a safe four-step synthetic scheme for preparation of **29** has been newly developed (Scheme 17).

Subsequent Michael addition – 1,3-elimination of chloroacetone **30** to diethylfumarate **28** was the first step. It was conducted according to recently reported protocol[34] with the only difference that chloroacetone (**30**) was gradually added to a stirred mixture of **28**, potassium carbonate and TEBAC in DMF instead of addition of **28** and **30** mixture into the reaction media as reported. This modification had been made taking a fact in consideration that unlike the highly reactive chloroacetone (**30**), the diethyl fumarate (**28**) turned to be inert towards possible self-condensation side-reactions under the reaction conditions. Therefore such addition order of the reagents, providing an excess of ester **28** against the ketone **30**, furnished a better yield of the ketoester **31**.

Scheme 17



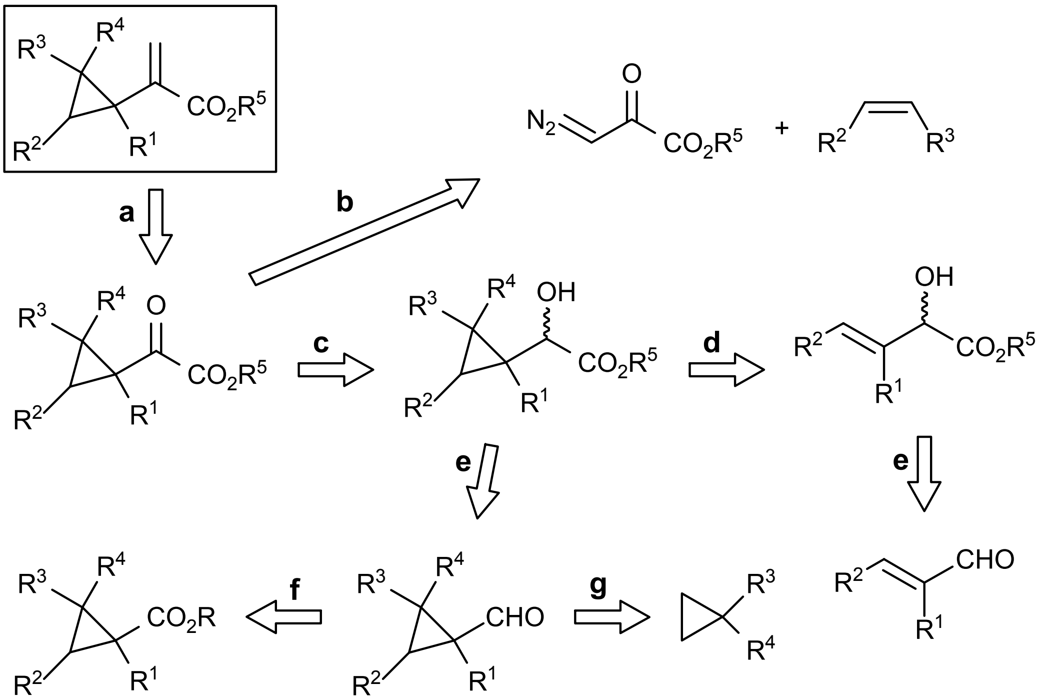
Preliminary attempted reduction of ketoester **31** by sodium borohydride, provided only a moderate yield of alcohol **32**, and gave also the corresponding diastereomeric lactones as by-products. The similar problem has been reported to arise by attempted reduction of various *cis*-1-alkoxycarbonyl-2-acetyl cyclopropanes[35] and was successfully overcome by reduction of a corresponding ketoester with sodium borohydride in the presence of one equivalent of cerium chloride in an accordance with the protocol for chemoselective reduction of keto-group in the presence of aldehyde.[36] Thus, the alcohol **32** was easily prepared in a large scale (26 g) and high yield; moreover, it was preferentially one diastereomer (d.e.~90% according to NMR, relative configuration had not been elucidated). The crude alcohol obtained, was smoothly converted to the corresponding bromide **33** in high yield by action of bromine-triphenylphosphine complex in methylene chloride according to DE MEIJERE[37] et al. Heating of the crude bromide **33** in a slight excess of neat DBU[38] at 100 °C with subsequent distillation of a crude product under reduced pressure, gave bulky amount of the target 1,2-diethoxycaronyl-3-vinyl cyclopropane (**29**) in high yield.

2. Synthesis of Alkyl Acrylates Bearing a Substituted Cyclopropane Attached to the Acrylate Double Bond. The "Main Strategy"

2.1. Introduction

Synthesis of acrylic acid derivatives bearing in 2-position variously substituted cyclopropane moiety was the central synthetic task of the project presented. Alkyl substituents were excluded from consideration because their introduction in vinylcyclopropane moiety had been previously shown to decrease conversion of monomers to the corresponding polymer.[39] Here only cyclopropylacrylates, substituted with vinyl, alkylidene, alkoxycarbonyl group, or those condensed with cycloalkanes, i.e. 2-(bicyclo[*n*.1.0]alk-*m*-yl)acrylates (*m* = 1, *n*+3) are concerned. The synthetic approaches to this class of substances are figured out on the Scheme 18.

Scheme 18



As it is shown on this scheme, target cyclopropylacrylates could be prepared by WITTIG methylenation **a** of a substituted cyclopropyl oxopyruvate. Two examples of cyclopropyl oxopyruvate and its vinylic derivative **13** methylenation leading to corresponding cyclopropylacrylates in moderate to good yields had been previously described in literature;

so this step seemed to be reliable enough. Substituted cyclopropyl oxoacetates are available via two different ways. Rh^{II}-catalyzed addition of alkyl diazopyruvates to various cycloalk(adi)enes (route **b**) is satisfactory documented in literature and, in spite of moderate yields and doubtful availability of used diazocompounds (they are synthesized from diazomethane and corresponding monoalkoxy oxalyl chlorides), this method combined with WITTIG reaction is the shortest way towards 2-bicycliclo[*n*.1.0]alk-(*n*+3)-yl acrylates. Another opportunity for the synthesis of substituted cyclopropyl oxoacetates included oxidation of the corresponding α-hydroxyacetates (route **c**). They can be obtained from already accessible substituted formylcyclopropanes (route **e**) or α,β-unsaturated aldehydes by subsequent SIMMOMS-SMITH cyclopropanation **d** of the α-alkenyl-α-hydroxyacetates prepared (route **e**) applying a preparative protocol for PINNER alcoholysis of cyanohydrins. Formylcyclopropanes could be prepared either from the corresponding cyclopropanecarboxylic acids, or by formylation of lithiated alkylidene cyclopropanes, some of which are accessible in a large scale.

Although the presented scheme might not always provide the shortest and most efficient route to some target products, its preparative utility in common sense is indisputable because it is based mostly on good developed preparative reactions, which may provide target acrylates preparation in at least 5 g scale with a high grade of reliability.

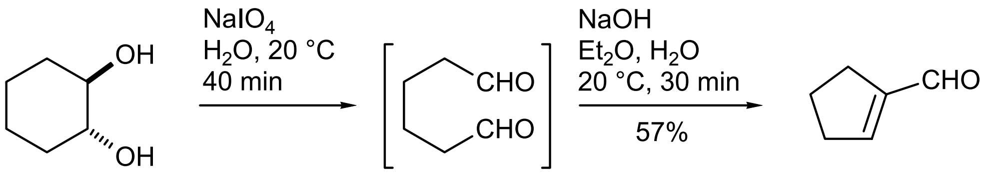
In the next parts of this chapter, the synthesis of the intermediate products starting from aldehydes towards target cyclopropylacrylates directed from **f** to **a** (Scheme 18) will be detailed.

2.2. Synthesis of cycloalk-1-enecarbaldehydes and substituted formylcyclopropanes.

1-Formyl substituted cyclopentene and cyclohexene were synthesized in accordance with previously described protocols.

Cyclopent-1-enecarboxaldehyde **36** was prepared in moderate yield (57%) starting from commercially available *trans*-1,2-cyclohexanediol **34** by "one-pot" oxidation with sodium *metha*-periodate and subsequent base-catalyzed intramolecular crotonic condensation of intermediately formed adipinaldehyde **35**,[40] with the only difference that when sodium hydroxide was added and the reaction mixture was stirred for 30 min, it was immediately neutralized by adding of 20% aqueous sulfuric acid and then worked up in a usual manner. This improvement let to suppress significantly a formation of undesirable resin-like by-products usually originated from base-catalysed self-condensation reactions, occurring when the standard work-up procedure is applied.

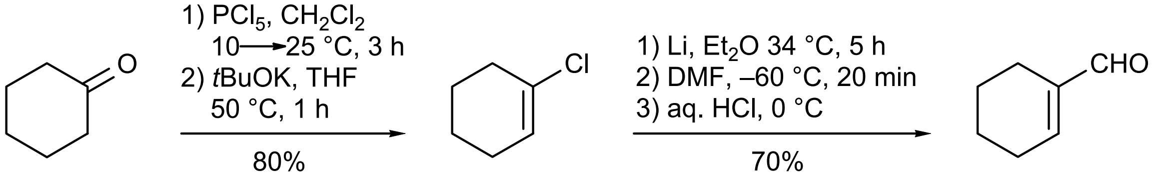
Scheme 19



34 **35** **36**

Cyclohex-1-enecarboxaldehyde **39** was prepared in three steps starting from cyclohexanone according to BRANDSMA and VERKRUIJSSE[41] (Scheme 20). Thus, chlorination of cyclohexanone (**37**) afforded a crude mixture of *gem*-dichlorocyclohexane and 1-chlorocyclohexene **38** that was then smoothly converted into 1-chlorocyclohexene (**38**) after successive elimination of HCl by potassium *tert*-butoxide. Obtained alkenyl chloride **38** was lithiated with 0.5% of sodium doped lithium and subsequently treated with DMF, giving after hydrolysis the target aldehyde **39** in good yield (70%).

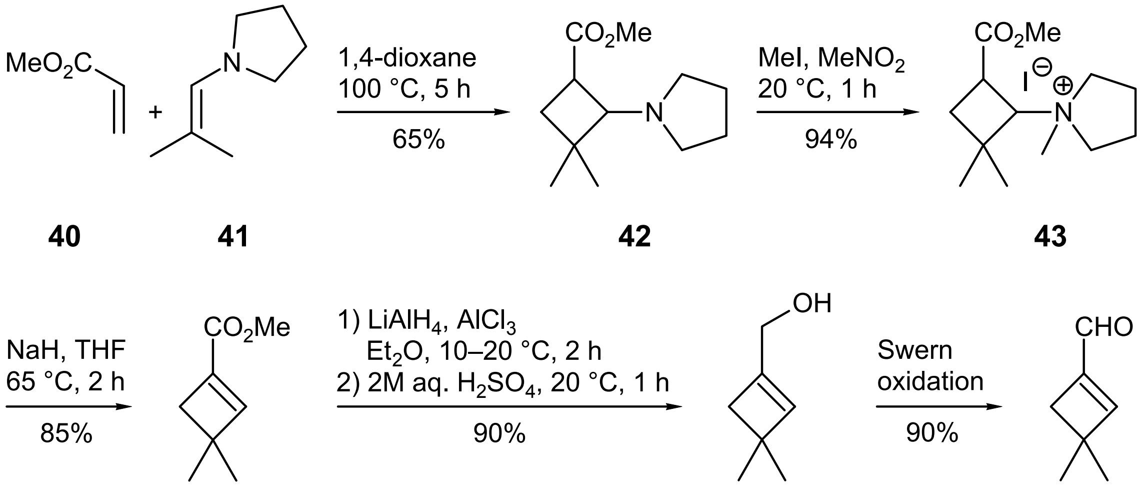
Scheme 20



37 **38** **39**

3,3-Dimethylcyclobut-1-enecarboxaldehyde (**46**) was synthesized by five step reaction sequence starting from β,β-disubstituted enamines [2+2] cycloaddition to EWG-substituted alkenes discovered by BRANNOCK et al.[42] Thus, refluxing of an equimolar mixture of methyl acrylate (**40**) and 1-(2-methylprop-1-enyl)pyrrolidine[43] (**41**) in dioxane,[44] provided corresponding cyclobutane derivative **42** in good yield (65%) (Scheme 21). Subsequent quaternization of **42** with methyl iodide in nitromethane gave almost quantitatively the corresponding methiodide **43**. It was subjected to original elimination protocol and gave, after refluxing with suspended in THF sodium hydride and corresponding work-up, methyl (3,3-dimethyl-1-cyclobutene)carboxylate **44** in high yield. In spite of obvious advantages of presented elimination protocol in comparison with the previously published one[44] (1 mol/L and 85% yield against 0.1 mol/L, 63% yield), it seems problematic to scale this procedure over 300 mmol, because difficulties increased to keep the reaction rate under control. If necessary, this complication could be overcome by gradual addition of solid methiodide **43** into the refluxing reaction mixture after the reaction has got started.

Scheme 21



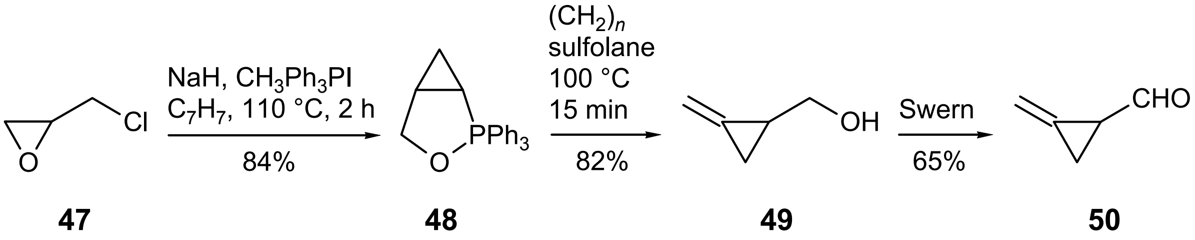
40 **41** **42** **43**

44 **45** **46**

Preliminarily attempted reduction of the ester **44** with $LiAlH_4$ in various versions encountered several difficulties connected with the formation of some amount of a dimeric derivative of alcohol **45**, so the yield did not exceed 40%. However, it was found that only the action of ethereal solution of AlH_3 (in situ generated from $LiAlH_4$ and $AlCl_3$ according to a thoroughly optimized by GASTAMINZA et al. procedure[45]) is able to smoothly reduce ester **44** to the corresponding alcohol. After the preparative adaptation of this protocol, 20.1 g of alcohol **45** in 90% yield was obtained. SWERN oxidation of **45** followed by acidic work-up procedure (GP 3) provided a significant amount of aldehyde (18.4 g) **46** in high yield.

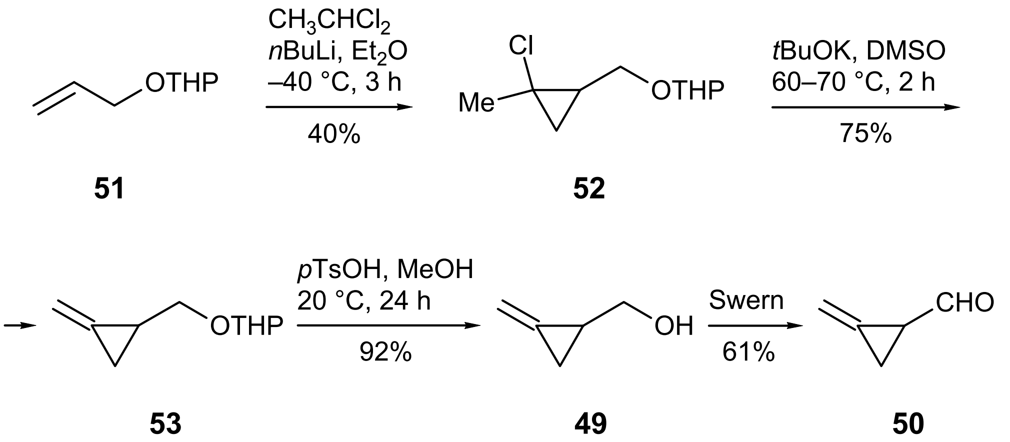
2-Methylenecyclopropylcarboxaldehyde **50** was first synthesized by LE CORRE[46] via SWERN oxidation of the corresponding 2-methylenecyclopropylcarbinol **49** obtained by a reaction of epichlorohydrin **47** with ylide, in situ generated from methyl triphenylphosphonium iodide and sodium hydride, and subsequent treatment of the obtained phosphacycle **48** with formaldehyde in sulfolane (Scheme 22). In spite of doubtless advantages of this approach for the synthesis of enantiomerically pure 2-alkylidene cyclopropyl carbinols (an efficient resolution procedure for the tartrate of **48** is also given in this paper), synthetic availability of the presented scheme towards racemic **49** seems to be not very useful because 2 mol of expensive methyl triphenylphosphonium iodide per 1 mol of epichlorohydrin is required. Therefore a real yield of this reaction sequence could be assumed as the halved one.

Scheme 22



An attempt preliminary undertaken to prepare 2-methylenecyclopropylcarboxaldehyde (**50**), was based on 1-(tetrahydropyran-2'-yl)oxymethyl-2-metylidenecyclopropane[47] (**53**). This compound was easily prepared in two steps from the corresponding THP-protected allyl alcohol **51** by addition of generated from 1,1-dichloroethane and *n*-butyl lithium 1-(chloromethyl)carbene and subsequent elimination of HCl by potassium *tert*-butoxide in DMSO.[48]

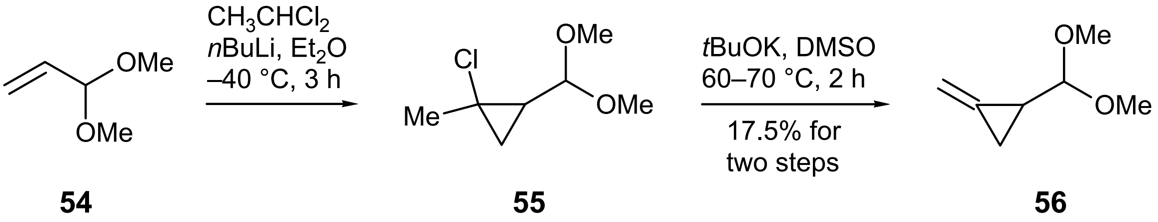
Scheme 23



Deprotection of **53**, followed by SWERN oxidation of obtained alcohol **49**, gave the corresponding aldehyde **50** in good yield (Scheme 23). However, the poor yield of the key methylenecyclopropane intermediate **53** on the first step and relatively low efficiency of SWERN oxidation of alcohol **49** invoked further attempts to modify the presented scheme.

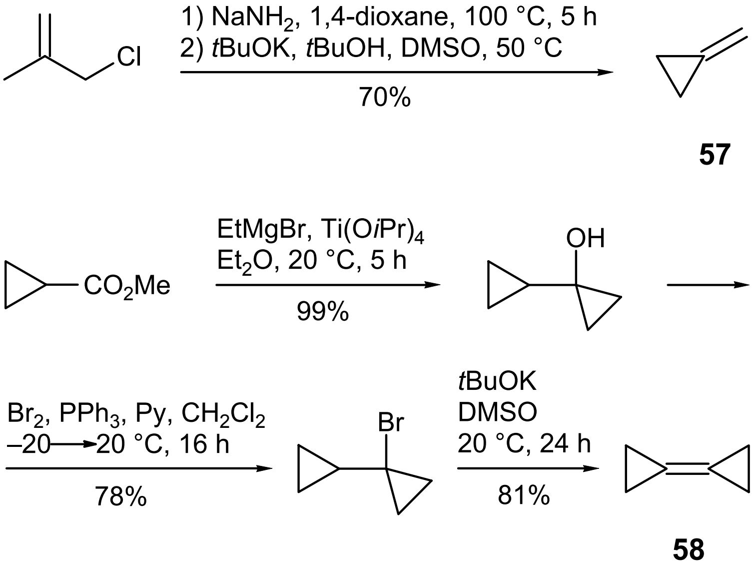
At first, the possibility to exclude SWERN oxidation was tested. Thus, 1,1-dimethoxyprop-2-ene (**54**) was subjected to the described above procedure of “methylenecarbene equivalent” addition to double bond (Scheme 24). That gave a protected analogue **56** of the target aldehyde **50** in 17.5% yield. In spite of low yield (however, it is a little bit higher than provided according to the previous scheme 16.8%) this approach appeared preferable because the reaction sequence was two times shorter, and chemically more stable acetal **56** was obtained.

Scheme 24



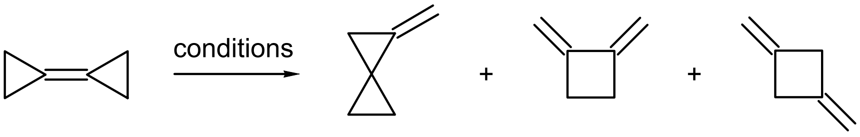
The next attempts to synthesize aldehyde **50** and its homologues were focused on formylation of the corresponding 1-lithiated cyclopropanes derived from methylenecyclopropane[49] (**57**) and bicyclopropylidene[50] (**58**) available on a centigram scale (Scheme 25).

Scheme 25



Moreover, bicyclopropylidene (**58**) is known to undergo the thermal rearrangements in gas phase to give together with the isomeric dimethylenecyclobutanes **60** and **61**, also the methylenedispiro[2.2]pentane[18] (**59**) (Scheme 26). The development of a preparative pyrolitic procedure able to provide a sufficient amount of **59** as potential building block for the corresponding methylenedispiro[2.2]pentylacrylates, seemed to be very attractive.

Scheme 26



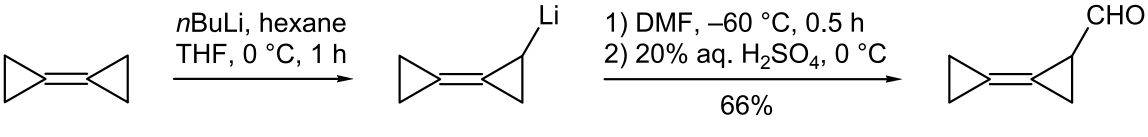
58 **59** **60** **61**

Table 3. Selected results of the optimization experiments towards **59**.

Entry	Conditions	Yield, %	Product ratio **59**	 **60**	 **61**
1	Quartz tube (30×600 mm), 350 C, 250 mL/min	90	95	<5%	
2	Cu tube (1000×2 mm), 350 °C, 100 mL/min	73	88	8	4
3	CuO coated tube (1000×2 mm), 350 °C, 100 mL/min	50	–	2	1

After the series of optimization experiments,[51] it was found that passed through a pre-heated to 350 °C quartz tube (3×60 cm) at flow rate 250 mL/min bicyclopropylidene (**58**) had undergone a clean rearrangement to methylenespiropentane **59**. The last was obtained in 90% yield and >95% purity on a preparative scale (17.4 g)[52] (Table 3). It is interesting to mention that the presence of copper oxide in reaction zone completely changed the rearrangement direction towards the isomeric dimethylenecyclobutanes **60** and **61** (entry 3). Thus, in view of the ready availability of **58**, this rearrangement constitutes the most convenient preparative approach to **58**, in comparison with two known traditional syntheses.[18, 53]

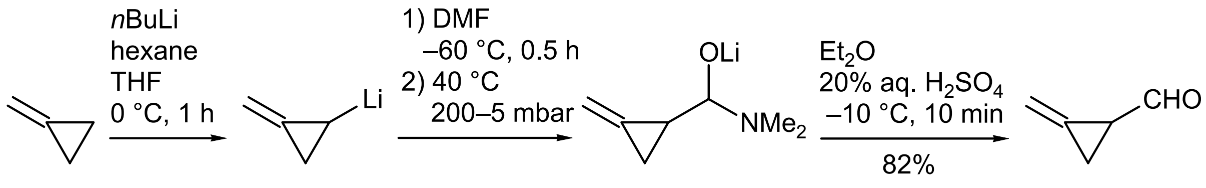
Scheme 27



58 **62** **63**

As it was previously found, bicyclopropylidene **58** had smoothly undergone lithiation by treatment with *n*-buthyl lithium in THF/hexane mixture to yield corresponding lithio bicyclopropylidene almost quantitatively. It was than trapped with various electrophiles. Thus, lithiated bicyclopropylidene **62** prepared according to DE MEIJERE et al.,[54] was formylated with dimethylformamide according to BRANDSMA,[41] to give after improved work-up procedure bicyclopropylidenecarboxaldehyde **63** in good yield[55] (Scheme 27).

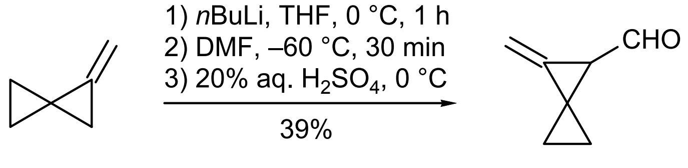
Scheme 28



57 **64** **65** **50**

Although the direct lithiation of methylenecyclopropane (**57**) as well as subsequent trapping of the corresponding lithiated compound **64** with various C-electrophiles is good described,[56] an extension of this approach towards aldehyde **50** turned to be problematic. Thus, successful lithiation of **57** is known to be possible only in highly basic systems like *n*BuLi/hexane/THF. Therefore, the separation of low-boiling and thermally unstable product **50** from the solvents looks to be rather difficult. On the other hand, methyl lithium in ether appeared too weak to lithiate the methylenecyclopropane (**57**). This difficulty has been successfully overcome by solvent evaporation under reduced pressure from the reaction mixture containing O-lithiated hemi-aminal **65**. This intermediate **65** was then dissolved in anhydrous ether and poured under argon into pre-cooled aqueous sulfuric acid. This improvement let to prepare, after the corresponding work-up, 16.8 g of the target aldehyde **50** in high yield[55] (Scheme 28).

Scheme 29



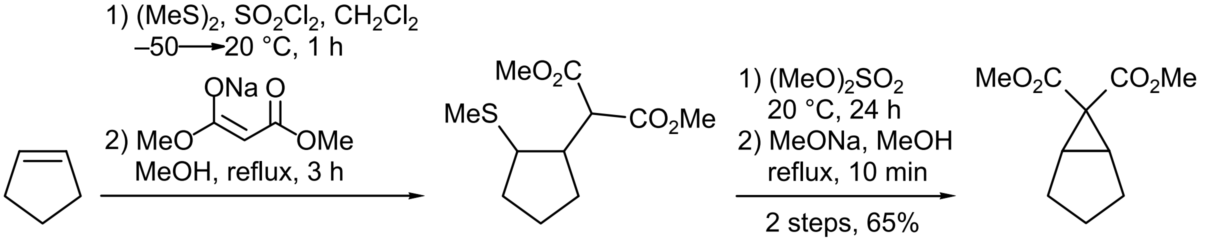
59 **66**

Lithiation of methylenespiropentane **59** according to the presented procedure, was complicated by some side reactions, and after corresponding work-up afforded the desired 2-methylenespiro[2.2]pentane-1-carbaldehyde **66** only in moderate yield (Scheme 29).

Thus, alkylidene substituted cyclopropylcarboxaldehyde **50**, **63**, **66** were synthesized in 39–82% yield on a preparative scale starting from the corresponding hydrocarbons **57-59** via one-pot lithiation-formylation procedure.

Synthesis of monoalkoxycarbonyl-substituted cyclopropanecarboxaldehydes was performed proceeding from the corresponding cyclopropanedicarboxylic acid esters. Thus, as a starting material, commercially available 1,1-cyclopropanedicarboxylic acid diethyl ester (**67**) and 1,2-cyclopropanedicarboxylic acid dimethyl ester (**68**) were used, as well as bicyclic *gem*-diester **70**, that prepared according to OHISHI[57] in two steps starting from cyclopentene (**69**) (Scheme 30).

Scheme 30



69 **70**

Although the classical protocol for partial hydrolysis of diesters [58] (NaOH/aq. EtOH), being applied to 1,1-cyclopropanedicarboxylic acid diethylester (**67**), provided the corresponding monoester **71** in good yield (77%), it turned to be ineffective when the methyl esters **68** and **70** were subjected to this one. Thus, only moderate chemoselectivity had been achieved in that case, so that distribution of products appeared to be close to the statistic one. Therefore, a novel protocol for hydrolysis has been developed. Thus, bicyclic diester **70** was found to be smoothly hydrolyzed by stirring with lithium hydroxide monohydrate suspended in THF/MeOH mixture at ambient temperature, giving the desired monoester **72** with the excellent chemo- and regioselectivity in high yield as the only isomer (Scheme 31). Its configuration was elucidated by X-Ray analysis as *exo*-[59] (Figure 4). It is necessary to note that after the diester **70** was subjected to the parent hydrolysis protocol[60] (Table 4, entry 2), only a mixture of isomeric half-esters in lower yield was obtained (compare with entry 3).

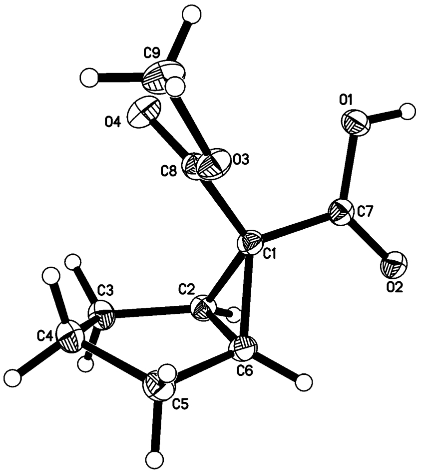
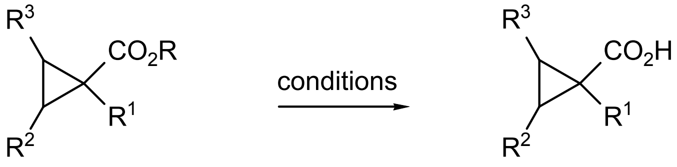


Figure 4

Scheme 31



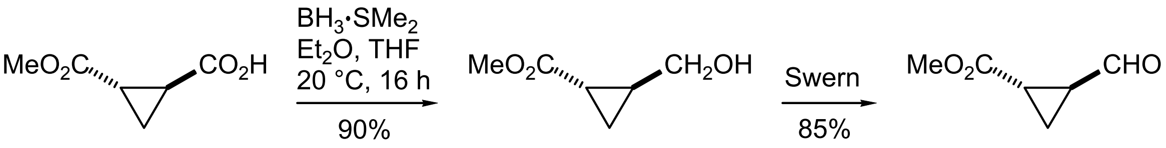
67,68,70 **71-73**

Table 4. Synthesis of cyclopropane containing half-esters **71-73**.

Entry	Ester	R	R^1	R^2	R^3	Product	Conditions	Yield, %
1	**67**	Et	CO_2Et	H	H	**71**	1 N NaOH, EtOH, 20 °C, 16 h	77
2	**70**	Me	CO_2Me	$(CH_2)_3$		**72**	NaOH, MeOH, THF, 20 C, 16 h	60
3	**70**	Me	CO_2Me	$(CH_2)_3$		**72**	LiOH·H_2O, MeOH, THF, 20 C, 24 h	83
4	**68**	Me	H	CO_2Me	H	**73**	see entry 3	70

Application of this novel protocol provided good chemoselectivity by partial hydrolysis even in the case of dimethyl *trans*-1,2-cyclopropanedicarboxylate **68** affording the corresponding half-ester **73** in the highest yield in comparison to those previously reported (enzymatic procedures were out of consideration).

Scheme 32

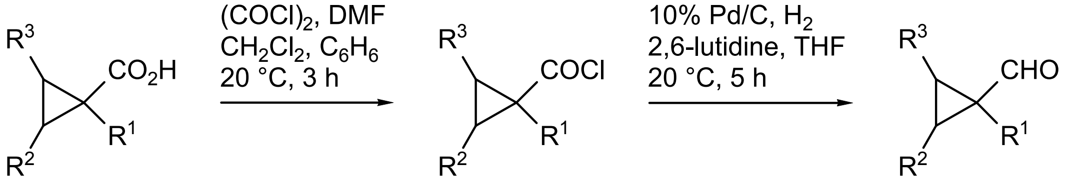


73 **74** **75**

Obtained half-esters could be transformed into the corresponding aldehydes by two different reaction sequences. The first one, previously reported by BALDWIN,[61] after reduction of half-ester **73** with $BH_3 \cdot SMe_2$ and successive SWERN oxidation resulted in the respective aldehyde **75** in 76% overall yield (Scheme 32).

Unfortunately, attempted reductions of *gem*-substituted half-esters **71** and **72** according to this protocol had been found to give only a complex mixture of products. Therefore, more general approach to alkoxycarbonyl substituted aldehydes based on BURGSTAHLER modification[62] of ROSENMUND reduction was then developed (Scheme 33).

Scheme 33



71-73 **75-77**

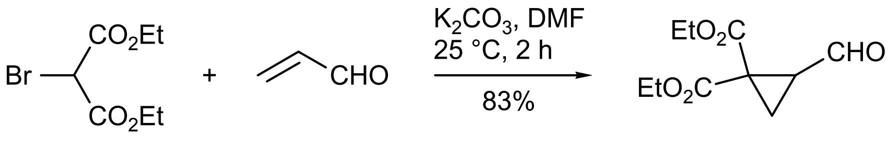
Table 5. Synthesis of aldehydes **75-77** by modified Rosenmund reduction.

Entry	Half-ester	R^1	R^2	R^3	Aldehyde	Yield, %
1	**73**	H	H	CO_2Me	**75**	85
2	**71**	CO_2Et	H	H	**76**	62
3	**72**	CO_2Me	$(CH_2)_3$		**77**	88

Thus, the titled half-esters **71-73** were smoothly converted into the corresponding acyl chlorides. They were successfully hydrogenated over 10% Pd/C in the presence of equimolar amount of 2,6-lutidine to give the respective aldehydes **75-77** in good yields (Table 5).

Finally, condensation of diethyl α-bromomalonate (**78**) with 2-propenal (**79**) conducted according to literature[63] gave 2-formyl-1,1-cyclopropanedicarboxylic acid diethyl ester (**80**) in high yield (Scheme 34).

Scheme 34



78 **79** **80**

Surprisingly, yield of the presented reaction was significantly higher than the reported one (60%) for the corresponding dimethyl α-bromomalonate used in the original procedure.

2.3. *Two-step synthesis of α-hydroxyacetates from cycloalkenyl- and cyclopropyl aldehydes*

Scheme 35

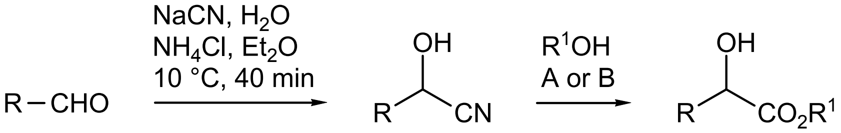
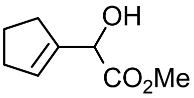
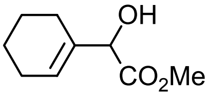
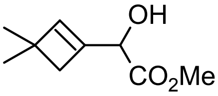
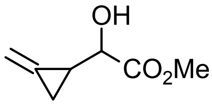
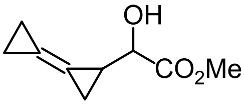
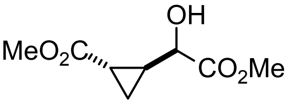
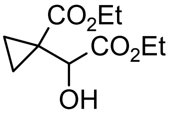
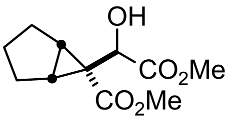
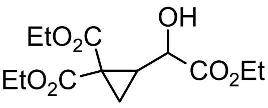


Table 6. Synthesis of various α-hydroxyacetates. Yields and conditions.

Entry	Aldehyde	Product, **81-89**		Conditions[a]	Yield, %
1	**36**		**81**	A	77
2	**39**		**82**	A	53 42 (Lit.[66])
3	**46**		**83**	A B	54 69
4	**40** **56**		**84**	A B	62 42
5	**63**		**85**	A	76
6	**75**		**86**	A B	44 63
7	**76**		**87**	A B	12 67
8	**77**		**88**	B	94[b]
9	**80**		**89**	A B	51 82[b]

[a] Method A: HCl, R^5OH, Et_2O, 2 °C, 16 h. Method B: HCl, R^5OH, −10 → 20 °C, 2 h. – [b] Yield of the crude product is given.

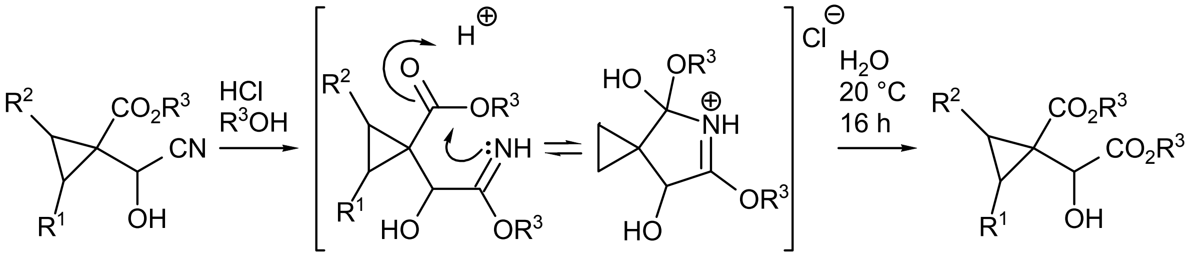
Among the variety of preparation procedures applied more or less successfully during the last century to cyanohydrins synthesis and PINNER alcoholysis of nitriles, those were chosen which provided required α-hydroxyacetates in good yields under the mildest conditions. Thus, for cyanohydrin synthesis, GUAY and BRASSARD[64] protocol was used to provide after some modifications crude product in yield around 90%. It should be noted that stabilization of cyanohydrin with acid is often essential for a reasonable yield achievement. This resulted from the fact that some cyanohydrins were unstable even at room temperature, so up to a half of crude product could be lost by evaporation of solvent under reduced pressure. Due to the same reason, it was preferable to subject freshly prepared cyanohydrin immediately to further transformations.

Alcoholysis of obtained crude cyanohydrins was initially conducted according to WARMERDAM et al. protocol[65] which let to alcoholyze enantiomerically pure cyanohydrins with stereogenic center in 2-position without racemization. Thus, application of this protocol to unsaturated cyanohydrins (entry 1-5) led to the corresponding hydroxyacetates **81**-**85** in moderate to good yields (Table 6).

For α-hydroxyacetates bearing alkylidenecyclopropane moiety (entry 4, 5), method A was the only one to get the highest yields. Besides, it provided good yields of 1-cycloalkenylhydroxyacetates, too (entry 1-3). However, Method A showed significantly lower efficiency in attempted preparations of the alkoxycarbonyl substituted cyclopropane derivatives **86-89**. Moreover, in the case of compound **87** bearing *gem*-alkoxycarbonyl substituent (*gem*- is referred to the reaction center), the yield turned to be drastically decreased (entry 7). Therefore, taking in consideration higher chemical stability of compounds **86-89** in large excess of HCl, it was decided to try another protocol,[66] namely alcoholysis of cyanohydins in saturated at 0 °C alcoholic solution of hydrogen chloride. Its modification resulted in a highly efficient Method B. Hydroxyesters **86-89** were synthesized by this method, fast (reaction time did not exceed 2 h) and in good yields.

It should also be noted, that hydrolysis of the intermediate iminoester hydrochloride usually required 1–2 h, while overnight stirring at ambient temperature was necessary to solvolyze the respective iminoester hydrochlorides to the α-hydroxyesters **87** and **88** completely. This might be caused by formation of an intermediate pyrroline derivative, which would undergo hydrolysis slower as the corresponding iminoester hydrochloride (Scheme 36).

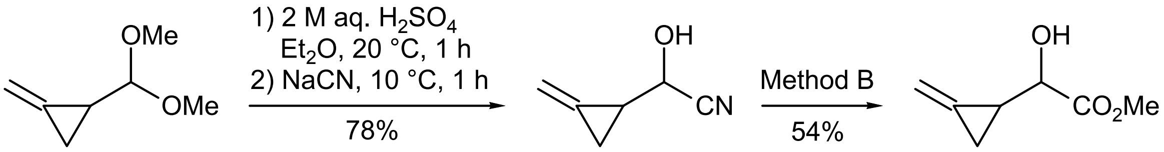
Scheme 36



87: $R^1 = R^2 = H$, $R^3 = Et$
88: $R^1R^2 = (CH_2)_3$, $R^3 = Me$

High synthetic utility of the Method B could also be illustrated by entry 3 (Table 6). An essential feature of this method is using of a large excess of HCl providing significantly higher reaction rate at low temperature (–20 °C), along with the mild reaction conditions preventing, as far as possible, side reactions. Thus, this method turned to be mild enough to alcoholyze in good yield cyanohydrin **90** alternatively prepared from the corresponding dimethyl acetal **56** (Scheme 37).

Scheme 37

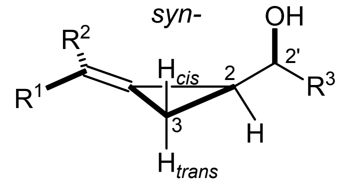
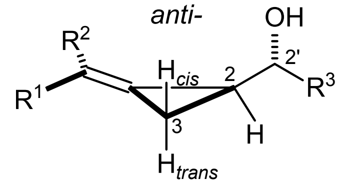


56 **90** **84**

Interesting to note that compounds **84-86** appeared to be separable by column chromatography to give pure *syn-* and *anti-* diastereomers. Moreover, in the case of methylenecyclopropanes **84**, **85**, the members of each diastereomeric series showed similar chemical shifts and coupling constants value for the respective protons of methylenecyclopropane system (Table 7). Configuration of diastereomers of the first series (Table 7) was unambiguously assigned by X-Ray structure analysis[67] as *syn-* (Figure 5). Obtained spectroscopic data are in a good accordance with those previously published for the similar structures.[68] Thus, *anti*-methylenecyclopropyl alkyl carbinols had been previously reported to display decreased polarity (*i.e.* higher R_f-values) and lower or any difference between signals of methylene protons (Δδ) at about 5.5 ppm. Such behavior was connected with an opportunity of weak intramolecular hydrogen bonding between methylene double bond and hydroxy-group, that evidence was previously confirmed by IR-spectroscopy.[69]

Such bonding is shown to be possible only for *anti*-diastereomers because of clear steric reasons (Figure 5).

Table 7. Selected chemical shifts and coupling constants for *syn*- and *anti*- substituted methylenecyclopropyl carbinols.

Compound	R^1 R^2 R^3	 δ(H), Δδ(R^1R^2), ppm; ^3J, Hz						 δ(H), Δδ(R^1R^2), ppm; ^3J, Hz				
		3_{cis} $^3J_{2-3}$	3_{trans} $^3J_{2-3}$	2 $^3J_{2\text{-H}-2'\text{-H}}$	2'	Δδ	R_f	3_{cis}– 3_{trans}	2 $^3J_{2\text{-H}-2'\text{-H}}$	2'	Δδ	R_f
84	H H CO_2Me	1.17 4.9	1.36 8.9	1.72 7.8	3.78	0.05	0.20	1.20 1.36	1.80 6.2	3.98	0.00	0.28
85	$(CH_2)_2$ CO_2Me	1.27 5.0	1.46 9.0	1.82 7.5	3.82	–	0.11	1.33 1.47	1.93 6.0	4.06	–	0.16
Lit.[68]	H H nC_7H_{15}	0.97	m[a]		3.21	0.07	0.26	0.90*	m	3.12	0.00	0.39

[a] Chemical shift for one of the 3-H is given; another cyclopropyl protons are overlapped with signals of nC_7H_{15}-group ones; coupling constants were not determined.

***syn*-84**

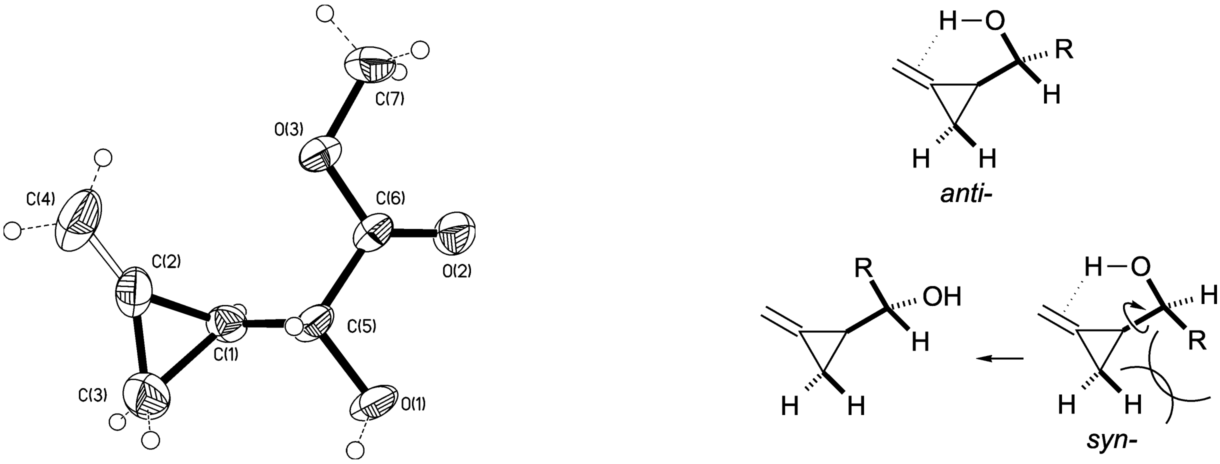


Figure 5

In general, eight new α-hydroxyacetates bearing cycloalkene or cyclopropane moiety, were synthesized in 53–94% yield on a preparative scale via optimized two-step procedure for cyanohydrin formation from aldehydes with successive PINNER alcoholysis.

2.4. SIMMONS-SMITH cyclopropanation of 2-(cycloalkene-1-yl)-2-hydroxyacetates

SIMMONS-SMITH reaction is used widely for the transformation of electron rich double bond into corresponding cyclopropane moiety. It was chosen as a key step to produce 2-bicyclo[n.1.0]alk-1-ylacrylates (Scheme 18). A lot of versions of this reaction including protocols for enantioselective cyclopropanation of prochiral double bond, are known to provide a variety of natural and synthetic products.[70] These synthetic procedures could be divided into two main classes: methods using active metals (Zn/Cu, Zn/Ag, Sm) and methods using alkylmetals ($ZnEt_2$, $AlMe_3$). This division originates from the mode used to generate active carbenoid species from various methylene halides (CH_2Br_2, CH_2ICl, CH_2I_2).

Initially, a modification of the classical SIMMONS SMITH protocol[71] referred to the first of these two divisions, was tested. It was recently used for the cyclopropanation of 1-cyclopentenylmethanol to give the corresponding bicyclic alcohol in 79% yield.[72] Unfortunately, it was found that the satisfactory conversion of the starting material **81** to the desired bicyclic compound **91** under these conditions could not be achieved (Table 8, entry 1). This process required complete alkene conversion towards an appropriate cyclopropane because of impossibility to separate the product from contaminating starting material (equal boiling points and R_f). The same situation occurred after oxidation of the crude reaction mixture to the mixture of corresponding oxoacetates. Partial chromatographic separation from the impurity derived from uncompleted cyclopropanation, became possible only after successive WITTIG methylenation, which would be discussed later.

Thus, further search of the appropriate cyclopropanation protocol was switched over to the methods of the second group involving diethyl zinc mediated carbenoid preparations. Cyclopropanation under FURUKAWA's conditions[73] was readily excluded from consideration because of obvious insolubility of the intermediate zinc alcoholates (derived from α-hydroxyacetates) in hydrocarbons, that could cause explosion of a reaction mixture.

Scheme 38

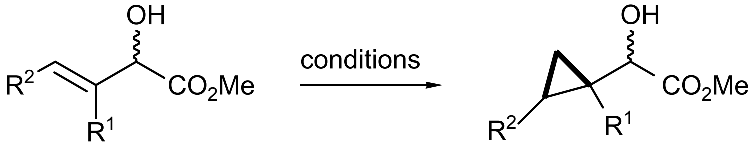
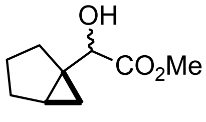
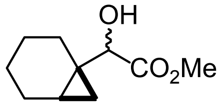
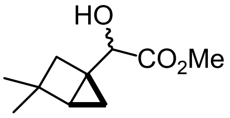


Table 8. Cyclopropanations of cycloalkene-1-yl hydroxyacetates **80-81**.

Entry	Alkene	R^1R^2	Product	Conditions[a]; [alkene], mol/L	Yield, %[b]
1	**81**	$(CH_2)_3$	 **91**	A; [1.000]	80(82)
2				B; [0.125]	92(100)
3				C, [0.167]	95(99)
4				D, [0.500]	95(100)
5	**82**	$(CH_2)_4$	 **92**	C, [0.167]	97(99)
6	**83**	$(CH_3)_2CCH_2$	 **93**	E, [0.100]	92(97)
7				F, [0.420]	92(99)

[a] A: 5×Zn, 0.5×CuCl, 2.5×CH_2I_2;Et_2O, reflux, 48 h; B: 3×Et_2Zn, 3×CH_2I_2, CH_2Cl_2, –20 °C, 3 h, 20 °C, 12 h; C: 3×Et_2Zn, 6×CH_2I_2, 3×DME, CH_2Cl_2, –20→20 °C, 14 h; D: 2.1×Et_2Zn, 2.1×CF_3CO_2H, 2.1×CH_2I_2, CH_2Cl_2, –20 °C, 3 h, 20 °C, 12 h; E: 5×Et_2Zn, 10×CH_2I_2, 5×DME, CH_2Cl_2, –20→20 °C, 18 h, 20 °C, 45 h; F: 2.5×Et_2Zn, 2.5×CF_3CO_2H, 2.5×CH_2I_2, CH_2Cl_2, –20 °C, 3 h, 20 °C, 12 h. – [b] Isolated yield of the starting material/product mixture, % (conversion, %) are given.

At first, a cyclopropanation was tested which involved prepared from equimolar amounts of $ZnEt_2$ and CH_2I_2, i.e. $EtZnCH_2I$[74], FURUKAWA-type carbenoid used by BARRETT et al.[75] for the cyclopropanation of some allylic alcohols. According to this protocol, α-hydroxyacetate **81** was smoothly converted into the corresponding bicyclic hydroxyacetates **91** in high yield and 100% conversion of the starting material. Unfortunately, this protocol could be used only in up to 20 mmol scale. Attempts to increase reaction scale over 20 mmol, caused explosion of the reaction mixture. This problem was overcome by CHARETTE et al.[76] They suggested to apply for cyclopropanation $Zn(CH_2I)_2{\cdot}DME$ complex, good soluble in methylene chloride, more thermally stable, though less reactive in comparison to $EtZnCH_2I$ or $Zn(CH_2I)_2$. This reagent was successfully used for a lot of preparative cyclopropyl carbinol syntheses including their enantioselective variations. When the titled protocol has been applied to cyclopropanate cycloalkenyl hydroxyacetates **81**, **82**, the corresponding bicyclic compounds **91**, **92** were obtained in almost quantitative yield and excellent conversion of the starting material. Cyclopropanation of cyclobutene compound **83** by this procedure turned to be complicated because in general the activity decreased of cyclobutenes to be cyclopropanated.[77] Nevertheless, corresponding bicyclo[2.1.0]pentane **93** was obtained in high yield and good conversion grade after continuous stirring of **83** in the presence of 5 equivalents of $Zn(CH_2I)_2 \cdot DME$ (Table 8, entry 6).

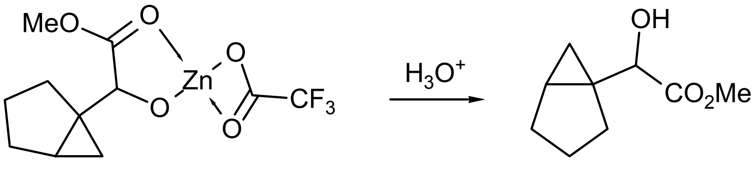
Although this method provided excellent yields of compounds **91** and **92** and unusually high yield of **93**, it could not be recommended as a tool for large scale preparations because of relatively high dilution of reaction mixture and large excess of the expensive reagents required (Table 8, entries 3, 5 and 6). Therefore, 150 mmol seems to be the limit for the reasonable synthetic applications of this protocol. On the other hand, cyclopropanation with $Zn(CH_2Cl)_2$ according to DENMARK's procedure[78] was also excluded from consideration notwithstanding more economical carbenoid consume (200 mol % Et_2Zn, 400 mol % CH_2ICl), because no published data concerning application of this protocol in a scale higher than 5 mmol had been published.

A highly efficient cyclopropanation protocol has been recently reported[79] to provide cyclopropanation of various alkenes (including substituted allyl alcohols) by a new type of carbenoid particle $CF_3CO_2ZnCH_2I$, so-called "SHI's carbenoid". This reagent has been recently found to cyclopropanate substituted allyl alcohols with high diastereoselectivity.[80] Unprecedented cyclopropanation of substituted electron poor vinyl chloride with SHI's carbenoid has been recently reported[81] to give corresponding cyclopropyl chloride in high yield with excellent diastereoselectivity.

Reported originally in 10 mmol scale, SHI's protocol appeared to be easily scaled, and after some optimizations was transformed into the large-scale preparation procedure. It enabled cyclopropanation of 0.5 mol of α-hydroxy acetate in a 2 L reaction flask. Moreover, SHI's carbenoid appeared to be active enough (only 2.5 equivalents of $CF_3CO_2ZnCH_2I$ was required) to cyclopropanate essentially less reactive methyl 3,3-dimethylcyclobuten-1-yl hydroxyacetate **83** to give **93** in high yield and with 99% conversion of the starting material.

It should be also mentioned that original work-up procedure was essentially remade. Thus, it was found that aqueous NH_4Cl was not able to destroy unusually stable Zn-alcoholate **94** (Scheme 39). It can be illustrated by the following example. Crude viscous oil obtained after original work-up procedure (weighed approximately two times more then it would be expected for 100% yield of product), was subjected to a distillation under reduced pressure. After continuous heating at 100 °C (0.1 Torr), only a little amount of methylene iodide and a few drops of product **91** were obtained. The cube residue was than subjected to acidic work-up procedure to give about 80% of **91** in satisfactory purity. High stability of **91** and respective intermediates could be attributed to electron-withdrawing methoxycarbonyl group, which prevents $E1_{cA}$ elimination of hydroxy group with successive rearrangements of cyclopropylmethyl cation formed. Therefore, acidic work-up procedure applied, did not reduce yields of cyclopropanated α-hydroxyacetates **91-93**.

Scheme 39



94 **91**

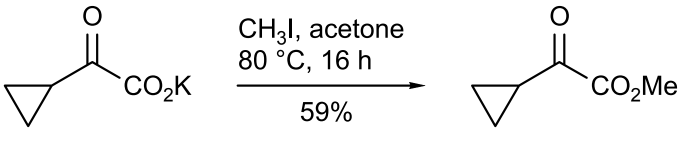
It should be also noted that cyclopropanation of compounds **81**, **82** resulted in the corresponding products **91**, **92** as mainly one of two possible diastereomers. According to ^{1}H NMR spectra of these products, diastereomeric excess may be assumed as > 80%, whereas cyclopropanation of compound **83** gave the respective bicyclo[2.1.0]pentane **93** as 7:4 mixture of diastereomers. Relative configuration of the major isomer was not elucidated.

2.5. *Synthesis of substituted alkyl cyclopropyl oxoacetates.*

2.5.1. Synthesis of methyl cyclopropyloxoacetate.

Although the title compound is described in literature,[82] there is no reliable protocol for its preparation. Nevertheless, methyl cyclopropyloxoacetate **96** was synthesized via alkylation of accessible potassium cyclopropyloxoacetate **95** prepared in a large scale by oxidation of methyl cyclopropyl ketone with potassium permanganate as it was previously reported[83] (Scheme 40).

Scheme 40



95 **96**

2.5.2. Oxidation of the α-cyclopropyl-α-hydroxyacetates to the corresponding α-oxoesters

Alkyl 2-cyclopropyl-2-hydroxyacetates **84-89,91,92** were oxidized by an active manganese dioxide according to a previously published protocol[84] to give the corresponding α-oxoacetates in good yields (71–88%) (Scheme 40, Table 8).

Scheme 41

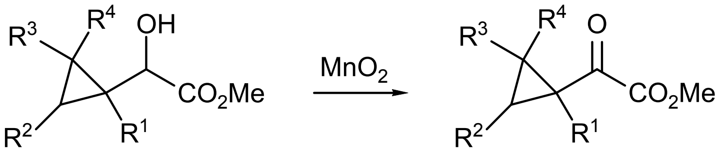
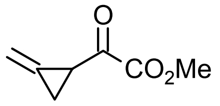
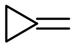
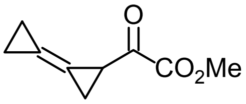
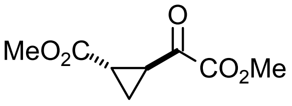
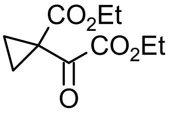
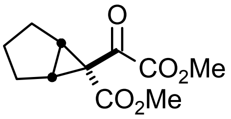
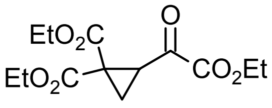
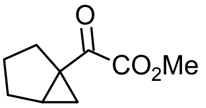
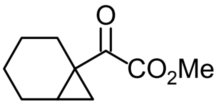
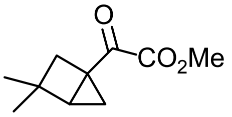


Table 9. Oxidation of various alkyl α-cyclopropyl-α-hydroxyacetates.

Entry	Alcohol	R^1	R^2	R^3	R^4	R^5	Product		Yield, %
1	**84**	H	H	$CH_2=$		Me		**97**	88
2	**85**	H	H			Me		**98**	75
3	**86**	H	CO_2Me	H	H	Me		**99**	71
4	**87**	CO_2Et	H	H	H	Et		**100**	85
5	**88**	CO_2Me	$(CH_2)_3$		H	Me		**101**	84
6	**89**	H	H	CO_2Et	CO_2Et	Et		**102**	78
7	**91**	$(CH_2)_3$		H	H	Me		**103**	83 97[a]
8	**92**	$(CH_2)_4$		H	H	Me		**104**	83
9	**93**	$(CH_3)_2CCH_2$		H	H	Me		**105**	0 73[b]

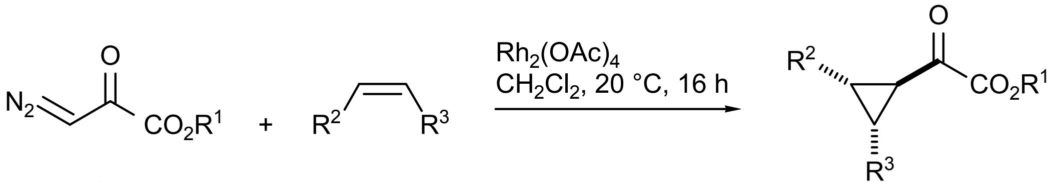
[a] SWERN oxidation had been applied. – [b] The yield was determined by GC analysis of the crude reaction mixture obtained after SWERN oxidation of **93**.

This protocol allowed to oxidize crude α-hydroxyacetates smoothly to give satisfactory pure oxoderivatives **97-104** in 50–200 mmol scale. Further scaling of this procedure turned to be problematic due to a relatively high dilution (0.16 mol/L). Therefore original SWERN protocol[85] was used for a large scale preparation of oxoacetate **103**. This method provided almost quantitative oxidation of the alcohol **91** in 0.5 mol scale. Moreover, an application of SWERN protocol made oxidation of the bicyclopentane alcohol **93** into the respective crude oxoester **105** possible, and provided satisfactory yield. This compound readily undergoes various side reactions, because of high lability of the endocyclic bond. A similar behavior of the endocyclic bond in 1-EWG-substituted bicycles has been previously described for methyl 2-oxobicyclo[3.1.0]hexane-1-carboxylate.[86]

2.5.3. Synthesis of alkyl (bicyclo[*n*.1.0]alk-(*n*+3)-yl)oxoacetates by Rh^{II}–catalyzed addition of alkyldiazopyruvates to cycloalkenes

Addition of alkyl diazopyruvates to alkenes (Scheme 42) is less described in literature than the analogous reactions with diazoacetic esters. Thus, only four articles concerning chemical behavior of alkyldiazopyruvates in presence of some alkenes were found.[20, 22, 87, 88] In general, this reaction is characterized by moderate yields and is usually accompanied with some side reactions.

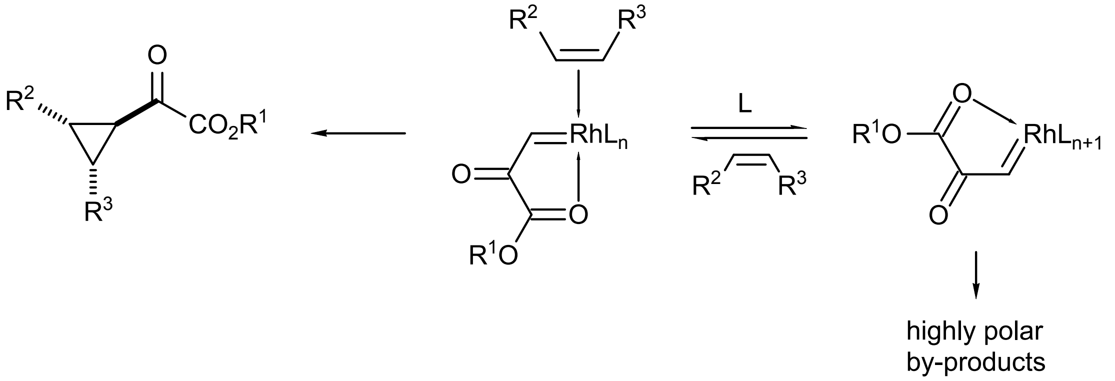
Scheme 42



12: R^1 = Et
106: R^1 = Me

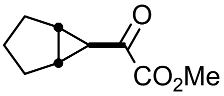
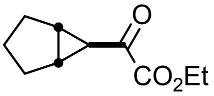
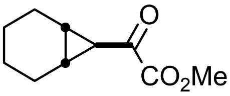
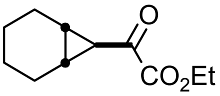
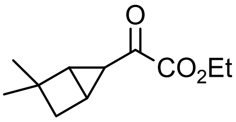
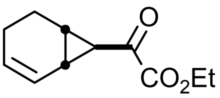
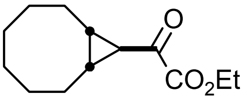
These complications could be attributed to the increased Lewis base strength of product, which may compete as ligand (L) with the complexed to Rh-carbene alkene. It would decrease concentration of the leading to desired cyclopropane product intermediate (Scheme 43).

Scheme 43



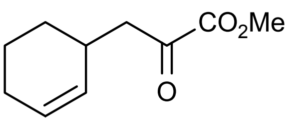
Otherwise, intermediate bearing no alkene complexed would form highly polar insertion products. Their contents in crude reaction mixture could reach 50%. Interesting to mention that no signals of the diazocompound dimerization product had been observed in ^{1}H NMR spectra of reaction mixture (no olefinic singlet about 7 ppm). This can be attributed to a modified procedure applied (see p. 7).

Table 10. Rh$_2$(OAc)$_4$ catalyzed addition of alkyldiazopyruvates to various alkenes.

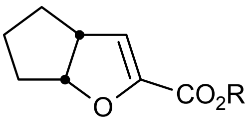
Entry	Alkene	R^1	R^{2}R^3	Product		Yield, %
1	**69**	Me	(CH$_2$)$_3$		**111**	49
2	**69**	Et	(CH$_2$)$_3$		**112**	48
3	**107**	Me	(CH$_2$)$_4$		**113**	55
4	**107**	Et	(CH$_2$)$_4$		**114**	49
5	**108**	Et	(CH$_3$)CCH$_2$		**115**	35
6	**109**	Et	(CH$_2$)$_2$CH=CH		**116**	58
7	**110**	Et	(CH$_2$)$_6$		**117**	35

On the other hand, 3-(cyclohexen-1-yl)pyruvic acid methyl ester **118** was detected among the by-products derived from alkenes. Its formation could be attributed to C–H insertion of the respective carbene into allylic position of cyclohexene **107**.[87] Moreover, cyclopentene **69** has been also found to give some amounts of dihydrofuranes **119** and **120** in reaction with both diazopyruvates **106** and **12**. It seems unusual because the formation of such products (it could be referred to formal 1,3-dipolar addition of α-oxocarbene to alkene double bond) has been described in literature[89] only for reactions of electron-reach vinyl ethers with higly electrophilic carbenes derived from diazocompounds of type EWG-CN_2COR (Scheme 44).

Scheme 44



118

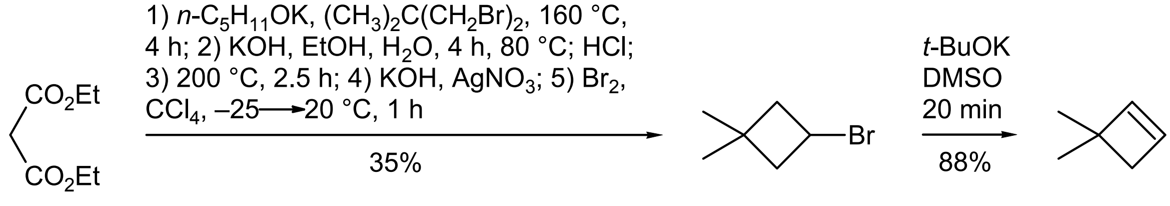


119: R = Me
120: R = Et

In general, Rh^{II}-catalyzed addition of diazopyruvates to cycloalkenes resulted in the corresponding bicyclic products in moderate yields, which were increased by use of large, usually 2.5–5-fold, excess of alkene (Table 10, entry 1-3). Besides, visibly higher yields (compound **114** had been synthesized before the general procedure was completely optimized) were reached for bicyclo[4.1.0]heptane derivatives and especially for the addition of ethyl diazopyruvate **12** to 1,3-cyclohexadiene (**109**). These outcomes could be more or less successfully explained in terms of the outlined on Scheme 42 equilibrium. Thus, positive influence of cycloalkene concentration on the cyclopropanated product formation is obvious. The highest product yield achieved in case of cyclohexadiene **109** is undoubtedly connected with significantly higher π-donating ability of diene in respect to alkene. Higher yields of bicyclo[4.1.0]heptanes could be attributed to higher steric volume of cyclohexene in comparison to cyclopentene (by approximately equal π-donating ability), so the coordination of bulky product ("L" on Scheme 43) on Rh^{II}-species is less preferable, and successive leaving of the initially complexed alkene is impeded.

Interestingly, that in all cases except bicyclo[2.1.0]pentane derivative **115**, only *exo*-isomers were obtained, that was confirmed by ^{1}H NMR spectroscopy. Thus, exocyclic cyclopropane proton in oxoesters **111-114,116,117** showed characteristic triplet at 2.2–2.6 ppm with a small coupling constant $^3J_{trans}$ = 2.8–4.8 Hz.

Scheme 45



2 **121** **108**

Addition of ethyl diazopyruvate **12** to 3,3-dimethylcyclobutene **108** gave the respective oxopyruvate **115** as 3.8:1 mixture of *exo-*/*endo*-isomers. Starting alkene **108** was obtained by dehydrobromination of 1-bromo-3,3-dimethylcyclobutane (**121**) prepared in five steps according to FITJER[90] (Scheme 45).

2.6. Synthesis of the substituted cyclopropylacrylates by WITTIG olefination

2.6.1. Synthesis of 2-substituted alkyl acrylates

Initially, the methylenation of α-oxoacetates was tested on **96** as a model compound, applying various WITTIG olefination protocols. Thus, the ylide generated from methyltriphenylphosphonium bromide with such bases as sodium hydride in tetrahydrofuran and with *n*-butyllithium in tetrahydrofuran or diethyl ether[82] led to only partial conversion of **96** providing the α-methyleneacetate **122** in moderate yields (<55%). This may be attributed to partial enolization, since about 40% of **96** could be recovered from the reaction mixture. Reaction of **96** with the ylide generated from methyltriphenylphosphonium bromide with sodium hydride in dimethylsulfoxide or with potassium *tert*-butoxide in tetrahydrofuran gave only mixtures of products. It was found, that only the ylide generated with lithium diisopropylamide (LDA) in tetrahydrofuran according to the protocol of WENKERT et al.,[20] which had previously been successfully applied for the methylenation of **13** to **125**, smoothly converted compounds **96-98**, **116** to the respective acrylates **122-124**, **138** in good yields (65–80%). However, even this method has some drawbacks. Generation of the ylide with LDA required 2 h of stirring at low temperature (–40 °C) and 2 h at ambient temperature, moreover, methylenation of α-oxoesters with an additional alkoxycarbonyl group turned out to be problematic. Thus, attempts to methylenate **99** according to this protocol gave the desired product **124** only in moderate yield (44%). Therefore, an improved methylenation protocol was developed. It turned out, that generation of the ylide from methyltriphenylphosphonium bromide with *n*-butyllithium in the presence 5–10 mol% of diisopropylamine proceeds as fast as without it, and provides a homogenous ylide solution just upon warming the reaction mixture from −78 °C to ambient temperature within 1 h. On the other hand, the ylide thus generated smoothly reacts with a keto-group at −50 °C, while ester groups are completely inert under these conditions. The catalytic amount (5–10 mol%) of diisopropylamine apparently is enough to reprotonate the enolate[91] formed by deprotonation of the α-oxoester. It is remarkable, that the added amine did not lead to any side reactions like MICHAEL addition to the formed acrylate or aminolysis of the ester group, and the yield of **126** was increased to 79%. This improved protocol may, of course, be used for the methylenation of compounds **96-98**, **116** to furnish better yields of **122-124**, **138**, which had been synthesized before the new procedure was developed. Thus, ethyl 2-methylenecyclopropylacrylate **141** was obtained in 75% yield from oxoester **140** by this improved procedure compared to 65% for the methyl ester **123** (R^5 = Me) achieved with the previously applied protocol (Table 11).

Scheme 46

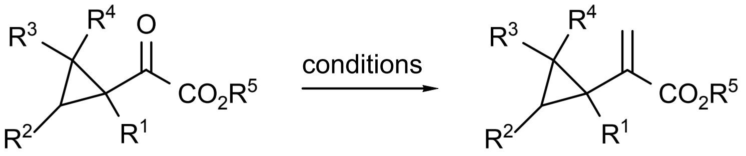
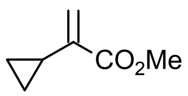
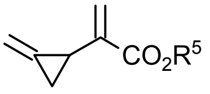
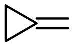
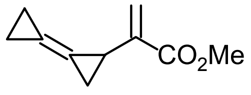
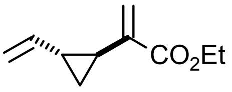
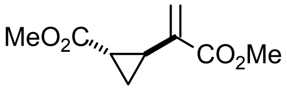
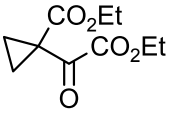
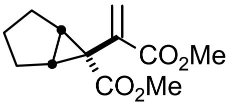
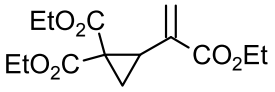
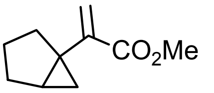
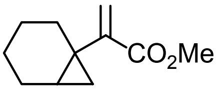
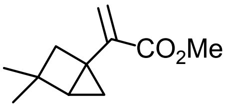
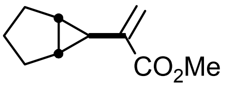
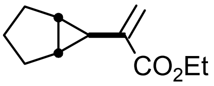
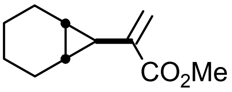
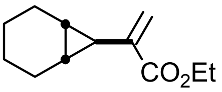
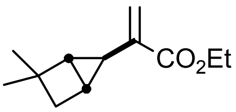
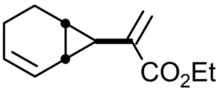
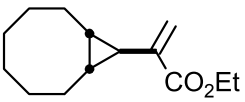


Table 11. Wittig methylenation of various cyclopropyloxoacetates.

Entry	Oxoester	R^1	R^2	R^3	R^4	R^5	Product		Yield, %
1	**96**	H	H	H	H	Me		**122**	74[a]
2	**97**	H	H	CH_2=		Me		**123**	65[a]
3	**140**					Et		**141**	75[b]
4	**98**	H	H			Me		**124**	80[a]
5	**13**	H	CH_2=CH	H	H	Et		**125**	79[a]
6	**99**	H	CO_2Me	H	H	Me		**126**	44[a] 79[b]

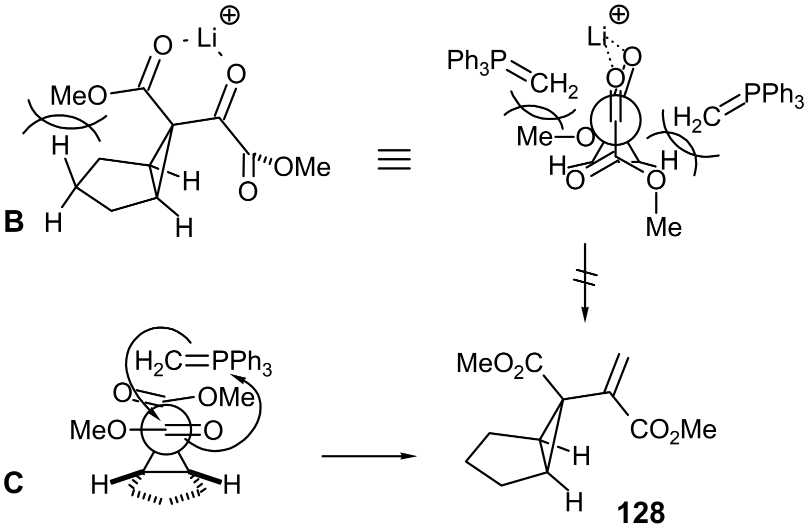
Entry	Oxoester	R^1	R^2	R^3	R^4	R^5	Product	Yield, %
7	**100**	CO_2Et	H	H	H	Et	 **127**	73[b]
8	**101**	CO_2Me	$(CH_2)_3$		H	Me	 **128**	19[b] 78[c]
9	**102**	H	H	CO_2Et	CO_2Et	Et	 **129**	81[b]
10	**103**	$(CH_2)_3$		H	H	Me	 **130**	85[b]
11	**104**	$(CH_2)_4$		H	H	Me	 **131**	81[b]
12	**105**	$(CH_3)_2CCH_2$		H	H	Me	 **132**	36[d]
13	**111**	H	$(CH_2)_3$		H	Me	 **133**	85[b]
14	**112**	H	$(CH_2)_3$		H	Et	 **134**	86[b]
15	**113**	H	$(CH_2)_4$		H	Me	 **135**	92[b]
16	**114**	H	$(CH_2)_4$		H	Et	 **136**	92[b]
17	**115**	H	$(CH_3)_2CCH_2$		H	Et	 **137**	66[b]
18	**116**	H	$(CH_2)_2CH{=}CH$		H	Et	 **138**	76[a]
19	**117**	H	$(CH_2)_4$		H	Et	 **139**	77[b]

[a] Ph_3PCH_3Br, LDA, THF, –40 °C, 2 h, 20 °C 2 h (GP 9A). – [b] Ph_3PCH_3Br, *n*BuLi, 10 mol% *i*Pr_2NH, THF, –78→10 °C, 1 h (GP 9B). – [c] Ph_3PCH_3Br, *t*BuOK, THF, 20 C, 1 h. – [d] Overall yield for two step SWERN-WITTIG sequence is given.

In this respect the attempted methylenation of **101** gave an unusual result in that predominantly the starting material was recovered. Most probably, complexation of the oxo- and the *endo*-methoxycarbonyl groups of **101** with a lithium cation forming a six-membered cyclic chelate lead to an orientation of the keto-carbonyl group which sterically disfavors addition of the bulky ylide (Scheme 47). Indeed, methylenation of **101** was successful (78%

yield) with so-called “salt-free” ylide, generated from methyltriphenylphosphonium bromide with potassium *tert*-butoxide in tetrahydrofuran.

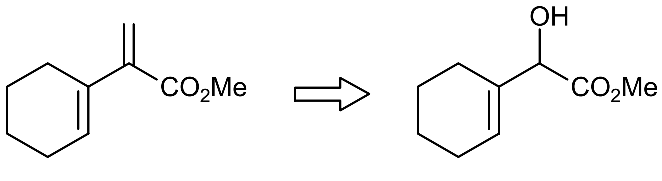
Scheme 47



128

Interesting to note, that after the oxoester **104** was subjected to methylenation according to GP 9B, a trace amount of 2-cyclohexene-1-yl acrylate **142**[92] was isolated by purification of the target compound **131**. Its presence originated from methylenation of **82**, which did not take part in SIMMONS-SMITH cyclopropanation (Scheme 48).

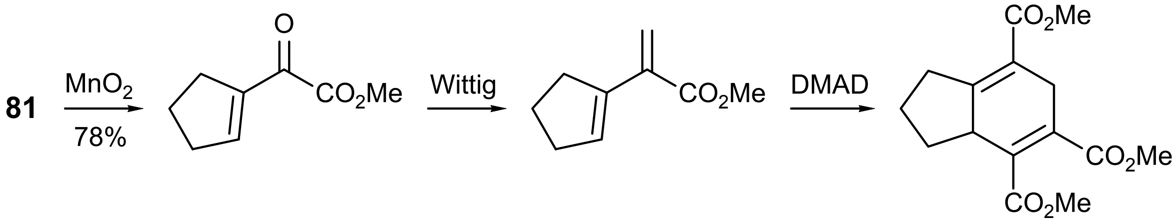
Scheme 48



142 **82**

On the other hand, no examples had been found to concern a direct alkylenation of alkenyl oxopyruvates with highly basic alkylidenetriphenyl phosphoranes. This intriguing opportunity, which might be useful in syntheses of various EWG-activated dienes, was checked as follows (Scheme 49).

Scheme 49



143 **144** **145**

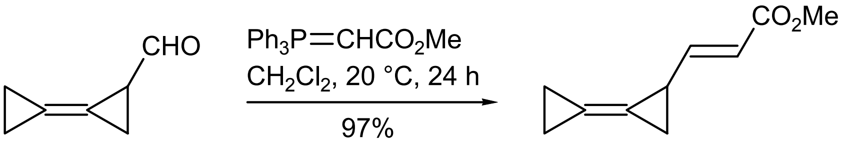
Methyl (cyclopenten-1-yl)hydroxyacetate (**81**) was oxidized with MnO_2 to give methyl (cyclopentene-1-yl)oxoacetate (**143**) in good yield. This oxoester was then subjected to methylenation with the ylide prepared according to GP 9B, but at 4-fold dilution of reaction mixture in respect to GP 9B. Unfortunately, methyl cyclopentene-1-yl acrylate turned out more reactive then its higher homolog **142**. Thus, after the reaction mixture was stirred for 5 h at ambient temperature, traces of more polar dimeric **144** were detected, which became the major product after additional stirring of the mixture for 16 h. Nevertheless, the clear evidence of the cyclopentenyl acrylate **144** formation was obtained after the crude product has been allowed to react with dimethyl acetylenedicarboxylate (DMAD), yielding corresponding DIELS-ALDER adduct **145**.

2.6.2. Synthesis of some 3-cyclopropylacrylates by WITTIG olefination. Thermal rearrangements of substituted methylenecyclopropylacrylates.

Besides of a wide variety of synthesized alkyl 2-cyclopropylacrylates, it was currently decided to prepare some easily accessible alkyl 3-cyclopropylacrylate in order to compare its behavior in radical polymerization with the respective 2-substituted analogues.

Thus, WITTIG olefination of the bicyclopropylidenecarboxaldehyde **63** with (methoxycarbonyl)methylene triphenylphosphorane in CH_2Cl_2 afforded methyl 3-bicyclopropylidenylacrylate (**146**) in high yield[52, 93] (Scheme 50).

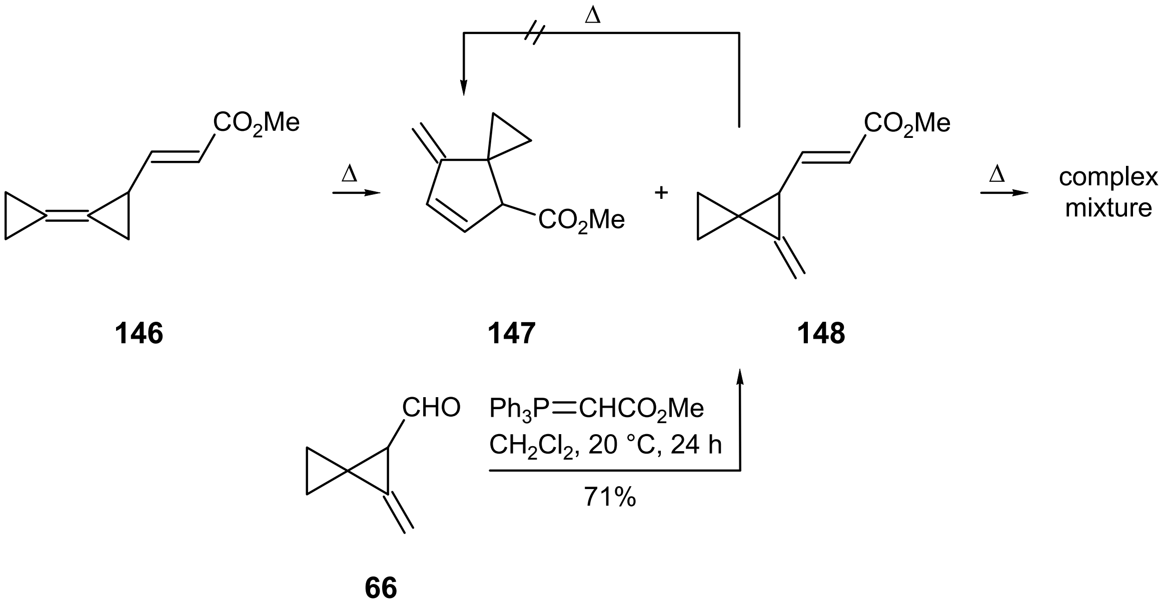
Scheme 50



63 **146**

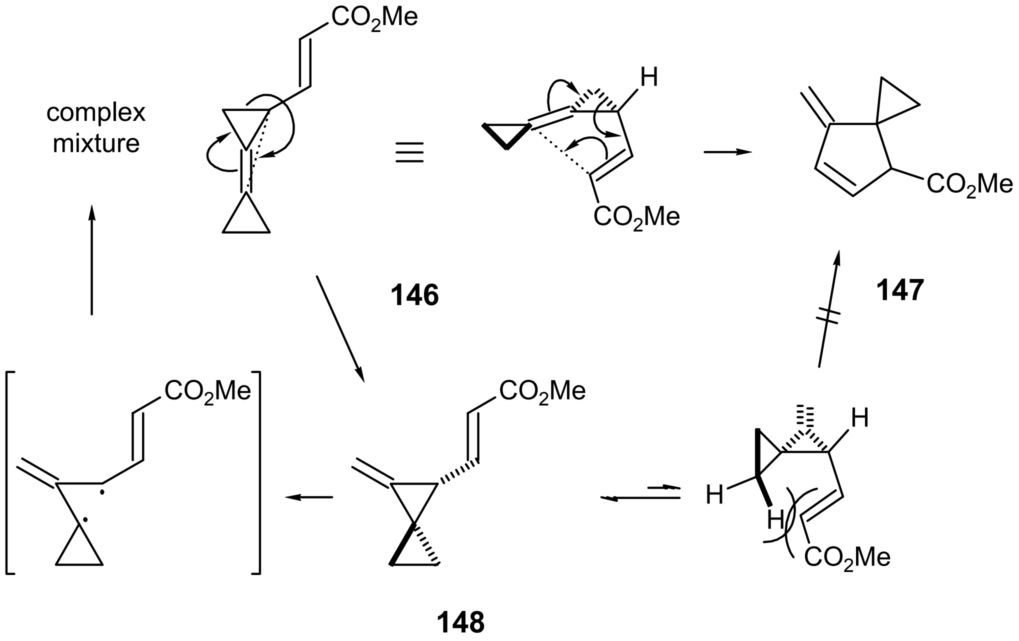
It was found that compound **146** undergoes thermal rearrangement by heating over 60 °C to give among unidentified products, methylenespiropentane compound **147** and methylenespiroheptane **148** (Scheme 51). After heating of the compound **146** at 160 °C for 1 h, methyl 7-methylenespiro[2.4]hept-5-ene-4-carboxylate (**147**) was isolated as the only product in 50% yield. On the other hand, prepared from the aldehyde **66**, methyl (*E*)-3-(2-methylenespiro[2.2]pent-1-yl)propenoate (**148**) gave under the same conditions only a complex mixture of poly- and oligomeric products. This fact could be considered as indirect evidence that the rearrangement of **146** towards **147** occurs via the five-membered cyclic transition state as a concerted process (Scheme 52).

Scheme 51



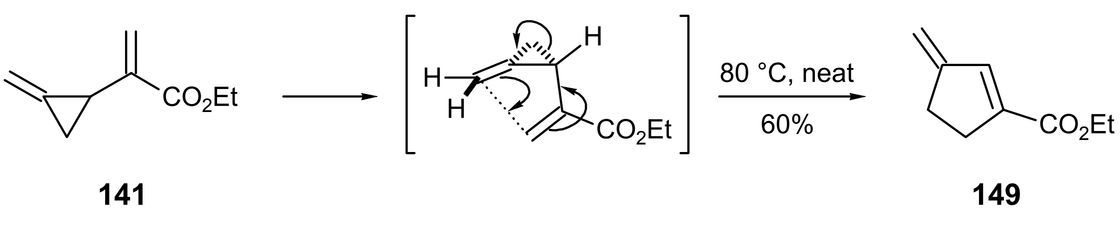
Alternatively, a *proximal* bond cleavage of **146** resulted also in methylenespiropentane compound **148**, which, however, could not been rearranged to **147** via concerted process, because it would require a sterically disfavored four-membered cyclic transition state (Scheme 52). Therefore, by heating, the compound **148** forms unselectively a complex mixture of oligomeric products, originated from all possible biradicals.

Scheme 52



Besides, it was also noted that 2-alkylidenecyclopropylacrylates readily undergo rearrangement under heating at 100 °C. Moreover, this process has been found to be significantly exothermic. Thus, attempted distillation of the ethyl 2-methylenecyclopropylacrylate **141** gave ethyl 4-(methylidenecyclopent-1-ene)-1-carboxylate **149** in good yield (Scheme 53).

Scheme 53



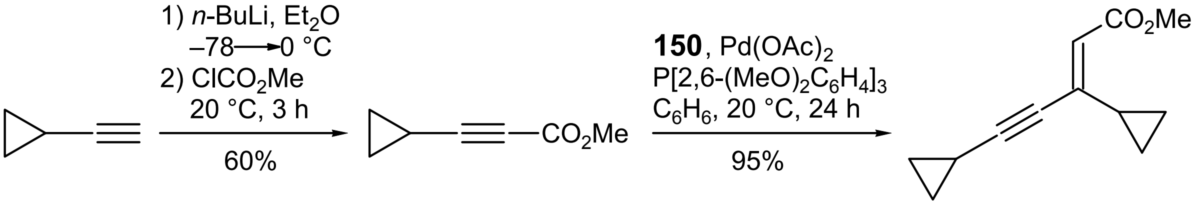
Rearrangement of **141** towards **149** may occur via five-membered transition state (analogously to **146**→**147**) as a concerted process.

3. Miscellaneous Preparations.

3.1. Synthesis of methyl (2E)-3,5-dicyclopropylpent-2-en-4-ynoate via Pd^0 catalyzed cross coupling of acetylenes

Recently developed by TROST et al. procedure for Pd^{II}-catalyzed addition of terminal alkynes to acceptor alkynes[94] was successfully used for the preparation of 3,3-disubstituted cyclopropyl containing acrylate.

Scheme 54



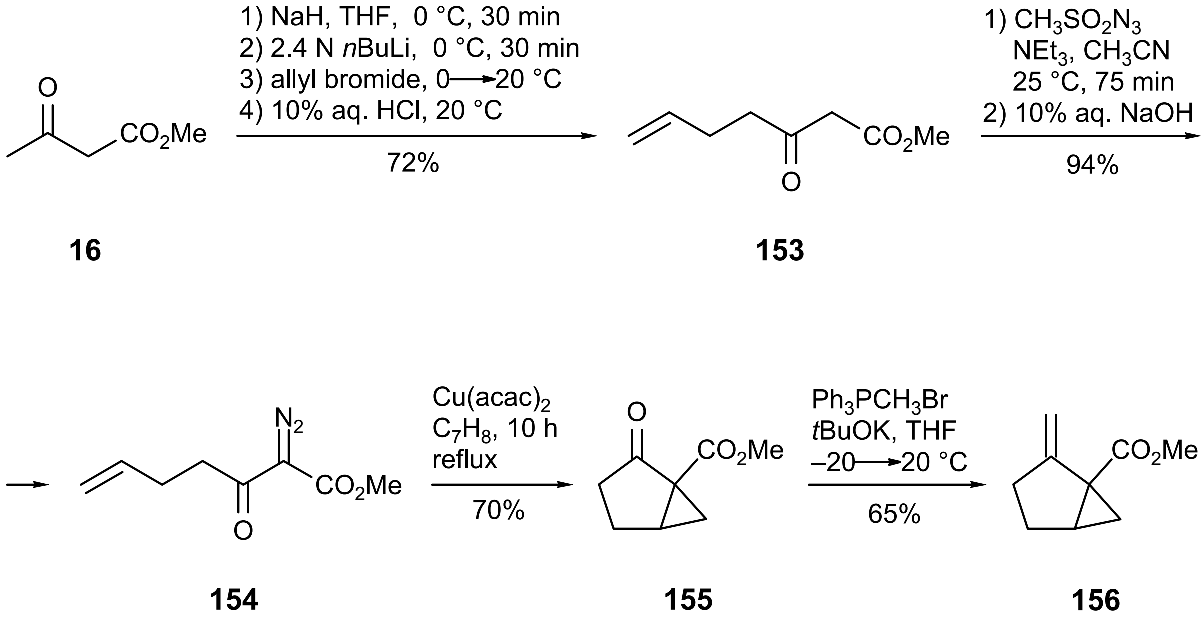
150 **151** **152**

Thus, starting from commercially accessible cyclopropylacetylene **150**, acrylate **152** was easily prepared in good yield by methoxycarbonylation of the lithiated cyclopropyl acetylene[95] and subsequent Pd^{II}-catalyzed cross coupling of the obtained 3-cyclopropylpropynoate (**151**) with cyclopropyl acetylene (Scheme 54).

3.2. Synthesis of methyl 2-methylenebicyclo[3.1.0]hexane-1-carboxylate

The titled compound was prepared in four steps starting from methyl acetoacetate. Thus, alkylation of the derived from methyl acetoacetate dianion with allyl bromide according to WEILER[96] gave 3-oxohept-6-enoate **153** successively converted into the corresponding diazoester **154**,[97] which was than cyclized in refluxing toluene in the presence of 2.5 mol% of copper(II)acetylacetonate affording methyl 2-oxobicyclo[3.1.0]hexane-1-carboxylate[86] (**155**) in good overall yield (47% for three steps). Prepared bicyclic oxoester **155** was smoothly methylenated with the ylide generated from methyl triphenylphosphonium bromide and potassium *tert*-butoxide in THF, to give the target compound **156** in good yield (Scheme 55).

Scheme 55


O
CO$_2$Me
1) NaH, THF, 0 °C, 30 min
2) 2.4 N *n*BuLi, 0 °C, 30 min
3) allyl bromide, 0 → 20 °C
4) 10% aq. HCl, 20 °C
72%
CO$_2$Me
O
1) CH$_3$SO$_2$N$_3$
NEt$_3$, CH$_3$CN
25 °C, 75 min
2) 10% aq. NaOH
94%
16
153
N$_2$
CO$_2$Me
O
Cu(acac)$_2$
C$_7$H$_8$, 10 h
reflux
70%
O
CO$_2$Me
Ph$_3$PCH$_3$Br
*t*BuOK, THF
–20 → 20 °C
65%
CO$_2$Me
154
155
156

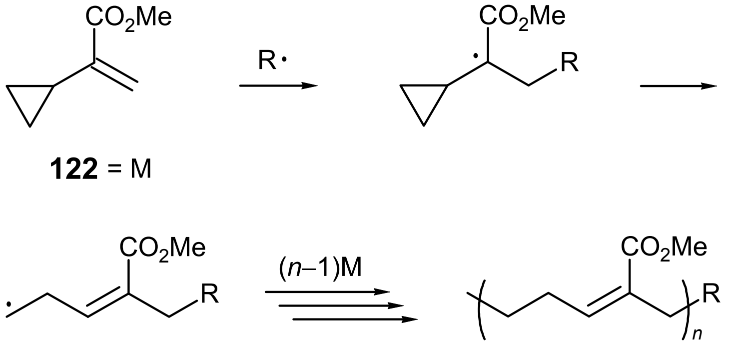
4. Polymerization of the Cyclopropylalkene-substituted Monomers. Preliminary Results and Discussion

Synthesized monomers depending on its behavior by radical ring-opening polymerization could be conditionally divided on two groups: compounds, bearing one ore two cyclopropyl groups along with variously attached double bond, namely “monocyclic monomers”, and bicyclic alkyl acrylates.

4.1. Polymerization of monocyclic monomers

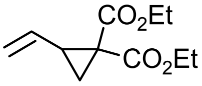
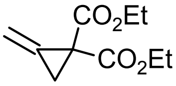
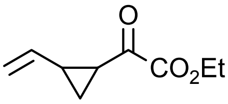
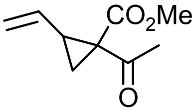
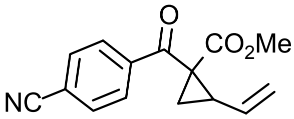
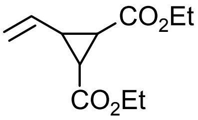
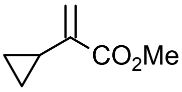
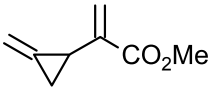
The polymerization of the titled monomers was carried out in chlorobenzene solution using AIBN as an initiator. The results show (Table 12) that polymers with a number-average molecular weight ($\overline{M}_n$) of 118900 and 86300 g/mol, respectively, were formed in the case of **122** and **124**, respectively, while the radical polymerizations of **5**, **13**, **29**, **123**, **127**, **129**, **146**, and **152** led to the formation of oligomeric products only. The ^{1}H NMR and ^{13}C NMR spectra of obtained poly(**122**) confirmed the opening of the cyclopropane ring with a formation of 1,5-disubstituted ring-opened unit (Scheme 56). This ring-opening polymerization which occurs instead of a simple vinyl-group polymerization, is typical for vinylcyclopropanes.[9]

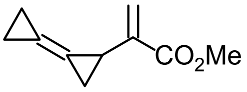
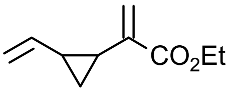
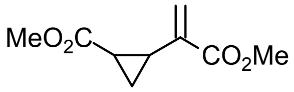
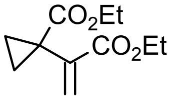
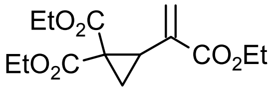
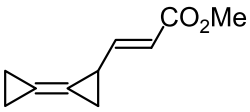
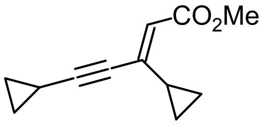
Scheme 56



Monomer **125** resulted in an insoluble cross-linked polymer, which was expected on the basis of the bifunctionality of this monomer. In contrast to this, poly(**126**) was also insoluble in tetrahydrofuran, but could be dissolved in other solvents, for example, in chloroform or chlorobenzene. Unfortunately, the polymerization of substituted cyclopropanes resulted in significantly lower polymer yields in comparison to the 1,1-diethoxycarbonyl-2-vinylcyclopropane (DECVCP), which was used as a benchmark for the reactivity in the radical polymerization of the vinylcyclopropane derivatives. The low polymer yield and $\overline{M}_n$ value of monomer **5** and **123** could be attributed to methylene substituent found to affect the formation of high molecular weight polymers adversely. Thus, 1,1-diethoxycarbonyl-2-methylenecyclopropane **5** did not form polymers in dichlorobenzene in the presence of AIBN within 15 h. The polymerization behavior of **124** can be also explained on this basis. The substitution of the methylene hydrogens in **123** by an ethylene bridge leads to monomer **124** in which the former radical accessible methylene group is now changed into a corresponding tetrasubstituted double bound. In contrast to a vinyl group, tetrasubstituted double bonds usually are not able to attach the initiating radicals and therefore could be detected in poly(**124**) by ^{13}C NMR spectroscopy.

Table 12. Polymerization of the synthesized monomers and DECVCP (2.0 mol/L) in chlorobenzene and in the presence of AIBN (2.0 mol%) at a temperature of 65 °C, with polymerization time (t_P) of 15 h.

Entry	Monomer	Polymer yield (%)	$\overline{M}_n$ [g/mol]	$\overline{M}_w$ [g/mol]	T_G [°C]
1	 [a]	95	67500	128700	40
2	 **5**	4	24585	–	–
3	 **13**	67	–	–	[b]
4	 **23**	89	30100	–	42
5	 **24**	70 47	8400 31500	–	–
6	 **29**	83	28100	–	5
7	 **122**	71	118900[c]	419000	–
8	 **123**	15	5300	7800	–

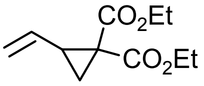
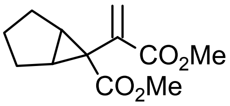
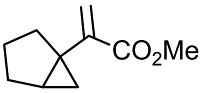
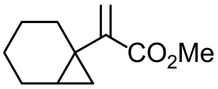
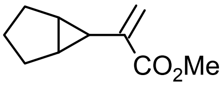
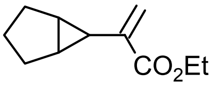
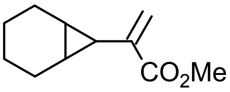
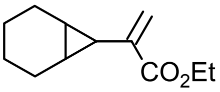
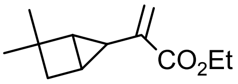
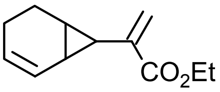
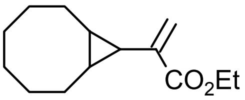
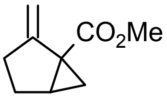
Entry	Monomer	Polymer yield (%)	$\overline{M}_n$ [g/mol]	$\overline{M}_w$ [g/mol]	T_G [°C]
9	 **124**	43	86300	156100	–
10	 **125**	42[d]	–	–	–
11	 **126**	67[d]	–	–	–
12	 **127**	57	50500	–	–20
13	 **129**	17	2900	8500	–
14	 **146**	25	13500	–	[b]
15	 **152**	92	–	–	[b]

[a] DECVCP. – [b] Viscous oil. – [c] Polymer was not completely soluble in THF. – [d] Polymer was not soluble in THF.

4.2. Polymerization of the bicyclic alkyl acrylates

The polymerizations of bicylic monomers were also carried out in chlorobenzene solutions with AIBN as an initiator. The promising results demonstrate (Table 13) a significant influence of the second ring size on the radical polymerization of bicyclic monomers. The highest polymer yields were obtained in the polymerizations of **128**, **130**, **131**, **133-136**, i.e. of monomers with an annelated 5- or 6-membered ring. In the case of **130**, **133** and **135**, the polymer yields (100, 99 and 98%, respectively) and the glass transition temperatures (T_g) of 90, 57 and 93 °C were significantly higher than those observed for DECVCP. In contrast, bicyclo[2.1.0]pentyl- and bicyclo[6.1.0]nonyl-group contained monomers **137** and **139**, respectively, gave low or even very low polymer yields. In comparison to **128**, **130** and **133**, compounds **137** and **139** showed a significant reduction of both the polymer yield and $\overline{M}_n$ value. It is well documented in the literature[9] that the introduction of a second substituent in the same position of the cyclopropane ring may cause a significant decrease of the monomer reactivity in the radical polymerization due to steric interactions. The drastically lower polymer yield in the radical polymerization of **138**, which contains an annelated cyclohexene ring, in comparison to **136** can probably be attributed to the presence of allylic hydrogen atoms in the monomer structure. This, in general, causes a degradative chain transfer in the radical polymerization with the formation of less reactive and therefore slower propagating radicals.[98]

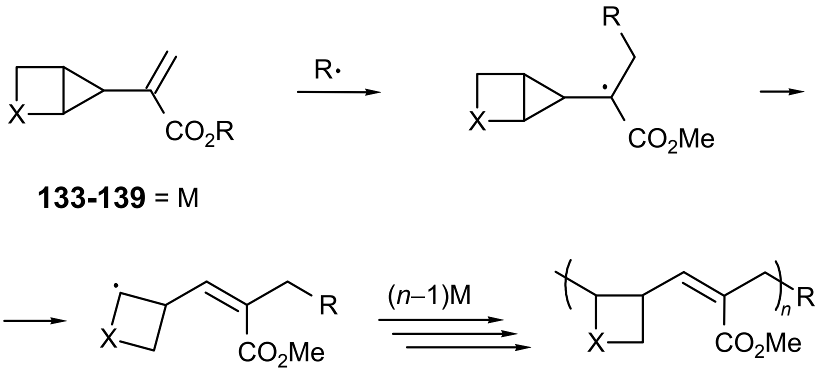
Table 13. Polymerization of the synthesized monomers and DECVCP (2.0 mol/L) in chlorobenzene and in the presence of AIBN (2.0 mol%) at a temperature of 65 °C, with polymerization time (t_P) of 15 h.

Entry	Monomer		Polymer yield (%)	$\overline{M}_n$ [g/mol]	$\overline{M}_w$ [g/mol]	T_G [°C]
1		[a]	95	67500	128700	40
2		**128**	30	14600	23100	55
3		**130**	100	120200	298000	90
4		**131**	54	23400	–	59
5		**133**	99	113000	380800	57
6		**134**	91	181300	204600	40
7		**135**	98	58500	124100	98
8		**136**	94	–	–	53
9		**137**	37	21000	30900	46
10		**138**	27	19800	22400	–
11		**139**	2	–	–	–
12		**156**	9	–	–	–

[a] DECVCP.

The ^{1}H NMR and ^{13}C NMR spectra of the polymers obtained, for example, in radical polymerization of the bicyclic monomers **133** or **135** confirmed the opening of the cyclopropane rings with a formation of 1,5-disubstituted ring-opened units containing the unchanged second ring (Scheme 57).

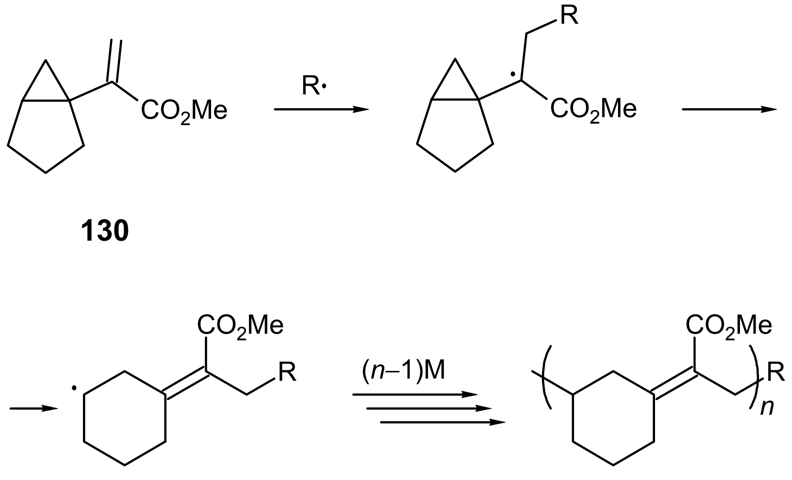
Scheme 57



133-139 = M

On the other hand, polymerization of the 1-substituted alkylacrylates **130**, **131** involves cleavage of the endocyclic bond to give corresponding polymers with cycloalkylidene unit (Scheme 58). Thus, the increased value of (T_g) for **130**, that is essentially higher then that for **134** (in spite of its $\overline{M}_n$ values are 120200 and 181300, respectively), could be attributed to the appearance of a rigid cyclohexylidenic fragment poly(**130**) that was evidenced by ^{13}C NMR. It is also clear, that reduced $\overline{M}_n$ values of **131** and **137** could be caused by increased sterical hindrance of radical center formed.

Scheme 58



130

As mentioned above, 2-vinylcyclopropane-1,1-dicarboxylates are less reactive in the radical copolymerization with methacrylates. In order to elucidate this aspect, the radical copolymerizations of MMA with **122**, **130**, **133** and **135** were carried out in chlorobenzene solutions in the presence of AIBN (Table 14). The composition of the copolymers formed could be determined by ^{1}H NMR spectroscopy, using the intensity ratio of the peaks at 3.69 ppm assigned to the OCH_3 protons of **122**, **130**, **133** or **135** and at 3.60 ppm assigned to the OCH_3 protons of the MMA units. The copolymers formed with **133**, **135** and especially **130**, contained visibly less units derived from MMA, in comparison to the copolymer of **122**. Taking into consideration the fact that the molar composition of a copolymer of DECVCP and MMA obtained under similar conditions[12] was 1.0 : 0.09, it can be concluded that 2-cyclopropylacrylates, especially the bicyclic monomers **130**, **133** and **135**, demonstrated a drastically improved reactivity in the radical polymerization, in comparison to DECVCP.

Table 14. Copolymerization of MMA (1.0 mol/L) with 122, 130, 133, 135 (1.0 mol/L) in chlorobenzene and in the presence of AIBN (2.0 mol%) at a temperature of 65 °C, with t_P of 2 h.

Entry	Comonomer	Polymer yield (%)	$\overline{M}_n$ [g/mol]	$x_{CM} : x_{MMA}$[a]	T_G [°C]
1	**122**	8.6	13300	1.0 : 5.0	–
2	**130**	72.8	67700	1.0 : 0.9	–
3	**130**	20.7[b]	84300	1.0 : 0.6	85
4	**133**	27.7	34300	1.0 : 1.4	62
5	**135**	10.1	17900	1.0 : 1.1	95

[a] Molar composition of the copolymer: [Comonomer] : [MMA]. – [b] t_P = 15 min.

Finally, it should be mentioned that monomer **130** can substitute commercially available dilutents in dental composites.[99] Thus, methyl 2-(bicyclo[3.1.0]hex-1-yl)acrylate is the first monomer that undergoes radical ring-opening polymerization with a reactivity higher than that of MMA, shows lower volume shrinkage than MMA, and may form polymers with a number-average molecular weight higher than 100000 g/mol. Moreover, it was found from *in vitro* single cell gel electrophoresis that **130** is not mutagenic and shows relatively low cytotoxity (XTT_{50} value 312.5 μg/mL).[100]

5. Synthesis of the 2-(Bicyclo[3.1.0]hex-1-yl)acrylic Acid and Its Esters

Since 2-bicyclo[3.1.0]hexyl acrylate derivatives have been find to be the most promising class of substances which may generate new low-shrinking monomers, it was decided to focus the further investigations on a development of possible synthetic approaches towards structurally modified compounds, parent to **130**.

At first, various 2-(bicyclo[3.1.0]hex-1-yl)acrylates had to be prepared. That required a reliable hydrolysis protocol for methyl ester **130** in order to obtain the corresponding acid **157**. Unfortunately, previously described in literature hydrolytic procedures including ultrasound induced methods, gave acid **157** contaminated with a significant amount of the corresponding β-hydroxyderivative as a product of MICHAEL addition of water to the acrylic double bond.

Then, original hydrolysis protocol was developed. Thus, it was found that continuous stirring of ester **130** with suspension of lithium hydroxide in aqueous acetone at ambient temperature gave pure acid **157** in high yield (Scheme 59). Generality of this new protocol could be also illustrated by hydrolysis of ethyl esters **136** and **141** (Table 15).

Scheme 59

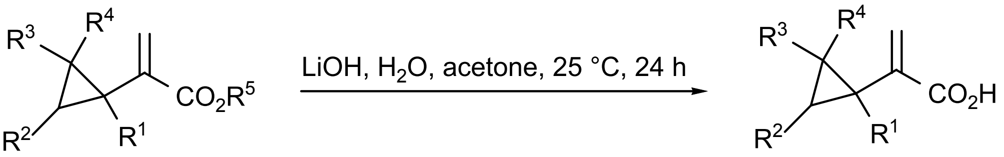
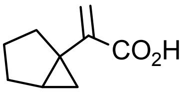
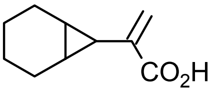
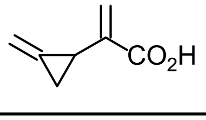
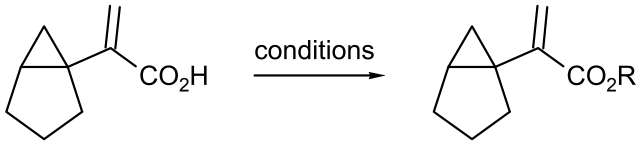


Table 15. Hydrolysis of selected alkyl acrylates.

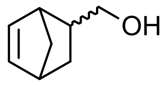
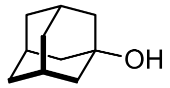
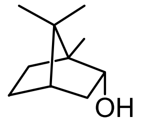
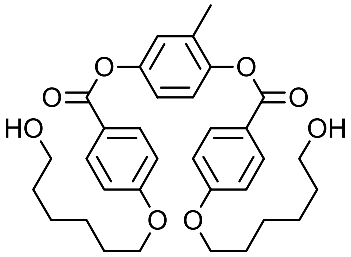
Entry	Ester	R^1	R^2	R^3	R^4	R^5	Product		Yield, %
1	**130**	$(CH_2)_3$		H	H	Me		**157**	86
2	**136**	H	$(CH_2)_4$		H	Et		**158**	81
3	**141**	H	H	$CH_2=$		Et		**159**	95

Scheme 60



157 **168-175**

Table 16. Esterification of 2-(bicyclo[3.1.0]hex-1-yl)acrylic acid.

Entry	Alcohol		Conditions[a]	Ester	Yield, %
1	PhCH$_2$OH	**160**	A, 5 mol % DMAP	**168**	86
			B		61
	PhCH$_2$Cl	**161**	K_2CO_3, KI, DMF, 25 °C, 12 h		90
2		**162**	A, 5 mol % DMAP	**169**	65
			B		64
			NEt_3, DIC, 10 mol % DMAP, 25 °		48
			1) *p*TsCl, NEt_3, 2) DMAP 10 mol %		42
3		**163**	A, 20 mol % DMAP	**170**	76
4		**164**	B	**171**	34
			A, 110 mol % DMAP	**172**	63
			Yamaguchi conditions		70
5	$(CH_2OH)_2$	**165**	DCC, NEt_3, 10 mol % DMAP	**173**	15
6	$[(CH_2)_3OH]_2$	**166**	B	**174**	84
7		**167**	B	**175**	70

[a] Method A: 1) $(COCl)_2$, CH_2Cl_2, DMF; 2) NEt_3, DMAP, 0→20 °C (GP 11A). – B: MITSUNOBU protocol (GP 11B).

Obtained bicyclic acid was subjected to esterification with various alcohols. As a main esterification method, standard MITSUNOBU protocol[101] was chosen, which let to prepare the respective bicyclic esters easy from various primary alcohols **160, 163-167**, including diols (Scheme 60, Table 16).

In spite of clear advantages of this method, it turned to be ineffective towards sterically congested esters. Thus, after the equimolar mixture of the acid **157**, (1*S*)-*endo*-(−)-borneol **164**, DEAD and PPh_3 was stirred for one week under MITSUNOBU conditions, inverted at C-1 position of the bornyl ester **171** was obtained in low yield. Its formation route might be similar to that reported for epimerization of 2-*endo*-norborneol in the presence of benzoic acid under MITSUNOBU conditions.[101]

Nevertheless, successful esterification of such sterically congested alcohols as borneol, became possible after the original esterification protocol had been developed. Thus, it was found that acyl chloride **176** prepared from bicyclic acid **157**, is able to acylate borneol in the presence of equimolar amount of DMAP by continuous stirring at room temperature, giving the target ester **172** in good yield (Table 16). This method could be a good alternative to YAMAGUCHI protocol,[102] which also provided satisfactory yield of ester **172**, but the purification of the target product was significantly complicated because of some amount (about 30%) of the corresponding bornyl 2,4,6-trichlorobezoate presence in reaction mixture.

Thus, efficient preparation methods for bicyclic acid **157**, acyl chloride **176** and the novel method for esterification of highly congested alcohols were developed and successfully applied for the preparative syntheses of the target esters bearing 2-bicyclo[3.1.0]hexyl moiety.

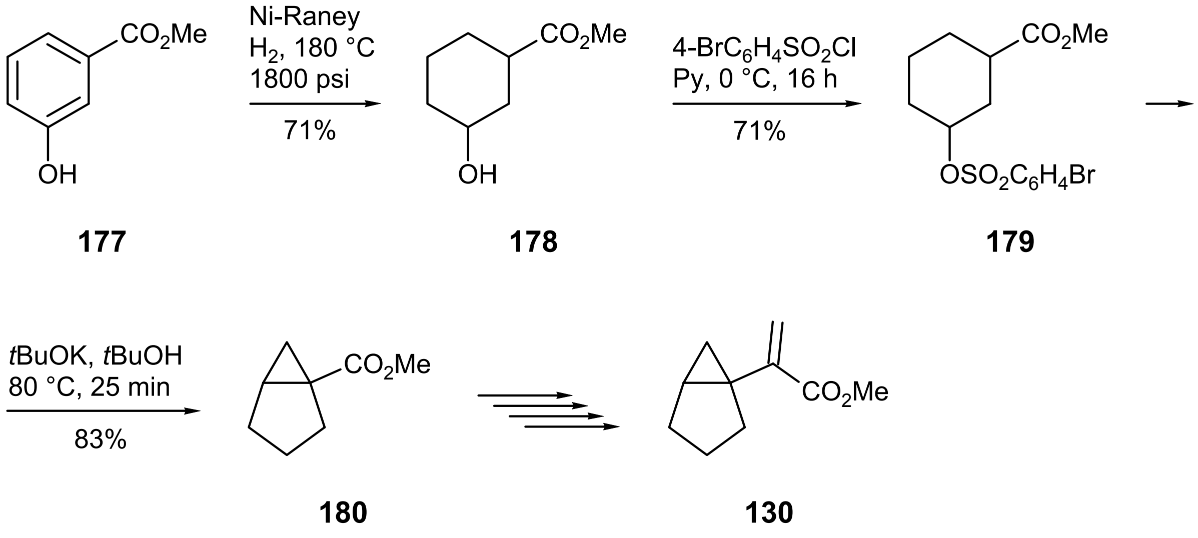
6. Alternative Approaches to the 2-(Bicyclo[3.1.0]hex-1-yl)acrylates

6.1. Introduction

Synthetic approaches which might result in 1-substituted bicyclo[3.1.0]hex-1-yl acrylates could be conditionally divided on two main classes. The first one would include transformations of functional groups attached to bicyclo[3.1.0]hexane moiety, already prepared via reliable preparative method; another one would concern methods providing construction of required bicyclic system from acyclic unsaturated precursors.

The oldest approach to construct this bicyclic system, namely 1,3-elimination in EWG-activated cyclohexane system, is known since 1957. Thus, methyl bicyclo[3.1.0]hexylcarboxylate[103] (**180**) was easily prepared by NELSON and MORTIMER from methyl 3-hydroxybenzoate **177** by a catalytic hydrogenation with successive brosylate **179** formation and its 1,3-elimination (Scheme 61).

Scheme 61



This nice three-step sequence has a serious drawback in terms of the considered here problematic, which is obvious. Thus, transformation of **180** to the desired acrylate **130** required five additional steps (subsequent hydrolysis, reduction, hydroxyacetate formation, oxidation, Wittig reaction). Therefore, this approach was readily excluded from consideration.

6.2. Investigation of preparative potential of Shapiro reaction towards acrylate synthesis

Although the general preparative availability of the presented approach looks doubtful,[104] it could appear an useful tool for direct introduction of the bulky electrophilic moiety into bicyclo[3.1.0]fragment. Thus, variety of mono- and bicyclic lithioalkenes became recently accessible in a half-preparative scale by Shapiro reaction, due to an essential optimization of reaction conditions and the right choice of the respective reagents and solvent systems.[105] Such progress became possible when *exact*, *i.e.* stoichiometric amount of base (predominantly, *n*BuLi) had been used for deprotonation of **Tris**-sulfonylhydazones in newly developed procedures, enabled to generate lithioalkene at low temperature (< –70 °C) and to involve it almost quantitatively in reaction with desired electrophile. Therefore, it was decided to test this reaction towards the preparation of bicyclic acid **157** derivatives.

Thus, 1-acetylcyclopentene[106] (**181**) was smoothly cyclopropanated with dimethylsulfoxonium methylide according to a previously described procedure,[107] to give 1-acetylbicyclo[3.1.0]hexane **182** in good yield. This ketone was then almost quantitatively converted into the corresponding arylsulfonylhydrazones[105] **183** and **184**, which were then subjected to Shapiro reaction under various conditions (Scheme 62, Table 17).

Scheme 62

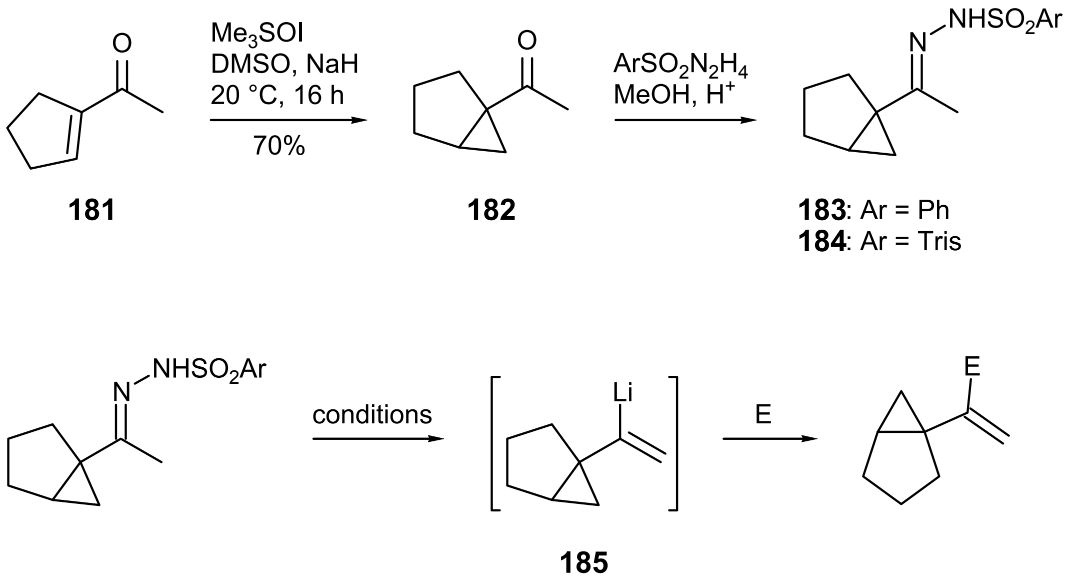
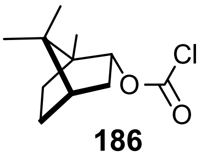


Table 17. Selected results of attempted trapping of lithioalkene **185** with electrophiles.

Entry	Hydrazone	Ar	Conditions	Electrophile	Product	Yield, %
1	**181**	Ph	MeLi, Et_2O, –70, C_6H_6, TMEDA	CO_2, THF, –70 –60 °C, 30 min	**157**	35
2	**182**	Tris	Hexane, C_6H_6, TMEDA, –40 °C, 3 h	 **186**	**172**	17[a]

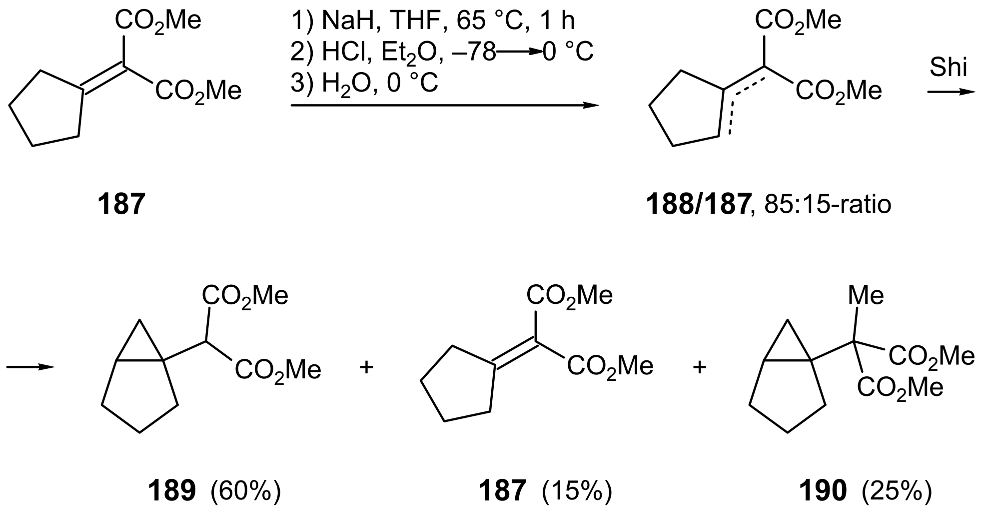
[a] Product contaminated with 40% of the corresponding bornyl pentanoate. Yield was estimated by GC.

Unfortunately, the titled hydrazones **183** and **184** turned out too low soluble to be deprotonated under –50 °C in routinely used for this reaction solvents; by warming, formation of a mixture of **185**, the base used and originated from **185** alkene occurred. This alkene is a result of competitive deprotonation of hydrazone or initially formed N-anion with lithioalkene **185**. Although a clear evidence of desired products **157** and **172** formation has been obtained, further attempts in this direction were cancelled, because the efficient esterification protocol (GP 11A) had been already developed.

6.3. SIMMONS-SMITH cyclopropanation of 2-(cyclopenten-1-yl)malonic acid derivatives with SHI's carbenoid.

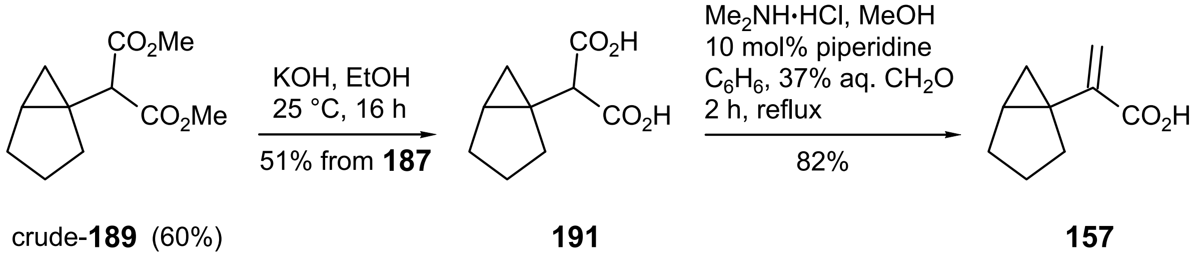
Investigation of SHI's carbenoid reactivity towards cyclopropanation of various cycloalkenes showed that malonic ester derivatives were relatively resistant to be involved as C-H acids into reactions with the titled carbenoid. Thus, after the cyclopentenyl malonic acid dimethyl ester[108] (**188**) has been allowed to react with Shi's carbenoid solution according to standard procedure, bicyclic diester **189** was obtained in 60% yield (GC) as major product among the unchanged starting cyclopentylidenemalonate[109] (**187**) (~15%) and methylated bicyclic product **190** (Scheme 63).

Scheme 63



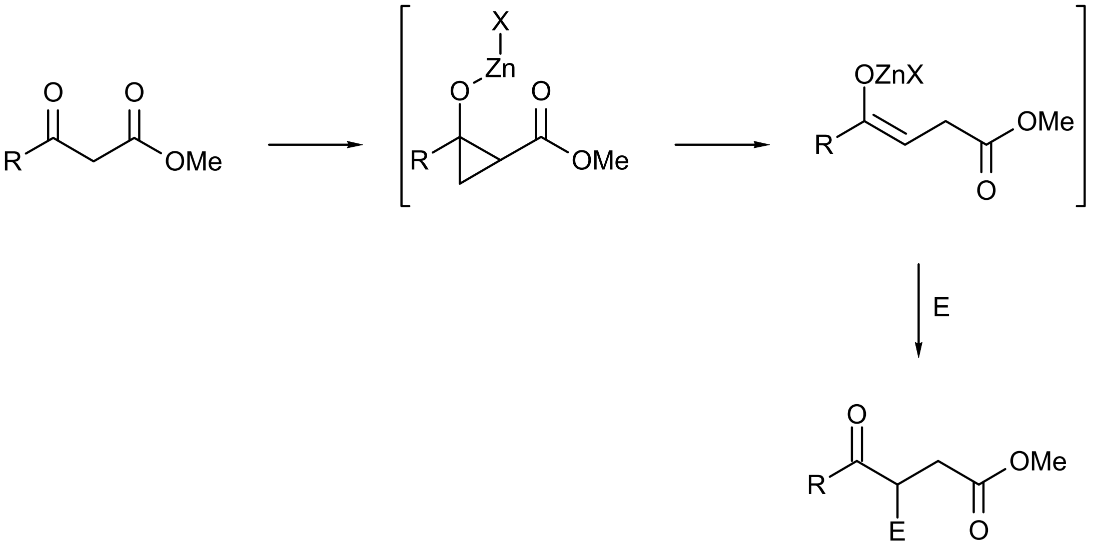
This inseparable mixture was successfully hydrolyzed by aqueous KOH to afford after crystallization pure diacid **191** in good yield. This dicarboxylic acid was then smoothly converted into the corresponding acrylic acid **157** according to original protocol developed on the basis of MANNICH decarboxylation-methylenation procedure[110] (Scheme 64).

Scheme 64



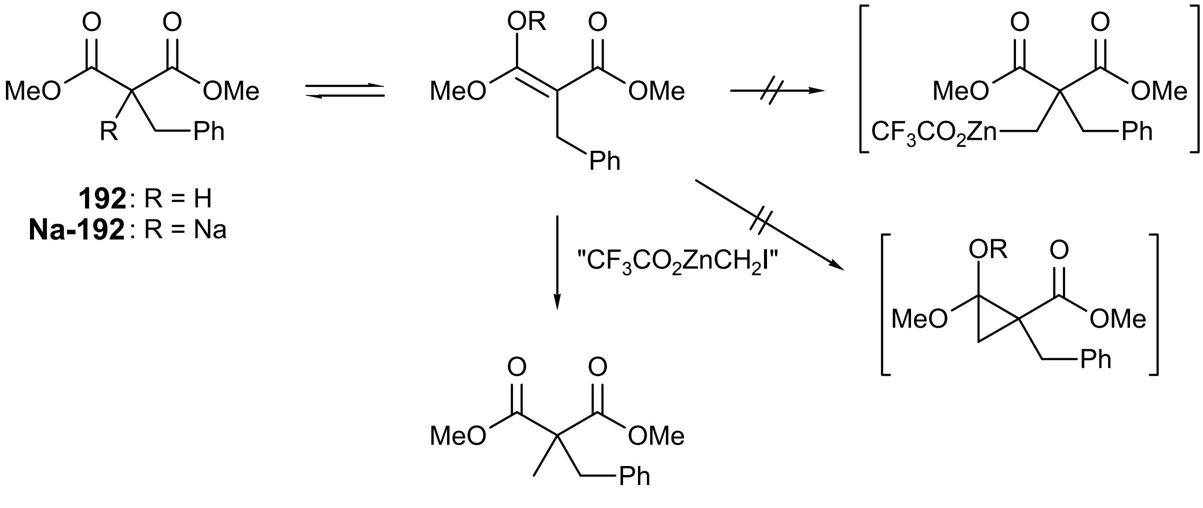
Malonic ester derivatives should be also noted to form no 1,4-dicarbonyl compound by treatment with Shi's carbenoid, giving instead it only the respective α-methylated malonic ester (like **190**). This outcome seems to be some like unusual because the formation of 1,4-dicarbonyl compounds resulted by reaction between β-ketoesters and FURAKAWA-type carbenoid ($EtZnCH_2I$) is well documented in literature.[111] Thus, an initial enolate cyclopropanation followed by Zn-cyclopropanolate cleavage (Scheme 65), provided the respective levulinic Zn-enolate, which was then trapped with various aldehydes (similarly to REFORMATSKY reaction).

Scheme 65



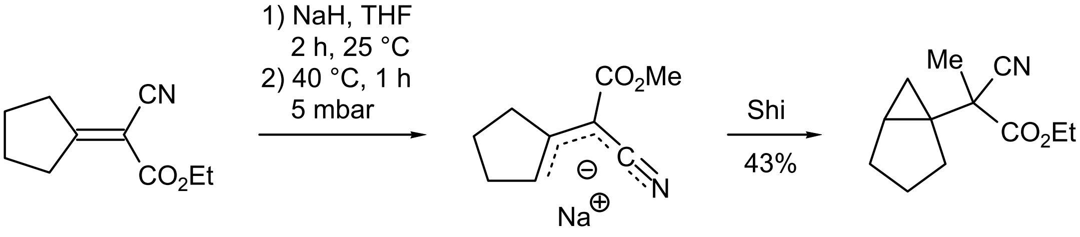
In this respect an attempt had been undertaken to capture Zn-organyl suggested to appear after ordinary enolate alkylation (Na-enolate was also tested) of the model compound **192** with SHI's carbenoid (Scheme 66). However, only compound **193** was isolated in moderate ("neutral conditions") to good (in the case of Na-enolate) yield as the major product after compound **192** subjected to SHI's protocol was treated with benzaldehyde. Therefore, it was supposed that methylation of α-position of malonic esters occured either by CH_2-insertion of the slowly decomposed carbenoid (in the case of "neutral media") or by an alkylation of Na-enolate (in the second case a complete methylation took place) with the originated from carbenoid decomposition methyl iodide.[73, 76]

Scheme 66



On the other hand, obtained from α,β-unsaturated CH-acids Na-enolates are known to undergo alkylation with a regioselectivity lack, giving a mixture of 2- and 4- alkylated derivatives.

Scheme 67



194 **195**

In this respect described here features of SHI's carbenoid may be used for "one-pot" methylation-cyclopropanation of (cyclo)alkylidene malonates and their analogues, which are readily accessible via KNOEVENAGEL reaction. Thus, easily prepared according to literature[112] cyclopentylidenecyanoacetic acid ethyl ester (**194**) was converted into the corresponding Na-enolate and, after the solvent replacement, treated with three equivalents of SHI's carbenoid to give the respective α-methylated bicyclo[3.1.0]hexane compound (**195**) in moderate yield (Scheme 67).

6.4. *Synthesis of 2-(bicyclo[3.1.0]hex-1-yl)acrylates via Pd^0 catalyzed 5-*exo-*trig/3-*exo-*trig cascade cyclization of 1,6-enynes*

6.4.1. Introduction

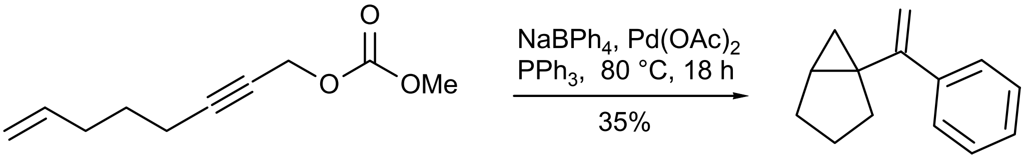
Among the wide variety of recently developed transition metal assisted enyne cyclizations, affording bicyclohexane derivatives with various substitution patterns on bicyclic system more or less successfully,[113] Pd-catalyzed cyclization of 1,6-enynes has been chosen, because it would directly result bicyclo[3.1.0]hexylacrylates required starting from relatively easy accessible acyclic precursors.

6.4.2. Preliminary experiments

A principal possibility of the 5-*exo-trig*/3-*exo-trig* cyclization of 1,6-enynes towards bicyclo[3.1.0]hexylacrylates had been recently reported by GRIGG.[114] Later, OPPOLZER[115] has developed this approach towards diastereoselective synthesis of enantiomerically pure (−)-α-Thujone. This article was chosen as a starting point for further investigations in this field because actually it was the only published example of the titled cyclization afforded various bicyclo[3.1.0]hexyl acrylic moiety in high yield by complete conversion of the starting 1,6-enines. Moreover, the viable procedures concerned the used catalytic system preparation had been documented in details.

First, a principal possibility to involve into the titled cyclization an *unsubstituted* enyne, which never before were cyclized to the respective bicyclo[3.1.0]hexane moiety via Pd-catalyzed process, was tested. There is a suggestion that unsubstituted 1,6-enynes would not undergo cyclization readily because of two reasons. Enyne conformation enabling this process (when unsaturated fragments are next to each other) is sterically disfavored unlike the widely used for this purposes 5-mono- and 5,5-disubstituted precursors.[114-116] On the other hand, a complexation of the hard nucleophilic substituent (for example, alkoxycarbonyl group of a *gem*-5,5-EWG-disubstituted 1,6-enyne) was suggested to stabilize an intermediate Pd-specie, thus preventing the β-hydride elimination of PdL_n resulted in a "Pd-black" formation.[116] In order to clear this question up, enyne **196** was subjected to the previously described by GRIGG[114] simple protocol for anionic capture of bicyclo[3.1.0]hexyl-Pd spices with sodium tetraphenylborate. Thus, heating of enyne **196** at 80 °C for 18 h in the presence of 10 mol% $Pd(OAc)_2$ and 20 mol% PPh_3 with 1 equivalent of $NaBPh_4$, resulted in desired cyclized product **197** (Scheme 68).

Scheme 68

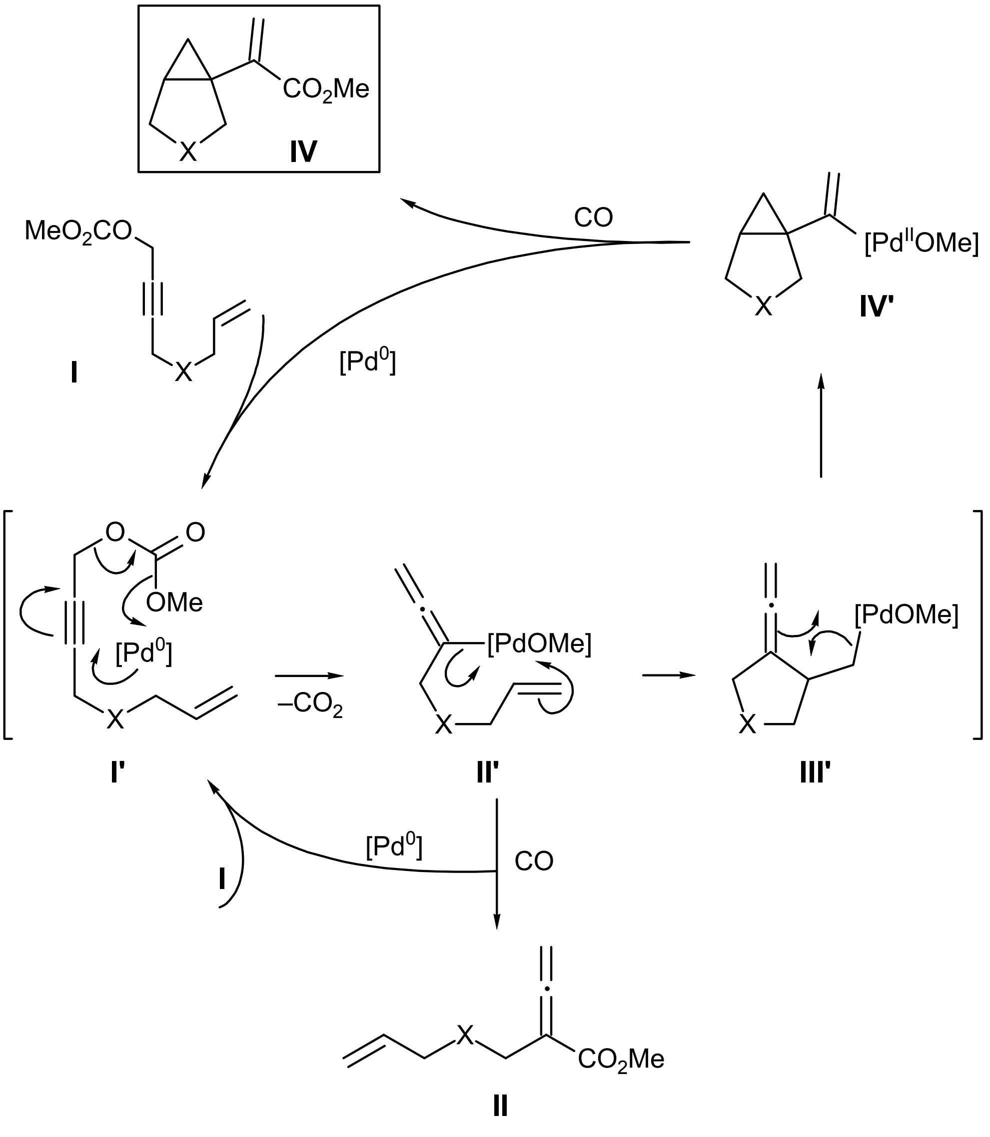


196 **197**

After the successful formation of desired product **197** had been evidenced, attempts to involve bicyclic vinyl palladium species into carbonylation process were undertaken. Preliminary GRIGG's[114] original protocol for methoxycarbonylative trapping of [3.1.0]bicyclohexyl palladium unit had been tested to produce only a complex mixture of unidentified products along with the starting material. In general, after the various reaction conditions were screened, it was concluded (besides, almost in the all cases target acrylate was found, but in a very low yield; <20% according to ^{1}H NMR spectra of reaction mixture), that the yield of a cyclized product was reduced at increased temperature and pressure. Increased temperature decreased "life-time" of the catalytic Pd-species, resulting in fast formation of the "Pd-black" as β-elimination product. An increased pressure gives rise a simple non-cyclized allenic methoxycarbonylation product, that was previously reported by TSUJI[117] (Scheme 69, cycle **I→II'→II**). Later it was also found that introduction of hard basic or nucleophilic groups into substrate (in the first approximation, it may be connected with the quantity of heteroatoms, namely oxygen atoms, in substrate, and their steric accessibility to be coordinated with Pd) significantly decreased the yield of bicyclic product and required an increased catalyst loading.

From these preliminary considerations is clear that only the nature of the catalytic species and its concentration had to be chosen as variable parameters for the process optimization. Thus, methylcarbonate leaving group had been already shown[116, 117] is actually the best one (it has the highest lability, that means lowest activation parameters for the oxidative addition of [Pd^0] to the substrate; step **I'→II'**). It is also obvious that characterized with clearly negative ΔS double cyclization process should be therefore conducted at the lowest possible temperature and CO pressure to avoid the by-product **II** formation (Scheme 69).

Scheme 69



X = CH$_2$, O, C(CO$_2$Et), C(CO$_2$Me)$_2$

Thus, the further investigations were switched over to search an appropriate ligand. It was found that only tri-(2-furyl)phosphine used by OPPOLZER for the same purposes,[115] provided almost 100% conversion of **196** towards the cyclized product **130**. Less expensive substituted phosphine (PPh$_3$, P(*o*-tolyl)$_3$, P[2,6-di-(MeO)$_2$Ph]$_3$) along with the HERMANN's catalyst[118] turned to be inefficient because of immediate "Pd-black" formation.

Some attempts were also undertaken to avoid the usage Pd$_2$(dba)$_3$. Its clear drawbacks are air sensitivity, high price, and occurrence of dibenzalacetone in the reaction mixture that sometimes complicated target product isolation. Taking in consideration a fact that a required Pd^0 catalytic specie might be generated from the precatalyst (cheap and air stable Pd(OAc)$_2$ would be most advantageous) and three equivalents of phosphine ligand (1 eq. promoted reduction of Pd^{II} to Pd^{0}, the another two are consumed to complexate with Pd^{0}),[119] it was decided to search for some promoting substance, which would reduce the $Pd(OAc)_2$ in the presence of 2 eq. of the $P(2\text{-furyl})_3$ giving "$Pd[P(2\text{-furyl})_3]_2$" stable for a longer time under reaction conditions. Thus, trimethyl phosphite was found to be an efficient Pd^{II}-reducing and, at the same time, catalyst supporting dopand, which enabled the required cascade cyclization of unsubstituted 1,6-enynes **I** (X = CH_2, O) towards the respective methyl 2-(bicyclo[3.1.0]hex-1-yl)acrylates **IV** (Scheme 69). 5,5-EWG disubstituted precursors were found to be unreactive towards the titled catalytic system (CSA), and only an unchanged starting material was recovered after continuous stirring under standard reaction conditions. Nevertheless, a combination of $P(2\text{-furyl})_3$ with tetramethyl ammonium bromide (CSB) was found to be useful to afford the corresponding *gem*-3,3-disubstitutes bicyclo[3.1.0]hex-1-yl acrylate (X = $C(CO_2Et)_2$) in high yield with a complete conversion of the starting material. This outcome is essential for preparative synthesis of the pure product, because all the participants of presented cyclization (starting material, by-products and product) have the very close to each other R_f-values.

In general, it should also be noted that any bulky species, being able for coordination bonding with the Pd^{0}-catalytic species, would decrease the yield of cyclization product (Scheme 69, steps **II'→III'→IV'→IV**) due to sterical reasons. Thus, in addition to negative influence of increased basic and nucleophilic substrate hardness onto yield of **IV** noted in the following range X = $CH_2 > O \gg C(CO_2Et)_2 > C(CO_2Me)_2$ (from left to right yield is decreased, reaction time is increased and Lewis base strength of the substrate is increased), it was found that, in spite of clearly higher reaction rate, a significant amount (up to 15%) of allene **II** was detected in the reaction mixture, after the unsubstituted 1,6-enyne was allowed to react in the presence of CSB. Moreover, a slightly increased yield of allene **II** (X = CH_2, O) was also noted, when more bulky cetyltrimethylammonium bromide was used as an activator instead of the tetramethylammonium bromide.

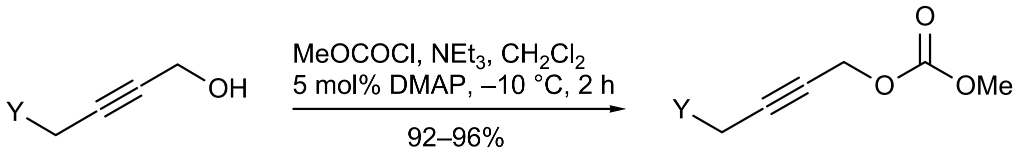
6.4.3. Preparative development

The successful development of the catalytic system based on $Pd(AcO)_2$ and $P(2\text{-furyl})_3$ in the presence of some activating dopand instead of the combination of $P(2\text{-furyl})_3$ /$Pd(dba)_2$ used by OPPOLZER,[115] had become an ultimative goal towards the preparative realization of the 1,6-enyne cyclization. After that, only a viable preparative access to the corresponding precursors had to be developed.

6.4.3.1. Syntheses of the starting 1,6-enynes

The syntheses of the starting propargylic alcohols **198-200** are well documented in the literature. Thus, the dianion obtained after deprotonation of propargylic alcohol with lithium amide, was alkylated with commercially available 5-bromopentene according to PAGE et al.[120] to give the unsaturated alcohol **198** in good yield (80%). Alkylation of 2-butyn-1,4-diol with allyl bromide in the presence of excess NaH according to a modified protocol by LEWIS et al.[121] gave the corresponding enyne alcohol **199** (55% yield). 4-Chlorobut-2-yn-1-ol (**200**) was prepared on a multigram scale according to BAILEY and FUJIWARA[122] in moderate yield (55%).

Scheme 70



198-200

196, 201, 202

Table 18. O-Methoxycarbonylation of the substituted propargylic alcohols **198-200**.

Entry	Alcohol	Y	Product	Yield, %
1	**198**	$CH_2=CH(CH_2)_2$	**196**	94
2	**199**	$CH_2=CHCH_2O$	**201**	92
3	**200**	Cl	**202**	98

The obtained alcohols **198-200** were smoothly converted into the respective carbonates in almost quantitative yields according to the original protocol (GP 12) (Scheme 70, Table 18).

Alkylation of dimethyl (**203**) and diethyl (**204**) allylmalonate with 4-chloro-2-butynyl methyl carbonate (**202**) afforded the corresponding enynes **205** and **206** in moderate yields (Scheme 71, Table 19). As can be seen in Table 19, the use of a more polar solvent (DMF) furnished a better yield of the target product, despite some complication of the work-up procedure.

Scheme 71

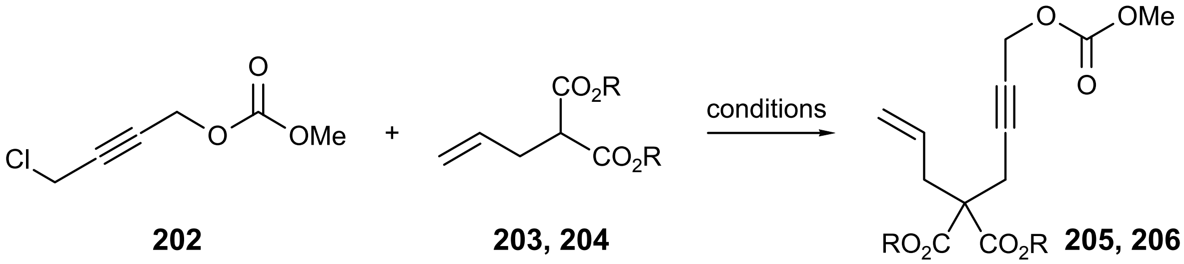


Table 19. Alkylation of allylmalonic acid esters with substituted propargyl chloride **202**.

Entry	Ester	R	Conditions	Product	Yield, %
1	**203**	Me	NaH, THF, 25 °C, 24 h	**205**	40
2	**204**	Et	NaH, DMF, 25 °C, 24 h	**206**	55

6.4.3.2. Protocol for 5-*exo-trig*/3-*exo-trig* cascade cyclizations of various 1,6-enynes

The enynes **196**, **201**, **205**, **206** synthesized on a multigram scale, were smoothly transformed into the corresponding 2-bicyclo[3.1.0]hex-1-ylacrylates **130**, **207-209** in good to high yields by continuous stirring in the presence of 2–5 mol% of the Pd catalytic system under 1 bar of carbon monoxide at an initial catalyst concentration of 4 mmol/L.

As can be seen in Table 20, the highest yield and the shortest reaction time was achieved for compound **130** (no oxygen atoms attached to the cycle formed), whereas the highest loading volume of the catalyst and longest conversion time was required for compound **208** (the strongest Lewis base, which is less sterically congested). It should also be noted that activation of Pd with tetramethylammonium bromide provided a more reactive, but less selective catalytic species. Thus, after **196** had been stirred under 1 bar of CO in the presence of 2 mol% CSB (Exp. Part), 100% conversion of the precursor to the products was achieved after only 1 h, but a significant amount of the allenic derivative **210** (compound **II** Scheme 69, Y = CH_2) was formed (~12%, GC, it displays a characteristic triplet of the allenic protons at ~5.1 ppm). A similar situation was observed when **201** had been allowed to react in the presence of CSB.

Scheme 72

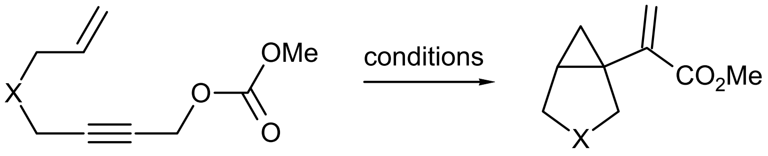
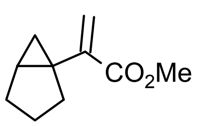
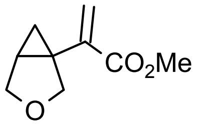
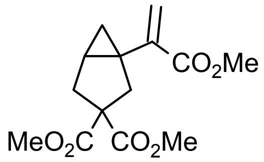
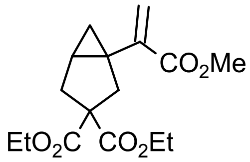


Table 20. Yields and reaction conditions for enyne cyclizations.

Entry	Enyne	X	Product		Conditions[a]	Yield, %, (purity)
1	**196**	CH_2		**130**	A, 2 mol % Pd^0,16 h	94 (98)
2	**201**	O		**207**	A, 2 mol % Pd^0,48 h	87 (98)
3	**205**	$C(CO_2Me)_2$		**208**	B, 5 mol % Pd^0, 68 h	63 (96)
4	**206**	$C(CO_2Et)_2$		**209**	B, 4.5 mol % Pd^0, 50 h	86 (98)

[a] A: 1 eq. $Pd(OAc)_2$, 2.2 eq. $P(2\text{-fur})_3$, 2.5 eq. mol % $P(OMe)_3$, 25 °C, 1 bar CO, $[Pd^0]$ = 4 mmol/L. B: as A, but instead of $P(OMe)_3$ 1.1 eq. of Me_4NBr had been used.

Thus, a highly efficient preparative protocol for a 5-*exo-trig*/3-*exo-trig* cascade cyclization of various 1,6-enynes involving a new catalytic system with the lowest loading volume among the published ones has been developed. Application of this method led to the synthesis of **130** as well as its structural analogues, which were inaccessible by other synthesis routes, in high yields.

C. EXPERIMENTAL PART

1. General Notes

The synthesized compounds were characterized by the following conditions and instruments. Melting points (uncorrected) were measured on a Dr. Tottoli device (Büchi®). – IR: Bruker IFS 66. – ^{1}H NMR: Bruker AM 250 (250 MHz), Varian Unity 300 (300 MHz), Varian Inova 600 (600 MHz); δ (ppm) = 0 for tetramethylsylane, 2.49 for dimethylsulfoxide-*d*$_6$, 7.16 for benzene-*d*$_6$ and 7.26 for chloroform-*d*$_1$. The signals were characterized: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept = septet, dd = doublet of doublets, dt = doublet of triplets, tt = triplet of triplets, m = multiplet. – ^{13}C NMR: Mercury 200 (50.3 MHz), Bruker AM 250 (62.9 MHz); δ (ppm) = 0 for tetramethylsylane, 39.5 for dimethylsulfoxide-*d*$_6$, 77.0 for chloroform-*d*$_1$, 128.0 for benzene-*d*$_6$. The characterization was performed with the help of APT (Attached Proton Test), where + = primary or tertiary (positive APT signal), – = secondary or quaternary carbon atom (negative APT signal); DEPT (Distortionless Enhancement by Polarization Transfer), where + = primary or tertiary (positive DEPT signal), – = secondary (negative DEPT signal), C_{quat} = quaternary carbon atom (zero DEPT signal). – MS: Finnigan MAT 95. – HRMS (High Resolution MS): Finnigan MAT 95. – Elemental analysis: LECO CHN-2000. – Gas chromatography (GC): Varian CP-3800; capillary columns CP-Sil 8 CB (30 m) and CP Sil 5 CB (50 m) were used. – Thin layer chromatography (TLC): Macherey-Nagel Alugram® SIL G/UV$_{254}$ 0.25 mm silica with fluorescent indicator. – Developer: molybdenum phosphoric acid solution (5% in ethanol) or potassium permanganate solution (saturated aqueous solution). – Column chromatography: Merck Silica gel 60 (0.063–0.200 mm, 70–230 mesh ASTM); the quantity was characterized as volume (mL). Flash chromatography: Merck Silica gel 60 (0.040–0.063 mm, 230–400 mesh ASTM); “dry column” technique[123] was applied. The column dimensions were characterized as “diameter of a column × height of the silica gel layer” (∅ mm × mm). Solvents were dried and purified according to conventional methods of the laboratory if necessary.

2. Synthetic Procedures and Spectral Data of the Synthesized Compounds.

The following compounds were synthesized according to the literature: dimethyl isopropylidenemalonate,[19] diethyl isopropylidenemalonate,[124] diethyl 2-methylene-1,1-cyclopropanedicarboxylate,[18] 4-(methoxycarbonyl)benzoyl chloride,[125] (*Z*)-1,4-dibromobut-2-ene,[26] methylenecyclopropane,[49] bicyclopropylidene,[50] 3,3-dimethoxyprop-1-ene,[126] 1,3-dibromo-2,2-dimethylpropane,[127] 3-bromo-1,1-dimethylcyclobutane,[90] 1-(tetrahydropyran-2'-yl)oxymethyl-2-metylenecyclopropane,[47, 48] (*E*)-2-(methoxycarbonyl)cyclopropylmethanol,[61] 1-(ethoxycarbonyl)cyclopropanecarboxylic acid,[58] dimethyl bicyclo[3.1.0]hexane-6,6-dicarboxylate,[57] 1-pyrrolidinoisobutene,[43] methyl 3,3-dimethyl-2-(pyrrolidin-1-yl)-cyclobutanecarboxylate,[44] cyclopent-1-enecarbaldehyde,[40] cyclohex-1-enecarbaldehyde,[41] diethyl 2-formylcyclopropane-1,1-dicarboxylate,[63] potassium cyclopropyloxoacetate,[82] methyl and ethyl diazopyruvate,[21] ethyl (2-ethenylcyclopropyl)oxoacetate and ethyl 2-(2-ethenylcyclopropyl)propenoate,[20] methyl 3-(cyclopropyl)prop-2-ynoate,[95] methyl 3-oxohept-6-eno-ate,[96] methyl 2-diazo-3-oxohept-6-enoate,[97] 1-acetylcyclopentene,[106] (bicyclo[3.1.0]hex-1-yl)-ethanone,[107] benzenesulfonylhydrazide and 1,3,5-triisopropylphenylsulfonylhydrazide,[128] (1*S*)-*endo*-(−)-bornyl chloroformate,[129] dimethyl 2-(cyclopentylidene)malonate,[109] ethyl cyano(cyclopentylidene)acetate,[112] 4-chlorobut-2-yn-1-ol[122] and oct-7-en-2-yn-1-ol.[120] The 1,4-di-[4-(6-hydroxyhexyloxy)phenylcarbonyloxy]-2-methylbenzene was provided from Chisso Petrochemical Corporation, Ichihara, Japan.

2.1. General Procedures.

General procedure for partial hydrolysis of diesters with lithium hydroxide (GP 1). To a vigorously stirred solution of the respective diester (100 mmol) in anhydrous THF (400 mL) was added dropwise at ambient temperature a solution of $LiOH\cdot H_2O$ (4.2 g, 100 mmol) in anhydrous methanol (100 mL) within 30 min, and the mixture was stirred for an additional 24 h. Then the solvents were completely evaporated under reduced pressure (T_{bath} 40 °C), the residue was dissolved in a minimal amount of water (50–100 mL) and extracted with ether (2 × 50 mL). The aqueous phase was acidified with 12 N HCl to pH=1 (8–9 mL), saturated with NaCl and extracted with ether (5 × 100 mL). The combined extracts were dried over Na_2SO_4, and the solvents evaporated under reduced pressure to give a crude product, which was purified by distillation under reduced pressure or recrystallized from an appropriate solvent.

General procedure for the formylation of lithiated methylenecyclopropanes with dimethylformamide (GP 2). To –78 °C (dry ice-acetone bath) cold anhydrous THF (100 mL), kept under nitrogen were added with stirring *n*BuLi (40 mL of 2.45 N solution in hexanes, 98 mmol) and corresponding methylenecyclopropane (100 mmol). The cooling bath was removed, the reaction mixture was warmed to 0 °C, stirred at this temperature for 1 h and cooled to −78 °C again. Then anhydrous DMF (8 mL, 103 mmol) was gradually added with vigorous stirring at such a rate to keep the internal temperature of the mixture under –70 °C. After the addition was complete, the cooling bath was removed and the reaction mixture was worked up in different ways depending on the nature of product.

General procedure for the aldehyde synthesis by SWERN oxidation of primary alcohols (GP 3). To a vigorously stirred solution of oxalyl chloride (18 mL, 210 mmol) in anhydrous CH_2Cl_2 (350 mL) chilled at –78 °C (dry ice/acetone bath) under nitrogen, was added a solution of anhydrous DMSO (32 mL, 450 mmol) in CH_2Cl_2 (16 mL) at such a rate that the temperature of the reaction mixture did not exceed –70 °C (about 30 min). After the mixture was stirred at –70 °C for an additional 30 min, a solution of the respective alcohol (174 mmol) was added in one portion by vigorous stirring keeping the temperature of the reaction mixture under −70 °C. The mixture was stirred at this temperature for an additional 30 min and anhydrous triethylamine (121 mL, 870 mmol) was gradually added at −60 °C. After the addition was complete, the cooling bath was removed and the stirred mixture was allowed to reach room temperature. Then water (100 mL) was added and the mixture was acidified with 12 N aqueous HCl (75 mL) at 0 °C (ice/salt bath). The organic layer was separated and the aqueous phase was extracted with diethyl ether (3 × 150 mL). Combined organic layers were washed with water (100 mL), brine (2 × 100 mL) and dried over $MgSO_4$. Evaporation of the solvents and purification of crude product was conducted depending on the product nature.

General procedure for the two-step synthesis of aldehydes from carboxylic acids by ROSENMUND reduction of acid chlorides (GP 4). To a stirred solution of the respective carboxylic acid (100 mmol) in anhydrous CH_2Cl_2 (50 mL), anhydrous DMF (0.05 mL) and oxalyl chloride (15.2 g, 10.3 mL, 120 mmol) were added at ambient temperature, and the mixture was stirred until the gas evolution had ceased (1–2 h). Then the solvent was evaporated under reduced pressure (15–20 Torr) without heating until the temperature of the reaction flask had reached about 20 °C, anhydrous benzene (50 mL) was added to the residue and evaporation was repeated under the same conditions. The resulting crude acid chloride was added under hydrogen to a suspension of 10% Pd/C (1.5 g, 1.4 mmol) in anhydrous degassed THF (500 mL) containing freshly distilled 2,6-lutidine (10.7 g, 11.6 mL, 100 mmol). The mixture was stirred at ambient temperature until the hydrogen absorption had been ceased (2–12 h), then the solvent was evaporated under reduced pressure at ambient temperature. The residue was triturated with anhydrous ether (100 mL), the solution diluted with pentane (200 mL) under stirring, filtered through Celite® which was subsequently washed with a 2:1 mixture of ether and pentane (2 × 50 mL). The filtrate was evaporated under reduced pressure at ambient temperature to give the crude aldehyde, which was purified by distillation under reduced pressure.

General procedure for the two-step synthesis of α-hydroxycarboxylic esters from aldehydes (GP 5). To a stirred suspension of NH_4Cl (13.9 g, 260 mmol) and the respective aldehyde (200 mmol) in 70 mL of a 1:1 mixture of water and diethyl ether was added with cooling (ice-water bath) a solution of NaCN (11.3 g, 230 mmol) in water (25 mL) within 20 min so that the temperature of the mixture was kept at 10 °C. After the addition was complete, the mixture was stirred at this temperature for an additional 20 min. The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (3 × 50 mL). The combined extracts were washed with brine (2 × 50 mL), acidified with a few drops of ortho-phosphoric acid, dried over $MgSO_4$, filtered and evaporated under reduced pressure at ambient temperature to give the crude product, which was converted into alkyl α-hydroxyacetates by two different methods.

Method A. To the crude cyanohydrine were added under nitrogen anhydrous MeOH (16 mL, 400 mmol) and diethyl ether (25 mL). This mixture was added in one portion with stirring into a pre-cooled (–10 °C, ice/salt bath) solution prepared by saturating anhydrous diethyl ether (100 mL) at 0 °C with dry HCl and subsequent dilution with the same solvent (175 mL). The mixture was stirred at 0–2 °C for 18 h, then the solid was filtered off, washed with anhydrous diethyl ether (50 mL) and dried under reduced pressure at ambient temperature to give a slightly gray powder, which was then added with stirring into water (100 mL) kept at 0 °C (ice bath). The mixture was stirred at 0 °C for 30 min and at ambient temperature for 1 h. The aqueous phase was saturated with NaCl and extracted with ethyl acetate (4 × 50 mL). The combined organic layers were washed with brine (50 mL) and dried over $MgSO_4$. The solvent was evaporated, and the residue distilled under reduced pressure, or was used for the next step without additional purification.

Method B. A three-necked pointed-bottom 250-mL flask was equipped with a septum, thermometer and gas inlet tube, which almost reached the bottom of the flask. The outer neck of the inlet tube was fitted with a bubbler charged with paraffin, and this in turn was connected with a $CaCl_2$-drying tube. The reaction flask was immersed in a dry ice/acetone bath, and a slow stream of dry hydrogen chloride was passed through the system. Then a solution of the crude cyanohydrine (200 mmol) in the respective anhydrous alcohol (100 mL) was added by syringe at such a rate to keep the temperature of the reaction mixture under −10 °C (about 30 min, cooling with dry ice/acetone bath). At the same time the stream of HCl was adjusted as to keep the pressure in the reaction flask slightly above ambient (control by bubbler). After the addition of the solution was complete, the mixture was saturated with hydrogen chloride at –20 °C and the cooling bath was removed. After stirring at ambient temperature for an additional 2 h, the mixture was evaporated under reduced pressure at ambient temperature. To the stirred residue was added ice water (100 mL) at 0 °C, and the mixture was stirred at this temperature for an additional 30 min. The ice bath was removed, and the mixture was stirred at ambient temperature for an additional time (1 h or 16 h for *gem*-alkoxycarbonyl substituted cyanohydrines). The organic layer was separated, and the aqueous phase was extracted with ethyl acetate (4 × 50 mL). The combined organic phases were washed with brine (50 mL) and dried over $MgSO_4$. The crude product obtained after evaporation of the solvent was distilled under reduced pressure or used for the next step without further purification.

General procedure for SIMMONS-SMITH cyclopropanation of 2-hydroxy-2-alkenyl acetates adopted from CHARETT's original protocol (GP 6A). To a stirred under nitrogen, –25 °C cold solution of 1,2-dimethoxyethane (46.7 mL, 450 mmol) in anhydrous CH_2Cl_2 (450 mL), diethyl zink (46.1 mL, 450 mmol) was added in one portion. Then methylene iodide (72.6 mL, 900 mmol) was gradually added to this solution with occasional cooling (dry ice/aceton bath) at such a rate that the mixture temperature did not exceed −20 °C (40−60 min). After the addition was complete, the mixture was stirred at −15 °C for additional 15 min, chilled to −25 °C and gradually added via PTFE tube within 30 min into a stirred under nitrogen solution of the respective alkene (150 mmol) in anhydrous CH_2Cl_2 (450 mL), keeping the internal mixture temperature between −14 and −11 °C (ice/salt bath). After the addition was complete, the mixture was stirred at this temperature for additional 2 h and allowed to reach ambient temperature (the cooling bath was not removed) by stirring for 12 h. Then the mixture was cooled to –5 °C (ice/salt bath) and 1 M aqueous H_2SO_4 (300 mL) was gradually added (a first 30 mL – very slowly and carefully, then – faster). After additional stirring for 30 min at ambient temperature organic layer was separated and the aqueous one was extracted with CH_2Cl_2 (3×100 mL). The combined organic phases were washed with 5% aqueous $Na_2S_2O_3$ (200 mL) and dried over $MgSO_4$. The residue obtained after evaporation of the solvents, was distilled under reduced pressure to yield pure product.

General procedure for SIMMONS-SMITH cyclopropanation of 2-hydroxy-2-alkenyl acetates with SHI's carbenoid (GP 6B). To a well stirred solution of $ZnEt_2$ (50 mL, 0.488 mol) in anhydrous CH_2Cl_2 (450 mL) chilled at –15 °C (ice/salt bath), trifluoroacetic acid (36 mL, 0.486 mol) was added within 1 h so that the temperature did not exceed 0 °C. *Caution! Gas evolution! Full size adapters, gas inlets and bubblers with paraffin oil must be used to avoid clogging of holes with the solid particles of the reaction mixture.* After additional stirring at 0 °C for 15 min, CH_2I_2 (40 mL, 0.496 mol) was added all at once, keeping the temperature around 0 °C with occasional cooling (ice/salt bath), and the reaction mixture was vigorously stirred at this temperature until it had become completely homogeneous (25–30 min). To this carbenoid solution the respective alkene (0.24 mol) was added dropwise at 0 °C within 15 min. After stirring at this temperature for additional 30 min, the cooling was removed and the mixture was stirred overnight at ambient temperature. Then the vigorously stirred reaction mixture was cooled to 0 °C (ice/salt bath), and 2 M aqueous H_2SO_4 (250 mL) was gradually added (a first 50 mL – slowly and carefully). The phases were separated and the aqueous layer was extracted with diethyl ether (3 × 200 mL). The combined organic phases were subsequently washed with 2 N NaOH (250 mL), brine (2 × 150 mL) and dried over $MgSO_4$. The residue obtained after evaporation of the solvents, was distilled under reduced pressure or subjected to column chromatography to yield pure product.

General procedure for the oxidation of α-hydroxy esters to α-oxoesters with active manganese dioxide (GP 7). To a well stirred solution of the respective α-hydroxy ester (80 mmol) in anhydrous diethyl ether (500 mL) was added active MnO_2 (Fluka®) (2 × 40 g) in two portions with an interval of 2 h. The suspension was stirred at ambient temperature (1–4 h) until the starting material had been completely consumed (TLC control). The mixture was filtered through Celite®, which was washed with diethyl ether (2 × 150 mL). The solvent was evaporated from the combined filtrates under reduced pressure at ambient temperature to give sufficiently pure (> 95% according to GC) α-oxoester, which could be used without additional purification.

General procedure for the synthesis of alkyl oxoacetates by $Rh_2(OAc)_4$-catalyzed addition of alkyl 3-diazopyruvates to cyclic alkenes (GP 8). To a well stirred solution of $Rh_2(OAc)_4$ (0.14–0.39 mol%) and the respective cycloalkene (200–500 mmol) in anhydrous degassed CH_2Cl_2 (400 mL) was added a solution of the corresponding alkyl 3-diazopyruvate (200 mmol) in the same solvent (400 mL) within 16 h. After the addition was complete, the reaction mixture was evaporated under reduced pressure at ambient temperature. The residue was triturated with pentane (110 mL), passed through a pad (∅65 × 30 mm) of flash silica gel and washed with pentane/diethyl ether, 10:1 (3 × 150 mL). The slightly yellow oil obtained after evaporation of the solvent was purified by column chromatography on silica gel.

General procedure for the WITTIG methylenation of carbonyl compounds adopted from WENKERT's original protocol (GP 9A). To a well stirred solution of LDA (prepared by adding of 2.44 N hexane solution of *n*BuLi (26 mL, 63 mmol) to a −78 °C cold solution of diisopropylamine (9.3 mL, 66 mmol) in 600 mL of anhydrous THF) was added under argon methyltriphenylphosphonium bromide (23.6 g, 63 mmol) at −78 °C, and kept at –40 °C for 2 h. Then the cooling bath was removed, the mixture was stirred for additional 2 h at ambient temperature, cooled to −10 °C (ice-salt bath), and the respective carbonyl compound (60 mmol) dissolved in anhydrous THF (40 mL) was added by vigorous stirring so that the temperature did not exceed −5 °C. Then the mixture was allowed to reach an ambient temperature, stirred for additional 4 h and acidified with 1 M aqueous H_2SO_4 (50 mL). Brine (50 mL) was then added, the organic phase was separated and the aqueous phase was extracted with ether (2 × 200 mL). The combined organic layers were washed with brine (2 × 200 mL) and dried over $MgSO_4$. The residue obtained after evaporation of the solvents was subjected to column chromatography on silica gel.

General procedure for the WITTIG methylenation of α-oxoesters to 2-substituted alkyl acrylates (GP 9B). To a well stirred suspension of methyltriphenylphosphonium bromide (37.5 g, 105 mmol) in anhydrous THF (250 mL), kept at −78 °C (dry ice/acetone bath) under nitrogen, was added diisopropylamine (1.4 mL, 10 mmol), and then a 2.5 M *n*BuLi solution in hexane (40 mL, 100 mmol). After the slight warming of the reaction mixture had ceased, the cooling bath was removed, and the mixture was allowed to warm up to ambient temperature (about 1 h), then cooled to −78 °C again, and a solution of the respective carbonyl compound (100 mmol) in anhydrous THF (20 mL) was added with vigorous stirring so that the temperature did not exceed −50 °C. After stirring for an additional 30 min at this temperature, the cooling bath was removed, the reaction mixture was stirred overnight (12 h) and then acidified with 5% aqueous H_2SO_4 (~10 mL). Brine (50 mL) was then added, the organic phase was separated and the aqueous phase was extracted with ether (2 × 100 mL). The combined organic layers were washed with brine (2 × 100 mL) and dried over $MgSO_4$. BHT (10 mg) was added, and the major part of the solvents was removed at ambient temperature on a rotary evaporator until the volume of the residue was reduced to 50–60 mL. To the stirred liquid residue (a spontaneously solidified residue may be homogenized by adding a minimal amount of warm dichloromethane) pentane (500 mL) was gradually added. The stirring continued at 0 °C until the $OPPh_3$ crystallization was complete, then the solid was filtered off and washed with pentane/ether, 5:1 (2 × 50 mL). The combined filtrates were evaporated under reduced pressure at ambient temperature. In the cases of relatively low-boiling compounds the solvents were distilled off at ambient pressure at a bath temperature under 60 °C, and the remaining solvent was removed under reduced pressure (~10 Torr) at ambient temperature (the evaporation was stopped as soon as the contents of the distillation flask had reached room temperature). The obtained crude product was purified by column chromatography or distilled under reduced pressure.

General procedure for hydrolysis of the 2-substituted alkyl acrylates with lithium hydroxide (GP 10). To a vigorously stirred solution of a respective alkyl acrylate (100 mmol) and BHT (10 mg) in acetone (210 mL) was added dropwise under nitrogen a solution of lithium hydroxide monohydrate (4.62 g, 110 mmol) in water (70 mL). The mixture was stirred at ambient temperature until the starting material had been completely consumed (24–48 h, TLC control). The reaction mixture was then concentrated under reduced pressure ($T_{bath} < 40$ °C) to a volume of ~60 mL and washed with ether (2 × 50 mL). The aqueous layer was separated, mixed with ether (100 mL), cooled to 0 °C and acidified with 12 N HCl (9–10 mL) to pH = 1. The organic phase was separated and the aqueous one was extracted with ether (4 × 50 mL). The combined ethereal layers were washed with brine (2 × 50 mL) and dried over Na_2SO_4. Obtained after evaporation of the solvent under reduced pressure residue was dissolved in CCl_4 (200 mL) and evaporated again to give a target acid, that was pure and dry enough for subsequent esterification according to any of the applied methods. Analytical samples of the synthesized acids were obtained after additional purification of crude product by recrystallization or by column chromatography with subsequent “Kugelrohr” distillation.

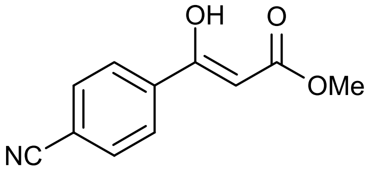
General Procedure for DMAP-catalyzed alcoholysis of 2-(bicyclo[3.1.0]hex-1-yl)acryloyl chloride (GP 11A). To a stirred solution of the respective alcohol (20 mmol), anhydrous triethylamine (20–25 mmol) and DMAP (5–120 mol%, depending on the alcohol nature) in anhydrous CH_2Cl_2 (35 mL), kept at −5 °C (ice/salt bath) under nitrogen, was added solution of acid chloride () (3.41 g, 20 mmol) in the same solvent (5 mL) at such a rate that the temperature of the reaction mixture did not exceed 0 °C (10–30 min). Then, the cooling bath was removed and the mixture was stirred at ambient temperature for additional time (12–48 h). After that, the most of solvent was evaporated under reduced pressure at ambient temperature, the residue was suspended by stirring in pentane (~80 mL) and filtered through a short pad of flash silica gel (~20 mL). The silica gel was rinsed with pentane/ether, 10:1 mixture (40 mL), and the combined filtrates were evaporated under reduced pressure to give crude product, which was purified by flash or column chromatography on silica gel.

General Procedure for MITSUNOBU esterification (GP 11B). To a stirred solution of the respective carboxylic acid (20 mmol), alcohol (20 mmol) and PPh_3 (5.3 g, 20 mmol) in anhydrous THF (50 mL), kept at –78 °C (dry ice-acetone bath) under nitrogen, was added dropwise diethyl azodicarboxylate (3.53 g, 20 mmol) at such a rate that the internal temperature of the mixture did not exceed −70 °C. After stirring for an additional 30 min, the cooling bath was removed, the reaction mixture was allowed to reach ambient temperature, and then the most of solvent was evaporated under reduced pressure at ambient temperature. To the stirred residue pentane (100 mL) was added, stirring was continued for about 1 h, then the suspension was filtered through a pad of flash silica gel (∅65 × 30 mm), that was then washed with pentane/ether, 20:1 mixture (2 × 100 mL). The combined organic filtrates were evaporated under reduced pressure at ambient temperature to give a crude product, which was purified by flash" or column chromatography on silica gel.

General Procedure for methoxycarbonylation of alcohols (GP 12). To a stirred solution of the respective alcohol (100 mmol), NEt_3 (14.6 mL, 105 mmol) and DMAP (0.62 g, 5 mmol) in anhydrous CH_2Cl_2 (100 mL), chilled to –10 °C (ice/salt bath) under nitrogen, methyl chlorocarbonate (9.3 mL, 120 mmol) dissolved in the same solvent (40 mL) was added within 2 h keeping the temperature of the mixture under –10 °C. After stirring at this temperature for additional 30 min, the cooling was removed and the mixture was concentrated under reduced pressure at ambient temperature to ~40 mL. The stirred residue was then diluted with three volumes of pentane and a suspension obtained was filtered through a pad of flash silica gel

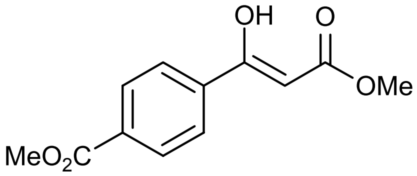
(20 mL), which was rinsed with pentane/CH_2Cl_2, 4:1 mixture (2 × 20 mL). The solvents were evaporated under reduced pressure to give crude product, which was purified by flash chromatography or distilled under reduced pressure.

2.2. *Synthesis of EWG-Disubstituted Vinylcyclopropanes*



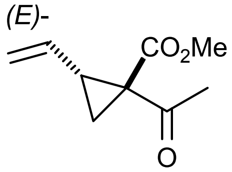
Methyl 3-(4-cyanophenyl)-3-oxyprop-2-enoate (**19**). To a stirred suspension of NaH (9.2 g of 60% dispersion in mineral oil, 230 mmol) in anhydrous DME (40 mL) a solution of methyl *para*-cyanobenzoate (**18**) (22.7 g, 141 mmol) in the same solvent (40 mL) was added all at once and the mixture was heated to reflux. Then, the heating bath was removed and a solution of methyl acetate (11.5 g, 155 mmol) in anhydrous DME (20 mL) was gradually added at such a rate to keep a gentle reflux of reaction mixture (about 2 h; occasional heating sometimes could be necessary until the reaction has got started). After the addition was complete, the mixture was stirred at reflux for additional 1 h, cooled to room temperature and the excess of NaH was decomposed by gradual adding of methanol (~4.5 mL) with occasional cooling (ice water bath). The resulted mixture was poured into water (1000 mL) containing 12 N HCl (20 mL) and stirred for 1 h. The solid material was filtered off, rinsed with water (500 mL), hexane (500 mL) and dried under reduced pressure (0.1 Torr, overnight). Recrystallization of the crude product from methanol (200 mL) gave 24 g (84%) of pure **19** as a yellow plates. – M. p. 95–96 °C. – IR (KBr): ν = 3431 (OH), 3121 (OH), 3051, 3001, 2952, 2225 (CN), 1653 (C=O), 1625 (C=C), 1561, 1508, 1441, 1381, 1347, 1290, 1268, 1223, 1119, 1082, 1009, 943, 854, 811, 785, 742 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 3.82 (s, 3 H, OCH_3), 5.72 (s, 1 H), 7.68–7.73 (m, AA', 2 H, Ar-$H_{2,6}$), 7.84–7.89 (m, BB', 2 H, Ar-$H_{3,5}$), 12.48 (s, 1 H, OH). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 51.8 (+, OCH_3), 89.3 (+, CH), 114.5, 118.2 (C_{quat}, CN, Ar-C), 126.5 (+, Ar-C), 132.3 (+,Ar-C), 137.4 (C_{quat}, Ar-C), 168.7 (C_{quat}, 3-C), 173.0 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 203 (26) [M^+], 172 (8) [$M^+ - CH_3O$], 171 (12) [$M^+ - CH_3OH$], 130 (100) [$M^+ - CH_2CO_2CH_3$], 102 (19) [$M^+ - CH_2CO_2CH_3 - CO$], 89 (2), 69 (6), 51 (2). – Anal. Calculated for $C_{11}H_9NO_3$ (203.20): C 65.02, H 4.46, N 6.89. Found: C 64.97, H 4.70, N 6.95.

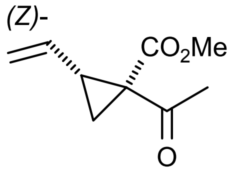
Methyl 3-(4-methoxycarbonylphenyl)-3-oxyprop-2-enoate (**21**). To a stirred solution of LDA



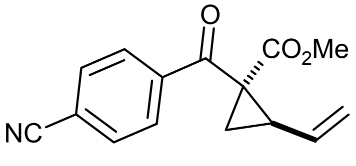
(prepared from 167 mL of 2.4 N solution of *n*BuLi in hexanes, 0.4 mol) and freshly distilled diisopropylamine (40.5 g, 56.3 mL, 0.4 mol) in 350 mL of anhydrous THF) chilled to –78 °C, methyl acetate (29.6 g, 0.4 mol) was gradually added at such a rate to keep the internal temperature under –70 °C (about 30 min). The mixture was stirred at this temperature for an additional 1 h and then, a solution of **20** (39.7 g, 0.2 mol) in anhydrous THF (200 mL) was gradually added within 4 h so that the mixture temperature did not exceed –70 °C. After the addition has been complete, a solution of glacial acetic acid (12 g) in ether (20 mL) was gradually added and the mixture was allowed to warm to 20 °C. Then the reaction mixture was poured into –10 °C cold 4 M aqueous HCl (200 mL), organic layer was separated and the aqueous phase was extracted with ether (3 × 100 mL). The combined organic layers were washed with brine (2 × 100 mL) and dried over $MgSO_4$. Obtained after evaporation of the solvents under reduced pressure residue was recrystallized from methanol to give 19 g (40%) of pure **21** as a colorless powder. – M. p. 81.0–81.5 °C. – IR (KBr): ν = 3434 (OH), 3039, 3013, 2958, 2839, 1725 (C=O), 1646 (C=O), 1624 (C=C), 1602, 1569, 1509, 1443, 1432, 1413, 1393, 1312, 1284, 1262, 1207, 1179, 1108, 1070, 1009, 960, 943, 867, 845, 801, 773, 724, 702 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 3.80 (s, 3 H, OCH_3), 3.93 (s, 3 H, OCH_3), 5.72 (s, 1 H), 7.80–7.84 (m, AA', 2 H, Ar-$H_{2,6}$), 8.04–8.08 (m, BB', 2 H, Ar-$H_{3,5}$), 12.45 (s, 1 H, OH). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 51.6, 52.3 (+, OCH_3), 88.6 (+, CH), 126.0 (+, Ar-C), 129.7 (+, Ar-C), 132.3, 137.3 (C_{quat}, Ar-C), 166.3 (C_{quat}, CO_2Me), 169.9 (C_{quat}, 3-C), 173.2 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 236 (23) [M^+], 205 (8) [$M^+ - CH_3O$], 204 (6) [$M^+ - CH_3OH$], 173 (5) [$M^+ - CH_3OH - CH_3O$], 163 (100) [$M^+ - CH_2CO_2CH_3$], 135 (10) [$M^+ - CH_2CO_2CH_3 - CO$], 120 (2), 103 (7), 89 (2), 76 (5), 50 (3). – Anal. Calculated for $C_{12}H_{12}O_5$ (236.22): C 61.01, H 5.12. Found: C 60.77, H 5.26.

(E/Z)-Methyl 1-acetyl-2-vinylcyclopropanecarboxylate (**23**) was prepared by alkylation of methyl acetoacetate (11.8 mL, 109 mmol) with 1,4-dibromobut-2-ene (26.9 g, 126 mmol) according to the previously reported procedure.[27] Rectification of the crude mixture under reduced pressure gave 15.4 g (84% yield, *E/Z*-ratio is 2:1 according to GC) of **23** contaminated with approximately 10% of some by-product. Column chromatography of this crude mixture on 1 L of silica gel, eluting with hexane/*t*BuOMe, 10:1, yielded 13.1 g (71%) (> 96% purity according to GC) of pure **23** as a *E/Z*, 2:1 isomeric mixture. A small amount of the both sufficiently pure isomers of **23** were isolated by column chromatography of an aliquot of the isomeric mixture (0.5 g) on 100 g of silica gel under the same conditions as above. – *(E)-***23** *(major isomer)*. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.53 (dd, ^3J = 8.9 Hz, ^2J = 4.5 Hz, 1 H, 3-H$_{cis}$), 1.84 (dd, ^3J = 7.5 Hz, ^2J = 4.5 Hz, 1 H, 3-H$_{trans}$), 2.30 (s, 3 H, CH$_3$), 2.62 (ddd, ^3J = 8.9 Hz, ^3J = 7.6 Hz, ^3J = 7.5 Hz, 1 H, 2-H), 3.73 (s, 3 H, OCH$_3$), 5.08–5.29 (m, ABC-system, 3 H, CH=CH$_2$). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 20.1 (–, C-3), 30.5 (+, C-2), 33.6 (+, CH$_3$), 42.4 (C$_{\text{quat}}$, C-1), 52.4 (+, OCH$_3$), 119.0 (–, C-2'), 132.6 (+, C-1'), 170.8 (C$_{\text{quat}}$, CO$_2$Me), 200.9 (C$_{\text{quat}}$, C=O). – *(Z)-***23** *(minor isomer)*. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.58 (dd, ^3J = 8.8 Hz, ^2J = 4.5 Hz, 1 H, 3-H$_{trans}$), 1.75 (dd, ^3J = 7.8 Hz, ^2J = 4.5 Hz, 1 H, 3-H$_{cis}$), 2.37 (s, 3 H, CH$_3$), 2.59 (ddd, ^3J = 8.8 Hz, ^3J = 7.8 Hz, ^3J = 7.8 Hz, 1 H, 2-H), 3.76 (s, 3 H, OCH$_3$), 5.13 (dd, ^3J = 10 Hz, ^2J = 1.8 Hz, 1 H, 2'-H$_{trans}$), 5.28 (dd, ^3J = 17 Hz, ^2J = 1.8 Hz, 1 H, 2'-H$_{cis}$), 5.41–5.55 (ddd, ^3J = 17 Hz, ^3J = 10 Hz, ^3J = 7.8 Hz, 1 H, 1'-H). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 23.2 (–, C-3), 29.5 (+, C-2), 34.5 (+, CH$_3$), 43.1 (C$_{\text{quat}}$, C-1), 52.3 (+, OCH$_3$), 118.9 (–, C-2'), 133.0 (+, C-1'), 169.3 (C$_{\text{quat}}$, CO$_2$Me), 201.9 (C$_{\text{quat}}$, C=O).



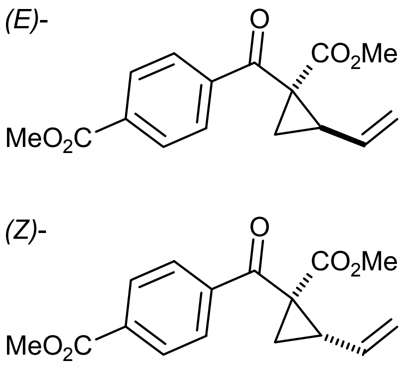


(E)-Methyl 1-(4-cyanophenyl)carbonyl-2-vinylcyclopropanecarboxylate (**24**). To a vigorously stirred suspension of finely powdered and flame-dried K$_2$CO$_3$ (41.5 g, 300 mmol) in 200 mL of a 1:1 mixture of anhydrous THF and methanol were subsequently added **19** (23.6 g, 116 mmol) and 1,4-dibromobut-2-ene (26.5 g, 124 mmol) at ambient temperature. The mixture was stirred at 25 °C for 76 h and then completely evaporated under reduced pressure. The residue was suspended in CH$_2$Cl$_2$ (250 mL), filtered through a pad of Celite® and the solvent was removed under reduced pressure to give about 30 g of slightly yellow oil. This one was dissolved in 2-propanol (100 mL), diluted with hexane (300 mL) and allowed to crystallize at ambient temperature. It gave 10.7 g (42%) of



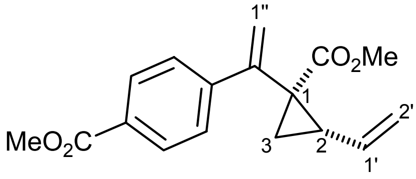
24 as a colorless prisms. – M. p. 101–102 °C. – IR (KBr): ν = 3083, 3017, 2959, 2853, 2231 (CN), 1721 (C=O), 1680 (C=O), 1634 (C=C), 1603, 1563, 1440, 1402, 1338, 1319, 1300, 1269, 1209, 1156, 1110, 1079, 1056, 1009, 982,930, 851, 831,749, 724, 703 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.70 (dd, ^3J = 9 Hz, ^2J = 5 Hz, 1 H, 3-H_{cis}), 1.98 (dd, ^3J = 7.5 Hz, ^2J = 5 Hz, 1 H, 3-H_{trans}), 2.94 (ddd, ^3J = 9 Hz, ^3J = 8.5 Hz, ^3J = 7.5 Hz, 1 H, 2-H), 3.56 (s, 3 H, OCH_3), 5.03 (dd, ^3J = 10 Hz, ^2J = 2.2 Hz, 1 H, 2'-H_{trans}), 5.13 (ddd, ^3J = 15.5 Hz, ^3J = 10 Hz, ^3J = 8.5 Hz, 1 H, 1'-H), 5.35 (dd, ^3J = 15.5 Hz, ^2J = 2.2 Hz, 1 H, 2'-H_{cis}), 7.71–7.76 (m, AA', 2 H, Ar-$H_{2,6}$), 7.85–7.90 (m, BB', 2 H, Ar-$H_{3,5}$). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.9 (–, C-3), 33.6 (+, C-2), 39.6 (C_{quat}, C-1), 52.7 (+, OCH_3), 116.1, 117.9 (C_{quat}, CN, Ar-C), 119.5 (–, C-2'), 128.8, 132.4, (+, Ar-C), 132.5 (+, C-1'), 140.6 (C_{quat}, Ar-C), 170.8 (C_{quat}, CO_2Me), 192.4 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 255 (15) [M^+], 224 (5) [M^+ – CH_3O], 223 (6) [M^+ – CH_3OH], 222 (9), 196 (4) [M^+ – CO_2CH_3], 195 (9) [M^+ – CO – CH_3OH], 167 (3), 140 (2), 130 (100), 125 (12), 105 (3), 102 (35), 93 (4), 71 (4), 41 (1). – Anal. Calculated for $C_{15}H_{13}NO_3$ (255.28): C 70.58, H 5.13, N 5.49. Found: C 70.35, H 5.35, N 5.32.

(E/Z)-Methyl 1-(4-methoxycarbonylphenyl)carbonyl-2-vinylcyclopropanecarboxylate (**25**). A mixture of **21** (5.75 g, 24 mmol), 1,4-dibromobut-2-ene (5.77 g, 27 mmol) and K_2CO_3 (8.75 g, 63 mmol) suspended in 40 mL of 1:1 mixture of anhydrous tetrahydrofurane and methanol were vigorously stirred at ambient temperature for 76 h. The solvents were evaporated under reduced pressure to give a residue, which was then triturated with ether (200 mL). This suspension was filtered through Celite®, washed with water (50 mL), brine (100 mL) and dried over $MgSO_4$. The residue obtained after evaporation of the solvents under reduced pressure (6.5 g) was dissolved in methanol (150 mL) and chilled at –20 °C. After the dimethylterephtalate (0.8 g) was filtered off, the filtrate was evaporated under reduced pressure. It gave 5.7 g of a slightly yellow oil that was a diastereomeric mixture of **25** (*E/Z*~5:1), contaminated with some unidentified by-products (about 20%) according to ^1H NMR data. A small amount of *(Z)*-**25** was crystallized off from the crude mixture and fully characterized. – *(E)*-**25** *(major isomer)*. – Colorless oil. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.65 (dd, ^3J = 9 Hz, ^2J = 4.8 Hz, 1 H, 3-H_{cis}), 1.96 (dd, ^3J = 7.3 Hz, ^2J = 4.8 Hz, 1 H, 3-H_{trans}), 2.93 (ddd, ^3J = 9 Hz, ^3J = 8.5 Hz, ^3J = 7.3 Hz, 1 H, 2-H), 3.53 (s, 3 H, OCH_3), 3.92 (s, 3 H,



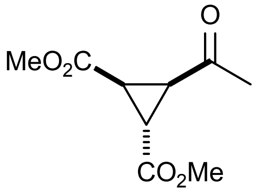
OCH_3), 4.99 (dd, ^3J = 10 Hz, ^2J = 1.8 Hz, 1 H, 2'-H_{trans}), 5.14 (ddd, ^3J = 16.5 Hz, ^3J = 10 Hz, ^3J = 8.5 Hz, 1 H, 1'-H), 5.59 (dd, ^3J = 16.5 Hz, ^2J = 1.8 Hz, 1 H, 2'-H_{cis}), 7.82–7.87 (m, AA', 2 H, Ar-$H_{2,6}$), 8.06–8.11 (m, BB', 2 H, Ar-$H_{3,5}$). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.8 (–, C-3), 33.3 (+, C-2), 39.7 (C_{quat}, C-1), 52.4, 52.6 (+, OCH_3), 119.1 (–, C-2'), 128.4, 129.7 (+, Ar-C), 132.7 (+, C-1'), 133.6, 140.7 (C_{quat}, Ar-C), 166.2, 171.1 (C_{quat}, CO_2Me), 193.0 (C_{quat}, C=O). – *(Z)-***25** *(minor isomer)*. – Colorless prisms, m. p. 117–118 °C. – IR (KBr): ν = 3089, 3039, 3001, 2954, 2842, 1740 (C=O), 1718 (C=O), 1683 (C=O), 1632 (C=C), 1573, 1502, 1436, 1406, 1314, 1289, 1267, 1212, 1195, 1145, 1113, 1061, 1009, 982, 926, 889, 870, 824, 781, 719 cm^{-1}. – ^1H NMR (600 MHz, $CDCl_3$): δ = 1.70 (dd, ^3J = 9 Hz, ^2J = 4.8 Hz, 1 H, 3-H_{trans}), 1.96 (dd, ^3J = 7.8 Hz, ^2J = 4.8 Hz, 1 H, 3-H_{cis}), 2.72 (ddd, ^3J = 9 Hz, ^3J = 8.8 Hz, ^3J = 7.8 Hz, 1 H, 2-H), 3.51 (s, 3 H, OCH_3), 3.94 (s, 3 H, OCH_3), 5.22 (dd, ^3J = 10 Hz, ^2J = 1.5 Hz, 1 H, 2'-H_{trans}), 5.39 (dd, ^3J = 17 Hz, ^2J = 1.5 Hz, 1 H, 2'-H_{cis}), 5.77 (ddd, ^3J = 17 Hz, ^3J = 10 Hz, ^3J = 8.8 Hz, 1 H, 1'-H), 7.86–7.91 (AA', 2 H, Ar-$H_{2,6}$), 8.08–8.12 (BB', 2 H, Ar-$H_{3,5}$). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 22.0 (–, C-3), 31.1 (+, C-2), 40.6 (C_{quat}, C-2), 52.5 (+, 2OCH_3), 119.2 (–, C-2'), 128.0, 129.7 (+, Ar-C), 132.7 (+, C-1'), 133.6, 140.5 (C_{quat}, Ar-C), 166.1, 169.5 (C_{quat}, CO_2Me), 193.8 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 288 (10) [M^+], 257 (10) [$M^+ - CH_3O$], 197 (8), 163 (100), 135 (14), 125 (11), 103 (6), 93 (3), 71 (3), 57 (18), 43 (4). – Anal. Calculated for $C_{16}H_{16}O_5$ (288.30): C 66.66, H 5.59. Found: C 66.60, H 5.74.

(Z)-Methyl 1-[1-(4-methoxycarbonylphenyl)ethen-1-yl]-2-vinylcyclopropanecarboxylate (**26**).

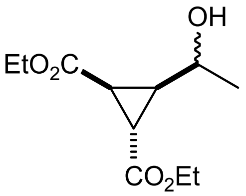


According to GP 9A, methylenation of a crude (*E/Z*)-mixture of **25** (5.76 g, 20 mmol) after column chromatography of the crude product on 500 mL of silica gel, eluting with hexane/*t*BuOMe, 5:1, gave 0.40 g (7%) of pure **26** along with 4.90 g (85% yield) of the enriched with (*E*)-isomer (according to ^1H NMR) starting material **25** was recovered. – Colorless prisms, m. p. 84–85 °C. – IR (KBr): ν = 3091, 3005, 2954, 2903, 2848, 1943, 1866, 1823, 1725 (C=O), 1708 (C=O), 1627 (C=C), 1605 (C=C), 1563, 1507, 1439, 1405, 1371, 1298, 1277, 1247, 1196, 1145, 1110, 1085, 1051, 1012, 955, 965, 948, 931, 905, 880, 863, 833, 786, 748, 726, 688, 649, 628 cm^{-1}. – ^1H NMR (600 MHz, $CDCl_3$): δ = 1.43 (dd, ^3J = 9.1 Hz, ^2J = 5 Hz, 1 H, 3-H_{trans}), 1.91 (dd, ^3J = 7.5 Hz, ^2J = 5 Hz, 1 H, 3-H_{cis}), 2.14 (ddd, ^3J = 9.1 Hz, ^3J = 9.1 Hz, ^3J = 7.5 Hz, 1 H, 2-H), 3.52 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 5.15 (dd, ^3J = 10.3 Hz, ^2J = 1.8 Hz, 1 H, 2'-H_{trans}), 5.30 (dd, ^3J = 17 Hz, ^2J = 1.8 Hz, 1 H, 2'-H_{cis}), 5.38 (s, 1 H, 1''-H_{trans}), 5.77 (s, 1 H, 1''-H_{cis}), 5.91 (ddd,

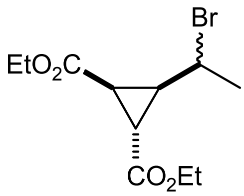
^3J = 17 Hz, ^3J = 10.3 Hz, ^3J = 9.1 Hz, 1 H, 1'-H), 7.52–7.56 (m, AA', 2 H, Ar-$H_{2,6}$), 7.94–7.98 (m, BB', 2 H, Ar-$H_{3,5}$). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 22.5 (–, C-3), 32.9 (+, C-2), 35.8 (C_{quat}, C-1), 51.9, 52.1 (+, OCH_3), 117.0, 117.4 [–, C-2'(1")*], 125.7 (+, Ar-C), 129.0 (C_{quat}), 129.5 (+, C-Ar), 134.6 (+, C-1'), 143.6, 145.3 (C_{quat}, C-Ar), 166.6, 171.7 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 286 (90) [M^+], 271 (9) [$M^+ - CH_3$], 258 (31) [$M^+ - C_2H_4$], 255 (38) [$M^+ - CH_3O$], 239 (6), 227 (100) [$M^+ - CO_2CH_3$], 213 (10), 195 (56) [$M^+ - CO_2CH_3 - CH_3OH$], 183 (12), 167 (82), 152 (25), 149 (16), 145 (15), 133 (14), 128 (21), 115 (21), 102 (10), 91 (24), 77 (12), 71 (18), 59 (43), 51 (7), 41 (14). – Anal. Calculated for $C_{17}H_{18}O_4$ (286.32): C 71.31, H 6.34. Found: C 70.97, H 6.61.



Dimethyl 3-acetylcyclopropane-1,2-dicarboxylate (**31**). To a vigorously stirred suspension of finely powdered, freshly flame-dried K_2CO_3 (80 g 580 mmol) and TEBAC (3.2 g, 17 mmol) in anhydrous DMF (200 mL) diethylfumarate (43 mL, 239 mmol) was added in one portion. The mixture was warmed to 40 °C, then the heating bath was removed and chloroacetone (34.7 g, 375 mmol) was gradually added by syringe pump within 5 h. After the addition was complete, the mixture was stirred at ambient temperature for additional 9 h and filtered through a pad of Celite®. The residue on the filter was washed with *t*BuOMe (3 × 100 mL) and the combined filtrates were evaporated under reduced pressure (T_{bath} < 80 °C, 5 Torr) to give 67.7 g of crude mixture, which was fractionated under reduced pressure (0.1 Torr). After the low-boiling fraction (DMF, diethyl fumarate, etc.) was separated off, the following fractions were obtained and checked by GC. Fraction I: 70–92 °C (1.8 g, 71% of **31**). – II: 92–95 °C (33 g, 98% purity). Total yield: 61%. The spectral data of the synthesized product **31** are identical to those reported in the literature.[34]



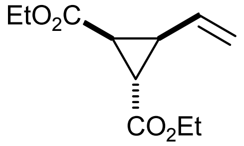
Diethyl 3-(1-hydroxyethyl)cyclopropane-1,2-dicarboxylate (**32**). To a vigorously stirred solution of **31** (27.67 g, 121 mmol) and $CeCl_3 \cdot 7H_2O$ (45.2 g, 121 mmol) in 50% aqueous ethanol (250 mL) chilled at –15 °C, $NaBH_4$ (4.6 g, 122 mmol) was added in a small portions within 15 min by occasional cooling (dry/ice acetone bath) so, that the internal temperature of the mixture was kept between –12 ° and –15 °C. After the addition had been completed, the stirring was continued at the same temperature until the gas evolution has been ceased (about 30 min). Then, the cooling bath was removed and the mixture was allowed to warm to room temperature (~20 °C). The mixture was concentrated under reduced pressure at ambient temperature to ~150 mL and extracted with ether (5 × 100 mL). The combined extracts were washed with half-saturated brine (100 mL), brine (150 mL) and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure gave 26.2 g (94%) of viscous colorless oil, that is pure (according to ^{1}H NMR data) alcohol **32** as only one diastereomer (*de* < 90%). – IR (film): ν = 3446 (OH), 3062, 2980, 2941, 2908, 2875, 1724 (C=O), 1448, 1372, 1331, 1265, 1192, 1141, 1095, 1075, 1039, 979, 924, 888, 859, 833, 781, 747 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.19–1.30 (m, 6 H, CH_3), 1.31 (d, ^3J = 6.3 Hz, 3 H, 2'-H), 1.88 (ddd, ^3J = 9.1 Hz, ^3J = 8.5 Hz, ^3J = 6 Hz, 1 H, 3-H), 2.23 (dd, ^3J = 6 Hz, ^3J = 4.9 Hz, 1 H, 2-H_{cis}), 2.29 (dd, ^3J = 9.1 Hz, ^3J = 4.9 Hz, 1 H, 1-H_{trans}), 2.37–2.45 (m, 1 H, OH), 3.89 (dq, ^3J = 8.5 Hz, ^3J = 6.3 Hz, 1 H, 1'-H), 4.12, 4.16 (q, *J* = 7 Hz, 4 H, OCH_2). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.0 (+, CH_3), 23.0, 26.2, 26.6, 35.8 (+), 62.2, 61.4 (–, OCH_2), 64.9 (+, C-1'), 171.0, 171.2 (C_{quat}, CO_2Et). – MS (70 eV, DCI, NH_3), *m/z* (%): 478.6 (1) [2M + NH_4^+], 248.2 (96) [M + NH_4^+], 231.2 (100) [M + H^+], 213.2 (46), 202 (4), 157 (5), 111 (6). – Anal. Calculated for $C_{11}H_{18}O_5$ (230.26): C 57.38, H 7.88. Found: C 57.36, H 8.05.



Diethyl 3-(1-bromoethyl)cyclopropane-1,2-dicarboxylate (**33**). To a stirred and pre-cooled to –20 °C (dry ice/acetone bath) solution of PPh_3 (13.77 g, 53 mmol) in anhydrous CH_2Cl_2 (50 mL), Br_2 (2.7 mL, 52 mmol) was gradually added within 10 min so, that the internal temperature of the reaction mixture was kept under –10 °C (ice/salt bath). After the mixture had become colorless or slightly yellow (colorization of mixture could been caused by partial decomposition of the reagent on upper and therefore warmest part of reaction flask; it is stable enough only under –10 °C), a solution of alcohol **32** (11.51 g, 50 mmol) and anhydrous pyridine (4 mL, 50 mmol) in the same solvent (5 mL) was gradually added at such a rate to keep the internal temperature of the mixture under –10 °C. The mixture was stirred at this temperature for additional 30 min, the cooling bath was removed and the stirring was continued at ambient temperature for 16 h. The mixture was filtered, the residue was washed with CH_2Cl_2 (2 × 20 mL) and the combined filtrates were concentrated under reduced pressure until the PPh_3O has started to crystallize. Then, the stirred residue was diluted by gradual adding of pentane (100 mL) and stirring was continued for 1 h. The PPh_3O was filtered off, washed with pentane/ether, 5:1 mixture (2 × 20 mL) and the combined filtrates were evaporated under reduced pressure to give brown oil, which was purified by flash" chromatography on 100 mL of flash silica gel, eluting with pentane/ether, 10:1, to yield 13.5 g (92%) of pure **33** as a diastereomeric mixture (9:1, according to ^{1}H NMR). – IR (film): ν =

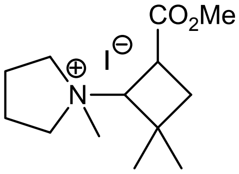
3061, 2983, 2935, 2908, 2875, 1718, 1457, 1370, 1329, 1277, 1204, 1179, 1142, 1096, 1059, 1037, 971, 946, 915, 858, 839, 784, 742, 668, 618 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.26, 1.27 (t, ^3J = 7 Hz, CH_3), 1.68 (d, ^3J = 6.8 Hz, 3 H, CH_3), 2.19–2.30 (m, 1 H, 3-H), 2.35 (dd, ^3J = 5.3 Hz, ^3J = 5.3 Hz, 1 H, 2-H_{cis}), 2.47 (dd, ^3J = 9 Hz, ^3J = 5.3 Hz, 1 H, 1-H_{trans}), 4.11–4.28 (m, 5 H, $2CH_2O$ + 1'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.1, 14.2 (+, CH_3), 26.1 (+, CH_3), 29.2, 30.9, 37.4 (+, *c*Pr-C), 45.5 (+, CHBr), 61.3, 61.4 (–, CH_2O), 169.3, 170.6 (C_{quat}, CO_2Et). – MS (70 eV, DCI, NH_3), *m/z* (%): 604 (1) [2M + NH_4^+], 312/310 (100/99) [M + NH_4^+], 230 (3) [M^+ + NH_4^+ – HBr], 221/219 (20/22) [M + NH_4^+ – $CO_2C_2H_5$ – NH_3], 213 (23) [M^+ + NH_4 – HBr – NH_3], 184 (2), 139 (1), 111 (1).

Diethyl 3-ethenylcyclopropane-1,2-dicarboxylate (**29**). A mixture of bromide **33** (14.6 g, 50 mmol) and DBU (8.1 mL, 54 mmol) was stirred at 100 °C for 2 h. The volatile material was "bulb-to-bulb" distilled off, dissolved in ether (150 mL), washed with 5% aqueous H_2SO_4 (50 mL), water (50 mL), brine (50 mL) and dried over $MgSO_4$. Obtained after evaporation of the solvent under reduced pressure colorless liquid was a pure **29** (98% according to GC). Yield: 9.5 g (89%). This product was distilled under reduced pressure to give 8.3 g of **29** (98.6% according to GC). – B. p. 63–64 °C (0.1 Torr). The spectral data of the synthesized compound are identical to those reported in the literature.[30]

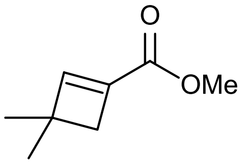


2.3. *Synthetic Procedures and Spectral Data of the Compounds Prepared According to the "Main Strategy"*

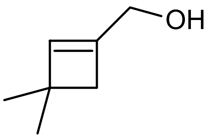
N-(1-Carbomethoxy-3,3-dimethyl-2-cyclobutyl)-N-methyl pyrrolidinium iodide (**43**). To a solution of methyl 3,3-dimethyl-2-(pyrrolidin-1-yl)-cyclobutanecarboxylate **42** (54.7 g, 259 mmol) in anhydrous nitromethane (130 mL) CH_3I (20 mL, 320 mmol) was added in one portion with occasional cooling (cold water) and allowed to stand at ambient temperature for 1 h. The solvent was evaporated under reduced pressure (T_{bath} < 50 °C) and the solid residue was recrystallized from the methanol/acetone mixture. It was obtained 86.2 g (94%) of **43** as a colorless crystals, which spectral data were identical to them reported in the literature.[44]



Methyl (3,3-dimethyl-1-cyclobutene)carboxylate (**44**). A 1 L, three-necked oven-dried flask, equipped with septum, mechanical stirrer and Dimroth reflux condenser with bubbler, was charged under nitrogen with the salt **43** (106 g, 300 mmol) and NaH (12.6 g of 60% suspension in mineral oil, 315 mmol). An anhydrous THF (300 mL) was added by *cannula*, and the mixture was heated by stirring (T_{bath} 80 °C) until the vigorous hydrogen evolution has been started (30–40 min). Then the heating bath was removed and the reaction rate was controlled by stirring and, if it is necessary, with occasional cooling (ice water bath). After the gas evolution has been ceased, the mixture was refluxed for an additional 1 h, cooled to room temperature and filtered through a short pad of Celite®. The most of solvent and 1-methylpyrrolidine were distilled off through a 10-cm Raschig rings filled column (T_{bath} < 100 °C), the residue was dissolved in diethyl ether (150 mL), and washed with 20% aqueous H_2SO_4 (~50 mL). The aqueous layer was extracted with ether (50 mL), the combined organic phases were washed with brine (50 mL) and dried over $MgSO_4$. Obtained after evaporation of the solvents at ambient pressure residue was "bulb-to-bulb" distilled to yield 35.7 g (85%) of methyl 3,3-dimethylcyclobuthen-1-yl carboxylate (**44**) as a slightly yellow liquid, which spectral data were identical to them reported in the literature.[44] – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 25.3 (+, $2CH_3$), 41.0 (C_{quat}, C-3), 42.5 (–, C-4), 51.3 (+, OCH_3), 134.7 (C_{quat}, C-1), 155.5 (+, C-2), 163.6 (C_{quat}, CO_2Me).

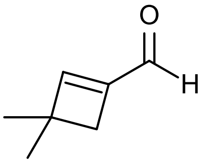


(3,3-Dimethylcyclobuten-1-yl)methanol (**45**). To a stirred solution of $LiAlH_4$ (14.2 g, 375 mmol) in anhydrous diethyl ether (700 mL) a freshly prepared solution of $AlCl_3$ (16.7 g, 125 mmol) in 300 mL of the same solvent was gradually added within 30–40 min so that the mixture temperature was kept at 0–2 °C (ice/salt bath). After the addition was complete, the mixture was readily warmed to 20 °C and stirred at this temperature for 20 min. Then methyl 3,3-dimethylcyclobuthen-1-yl carboxylate (**44**) (28 g, 200 mmol) was added within 15 min by vigorous stirring (ice bath), keeping the temperature of the mixture at 8–10 °C (ice-salt bath). After that, the mixture was immediately warmed up to 20 °C (warm water bath) and kept at this temperature for 50 min. Then, a 2 M aqueous H_2SO_4 (63 mL) was gradually added to the vigorously stirred and cooled (ice/salt bath) reaction mixture. The mixture was stirred at 20 °C for additional 1 h and filtered through a short pad of Celite®, which was then washed with ether (2×100 mL). The organic phase was dried over $MgSO_4$, filtered and evaporated under reduced pressure at ambient temperature. The residue was distilled under reduced pressure to

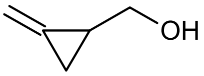


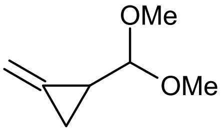
yield 20.1 g (90%) of **45** as a viscous colorless oil. – B. p. 89–90 °C (75 mbar). – IR (film): ν = 3323, 3031, 2954, 2914, 2862, 1637 (C=C), 1461, 1361, 1282, 1226, 1123, 1028, 961, 907, 802 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.18 (s, 6 H, CH_3), 1.40 (br. s, 1 H, OH), 2.19 (s, 2 H, 4-H), 4.09 (d, ^4J = 1.8 Hz, 2 H, 1'-H), 5.99 (t, ^4J = 1.8 Hz, 1 H, 2-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 26.5 (+, $2CH_3$), 40.5 (C_{quat}, C-3), 43.0 (–, C-4), 61.6, (–, C-1'), 137.9 (+, C-2), 144.0 (C_{quat}, C-1). – MS (70 eV, EI), *m/z* (%): 122 (3), [M^+], 97 (18), 94 (10) [$M^+ - C_2H_4$], 93 (8), 91 (3), 83 (13), 81 (11) [$C_6H_9^+$], 79 (100) [$C_6H_7^+$], 77 (17) [$C_6H_5^+$], 69/70/71 (6/2/1), 65/66/67 (5/3/5), 55/56/57 (14/12/3), 53 (17), 43 (21), 41 (39). – MS (HR-EI): 112.0888 ($C_7H_{12}O$, calcd. 112.0888).

3,3-Dimethyl-1-cyclobutenecarbaldehyde (**46**). Alcohol **45** (19.5 g, 174 mmol) was subjected to GP 3. After the reaction mixture was worked up by usual manner, the solvents were distilled off through a 10-cm Raschig rings filled column at a moderate rate (2–3 drops/s, T_{bath} < 60 °C) under ambient pressure. The residue was distilled under reduced pressure to yield 18.4 g (90%) of pure **46** as a slightly yellow liquid. – B. p. 61–63 °C (60 mbar). – IR (film): ν = 3042, 2960, 2928, 2866, 2790, 2699, 1683(C=O), 1592 (C=C), 1462, 1437, 1366, 1299, 1279, 1174, 1125, 953, 912, 832, 737, 669 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.25 (s, 6 H, $2CH_3$), 2.39 (s, 2 H, 4-H), 6.99 (s, 1 H, 2-H), 9.56 (s, 1 H, CHO). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 25.4 (+, $2CH_3$), 40.6 (–, C-4), 42.5 (C_{quat}, C-3), 143.0 (C_{quat}, C-1), 160.3 (+, C-2), 188.0 (+, CHO). – MS (DCI, NH_3, 70 eV), *m/z* (%): 145 (72) [$M + NH_3 + NH_4^+$], 128 (100) [$M + NH_4^+$], 110 (35) [M^+], 109 (30) [$M - H^+$]. – Anal. Calculated for $C_7H_{10}O$ (110.15): C 76,33, H 9,15. Found: C 76.09, H 8.98.

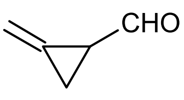


2-Methylenecyclopropylmethanol (**49**). A solution of 1-(tetrahydropyran-2'-yl)oxymethyl-2-metylidenecyclopropane (**53**) (20.2 g, 120 mmol) and *p*TsOH·H_2O (2.3 g, 12 mmol) in methanol (480 mL) was stirred at ambient temperature for 24 h. Then $NaHCO_3$ (1.01 g, 12 mmol) was added and methanol was distilled off through a 40 cm Vigreux column under reduced pressure (90 Torr, T_{bath} 40 °C). The residue was triturated with CH_2Cl_2 (50 mL), filtered, the solid was washed on the filter (2×10 mL) and the filtrate was evaporated at atmospheric pressure. The residue was distilled under reduced pressure to give 9.3 g (92%) of pure **49** as a colorless liquid. – B. p. 68–70 °C (46 Torr). The spectral data of the synthesized product were identical to those reported in the literature.[46]

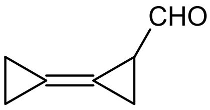




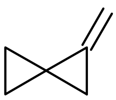
1-(Dimethoxymethyl)-2-methylenecyclopropane (**56**). To a stirred solution of 3.3-dimethoxyprop-1-ene (21.5 g, 210 mmol) and 1,1-dichloroethane (26.6 mL, 316 mmol) in anhydrous ether (125 mL) chilled to –40 °C under nitrogen *n*BuLi (106 mL of 2.4 N solution in hexanes, 254 mmol) was gradually added within 3 h keeping the temperature of the mixture between –40 and –35 °C with occasional cooling (dry ice/acetone bath). After the addition has been completed, the cooling bath was removed, the reaction was allowed to warm to 20 °C and quenched with ice water (50 mL). Organic phase was separated, washed with water (50 mL), brine (50 mL) and dried over $MgSO_4$. Solvent was evaporated under normal pressure through a 30-cm Vigreux column (T_{bath} < 160 °C) and the residue was “bulb-to-bulb” distilled (0.1 Torr, T_{bath} < 100 °C). It gave 14.25 g of colorless liquid (^{1}H NMR spectra showed no olefinic protons) used in the next step without additional purification. Thus, the crude chloride () (14.25 g) was gradually added to a stirred solution of *t*BuOK (11.6 g, 103 mmol) in anhydrous DMSO (52 mL) at 60 °C and stirred at this temperature for additional 2 h. A volatile material was “bulb-to-bulb” distilled off (T_{bath} < 100 °C, 10 Torr) diluted with pentane (150 mL), washed with water (2 × 50 mL), brine (50 mL) and dried over $MgSO_4$. Solvent was distilled off through a 10-cm Raschig rings filled column (T_{bath} < 100 °C) and the residue was fractionated under reduced pressure by 20-cm Vigreux column to give 4.7 g (17.5% for two steps) of **56** as a colorless liquid. – B. p. 70 °C (80 mbar). – IR (film): ν = 3070, 3050, 2996, 2957, 2935, 2902, 2831, 2738, 2666, 1454, 1382, 1349, 1321, 1273, 1190, 1141, 1108, 1086, 1064, 1042, 982, 954, 889, 828, 751 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.12 (dddd, ^2J = 9.2 Hz, ^3J = 5.1 Hz, ^4J = 2.5 Hz, ^4J = 2.2 Hz, 1 H), 1.32 (dddd, ^2J = 9.2 Hz, ^3J = 9.1 Hz, ^4J = 2.5 Hz, ^4J = 2.2 Hz, 1 H), 1.76 (ddddd, ^3J = 9.1 Hz, ^3J = 5.9 Hz, ^3J = 5.1 Hz, ^4J = 2.5 Hz, ^4J = 2.2 Hz, 1 H), 3.36 (s, 6 H, OCH_3), 4.08 (d, ^3J = 5.9 Hz, 1 H), 5.45–5.51 (m, 2 H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 6.6 (–, C-3), 17.7 (+, C-1), 52.7, 53.3 (+, OCH_3), 104.6 (–, C-1''), 104.8 (+, CH, C-1'), 130.1 (C_{quat}, C-2). – MS (70 eV, DCI, NH_3), *m/z* (%): 146 (11) [M + NH_4^+], 127 (5), [M – H^+], 113 (100) [M – CH_3^+], 111 (45), 105 (12), 103 (40), 101 (6). – Anal. Calculated for $C_7H_{12}O_2$ (128.17): C 65.60, H 9.44. Found: C 65.33, H 9.43.



2-Methylenecyclopropanecarbaldehyde (**50**) was prepared in two ways. *A)* Swern oxidation of 2-methylenecyclopropylmethanol (9.3 g) **49** according to GP 3 gave 5.75 g (61% yield) of the target aldehyde. *B)* Formylation of lihtiated methylenecyclopropane (**57**) according to GP 2 gave 82% of aldehyde after the improved work up procedure had been applied. Thus, after the DMF (20 mL, 258 mmol) was added to the solution of 1-lithio-2-methylenecyclopropane (prepared from 2.4 N solution *n*BuLi in hexanes (105 mL, 252 mmol) and 14.9 g (275 mmol) of methylenecyclopropane in 250 mL of anhydrous THF), cooling bath was removed, the reaction mixture was allowed to reach ambient temperature, and the volatile material was completely evaporated under reduced pressure (T_{bath} < 40°C) to give a slightly yellow amorphous solid. This residue was dissolved in anhydrous ether (400 mL) and poured under argon into a stirred –10 °C cold 2 M aqueous H_2SO_4 (200 mL) keeping the internal temperature under 10 °C (ice/salt bath). The organic layer was separated, the aqueous one was saturated with NaCl, and extracted with ether (3×50 mL). The combined organic phases were washed with brine (2×100 mL) and dried over $MgSO_4$. The solvent was distilled off at atmospheric pressure through a 10-cm Raschig rings filled column at a moderate rate (2–3 drops/s, T_{bath} < 60 °C; at the end of distillation the bath temperature was increased for a short time up to 80 °C). The residue was "bulb-to-bulb" distilled under reduced pressure to yield 16.8 g (82%) of **50** as a slightly yellow liquid, the spectral data of which were identical to those reported in the literature.[46]

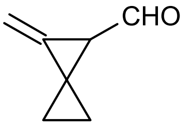


Bicyclopropylidenecarbaldehyde (**63**). After the bicyclopropylidene **58** (8.1 g, 100 mmol) was subjected to GP 2, the resulting reaction mixture was treated with 2 M aqueous H_2SO_4 (50 mL) at 0 °C, organic layer was separated and the aqueous one was extracted with ether (2 × 50 mL). Combined extracts were washed with brine (2 × 50 mL) and dried over $MgSO_4$. The solvents were distilled off through a 20-cm Vigreux column (T_{bath} < 80 °C), and the residue was "bulb-to-bulb" distilled (T_{bath} < 80 °C, 10 Torr) to give slightly yellow liquid (it contains target aldehyde contaminated with THF and a few amount of ether according to ^{1}H NMR data), which was finally purified by distillation under reduced pressure to yield 7.1 g (66%) of pure **63** as a slightly yellow liquid. – B. p. 104 °C (75 mbar). – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.21–1.34 (m, 4 H), 1.89–1.95 (m, 2 H), 2.46–2.51 (m, 1 H), 8.62 (d, ^3J = 6.5 Hz, 1 H, CHO). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 3.6, 4.0 [–, C-2'(3')*], 10.3 (–, C-2), 28.5 (+, C-1), 108.0, 116.2 [C_{quat}, C-1(1')], 198.5 (+, CHO).

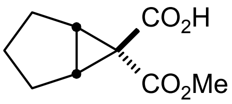


Methylenedispiro[2.2]pentane (**59**). Bicyclopropylidene **58** (19.3 g, 22.6 mL, 241 mmol) was slowly added by syringe pump over 4.7 h to a pre-heated (80 °C) 50-mL pointed-bottom flask under a constant stream of nitrogen (250 mL/min through a capillary which almost reached the bottom of the flask). The flask was connected to a quartz tube (3 × 60 cm) that had been filled with quartz rings and pre-heated to 350 °C. The product was collected in a cold (–196 °C) trap. After the addition was complete, the stream of nitrogen was passed through the apparatus for an additional 20 min, and the cold trap was allowed to warm up to 20 °C. Its contents (17.4 g) was methylenespiropentane (**59**) of ≥ 95% purity, as a colorless or slightly yellow liquid, yield 90%. Its NMR spectroscopic data are identical to those reported in the literature.[18] Attempted distillation of **59** at atmospheric pressure did not increase its purity, but only reduced the yield due to partial polymerization. – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.1 (–, 3 CH_2), 10.7 (C_{quat}, C-3), 98.4 (–, C-1'), 137.5 (C_{quat}, C-1).

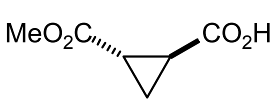
2-Methylenespiro[2.2]pentane-1-carbaldehyde (**66**). After the exact procedure described for the compound **63** has been applied to methylenespiropentane **59** (4 g, 50 mmol), 2.8 g (39%) of target aldehyde **66** was obtained. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.15–1.50 [m, 4 H, 4(5)-H], 2.55 (ddd, ^3J = 6.8 Hz, ^4J = 2 Hz, ^4J = 1 Hz, 1 H, 1-H), 5.39 (d, ^2J = 2 Hz, 1 H), 5.47 (d, ^2J = 1 Hz, 1 H), 8.85 (d, ^3J = 6.8 Hz, 1 H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 8.4 9.1 [–, C-4(5)], 17.0 (C_{quat}, C-3), 34.1 (+, C-1), 102 (–, C-1'), 132.8 (C_{quat}, C-2), 199.5 (+, CHO).



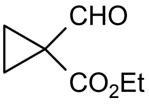
exo-6-(Methoxycarbonyl)bicyclo[3.1.0]hexane-6-carboxylic acid (**72**). The colorless solid (15.53 g) obtained after hydrolysis of diester **70** with LiOH according to GP 1, was recrystallized from a mixture of toluene and cyclohexane, 1:2 (250 mL), to yield 13.92 g of pure **72** as colorless prisms. A second crop (1.29 g) was obtained after evaporation of the mother liquor and recrystallization of the residue from the same solvent (about 25 mL). The overall yield of **72** was 15.21 g (83%). – M. p. 137–137.5 °C. – IR (KBr): ν = 3450 (OH), 3045, 3023, 2968, 2875, 1747 (C=O), 1700 (C=O), 1443, 1371, 1316, 1283, 1233, 1193, 1162, 1110, 1050, 1022, 938, 872, 806, 768 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.83 (m, 1 H), 1.67 (m, 1 H), 1.85–2.10 (m, 4 H), 2.20 [m, 2 H, 1(5)-H], 3.73 (s, 3 H, OCH_3), 11.22 (bs, 1 H, COOH). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 21.3 (–, C-3), 26.4 [–, C-2(4)], 35.7 [+, C-1(5)], 35.8 (C_{quat}, C-6), 52.7 (+, OCH_3), 167.6 (C_{quat}, COOH), 176.8 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 184 (22) [M^+], 166 (96) [$M^+ - H_2O$], 155 (21) [$M^+ - H - C_2H_4$], 153 (73) [$M^+ - CH_3O$], 152 (70) [$M^+ - CH_3OH$], 138 (36) [$M^+ - CO - H_2O$], 134 (100) [$M^+ - CH_3OH - H_2O$], 124 (78) [$M^+ - CO - CH_3OH$], 107 (21), 106 (36), 93 (15), 79 (90), 77 (34) [$C_6H_5^+$], 67 (27), 53 (12), 41 (19) [$C_3H_5^+$]. – Anal. Calculated for $C_9H_{12}O_4$ (184.19): C 58.69, H 6.57. Found: C 58.89, H 6.83.



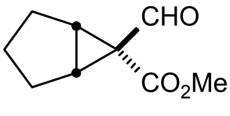
trans-2-Methoxycarbonylcyclopropanecarboxylic acid (**73**). A crude mixture (25 g) obtained after hydrolysis of the diester **68** (31 g, 196 mmol) with LiOH according to GP 1, was "bulb-to-bulb" distilled under reduced pressure (T_{bath} 100–110 °C/0.1 Torr) to give 20 g (70%) of pure ester **73**, the physical properties and ^{1}H NMR spectra of which were identical to those reported in the literature.[61, 130] – IR (film): ν = 3116, 3078, 3018, 2958, 2751, 2702, 2658, 2560, 1731 (C=O), 1698 (C=O), 1436, 1376, 1327, 1305, 1207, 1175, 1115, 1087, 1055, 1006, 918, 853, 820, 744, 651, 629 cm^{-1}. – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 15.8 (–, C-3), 22.0 22.7 [+, C-1(2)*], 52.3 (+, OCH_3), 171.8 (C_{quat}, CO_2Me), 178.1 (C_{quat}, CO_2H). – MS (70 eV, EI), *m/z* (%): 144 (1) [M^+], 143 (1) [M^+ – H], 127 (4) [M^+ – OH], 126 (4) [M^+ – H_2O], 113 (100) [M^+ – OCH_3], 112 (54) [M^+ – CH_3OH], 99 (23) [M^+ – CO_2 – H], 98 (58) [M^+ – CO – H_2O], 95 (6), 85 (27) [M^+ – CO_2Me], 84 (51) [M^+ – CO_2Me – H], 71 (4), 69 (10), 68 (20), 67 (6), 59 (32), 57 (16), 55 (18), 45 (16), 43 (6), 42 (6), 41 (20). – Anal. Calculated for $C_6H_8O_4$ (144.13): C 50.00, H 5.59. Found: C 49.74, H 5.36.



Ethyl 1-formylcyclopropanecarboxylate (**76**). According to GP 4, 1-ethoxycarbonylcyclopropanecarboxylic acid (**67**) (36.8 g, 233 mmol) after distillation of the crude product under reduced pressure, gave 20.5 g (62 %) of pure **76**, which spectral data and physical property were identical to those reported in the literature.[131] – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.1 (+, CH_3), 22.5 [–, C-2(3)], 33.4 (C_{quat}, 1-C), 61.3, (–), 171.0 (C_{quat}, CO_2Et), 198.8 (+, CHO).

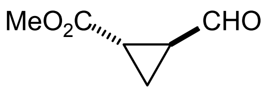


Methyl exo-6-formylbicyclo[3.1.0]hexane-6-carboxylate (**77**). According to GP 4, the half-ester **72** (14.7 g, 80 mmol) after distillation of the crude product under reduced pressure, gave 11.8 g (88%) of pure **77** as a colorless oil. – B. p. 66–67 °C (7 mbar). – IR (film): ν = 2955, 2918, 2894, 2866, 2791, 2753, 2716, 1739 (CHO), 1701 (C=O), 1480, 1438, 1405, 1372, 1330, 1293, 1232, 1199, 1156, 1109, 1091, 1054, 1030, 987, 964, 945, 893, 870, 832, 809, 757 cm^{-1} – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.93–1.14 (m, 1 H), 1.66–1.80 (m, 1 H), 1.91–2.12 [m, 4 H, 2(4)-H], 2.20–2.26 [m, 2 H, 1(5)-H], 3.78 (s, 3 H, OCH_3), 9.15 (s, 1 H, CHO). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 22.3 (–, C-3), 26.2 [–, C-2(4)], 35.3 [+, C-1(5)], 45.2 (C_{quat}, C-6), 52.5 (+, OCH_3), 168.6 (C_{quat}, CO_2Me), 195.5 (+, CHO). – MS (70 eV, EI), *m/z* (%): 168 (9) [M^+], 167 (100) [M^+ – H], 135 (13), [M^+ – CH_3OH – H], 108 (3) [M^+ – CO – CH_3OH], 107 (4), 79 (5)

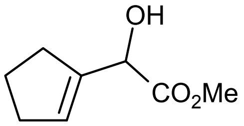


$[C_6H_7^+]$, 67 (6). – Anal. Calculated for $C_9H_{12}O_3$ (168.19): C 64.27, H 7.19. Found: C 64.07, H 7.03.

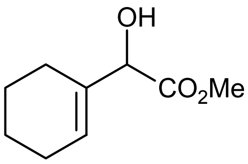
Methyl trans-2-formylcyclopropanecarboxylate (**75**) was prepared in two ways. *A)* Swern oxidation of *(E)*-2-(methoxycarbonyl)cyclopropyl methanol (**74**) (13.4 g, 103 mmol) according to GP 3 yielded 11.2 g (85%) of **75**. *B)* According to GP 4, the half-ester **73** (15.1 g, 105 mmol) after distillation of the crude product under reduced pressure, gave 11.4 g (85%) of pure **75** as a colorless oil, 1H- and ^{13}C NMR spectra of which were identical to those reported in the literature.[61] – B. p. 81–82 °C (12 Torr). – IR (film): ν = 3105, 3062, 3013, 2958, 2849, 2740, 1736 (C=O), 1715 (C=O), 1436, 1387, 1322, 1284, 1207, 1175, 1082, 1060, 1022, 946, 913, 864, 850, 820, 749, 735, 667 cm^{-1} – MS (70 eV, EI), *m/z* (%): 128 (4) $[M^+]$, 113 (1) $[M^+ - CH_3]$, 99 (4) $[M^+ - CHO]$, 97 (19) $[M^+ - OCH_3]$, 96 (20) $[M^+ - CH_3OH]$, 85 (2), 71 (6), 69 (53) $[M^+ - CO_2CH_3]$, 68 (33) $[M^+ - CH_3OH - CO]$, 59 (18), 55 (9), 45 (2), 43 (5), 42 (9), 41 (100) $[C_3H_5^+]$, 40 (22) $[C_3H_4^+]$.



Methyl (cyclopenten-1-yl)hydroxyacetate (**81**). According to GP 5A, the aldehyde **36** (40 g, 416 mmol) after distillation of the crude product, gave 50 g (77%) of pure **81** as a colorless liquid. – B. p. 51–52 °C (0.1 Torr). – IR (film): ν = 3477, 3048, 2954, 2899, 2855, 1740, 1644, 1439, 1264, 1208, 1143, 1074, 979, 954, 724 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.84 (tt, ^3J = 7.5 Hz, ^3J = 7.5 Hz, 2 H, 4-H), 2.10–2.42 (m, 4 H), 3.32 (s, 1 H, OH), 3.72 (s, 3 H, OCH$_3$), 4.72 (s, 1 H), 5.69–5.75 (m, 1 H, 2-H). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 23.0 (–, C-4), 31.2 32.1 [–, C-3(5)], 52.4 (+, OCH$_3$), 70.1 (+, C-2'), 129.3 (+, C-2), 140.6 (C$_{quat}$, C-1), 173.6 (C$_{quat}$, CO$_2$Me). – MS (70 eV, EI), *m/z* (%): 156 (14) $[M^+]$, 138 (4) $[M^+ - H_2O]$, 124 (5), 107 (3), 97 (100) $[M^+ - CO_2CH_3]$, 79 (17) $[M^+ - CO_2CH_3 - H_2O]$, 67 (22). – Anal. Calculated for $C_8H_{12}O_3$ (156.18): C 61.52, H 7.74. Found: C 61.19, H 7.41.

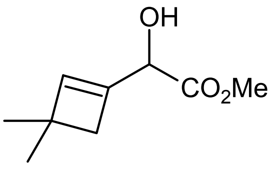


Methyl (cyclohexen-1-yl)hydroxyacetate (**82**). According to GP 5A, the aldehyde **39** (16.5 g, 150 mmol) after distillation of the crude product, yielded 13.5 g (53%) of pure **82** as a colorless liquid, ^{1}H NMR and ^{13}C NMR spectra of which were identical to those reported in the literature.[65] – IR (film): ν = 3490, 3001, 2930, 2859, 2838, 2660, 1738, 1672, 1438, 1396, 1259, 1211, 1140, 1088, 1068, 1042, 1010, 984, 923, 845, 800, 708 cm^{-1}. – MS (70 eV, EI), *m/z*



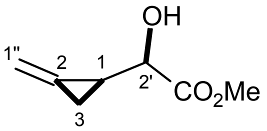
(%): 170 (6) [M^+], 152 (7) [$M^+ - H_2O$], 138 (2), 124 (2), 111 (100) [$M^+ - CO_2CH_3$], 93 (23) [$M^+ - CO_2CH_3 - H_2O$], 91 (10), 81 (29), 77 (15) [$C_6H_5^+$], 67 (94), 55 (45), 53 (19), 43 (10), 41 (17). Anal. Calculated for $C_9H_{14}O_3$ (170,21): C 63.51, H 8.29. Found: C 63.83, H 8.09.

Methyl (3,3-dimethylcyclobuten-1-yl)hydroxyacetate (**83**). According to GP 5A, the aldehyde **46** (16.7 g, 151 mmol) after distillation of the crude product, gave 13.9 g (54% yield) of pure **83**. According to GP 5B, the aldehyde **46** (12.7 g, 115 mmol) after distillation of the crude product, yielded 13.5 g (69%) of pure **83** as a colorless liquid. – B. p. 48–50 °C (0.1 Torr). – IR (film): ν = 3477 (OH), 3037, 2957, 2921, 2863, 1743 (C=O), 1628 (C=C), 1452, 1437, 1363, 1281, 1220, 1129, 1077, 1011, 984, 939, 907, 843, 797, 744 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.15 (s, 3 H, CH_3), 1.16 (s, 3 H, CH_3), 2.21 (s, 2 H, 4-H), 2.91 (s, 1 H, OH), 3.80 (s, 3 H, OCH_3), 4.63 (d, ^4J = 1.5 Hz, 1 H, 2'-H), 6.08 (d, ^4J = 1.5 Hz, 1 H, 2-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 26.1 (+, $2CH_3$), 40.4 (C_{quat}, C-3), 42.9 (–, C-4), 52.6 (+, OCH_3), 69.7 (+, C-2'), 140.0 (C_{quat}, C-1), 140.9 (+, C-2), 172.8 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 170 (1) [M^+], 153 (5), [$M^+ - OH$], 139 (13) [$M^+ - OCH_3$], 121 (5) [$M^+ - H_2O - OCH_3$], 111 (100), [$M^+ - CO_2CH_3$], 95 (22), 93 (57) [$M^+ - CO_2CH_3 - H_2O$], 91 (14), 81 (33) [$C_6H_9^+$], 77 (17) [$C_6H_5^+$], 67 (19), 65 (6), 55 (59), 53 (18), 43 (32), 41 (46). – MS (HR-EI): 170.0943 ($C_9H_{14}O_3$, calcd. 170.0943).

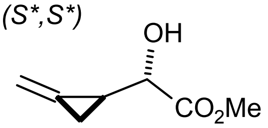


Methyl 2-methylenecyclopropylhydroxyacetate (**84**) was prepared in two ways. *A*). According to GP 5A the aldehyde **50** (4.94 g, 60 mmol) gave 5.3 g (62% yield) of crude **84** as a 1:1 mixture of diastereomers, which was used for the next step without additional purification. *B*). A solution of the acetal **56** (3 g, 23 mmol) in diethyl ether (4 mL) was stirred with 2 M aqueous H_2SO_4 (12 mL) at ambient temperature for 1 h, then it was cooled to 0 °C and a solution of NaCN (1.32 g, 27 mmol) in water (3 mL) was gradually added within 10 min. The mixture was stirred for an additional 30 min at 10 °C and worked up by usual manner to give a crude cyanohydine (2 g, 78%), which was converted to the corresponding α-hydroxyester according to GP 5B to give 1.6 g of **84** as a crude 1:1 diastereomeric mixture. This one was subjected to column chromatography on 100 g of silica gel, eluting with pentane/diethyl ether, 5:1, to lead to complete separation of the two diastereomers of **84** and gave 0.7 g of each of them. Total yield: 1.4 g (42% from the dimethylacetal **56**). – *(S*,R*)*-**84** (R_f = 0.20). – Colorless prisms,

(S,R*)*



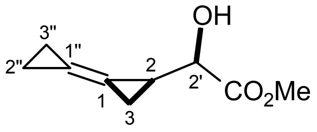
(S,S*)*



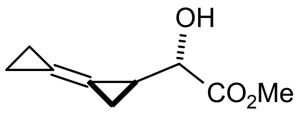
m. p. 41–42 °C. – IR (film): ν = 3451 (OH), 3078, 3050, 2996, 2957, 2902, 2853, 1739 (C=O), 1437, 1404, 1251, 1207, 1119, 1092, 1075, 1026, 1004, 986, 894, 850, 790, 735 cm^{-1}. – ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.17 (dddd, ^2J = 9.4 Hz, ^3J = 4.9 Hz, ^4J = 2.5 Hz, ^4J = 2.2 Hz, 1 H, 3-H$_{cis}$), 1.36 (dddd, ^2J = 9.4 Hz, ^3J = 8.9 Hz, ^4J = 2.5 Hz, ^4J = 1.9 Hz, 1 H, 3-H$_{trans}$), 1.72 (ddddd, ^3J = 8.9 Hz, ^3J = 7.8 Hz, ^3J = 4.9 Hz, ^4J = 2.3 Hz, ^4J = 1.9 Hz, 1 H, 1-H), 2.68 (d, ^3J = 5.6 Hz, 1 H, OH), 3.78 (dd, ^3J = 7.8 Hz, ^3J = 5.6 Hz, 1 H, 2'-H), 3.82 (s, 3 H, OCH$_3$), 5.46–5.49 (m, 1 H, 1''-H$_{trans}$), 5.51–5.53 (m, 1 H, 1''-H$_{cis}$). – ^{13}C NMR (50.3 MHz, CDCl$_3$, APT): δ = 7.6 (–, C-3), 19.1 (+, C-1), 52.6 (+, OCH$_3$), 72.1 (+, C-2'), 105.5 (–, C-1''), 130.7 (–, C-2), 174.5 (–, CO$_2$Me). – MS (70 eV, DCI, NH$_3$), *m/z* (%): 160 (100) [M + NH$_4^+$]; MS (70 eV, EI), *m/z* (%): 141 (0.5) [M$^+$ – H], 125 (22) [M$^+$ – OH], 114 (4), 113 (11), 111 (3) [M$^+$ – OCH$_3$], 110 (6), 103 (6), 102 (2), 99 (4), 90 (5), 86 (2), 85 (7), 84 (6), 83 (100), 82 (81), 81 (12), 74 (2), 71 (13), 69 (4), 66 (3), 65 (8), 61 (14), 59 (36), 57 (6), 56 (4), 55 (74), 54 (36), 53 (32), 52 (4), 51 (9), 50 (5), 43 (21), 42 (5), 41 (11). – Anal. Calculated for C$_7$H$_{10}$O$_3$ (142.15): C 59.14, H 7.09. Found: C 58.88, H 6.82. – *(S*,S*)*-**84** (*R*$_\text{f}$ = 0.28). – Colorless oil. – IR (film): ν = 3467 (OH), 3078, 3049, 2996, 2957, 2908, 2853, 1734 (C=O), 1437, 1399, 1273, 1207, 1135, 1115, 1095, 1075, 1009, 987, 894, 856, 834, 768, 729 cm^{-1}. – ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.20–1.36 (m, 2 H, 3-H), 1.76–1.85 (m, 1 H, 1-H), 2.51 (bs, 1 H, OH), 3.81 (s, 3 H, OCH$_3$), 3.98 (d, ^3J = 6.2 Hz, 1 H), 5.47–5.52 (m, 2 H). – ^{13}C NMR (50.3 MHz, CDCl$_3$, APT): δ = 6.6 (–, C-3), 18.5 (+, C-1), 52.5 (+, OCH$_3$), 70.7 (+, CH), 105.4 (–, C-1''), 130.7 (–, C-2), 174.5 (–, CO$_2$Me). – MS (70 eV, DCI, NH$_3$), *m/z* (%): 302 (46) [2M + NH$_4^+$], 160 (100) [M + NH$_4^+$]; MS (70 eV, EI), *m/z* (%): 141 (0.1) [M$^+$ – H], 125 (17) [M$^+$ – OH], 114 (4), 113 (11) [M$^+$ – OCH$_3$], 111 (3), 110 (5), 103 (3), 102 (2), 99 (4), 90 (3), 88 (4), 87 (3), 86 (27), 85 (18), 84 (47), 83 (100), 82 (84), 81 (13), 71 (9), 65 (7), 61 (9), 59 (27), 57 (4), 56 (4), 55 (75), 54 (40), 53 (28), 52 (3), 51 (7), 50 (3), 49 (6), 47 (11), 43 (15), 42 (5), 41 (8). – Anal. Calculated for C$_7$H$_{10}$O$_3$ (142.15): C 59.14, H 7.09. Found: C 58.88, H 6.82.

Methyl bicyclopropylidenylhydroxyacetate (**85**). According to GP 2A the aldehyde **63** (11.8 g, 109 mmol) gave 13.9 g (76% yield) of crude **85** as a 1:1 mixture of diastereomers, which was used for the next step without additional purification. Analytical samples of both diastereomers were obtained by column chromatography of the crude reaction mixture (200 mg) on 25 g of silica gel, eluting with hexane/*t*BuOMe, 5:1, which led to complete separation of the two diastereomers of **85** and gave 80 mg of each of them. – *(S*,R*)*-**85** (R_f = 0.11). – Colorless prisms, m. p. 59–60 °C. – IR (film): ν = 3462 (OH), 3050, 2985, 2957, 2853, 1739 (C=O), 1437, 1410, 1267, 1207, 1124, 1081, 1026, 998, 965, 938, 899, 867, 828, 757 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.17–1.22 [m, 4 H, 2"(3")-H], 1.27 (ddtt, ^2J = 9 Hz, ^3J = 5 Hz, ^5J = 2.1 Hz, ^5J = 2.1 Hz, 1 H, 3-H_{cis}), 1.46 (ddtt, ^2J = 9 Hz, ^3J = 9 Hz, ^5J = 2.1 Hz, ^5J = 2.1 Hz, 1 H, 3-H_{trans}), 1.82 (dddtt, ^3J = 9 Hz, ^3J = 7.5 Hz, ^3J = 5 Hz, ^5J = 2.1 Hz, ^5J = 2.1 Hz, 1 H, 2-H), 2.88 (bs, 1 H, OH), 3.81 (s, 3 H, OCH_3), 3.82 (d, ^3J = 7.5 Hz, 1 H, 2'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 2.9 3.1 [–, C-2"(3")], 8.1 (–, C-3), 19.7 (+, C-2), 52.5 (+, OCH_3), 72.5 (+, C-2'), 110.1, 113.5 [C_{quat}, C-1(1")], 174.7 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 168 (5) [M^+], 167 (14) [M^+ – H], 151 (1) [M^+ – OH], 139 (3), 125 (3), 109 (22) [$M^+ - CO_2CH_3$], 108 (22) [$M^+ - CO - CH_3OH$], 95 (5), 91 (36) [$C_7H_7^+$], 81 (64) [$C_5H_5O^+$], 79 (100) [$C_6H_7^+$], 77 (62), 69 (30), 65 (34), 63 (15), 59 (50), 57 (23), 55 (18), 53 (76), 51 (55), 43 (27), 41 (84). – Anal. Calculated for $C_9H_{12}O_3$ (168.19): C 64.27, H 7.19. Found: C 64.04, H 6.96. *(S*,S*)*-**85** (R_f = 0.16). – Colorless prisms, m. p. 31–32 °C. – IR (film): ν = 3495 (OH), 3050, 2979, 2957, 2817, 1739 (C=O), 1437, 1410, 1267, 1229, 1207, 1130, 1086, 1020, 998, 965, 943, 910, 878, 856, 823, 762 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.17–1.23 [m, 4 H, 2"(3")-H], 1.33–1.47 (m, 2 H, 3-H), 1.88–1.98 (m, 1 H, 2-H), 2.46 (bs, 1 H, OH), 3.80 (s, 3 H, OCH_3), 4.06 (d, ^3J = 6 Hz, 1 H, 2'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 3.1 [–, C-2"(3")], 6.8 (–, C-3), 18.9 (+, C-2), 52.5 (+, OCH_3), 70.7 (+, C-2'), 110.1, 113.2 [C_{quat}, C-1(1")], 174.7 (C_{quat}, CO_2Me). – MS (70 eV, DCI, NH_3), *m/z* (%): 203 (3) [$M + NH_3 + NH_4^+$], 186 (100) [$M^+ + NH_4^+$]. – Anal. Calculated for $C_9H_{12}O_3$ (168.19): C 64.27, H 7.19. Found: C 64.12, H 6.89.

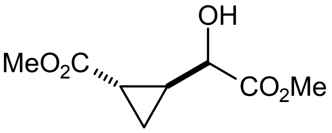
(S*,R*)



(S*,S*)

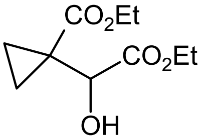


Methyl (1-ethoxycarbonylcycloprop-2-yl)hydroxyacetate (**86**). According to GP 5A, the



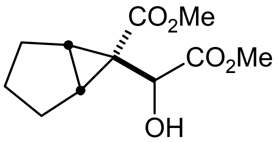
aldehyde **75** (11.56 g, 90 mmol) gave 7.4 g (44%) of **86** as a crude 1:1 mixture of diastereomers, which was used for the next step without additional purification. According to GP 5B, the aldehyde **75** (3.46 g, 27 mmol) gave 3.21 g (63%) of the crude **86**. An aliquot of this diastereomeric mixture (1.6 g) was subjected to column chromatography on 200 mL of silica gel, eluting with hexane/ethyl acetate, 5:1, to give the following fractions, which were monitored by GC. Fraction I: 400 mg of the first diastereomer (95% purity). – II: 1 g of a diastereomeric mixture. – III: 200 mg of the second diastereomer (96% purity). – *First diastereomer*. – Colorless oil. – IR (film): ν = 3479 (OH), 3012, 2957, 2908, 2853, 1728 (C=O), 1437, 1399, 1349, 1305, 1273, 1207, 1174, 1116, 1102, 1020, 982, 960, 940, 906, 866, 843,817, 773, 735 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.98–1.11 (m, 2 H, 3-H), 1.73–1.85 [m, 2 H, 1(2)-H], 2.89 (bs, 1 H, OH), 3.65 (s, 3 H, OCH$_3$), 3.80 (s, 3 H, OCH$_3$), 4.14 (d, ^3J = 4.2 Hz, 1 H, C-2'). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 10.2 (–, C-3), 16.4, 24.0 [+, C-1(2)], 51.8, 52.8 (+, OCH$_3$), 68.4 (+, C-2'), 174.0, 174.4 (C$_{quat}$, CO$_2$Me). – *Second diastereomer*. – Colorless prisms (recrystallyzed from hexane/*t*BuOMe), m. p. 59–60 °C. – IR (film): ν = 3473 (OH), 3012, 2957, 2908, 2853, 1734 (C=O), 1437, 1393, 1267, 1207, 1174, 1146, 1108, 1086, 1026, 982, 954, 927, 905, 866, 845, 779, 735, 680 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.09–1.24 (m, 2 H, 3-H), 1.70–1.84 [m, 2 H, 1(2)-H], 2.82 (bs, 1 H, OH), 3.66 (s, 3 H, OCH$_3$), 3.82 (s, 3 H, OCH$_3$), 3.99 (d, ^3J = 5.3 Hz, 1 H, 2'-H). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 11.6 (–, C-3), 16.1, 24.5 [+, C-1(2)], 51.8, 52.9 (+, OCH$_3$), 69.4 (+, C-2'), 173.9, 174.4 (C$_{quat}$, CO$_2$Me). – The following data were obtained for the diastereomeric mixture. – MS (70 eV, EI), *m/z* (%): 188 (1) [M$^+$], 157 (6) [M$^+$ – CH$_3$O], 129 (100) [M$^+$ – CO$_2$CH$_3$], 99 (12), 97 (96), 87 (8), 69 (33), 59 (21), 55 (17), 53 (3), 43 (5), 41 (27). – Anal. Calculated for C$_8$H$_{12}$O$_5$ (188.18): C 51.06, H 6.43. Found: C 50.81, H 6.63.

Ethyl (1-ethoxycarbonylcycloprop-1-yl)hydroxyacetate (**87**). According to GP 5B, the crude

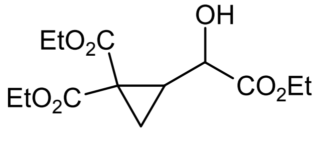


cyanohydrin (24 g, 142 mmol) obtained from the aldehyde **76** (22 g, 155 mmol) after work-up (the iminoester hydrochloride was hydrolyzed by stirring of the aqueous mixture for 16 h at ambient temperature) yielded 22.5 g (67%) of crude **87** as a colorless oil, which was used for the next step without additional purification. Flash chromatography of the crude product (0.5 g), eluting with pentane/diethyl ether, 10:1 to 5:1 with subsequent "Kugelrohr" distillation, gave 0.4 g of an analytical sample of **87** as a colorless oil. – IR (film): ν = 3496 (OH), 3109, 2983, 2948, 2916, 2885, 1734 (C=O), 1472, 1447, 1401, 1375, 1354, 1258, 1219, 1182, 1166, 1096, 1030, 987, 952, 919, 863, 757 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.00 – 1.39 [m, 4 H, 2(3)-H], 1.21(t, ^3J = 7.2 Hz, 3 H, CH_3), 1.28 (t, ^3J = 7.2 Hz, 3 H, CH_3), 2.92 (bs, 1 H, OH), 3.55 (s, 1 H, 2'-H), 4.05–4.16 (m, AB, 2 H, OCH_2), 4.19–4.32 (m, AB, 2 H, OCH_2). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.7 [–, C-2(3)*], 14.0, 14.1 (+, CH_3), 14.9 [–, C-2(3)*], 60.9 61.8 (–, OCH_2), 74.1 (+, C-2'), 172.9, 173.3 (C_{quat}, CO_2Et). – MS (70 eV, DCI, NH_3), *m/z* (%): 450.5 (1) [2M + NH_4^+], 234.2 (100) [M + NH_4^+], 217 (49) [M + H^+], 206 (6), 188 (2), 160 (7), 143 (14), 114 (9). – Anal. Calculated for $C_{10}H_{16}O_5$ (216.23): C 55.55, H 7.46. Found: C 55.34, H 7.40.

Methyl exo-(6-ethoxycarbonylbicyclo[3.1.0]hex-6-yl)hydroxyacetate (**88**). According to GP 5B, the crude cyanohydrine (13.6 g, 69.6 mmol) obtained from the aldehyde **77** (11.8 g, 70.2 mmol) after work-up (the iminoester hydrochloride was hydrolyzed by stirring the aqueous mixture for 16 h at ambient temperature) gave 14.9 g (94%) of crude **88** as a colorless oil, which was used for the next step without additional purification. flash" chromatography of the crude product (0.71 g), eluting with pentane/diethyl ether, 10:1 to 5:1, and subsequent "Kugelrohr" distillation gave 0.60 g (84%) of an analytical sample of **88** as a colorless oil. – IR (film): ν = 3487 (OH), 3029, 2953, 2865, 1736 (C=O), 1436, 1393, 1349, 1295, 1267, 1202, 1153, 1137, 1098, 1060, 1027, 989, 946, 853, 842, 706 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.91–1.11 (m, 1 H), 1.58–1.72 (m, 1 H), 1.75–1.90 (m, 5 H), 1.92–2.05 (m, 1 H, 1(5)*-H), 3.02 (bs, 1 H, OH), 3.60 (s, 1 H, 2'-H), 3.65 (s, 3 H, OCH_3), 3.79 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 23.2 (–, C-3), 25.9, 26.3 [–, C-2(4)], 30.0, 30.3 [+, C-1(5)], 36.9 (C_{quat}, C-6), 52.0, 52.7 (+, OCH_3), 75.3 (+, C-2'), 170.3, 173.4 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 228 (2) [M^+], 227 (3) [M^+ – H], 197 (2) [M^+ – CH_3O], 178 (10), 169 (33) [M^+ – CO_2CH_3], 159 (11), 137 (100), 118 (11), 109 (21), 91 (15), 81 (24) [$C_6H_9^+$], 79 (22) [$C_6H_7^+$], 77 (8) [$C_6H_5^+$], 72 (11), 67 (30), 53 (6), 41 (5). – Anal. Calculated for $C_{11}H_{16}O_5$ (228.24): C 57.88, H 7.07. Found: C 57.60, H 6.85.

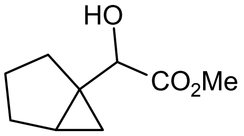


Ethyl [1,1-bis(ethoxycarbonyl)cycloprop-2-yl]hydroxyacetate (**89**). According to GP 5A, the aldehyde **80** (8.57 g, 40 mmol) gave 5.92 g (51%) of crude **89**. According to GP 5B, the aldehyde **80** (8.57 g, 40 mmol) gave 9.46 g (82%) of crude **89**, which was used for the next step without additional purification. A sample of 0.5 g of the crude **89** was subjected to

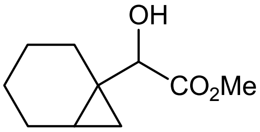


chromatography on silica gel, eluting with hexane/ethyl acetate, 5:1, to give 0.4 g (80%) pure () as a mixture of diastereomers (~65:35 according to ^{1}H NMR), which were not separated. It was not possible to obtain correct elemental analysis data because **89** partially underwent lactonization upon either column chromatography on silica gel or distillation under reduced pressure. In both cases formation of some amounts (5–10%) of diethyl 2-oxo-3-oxabicyclo[3.1.0]hexane-1,4-dicarboxylate was detected by GC and ^{1}H NMR spectroscopy. – IR (film): ν = 3490 (OH), 3100, 2985, 2941, 2908, 2875, 1734 (C=O), 1465, 1443, 1371, 1322, 1262, 1207, 1130, 1097, 1026, 938, 855, 784, 724, 702 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.22–1.32 (3 t, ^3J = 7.2 Hz, 9 H, CH_3), 1.35 (dd, ^3J = 9 Hz, ^2J = 5 Hz, 0.67 H, 3-H_{cis}), 1.49 (dd, ^3J = 9 Hz, ^2J = 5 Hz, 0.34 H, 3-H_{cis}), 1.69 (dd, ^3J = 7.2 Hz, ^2J = 5 Hz, 1 H, 3-H_{trans}), 2.13–2.22 (m, 1 H, 2-H), 2.87 (d, ^3J = 5.5 Hz, 0.68 H, OH), 3.09 (d, ^3J = 4.6 Hz, 0.26 H, OH), 3.96 (dd, ^3J = 8.2 Hz, ^3J = 4.6 Hz, 0.3 H, 2'-H), 4.09–4.32 (3 q, ^3J = 7.2 Hz, 6 H, OCH_2), 4.39 (dd, ^3J = 5.5 Hz, ^3J = 5.5 Hz, 0.77 H, 2'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.9, 14.0, 14.1 (+, CH_3), 15.6, 17.9 (–, C-3), 29.6, 30.4 (+, C-2), 32.4, 32.7 (C_{quat}, C-1), 61.5, 61.7, 61.8, 62.0, 62.3 (–, OCH_2), 66.6, 69.2 (+, C-2'), 167.6, 168.0, 169.4, 169.8, 172.8, 173.6 (C_{quat}, CO_2Et). – MS (70 eV, EI), *m/z* (%): 288 (1) [M^+], 243 (12) [$M^+ - C_2H_5O$], 215 (55) [$M^+ - CO_2C_2H_5$], 197 (6) [$M^+ - CO - C_2H_5OH - OH$], 173 (3), 169 (100) [$M^+ - C_2H_5OH - C_2H_5O - CO$], 157 (2), 141 (9), 127 (6), 123 (7), 113 (8), 99 (3), 97 (3), 95 (4), 85 (2), 69 (3), 68 (3), 41 (5).

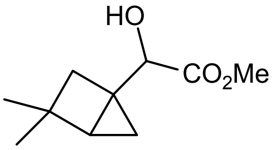
Methyl (bicyclo[3.1.0]hex-1-yl)hydroxyacetate (**91**) was prepared in two ways. *A).* Cyclopropanation of alkene **81** (23.4 g, 150 mmol) according to GP 6A yielded 24.4 g (95%) of pure **91** (>98% GC). *B).* According to GP 6B, the alkene **81** (74.7 g, 478 mmol) after distillation of the crude product gave 78 g (96%) of pure **91** as a colorless oil. – B. p. 62–63 °(2 mbar). – IR (film): ν = 3490, 3067, 3000, 2953, 2862, 1735 (C=O), 1438, 1273, 1226, 1201, 1085, 1026, 990, 946, 798, 776, 730 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.43–0.55 (m, 2 H, 6-H), 1.08–1.30 (m, 1 H), 1.36–1.81 (m, 6 H), 2.87 (bs, 1 H, OH), 3.79 (s, 3 H, OCH_3), 3.99 (s, 1 H, 2'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ =9.9 (–, C-6), 21.1 (–, C-3), 22.0 (+, C-5), 26.8 28.3 [–, C-2(4)], 31.6 (C_{quat}, C-1), 52.4 (+, OCH_3), 74.3 (+, C-2'), 175.0 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 170 (1) [M^+], 152 (25) [$M^+ - H_2O$], 137 (5), 120 (5), 111 (68) [$M^+ - CO_2Me$], 93 (25) [$M^+ - CO_2Me - H_2O$], 81 (100) [$C_6H_9^+$], 67 (68), 55 (15), 53 (8), 43 (10), 41 (14). – Anal. Calculated for $C_9H_{14}O_3$ (170.21): C 63.51, H 8.29. Found: C 63.28, H 7.99.



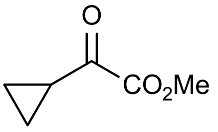
Methyl (bicyclo[4.1.0]hept-1-yl)hydroxyacetate (**92**). According to GP 6A, the alkene **82** (13.3 g, 78 mmol) after distillation of the crude product yielded 14 g (97%) of pure **92** as a colorless oil. – B. p. 61 – 62 °C (0.2 Torr). – IR (film): ν = 3487, 3061, 3001, 2930, 2857, 1734, 1454, 1432, 1245, 1212, 1094, 1064, 1023, 987 793 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.33 (dd, ^2J = 5.5 Hz, ^3J = 5.5 Hz, 1 H, 7-H$_{endo}$), 0.67 (dd, ^2J = 5.5 Hz, ^3J = 9.3 Hz, 1 H, 7-H$_{exo}$), 1.06–1.25 (m, 5 H), 1.53–1.70 (m, 3 H), 1.77–1.91 (m, 1 H), 2.91 (d, ^3J = 5.3 Hz, 1 H, OH), 3.43 (d, ^3J = 5.3 Hz, 1 H, 2'-H), 3,79 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 15.5 (+, C-6), 15.6 (–, C-7), 20.9 (–), 21.4 (–), 22.3 (C$_{quat}$, C-1), 23.1 (–), 24.5 (–), 52.4 (+, OCH_3), 78.8 (+, C-2'), 174.9 (C$_{quat}$, CO_2Me). – MS (70 eV, DCI, NH_3), *m/z* (%): 219 (3.2) [$M+NH_3+NH_4^+$], 201 (100) [$M+NH_3^+$], 184 (2.4) [M^+], 167 (2.4). – Anal. Calculated for $C_9H_{12}O_3$ (184.23): C 65,19, H 8,75. Found: C 65.40, H 8.80.



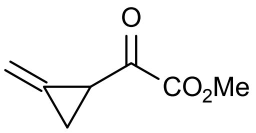
Methyl (3,3-dimethylbicyclo[2.1.0]pent-1-yl)hydroxyacetate (**93**). Alkene **83** (12.3 g, 72 mmol) was cyclopropanated according to GP 6B, but 2.5 mol of “Shi carbenoid” per 1 mol alkene was taken. It gave 17 g of crude product as yellow oil, which was purified by flash” chromatography on 100 mL of flash silica gel, eluting with pentane/ether, 10:1 to 5:1, to yield 12.7 g (95%) of **93**, as a mixture of diastereomers (7:4) contaminated with a small amount of the starting material (1.23% GC) and some unidentified product (2.5% GC). – Colorless oil. – IR (film): ν = 3484 (OH), 3056, 3026, 2956, 2930, 2864, 1738 (C=O), 1466, 1439, 1366, 1273, 1210, 1162, 1107, 1080, 1026, 1007, 990, 943, 909, 830, 777, 723 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.74–0.85 (m, 1 H), 0.78 (s, 3 H, CH_3), 0.94 (dd, *J* = 5 Hz, *J* = 1.8 Hz, 0.64 H), 0.99 (dd, *J* = 5 Hz, *J* = 1.8 Hz, 0.36 H), 1.13 (d, *J* = 11 Hz, 0.36 H), 1.19 (s, 1.9 H, CH_3), 1.23 (s, 1.1 H, Me), 1.30 (d, *J* = 11 Hz, 0.64 H), 1.50 (dd, *J* = 11 Hz, *J* = 2 Hz, 0.64 H), 1.53–1.61 (m, 1 H), 1.63 (dd, *J* = 11 Hz, *J* = 2 Hz, 0.36 H), 2.68 (d, ^3J = 6.5 Hz, 0.64 H, OH), 2.81 (d, ^3J = 6.5 Hz, 0.36 H, OH), 3.77 (s, 1.1 H, OCH_3), 3.80 (s, 1.9 H, OCH_3), 3.91 (d, ^3J = 6.5 Hz, 0.36 H, 2'-H), 4.06 (d, ^3J = 6.5 Hz, 0.64 H, 2'-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 17.1, 18.0 (–, C-5), 21.7 (C$_{quat}$, C-1), 22.6, 22.8 (+, CH_3), 28.2, 28.3 (+, C-4), 29.6, 29.8 (+, CH_3), 32.2, 32.3 (C$_{quat}$, C-3), 35.5, 37.3 (–, C-2), 52.2, 52.4 (+, OCH_3), 72.6, 72.7 (+, C-2'), 174.2, 174.5 (C$_{quat}$, CO_2Me). – MS (70 eV, DCI, NH_3), *m/z* (%): 219 (37) [$M + NH_3 + NH_4^+$], 202 (100) [$M + NH_4^+$], 166 (3), 149 (2), 123 (8), 106 (9). – Anal. Calculated for $C_{10}H_{16}O_3$ (184.23): C 65.19, H 8.75. Found: C 64.95, H 9.08.



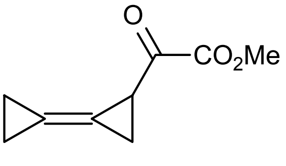
Methyl cyclopropyloxoacetate (**96**). A mixture of potassium cyclopropyloxoacetate (**95**) (7.61 g, 50 mmol), CH_3J (4 mL, 64 mmol) and anhydrous acetone (50 mL) was placed in a screw-capped Pyrex® bottle and was stirred at 80 °C for 16 h. The reaction mixture was cooled to ambient temperature, filtered through Celite®, which was subsequently washed with ether (50 mL). The solvents were evaporated at ambient pressure, and the residue was distilled under reduced pressure to give 3.78 g (59%) of pure **96**, the spectral data of which were identical to those reported in the literature.[82]



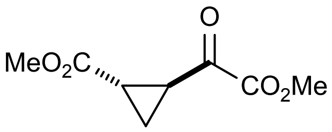
Methyl 2-methylenecyclopropyloxoacetate (**97**). According to GP 7, oxidation of crude **84** (6.2 g, 44 mmol) with active MnO_2 yielded 5.4 g (88%) of pure **97** as a colorless oil. An analytical sample was obtained by “Kugelrohr” distillation of crude **97**. – IR (film): ν = 3083, 3065, 3001, 2957, 2902, 2853, 1734 (C=O), 1715 (C=O), 1437, 1393, 1327, 1267, 1196, 1157, 1092, 1042, 1009, 965, 899, 839, 801, 724 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.89 (dddd, ^3J = 8.4 Hz, ^2J = 8.4 Hz, ^4J = 2.5 Hz, ^4J = 2.5 Hz, 1 H, 3-H_{trans}), 2.10 (dddd, ^2J = 8.4 Hz, ^3J = 5 Hz, ^4J = 2.5 Hz, ^4J = 2.5 Hz, 1 H, 3-H_{cis}), 3.30 (dddd, ^3J = 8.4 Hz, ^3J = 5 Hz, ^4J = 2.5 Hz, ^4J = 2.5 Hz, 1 H, 1-H), 3.89 (s, 3 H, OCH_3), 5.47 (ddd, ^4J = 2.5 Hz, ^4J = 2.5 Hz, ^4J = 2.5 Hz, 1 H), 5.53 (ddd, ^4J = 2.5 Hz, ^4J = 2.5 Hz, ^4J = 2.5 Hz, 1 H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.9 (–, C-3), 23.4 (+, C-1), 53.1 (+, OCH_3), 104.5 (–), 132.3 (C_{quat}, C-2), 161.2 (C_{quat}, CO_2Me), 191.1 (C_{quat}, CO). – MS (70 eV, EI), *m/z* (%): 140 (4) [M^+], 112 (2) [M^+ – CO], 109 (2) [M^+ – CH_3O], 81 (100) [M^+ – CO_2CH_3], 59 (8) [$CO_2CH_3^+$], 53 (64), [$C_4H_5^+$], 52 (6), 51 (7), 50 (4), 41 (1). – Anal. Calculated for $C_7H_8O_3$ (140.14): C 59.99, H 5.75. Found: C 59.69, H 5.50.



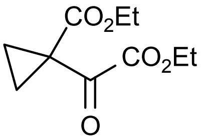
Methyl bicyclopropylidenyloxoacetate (**98**). According to GP 7, oxidation of crude **85** (13.87 g, 82 mmol) after distillation under reduced pressure gave 10.3 g (75%) of pure **98** as a slightly yellow oil, which crystallized at 0 °C. – B. p. 55–56 °C (0.1 Torr). – IR (film): ν = 3061, 2985, 2957, 2847, 1734 (CO_2Me), 1712 (C=O), 1437, 1411, 1349, 1278, 1229, 1196, 1155, 1087, 1071, 1015, 976, 933, 834, 811, 716 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.13–1.35 [m, 4 H, 2'(3')-H], 1.97 (ddtt, ^3J = 7.8 Hz, ^2J = 7.8 Hz, ^5J = 2.5 Hz, ^5J = 2.5 Hz, 1 H, 3-H_{trans}), 2.17 (ddtt, ^2J = 7.8 Hz, ^3J = 5 Hz, ^5J = 2.5 Hz, ^5J = 2.5 Hz, 1 H, 3-H_{cis}), 3.34 (ddtt, ^2J = 7.8 Hz, ^3J = 5 Hz, ^5J = 2.5 Hz, ^5J = 2.5 Hz, 1 H, 2-H), 3.85 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 3.7 4.2 [–, C-2'(3')], 15.4 (–, C-3), 23.7



(+, C-2), 52.9 (+, OCH_3), 112.4, 113.5 [C_{quat}, C-1(1')], 161.3 (C_{quat}, CO_2Me), 191.7 (C_{quat}, C=O). – MS (70 eV, DCI, NH_3), *m/z* (%): 184 (21) [$M + NH_4^+$], 167 (100) [$M + H^+$], 152 (2), 135 (5), 126 (8), 124 (1), 107 (3). – Anal. Calculated for $C_9H_{10}O_3$ (166.17): C 65.05, H 6.07. Found: C 64.82, H 6.11.

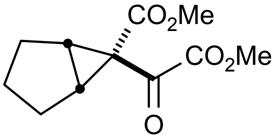


Methyl (1-methoxycarbonylcycloprop-2-yl)oxoacetate (**99**). According to GP 7, oxidation of crude **86** (7.4 g, 39 mmol) gave 5.2 g (71%) of **99** as a slightly yellow oil, which was used in the next step without additional purification. An a analytical sample was obtained by column chromatography of crude product (0.20 g) on silica gel (25 g) eluting with pentane/ether, 10:1 and subsequent “Kugelrohr” distillation. It gave 0.16 g (80%) of pure **99** as a colorless oil. – IR (film): ν = 3111, 3078, 3012, 2958, 2908, 2853, 1739 (CO_2Me), 1719 (C=O), 1441, 1404, 1343, 1275, 1209, 1174, 1087, 1053, 995, 931, 888, 847, 817, 784, 756, 718, 675 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.56 (ddd, ^3J = 9 Hz, ^3J = 5.8 Hz, ^2J = 3.5 Hz, 1 H, 3-H_{trans}), 1.64 (ddd, ^3J = 9 Hz, ^3J = 6.5 Hz, ^2J = 3.5 Hz, 1 H, 3-H_{cis}), 2.31 (ddd, ^3J = 9 Hz, ^3J = 6.5 Hz, ^3J = 4 Hz, 1 H, 1 H, 1-H), 3.23 (ddd, ^3J = 9 Hz, ^3J = 5.8 Hz, ^3J = 4 Hz, 1 H, 2-H), 3.69 (s, 3 H, OCH_3), 3.88 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.1 (–, C-3), 26.1 26.2 [+, C-1(2)*], 52.3 53.2 (+, OCH_3), 160.5 171.3 (C_{quat}, CO_2Me), 190.7 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 186 (2) [M^+], 155 (6) [$M^+ - CH_3O$], 128 (6), 127 (100) [$M^+ - CO_2CH_3$], 99 (9) [$M^+ - C_2H_4 - CO_2CH_3$], 95 (4), 71 (10), 59 (13), 55 (2), 41 (6). – Anal. Calculated for $C_8H_{10}O_5$ (186.16): C 51.61, H 5.41. Found: C 51.31, H 5.66.

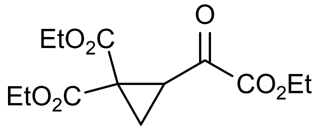


Ethyl (1-ethoxycarbonylcycloprop-1-yl)oxoacetate (**100**). Crude **87** (15 g, 69 mmol) was oxidized according to GP 7 to give 12.6 g (85%) of sufficiently pure **100** (according to NMR data) as a slightly yellow oil, which was used in the next step without further purification. An analytical sample was obtained as described above for compound **99**. – IR (film): ν = 3111, 2986, 2916, 2913, 2880, 1739 (C=O), 1718 (C=O), 1470, 1447, 1371, 1315, 1253, 1182, 1092, 1060, 1037, 1025, 956, 877, 858, 790, 750, 726 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.24 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.37 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.60–1.72 [m, AA’BB’, 4 H, 2(3)-H], 4.18 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 4.35 (q, ^3J = 7.2 Hz, 2 H, OCH_2). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.9 (+, CH_3), 20.5 [–, C-2(3)], 32.9 (C_{quat}, C-1), 61.6, 62.3 (–, OCH_2), 163.0, 169.8 (C_{quat}, CO_2Et), 191.8 (C=O). – MS (70 eV, DCI, NH_3), *m/z* (%): 446 (1) [$2M + NH_4^+$], 249 (37) [M + NH_3 + NH_4^+], 232 (100) [M + NH_4^+], 215 (2) [M + H^+], 181 (9), 164 (8), 147 (1). – Anal. Calculated for $C_{10}H_{14}O_5$ (214.22): C 56.07, H 6.59. Found: C 55.85, H 6.90.

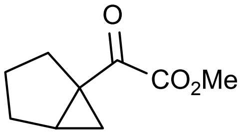
Methyl exo-(6-methoxycarbonylbicyclo[3.1.0]hex-6-yl)oxoacetate (**101**). Oxidation of crude **88** (11.7 g, 51 mmol) according to GP 7 gave 9.8 g (84%) of a colorless oil, pure according to its ^1H NMR data. An analytical sample was obtained by "Kugelrohr" distillation of crude **101**. – IR (film): ν = 3034, 2957, 2869, 1739, 1701, 1437, 1360, 1311, 1289, 1234, 1196, 1152, 1075, 1031, 1004, 982, 949, 905, 878, 856, 846, 817, 779, 751, 718 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.02–1.22 (m, 1 H), 1.66–1.81 (m, 1 H), 1.93–2.16 [m, 4 H, 2(4)-H), 2.32–2.38 (m, 2 H 1(5)-H], 3.75 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 22.4 (–, C-3), 26.7 [–, C-2(4)], 41.5 [+, C-1(5)], 43.3 (C_{quat}, C-6), 52.5 (+, OCH_3), 53.0 (+, CH_3), 161.7, 168.3 (C_{quat}, CO_2Me), 189.0 (C_{quat}, C=O). – MS (70 eV, DCI, NH_3), *m/z* (%): 470 (1) [2M + NH_4^+], 244 (100) [M + NH_4^+]. – Anal. Calculated for $C_{11}H_{14}O_5$ (226.23): C 58.40, H 6.24. Found: C 58.15, H 5.95.



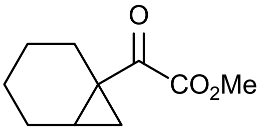
Ethyl [1,1-bis(ethoxycarbonyl)cycloprop-2-yl]oxoacetate (**102**). Crude **89** (5.92 g, 21 mmol) was oxidized according to GP 7 to give 4.7 g (78%) of sufficiently pure **102** (according to ^1H NMR data) as a colorless oil, which was successfully used in the next step without additional purification. An analytical sample was obtained as described above for compound **99**. – IR (film): ν = 3111, 2985, 2941, 2908, 2875, 1734 (C=O), 1720 (C=O), 1470, 1447, 1371, 1323, 1258, 1205, 1174, 1135, 1086, 1058, 1022, 860, 720, 691 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.22 (t, ^3J = 7.2 Hz, 3 H, CH_3) 1.26 (t, ^3J = 7.2 Hz, 3 H, CH_3) 1.36 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.81 (dd, ^3J = 8.4 Hz, ^2J = 4.5 Hz, 1 H, 3-H_{cis}), 2.04 (dd, ^3J = 7.2 Hz, ^2J = 4.5 Hz, 1 H, 3-H_{trans}), 3.56 (dd, ^3J = 8.4 Hz, ^3J = 7 Hz, 1 H, 2-H), 4.11–4.26 (m, 4 H, 2 OCH_2), 4.35 (q, ^3J = 7.2 Hz, 2 H, OCH_2). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.8, 13.9 (+, CH_3), 21.5 (–, C-3), 30.5 (+, C-2), 40.6 (C_{quat}, C-1), 62.0, 62.5, 62.9 (–, OCH_2), 159.9, 165.2, 168.0 (C_{quat}, CO_2Et), 188.9 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 286 (1) [M^+], 241 (5) [M^+ – C_2H_5O], 213 (88) [M^+ – $CO_2C_2H_5$], 185 (48) [M^+ – $CO_2C_2H_5$ – CO], 157 (100), 139 (56), 113 (8), 95 (17), 84 (11), 71 (11), 67 (27), 55 (20), 43 (11), 41 (12). – Anal. Calculated for $C_{13}H_{18}O_7$ (286.28): C 54.54, H 6.34. Found: C 54.62, H 6.10.



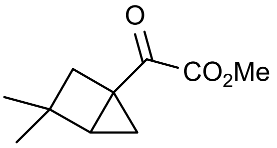
Methyl (bicyclo[3.1.0]hex-1-yl)oxoacetate (**103**) was obtained by oxidation of **91** in two ways. *A)* According to GP 3, alcohol **91** (78 g, 458 mmol) after distillation of the crude reaction mixture gave 75 g (97% yield) of pure product **103** as a slightly yellow liquid. *B)* Oxidation of crude **91** (22.8 g, 134 mmol) according to GP 7 yielded 18.7 g (83%) of sufficiently pure **103**. – B. p. 80–81 °C (2 mbar). – IR (film): ν = 3008, 2957, 2869, 1734 (C=O), 1684 (C=O), 1453, 1437, 1382, 1293, 1240, 1179, 1081, 1039, 1003, 929, 866, 794 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.14, (dd, ^2J = 5.5 Hz, ^3J = 5.5 Hz, 1 H, 6-H_{endo}), 1.18–1.36 (m, 1 H), 1.60–1.94 (m, 5 H), 2.08–2.22 (m, 1 H), 2.31–2.38 (m, 1 H), 3.79 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.0 (–, C-6), 20.4 (–, C-3), 26.5, 26.9 [–, C-2(4)], 33.9 (+, C-5), 39.3 (C_{quat}, C-1), 52.3 (+, OCH_3), 163.3 (C_{quat}, CO_2Me), 195.8 (C_{quat}, C=O). – MS (70 eV, EI), m/z (%): 168 (0.6) [M^+], 140 (2) [$M^+ - C_2H_4$], 109 (100) [$M^+ - CO_2CH_3$], 81 (81) [$C_6H_9^+$], 79 (41) [$C_6H_7^+$], 77 (12), 65(6), 59 (6), 53 (23), 51 (5), 41 (22). – Anal. Calculated for $C_9H_{12}O_3$ (168.19): C 64.27, H 7.19. Found: C 64.55, H 6.96.



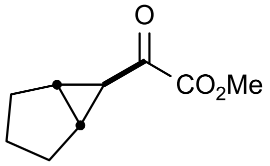
Methyl (bicyclo[4.1.0]hept-1-yl)oxoacetate (**104**). Oxidation of crude **92** (13.57 g, 74 mmol) according to GP 7 gave 11.1 g (83%) of sufficiently pure **104** as a colorless oil, which was used in the next step without additional purification. An analytical sample was obtained by “Kugelrohr” distillation of crude **104**. – Colorless liquid. – IR (film): ν = 3078, 3001, 2937, 2862, 1738 (C=O), 1688 (C=O), 1451, 1440, 1382, 1313, 1267, 1219, 1150, 1124, 1091, 1065, 1034, 1013, 954, 930, 894, 834, 795, 728, 639 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.95 (dd, ^3J = 6.5 Hz, ^2J = 4.5 Hz, 1 H, 7-H_{endo}), 1.09–1.43 (m, 4 H), 1.58–1.68 (m, 2 H), 1.74–1.98 (m, 3 H), 2.45 (m, 1 H), 3.82 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.7, 21.0, 23.0, 23.1, 23.4 (–), 25.5 (+, C-6), 29.2 (C_{quat}, C-1), 52.2 (+, OCH_3), 164.6 (C_{quat}, CO_2Me), 198.3 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 182 (2) [M^+], 124 (8), 123 (100) [$M^+ - CO_2CH_3$], 95 (52) [$M^+ - CO_2CH_3 - CO$], 79 (4) [$C_6H_7^+$], 77 (3) [$C_6H_5^+$], 67 (17), 55 (10), 53 (6), 41 (11). – Anal. Calculated for $C_{10}H_{14}O_3$ (182.22): C 65.91, H 7.74. Found: C 66.03, H 7.58.

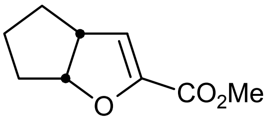


Methyl (3,3-dimethylbicyclo[2.1.0]pent-1-yl)oxoacetate (**105**). According to GP 3, the alcohol **93** (3.68 g, 20 mmol) gave a crude mixture, which was worked up as follows. The residue obtained after evaporation of the solvents under reduced pressure at ambient temperature, was triturated by stirring with a small amount of *t*BuOMe (about 10 mL) to start a triethylamine hydrochloride crystallization, diluted by stirring with a three fold excess of pentane, filtered and evaporated again under reduced pressure. It gave 3.6 g of a crude product (73% GC), which was used in the next step without additional purification. Attempts to purify the product by column chromatography caused only its complete decomposition. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.89 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3), 1.42 (d, ^2J = 11.3 Hz, 1 H, 2-H_{endo}), 1.77 (dd, ^3J = 5 Hz, ^2J = 3.5 Hz, 1 H, 5-H_{endo}), 2.10–2.20 (m, 2 H, 2-H_{exo}, 4-H), 2.77 (dd, ^3J = 6 Hz, ^2J = 3.5 Hz, 1 H, 5-H_{exo}), 3.78 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 23.2 (+, CH_3), 27.5 (–, C-5), 29.3 (C_{quat}, C-1), 29.5 (+, CH_3), 32.6 (C_{quat}, C-3), 36.1 (–, C-2), 45.8 (+, C-4), 52.4 (+, OCH_3), 161.8 (C_{quat}, CO_2Me), 192.5 (C_{quat}, C=O).

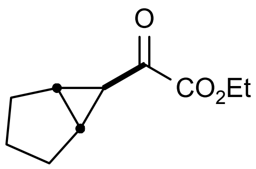


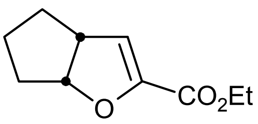
Methyl exo-(bicyclo[3.1.0]hex-6-yl)oxoacetate (**111**). Addition of methyl diazopyruvate (**106**) (19.8 g, 155 mmol) to cyclopentene (27 mL, 308 mmol) in the presence of 0.26 mol% of $Rh_2(OAc)_4$ (176 mg, 0.4 mmol) according to GP 8 gave 25.7 g of a slightly yellow oil, which was subjected to chromatography on 2 L of silica gel, eluting with pentane/diethyl ether, 10:1, to give 12.7 g (49%) of pure **111** (>98% purity according to GC) as a slightly yellow oil. Further elution with the same solvent gave 350 mg of pure (**119**) (>96% purity according to GC). – IR (film): ν = 3037, 2956, 2886, 2865, 1735 (C=O), 1706 (C=O), 1448, 1438, 1406, 1327, 1290, 1249, 1227, 1169, 1100, 1074, 1044, 1017, 992, 976, 935, 887, 843, 804, 754 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.20 (dtt, ^2J = 13.3 Hz, ^3J = 10.8 Hz, ^3J = 9 Hz, 1 H), 1.60–1.94 (m, 5 H), 2.10–2.13 [m, 2 H, 1(5)-H], 2.57 (t, ^3J = 2.8 Hz, 1 H, 6-H), 3.85 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.9 (–, C-3), 27.4 (+, C-6), 27.5 [–, C-2(4)], 35.9 [+, C-1(5)], 52.9 (+, OCH_3), 161.6 (C_{quat}, CO_2Me), 192.6 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 168 (2) [M^+], 109 (100) [$M^+ - CO_2CH_3$], 85 (2), 81 (26) [$M^+ - C_2H_3O_2 - CO$], 79 (8) [$C_6H_7^+$], 71 (3), 67 (2), 55 (3), 53 (7), 41 (6). – Anal. Calculated for $C_9H_{12}O_3$ (168.19): C 64.27, H 7.19. Found: C 64.51, H 6.92. – *Methyl 4,5,6,6a-tetrahydro-3aH-cyclopenta[b]furan-2-carboxylate* (**119**).– Colorless oil. – IR (film): ν = 3116, 2957, 2870, 1734 (C=O), 1629 (C=C), 1437, 1360, 1316, 1295, 1267, 1223, 1196, 1135, 1108, 1086,





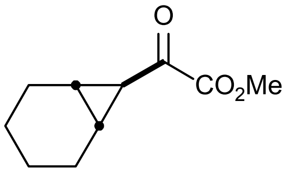
1015, 987, 943, 910, 888, 845, 817, 799, 773, 740 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.54–1.76 (m, 5 H), 2.05–2.12 (m, 1 H, 6-H), 3.45–3.53 (m, 1 H, 3a-H), 3.79 (s, 3 H, OCH_3), 5.14–5.20 (m, 1 H, 6a-H), 5.77 (d, ^3J = 3.1 Hz, 1 H, 3-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 23.2, 32.8, 35.4 (–), 47.4 (+, C-3a), 52.0 (+, OCH_3), 88.6 (+, C-6a), 114.5 (+, C-3), 148.0 (C_{quat}, C-2), 160.8 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 168 (16) [M^+], 139 (100) [$M^+ - C_2H_5$], 136 (20), 125 (14), 111 (6), 109 (67) [$M^+ - CO_2CH_3$], 97 (9), 95 (14), 81 (51) [$C_5H_5O^+$], 79 (30), 67 (23), 59 (14), 53 (20), 41 (25) [$C_3H_5^+$].



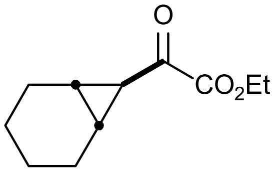


Ethyl exo-(bicyclo[3.1.0]hex-6-yl)oxoacetate (**112**). Addition of ethyl diazopyruvate (**12**) (14.2 g, 100 mmol) to cyclopentene (18 mL, 200 mmol) in the presence of 0.14 mol% of $Rh_2(OAc)_4$ (60 mg, 0.14 mmol) according to GP 8 gave 15.9 g of crude product as an oil, which was purified by column chromatography on 1 L of silica gel, eluting with hexane/*t*BuOMe, 20:1, to yield five fractions. – Fraction I: mixture of unidentified by-products (1.28 g). – II: 4.3 g (>60%) of **112**. – III: 1.25 g of **112** (80% purity). IV: 6.87 g (>97%) of **112**. – V: 0.25 g (about 90% pure) of **120**. The combined fractions II and III (5.75 g) were purified once more under the same conditions to yield 1.8 g of pure **112**. Total yield: 8.67 g (48%). – Slightly yellow oil. –IR (film): ν = 3041, 2963, 2946, 2868, 1728 (C=O), 1707 C=O), 1473, 1444, 1407, 1366, 1324, 1287, 1246, 1221, 1168, 1098, 1073, 1040, 1020, 991, 946, 888, 839, 806, 740 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.10–1.37 (m, 1 H), 1.36 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.60–1.97 (m, 5 H), 2.10–2.12 [m, 2 H, 1(5)-H], 2.56 (t, J = 2.8 Hz, 1 H, 6-H), 4.30 (q, ^3J = 7.2 Hz, 2 H, OCH_2). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.0 (+, CH_3), 20.0 (–, C-3), 27.3 (+, C-6), 27.5 [–, C-2(4)], 35.8 [+, C-1(5)], 62.3 (–, OCH_2), 161.3 (C_{quat}, CO_2Et), 193.0 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 182 (4) [M^+], 111 (8), 109 (100) [$M^+ - CO_2C_2H_5$], 81 (23), 79 (10) [$C_6H_7^+$], 67 (3), 55 (4), 53 (7), 41 (3). – MS (HR-EI): 182.0943 ($C_{10}H_{14}O_3$, calcd. 182.0943). *–Ethyl 4,5,6,6a-tetrahydro-3aH-cyclopenta[b]furan-2-carboxylate* (**120**). – Colorless oil. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.35 (t, ^3J = 7 Hz, 3 H, CH_3), 2.56–2.80 (m, 5 H), 2.04–2.14 (m, 1 H, 6-H), 3.43–3.54 (m, 1 H, 3a-H), 4.24 (q, ^3J = 7 Hz, 2 H, OCH_2), 5.12–5.21 (m, 1 H, 6a-H), 5.74 (d, ^3J = 3.8 Hz, 1 H, 3-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.1 (+, CH_3), 23.2, 32.7, 35.4 (–), 47.4 (+, C-3a), 61.0 (–, OCH_2), 88.5 (+, C-6a), 114.1 (+, C-3), 148.3 (C_{quat}, C-2), 160.4 (C_{quat}, CO_2Et).

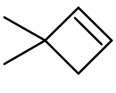
Methyl exo-(bicyclo[4.1.0]hept-7-yl)oxoacetate (**113**). Addition of methyl diazopyruvate (25.6 g, 200 mmol) to cyclohexene (50 mL, 500 mmol) in the presence of 0.31 mol% of $Rh_2(OAc)_4$ (0.28 g, 0.63 mmol) according to GP 8 gave 31 g of crude product as a yellow oil, which was separated into four fractions by column chromatography on 2 L of silica gel, eluting with hexane/*t*BuOMe, 10:1, as analyzed by GC. – Fraction I: 2.16 g (92% purity) of 3-(cyclohexen-1-yl)pyruvic acid methyl ester (**118**). – II: 1 g containing **113** (50%) and some unidentified products (~50% total). – III: 2.8 g (73% purity) of **113**.– IV: 19.9 g (55%) of **113** (> 99.5% purity). – IR (film): ν = 3011, 2935, 2860, 1734 (C=O), 1703 (C=O), 1449, 1413, 1306, 1259, 1203, 1172, 1152, 1100, 1077, 1037, 1017, 973, 950, 890, 843, 779, 755, 720 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.24–1.36 (m, 4 H), 1.68–1.79 (m, 2 H), 1.85–1.95 (m, 4 H), 2.58 (t, ^3J = 3.4 Hz, 1 H, 7-H), 3.86 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 20.7 [–, C-3(4)], 23.1 [–, C-2(5)], 30.5 [+, C-1(6)], 32.1 (+, C-7), 52.9 (+, OCH_3), 161.7 (C_{quat}, CO_2Me), 193.1 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 182 (1) [M^+], 123 (100) [$M^+ - CO_2CH_3$], 95 (45) [$C_7H_{11}^+$], 93 (4) [$C_7H_9^+$], 91 (3) [$C_7H_7^+$], 81 (19) [$C_6H_9^+$], 79 (19) [$C_6H_7^+$], 77 (6) [$C_6H_5^+$], 67 (39), 66 (5), 65 (5), 59 (4), 55 (61), 53 (20), 51 (4), 41 (42). – MS (HR-EI): 182.0943 ($C_{10}H_{14}O_3$, calcd. 182.0943).



Ethyl exo-(bicyclo[4.1.0]hept-7-yl)oxoacetate (**114**). Addition of ethyl diazopyruvate (14.2 g, 100 mmol) to cyclohexene (20 mL, 200 mmol) in the presence of 0.14 mol% of $Rh_2(OAc)_4$ (60 mg, 0.14 mmol) according to GP 8 gave 18.5 g of crude product as a yellow oil, which was subsequently purified by column chromatography on 850 mL of silica gel, eluting with hexane/*t*BuOMe, 20:1, to yield 9.6 g (49%) of pure **114**, the spectral data of which were identical to those reported in the literature.[87, 88]



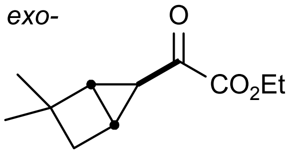
3,3-Dimethylcyclobutene-1 (**108**). To a stirred solution of *t*BuOK (52 g, 460 mmol) in anhydrous DMSO (460 mL), kept at 20 °C (cold water bath) under nitrogen, was added 1-bromo-3,3-dimethylcyclobutane (**121**) (49.3 g, 300 mmol) in one portion. The mixture was stirred at ambient temperature for 20 min, the volatile material was "bulb-to-bulb" distilled (T_{bath} 50 °C/20 Torr) into a −78 °C (dry ice/acetone bath) cold, pointed-bottom Schlenk flask. After the distillation was complete, the crude product was transferred by *cannula* from the cooled collecting flask into a separating funnel, washed with water (2 × 20 mL), brine (10 mL) and placed in a storage bottle containing a small amount of BHT (~10



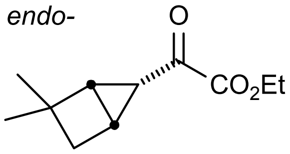
mg) and molecular sieves 4 Å (~1 g). The colorless liquid weighed 21.9 g (88%), it was pure 3.3-dimethylcyclobutene-1 (**108**) according to its ^{1}H NMR spectrum. – *d^2* 0.706. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.19 (s, 6 H, 2CH$_3$), 2.25 (d, ^3J = 1 Hz, 2 H, 4-H), 5.99 (dt, ^3J = 2.8 Hz, ^3J = 1 Hz, 1 H, 1-H), 6.09 (d, ^3J = 2.8 Hz, 1 H, 2-H). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 26.5 (+, 2CH$_3$), 44.6 (–), 44.9 (C$_{\text{quat}}$), 132.0 (+, CH, C–1), 146.5 (+, CH, C–2).

Ethyl (2,2-dimethylbicyclo[2.1.0]pent-5-yl)oxoacetate (**115**). Addition of ethyl diazopyruvate (24.4 g, 172 mmol) to 3,3-dimethylcyclobutene (**108**) (25 mL, 215 mmol) in the presence of 0.39 mol% of Rh$_2$(OAc)$_4$ (300 mg, 0.68 mmol) according to GP 8 gave 29.1 g of crude product as a yellow oil, which was separated by column chromatography on 2 L of silica gel, eluting with hexane/*t*BuOMe, 20:1, to yield 2.27 g of an intermediate fraction containing about 70% of **115** and 11.7 g (35%) of pure **115** (purity >98% according to GC) as a 3.8:1 mixture of *exo-* and *endo-* isomers. A small amount (250 mg) of pure *exo*-**115** was isolated by column chromatography of an aliquot of the mixture of *exo-* and *endo*-isomers (2 g) on 200 g of silica gel under the same conditions as above, but only from the latest fractions. – *exo*-**115**. – IR (film): ν = 3039, 2959, 2930, 2867, 1733 (C=O), 1712 (C=O), 1465, 1443, 1385, 1368, 1303, 1271, 1240, 1146, 1082, 1030, 1015, 986, 938, 914, 880, 834, 790, 739 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.90 (s, 3 H, CH$_3$), 1.29 (s, 3 H, CH$_3$), 1.37 (t, ^3J = 4 Hz, 3 H, CH$_3$), 1.42 (d, ^2J = 11.5 Hz, 1 H, 3-H$_{endo}$), 1.79 (ddd, ^2J = 11.5, ^3J = 4 Hz, ^4J = 0.5 Hz, 1 H, 3-H$_{exo}$), 2.10 (dd, ^3J = 4.8 Hz, ^4J = 0.5 H, 1 H, 1-H), 2.17 (dd, ^3J = 4.8 Hz, ^3J = 4 Hz, 1 H, 4-H), 4.33 (q, ^3J = 4 Hz, 2 H, OCH$_2$). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 14.0 (+, CH$_3$), 23.3 (+, CH$_3$), 26.4 (+, CH), 29.5 (+, CH$_3$), 34.1 (+, CH), 36.3 (C$_{\text{quat}}$), 38.1 (–, C-3), 41.8 (+, CH), 62.4 (–, OCH$_2$), 161.0 (C$_{\text{quat}}$, CO$_2$Et), 192.3 (C$_{\text{quat}}$, C=O). – MS (70 eV, DCI, NH$_3$), *m/z* (%): 410 (4) [2M + NH$_4^+$], 231 (19), [M + NH$_3$ + NH$_4^+$], 214 (100) [M + NH$_4^+$], 185 (1) [M + NH$_4^+$ – C$_2$H$_5^+$], 135 (2), 95 (1). – Anal. Calculated for C$_{11}$H$_{16}$O$_3$ (196.24): C 67.32, H 8.22. Found: C 67.19, H 7.96.

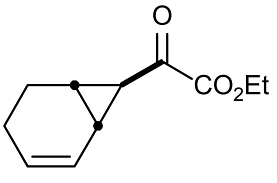
exo-



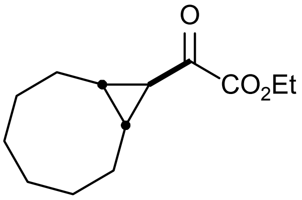
endo-



Ethyl exo-(bicyclo[4.1.0]hept-2-en-7-yl)oxoacetate (**116**). Addition of ethyl diazopyruvate (10.0 g, 70 mmol) to 1,3-cyclohexadiene (13 mL, 137 mmol) in the presence of 0.32 mol% of $Rh_2(OAc)_4$ (100 mg, 0.22 mmol) according to GP 8 gave 10.7 g of crude product as a yellow oil, which was subjected to chromatography on 1 L of silica gel, eluting with hexane/*t*BuOMe, 20:1, to yield 7.9 g (58%) of pure **116**. – IR (film): ν = 3039, 2985, 2936, 2852, 1728, 1703, 1638, 1473, 1445, 1420, 1393, 1370, 1295, 1258, 1236, 1196, 1089, 1043, 1015, 961, 928, 858, 802, 757, 746, 684 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.35 (t, ^3J = 7.1 Hz, 3 H, CH_3), 1.63–2.23 (m, 6 H), 3.02 (m, 1 H, 7-H), 4.31 (q, ^3J = 7.1 Hz, 2 H, OCH_2), 5.58–5.66 [m, 1 H, 2(3)*-H], 5.92–5.60 [m, 1 H, 2(3)*-H]. – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.0 (+, CH_3), 17.9, 20.3 [–, C-4 (5)*], 28.3, 30.1 [+, C-1 (6)*], 30.9 (+, C-7), 62.4 (–, OCH_2), 124.9, 126.3 [+, C-2 (3)*], 161.0 (C_{quat}, CO_2Et), 191.8 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 194 (7) [M^+], 179 (2) [$M^+ - CH_3$], 165 (4), [$M^+ - C_2H_5$], 148 (6), 147 (7), 121 (73), 120 (48), 116 (15), 103 (14), 93 (100), 91 (64), 79 (34) [$C_6H_7^+$], 77 (57) [$C_6H_5^+$], 65 (13), 55 (27), 41 (7). – MS (HR-EI): 194.0943 ($C_{11}H_{14}O_3$, calcd. 194.0943).

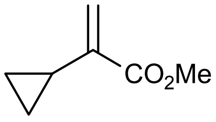


Ethyl exo-(bicyclo[6.1.0]non-9-yl)oxoacetate (**117**). Addition of ethyl diazopyruvate (14.2 g, 100 mmol) to cyclooctene (26 mL, 200 mmol) in the presence of 0.27 mol% of $Rh_2(AcO)_4$ (120 mg, 0.27 mmol) according to GP 8 gave 16.9 g of crude product as a yellow oil, from which excess cyclooctene was "bulb-to-bulb" distilled off at 60 °C/0.1 Torr, and the residue was subjected to chromatography on 1.5 L of silica gel, eluting with hexane/*t*BuOMe, 20:1, to yield 5.79 g of pure **117** and 6.5 g of crude product (~60% of **117** according to GC). The latter was purified on 700 mL of silica gel under the same conditions to give 2.12 g of pure **117**. Total yield: 7.91 g (35%). – IR (film): ν = 2988, 2925, 2852, 1749 (C=O), 1730 (C=O), 1704 (C=O), 1468, 1446, 1430, 1394, 1369, 1353, 1318, 1303, 1269, 1253, 1203, 1160, 1110, 1086, 1021, 978, 933, 881, 862, 828, 787, 756, 726 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.12–1.33 (m, 2 H), 1.32–1.44 (m, 4 H), 1.36 (t, ^3J = 7 Hz, 3 H, CH_3), 1.53–1.74 (m, 6 H), 2.01–2.06 (m, 1 H), 2.07–2.12 (m, 1 H), 2.29 (t, ^3J = 4 Hz, 1 H, 9-H), 4.31 (q, ^3J = 7 Hz, 2 H, OCH_2). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.0 (+, CH_3), 26.1, 26.3, 28.9 (–), 32.1 (+, C-9), 34.9 [+, C-1(8)], 62.3 (–, OCH_2), 161.3 (C_{quat}, CO_2Et), 193.2 (C_{quat}, C=O). – MS (70 eV, EI), *m/z* (%): 224 (1) [M^+], 151 (100) [$M^+ - CO_2C_2H_5$], 133 (2), 123 (2) [$C_9H_{15}^+$], 109 (3), 107 (3), 95 (3) [$C_7H_{11}^+$], 91 (3) [$C_7H_7^+$], 81 (20)

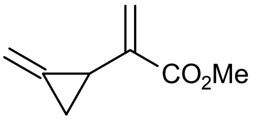


$[C_6H_9^+]$, 79 (5) $[C_6H_7^+]$, 77 (2) $[C_6H_5^+]$, 67 (14) $[C_5H_7^+]$, 55 (21) $[C_4H_7^+]$, 53 (6), 41 (13) $[C_3H_5^+]$.– MS (HR-EI): 224.1413 ($C_{13}H_{20}O_3$, calcd. 224.1413).

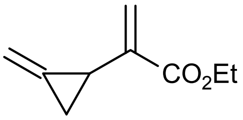
Methyl 2-cyclopropylpropenoate (**122**). Oxoester **96** (7.7 g, 60 mmol) was converted to the corresponding methyl 2-cyclopropyl acrylate **122** according to GP 9A. The 5.6 g (74%) of **122** obtained as a colorless liquid had the same physical properties and spectral data as reported in the literature.[82]



Methyl 2-(2-methylenecyclopropyl)propenoate (**123**). Methylenation of the oxoester **97** (5.4 g, 39 mmol) according to GP 9A gave 3.66 g of crude product, which was purified by column chromatography on 300 mL of silica gel, eluting with pentane/ether, 20:1, to yield 3.5 g (65%) of pure **123** as a colorless liquid. – IR (film): ν = 3078, 3049, 2996, 2952, 2908, 2847, 1728 (C=O), 1624 (C=C), 1437, 1393, 1338, 1267, 1253, 1190, 1146, 1092, 1059, 1026, 993, 943, 894, 861, 812, 751, 702 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.22 (dddd, ^2J = 8.6 Hz, ^3J = 5 Hz, ^4J = 2.5 Hz, ^4J = 2 Hz, 1 H, 3-H_{cis}), 1.60 (dddd, ^3J = 9.1 Hz, ^2J = 8.6 Hz, ^4J = 2.5 Hz, ^4J = 2 Hz, 1 H, 3-H_{trans}), 2.41 (ddddd, ^3J = 9.1 Hz, ^3J = 5 Hz, ^4J = 2.5 Hz, ^4J = 2 Hz, ^4J = 1.3 Hz, 1 H, 1-H), 3.79 (s, 3 H, OCH_3), 5.49 (dd, ^2J = 1.2 Hz, ^4J = 1.3 Hz, 1 H, 3'-H_{trans}), 5.51–5.55 (m, 2 H, 1''-H), 6.05 (d, ^2J = 1.2 Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.4 (–, C-3), 16.4 (+, C-1), 52.0 (+, OCH_3), 105.0 (–, C-1''), 122.8 (–, C-3'), 133.4 (C_{quat}, C-2), 139.9 (C_{quat}, C-2'), 167.3 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 138 (39) $[M^+]$, 137 (24) $[M^+ - H]$, 123 (3) $[M^+ - CH_3]$, 110 (6), 108 (4), 107 (59) $[M^+ - OCH_3]$, 105 (10), 95 (4), 93 (4), 91 (3), 80 (8), 79 (100), 77 (93), 67 (4), 65 (2), 63 (3), 59 (12), 53 (11), 51 (17), 41 (3). – Anal. Calculated for $C_8H_{10}O_2$ (138.16): C 69.54, H 7.30. Found: C 69.30, H 7.32.

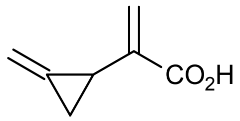


Ethyl 2-(2-methylenecyclopropyl)propenoate (**141**) was prepared from the aldehyde **50** (10.1 g 123 mmol) by subsequent applying of GP 5A, GP 7 and GP 9B without purification of intermediate products. It was obtained 8.26 g of crude product, which was purified by column chromatography on 1 L of silica gel, eluting with pentane/ether, 20:1, to give 7.49 g (overall yield: 40%) of pure **141** as a colorless liquid. – IR (film): ν = 3078, 3050, 2982, 2941, 2908, 2875, 1718 (C=O), 1628 (C=C), 1447, 1399, 1371, 1339, 1265, 1250, 1147, 1094, 1028, 944, 892, 867, 813, 749, 703 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.02 (dddd, ^2J = 8.6 Hz, ^3J = 5 Hz, ^4J = 2.5 Hz, ^4J = 2 Hz, 1 H, 3-H_{cis}), 1.31 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.58 (dddd, ^3J = 9.1 Hz, ^2J = 8.6 Hz, ^4J =

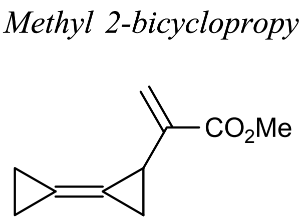


2.5 Hz, $^4J = 2$ Hz, 1 H, 3-H$_{trans}$), 2.41 (ddddd, $^3J = 9.1$ Hz, $^3J = 5$ Hz, $^4J = 2.5$ Hz, $^4J = 2$ Hz, $^4J = 1.3$ Hz, 1 H, 1-H), 4.23 (q, $^3J = 7.2$ Hz, 2 H, OCH$_2$), 5.46 (dd, $^2J = 1.2$ Hz, $^4J = 1.3$ Hz, 1 H, 3'-H$_{trans}$), 5.48–5.54 (m, 2 H, 1''-H), 6.04 (d, $^2J = 1.2$ Hz, 1 H, 3'-H$_{cis}$). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 13.3 (–, C-3), 14.2 (+, CH$_3$), 16.4 (+, C-1), 60.8 (–, OCH$_2$), 104.8 (–, C-1''), 122.4 (–, C-3'), 133.5 (C$_{quat}$, C-2), 140.2 (C$_{quat}$, C-2'), 166.8 (C$_{quat}$, CO$_2$Et). – MS (70 eV, EI), *m/z* (%): 152 (10) [M$^+$], 124 (29) [M$^+$ – C$_2$H$_4$], 123 (42) [M$^+$ – C$_2$H$_5$], 107 (52) [M$^+$ – C$_2$H$_5$O], 96 (10), 95 (8), 79 (100) [C$_6$H$_7$$^+$], 77 (74) [C$_6H_5$$^+$], 67 (4), 53 (11), 51 (12), 41 (4). – Anal. Calculated for C$_9$H$_{12}$O$_2$ (152.19): C 71.03, H 7.95. Found: C 70.84, H 7.79.

2-(2-Methylenecyclopropyl)propenoic acid (**159**). Hydrolysis of ethyl 2-(2-methylenecyclopropyl)propenoate (**141**) (800 mg, 5.2 mmol) according to GP 10 gave 650 mg (99%) of **159** as a colorless liquid, which showed any impurities in its ^{1}H NMR spectra and therefore was used for the esterification without additional purification. An analytical sample was obtained by "Kugelrohr" distillation of the crude product (30 mg). – IR (film): ν = 3078 (OH), 2996, 2913, 2880, 2666, 2600, 2557, 1701 (C=O), 1624 (C=C), 1432, 1338, 1278, 1157, 1119, 1092, 1031, 949, 889, 817, 784, 757, 735, 691 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.07 (dddd, $^2J = 8.6$ Hz, $^3J = 5$ Hz, $^4J = 2.5$ Hz, $^4J = 2$ Hz, 1 H, 3-H$_{cis}$), 1.63 (dddd, $^3J = 9.1$ Hz, $^2J = 8.6$ Hz, $^4J = 2.5$ Hz, $^4J = 2$ Hz, 1 H, 3-H$_{trans}$), 2.43 (ddddd, $^3J = 9.1$ Hz, $^3J = 5$ Hz, $^4J = 2.5$ Hz, $^4J = 2$ Hz, $^4J = 1.3$ Hz, 1 H, 1-H), 5.53–5.59 (m, 2 H, 1''-H), 5.63 (dd, $^2J = 1.2$ Hz, $^4J = 1.3$ Hz, 1 H, 3'-H$_{trans}$), 6.22 (d, $^2J = 1.2$ Hz, 1 H, 3'-H$_{cis}$), 12.04 (bs, 1 H, OH). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 13.4 (–, C-3), 16.1 (+, C-1), 105.2 (–, C-1''), 125.1 (–, C-3'), 133.2 (C$_{quat}$, C-2), 139.5 (C$_{quat}$, C-2'), 172.5 (C$_{quat}$, CO$_2$H). – MS (70 eV, EI), *m/z* (%): 124 (34) [M$^+$], 123 (18) [M$^+$ – H], 120 (11), 119 (36), 117 (39), 105 (5), 95 (9), 84 (3), 82 (6), 79 (100) [M$^+$ – H – CO$_2$], 77 (54) [C$_6$H$_5$$^+$], 67 (3), 53 (9), 51 (14), 47 (4), 41 (2).

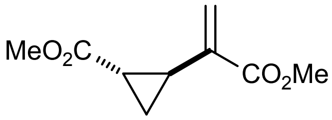


Methyl 2-bicyclopropylidenylpropenoate (**124**). Methylenation of the oxoester **98** (6.5 g, 39 mmol) according to GP 9A, after subsequent flash" chromatography of the crude product on 100 mL of flash silica gel, eluting with pentane/ether, 20:1, gave 5.17 g (80%) of pure **124** as a slightly yellow oil. – IR (film): ν = 3111, 3050, 2981, 2952, 2908, 2842, 1723 (C=O), 1624 (C=C), 1437, 1413, 1357, 1282, 1251, 1194, 1143, 1086, 1067, 1019, 996, 961, 938, 878, 857, 834, 814, 783, 746, 694 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.04–1.12 (m, 1 H, 3-H$_{cis}$), 1.16–1.27 (m, 4 H, 2''(3'')-H), 1.64–1.75 (m, 1 H, 3-H$_{trans}$), 2.45–2.54

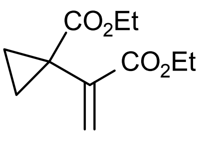


(m, 1 H, 2-H), 3.78 (s, 3 H, OCH_3), 5.41 (m, 1 H, 3'-H_{trans}), 6.02 (m, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 3.0, 3.2 [–, C-2"(3")], 13.8 (–, C-3), 16.7 (+, C-2), 51.8 (+, OCH_3), 112.5, 112.8 [C_{quat}, C-1(1")], 123.0 (–), 140.4 (C_{quat}, C-2'), 167.4 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 164 (17) [M^+], 149 (10) [$M^+ - CH_3$], 136 (8) [$M^+ - C_2H_4$], 133 (13) [$M^+ - CH_3O$], 121 (8), 105 (100) [$M^+ - CH_3O - CO$], 104 (26) [$M^+ - CH_3OH - CO$], 103 (25) [$M^+ - CH_3OH - CO - H$], 91 (10) [$C_7H_7^+$], 79 (27) [$C_6H_7^+$], 77 (31) [$C_6H_5^+$], 65 (10), 59 (6), 53 (6), 51 (12), 41 (2). – Anal. Calculated for $C_{10}H_{12}O_2$ (164.20): C 73.15, H 7.37. Found: C 73.02, H 7.15.

Methyl 2-(1-methoxycarbonylcycloprop-2-yl)propenoate (**126**). Methylenation of oxoester **99** (5.4 g 29 mmol) according to GP 9A yielded 2.41 g (44%) of **126**. According to GP 9B, 4.7 g (25 mmol) of **99** gave after flash" chromatography of the crude mixture on 100 mL of flash" silica gel, eluting with pentane/ether, 10:1, 3.64 g (79%) of pure **126** as a colorless oil. – IR (film): ν = 3001, 2955, 2949, 2853, 1729 (C=O), 1629 (C=C), 1439, 1393, 1344, 1273, 1207, 1175, 1135, 1086, 1058, 991, 935, 843, 814, 743 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.15 (ddd, ^3J = 8.5 Hz, ^3J = 6.8 Hz, ^2J = 4.5 Hz, 1 H, 3-H_{cis}), 1.41 (ddd, ^3J = 9.3 Hz, ^3J = 4.8 Hz, ^2J = 4.5 Hz, 1 H, 3-H_{trans}), 1.73 (ddd, ^3J = 8.5 Hz, ^3J = 4.8 Hz, ^3J = 4.8 Hz, 1 H, 2-H), 2.33 (ddd, ^3J = 9.3 Hz, ^3J = 6.8 Hz, ^3J = 4.8 Hz, 1 H, 1-H), 3.69 (s, 3 H, OCH_3), 3.76 (s, 3 H, OCH_3), 5.43 (s, 1 H, 3'-H_{trans}), 6.14 (s, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 15.1 (–, C-3), 22.0, 22.6 [+, C-1(2)], 51.9, 52.0 (+, OCH_3), 123.7 (–, C-3'), 139.0 (C_{quat}, C-2'), 166.6 (C_{quat}, C-1'), 173.5 (C_{quat}, C-1"). – MS (70 eV, EI), *m/z* (%): 184 (8) [M^+], 169 (2) [$M^+ - CH_3$], 153 (44) [$M^+ - OCH_3$], 152 (100) [$M^+ - CH_3OH$], 142 (2), 129 (6), 125 (31) [$M^+ - CO_2CH_3$], 124 (57) [$M^+ - CO_2CH_3 - H$], 109 (7), 108 (6), 97 (11), 96 (17), 93 (58), 81 (9), 79 (16), 75 (10), 64 (19), 65 (30), 59 (57) [CO_2Me^+], 55 (14), 53 (13), 41 (14). – MS (HR-EI): 184.0736 ($C_9H_{12}O_4$, calcd. 184.0736).

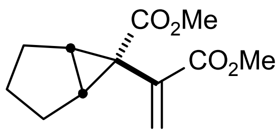


Ethyl 2-(1-ethoxycarbonylcycloprop-1-yl)propenoate (**127**). Oxoester **100** 7.5 g (35 mmol) was converted into **127** according to GP 9. A crude product (6.8 g) was subjected to column chromatography on 650 mL of silica gel, eluting with hexane/*t*BuOMe, 10:1, to give 5.4 g (73%) of pure **127** as a colorless oil. – IR (film): ν = 3105, 2983, 2941, 2908, 2875, 1724 (C=O), 1636 (C=C), 1465, 1447, 1419, 1369, 1333, 1302, 1233, 1184, 1115, 1030, 969, 862, 816, 757, 734, 695 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.98–1.03 [m, AA', 2 H, 2(3)*-H], 1.18 (t, ^3J = 7.2 Hz, 3 H, CH_3),



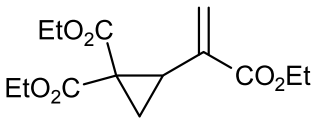
1.28 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.45–1.49 [m, BB', 2 H, 2(3)*-H], 4.09 (q, ^3J = 7.2 Hz, 2 H, CH_3), 4.21 (q, ^3J = 7.2 Hz, 2 H, CH_3), 5.58 (d, ^2J = 1 Hz, 1 H, 3'-H_{trans}), 6.26 (d, ^2J = 1 Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.0, 14.1 (+, CH_3), 16.2 [–, C-2(3)], 26.3 (C_{quat}, C-1), 60.7, 61.0 (–, OCH_2), 125.9 (–, C-3'), 139.7 (C_{quat}, C-2'), 166.4 (C_{quat}, C-1'), 173.4 (–, CO_2Et). – MS (70 eV, EI), *m/z* (%): 212 (30) [M^+], 184 (6) [$M^+ - C_2H_4$], 183 (40) [$M^+ - C_2H_5$], 167 (46) [$M^+ - C_2H_5O$], 168 (19) [$M^+ - C_2H_5OH$], 155 (27), 139 (46) [$M^+ - CO_2C_2H_5$], 138 (100) [$M^+ - CO_2C_2H_5 - H$], 125 (7), 111 (17), 110 (19), 97 (2), 93 (9), 82 (13), 69 (3), 67 (12), 66 (21), 65 (18), 55 (7), 43 (6), 41 (6). – MS (HR-EI): 212.1048 ($C_{11}H_{16}O_4$, calcd. 212.1048).

Methyl 2-(6-carbomethoxycarbonylbicyclo[3.1.0]hex-6-yl)propenoate (**128**). Methylenation of the oxoester **101** (7.9 g, 35 mmol) according to GP 9B yielded only 1.5 g (19%) of **128** along with most of the starting material being recovered. Therefore, an improved protocol to methylenate **101** was developed. To an oven-dried 25-mL flask charged with methyltriphenylphosphonium bromide (0.82 g, 2.3 mmol) under argon was added all at once with stirring a freshly prepared solution of *t*BuOK (0.25 g, 2.2 mmol) in anhydrous THF (10 mL) at ambient temperature. After additional stirring at room temperature for 1 h, the ylide solution was cooled to –30 °C and oxoester () (0.45 g, 2 mmol) dissolved in the same solvent (2 mL) was added dropwise, keeping the temperature of the reaction mixture under –20 °C and continued stirring at this temperature for an additional 1 h. Then, the cooling bath was removed, and stirring was continued at ambient temperature for 16 h. The reaction was with a few drops of acetic acid. The major part of the solvents was removed under reduced pressure at ambient temperature. The residue was suspended in *t*BuOMe (10 mL) under stirring, poured into pentane (20 mL), and the mixture was filtered. The residue obtained after evaporation of the solvents from the filtrate was subjected to chromatography on silica gel (50 mL), eluting with hexane/*t*BuOMe, 10:1, to give 0.35 g (78%) of pure **128** as a colorless liquid. – IR (film): ν = 3111, 3023, 2952, 2869, 1734 (C=O), 1635 (C=C), 1437, 1371, 1295, 1233, 1196, 1152, 1102, 1048, 1026, 993, 954, 916, 867, 845, 812, 768, 685 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.34–1.52 (m, 1 H), 1.64–2.06 (m, 7 H), 3.58 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 5.62 (d, ^2J = 1 Hz, 1 H, 3'-H_{trans}), 6.19 (d, ^2J = 1 Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 25.5 (–, C-3), 26.4 [–, C-2(4)], 34.9 [+, C-1(5)], 35.9 (C_{quat}, C-6), 51.7, 51.9 (+, OCH_3), 126.8 (–, C-3'), 140.9 (C_{quat}, C-2'), 166.6, 170.6 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 224 (2) [M^+], 192 (100) [$M^+ - CH_3OH$], 177 (1), 164 (21) [$M^+ - CH_3OH - CO$], 160 (30), 151 (8), 149 (6),

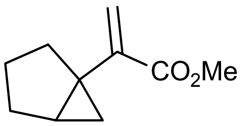


136 (12), 133 (23), 132 (23), 121 (4), 105 (42), 91 (9), 79 (15), 77 (15), 67 (16), 65 (6), 59 (9), 55 (2), 53 (3), 51 (4), 45 (2), 41 (4). – Anal. Calculated for $C_{12}H_{16}O_4$ (224.25): C 64.27, H 7.19. Found: C 64.21, H 7.00.

Ethyl 2-[1,1-bis(ethoxycarbonyl)cycloprop-2-yl]propenoate (**129**). Oxoester **102** (4.7 g, 16.4 mmol) was converted into **129** according to GP 9B. flash” chromatography of the crude product on flash” silica gel (60 mL), eluting with pentane/ether, 5:1, yielded 3.8 g (81%) of pure **129** as a colorless oil. – IR (film): ν = 3111, 2983, 2941, 2908, 2875, 1727 (C=O), 1635 (C=C), 1464, 1447, 1370, 1320, 1265, 1204, 1174, 1140, 1097, 1026, 954, 861, 816, 784, 709 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.14 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.24 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.27 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.56 (dd, ^3J = 8.8 Hz, ^2J = 5.3 Hz, 1 H, 3-H_{trans}), 1.78 (dd, ^3J = 8.3 Hz, ^2J = 5.3 Hz, 1 H, 3-H_{cis}), 2.90 (dd, ^3J = 8.8 Hz, ^3J = 8.3 Hz, 1 H, 2-H), 4.05 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 4.12–4.24 (m, 4 H, OCH_2), 5.45 (s, 1 H, 3'-H_{trans}), 6.23 (s, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.9, 14.0, 14.1 (+, CH_3), 17.6 (–, C-3), 28.3 (+, C-2), 36.3 (C_{quat}, C-1), 60.8, 61.3, 61.6 (–, OCH_2), 125.9 (–, C-3'), 135.3 (C_{quat}, C-2'), 165.9, 166.6, 169.3 (C_{quat}, CO_2Et). – MS (70 eV, EI), *m/z* (%): 284 (12) [M^+], 239 (74) [$M^+ - C_2H_5O$], 238 (67) [$M^+ - C_2H_5OH$], 211 (100) [$M^+ - CO_2C_2H_5$], 193 (7), 183 (8), 182 (8), 165 (41) [$M^+ - CO_2C_2H_5 - C_2H_5OH$], 155 (3), 137 (36), 120 (43), 110 (22), 101 (7), 93 (10), 83 (6), 82 (6), 81 (5), 65 (10), 53 (8), 41 (3). – Anal. Calculated for $C_{14}H_{20}O_6$ (284.31): C 59.14, H 7.09. Found: C 58.86, H 7.31.

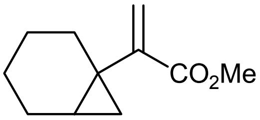


Methyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**130**). Methylenation of the oxoester **103** (75 g, 446 mmol) according to GP 9B gave a crude product (73–78 g), which was distilled under reduced pressure to yield 66.1 g (85%) of pure **130** (>98% purity according to GC) as a colorless liquid. – B. p. 64–65 °C (4 mbar). – IR (film): ν = 3073, 3001, 2953, 2862, 1725 (C=O), 1624 (C=C), 1436, 1366, 1323, 1302, 1216, 1174, 1123, 1018, 996, 941, 856, 812 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.62 (dd, ^3J = 6 Hz, ^2J = 4.9 Hz, 1 H, 6-H_{exo}), 0.63 (dd, ^2J = 4.9 Hz, ^3J = 4.2 Hz, 1 H, 6-H_{endo}), 1.11–1.30 (m, 1 H, 3-H), 1.44 (ddd, ^3J = 6 Hz, ^3J = 6 Hz, ^3J = 4 Hz, 1 H), 1.57–1.95 (m, 5 H), 3.73 (s, 3 H, OCH_3), 5.56 (d, ^2J = 1.7 Hz, 1 H, 3'-H_{trans}), 6.07 (d, ^2J = 1.7 Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.9 (–, C-6), 21.1 (–, C-3), 24.9 (+, C-5), 27.5 [–, C-2(4)*], 30.8 (C_{quat}, C-1), 32.1 [–, C-2(4)*], 51.5 (+, OCH_3), 124.5 (–, C-3'), 143.8 (C_{quat}, C-2'), 167.4 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 166 (37.3) [M^+], 151 (15.9), 138 (21.4),

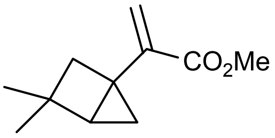


134 (58.7), 106 (95.6), 91 (100), 79 (39.3) [$C_6H_7^+$], 67 (20.6). –Anal. Calculated for ($C_{10}H_{14}O_2$): C 72.26, H 8.49. Found: C 72.59, H 8.24.

Methyl 2-(bicyclo[4.1.0]hept-1-yl)propenoate (**131**). Methylenation of the oxoester **104** (11.1 g, 61 mmol according to GP 9B gave after column chromatography of the crude product on 900 mL of silica gel, eluting with pentane/ether, 40:1, 8.85 g (81%) of pure **131** as a colorless liquid – IR (film): ν = 3067, 2998, 2932, 2857, 1725 (C=O), 1624 (C=C), 1454, 1432, 1318, 1281, 1270, 1256, 1209, 1156, 1132, 1095, 1075, 1025, 996, 946, 835, 816 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.44 (dd, ^3J = 5.5 Hz, ^2J = 4.8 Hz, 1 H, 7-H$_{endo}$), 0.73 (dd, ^3J = 9.3 Hz, ^2J = 4.8 Hz, 1 H, 7-H$_{exo}$), 0.93 (dddd, ^3J = 9.3 Hz, ^3J = 6.4 Hz, ^3J = 5.5 Hz, ^4J = 1.4 Hz, 1 H, 1-H), 1.08–1.43 (m, 4 H), 1.60–1.76 (m, 3 H), 1.87–2.01 (m, 1 H), 3.75 (s, 3 H, OCH_3), 5.49 (d, ^2J = 1.5 Hz, 1 H, 3'-H$_{trans}$), 6.05 (d, ^2J = 1.5 Hz, 1 H, 3'-H$_{cis}$). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 16.7 (–), 18.5 (+, C-6), 20.4, 21.7 (–), 22.2 (C$_{quat}$, C-1), 23.5 (–), 29.7 (–), 51.6 (+, OCH_3), 123.9 (–, C-3'), 147.4 (C$_{quat}$, C-2'), 167.6 (C$_{quat}$, CO_2Me). – MS (70 eV, EI), *m/z* (%): 180 (71) [M^+], 165 (8) [$M^+ - CH_3$], 152 (22) [$M^+ - C_2H_4$], 149 (40) [$M^+ - CH_3O$], 148 (90) [$M^+ - CH_3OH$], 137 (18) [$M^+ - C_3H_7$], 126 (24), 121 (80) [$M^+ - CO_2CH_3$], 120 (82) [$M^+ - C_2H_4 - CH_3OH$], 105 (59), 93 (57), 91 (86), 81 (100) [$C_6H_9^+$], 79 (98) [$C_6H_7^+$], 77 (52) [$C_6H_5^+$], 67 (41), 59 (23), 55 (28), 53 (27), 41 (53). – MS (HR-EI): 180.1150 ($C_{11}H_{16}O_2$, calcd. 180.1150).

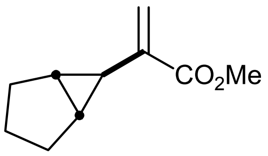


Methyl 2-(3,3-dimethylbicyclo[2.1.0]pent-1-yl)propenoate (**132**). Methylenation of the crude **105** (1.82 g) according to GP 9B gave 2 g of a crude product, which was subjected to flash” chromatography on 40 mL of flash silica gel, eluting with pentane/ether, 20:1, to yield 646 mg (36% from hydroxyester **93**) of pure **132** as a colorless oil. – IR (film): ν = 3023, 2985, 2954, 2930, 2864, 1723 (C=O), 1611 (C=C), 1465, 1436, 1361, 1308, 1264, 1234, 1205, 1174, 1132, 1112, 1089, 1048, 1020, 990, 941, 918, 863, 813, 784 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.833 (s, 3 H, CH_3), 1.12–1.16 (m, 2 H, 5-H), 1.25 (s, 3 H, CH_3), 1.50 (d, ^3J = 10.8 Hz, 1 H, 2-H$_{exo}$), 1.70 (dd, ^3J = 10.8 Hz, ^4J = 1.3 Hz, 1 H, 2-H$_{endo}$), 1.93 (^3J = 4 Hz, ^3J = 2.8 Hz, ^4J = 1.3 Hz, 1 H, 4-H), 3.71 (s, 3 H, OCH_3), 5.43 (d, ^2J = 1.5 Hz, 3'-H$_{trans}$), 6.07 (d, ^2J = 1.5 Hz, 3'-H$_{cis}$). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 21.6 (C$_{quat}$, C-1), 21.9 (–, C-5), 23.0 (+, CH_3), 30.2 (+, CH_3), 32.4 (C$_{quat}$, C-3), 33.2 (+, C-4), 40.8 (–, C-2), 51.5 (+, OCH_3), 122.8 (–, C-3'), 142.3 (C$_{quat}$, C-2'), 166.7 (C$_{quat}$, CO_2Me). – MS (70 eV, EI), *m/z*

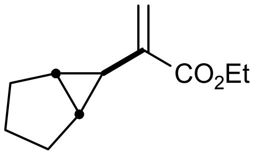


(%): 180 (10) [M^+], 165 (49) [$M^+ - CH_3$], 161 (6, 149 (15) [$M^+ - CH_3O$], 131 (40), 121 (79) [$M^+ - CO_2CH_3$], 105 (100), 95 (16), 93 (30), 91 (36), 79 (30) [$C_6H_7^+$], 77 (18) [$C_6H_5^+$], 74 (6), 71 (5), 69 (6), 67 (5), 65 (7), 59 (6), 57 (11), 55 (10), 53 (7), 51 (5), 43 (7), 41 (36). – Anal. Calculated for $C_{11}H_{16}O_2$ (180.24): C 73.30, H 8.95. Found: C 73.24, H 9.02.

Methyl exo-2-(bicyclo[3.1.0]hex-6-yl)propenoate (**133**). Methylenation of the oxoester **111** (11.44 g, 68 mmol) according to GP 9B gave 12.38 g of a crude product as a yellow oil, which was subjected to chromatography 1 L of silica gel, eluting with pentane/diethyl ether, 20:1, to yield 9.6 g (85%) of pure **133** as a colorless liquid. – IR (film): ν = 3105, 3026, 2952, 2861, 1724 (C=O), 1624 (C=C), 1437, 1408, 1336, 1294, 1280, 1252, 1229, 1193, 1174, 1137, 1081, 1053, 998, 926, 887, 844, 812 cm^{-1}. – ^1H NMR (300 MHz, $CDCl_3$): δ = 1.13–1.30 (m, 1 H), 1.37 [dd, $^3J = 3.7$ Hz, $^3J = 3.5$ Hz, 2 H, 1(5)-H], 1.56 (t, $^3J = 3.7$ Hz, 1 H, 6-H), 1.59–1.77 (m, 3 H), 1.85 [dd, $^2J = 12.4$ Hz, $^3J = 8$ Hz, 2 H, 2(4)-H_{exo}], 3.75 (s, 3 H, OCH_3), 5.18 (d, $^2J = 1$ Hz, 1 H, 3'-H_{trans}), 5.93 (d, $^2J = 1$ Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (50.3 MHz, $CDCl_3$, APT): δ = 18.9 (+, C-6), 20.9 (–, C-3), 27.7 [–, C-2(4)], 28.5 [+, C-1(5)], 51.8 (+, OCH_3), 119.5 (–, C-3'), 141.9 (–, C-2'), 167.7 (–, CO_2Me). – MS (70 eV, EI), *m/z* (%): 166 (37) [M^+], 151 (15) [$M^+ - CH_3$], 138 (13) [$M^+ - C_2H_4$], 135 (22) [$M^+ - CH_3O$], 134 (70) [$M^+ - CH_3OH$], 125 (8), 107 (46) [$M^+ - CH_3O - CO$], 106 (74) [$M^+ - CH_3OH - CO$], 105 (36) [$M^+ - CH_3OH - CO - H$], 100 (6), 93 (16), 91 (51) [$C_7H_7^+$], 79 (70) [$C_6H_7^+$], 77 (31) [$C_6H_5^+$], 67 (100), 65 (21), 59 (20), 53 (20), 51 (12), 43 (42), 41 (40). – Anal. Calculated for $C_{10}H_{14}O_2$ (166.22): C 72.26, H 8.49. Found: C 72.09, H 8.20.

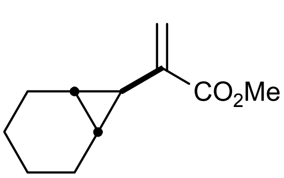


Ethyl exo-2-(bicyclo[3.1.0]hex-6-yl)propenoate (**134**). Methylenation of the oxoester **112** (8.5 g, 47 mmol) according to GP 9B gave 8.6 g of the crude product as yellow oil, which was "bulb-to-bulb" distilled (T_{bath} < 80 °C, 0.1 Torr) to yield 7.3 g (86%) of **134** in satisfactory purity (about 95% according to GC). This was purified by column chromatography on 700 mL of silica gel, eluting with pentane/diethyl ether, 20:1, to yield 5.94 g (70%, purity >99%) of **134** as a colorless liquid. – IR (film): ν = 3111, 3028, 2957, 2937, 2862, 1719 (C=O), 1626 (C=C), 1466, 1447, 1410, 1367, 1333, 1292, 1252, 1229, 1179, 1136, 1092, 1053, 1028, 924, 889, 848, 811 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.13–1.30 (m, 1 H), 1.28 (t, $^3J = 7.2$ Hz, 3 H, CH_3), 1.34–1.36 (m, 2 H), 1.51–1.76 (m, 4 H), 1.79–1.87 (m, 2 H), 4.18 (q, $^3J = 7.2$ Hz, 2 H, OCH_2), 5.15 (d, $^2J = 1$ Hz, 1 H, 3'-H_{trans}), 5.91 (d, $^2J = 1$ Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR

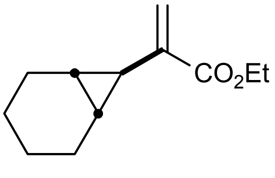


(62.9 MHz, $CDCl_3$, DEPT): δ = 14.2 (+, CH_3), 18.9 (+, C-6), 21.0 (–, C-3), 27.7 [–, C-2(4)], 28.5 [+, C-1(5)], 60.7 (–, OCH_2), 119.2 (–, C-3'), 142.2 (C_{quat}, C-2'), 167.3 (C_{quat}, CO_2Et). – MS (70 eV, EI), *m/z* (%): 180 (38) [M^+], 165 (2) [$M^+ - CH_3$], 151 (18) [$M^+ - C_2H_5$], 134 (47) [$M^+ - C_2H_5OH$], 123 (16), 109 (100), 107 (24), 106 (41), 105 (35), 91 (30), 81 (35) [$C_6H_9^+$], 79 (50) [$C_6H_7^+$], 77 (14) [$C_6H_5^+$], 67 (69), 53 (2), 41 (7). – Anal. Calculated for $C_{11}H_{16}O_2$ (180.24): C 73.30, H 8.95. Found: C 73.03, H 9.28.

Methyl exo-2-(bicyclo[4.1.0]hept-7-yl)propenoate (**135**). Methylenation of the oxoester **113** (18.2 g, 100 mmol) according to GP 9B gave 18.4 g of crude product, which was subjected to chromatography on 1.5 L of silica gel, eluting with hexane/*t*BuOMe, 20:1, to yield 16.5 g (92%) of pure **135**. – IR (film): ν = 2996, 2927, 2852, 1721 (C=O), 1627 (C=C), 1435, 1403, 1355, 1322, 1264, 1193, 1140, 1082, 1028, 1014, 1001, 916, 872, 842, 813, 773, 734 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.01–1.06 [ddd, ^3J = 5 Hz, ^3J = 4 Hz, J = 1 Hz, 2 H, 1(6)-H], 1.20–1.28 [m, 4 H, 2(5)-H], 1.48 (t, ^3J = 5 Hz, 1 H, 7-H), 1.64–1.75 [m, 2 H, 3(4)*-H], 1.80–1.93 [m, 2 H, 3(4)*-H], 3.76 (s, 3 H, OCH_3), 5.16 (s, 1 H, 3'-H_{trans}), 5.91 (d, J = 1 Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 21.0 [+, C-1(6)], 21.2, 23.3 (–), 24.0 (+, C-7), 51.9 (+, OCH_3), 118.8 (–, C-3'), 142.9 (C_{quat}, C-2'), 168.0 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 180 (24) [M^+], 165 (6) [$M^+ - CH_3$], 149 (9) [$M^+ - CH_3O$], 148 (18) [$M^+ - CH_3OH$], 137 (6), 121 (27) [$M^+ - CO_2Me$], 120 (37) [$M^+ - CH_3OH - CO$], 120 (28), 111 (3), 105 (17), 93 (29), 92 (36), 91 (70), 81 (100) [$C_6H_9^+$], 79 (86) [$C_6H_7^+$], 77 (51) [$C_6H_5^+$], 67 (34), 65 (15), 59 (15), 55 (10), 53 (17), 51 (6), 41 (79). MS (HR-EI): 180.1150 ($C_{11}H_{16}O_2$, calcd. 180.1150).



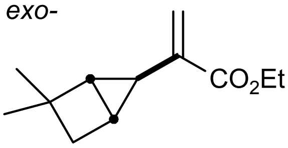
Ethyl exo-2-(bicyclo[4.1.0]hept-7-yl)propenoate (**136**). Methylenation of the oxoester **114** (8.9 g, 45 mmol) according to GP 9B gave 9.0 g of the crude product, which was subjected to chromatography on 700 mL of silica gel, eluting with hexane/*t*BuOMe, 20:1, to yield 8.1 g (92%) of pure **136**. – IR (film): ν = 3105, 2979, 2930, 2853, 1717 (C=O), 1629 (C=C), 1448, 1393, 1366, 1300, 1256, 1174, 1155, 1141, 1097, 1026, 932, 867, 845, 806, 768, 721 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.01–1.05 (m, 2 H), 1.20–1.28 (m, 4 H, 2(5)-H), 1.30 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.47 (t, ^3J = 5 Hz, 1 H, 7-H), 1.64–1.75 (m, 2 H, 3(4)*-H), 1.80–1.93 (m, 2 H, 3(4)*-H), 4.21 (q, ^3J = 7.2 Hz, 3 H, OCH_2), 5.15 (s, 1 H, 3'-H_{trans}), 5.91 (d, J = 1 Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.2 (+, CH_3), 20.9 [+, C-



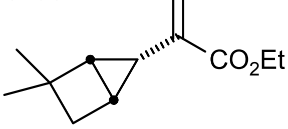
1(6)], 21.2 23.3 (–), 24.0 (+, C-7), 60.6 (–, OCH_2), 118.6 (–, C-3'), 143.1 (C_{quat}, C-2'), 167.5 (C_{quat}, CO_2Et). – MS (70 eV, EI), *m/z* (%): 194 (46) [M^+], 166 (34) [$M^+ - C_2H_4$], 165 (42) [$M^+ - C_2H_5$], 149 (26) [$M^+ - C_2H_5O$], 148 (59) [$M^+ - C_2H_5OH$], 137 (11) [$M - C_2H_4 – C_2H_5$], 123 (17), 121 (53) [$M^+ - CO_2C_2H_5$], 120 (55) [$M^+ - C_2H_5OH - CO$], 119 (55), 114 (13), 105 (21), 93 (34), 91 (50), 81 (100) [$C_6H_9^+$], 79 (62) [$C_6H_7^+$], 77 (30) [$C_6H_5^+$], 67 (32), 55 (14), 53 (16), 41 (15). – MS (HR-EI): 194.1307 ($C_{12}H_{18}O_2$ calcd. 194.1307).

Ethyl 2-(2,2-dimethylbicyclo[2.1.0]pent-5-yl)propenoate (**137**). Methylenation of a 3.8:1 mixture of *exo*- and *endo*-isomers of **115** (8.3 g, 42 mmol) according to GP 9B gave 6.7 g of a crude mixture, which was purified by column chromatography on 700 mL of silica gel, eluting with pentane/ether, 50:1, to give 5.2 g of *exo*-**137** (*exo-*/*endo-* ratio 94:2 according to GC) contaminated with some by-product (4%) and 210 mg of pure *endo*-**137**. Total yield: 66%. – *exo*-**137**. – Colorless oil. – IR (film): ν = 3111, 3045, 3023, 2957, 2924, 2864, 2721, 1723 (C=O), 1624 (C=C), 1465, 1465, 1443, 1410, 1384, 1366, 1311, 1262, 1212, 1152, 1124, 1108, 1026, 997, 872, 812, 784, 675 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.88 (s, 3 H, CH_3), 1.25 (s, 3 H, CH_3), 1.31 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.42 (d, ^2J = 11 Hz, 1 H, 3-H_{endo}), 1.47 (d, ^3J = 4.5 Hz, 1 H, 1-H), 1.59 (dd, ^3J = 4.5 Hz, ^3J = 4.5 Hz, 1 H, 4-H), 1.67 (dd, ^2J = 11 Hz, ^3J = 4.5 Hz, 1 H, 3-H_{exo}), 2.17 (s, 1 H, 5-H), 4.23 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 5.04 (s, 1 H, 3'-H_{trans}), 5.90 (s, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.2 (+, CH_3), 19.4 (+, CH), 23.3 (+, CH_3), 26.7 (+, CH) 30.3 (+, CH_3), 35.0 (C_{quat}, C-2), 36.1 (+, CH), 37.7 (–, C-3), 60.7 (–, OCH_2), 119.2 (–, C-3'), 140.6 (C_{quat}, C-2'), 167.1 (C_{quat}, CO_2Et). – MS (70 eV, EI), *m/z* (%): 194 (1) [M^+], 179 (17) [$M^+ - CH_3$], 165 (51) [$M^+ - C_2H_5$], 151 (10), 149 (12) [$M^+ - C_2H_5O$], 148(10) [$M^+ - C_2H_5OH$], 147 (12), 133 (39), 123 (6), 121 (38) [$M^+ - CO_2C_2H_5$], 120 (22), 119 (29), 105 (100), 95 (8), 93 (28), 91 (32), 81 (6), 79 (43) [$C_6H_7^+$], 77 (28) [$C_6H_5^+$], 67 (14), 65 (9), 55 (13), 53 (14), 51 (6), 43 (9), 41 (32). – Anal. Calculated for $C_{12}H_{18}O_2$ (194.27): C 74.19, H 9.34. Found: C 74.42, H 9.02. – *endo*-**137**. – Colorless oil. – IR (film): ν = 3105, 3037, 3016, 2985, 2953, 2936, 2902, 2865, 1722 (C=O), 1628 (C=C), 1464, 1446, 1383, 1364, 1300, 1275, 1249, 1188, 1163, 1110, 1030, 982, 946, 899, 855, 819, 777, 743 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.65 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3), 1.30 (t, J = 7.2 Hz, 3 H, CH_3), 1.42 (d, ^2J = 11.3 Hz, 1 H, 3-H_{endo}), 1.56 (dd, ^2J = 11.3 Hz, ^3J = 4.5 Hz, 1 H, 3-H_{exo}), 1.63–1.75 (m, 2 H), 1.80 (dddd, ^3J = 5.8 Hz, ^3J = 5.8 Hz, ^4J = 2.3 Hz, ^4J = 2.3 Hz, 1 H, 5-H), 4.23 (q, J = 7.2 Hz, 2 H, OCH_2), 5.73 (dd, ^2J = 2.3 Hz, ^4J = 2.3 Hz, 1 H, 3'-

exo-

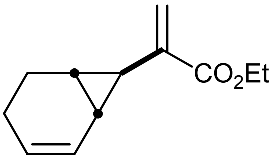


endo-

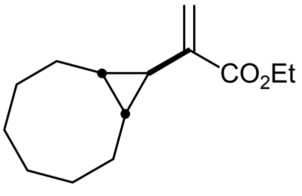


H_{trans}), 6.38 (dd, ^2J = 2.3 Hz, ^4J = 2.3 Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 11.9 (+, CH), 14.3 (+, CH_3), 23.4 (+, CH_3), 27.7, 31.0 (+, CH), 32.0 (–, C-3), 32.4 (+, CH_3), 33.5 (C_{quat}, C-2), 60.4 (–, OCH_2), 127.8 (–, C-3'), 137.1 (C_{quat}, C-2'), 167.8 (CO_2Et). – MS (70 eV, EI), *m/z* (%): 194 (1) [M^+], 179 (15) [$M^+ - CH_3$], 165 (88) [$M^+ - C_2H_5$], 151 (8), 149 (13) [$M^+ - C_2H_5O$], 148 (19) [$M^+ - C_2H_5OH$], 147 (21), 133 (41), 121 (47) [$M^+ - CO_2C_2H_5$], 120 (28), 119 (38), 105 (100), 95 (19), 93 (29), 91 (30), 79 (41) [$C_6H_7^+$], 77 (21) [$C_6H_5^+$], 67 (14), 65 (7), 55 (14), 53 (9), 43 (8), 41 (24). – Anal. Calculated for $C_{12}H_{18}O_2$ (194.27): C 74.19, H 9.34. Found: C 73.96, H 9.23.

Ethyl exo-2-(bicyclo[4.1.0]hept-2-en-7-yl)propenoate (**138**). Methylenation of the oxoester **116** (7.6 g, 39 mmol) according to GP 9A gave after flash" chromatography of the crude product on 120 mL of flash" silica gel, eluting with pentane/ether, 20:1, 5.7 g (76%) of pure **138** as a slightly yellow liquid. – IR (film): ν = 3032, 2981, 2928, 2853, 1718, 1624, 1457, 1444, 1409, 1395, 1368, 1339, 1301, 1260, 1174, 1140, 1099, 1061, 1044, 1027, 940, 923, 861, 845, 811, 789, 724, 696 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.29 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.29–1.36 (m, 1 H), 1.43–1.66 (m, 2 H), 1.77–2.08 (m, 4 H), 4.20 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 5.26 (dd, ^2J = 1 Hz, J = 1 Hz, 1 H, 3'-H_{trans}), 5.49 (ddd, ^3J = 9.5 Hz, ^3J = 6.5 Hz, ^4J = 2.5 Hz, 1 H), 5.98 (d, ^2J = 1 Hz, 1 H, 3'-H_{cis}), 6.01–6.08 (m, 1 H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.1 (+, CH_3), 17.9 (–, C-5), 20.7 (+, C-7), 20.8 (–, C-4), 23.8 [+, C-1(6)], 60.6 (–, OCH_2), 119.8 (–, C-3'), 123.8, 127.0 [+, C-2(3)], 141.6 (C_{quat}, C-2'), 167.0 (C_{quat}, CO_2Et). – MS (70 eV, EI), *m/z* (%): 192 (9) [M^+], 164 (2) [$M^+ - C_2H_4$], 163 (12) [$M^+ - C_2H_5$], 147 (15) [$M^+ - C_2H_5O$], 146 (40) [$M^+ - C_2H_5OH$], 145 (47), 131 (7), 119 (5) [$M^+ - CO_2C_2H_5$], 118 (44) [$M^+ - CO_2C_2H_5 - H$], 117 (98), 114 (100), 105 (7), 103 (6), 91 (66), 86 (42), 79 (87) [$C_6H_7^+$], 78 (51), 77 (61) [$C_6H_5^+$], 65 (11), 53 (5), 51 (4), 41 (14). – Anal. Calculated for $C_{12}H_{16}O_2$ (192.25): C 74.97, H 8.39. Found: C 74.71, H 8.32.

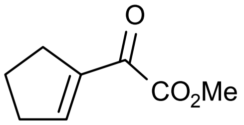


Ethyl exo-2-(bicyclo[6.1.0]non-9-yl)propenoate (**139**). Methylenation of the oxoester **117** (7.9 g, 35 mmol) according to GP 9B gave 8.0 g of a crude product, which was purified by chromatography on 700 mL of silica gel, eluting with hexane/*t*BuOMe, 40:1, to yield 6.0 g (77%, >99% purity according to GC) of **139** as a colorless oil. Yield: 6 g (77%, >99% purity according to GC). – IR (film): ν = 3105, 2982, 2923, 2851, 2687, 1720 (C=O), 1627 (C=C), 1466, 1446, 1407, 1369, 1321, 1300, 1268, 1252, 1161, 1138, 1026, 989, 937,

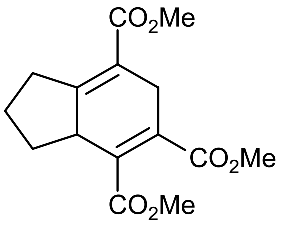


889, 862, 815, 779, 736, 683 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.77–0.90 (m, 2 H), 0.98–1.16 (m, 2 H), 1.19 (dt, ^3J = 5.3 Hz, ^4J = 1 Hz, 1 H, 9-H), 1.30 (t, ^3J = 7.2 Hz, 3 H, CH$_3$), 1.28–1.45 (m, 4 H), 1.48–1.74 (m, 4 H), 2.04 (m, 1 H), 2.10 (m, 1 H), 4.20 (q, ^3J = 7.2 Hz, 2 H, OCH$_2$), 5.22 (dd, ^2J = 1.3 Hz, ^4J = 1 Hz, 1 H, 3'-H$_{trans}$), 5.93 (d, ^2J = 1.3 Hz, 1 H, 3'-H$_{cis}$). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 14.2 (+, CH$_3$), 24.4 (+, C-9), 26.4 [+, C-1(8)], 26.5, 26.6, 29.4 (–), 60.6 (–, OCH$_2$), 119.1 (–, C-3'), 142.7 (C$_{\text{quat}}$, C-2'), 167.5 (C$_{\text{quat}}$, CO$_2$Et). – MS (70 eV, EI), *m/z* (%): 222 (88) [M$^+$], 193 (15) [M$^+$ – C$_2$H$_5$], 177 (18) [M$^+$ – C$_2$H$_5$O], 176 (22) [M$^+$ – C$_2$H$_5$OH], 165 (10), 149 (61) [M$^+$ – CO$_2$C$_2$H$_5$], 148 (40) [M$^+$ – CO$_2$C$_2$H$_5$ – H], 147 (31), 133 (11), 127 (15), 121 (15), 119 (14), 114 (19), 111 (40), 109 (80), 107 (22), 105 (18), 99 (11), 95 (24), 93 (31), 91 (28), 81 (62) [C$_6$H$_9^+$], 79 (46) [C$_6$H$_7^+$], 77 (21) [C$_6$H$_5^+$], 67 (100), 55 (34), 53 (17), 41 (45). – Anal. Calculated for C$_{14}$H$_{22}$O$_2$ (222.32): C 75.63, H 9.97. Found: C 75.40, H 10.20.

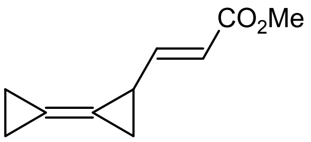
Methyl (cyclopenten-1-yl)oxoacetate (**143**). Hydroxyester **81** (7.81 g, 50 mmol) was subjected to GP 7. The only difference was that, the reaction mixture was stirred for 1 h after the second portion of MnO$_2$ had been added. The crude product (6.5 g) was distilled under reduced pressure to yield 5.93 g (78%) of pure **143** as a slightly yellow liquid. – B. p. 74–75 °C (2 mbar). – IR (film): ν = 2957, 2858, 2836, 1739 (C=O), 1668 (C=O), 1602 (C=C), 1437, 1371, 1306, 1284, 1251, 1223, 1157, 1020, 993, 954, 899, 834, 790, 751, 620 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.94 (tt, ^3J = 7.8 Hz, ^3J = 7.4 Hz, 2 H, 4-H), 2.51–2.69 [m, 4 H, 3(5)-H], 3.85 (s, 3 H, OCH$_3$), 7.16–7.20 (m, 1 H, 2-H). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 22.3 (–, C-4), 30.2, 34.8 [–, C-3(5)], 52.5 (+, OCH$_3$), 141.8 (C$_{\text{quat}}$, C-1), 153.1 (+, C-2), 163.3 (C$_{\text{quat}}$, CO$_2$Me), 182.9 (C$_{\text{quat}}$, C=O). – MS (70 eV, EI), m/z (%): 154 (1) [M$^+$], 126 (18) [M$^+$ – CO], 95 (100) [M$^+$ – CO$_2$CH$_3$], 67 (27) [C$_5$H$_7^+$], 65 (11) [C$_5$H$_5^+$], 41 (24) [C$_3$H$_5^+$].



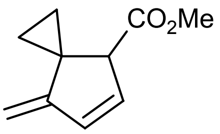
Trimethyl 2,3,3a,6-tetrahydro-1H-indene-4,5,7-tricarboxylate (**145**). After the **143** (3.2 g, 20 mmol) was subjected to GP 9B with only difference that the concentration of prepared ylide was four times lower (0.1 mol/L), a some amount of crude methyl 2-(cyclopenten-1-yl)propenoate **144** was isolated by flash" chromatography on 60 mL of flash silica gel, eluting with pentane to pentane/ether, 20:1. Further elution with pentane/ether, 10:1 yielded a mixture of isomeric dimers of **144** (2.4 g, 79%). To the combined fractions contained **144**, dimethyl acetylenedicarboxylate was added (1 g, 7 mmol),



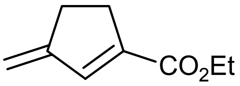
the solvents were evaporated at normal pressure (T_{bath} < 65 °C) and the mixture was allowed to stand at ambient temperature overnight. Then, the crude reaction mixture was subjected to column chromatography on 150 mL of silica gel, eluting with pentane/ether, 10:1, to yield 870 mg (15% from the oxoester**143**) of pure **145** as a colorless plates. – M. p. 55–56°C. – IR (KBr): ν = 3039, 2996, 2957, 2913, 2880, 2836, 1727 (C=O), 1717 (C=O), 1668 (C=C), 1640 (C=C), 1437, 1314, 1300, 1278, 1264, 1196, 1152, 1108, 1075, 1015, 954, 839, 790, 757 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 1.34–1.52 (m, 1 H), 1.59–1.79 (m, 1 H), 1.86–1.98 (m, 1 H), 2.03–2.14 (m, 1 H), 2.75–2.85 (m, 2 H), 2.92–3.08 (m, 1 H), 3.25–3.41 (m, 1 H), 3.45–3.71 (m, 1 H), 3.73 (s, 3 H, OCH_3), 3.77 (s, 3 H, OCH_3), 3.81 (s, 3 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 23.7 (–, C-2), 28.6, 29.9 [–, C-1(3)], 31.3 (–, C-6), 46.0 (+, C-3a), 51.4, 52.2, 52.3 (+, OCH_3), 117.6 (C_{quat}, C-7), 129.2, 139.1 [C_{quat}, C-4(5)], 156.5 (C_{quat}, C-7a), 166.4, 166.5, 168.8 (C_{quat}, CO_2Me). – MS (70 eV, EI), m/z (%): 294 (1) [M^+], 266 (5) [$M^+ - C_2H_4$], 262 (62) [$M^+ - CH_3OH$], 247 (11), 235 (35) [$M^+ - CO_2CH_3$], 231 (6), 203 (100) [$M^+ - 2CH_3OH - CO$], 191 (17), 175 (21), 148 (8), 145 (14), 131 (8), 119 (11), 117 (16), 115 (26) [$C_9H_7^+$], 105 (3), 103 (2), 91 (10), 59 (22), 41 (2).



Methyl 3-bicyclopropylidenylpropenoate (**146**). A solution of the aldehyde (**63**) (3.6 g, 33 mmol) and (carbomethoxy)methylenetriphenylphosphorane (14 g, 42 mmol) in anhydrous CH_2Cl_2 (300 mL) was stirred at ambient temperature for 24 h. The solvent was evaporated under reduced pressure at ambient temperature until the Ph_3PO had started to crystallize, then pentane (200 mL) was added by stirring and this suspension was filtered through flash" silica gel (50 mL as a 2 cm pad). The silica gel was washed with the pentane/ether, 10:1, mixture (2 × 50 mL). Concentration of the combined extracts under reduced pressure gave 5.28 g of crude product, which was purified by flash" chromatography on 120 mL of flash silica gel, eluting with pentane/ether, 20:1, to yield 4.9 g (90%) of pure **146**. ^1H NMR (250 MHz, $CDCl_3$): δ = 1.16–1.26 (m, 4 H, 2'(3')-H), 1.36–1.46 (m, 1 H, 3-H_{trans}), 1.75–1.87 (m, 1 H, 3-H_{cis}), 2.27–2.40 (m, 1 H, 2-H), 3.73 (s, 3 H, OCH_3), 5.92 (d, ^3J = 17.5 Hz, 1 H, 2"-H), 6.56 (dd, ^3J = 17.5 Hz, ^3J = 10.0 Hz, 3"-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 3.2 [–, C-2'(3')], 13.4 (–, C-3), 19.4 (+, C-2), 51.2 (+, OCH_3), 113.1 113.5 [C_{quat}, C-1(1')], 118.5 (+, C-2"), 151.4 (+, C-3"), 167.0 (C_{quat}). – MS (70 eV, EI), *m/z* (%): 164 (1) [M^+], 163 (3) [$M^+ - H$], 136 (8) [$M^+ - C_2H_4$], 133 (10), 132 (15), 124 (20) [$M^+ - C_3H_4$], 105 (100) [$M^+ - CO_2CH_3$], 104 (41), 103 (45), 91 (22), 79 (40) [$C_6H_7^+$], 77 (48) [$C_6H_5^+$]. – MS (HR-EI): 164.0837 ($C_{10}H_{12}O_2$, calcd. 164.0837).

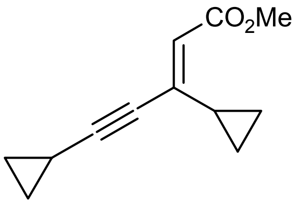


Methyl 7-methylenespiro[2.4]hept-5-ene-4-carboxylate (**147**). A solution of the acrylate **146** (1.00 g, 6 mmol) in diethylene glycol dimethyl ether (10 mL) was heated under reflux. After cooling to room temperature, it was poured into water (100 mL) and the mixture was extracted with pentane (3 × 10 mL). The combined extracts were washed with water (100 mL) and brine (100 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Column chromatography of the residue (0.82 g) on 100 mL of silica gel (eluent hexane/*t*BuOMe, 20/1) gave **147** (0.50 g, 50%) as a colorless oil. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.79–1.06 [m, 4 H, 1(2)-H], 3.55 (s, 1 H, 4-H), 3.65 (s, 3 H, OCH_3) 4.20–4.21 (m, 1 H, 1'-H), 4.69 (s, 1 H, 1'-H), 6.10–6.17 (m, 1 H, 6-H), 6.48 (dd, J = 5.8 Hz, J = 1.8 Hz, 1 H, 5-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.6, 19.2 [–, C-1(2)], 26.0 (C_{quat}, C-3), 51.7 (+, OCH_3), 57.3 (+, C-4), 97.6 (–), 134.2 (+, C-5), 136.9 (+, C-6), 157.2 (C_{quat}, C-7), 172.5 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 164 (25) [M^+], 136 (10) [$M^+ - C_2H_4$], 105 (100) [$M^+ - CO_2CH_3$], 103 (15), 79 (18) [$C_6H_7^+$], 77 (22) [$C_6H_5^+$]. – MS (HR-EI): 164.0837 ($C_{10}H_{12}O_2$, calcd. 164.0837).

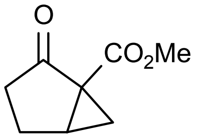


Ethyl 3-(methylene)cyclopent-1-enecarboxylate (**149**). Ethyl 2-(2-methylenecyclopropyl)-propenoate **141** (1.52 g, 10 mmol) was refluxed in degassed toluene (15 mL) for 2 h. Then the most of solvent was distilled off at ambient pressure. The residue obtained was distilled under reduced pressure to give 0.91 g (60%) of the pure **149**. – B. p. 74–75 °C (8 mbar). – IR (film): ν = 3084, 2985, 2935, 2859, 1712, 1629, 1602, 1448, 1397, 1371, 1344, 1322, 1300, 1262, 1234, 1212, 1168, 1141, 1075, 1020, 943, 910, 872, 806, 746, 680 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.30 (t, ^3J = 7.2 Hz, 3 H, CH_3), 2.59–2.75 (m, 4 H), 4.21 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 5.01–5.05 (m, 1 H, 1'-H), 5.14–5.18 (m, 1 H, 1'-H), 6.94–6.98 (m, 1 H, 2-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 14.3 (+, CH_3), 29.1, 30.8 [–, C-4(5)], 60.3 (–, OCH_2), 109.8 (–, C-1'), 141.7 [C_{quat}, C-1(3)*], 142.9 (+, C-2), 156.5 [C_{quat}, C-1(3)*], 165.6 (C_{quat}, CO_2Et).

2.4. Miscellaneous Preparations



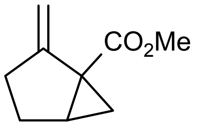
Methyl (2E)-3,5-dicyclopropylpent-2-en-4-ynoate (**152**). A solution of Pd(AcO)$_2$ (112 mg, 0.50 mmol) and TDMPP (221 mg, 0.50 mmol) in degassed benzene (50 mL) was stirred at ambient temperature for 15 min and methyl 3-cyclopropylpropynoate **151** (3.10 g, 25 mmol) was added all at once. After an additional 5 min, cyclopropyl acetylene (1.65 g, 25 mmol) was added in one portion and the reaction mixture was stirred at ambient temperature until complete consumption of the starting material (about 24 h, TLC control). The solvent was removed under reduced pressure at ambient temperature to give 5.1 g of crude product as brown oil, which was subjected to column chromatography on 500 mL of silica gel, eluting with hexane/*t*BuOMe, 30:1, to yield 4.5 g (95%) of pure **152** as a colorless oil, which solidified in a refrigerator. – IR (film): ν = 3093, 3010, 2949, 2902, 2842, 2219 (C≡C), 1717 (C=O), 1594 (C=C), 1457, 1436, 1388, 1362, 1311, 1268, 1194, 1159, 1130, 1054, 1029, 953, 922, 888, 856, 815, 768, 717, 668 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.68–0.74 (m, 2 H), 0.81–0.88 (m, 6 H), 1.26–1.38 (m, 1 H), 3.08–3.21 (m, 1 H), 3.68 (s, 3 H, OCH$_3$), 5.95 (s, 1 H, 2-H). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 0.1 (+), 8.4 9.0 (–), 12.6 (+), 51.0 (+, CH$_3$), 72.4, 99.5 [C$_{quat}$, C-4(5)], 120.8 (+, C-2), 147.4 (C$_{quat}$, C-3), 167.1 (C$_{quat}$, CO$_2$Me). – MS (70 eV, EI), *m/z* (%): 190 (64) [M$^+$], 175 (69) [M$^+$ – CH$_3$], 162 (51) [M$^+$ – C$_2$H$_4$], 159 (21) [M$^+$ – CH$_3$O], 147 (100) [M$^+$ – C$_2$H$_4$ – CH$_3$], 131 (25) [M$^+$ – CO$_2$Me], 119 (35), 115 (34), 103 (17), 91 (77), 89 (9), 77 (36) [C$_6$H$_5$], 69 (6), 65 (20), 63 (18), 59 (6), 55 (4), 53 (14), 51 (19), 43 (7), 41 (15). – MS (HR-EI): 190.0994 (C$_{12}$H$_{14}$O$_2$, calcd. 190.0994).



Methyl 2-oxobicyclo[3.1.0]hexane-1-carboxylate (**155**). To a stirred solution of Cu(acac)$_2$ (0.26 mg, 1 mmol) in anhydrous degassed toluene (45 mL) kept at 110 °C, diazoester **154** (7.33 g, 40 mmol) dissolved in the same solvent (15 mL) was added by syringe pump within 8 h. After refluxing for additional 2 h, the solvent was evaporated under reduced pressure (T$_{bath}$ < 40 °C, 5 Torr), the residue was suspended by stirring in ether (20 mL), diluted with pentane (100 mL) and filtered through a pad of flash silica gel (20 mL), which was then washed with the same solvent (2 × 20 mL). Evaporation of the combined filtrates under reduced pressure gave 5.2 g of crude product, which was purified by distillation under reduced pressure to yield 4.4 g

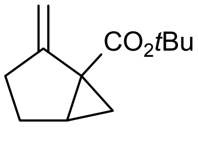
(70%) of pure **155** as a colorless liquid. – B. p. 69–70 °C (0.1 Torr). The spectral data of the synthesized compound are identical to those reported in the literature.[86]

Methyl 2-methylenebicyclo[3.1.0]hexane-1-carboxylate (**156**). To a stirred under argon



suspension of methyl triphenylphosphonium bromide (7.5 g, 21 mmol) in anhydrous THF (80 mL) was added *t*BuOK (20 mmol, 10 mL of 2 N solution in THF) all at once at ambient temperature. After stirring for additional 1 h at room temperature, the ylide solution was chilled to –30 °C (dry ice/acetone bath) and ketoester **155** (3.1 g, 20 mmol) was gradually added keeping the internal temperature between –35 ° and –30 °C with occasional cooling (dry ice/acetone bath). The mixture was stirred at this temperature for additional 1 h, the cooling was removed and the stirring was continued at ambient temperature for 24 h. Then the mixture was acidified with 5% aqueous H_2SO_4 (10 mL), diluted with brine (20 mL), organic layer was separated and the aqueous phase was extracted with ether (2 × 40 mL). The combined extracts were washed with brine (2 × 40 mL) and dried over $MgSO_4$. The solvents were evaporated under reduced pressure (50 °C, 500–200 mbar) and the residue was worked up according to GP 9B to give 3.1 g of crude oil, which was subjected to flash chromatography on 50 mL of flash silica gel, eluting with pentane/ether, 20:1 to 10:1, to yield 1.98 g (65%) of pure **156**. – IR (film): ν = 3104, 3051, 2995, 2953, 2871, 1728 (C=O), 1652 (C=C), 1437, 1374, 1326, 1251, 1192, 1121, 1067, 1046, 1029, 984, 965, 938, 924, 884, 858, 830, 774, 733 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.11 (dd, *J* = 5.5 Hz, *J* = 4.5 Hz, 1 H), 1.69–1.78 (m, 2 H), 1.83–1.99 (m, 1 H), 2.05–2.37 (m, 3 H), 3.68 (s, 3 H, OCH_3), 5.02–5.06 (m, 1 H), 5.52–5.56 (m, 1 H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 21.2 (–, C-6), 24.6 (–, C-4), 30.2 (–, C-3), 33.7 (+, C-5), 33.9 (C_{quat}, C-1), 51.6 (+, CH_3), 107.8 (–, C-1'), 146.9 (C_{quat}, C-2), 172.7 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 152 (50) [M^+], 137 (6) [$M^+ - CH_3$], 121 (21) [$M^+ - CH_3O$], 120 (14) [$M^+ - CH_3OH$], 93 (100) [$M^+ - CO_2Me$], 91 (74), 79 (8), 77 (42), 66 (10), 65 (11), 53 (4), 51 (5), 41(7). MS (HR-EI): 152.0837 ($C_9H_{12}O_2$, calcd. 152.0837).

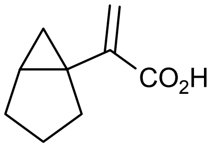
tert-Butyl 2-methylenebicyclo[3.1.0]hexane-1-carboxylate was isolated from reaction mixture,



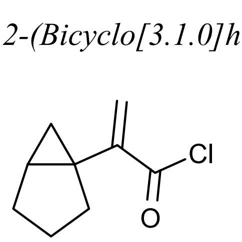
obtained after the **155** (1.67 g, 11 mmol) was allowed to react with 1.5 mol excess of methylenetriphenylphosphonium ylide under the described for **156** reaction conditions. Yield: 0.27 g (11%). – IR (film): ν = 3100, 3050, 3009, 2978, 2935, 2875, 1723 (C=O), 1651 (C=C), 1479, 1454, 1440, 1397, 1380, 1366, 1327, 1262, 1247, 1174, 1331, 1113, 1066, 1045, 1028, 966, 937, 833, 845, 829, 793, 740, 629, 600 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.04 (dd, *J* = 5.5 Hz, *J* = 4.5 Hz, 1 H), 1.45 (s, 9 H), 1.60–1.74 (m, 2 H), 1.81–1.99 (m, 1 H), 2.02–2.20 (m, 2 H), 2.21–2.28 (m, 1 H), 4.98–5.02 (m, 1 H), 5.51–5.55 (m, 1 H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 21.2 (–, C-6), 24.4 (–, C-4), 28.1 (+, CH_3), 30.5 (–, C-3), 33.1 (+, C-5), 34.6 (C_{quat}, C-1), 80.3 (C_{quat}, *t*-Bu), 107.5 (–, C-1"), 147.3 (C_{quat}, C-2), 171.4 (C_{quat}, CO_2*t*-Bu). – MS (70 eV, EI), *m/z* (%): 194 (1) [M^+], 193 (6) [M^+ – H], 138 (100) [M^+ – C_4H_8], 121 (40) [M^+ – C_4H_9O], 95 (23), 93 (66), 91 (23), 79 (23), 77 (19) [$C_6H_5^+$], 67 (10), 57 (29), 41 (18).

2.5. Synthesis of 2-(Bicyclo[3.1.0]hex-1-yl)propenoic Acid and Its Esters

2-(Bicyclo[3.1.0]hex-1-yl)propenoic acid (**157**). Hydrolysis of **130** (13.3 g, 80 mmol) according to (GP 10) gave 10.5 g (86%) of **157** (pure according to NMR data) as a colorless crystals, which had a tendency to rapidly polymerize without an added stabilizer (BHT) or in the presence of oxygen. – M. p. 60.5–61.0 °C. – IR (KBr): ν = 3436 (OH), 3067, 3028, 3005, 2958, 2937, 2861, 2731, 2601, 1694 (C=O), 1621 ($C=CH_2$), 1426, 1321, 1304, 1253, 1224, 1180, 1134, 1042, 1022, 954, 916, 804 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.60–0.70 (m, 2 H, 6-H), 1.13–1.34 (m, 1 H), 1.43–1.50 (m, 1 H, 1-H), 1.58–1.97 (m, 5 H), 5.71 (d, ^2J = 1.6 Hz, 1 H, 3'-H_{trans}), 6.28 (d, ^2J = 1.6 Hz, 1 H, 3'-H_{cis}), 11.90 (bs, 1 H, CO_2H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.0 (–, C-6), 21.2 (–, C-3), 24.9 (+, C-5), 27.5 [–, C-2(4)*], 30.6 (C_{quat}, C-1), 32.2 [–, C-2(4)*], 127.3 (–, C-3'), 143.3 ($C_{quat,}$, C-2'), 172.8 (C_{quat}, CO_2H). – MS (70 eV, EI), *m/z* (%): 152 (<0.1) [M^+], 107 (1), 78 (100), 77 (18) [$C_6H_5^+$], 52 (14), 51 (13). – Anal. Calculated for $C_9H_{12}O_2$ (152.19): C 71.03, H 7.95. Found: C 71.30, H 7.75.

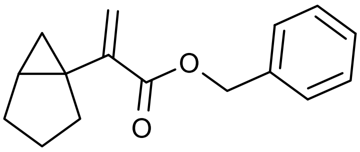


2-(Bicyclo[3.1.0]hex-1-yl)propenoyl chloride (**176**). To a stirred solution of the acid **157** (3.04 g, 20 mmol), BHT (2 mg, 0.01 mmol) and a few drops of DMF (~0.05 mL) in anhydrous CH_2Cl_2 (10 mL) was added oxalyl chloride (2.1 mL, 25 mmol) under argon at ambient temperature. The mixture was stirred at this temperature until the gas evolution had been ceased (~3 h), then the solvent was evaporated under reduced pressure (about 10 mbar) at ambient temperature. The evaporation was stopped as soon as the temperature of the reaction mixture had reached 20 °C. The crude mixture was dissolved in anhydrous carbon tetrachloride (20

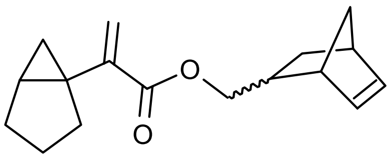


mL) and evaporated under reduced pressure by the same way, and the residue was "bulb-to-bulb" distilled (T_{bath} < 60 °C, 0.5 Torr) to yield 3.17 g (93%) of sufficiently pure **176**. The analytical sample was obtained by distillation of a crude reaction mixture under reduced pressure. – B. p. 63–64 °C (4 mbar). – IR (film): ν = 3067, 3029, 3001, 2963, 2941, 2864, 1755 (C=O), 1613 (C=C), 1476, 1418, 1399, 1366, 1305, 1273, 1234, 1185, 1163, 1141, 1020, 962, 949, 936, 905, 877, 817, 757, 735, 685, 663, 614, 570, 449 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.66 (dddd, ^3J = 8.4 Hz, ^2J = 4.9 Hz, ^4J = 0.8 Hz, ^4J = 0.8 Hz, 1 H, 6-H_{exo}), 0.72 (dd, ^2J = 4.9 Hz, ^3J = 4.3 Hz, 1 H, 6-H_{endo}), 1.14–1.34 (m, 1 H, 3-H), 1.48 (ddd, ^3J = 8.4 Hz, ^3J = 4.3 Hz, ^3J = 4.3 Hz, 1 H, 1-H), 1.60–1.98 (m, 5 H), 6.05 (s, 1 H), 6.53 (s, 1 H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.4 (–, C-6), 21.1 (–, C-3), 25.4 (+, C-1), 27.4 [–, C-2(4)*], 31.3 (C_{quat}, C-1), 32.1 [–, C-2(4)*], 133.1 (–, C-3'), 148.3 (C_{quat}, C-2'), 167.8 (C_{quat}, C-1'). – MS (70 eV, EI), *m/z* (%): 170/172 (7/2) [M^+], 142/144 (3/1) [M^+ – CO], 135 (36) [M^+ – Cl], 107 (100) [M^+ – Cl – CO], 91 (62) [$C_7H_7^+$], 79 (63) [$C_6H_7^+$], 77 (26), 67 (10), 65 (20), 63 (5), 53 (13), 51 (18), 41 (16).

Benzyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**168**) was prepared in three ways. *A)* Alcoholysis of the obtained from acid **157** (4.26 g, 28 mmol) crude acyl chloride **176** with benzyl alcohol in the presence of 5 mol % of DMAP according to GP 11A (the reaction mixture was stirred at ambient temperature for 2 h) gave 5.9 g (86% yield, 92% purity) of crude product which was finally purified by column chromatography on 700 mL of silica gel, eluting with hexane/toluene, 10:1 to 5:1, to yield 4.25 g (62%) of pure **168** (99.5% purity according to GC). – *B)* Esterification of the acid **157** (1.36 g, 9 mmol) according to GP 11B gave 1.82 g of crude product, which was purified by column chromatography under the same conditions to yield 1.31 g (61% with purity 99.5% according to GC) of **168**. – *C)* To a stirred suspension of finely powdered and flame-dried K_2CO_3 (5 g, 36.2 mmol) and KI (22.9 mmol) in anhydrous DMF (40 mL) under argon was added solution of acid () (3.3 g, 21.7 mmol) and benzyl chloride (2.9 g, 22.9 mmol) in 10 mL of the same solvent in one portion at ambient temperature. After stirring for additional 12 h the mixture was poured into 250 mL of *t*BuOMe and filtered through a short pad of Celite®, which was rinsed with 50 mL of the same solvent. The filtrate was washed with water (2×150 mL), brine (100 mL) and dried over anhydrous $MgSO_4$. Evaporation of the solvents under reduced pressure gave 5.2 g of a crude product, which was subjected to flash" chromatography on 100 mL of flash silica gel, eluting with pentane to pentane/ether, 20:1, to yield 4.75 g (90%) of



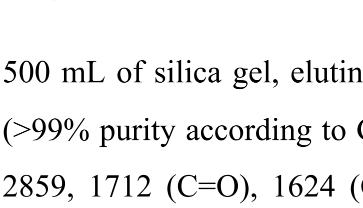
pure **168** (99.8% GC). – IR (film): ν = 3094, 3065, 3033, 2999, 2955, 2935, 2861, 1719 (C=O), 1623 (C=C), 1498, 1455, 1383, 1360, 1319, 1299, 1240, 1212, 1174, 1157, 1115, 1029, 1018, 955, 874, 812, 751, 735, 697 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.64 (dd, ^2J = 4.9 Hz, ^3J = 4.5 Hz, 1 H, 6-H_{endo}), 0.66 (dd, ^3J = 8.3 Hz, ^2J = 4.9 Hz, 1 H, 6-H_{exo}), 1.13–1.33 (m, 1 H), 1.46 (ddd, ^3J = 8.3 Hz, ^3J = 4.5 Hz, ^3J = 4.5 Hz, 1 H), 1.57–1.93 (m, 5 H), 5.20 (s, 2 H, OCH_2), 5.62 (d, ^2J = 1.5 Hz, 3'-H_{trans}), 6.17 (d, ^2J = 1.5 Hz, 3'-H_{cis}), 7.31–7.40 (m, 5 H, Ar-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.9 (–, C-6), 21.2 (–, C-3), 25.1 (+, C-5), 27.6 [–, C-2(4)*], 30.9 (C_{quat}, C-1), 32.2 [–, C-2(4)*], 66.2 (–, OCH_2), 125.1 (–, C-3'), 127.9 (+, C-Ar_{meta}), 128.0 (+, C-Ar_{para}), 128.5 (+, C-Ar_{ortho}), 136.1 (C_{quat}, C-Ar), 143.8 (C_{quat}, C-2'), 166.8 (C_{quat}, C-1'). – MS (70 eV, EI), *m/z* (%): 242 (1) [M^+], 197 (7), 151 (30) [$M^+ - C_7H_7^+$], 133 (16) [$M^+ - C_7H_7OH - H$], 105 (17) [$M^+ - C_7H_7OH - CO - H$], 91 (100), [$C_7H_7^+$], 79 (11) [$C_6H_7^+$], 77 (7) [C_6H_5], 65 (11), 43 (10), 41 (4). – Anal. Calculated for $C_{16}H_{18}O_2$ (242.31): C 79.31, H 7.49. Found: C 79.16, H 7.27.



(Bicyclo[2.2.1]hept-5-en-2-yl)methyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**169**) was prepared in four different ways. *A)* Alcoholysis of acyl chloride **176** (3.41 g, 20 mmol) with alcohol **162** (2.5 g, 20 mmol of commercially available *exo-*/*endo*-mixture) in the presence of 5 mol% DMAP according to GP 11A (the reaction mixture was stirred at ambient temperature for 12 h) gave 4.67 g of crude **169** (purity > 90%), which was purified by column chromatography on 500 mL of silica gel, eluting with hexane/toluene, 10:1 to 5:1, to yield 3.36 g of pure **169** (99.5% purity, yield: 65%). – *B)* Esterification of the acid **157** (1.36 g, 9 mmol) according to GP 11B gave 2.07 g of crude product, that was purified as above to yield 1.49 g **169** (64%, 99% purity). – *C)* To a stirred solution of alcohol **162** (250 mg, 2 mmol), DMAP (25 mg, 0.2 mmol), NEt_3 (0.31 mL, 2.2 mmol) and DIC (280 mg, 2.2 mmol) in anhydrous CH_2Cl_2 (4 mL) a solution of acid **157** (304 mg, 2 mmol) in the same solvent (1 mL) was added in one portion at ambient temperature. The reaction mixture was stirred at this temperature for 16 h, diluted with pentane (10 mL), filtered, the residue was washed with pentane (10 mL) and the combined filtrates were evaporated under reduced pressure. The residue was purified by flash" chromatography to yield 247 mg of **169** (48%, purity 95%). – *D)* To a stirred and pre-cooled to 0 °C solution of stabilized with BHT (1 mg) acid **157** (941 mg, 6.2 mmol) in anhydrous toluene (6 mL) were subsequently added NEt_3 (1.72 mL, 12.4 mmol) and dissolved in 4 mL of the same solvent *p*TsCl (1.18 g, 6.2 mmol). After the addition had been completed, the cooling bath was

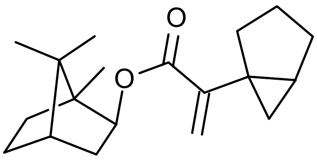
removed and the mixture was stirred at ambient temperature for 1 h. Obtained suspension was filtered under argon into reaction flask, containing a stirring bar, alcohol **162** (0.768 g, 6.2 mmol) and DMAP (76 mg, 0.6 mmol). The residue on the filter was washed under argon with anhydrous toluene (5 mL) and the resulting mixture was stirred at ambient temperature for 24 h. The solvent was removed under reduced pressure (T_{bath} < 40 °C) and the residue was stirred with pentane (50 mL) for 1 h. The suspension was filtered through a pad of flash silica gel (about 20 mL), which then was washed with pentane/ether, 20:1 mixture (2 × 20 mL). The combined filtrates were evaporated under reduced pressure and the residue was separated by column chromatography on 200 mL of silica gel, eluting with hexane/toluene, 5:1, to give 670 mg (42% yield, 95% purity) of product **169** and 670 mg (39%) of (bicyclo[2.2.1]hept-5-en-2-yl)carbinol tosylate. – IR (film): ν = 3061, 3031, 2960, 2862, 1719 (C=O), 1624 (C=C), 1449, 1391, 1363, 1325, 1287, 1213, 1175, 1113, 1016, 992, 940, 812, 723 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.55–0.68 (m, 3.03 H[132]), 1.14–1.36 (m, 3.33 H), 1.40–1.48 (m, 1.95 H), 1.58–1.97 (m, 7.08 H), 2.37–2.50 (m, 0.76 H), 2.70–2.90 (m, 2 H, 1"(4")-H), 3.66–3.75 (m, 0.77 H, OCH_2), 3.93 (dd, *J* = 11 Hz, *J* = 6.8 Hz, 0.80 H, OCH_2), 3.99–4.08 (m, 0.22 H, OCH_2), 4.20 (dd, *J* = 10.8 Hz, *J* = 6.8 Hz, 0.18 H, OCH_2), 5.55–5.58 (d, ^2J = 1.8 Hz, 0.7 H, 3'-H_{trans}), 5.94 (dd, ^3J = 5.8 Hz, ^3J = 3 Hz, 0.7 H, 6"-H), 6.08–6.16 (m, 2.3 H, 3'-H_{cis} + 5"-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.9 (–, C-6), 21.3 (–, C-3), 25.1 (+, C-5), 27.7 [–, C-2(4)*], 28.9 (–), 29.0 (–), 29.6 (–), 30.8 (C_{quat}, C-1), 32.3 [–, C-2(4)*], 37.7, 37.8, 38.0, 41.6, 42.2, 43.7, 44.0 (+), 45.0, 49.4 (–), 67.9, 68.6 (–, OCH_2), 124.5, 124.6, 124.7 (–, C-3'), 132.1, 136.2, 136.9, 137.5 [+, C-5"(6")], 144.1, 144.2 (C_{quat}, C-2'), 167.2 (C_{quat}, C-1'). – MS (70 eV, EI), *m/z* (%): 258 (2) [M^+], 193 (1), 152 (33) [$M^+ - C_8H_{10}$], 151 (20) [$M^+ - C_8H_{10} -$ H], 133 (6) [$M^+ - C_8H_{10} - H_2O - H$], 123 (2), 107 (86), [$M^+ - C_8H_{10} - CO_2 - H$], 91 (21), 79 (100) [$C_6H_7^+$], 77 (9) [$C_6H_5^+$], 66 (41), 53 (3), 41 (14). MS (HR-EI): 258.1620 ($C_{17}H_{22}O_2$, calcd. 258.1620).

Adamant-1-yl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**170**). Alcoholysis of acyl chloride **176** (3.32 g, 19.5 mmol) with alcohol **163** (2.96 g, 19.5 mmol) in the presence of 20 mol% DMAP according to GP 11A (the reaction mixture was stirred at ambient temperature for 36 h) gave 5.7 g of crude **170**, which was purified by column chromatography on 500 mL of silica gel, eluting with hexane/*t*BuOMe, 40:1, to yield 4.24 g (76%) of pure **170** (>99% purity according to GC) as a viscous colorless oil. – IR (film): ν = 3067, 3001, 2913, 2859, 1712 (C=O), 1624 (C=C), 1454, 1367, 1355, 1322, 1284, 1240, 1212, 1174, 1119,

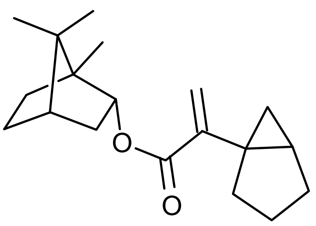


1053, 1015, 965, 938, 866, 812 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.59 (dd, ^2J = 4.9 Hz, ^3J = 4.4 Hz, 1 H, 6-H_{endo}), 0.63 (dd, ^3J = 8.3 Hz, ^2J = 4.9 Hz, 1 H, 6-H_{exo}), 1.11–1.32 (m, 1 H, 3-H), 1.40 (ddd, ^3J = 8.3 Hz, ^3J = 4.4 Hz, ^3J = 4.2 Hz, 1 H, 1-H), 1.56–1.96 (m, 5 H), 1.67 (bs, 6 H), 2.16 (bs, 9 H), 5.48 (d, ^2J = 1.8 Hz, 1 H, 3'-H_{trans}), 6.01 (d, ^2J = 1.8 Hz, 1 H, 3'-H_{cis}) – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.7 (–, C-6), 21.2 (–, C-3), 25.2 (+, C-1), 27.7 [–, C-2(4)*], 30.8 (+,C-3", C-5", C-7"), 30.9 (C_{quat}, C-1), 32.3 [–, C-2(4)*], 36.2 (–, C-4", C-6", C-10"), 41.4 (–, C-2", C-8", C-9"), 80.5 (C_{quat}, C-1"), 123.6 (–, C-3'), 145.7 (C_{quat}, C-2'), 166.2 (C_{quat}, C-1').–MS (70 eV, EI), *m/z* (%): 286 (2) [M^+], 243 (1), 150 (3) [$M^+ - C_{10}H_{15} - H$], 135 (100) [$M - C_{10}H_{15}O$, $C_{10}H_{15}^+$], 107 (6) [$M^+ - C_{10}H_{15}O - CO$], 93 (7), 79 (8) [$C_6H_7^+$], 67 (2), 55 (1), 41 (2).

(1R,S, 2'R)-exo-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**171**) was obtained from acid **157** (1.95 g, 12.8 mmol) and (1*S*)-*endo*-(−)-borneol (**164**) (1.98 g, 12,8 mmol) according to GP 11B. After the reaction mixture was stirred for 1 week at ambient temperature, it was worked up by usual manner to give a colorless viscous oil (4.24 g), which was subjected to column chromatography on 300 mL of silica gel, eluting with hexane/benzene, 5:1, to yield 1.24 g (34%) of the pure **171** that is mixture of two diastereomers (*R,R* and *R,S*, *de* ≈ 0). – IR (film): ν = 3105, 3067, 2954, 2879, 2771, 2727, 1717 (C=O), 1623 (C=C), 1473, 1456, 1390, 1369, 1322, 1300, 1240, 1212, 1175, 1119, 1086, 1053, 1015, 974, 943, 845, 812, 690 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.60–0.63 (m, 2 H, 6-H), 0.84 (s, 3 H, CH_3), 0.86 (s, 1.5 H, CH_3), 0.87 (s, 1.5 H, CH_3), 1.01 (s, 3 H, CH_3), 1.04–1.33 (m, 4 H), 1.39–1.48 (m, 1 H), 1.51–1.97 (m, 9 H), 4.69–4.75 (m, 1 H, 1'-H), 5.55 (d, *J* = 1.8 Hz, 1 H, 3"-H_{trans}), 6.07 (d, *J* = 1.8 Hz, 0.5 H, 3"-H_{cis}), 6.08 (d, *J* = 1.8 Hz, 0.5 H, 3"-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 11.6 (+, CH_3), 13.0 (–, C-6), 20.0, 20.1 (+, CH_3), 21.2 (–, C-3), 24.9 (+, C-5), 27.0 (–), 27.7 [–, C-2(4)*], 31.0 (C_{quat}, C-1), 32.4 [–, C-2(4)*], 33.9 (–), 38.9 (–), 45.0 (+, C-4'), 46.9 (C_{quat}, C-7'), 48.8 (C_{quat}, C-1'), 81.3 (+, C-2'), 124.5 (–, C-3"), 144.4 (C_{quat}, C-2"), 166.7 (C_{quat}, C-1"). – MS (70 eV, EI), *m/z* (%): 288 (7) [M^+], 262 (3), 245 (2), 203 (2), 180 (23), 166 (10), 152 (28) [$M^+ - C_{10}H_{16}$], 137 (100) [$C_{10}H_{17}^+$], 121 (4), 107 (20), 95 (15), 81 (70) [$C_6H_9^+$], 67 (14), 55 (6), 43 (6), 41 (10). – MS (HR-EI): 288,2089 ($C_{19}H_{28}O_2$, calcd. 288,2089).

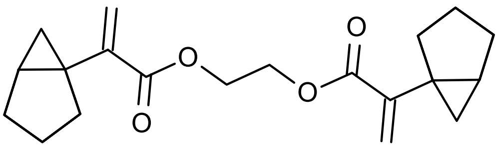


(1R,S, 2'S)-endo-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl 2-(bicyclo[3.1.0]hex-1-yl)propenoate

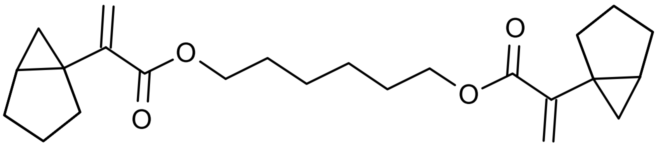


(**172**) was prepared in two ways. *A) Yamaguchi Protocol.* To a stirred solution of 2-(bicyclo[3.1.0]hex-1-yl)acrylic acid (**157**) (2.03 g, 13.3 mmol), NEt$_3$ (1.35 g, 13.3 mmol) and BHT (10 mg) in dry THF (25 mL) 2,4,6-trichlorobenzoylchloride (3.25 g, 13.3 mmol) was added under nitrogen at ambient temperature. The mixture was stirred for 2 h, then dry hexane (25 mL) was added, triethyl amine hydrochloride was filtered off and washed with hexane (2 × 5 mL) under argon. To the residue obtained after evaporation of the solvents under reduced pressure at 0 °C, a solution of DMAP (3.26 g, 26.6 mmol) and (1*S*)-*endo*-(–)-borneol (**164**) (4.10 g, 26.6 mmol) in dry toluene (50 mL) was added. The mixture was stirred at ambient temperature for 24 h, then filtered through Celite$^{®}$ and evaporated under reduced pressure. The residue was dissolved in a minimal amount of CH$_2$Cl$_2$ and diluted ten times with pentane by stirring. Obtained suspension was passed through a pad of a flash silica gel (~50 mL) and washed with pentane/ether, 20:1 mixture (2 × 50 mL). The residue, obtained after evaporation of the solvents, was purified by column chromatography on silica gel, eluting with hexane/benzene/1,2-dichloro ethane, 20:2:1, to yield 2.68 g (70%) of pure **172** as a colorless viscous oil. – *B).* Alcoholysis of acyl chloride **176** (3.41 g, 20 mmol) with (1*S*)-*endo*-(–)-borneol (**172**) (3.08 g, 20 mmol) in the presence of 110 mol% DMAP (2.69 g, 22 mmol) according to GP 11A (the reaction mixture was stirred at ambient temperature for 48 h) gave 4 g of crude **172**, which was purified by column chromatography on 500 mL of silica gel, eluting with hexane/toluene, 6:1, to yield 3.6 g (63%) of pure **172** (>98% purity according to GC) as a viscous colorless oil. – IR (film): ν = 3100, 3067, 3028, 2954, 2869, 1717 (C=O), 1623 (C=C), 1473, 1456, 1421, 1387, 1360, 1327, 1295, 1287, 1215, 1176, 1120, 1042, 1021, 993, 979, 941, 917, 892, 813, 692 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 0.60–0.68 (m, 2 H, 6-H), 0.85 (s, 1.5 H, CH$_3$), 0.86 (s, 1.5 H, CH$_3$), 0.88 (s, 3 H, CH$_3$), 0.92 (s, 3 H, CH$_3$), 0.95–1.04 (m, 1 H), 1.18–1.38 (m, 3 H), 1.40–1.47 (m, 1 H), 1.58–2.06 (m, 8 H), 2.40 (dddd, ^{3}J = 13.8 Hz, ^{3}J = 9.8 Hz, ^{3}J = 4.5 Hz, ^{3}J = 3.5 Hz, 1 H, 4'-H), 4.93 (dd, ^{3}J = 3.5 Hz, ^{3}J = 2 Hz, 0.5 H, 2'-H), 4.95 (dd, ^{3}J = 3.5 Hz, ^{3}J = 2 Hz, 0.5 H, 2'-H), 5.56 (d, ^{2}J = 1.8 Hz, 0.5 H, 3''-H$_{trans}$), 5.57 (d, ^{2}J = 1.8 Hz, 0.5 H, 3''-H$_{trans}$), 6.12 (d, ^{2}J = 1.8 Hz, 0.5 H, 3''-H$_{cis}$), 6.14 (d, ^{2}J = 1.8 Hz, 0.5 H, 3''-H$_{cis}$). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 12.9 (–, C-6), 13.6 (+, CH$_3$), 18.8 (+, CH$_3$), 19.7 (+, CH$_3$), 21.3 (–, C-3), 25.1 (+, C-5), 27.3, 27.7, 28.1 (–), 31.0 (C$_{\text{quat}}$, C-1), 32.4 [–, C-2(4)*], 36.9 (–), 44.8 (+, C-4'), 47.7(C$_{\text{quat}}$, C-7'), 48.8 (C$_{\text{quat}}$, C-1'), 80.2 (+, C-2'), 124.7 124.8 (–, C-3''), 144.4 (C$_{\text{quat}}$, C-2''), 167.6 (C$_{\text{quat}}$, C''-1). – MS (70 eV, EI), *m/z* (%): 288 (1) [M^{+}], 175 (4), 173 (7), 152 (20) [$M^+ - C_{10}H_{16}^+$], 137 (52) [$C_{10}H_{17}^+$], 121 (8), 109 (16), 107 (19) [$C_8H_{11}^+$], 95 (28), 93 (15), 91 (12), 81 (100) [$C_6H_9^+$], 79 (17) [$C_6H_7^+$], 77 (7) [$C_6H_7^+$], 69 (22), 67 (19), 57 (13), 55 (18), 53 (6), 43 (16), 41 (32). – MS (HR-EI): 288.2089 ($C_{19}H_{28}O_2$, calcd. 288.2089).

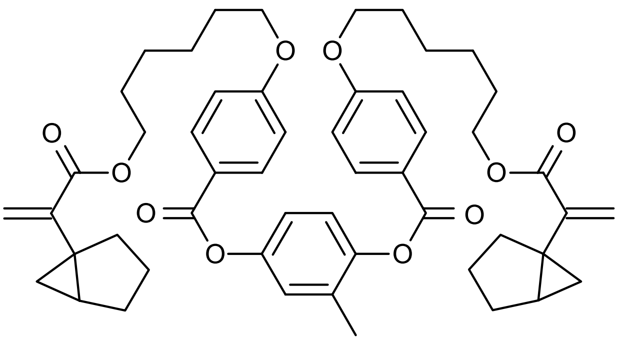
1,2-bis-[2-(Bicyclo[3.1.0]hex-1-yl)propenoyloxy]ethane (**173**). To a stirred solution of 1,2-ethanediol (0.122 g, 19.7 mmol), DCC (0.86 g, 4.2 mmol), NEt_3 (0.59 mL, 4.2 mmol) and DMAP (50 mg, 0.4 mmol) in anhydrous acetonitrile (10 mL) a solution of acid (0.60 g, 3.9 mmol) in 5 mL of the same solvent was added in one portion under nitrogen at ambient temperature. The mixture was stirred overnight (~16 h) and evaporated under reduced pressure at ambient temperature. The residue was dissolved in ether (50 mL), washed with 1 M aqueous H_2SO_4 (10 mL), water (10 mL), brine (20 mL) and dried over $MgSO_4$. A residue obtained after evaporation of solvent under reduced pressure was purified by column chromatography on 100 mL of silica gel, eluting with hexane/*t*BuOMe, 20:1, to yield 0.2 g (15%) of pure **173** as a colorless viscous oil. – IR (film): ν = 3065, 3028, 3000, 2955, 2861, 1723 (C=O), 1623 (C=C), 1476, 1451, 1410, 1370, 1316, 1288, 1241, 1208, 1173, 1112, 1055, 1009, 944, 887, 874, 812, 712, 691 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.62 (dd, $^3J = 6$ Hz, $^2J = 4.9$ Hz, 2 H, 6-H_{exo}), 0.63 (dd, $^2J = 4.9$ Hz, $^3J = 4.2$ Hz, 2 H, 6-H_{endo}), 1.12–1.33 (m, 2 H), 1.43 (ddd, $^3J = 6$ Hz, $^3J = 6$ Hz, $^3J = 4.2$ Hz, 2 H, 1-H), 1.54–1.64 (m, 2 H), 1.65–1.93 (m, 8 H), 4.39 (s, 4 H, OCH_2), 5.61 (d, $^2J = 1.8$ Hz, 2 H, 3'-H_{trans}), 6.13 (d, $^2J = 1.8$ Hz, 2 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.9 (–, C-6), 21.2 (–, C-3), 25.0 (+, C-5), 27.6 [–, C-2(4)*], 30.8 (C_{quat}, C-1), 32.2 [–, C-2(4)*], 62.2 (–, CH_2O), 125.4 (–, C-3'), 143.5 (C_{quat}, C-2'), 166.7 (C_{quat}, C-1'). – MS (70 eV, EI), *m/z* (%): 330 (2) [M^+], 302 (1), 268 (3), 240 (3), 223 (1), 179 (100), 160 (4), 149 (9), 134 (14), 106 (25), 91 (25), 79 (16) [$C_6H_7^+$], 57 (2), 41 (6). – MS (HR-EI): 330.1831 ($C_{20}H_{26}O_4$, calcd. 330.1831).



1,6-bis-{2-(Bicyclo[3.1.0]hex-1-yl)propenoyloxy}hexane (**174**) was prepared from acid **157** (11.0 g, 72.2 mmol) and 1,6-hexanediol (4.27 g, 36.1 mmol) according to GP 11B. The crude product (13.7 g) was purified by column chromatography on 1 L of silica gel (column ∅70 mm), eluting with hexane/*t*BuOMe, 20:1, to yield 11.7 g (84%) of pure diester **174** as a colorless viscous oil. – IR (film): ν = 3067, 3028, 3001, 2953, 2861,



1719 (C=O), 1624 (C=C), 1476, 1451, 1364, 1292, 1213, 1175, 1119, 1017, 987, 941,813 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.58–0.66 (m, 4 H), 1.12–1.33 (m, 2 H), 1.39–1.46 (m, 6 H), 1.57–1.74 (m, 8 H), 1.77–1.94 (m, 6 H), 4.13 (t, ^3J = 6.8 Hz, 4 H, OCH_2), 5.56 (d, ^2J = 1.8 Hz, 2 H, 3'-H$_{trans}$), 6.09 (d, ^2J = 1.8 Hz, 2 H, 3'-H$_{cis}$). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.9 (–, C-6), 21.2 (–, C-3), 25.1 (+, C-5), 25.7 (–), 27.6 [–, C-2(4)*], 28.5 (–), 30.8 (C$_{quat}$), 32.3 [–, C-2(4)*], 64.3 (–, CH_2O), 124.6 (–, C-3'), 144.1 (C$_{quat}$, C-2'), 167.1 (C$_{quat}$, C-1'). – MS (70 eV, EI), *m/z* (%): 386.3 (14) [M^+], 268 (20), 240 (24), 152 (38), 135 (100), 107 (94), 91 (38), 83 (24), 81 (9) [$C_6H_9^+$], 79 (36) [$C_6H_7^+$], 77 (10) [$C_6H_5^+$], 67 (11), 55 (36), 41 (14). – MS (HR-EI): 386.2457 ($C_{24}H_{34}O_4$, calcd. 386.24571). – Anal. Calculated for the corresponding polymer $(C_{24}H_{34}O_4)_n$ $(386.52)_n$: C 74.58, H 8.87. Found: C 74.39, H 8.57.



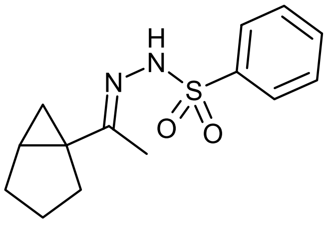
1,4-di-{4-[6-(2-(Bicyclo[3.1.0]hex-1-yl)propenoyloxy)hexyloxy]phenylcarbonyloxy}-2-methylbenzene (**175**). To a stirred suspension of 2-(bicyclo[3.1.0]hex-1-yl)acrylic acid (0.54 g, 3.6 mmol), 1,4-di-[4-(6-hydroxyhexyloxy)-phenylcarbonyloxy]-2-methylbenzene (**167**) (1 g, 1.8 mmol), PPh_3 (0.95 g, 3.6 mmol) in 40 mL of anhydrous THF/toluene, 1:1 mixture, kept at –78 °C (dry ice/acetone bath) under nitrogen, diethyl azodicarboxylate (0.63 g, 3.6 mmol) was gradually added so that the mixture temperature did not exceed –70 °C. After stirring at this temperature for an additional 1 h, the cooling bath was removed and the reaction mixture was stirred overnight at ambient temperature. The residue obtained after evaporation of the solvents under reduced pressure, was stirred with hexane/benzene, 2:1mixture for 2 h and then filtered. The filtrate was evaporated under reduced pressure at ambient temperature to give crude viscous oil, which was purified by flash” chromatography on 40 mL of flash silica gel, eluting with hexane/benzene/*t*BuOMe, 8:4:1, to yield 1.03 g (70%) of pure **175** as a very viscous colorless oil. – IR (film): ν = 3070, 3034, 3003, 2939, 2864, 2769, 1734 (C=O), 1719 (C=O), 1604 (C=C), 1580, 1509, 1493, 1473, 1453, 1421, 1394, 1362, 1314, 1255, 1215, 1160, 1116, 1073, 1005, 912, 894, 843, 811, 763, 728 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.61–0.67 (m, 4 H, 6-H), 1.07–1.18 (m, 2 H), 1.42–1.91 (m, 28 H), 2.24 (s, 3 H, CH_3), 4.05 (t, ^3J = 6.5 Hz, 4 H, CH_2OAr), 4.17 (t, ^3J = 6.5 Hz, 4 H, CH_2O_2C), 5.58 (d, ^2J = 1.8 Hz, 2 H, 3'-H$_{trans}$), 6.11 (d, ^2J = 1.8 Hz, 2 H, 3'-H$_{cis}$), 6.95–7.00 (m, 4 H, Ar-H), 7.06–7.19 (m, 3 H, Ar-H), 8.11–8.19 (m, 4 H, Ar-H). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.9 (–, C-6), 16.4

(+, CH_3), 21.2 (–, C-3), 25.1 (+, C-5), 25.7, 25.8 (–), 27.6 [–, C-2(4)*], 28.6, 29.0 (–), 30.9 (C_{quat}, C-1), 32.3 [–, C-2(4)*], 64.3 (–, CH_2O_2C), 68.0 (–, CH_2OAr), 114.2, 114.3 (+, C-Ar), 120.0 (+, C-Ar), 121.4, 121.5 (C_{quat}, C-Ar), 122.9, 124.1 (+, C-Ar), 124.6 (–, C-3'), 128.3 (+, C-Ar), 131.7 (C_{quat}, C-Ar), 132.3 (+, C-Ar), 144.1 (C_{quat}, C-2'), 147.0, 148.4 (C_{quat}, $COOC_{Ar}$), 163.4 163.5 (C_{quat}, CH_2OC_{Ar}), 164.5 164.9 (C_{quat}, $ArCO_2$), 167.2 (C_{quat}, C-1'). – MS (70 eV, DCI, NH_3), *m/z* (%): 850 (100) $[M + NH_4^+]$, 698 (1), 496 (4), 408 (3), 391 (6), 272 (21), 170 (28). – Anal. Calculated for $C_{51}H_{60}O_{10}$ (833.02): C 73.53, H 7.26. Found: C 72.87, H 7.03.

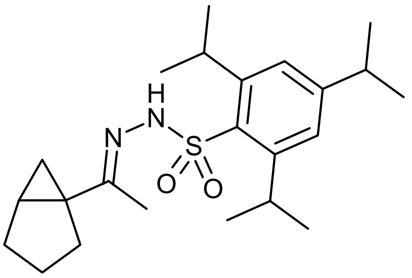
2.6. Alternative Approaches to Synthesis of the 2-(Bicyclo[3.1.0]hex-1-yl)acrylates

2.6.1. SHAPIRO reaction towards acrylate synthesis

N'-[(1E)-1-Bicyclo[3.1.0]hex-1-ylethylidene]benzenesulfonohydrazide (**183**). To a stirred solution of benzenesulfonylhydrazide (8.77 g, 51 mmol) in a warm methanol (30 mL) (bicyclo[3.1.0]hex-1-yl)ethanone (**182**) (6.35 g, 51 mmol) was added. The mixture was allowed to crystallize at ambient temperature for 5 h then a crystalline material was filtered, washed with cold methanol (2 × 5 mL) and dried under reduced pressure to give 11 g of pure **183** as a colorless powder. The mother liquor was evaporated under reduced pressure and the residue was recrystallized from toluene/cyclohexane, 1:3, to give 2.16 g of **183** as slightly yellow prisms. Overall yield: 13.16 g (93%). – M. p. 120–122 °C. – IR (KBr): ν = 3199, 3072, 3006, 2966, 2915, 2858, 1615 (C=N), 1450, 1401, 1342, 1327, 1285, 1167, 1134, 1094, 1044, 925, 752, 728, 681, 621580, 562, 550 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.68 (dd, ^2J = 5.3 Hz, ^3J = 5 Hz, 1 H, 6-H_{endo}), 0.78 (dd, ^3J = 7.8 Hz, ^2J = 5.3 Hz, 1 H, 6-H_{exo}), 1.08–1.32 (m, 1 H), 1.47–1.78 (m, 5 H), 1.58 (s, 3 H, 2'-C), 1.90–2.05 (m, 1 H, C-1), 7.47–7.59 (m, 3 H, Ph-H), 7.96–8.01 (m, 2 H, Ph-$H_{2,6}$). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.8 (+, CH_3), 13.3 (–, C-6), 20.6 (–, C-3), 25.3 (+, C-5), 26.9, 28.4 [–, C-2(4)*], 35.0 (C_{quat}, C-1), 128.2, 128.6 (+, C-Ph), 133.0 (+, C_{para}-Ph), 138.2 (C_{quat}, Ph).[133] – MS (70 eV, EI), *m/z* (%): 278 (1) $[M^+]$, 141 (5) $[C_6H_5SO_2^+]$, 138 (8) $[M^+ - C_6H_5SO_2]$, 137 (100) $[M^+ - C_6H_6 - SO_2]$, 109 (10) $[M^+ - C_6H_6 - SO_2 - N_2]$, 95 (36), 93 (13), 91 (8), 81 (6), 79 (21) $[C_6H_7^+]$, 77 (77) $[C_6H_5^+]$, 69 (5), 68 (5), 67 (10), 65 (9), 55 (21), 53 (17), 51 (34), 42 (28), 41 (51). – Anal. Calculated for $C_{14}H_{18}N_2O_2S$ (278.37): C 60.41, H 6.52, N 10.06. Found: C 60.20, H 6.24, N 9.82.



N'-[(1E,Z)-1-bicyclo[3.1.0]hex-1-ylethylidene]-2,4,6-tris(1-methylethyl)benzenesulfonohydrazide (**184**). To a stirred suspension of 1,3,5-triisopropyl benzenesulfonylhydrazide (7.46 g, 25 mmol) in methanol (20 mL) (bicyclo[3.1.0]hex-1-yl)ethanone (**182**) (3.11 g, 25 mmol) and 37% aqueous HCl (0.2 mL) were subsequently added at room temperature. After stirring for an additional 1 h, the mixture was chilled at –0 °C overnight and filtered. The product was washed with cold methanol (2 × 5 mL) and dried under reduced pressure (0.01 Torr) at room temperature for 12 h to yield 8.1 g (80%) of colorless powder, that is pure (*E/Z*) mixture of **184** (approximately 85/15, according to ^{1}H NMR data). – M. p. 170–171 °C (dec.). – IR (KBr): ν = 3261, 2960, 2931, 2866, 1601 (C=N), 1562, 1460, 1425, 1382, 1362, 1327, 1284, 1259, 1196, 1167, 1154, 1106, 1059, 1036, 940, 915, 881, 806, 757, 699, 663, 630, 613, 599 cm^{-1}. – ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.64 (dd, ^2J = 5.2 Hz, ^3J = 4.8 Hz, 1 H, 6-H), 0.77 (dd, ^3J = 8.2 Hz, ^2J = 5.2 Hz, 1 H, 6-H), 1.05–1.35 (m, 1 H), 1.25 (d, ^3J = 7 Hz, 6 H), 1.27 (d, ^3J = 7 Hz, 12 H), 1.45–1.98 (m, 6 H), 1.60 (s, 3 H, 2'-H), 2.91 (sept, ^3J = 7 Hz, 1 H), 4.24 (sept, J = 7 Hz, 2 H), 7.16 (s, 2 H, H-Ar), 7.40 (bs, 1 H, NH). – ^{13}C NMR (50.3 MHz, $CDCl_3$, APT): δ = 12.6 (+, CH_3, C-1'), 13.1 (–, C-6), 20.7 (–, C-3), 23.5 (+, 2 CH_3), 24.8 (+, 4 CH_3), 24.9 (+, CH), 26.9, 28.5 [–, C-2(4)*], 29.9 (+, 2 CH), 34.1 (+, C-5), 34.9 (C_{quat}, C-1), 123.5 (+, C-Ar), 131.6, 151.2, 152.9 (C_{quat}, C-Ar)[134]. – MS (70 eV, EI), *m/z* (%): 404 (9) [M^+], 282 (4) [$C_{14}H_{22}N_2O_2S^+$], 269 (6), 267 (4) [$C_{15}H_{23}O_2S^+$], 251 (8) [$C_{14}H_{19}O_2S^+$], 203 (4) [$C_{15}H_{23}^+$], 175 (4) [$C_{13}H_{19}^+$], 137 (100) [$M^+ - C_{15}H_{23}O_2S^+$], 124 (15), 123 (14), 119 (11), 118 (10), 95 (19), 93 (33), 91 (10), 79 (11) [$C_6H_7^+$], 77 (5) [$C_6H_5^+$], 69 (3), 67 (5), 55 (7), 53 (3), 43 (16), 41 (11). – Anal. Calculated for $C_{23}H_{36}N_2O_2S$ (404.61): C 68.27, H 8.97, N 6.92. Found: C 68.49, H 8.78, N 7.00.

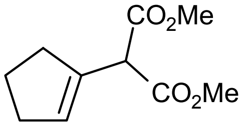


Attempted trapping of in situ generated 1-bicyclo[3.1.0]hexylethenyl lithium with CO_2. To a cooled (dry ice/acetone bath) as low as possible to keep benzene in solution (somewhere between –20 and –30°C) suspension of phenyl hydrazide **183** (2.78 g, 10 mmol) in benzene/TMEDA mixture (10:4.5 mL), was gradually added MeLi (20 mL of 1.6 M solution in ether, 32 mmol), the mixture was simultaneously chilled to –70 °C and stirred at this temperature for 30 min. Then the cooling bath was removed, the mixture was stirred at ambient temperature after the nitrogen evolution has been completely ceased (3 – 3.5 h, the mixture turned red-brown) and cooled to –50 °C (at lower temperature the mixture becomes heterogeneous). This solution was gradually added to a vigorously stirred anhydrous THF

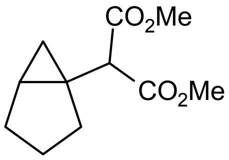
(25 mL) saturated with CO_2 at –70 C at such a rate to keep the internal temperature of the mixture under –60 °C. After the addition has been complete, the cooling was removed, the mixture was allowed to reach ambient temperature and evaporated under reduced pressure (T_{bath} < 40 °C). The residue was suspended in ether (100 mL) and acidified with 20% aqueous H_2SO_4 (about 20 mL). Organic layer was separated and the aqueous phase was extracted with ether (3 × 20 mL). The combined extracts were dried over Na_2SO_4, and the solvent was removed under reduced pressure. The residue was "Kugelrohr" distilled (100 °C/0.5 Torr) to give 0.53 g (35%) of crude acid **157**, which NMR spectra corresponded to those described above.

Attempted trapping of in situ generated 1-bicyclo[3.1.0]hexylethenyl lithium with (1S)-endo-(–)-bornyl chloroformate. To a stirred suspension of **184** (4 g, 10 mmol) in anhydrous hexane (30 mL) was added TMEDA (3.4 mL, 38 mmol) and the mixture was chilled under argon to −78 °C. Then *n*BuLi (8.5 mL of 2.48 N solution in hexanes, 21 mmol) was added dropwise at –70 °C and the mixture was stirred at this temperature for 1 h. Over this period the mixture turned only slightly yellow and was still heterogenous (expected red color of dianion was not observed). Then, solution of TMEDA (5 mL) in benzene (10 mL) was added, the mixture has been warmed to such a temperature so the evolution of nitrogen was not yet observed (between –50 and –40°C), and stirring was continued at this temperature. After 3 h the mixture turned orange and the solid starting material was partially dissolved. The cooling was removed and the mixture was allowed to warm to 0 °C. After the nitrogen evolution has been ceased, the mixture was chilled to –78 °C and (1*S*)-*endo*-(−)-bornyl chloroformate (**186**) (2.16 g, 10 mmol) was gradually added keeping the internal mixture temperature under −60 °C. After stirring at this temperature for 30 min, the cooling was removed, the mixture was allowed to reach an ambient temperature and poured into cooled to 0 °C 1 M aqueous H_2SO_4 (75 mL). The organic layer was separated and the aqueous phase was extracted with ether (2 × 25 mL). The combined organic phases were washed with water (50 mL), brine (50 mL) and dried over $MgSO_4$. The residue obtained after evaporation of the solvents under reduced pressure was triturated with pentane (50 mL), passed through a pad of flash silica gel (3 cm, 40 mL), and eluted with pentane/ether mixture, 40:1. After evaporation of the solvents it was obtained 0.8 g of colorless oil, that was **172** contaminated with ~40% (according to ^{1}H NMR) of (1*S*)-*endo*-(−)-bornyl pentanoate. Further elution of the silica gel with pentane/ether, 5:1 partially recovered the starting chloroformate **186**.

2.6.2. Simmons-Smith cyclopropanation of 2-(cyclopenten-1-yl)malonic acid derivatives with Shi carbenoid

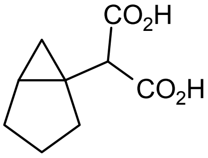


Dimethyl 2-(cyclopenten-1-yl)malonate (**188**). To a stirred suspension of NaH (285 mmol, 11.4 g of 60% dispersion in oil) in anhydrous THF (180 mL) dimethyl cyclopentylidenemalonate (**187**) (54.1 g, 273 mmol) was gradually added. After the hydrogen evolution had been ceased, the reaction mixture was stirred at ambient temperature for additional 30 min, chilled to −78 °C under argon and 4 N ethereal HCl (71.5 mL) was gradually added within 5 min by vigorous stirring and cooling (dry ice/acetone bath). The cooling bath was removed as soon as the exothermic reaction has been completed and the mixture was allowed to reach –10 °C. Then water (50mL) was gradually added at this temperature (cooling with ice/salt bath) Organic layer was separated and aqueous phase was extracted with ether (3 × 50 mL). The combined organic layers were washed with brine (2 × 100mL) and dried over $MgSO_4$. Evaporation of the solvents under reduced pressure gave 58.6 g of crude oil, which was distilled under reduced pressure to give 54 g of product **188** contaminated only with the starting material (85:15 ratio according to GC).



Dimethyl 2-(bicyclo[3.1.0]hexen-1-yl)malonate (**189**). To a stirred solution of prepared according to GP 6 Shi’s carbenoid (220 mmol) a crude **188** (22.1 g, 111 mmol) was gradually added so, that the temperature of the reaction mixture did not exceed 0 °C. After stirring at this temperature for 30 min, the cooling bath was removed and the mixture was allowed to react at ambient temperature for 24 h. The reaction was worked up by usual manner as described in GP 6. Obtained after evaporation of the solvents crude product (24.7 g) was distilled under reduced pressure to give 20.9 g of mixture (0.8% of starting material **188**, 60% of product **189**, 24% of **190** and 15% of dimethyl cyclopentylidenemalonate (**187**) according to GC) boiling between 62 ° and 67 °C at 0.1 Torr. Although isolation of pure **189** by means a simple rectification seems problematic and required special equipment (Spaltrohr) to produce bulky amounts of pure **189**, it is possible to obtain its analytical sample by column chromatography (eluent hexane/*t*BuOMe, 10:1, 100 mL of silica gel per 1 g of crude mixture). – IR (film): ν = 3067, 3000, 2954, 2864, 1739, 1436, 1311, 1245, 1149, 1050, 1031, 950, 910, 872, 801, 739 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.44 (dd, ^3J = 8.3 Hz, ^2J = 5.5 Hz, 1 H), 0.55 (dd, ^2J = 5.5 Hz, ^3J = 4.5 Hz, 1 H), 1.11−1.31 (m, 2 H), 1.54−1.89 (m, 5 H), 3.23 (s, 1 H, 2'-H), 3.73

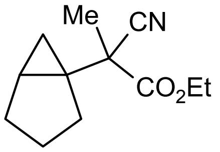
(s, 6 H, OCH_3). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 11.9 (–, C-6), 21.1 (–, C-3), 23.6 (+, C-5), 27.1 (–, C-4), 27.4 (C_{quat}, C-1), 29.5 (–, C-2), 52.2 (+, CH_3), 56.7 (+, CH), 169.2 169.3 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 212 (4) [M^+], 181 (2) [$M^+ - CH_3O$], 153 (36) [$M^+ - CO_2CH_3$], 152 (100) [$M^+ - CO_2CH_3 - H$], 137 (8), 133 (12), 121 (19), 101 (2), 93 (24), 80 (15) [$C_6H_8^+$], 79 (13), 77 (12) [C_6H_5], 65 (4), 59 (10), 53 (6), 41 (7). – Anal. Calculated for $C_{11}H_{16}O_4$ (212.25): C 62.25, H 7.60. Found: C 62.31, H 7.54.



2-(Bicyclo[3.1.0]hexen-1-yl)malonic acid (**191**). The previously obtained mixture (20.8 g) contained 60% of **189** was dissolved in ethanol (100 mL) and added to solution of KOH (25 g) in water (12 mL). After stirring at ambient temperature for 16 h, the reaction mixture was concentrated under reduced pressure (T_{bath} < 60 °C) and the residue was washed with ether (2 × 50 mL). The aqueous layer was separated, mixed with ether (100 mL) and acidified with 12 N HCl to pH=1 (35–36 mL) by cooling (ice bath). Organic layer was separated and aqueous phase was extracted with ethyl acetate (5 × 50 mL). The combined organic phases were washed with brine (100 mL) and dried over Na_2SO_4. A slightly brown solid obtained after evaporation of the solvents under reduced pressure was recrystallized from $CHCl_3$ to yield 10.4 g (51% from dimethyl cyclopentylidenemalonate) of pure diacid **191**. The analytical sample was obtained after additional crystallization from toluene. – M. p. 152 °C (dec). – IR (KBr): ν = 3424 (OH), 3080, 3006, 2959, 2870, 2672, 1718 (C=O), 1419, 1309, 1286, 1272, 1223, 1205, 1185, 1096, 1048, 1030, 1002, 927, 844, 787, 775, 711, 667 cm^{-1}. – ^1H NMR (250 MHz, DMSO-d^6): δ = 0.37–0.46 (m, 2 H, 6-H), 1.07–1.23 (m, 2 H), 1.44–1.76 (m, 5 H), 3.12 (s, 1 H, 2'-H), 7.53 (s, 1 H, COOH). – ^{13}C NMR (62.9 MHz, DMSO-d^6, DEPT): δ = 11.8 (–, C-6), 20.9 (–), 23.0 (+, C-5), 27.2 (C_{quat}, C-1), 27.3, 29.4 (–), 56.6 (+, C-2'), 170.5, 170.7 (C_{quat}, CO_2H). – MS (70 eV, DCI, NH_3), *m/z* (%): 386 (3) [$2M + NH_4^+$], 219 (64) [$M + NH_3 + NH_4^+$], 202 (100) [$M + NH_4^+$], 175 (6), 158 (11), 140 (12), 134 (13), 116 (2), 100 (6). – Anal. Calculated for $C_{11}H_{16}O_4$ (184.19): C 58.69, H 6.57. Found: C 58.84, H 6.30.

Decarboxylative methylenation of **191** *to 2-(bicyclo[3.1.0]hexen-1-yl)propenoic acid* (**157**). A mixture of diacid **191** (1.84 g, 10 mmol), dimethyl amine hydrochloride (0.9 g, 11 mmol), 37% aqueous CH_2O (3.8 mL, 50 mmol), piperidine (0.1 mL, 1 mmol), BHT (1 mg) and methanol (10 mL) in benzene (100 mL) was stirred by reflux for 2 h. Organic layer was separated and aqueous phase was extracted with ether (50 mL). The combined organic phases were washed with brine (2 × 50 mL) and dried over Na_2SO_4. The solvents were evaporated under reduced pressure, the residue was dissolved in CCl_4 (30 mL) and evaporated again to give a target acid **157** as a colorless crystals. Yield: 1.25 g (82%). The spectral data of the synthesized product were identical to them described above.

Ethyl 2-cyano-2-(bicyclo[3.1.0]hex-1-yl) propanoate (**195**). To a slowly stirred mixture of

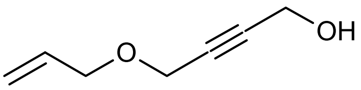


ethyl cyanocyclopentylidene acetate (**194**) (1.79 g, 10 mmol) and NaH (10 mmol, 0.4 g of 60% dispersion in oil) THF (20 mL) was carefully added by occasional cooling with ice water. After the hydrogen evolution has been ceased, the mixture was stirred for additional 30 min, completely evaporated under reduced pressure and dried for 1 h at 0.1 Torr. To the obtained solid residue a freshly prepared according to GP 6 Shi's carbenoid (30 mmol in 45 mL of CH_2Cl_2) was added under argon keeping the temperature of the both components under 0 °C (ice/salt bath). After additional stirring at 0 °C for 30 min, the cooling was removed and the mixture was allowed to react at ambient temperature for 40 h. Then 2 N aqueous NaOH (30 mL) was added, the mixture was passed through Celite®, organic layer was separated and aqueous phase was extracted with ether (3 × 30 mL). The combined organic phases were washed with 10% aqueous NaCl (50 mL), brine (50 mL) and dried over $MgSO_4$. A residue (2.6 g) obtained after evaporation of the solvents under reduced pressure was subjected to flash" chromatography on 40 mL of flash silica gel, eluting with pentane/ether, 10:1 to 5:1, to give 1.0 g (43% yield) of slightly yellow liquid, that was **195** as an approximately equal mixture of diastereomers (one spot on TLC, 85% purity according to GC). Column chromatography of this mixture on 100 mL of silica gel, eluting with hexane/*t*BuOMe, 10:1, let to separate these diastereomers partially; each of them was obtained with a purity grade (>90%) enough to characterize the both isomers by NMR-spectra. – *First diastereomer.* – Colorless oil. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.54 (dd, ^2J = 5.8 Hz, ^3J = 4.6 Hz, 1 H, 6-H$_{endo}$), 0.79 (ddd, J = ^{3}8.6 Hz, ^2J = 5.8 Hz, J = 1 Hz, 1 H, 6-H$_{exo}$), 1.12–1.38 (m, 1 H), 1.30 (t, J = 7 Hz, 3 H, CH_3), 1.51 (s, 3 H, CH_3), 1.45–1.74 (m, 6 H), 4.16–4.34 (AB, 4 H, OCH_2). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.5 (–, C-6), 14.9 (+, CH_3), 21.4 (+, CH_3, C-3'), 21.8 (–, C-3), 23.4 (+, C-5), 27.7, 29.4 [–, C-2(4)], 33.8 (C$_{quat}$, C-1), 47.6 (C$_{quat}$, C-2'), 63.2 (–, OCH_2), 120.3 (C$_{quat}$, CN), 169.3 (C$_{quat}$, C-1'). – .*Second diastereomer.* – Colorless oil. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.52 (dd, ^2J = 5.8 Hz, ^3J = 4.6 Hz, 1 H, 6-H$_{endo}$), 0.78 (dd, ^3J = 8.6 Hz, ^2J = 5.8 Hz, 1 H, 6-H$_{exo}$), 1.14–1.36 (m, 1 H), 1.29 (t, J = 7 Hz, 3 H, CH_3), 1.53 (s, 3 H, CH_3), 1.41–1.82 (m, 6 H), 4.23 (q, J = 7 Hz, 2 H, OCH_2). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.1 (–, C-6), 14.0 (+, CH_3), 20.5 (+, CH_3, C-3'), 20.8 (–, C-3), 22.5 (+, C-5), 27.0, 28.4 [–, C-

2(4)], 32.6 (C_{quat}, C-1), 46.7 (C_{quat}, C-2'), 62.4 (–, OCH_2), 119.5 (C_{quat}, CN), 168.5 (C_{quat}, C-1'). The following data were obtained for the diastereomeric mixture of **195**. – IR (film): ν = 3072, 2946, 2869, 2244 (CN), 1744 (C=O), 1448, 1377, 1312, 1295, 1245, 1230, 1163, 1145, 1113, 1020, 943, 856, 784, 762, 696, 631 cm^{-1}. – MS (70 eV, EI), *m/z* (%): 207 (1) [M^+], 167 (10), 162 (3) [$M^+ - C_2H_5O$), 148 (3), 134 (29) [$M^+ - CO_2C_2H_5$], 128 (6) 120 (2), 118 (2), 107 (17), 93 (7), 91 (4), 81 (100) [$C_6H_9^+$], 79 (21) [$C_6H_7^+$], 77 (4) [$C_6H_5^+$], 65 (3), 53 (5), 41 (7). – Anal. Calculated for $C_{12}H_{17}NO_2$ (207.27): C 69.54, H 8.27, N 6.76. Found: C 69.27, H 9.03, N 6.48.

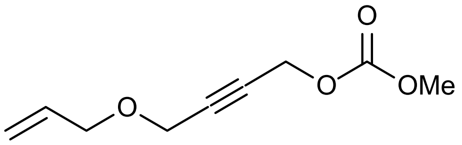
2.6.3. Synthesis of 2-(bicyclo[3.1.0]hex-1-yl)acrylates via Pd-catalyzed 5-*exo-trig*/3-*exo-trig* cascade cyclization of 1,6-enines.

2.6.3.1. Synthesis of acyclic precursors.

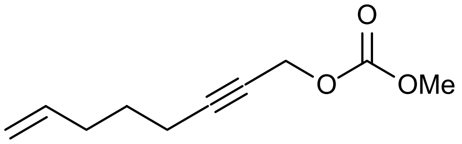


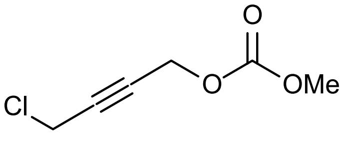
5-Oxaoct-7-en-2-yn-1-ol (**199**). To a stirred suspension of NaH (120 mmol, 4.8 g of 60% dispersion in oil) in anhydrous THF (50 mL) was gradually added 2-butyn-1,4-diol (17.2 g, 200 mmol) dissolved in anhydrous DMF (50 mL). After stirring under reflux for 1 h, a solution of allyl bromide (10.5 mL, 120 mmol) in anhydrous THF (30 mL) was gradually added by syringe pump within 2 h keeping a gentle refluxing of the reaction mixture. After the addition was complete, the mixture was stirred at reflux for additional 30 min and evaporated under reduced pressure ($T_{bath} < 70$ °C, 5 Torr). The residue was partitioned between ether (200 mL) and water (50 mL), organic layer was separated and the aqueous phase was extracted with ether (3 × 100 mL). The combined organic phases were washed with water (50 mL), brine (100 mL) and dried over $MgSO_4$. The residue (12.6 g) obtained after evaporation of the solvents, was purified by flash" chromatography on 100 mL of flash silica gel, eluting with pentane/ether, 5:1 to 2:1, to yield 8.2 g (55%, from allyl bromide) of pure alcohol **199**. Otherwise, by-product (1,4-bis-allyloxybutyn-2) and paraffin oil could be removed from the reaction mixture just by washing of dissolved in water (~100 mL) crude alcohol with hexane. After removing the low-polar by-products (TLC control), the pure product could be regenerated by saturation of the aqueous phase with NaCl and subsequent extraction with ether. This procedure requires further optimization if necessary to increase yield of product. Physical and spectral data of the synthesized compound **199** were identical to those reported in the literature.[121]

Methyl (5-oxa-oct-7-en-2-ynyl)carbonate (**201**). According to GP 12, alcohol **199** (11.4 g, 91 mmol) after distillation of the crude product under reduced pressure, gave 15.5 g (92%) of pure **201** as a colorless liquid. – B. p. 68–70 °C (0.2 Torr). – IR (film): ν = 3082, 3015, 2959, 2855, 2239 (C≡C), 2160, 1754 (C=O), 1649 (C=C), 1444, 1374, 1264, 1138, 1083, 1022, 994, 950, 901, 790 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 3.80 (s, 3 H, OCH$_3$), 4.04 (ddd, ^3J = 5.7 Hz, ^4J = 1.5 Hz, ^4J = 1.2 Hz, 2 H, 6-H), 4.18 (t, ^5J = 1.7 Hz, 2 H, 4-H), 4.77 (t, ^5J = 1.7 Hz, 2 H, 1-H), 5.21 (ddd, ^3J = 10.5 Hz, ^2J = 1.5 Hz, ^4J = 1.2 Hz, 1 H, 8-H$_{trans}$), 5.30 (ddd, ^3J = 17.3 Hz, ^2J = 1.5 Hz, ^4J = 1.5 Hz, 1 H, 8-H$_{cis}$), 5.88 (ddt, ^3J = 17.3 Hz, ^3J = 10.5 Hz, ^3J = 5.7 Hz, 1 H, 7-H). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 55.1 (+, CH$_3$), 55.6 (–, C-4), 57.2 (–, C-6), 70.6 (–, C-1), 79.7 (C$_{quat}$, C-3), 83.5 (C$_{quat}$, C-2), 118.0 (–, C-8), 133.7 (+, C-7), 155.1 (C$_{quat}$, CO$_2$Me). – MS (70 eV, DCI, NH$_3$), *m/z* (%): 386.4 (2) [2M + NH$_4^+$], 202.2 (100) [M + NH$_4^+$], 127 (1). – Anal. Calculated for C$_9$H$_{12}$O$_4$ (184.19): C 58.69, H 6.57. Found: C 58.96, H 6.24.

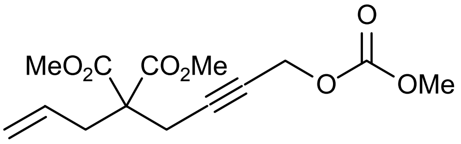


Methyl (oct-7-en-2-ynyl)carbonate (**196**). According to GP 12, alcohol **198** (8.1 g, 65 mmol) after distillation of the crude product under reduced pressure, gave 11.1 g (94%) of pure **196** as a colorless liquid. – B. p. 60–62 °C (0.2 Torr). – IR (film): ν = 3078, 3001, 2979, 2943, 2861, 2235 (C≡C), 1756 (C=O), 1640 (C=C), 1446, 1375, 1262, 1150, 1106, 1020, 994, 953, 916, 791 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 5.59 (tt, ^3J = 7.5 Hz, ^3J = 7.3 Hz, 2 H, 5-H), 2.12 (dddt, ^3J = 7.5 Hz, ^3J = 6.8 Hz, ^4J = 1.5 Hz, ^4J = 1 Hz, 2 H, 6-H), 2.22 (tt, ^3J = 7.3 Hz, ^5J = 2.3 Hz, 2 H, 4-H), 3.79 (s, 3 H, OCH$_3$), 4.71 (t, ^5J = 2.3 Hz, 2 H, 1-H), 4.96 (ddd, ^3J = 9.5 Hz, ^2J = 1.5 Hz, ^4J = 1 Hz, 1 H, 8-H$_{trans}$), 5.01 (ddd, ^3J = 17 Hz, ^2J = 1.5 Hz, ^4J = 1.5 Hz, 1 H, 8-H$_{cis}$), 5.76 (ddd, ^3J = 17 Hz, ^3J = 9.5 Hz, ^3J = 6.8 Hz, 1 H, 7-H). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 18.0 (–, C-4) 27.4 (–, C-5), 32.6 (–, C-6), 54.9 (+, CH$_3$), 56.2 (–, C-1), 73.6 (C$_{quat}$, C-3), 88.0 (C$_{quat}$, C-2), 115.2 (–, C-8), 137.6 (+, C-7), 155.2 (C$_{quat}$, CO$_2$Me). – MS (70 eV, DCI, NH$_3$), *m/z* (%): 200 (100) [M + NH$_4^+$], 123 (3), 108 (2), 107 (12), 106 (9). – Anal. Calculated for C$_{10}$H$_{14}$O$_3$ (182.22): C 65.91, H 7.74. Found: C 66.05, H 7.58.

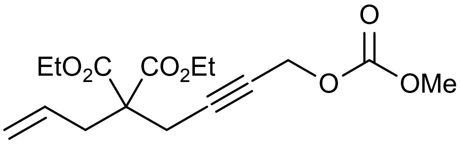




4-Chlorobut-2-ynyl methyl carbonate (**202**). According to GP 12, 4-chlorobut-2-yn-1-ol (10.4 g, 100 mmol) gave 16.0 g (98%) of sufficiently pure **202** as a slightly yellow liquid, which physical property and spectral data were identical to those reported in the literature.[135]



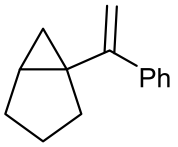
Methyl [5,5-bis(methoxycarbonyl)oct-7-en-2-ynyl]carbonate (**205**). To a stirred suspension of NaH (3.27 g of 60% dispersion in mineral oil, 82 mmol) in anhydrous THF (80 mL) dimethyl allyl malonate (**203**) (13.4 g, 78 mmol) was added dropwise at ambient temperature. After the reaction mixture had become homogeneous, a solution of **202** (13.3 g, 82 mmol) in the same solvent (40 mL) was gradually added at ambient temperature within 1 h. The reaction mixture was stirred for an additional 16 h and then evaporated under reduced pressure at ambient temperature. The residue was partitioned between ether (200 mL) and water (50mL) and the aqueous phase was extracted with ether (2×50 mL). The combined organic layers were washed with water (2×50 mL), brine (100 mL) and dried over $MgSO_4$. Evaporation of the solvents under reduced pressure gave 21.1 g of the crude residue, which was subjected to flash chromatography on 200 mL of flash silica gel, eluting with hexane/*t*BuOMe, 5:1, to yield 9.3 g (40%) of pure **205** as a slightly yellow viscous oil. The physical properties and spectral data of the compound synthesized were identical to those reported in the literature.[135]



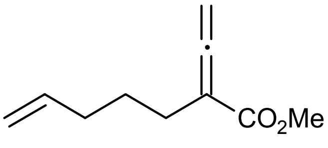
Methyl [5,5-bis(ethoxycarbonyl)oct-7-en-2-ynyl]carbonate (**206**). To a stirred suspension of NaH (1.9 g of 60% dispersion in mineral oil) in anhydrous DMF (45 mL) diethyl allyl malonate (**204**) (9.01 g, 45 mmol) was added in one portion and then **202** (7.4 g, 46 mmol) was added dropwise at 10 °C (ice water bath) within 30 min. The mixture was stirred at ambient temperature for 24 h, DMF was “bulb-to-bulb” distilled off (0.1 Torr, $T_{bath} < 60$ °C), the residue was diluted with ether (200 mL), washed with 5% aqueous H_2SO_4 (50 mL), water (50 mL), brine (50 mL) and dried over $MgSO_4$. Evaporation of the solvent under reduced pressure gave 14.3 g of a brown oil, which was purified by flash” chromatography on 100 mL of flash silica gel, eluting with pentane/ether, 10:1 to 5:1, to yield 8.1 g (55%) of pure **206** as a slightly yellow viscous oil. – IR (film): ν = 3081, 2983, 2963, 2941, 2908, 2875, 2239 (C≡C), 2156, 2046, 1755 (C=O, carbonate), 1734 (C=O), 1640 (C=C), 1443, 1370, 1328, 1267, 1218, 1189, 1139, 1096, 1069, 1031, 954, 901, 861, 792 cm^{-1}. – ^{1}H NMR (250 MHz, CDCl$_3$): δ = 1.23 (t, ^3J = 7.2 Hz, 6 H, CH$_3$), 2.76 (ddd, ^3J = 7.4 Hz, ^4J = 1.5 Hz, ^4J = 1 Hz, 2 H, 6-H), 2.82 (t, ^5J = 2.1 Hz, 2 H, 4-H), 3.79 (s, 3 H, OCH$_3$), 4.19 (q, ^3J = 7.2 Hz, 4 H, OCH$_2$), 4.67 (t, ^5J = 2.1 Hz, 2 H, 1-H), 5.10 (ddd, ^3J = 9.9 Hz, ^2J = 1.5 Hz, ^4J = 1 Hz, 1 H, 8-H$_{trans}$), 5.15 (ddd, ^3J = 17.3 Hz, ^2J = 1.5 Hz, ^4J = 1.5 Hz, 1 H, 8-H$_{cis}$), 5.60 (ddd, ^3J = 17.3 Hz, ^3J = 9.9 Hz, ^3J = 7.4 Hz, 1 H, 7-H). – ^{13}C NMR (62.9 MHz, CDCl$_3$, DEPT): δ = 14.0 (+, CH$_3$), 22.8 (–, C-4), 36.4 (–, C-6), 55.0 (+, OCH$_3$), 55.8 (–, C-1), 56.6 (C$_{quat}$, C-5), 61.6 (–, OCH$_2$), 76.5 (C$_{quat}$, C-3), 82.8 (C$_{quat}$, C-2), 119.8 (–, C-8), 131.7 (+, C-7), 155.1 (C$_{quat}$, OCO$_2$Me), 169.6 (C$_{quat}$, CO$_2$Et). – MS (70 eV, DCI, NH$_3$), *m/z* (%): 670.5 (1) [2M + NH$_4^+$], 344.3 (100) [M + NH$_4^+$], 327.3 (9) [M + H$^+$], 251.2 (4), 177 (2). – Anal. Calculated for $C_{16}H_{22}O_7$ (326.34): C 58.89, H 6.79. Found: C 58.58, H 7.08.

2.6.3.2. Preliminary experiments.

1-(1-Phenylethenyl)bicyclo[3.1.0]hexane (**197**). A solution of enyne **196** (911 mg, 5 mmol), PPh$_3$ (262 mg, 1 mmol), Pd(OAc)$_2$ (112 mg, 0.5 mmol) and NaBPh$_4$ (1.711 g, 5 mmol) in degassed anisole (10 mL) was stirred at 80 °C for 18 h. After cooling to room temperature, the mixture was diluted with pentane (50 mL) and filtered through a pad of flash silica gel (10 mL), which was rinsed with pentane (2 × 10 mL). The combined filtrates were evaporated under reduced pressure to give 1.2 g of crude oil, which was purified by column chromatography (150 mL of silica gel, eluent pentane) to yield 400 mg (35% yield) of pure **197**. Spectral data of the synthesized compound corresponded to literature.[113]



Methyl 2-(pent-4-enyl)buta-2,3-dienoate (**210**) was isolated as a by-product in attempted cyclization of (**196**) by following conditions. To a stirred solution of P(2-furyl)$_3$ (46 mg, 0.2 mmol) and PPh$_3$ (26 mg, 0.1 mmol) in degassed methanol (25 mL) was added Pd(OAc)$_2$ (22 mg, 0.1 mmol) under argon. After the mixture had become dark brown and completely homogenous (about 30 min), was added enyne **196** (364 mg, 2 mmol) all at once and the reaction atmosphere was replaced with CO. After stirring at ambient temperature for 5 h, the brown color is disappeared and no changes of reactions mixture were observed (less, then 50% conversion according TLC). Then, PPh$_3$ (50 mg) and LiI (50 mg) were added and the red-brown mixture was stirred overnight under 1 bar of CO. After the starting material was



completely consumed (< 3% according to GC), the mixture was evaporated under reduced pressure at ambient temperature to give 550 mg of residue, which was suspended by stirring with pentane (30 mL) and filtered through a pad of flash" silica gel (10 mL). This was washed with pentane/ether mixture, 10:1 (2 × 20 mL), and the combined filtrates were evaporated under reduced pressure to give 350 mg of the residue, which was then subjected to column chromatography on 50 mL of silica gel, eluting with pentane/ether, 20:1, to yield ~100 mg of **130**, about 60 mg of unindentified substance and 90 mg (27%) of the crude **210**, contaminated with 10–15% of **130**. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.55 (tt, ^3J = 7.5 Hz, ^3J = 7.5 Hz, 2 H, 5-H), 2.08 (tddd, ^3J = 7.5 Hz, ^3J = 7.5 Hz, ^5J = 1.5 Hz, ^5J = 1 Hz, 2 H, 6-H), 2.24 (tt, ^3J = 8 Hz, ^5J = 3 Hz, 2 H, 4-H), 3.74 (s, 3 H, OCH_3), 4.94 (ddd, ^3J = 10.3 Hz, ^2J = 2 Hz, ^5J = 1.5 Hz, 1 H, 8-H_{trans}), 5.00 (ddd, ^3J = 17.5 Hz, ^2J = 2 Hz, ^5J = 1 Hz, 1 H, 8-H_{cis}), 5.13 (t, ^5J = 3 Hz, 2 H, 1-H), 5.79 (ddd, ^3J = 17.5 Hz, ^3J = 10.3 Hz, ^3J = 7.5 Hz, 1 H, 7-H).

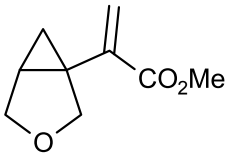
2.6.3.3. Preparative Pd-catalyzed cyclizations of 1,6-enines to 2-bicyclo[3.1.0]acrylates

Preparation of the Catalytic System A (CSA). To a stirred solution of P(2-furyl)$_3$ (232 mg, 1 mmol) and $P(OMe)_3$ (310 mg, 2.5 mmol) in thoroughly degassed methanol (125 mL) $Pd(OAc)_2$ (112 mg, 0.5 mmol) was added under argon. After stirring at ambient temperature for additional 1 h the solution is ready to use.

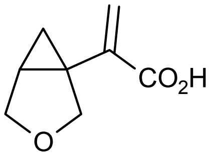
Catalytic System B (CSB) was prepared as it is described for the System A, but instead trimethylphosphite 1.1 eq. of tetramethylammonium bromide (154 mg, 0.1 mmol) was added.

Methyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**130**) was prepared by stirring of enyne **196** (0.91 g, 5 mmol) in presence 2 mol% of CSA (0.1 mmol, 25 mL of 0.004 M methanolic solution of the "Pd"-catalyst) under 1 bar of CO for 16 h (T = 25 °C) with subsequent flash" chromatography (20 mL of flash silica gel, eluent pentane/ether, 20:1) of the residue obtained after evaporation of solvent under reduced pressure at ambient temperature. Yield: 0.78 g (94%, 97.5% purity). The spectral data of the synthesized compound corresponded to those reported above.

Methyl 2-(3-oxabicyclo[3.1.0]hex-1-yl)propenoate (**207**). Enyne **201** (7.37 g, 40 mmol) was added all at once to 0.004 M solution of CSA (2 mol%, 0.8 mmol) in methanol (200 mL), the reaction atmosphere was replaced with CO and the mixture was vigorously stirred at 25 °C until the starting material has been completely consumed (about 48 h, GC control). Then, the solvent was removed under reduced pressure at ambient temperature and the residue was subjected to flash" chromatography on 100 mL of flash silica gel, eluting with pentane/ether, 10:1, to yield 5.86 g (87%) of **207** (purity 97.5%). – B. p. 61–62 °C (2 mbar). – IR (film): ν = 3076, 3001, 2957, 2924, 2859, 1730 (C=O), 1629 (C=C), 1437, 1396, 1377, 1350, 1309, 1217, 1132, 1096, 1080, 1069, 1047, 1019, 987, 949, 931, 911, 859, 815, 732, 703 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.82 (dd, ^3J = 5 Hz, ^2J = 4.5 Hz, 1 H, 6-H_{endo}), 0.85 (ddd, ^3J = 7.5 Hz, ^2J = 4.5 Hz, ^4J = 1 Hz, 1 H, 6-H_{exo}), 1.73 (ddd, ^3J = 7.5 Hz, ^3J = 5 Hz, ^3J = 2 Hz, 1 H, 5-H), 3.72 (dd, ^2J = 7.9 Hz, ^4J = 1 Hz, 1 H, 2-H_{exo}), 3.75 (s, 3 H, OCH_3), 3.84 (d, ^2J = 8.3 Hz, 1 H, 4-H_{endo}), 3.86 (d, ^2J = 7.9 Hz, 1 H, 2-H_{endo}; dd, ^2J = 8.3 Hz, ^3J = 2 Hz, 1 H, 4-H_{exo}), 5.67 (d, ^2J = 1.2 Hz, 1 H, 3'-H_{trans}), 6.25 (d, ^2J = 1.2 Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.9 (–, C-6), 24.5 (+, C-5), 30.8 (C_{quat}, C-1), 51.9 (+, CH_3), 69.8, 72.3 [–, C-2(4)], 127.2 (–, C-3'), 139.1 (C_{quat}, C-2'), 166.7 (C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 168 (4) [M^+], 153 (4) [$M^+ - CH_3$], 149 (7), 140 (9), 139 (8), 137 (17) [$M^+ - CH_3O$], 136 (37) [$M^+ - CH_3OH$], 125 (21), 109 (21), 108 (58) [$M^+ - CO_2CH_3$], 97 (10), 95 (13), 91 (8), 81 (29), 79 (100), 77 (55) [$C_6H_5^+$], 71 (8), 69 (12), 67 (11), 65 (6), 59 (21), 57 (22), 55 (18), 53 (28), 51 (17), 45 (9), 43 (20), 41 (88).

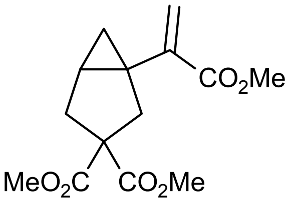


Methyl 2-(3-oxabicyclo[3.1.0]hex-1-yl)propenoic acid (**211**). According to GP 10, a crude **207** (0.6 g, 85% GC) after recrystallization of the crude product from toluene/cyclohexane, 4:1, gave 0.35 g (80%) of pure acid **211** as a colorless crystals. – M. p. 86.5–87.0 °C. – IR (KBr): ν = 3440 (OH), 3076, 2999, 2967, 2946, 2924, 2896, 2858, 2733, 2657, 2619, 1683 (C=O), 1621 (C=C), 1449, 1432, 1373, 1354, 1318, 1301, 1258, 1238, 1204, 1143, 1097, 1081, 1044, 1017, 1007, 973, 933, 897, 869, 815, 732, 698, 664, 606 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.86 (dd, ^3J = 5.1 Hz, ^2J = 4.8 Hz, 1 H, 6-H_{endo}), 0.90 (ddd, ^3J = 7.5 Hz, ^2J = 4.8 Hz, ^4J = 0.8 Hz, 1 H, 6-H_{exo}), 1.76 (ddd, ^3J = 7.5 Hz, ^3J = 5 Hz, ^3J = 2.1 Hz, 1 H, 5-H), 3.78 (dd, ^2J = 7.9 Hz, ^4J = 0.8 Hz, 1 H, 2-H_{exo}), 3.89 (d, ^2J = 8.3 Hz, 1 H, 4-H_{endo}), 3.91 (d, ^2J = 7.9 Hz, 1 H, 2-H_{endo}; dd, ^2J = 8.3 Hz, ^3J = 2.1 Hz, 1 H, 4-H_{exo}), 5.80 (d, ^2J = 1 Hz, 1 H, 3'-H_{trans}), 6.41 (d, ^2J = 1 Hz, 1 H, 3'-H_{cis}), 11.34 (bs, 1 H, OH). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.9

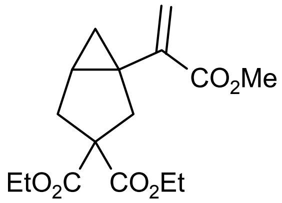


(–, C-6), 24.4 (+, C-5), 30.5 (C_{quat}, C-1), 69.8, 72.2 [–, C-2(4)*], 129.7 (–, C-3'), 138.6 (C_{quat}, C-2'), 171.5 (C_{quat}, C-1'). – MS (70 eV, EI), *m/z* (%): 154 (15) [M^+], 139 (7), 136 (19) [$M^+ - H_2O$], 126 (16), 125 (17), 123 (8), 111 (31), 109 (16), 108 (32), 107 (15), 98 (9), 96 (8), 95 (6), 93 (7), 83 (10), 81 (28), 79 (100), 77 (45), 69 (27), 67 (13), 65 (14), 55 (11), 53 (32), 51 (30), 45 (11), 43 (16), 41 (85). – Anal. Calculated for $C_8H_{10}O_3$ (154.16): C 62.33, H 6.54. Found: C 62.50, H 6.33.

Methyl 2-{3,3-bis(methoxycarbonyl)bicyclo[3.1.0]hex-1-yl}propenoate (**208**). Enyne **205** (596 mg, 2 mmol) was stirred in the presence of 5 mol% of CSB (0.1 mmol of catalyst, 25 mL of 0.004 M solution in MeOH) under 1 bar of CO at 25 °C for 68 h, the solvent was evaporated under reduced pressure and the residue was purified by column chromatography on 100 mL of silica gel, eluting with pentane/ether, 5:1, to give 360 mg (63% yield) of **208** as a viscous colorless oil (96% purity according to GC). – IR (film): ν = 3073, 3006, 2954, 2845, 1736 (C=O), 1629 (C=C), 1435, 1373, 1320, 1294, 1251, 1215, 1172, 1132, 1092, 1071, 997, 947, 867, 851, 817, 696 cm^{-1}. – ^1H NMR (250 MHz, $CDCl_3$): δ = 0.48 (dd, ^2J = 5.7 Hz, ^3J = 4.5 Hz, 1 H, 6-H_{endo}), 0.75 (ddd, ^3J = 7.9 Hz, ^2J = 5.7 Hz, ^4J = 1.5 Hz, 1 H, 6-H_{exo}), 1.51–1.59 (m, 1 H, 5-H), 2.59 (dd, ^2J = 13.5 Hz, J = 1.5 Hz, 1 H), 2.61–2.63 (m, 3 H), 3.69 (s, 3 H, CH_3), 3.73 (s, 3 H, CH_3), 3.75 (s, 3 H, CH_3), 5.60 (d, ^2J = 1.2 Hz, 3'-H_{trans}), 6.16 (d, ^2J = 1.2 Hz, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 16.2 (–, C-6), 24.8 (+, C-5), 31.1 (C_{quat}, C-1), 36.1 (–, C-4), 40.2 (–, C-2), 52.8, 52.9, 57.8 (+, 3 CH_3), 59.7 (C_{quat}, C-3), 125.9 (–, C-3'), 142.0 (C_{quat}, C-2'), 166.9 (C_{quat}, C-1'), 171.9, 173.2 (2 C_{quat}, CO_2Me). – MS (70 eV, EI), *m/z* (%): 282 (2) [M^+], 251 (28) [$M^+ - CH_3O$], 250 (48) [$M^+ - CH_3OH$], 222 (33) [$M^+ - CH_3OH - CO$], 191 (24) [$M^+ - CH_3OH - CH_3O - CO$], 190 (51) [$M^+ - 2CH_3OH - CO$], 163 (100), 147 (6), 131 (27), 103 (55), 91 (7), 77 (12) [$C_6H_5^+$], 59 (13), 41 (3). – Anal. Calculated for $C_{14}H_{18}O_6$ (282.29): C 59.57, H 6.43. Found: C 59.30, H 6.77.



Methyl 2-{3,3-bis(ethoxycarbonyl)bicyclo[3.1.0]hex-1-yl}propenoate (**209**). Enyne **206** (7.35 g, 22.5 mmol) was added all at once to a solution of CSB (4.44 mol % of "Pd^0"; prepared from 224 mg, 1 mmol of $Pd(OAc)_2$, 505 mg, 2.18 mmol of $P(2\text{-furyl})_3$ and 167 mg, 1.08 mmol of Me_4NBr) in methanol (300 mL), the reaction atmosphere was replaced with CO and the mixture was vigorously stirred at 25 °C until the starting material has been completely consumed (50 h, GC control). Then, the solvent was removed



under reduced pressure to give 8.16 g of crude product, which was purified by flash" chromatography on 100 mL of flash silica gel, eluting with pentane/ether, 10:1 to 5:1, to yield 6.03 g (86%) of pure the **209** (97.5% according to GC) as a colorless oil. – IR (film): ν = 3074, 2983, 2957, 2908, 2878, 1728 (C=O), 1629 (C=C), 1438, 1384, 1367, 1325, 1295, 1245, 1212, 1198, 1177, 1124, 1092, 1069, 1058, 1018, 1000, 955, 898, 861, 817, 766, 696 cm^{-1}. – ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.52 (dd, ^2J = 5.6 Hz, ^3J = 4.5 Hz, 1 H, 6-H_{endo}), 0.74 (ddd, ^3J = 7.9 Hz, ^2J = 5.6 Hz, ^4J = 1.5 Hz, 1 H, 6-H_{exo}), 1.21 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.24 (t, ^3J = 7.2 Hz, 3 H, CH_3), 1.51–1.59 (m, 1 H, C-5), 2.51–2.62 (m, 3 H), 2.71 (d, ^2J = 13.5 Hz, 1 H), 3.75 (s, 3 H, OCH_3), 4.15 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 4.17 (q, ^3J = 7.2 Hz, 2 H, OCH_2), 5.59 (d, ^2J = 1.2 Hz, 1 H, 3'-H_{trans}), 6.15 (d, ^2J = 1.2 Hz, 1 H, 3'-H_{cis}). – ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.9 (+, 2 CH_3), 16.3 (–, C-6), 24.9 (+, C-5), 31.2 (C_{quat}, C-1), 36.0 (–, C-4), 40.2 (–, C-2), 51.8 (+, OCH_3), 59.9 (C_{quat}, C-3), 61.6, 61.7 (–, 2 CH_2), 125.8 (–, C-3'), 142.2 (C_{quat}, C-2'), 167.0 (C_{quat}, C-1'), 171.6 172.9 (C_{quat}, CO_2Et). – MS (70 eV, EI), *m/z* (%): 310 (8) [M^+], 279 (17) [$M^+ - CH_3O$], 278 (55) [$M^+ - CH_3OH$], 265 (36) [$M^+ - C_2H_5O$], 250 (25) [$M^+ - C_2H_5O - CH_3$], 236 (20), [$M^+ - C_2H_5OH - CO$], 218 (4), 205 (15) [$M^+ - CO_2CH_3 - C_2H_5OH$], 190 (55) [$M^+ - 2C_2H_5OH - CO$], 177 (100) [$M^+ - CO_2CH_3 - C_2H_5OH - CO$], 163 (32), 149 (18), 147 (26), 131 (43), 105 (26), 103 (81), 91 (12), 79 (12), 77 (20), 65 (3), 59 (4), 55 (4), 53 (3), 51 (2), 41 (3). – Anal. Calculated for $C_{16}H_{22}O_6$ (310.34): C 61.92, H 7.15. Found: C 61.57, H 7.36.

D. SUMMARY

Twenty-eight new alkyl 2-cyclopropylacrylates with various substitution patterns were synthesized from readily available precursors applying appropriately modified variants of standard transformations.

Thus, cyanohydrin formation from an aldehyde, alcoholysis of a cyanohydrin to an α-hydroxycarboxylic acid ester, SIMMONS-SMITH cyclopropanations of cycloalken-1-yl hydroxyacetates, oxidation and WITTIG methylenation of an α-ketocarboxylic acid ester afforded target cyclopropylacrylates on overall yields ranged from 33 to 54%. The α-ketocarboxylates **13**, **111-117** were prepared by dirhodium tetraacetate-catalyzed cyclopropanation of the corresponding alkenes with methyl or ethyl diazopyruvate in 32–58% yield.

The diastereoselectivity of double alkylation of unsymmetrical 1,3-dicarbonyl compounds towards the corresponding vinylcyclopropane derivatives was elucidated.

A preparative-scale procedure for the vapor-phase pyrolysis of bicyclopropylidene to methylenespiropentane (**59**) was developed to provide pure methylenespiropentane on a 17.4 g scale. A large-scale preparative protocol for 2-methylenecyclopropanecarboxaldehyde (**50**) was also developed.

Two new highly efficient methods for the ester hydrolysis leading to the corresponding half-esters or acrylic acids were developed. Thus, hydrolysis of 6,6-bis(methoxycarbonyl)bicyclo[3.1.0]hexane (**70**) was achieved with an excellent regioselectivity to give the respective half-ester **72** as the pure *exo*-isomer. Various acrylic esters had been found are smoothly hydrolyzed with lithium hydroxide in aqueous acetone. A new esterification procedure for the synthesis of esters from sterically congested alcohols was also developed.

The cyclopropanations of EWG-substituted α-cyclopenteylacetic esters **187** and **194** or their isomeric precursors with "SHI carbenoid" ($CF_3COOZnCH_2I$) were investigated. This reagent has been found to cyclopropanate double bond bearing strongly chelating β-dicarbonylic fragment, which usually decreases reactivity of carbenoid, whereas this turned to be enormous inert towards C–H-acidic α-position of the substrate. Thus, according to this protocol (cyclo)alkylidenemalonates and their analogues, which are readily accessible by the KNOEVENAGEL reaction, could be converted in the respective cyclopropanes by the "one-pot" methylation-cyclopropanation process.

The behavior of the synthesized cyclopropylacrylates under radical-initiated homo- and copolymerization conditions was investigated (IVOCLAR Vivadent). The radical homopolymerizations of the titled monomers were carried out with 2,2′-azabisisobutyronitrile (AIBN) as an initiator in chlorobenzene at 65 °C. The highest polymer yields were obtained in the polymerizations of monomers with an annelated 5- or 6-membered ring. In the case of **133** and **135** both the polymer yields (99 and 98%, respectively) and the glass transition temperatures (T_g) of 57 and 93 °C were significantly higher than those observed for the polymer from 1,1-diethoxycarbonyl-2-vinylcyclopropane (DECVCP) used as a benchmark for the monomer reactivities in the radical polymerizations of all the vinylcyclopropane derivatives. The bicyclic monomer **130** as well as parent esters **168-175**, also showed improved reactivities in comparison to DECVCP in the radical-initiated copolymerization with methyl methacrylate. It was concluded that monomer **130** can be applied to substitute commercially available dilutents in dental composites.[99] Thus, methyl 2-(bicyclo[3.1.0]hex-1-yl)acrylate is the first monomer that undergoes radical ring-opening polymerization with a reactivity higher than that of MMA, shows lower volume shrinkage than MMA, and may form polymers with a number-average molecular weight higher than 100000 g/mol. Moreover, it was found from in-vitro single cell gel electrophoresis that **130** is not mutagenic and shows a relatively low cytotoxity (XTT_{50} value 312.5 µg/mL).[100]

An efficient large preparative scale protocol was developed which allows one to obtain the monomer **130** in three steps from hydroxyacetate **81** on a 50 g scale in 75% overall yield.

A highly efficient preparative protocol for 5-*exo-trig*/3-*exo-trig* cascade cyclizations of various 1,6-enynes has been developed which involved a new catalytic system characterized by the lowest loading volume among the published ones. By this approach, the bicyclic 2-cyclopropylacrylate **130** as well as its structural analogues **207-209**, which are promising new low-shrinkage monomers and are inaccessible by other synthetic routes, can be synthesized in high yield.

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[132] The real values of signal intensities are given because it was impossible to make a complete assignment for this isomeric mixture. Therefore the sum of real intensities is more then the theoretical value. The same situation could be observed in ^{1}H NMR spectra of used alcohol **162**, where the sum of multiplet intensities between 1.0 and 1.9 ppm is “5.26” instead the required value of “4.7”.

[133] An expected about 185 ppm signal for C-1' (quaternary carbon atom of imino group) was unable to observe even after 9 h of acquisition because its very low intensity.

[134] An expected about 185 ppm signal for C-1' (quaternary carbon atom of imino group) was unable to observe even after 9 h of acquisition because its very low intensity.

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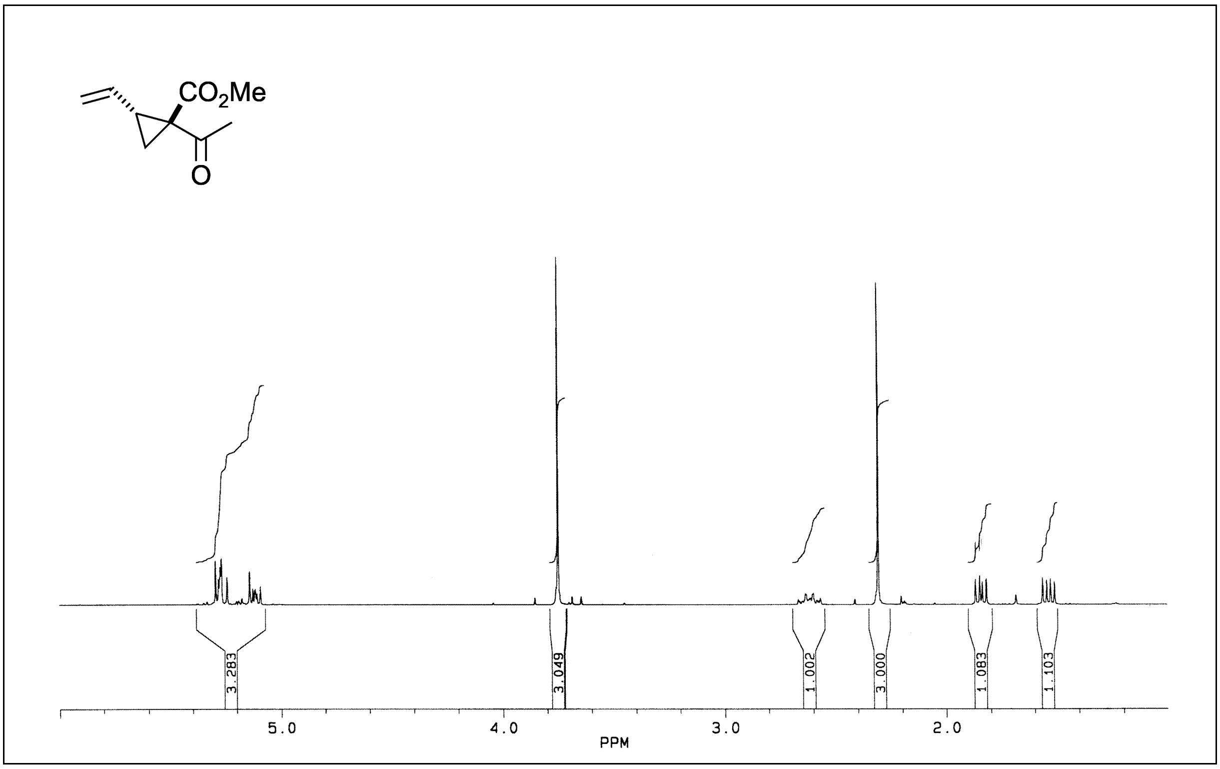
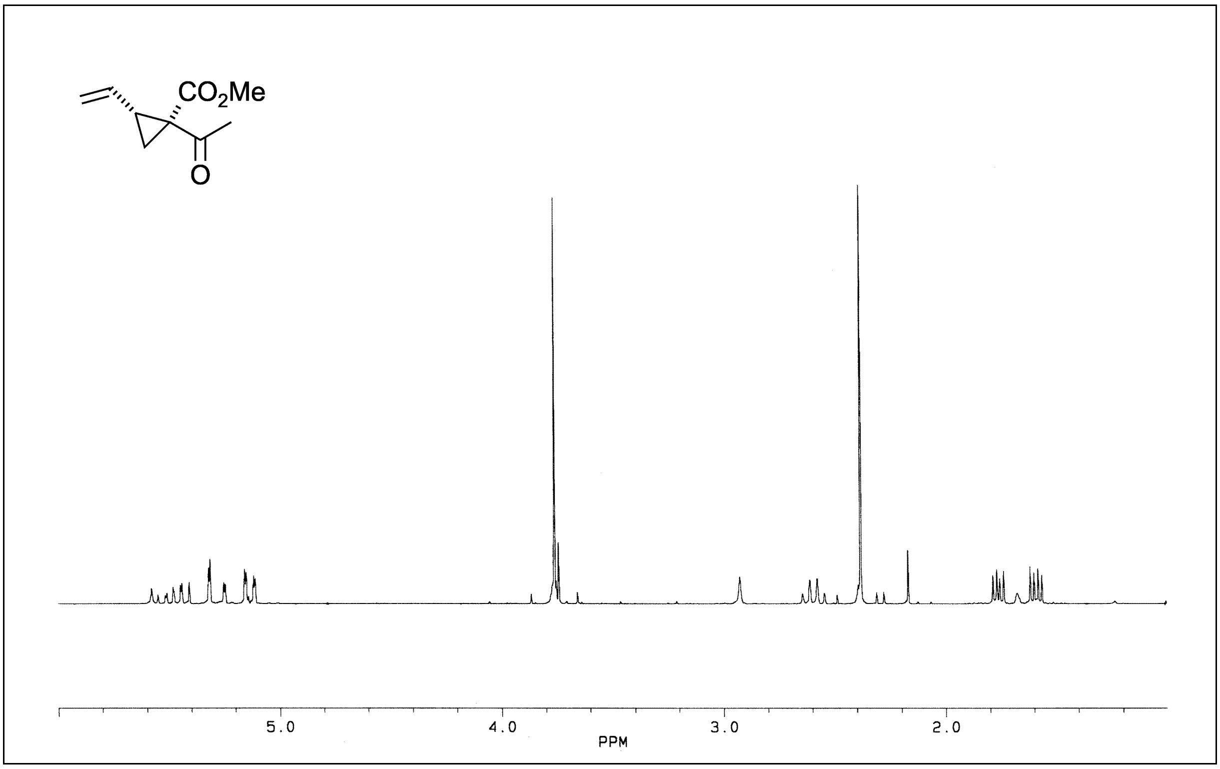
F. SPECTRAL DATA

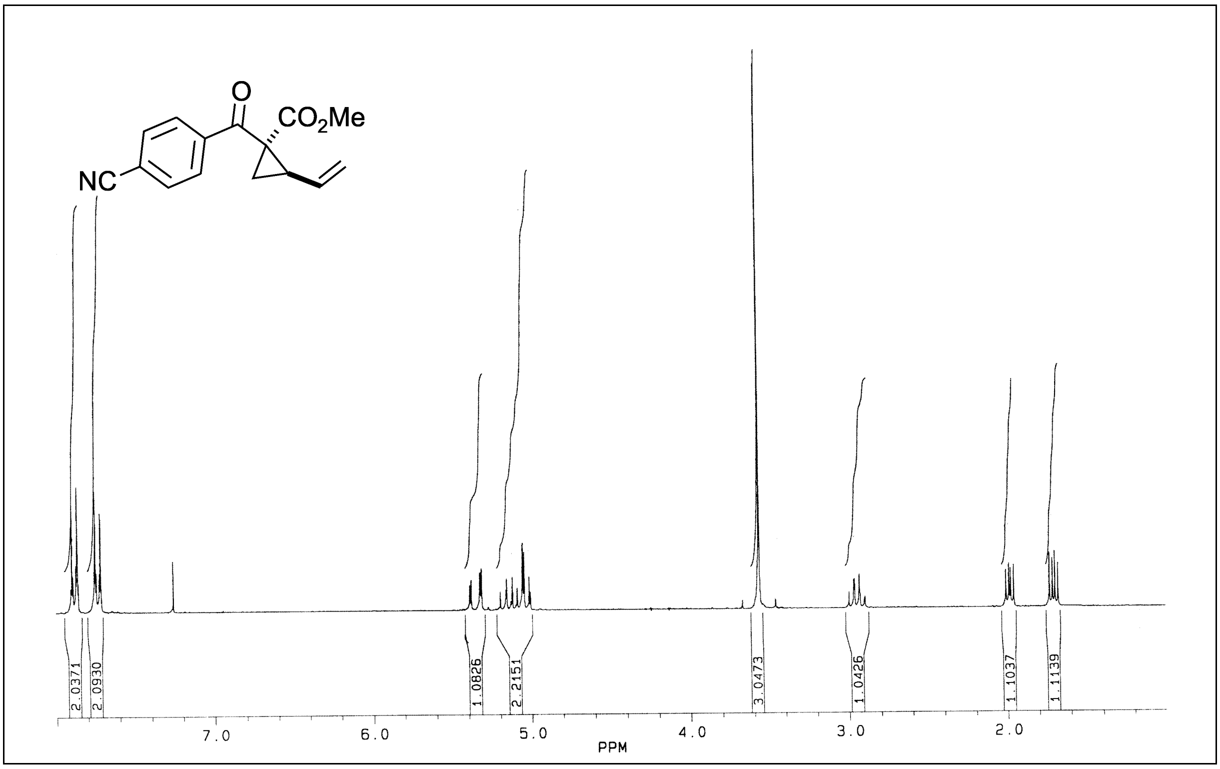
1. ^{1}H-NMR spectra



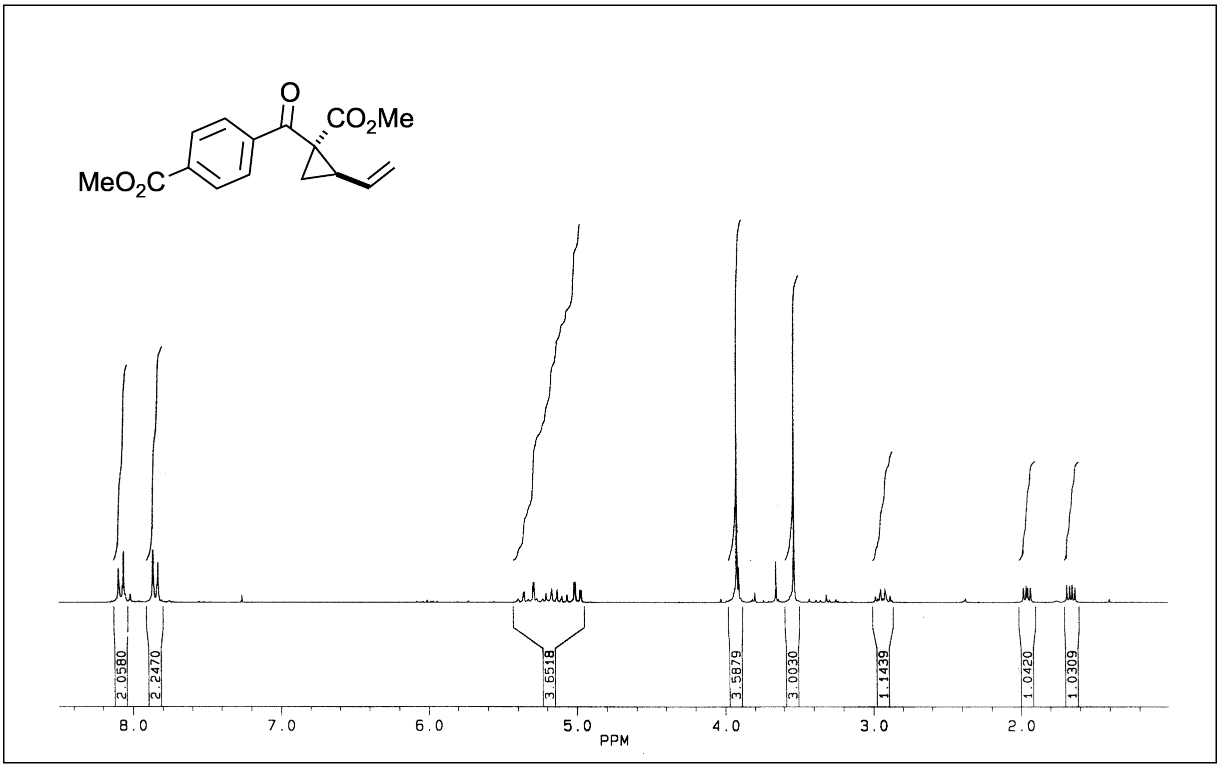
(*E*)-Methyl 1-acetyl-2-ethenylcyclopropanecarboxylate (***E*-23**)



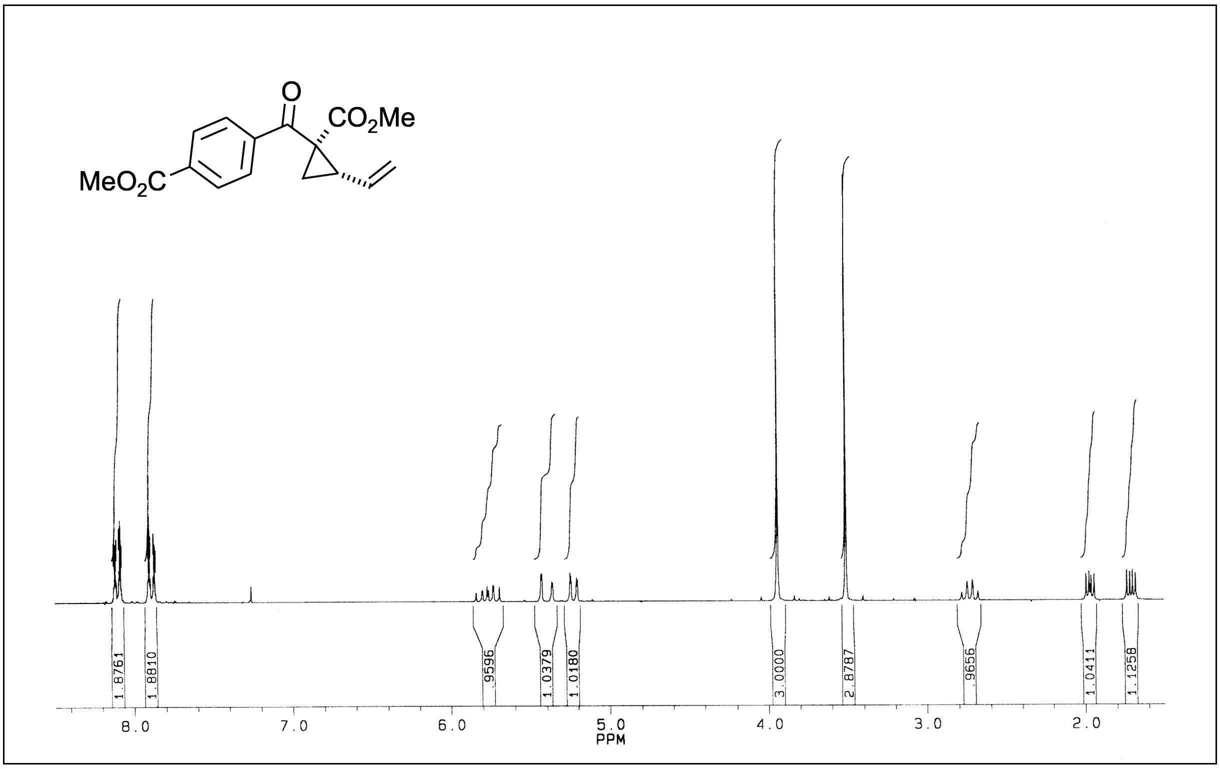
(*Z*)-Methyl 1-acetyl-2-ethenylcyclopropanecarboxylate (***Z*-23**)



(*E*)-Methyl 1-(4-cyanophenyl)carbonyl-2-ethenylcyclopropanecarboxylate (***E*-24**)



(*E*)-Methyl 1-(4-methoxycarbonylphenyl)carbonyl-2-ethenylcyclopropanecarboxylate (***E*-25**)



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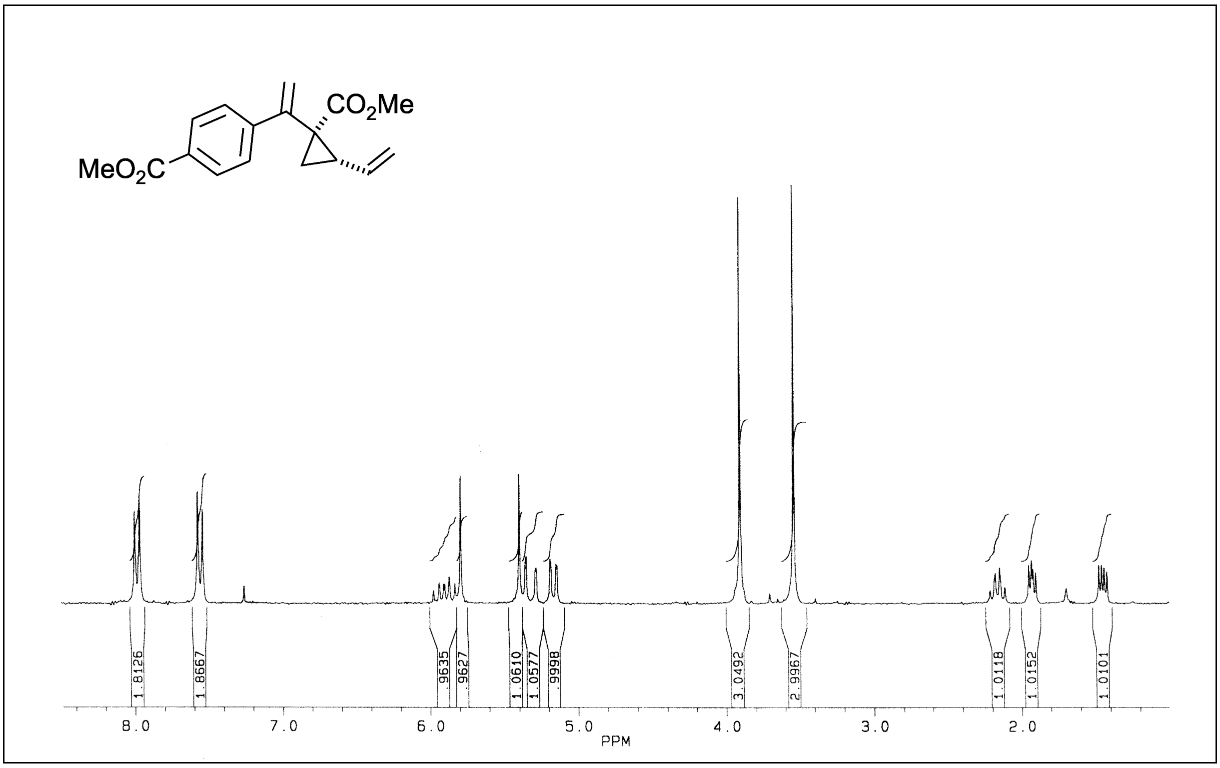
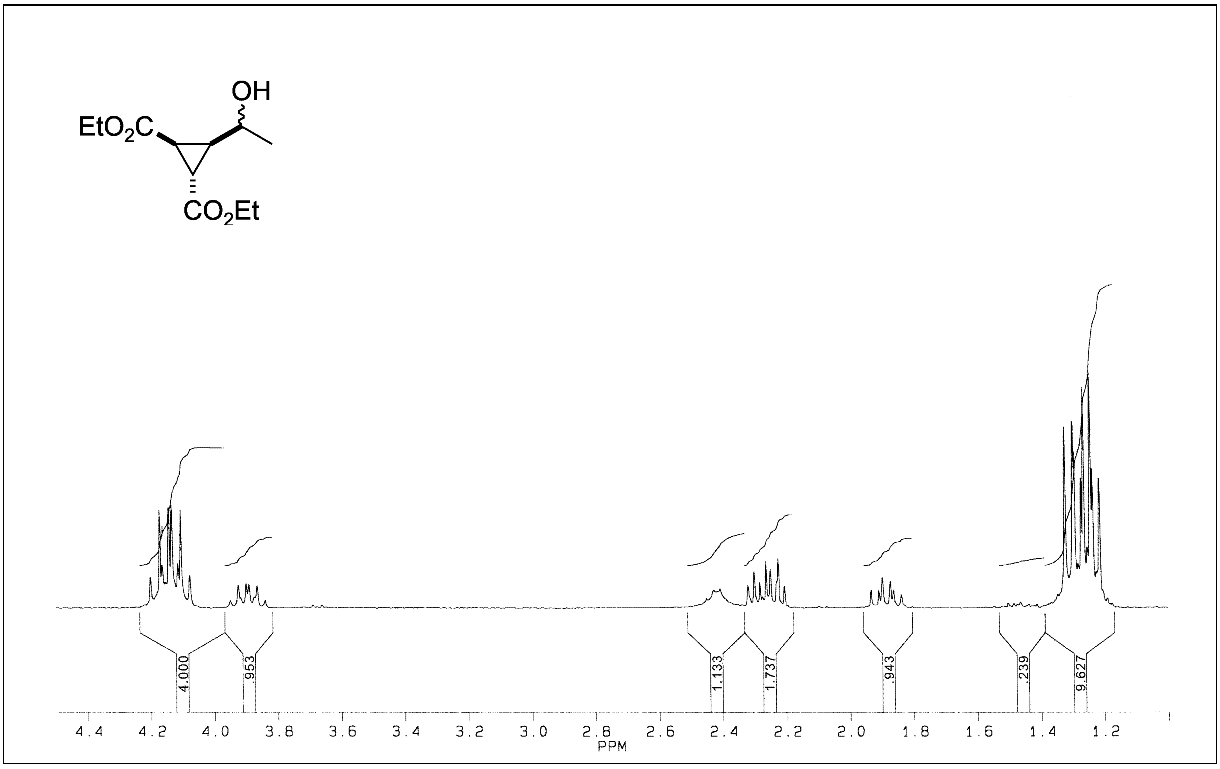
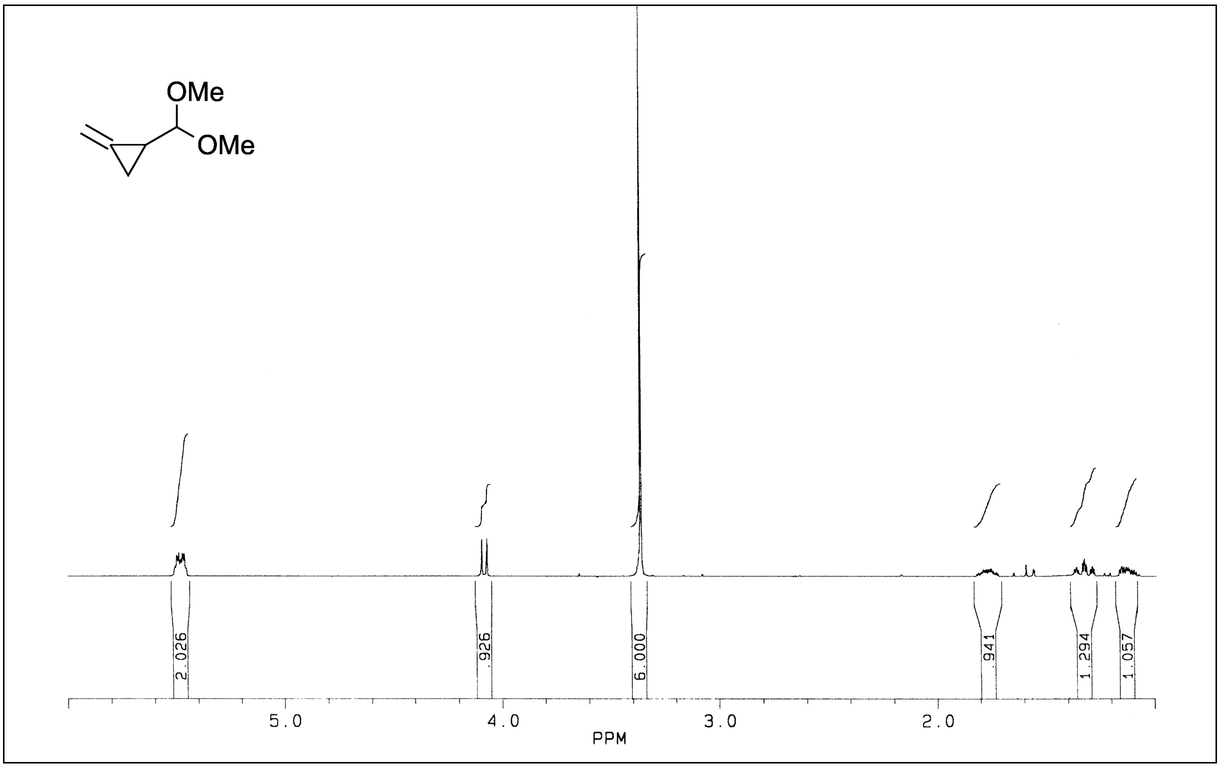


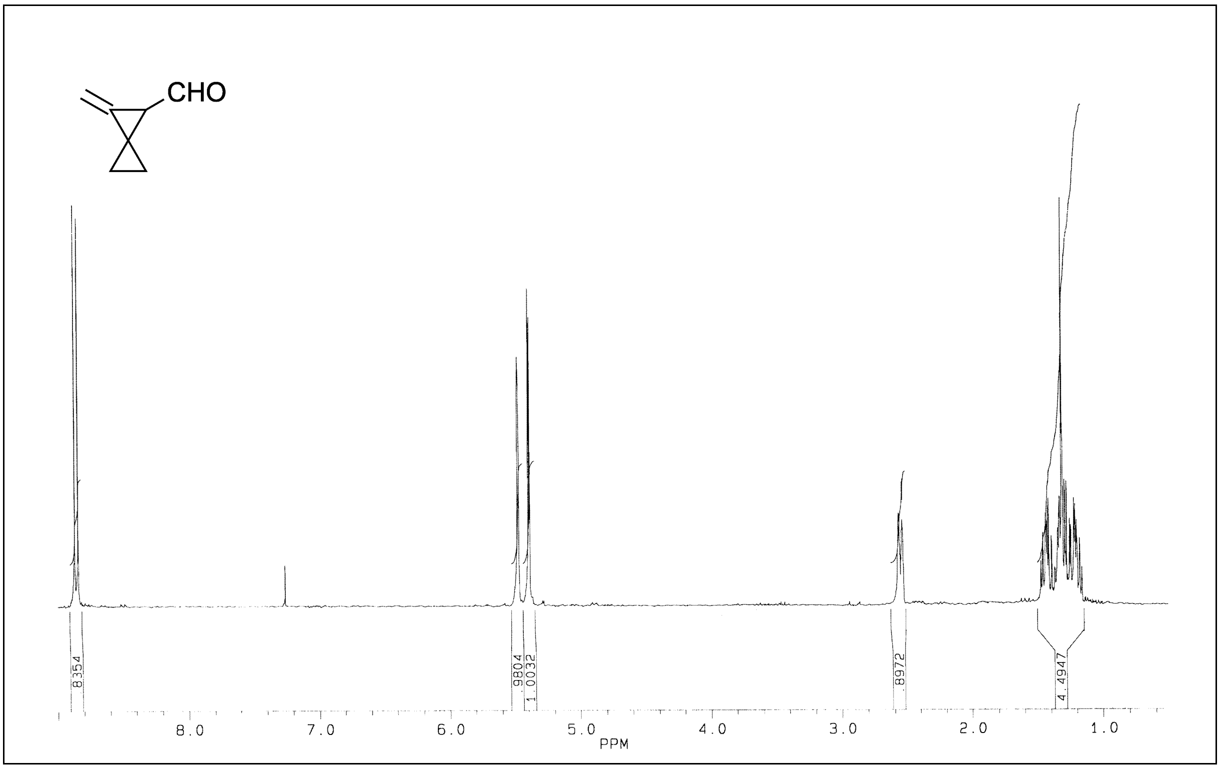
(*Z*)-Methyl 1-[1-(4-methoxycarbonylphenyl)ethen-1-yl]-2-ethenylcyclopropanecarboxylate (**26**)



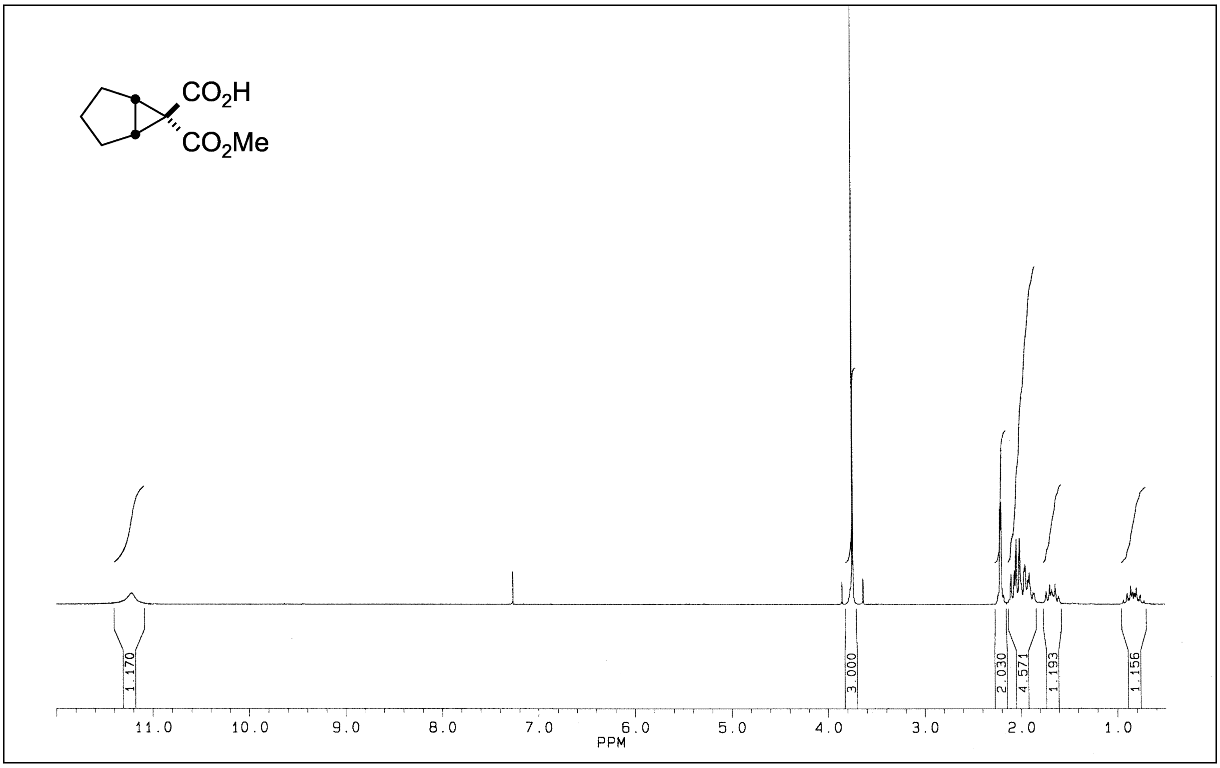
Diethyl 3-(1-hydroxyethyl)cyclopropane-1,2-dicarboxylate (**32**)



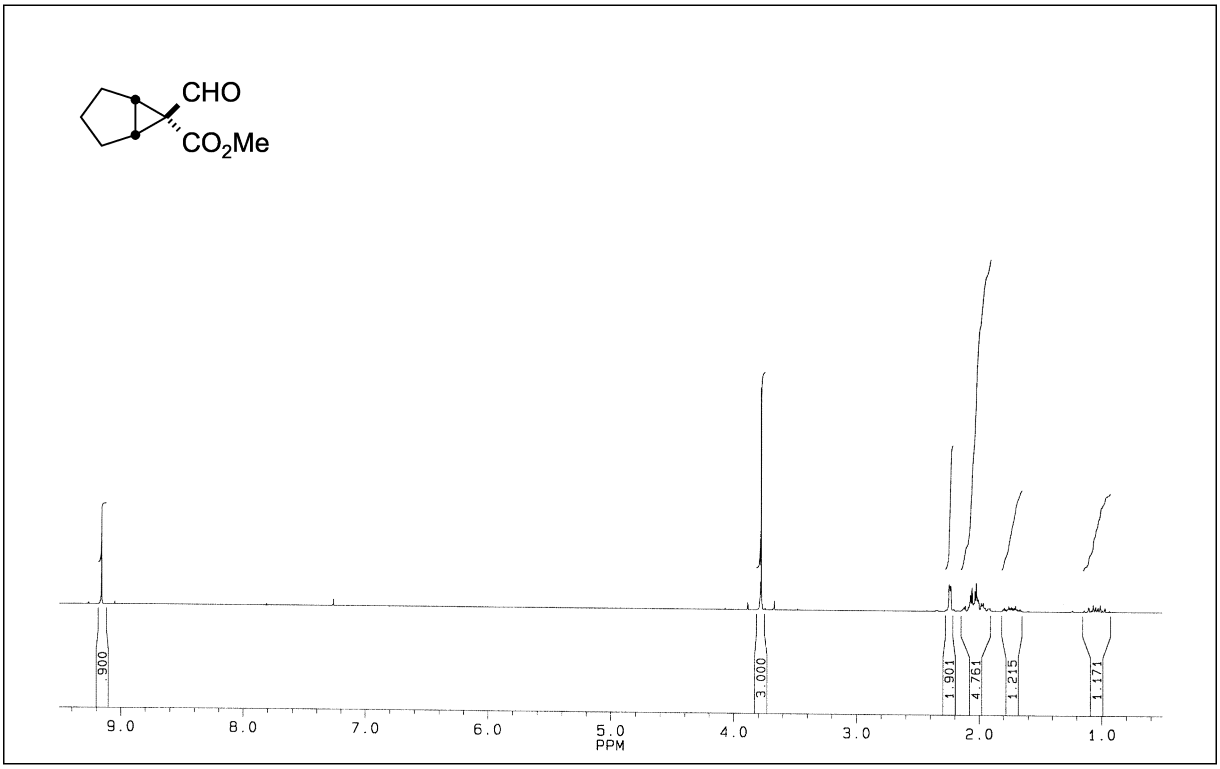
1-(Dimethoxymethyl)-2-methylenecyclopropane (**56**)



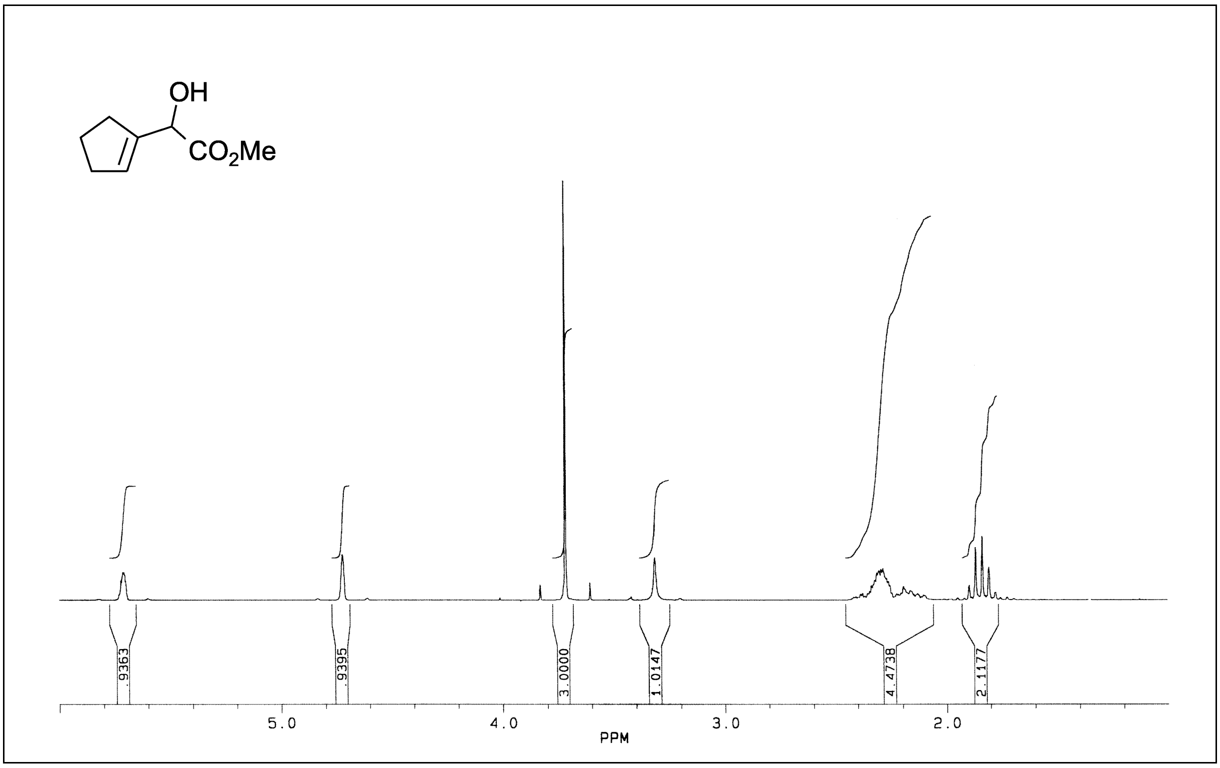
2-Methylenespiro[2.2]pentane-1-carbaldehyde (**66**)



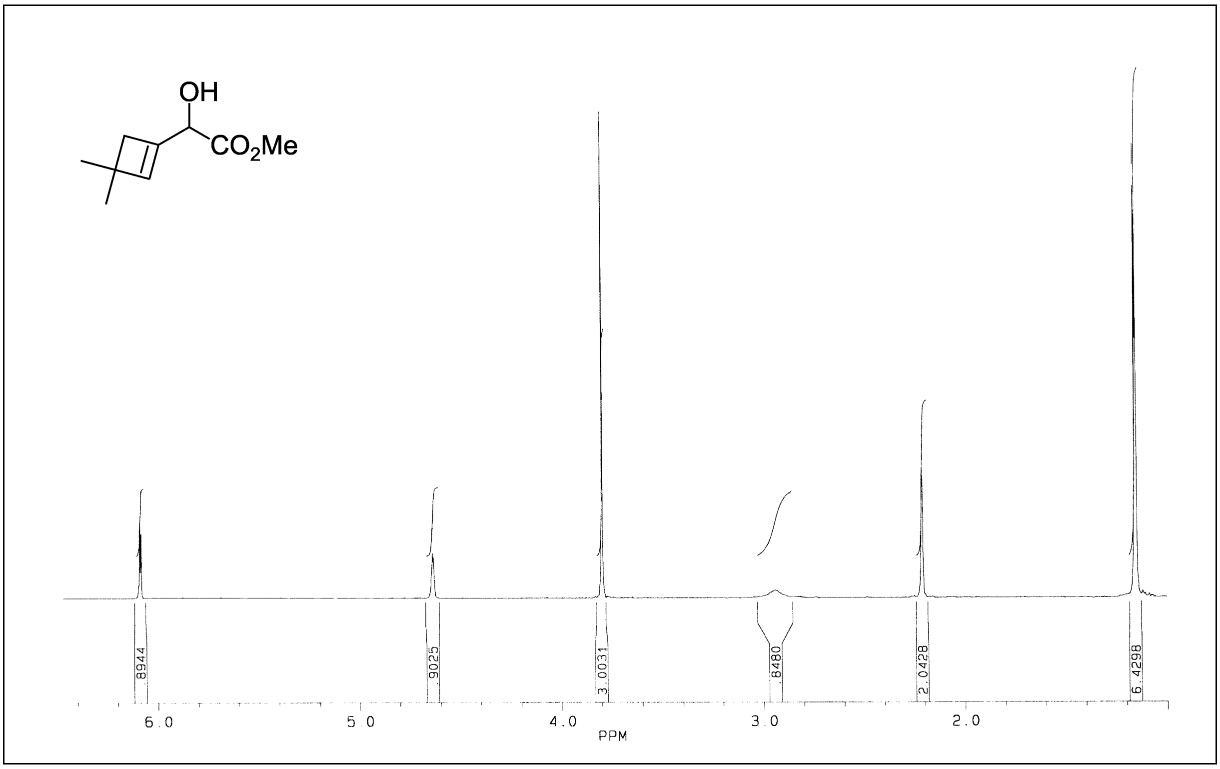
exo-6-Methoxycarbonylbicyclo[3.1.0]hexane-6-carboxylic acid (**72**)



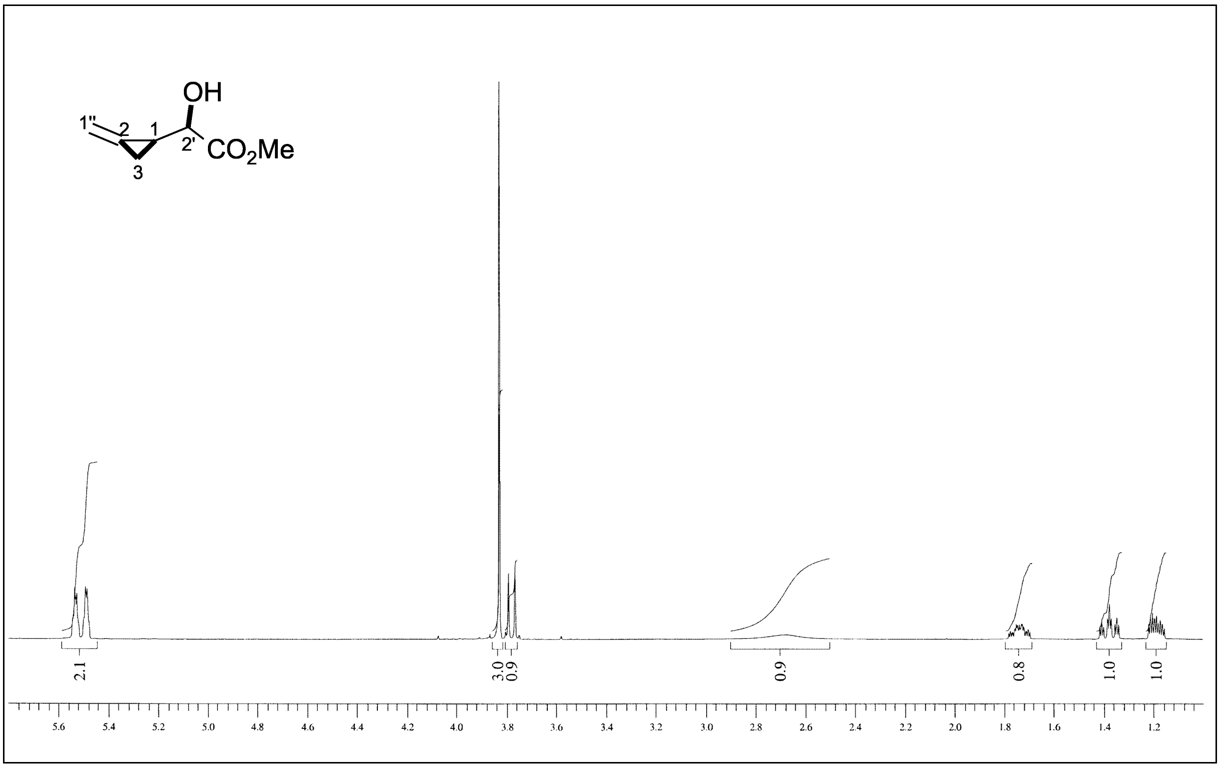
Methyl *exo*-6-formylbicyclo[3.1.0]hexane-6-carboxylate (**77**)



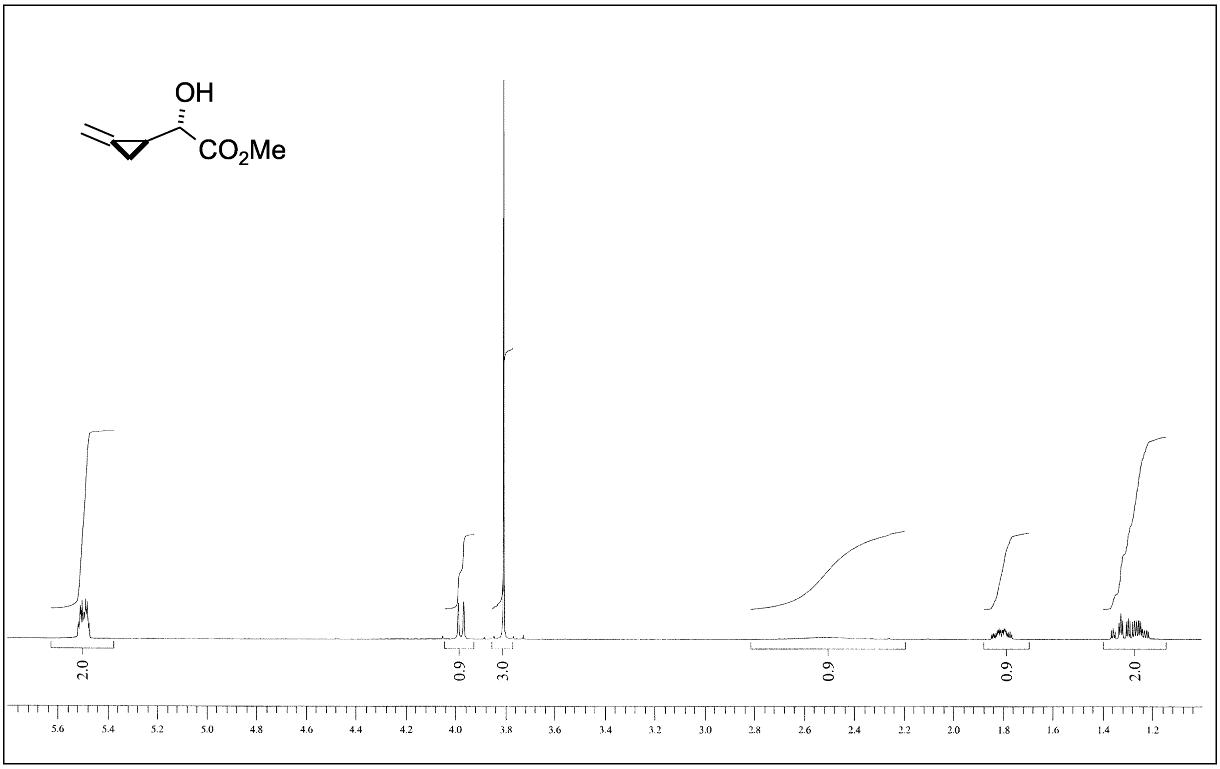
Methyl (cyclopenten-1-yl)hydroxyacetate (**81**)



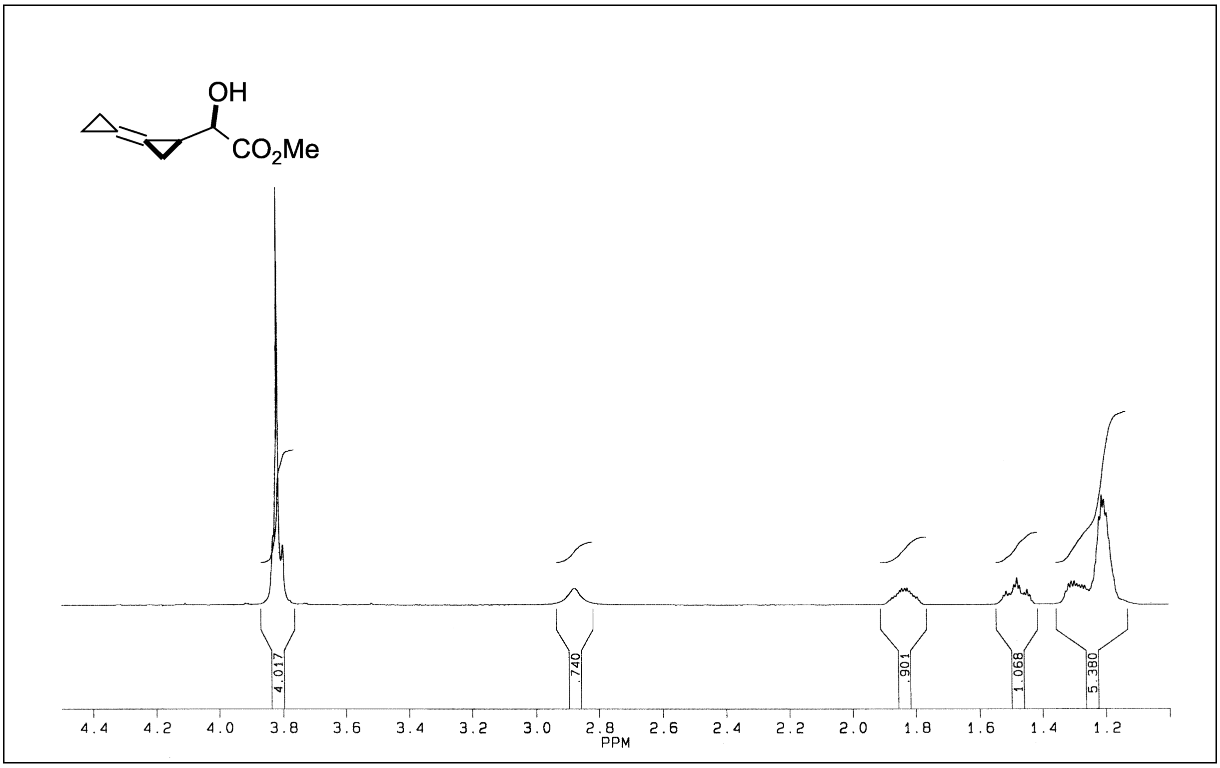
Methyl (3,3-dimethylcyclobuten-1-yl)hydroxyacetate (**83**)



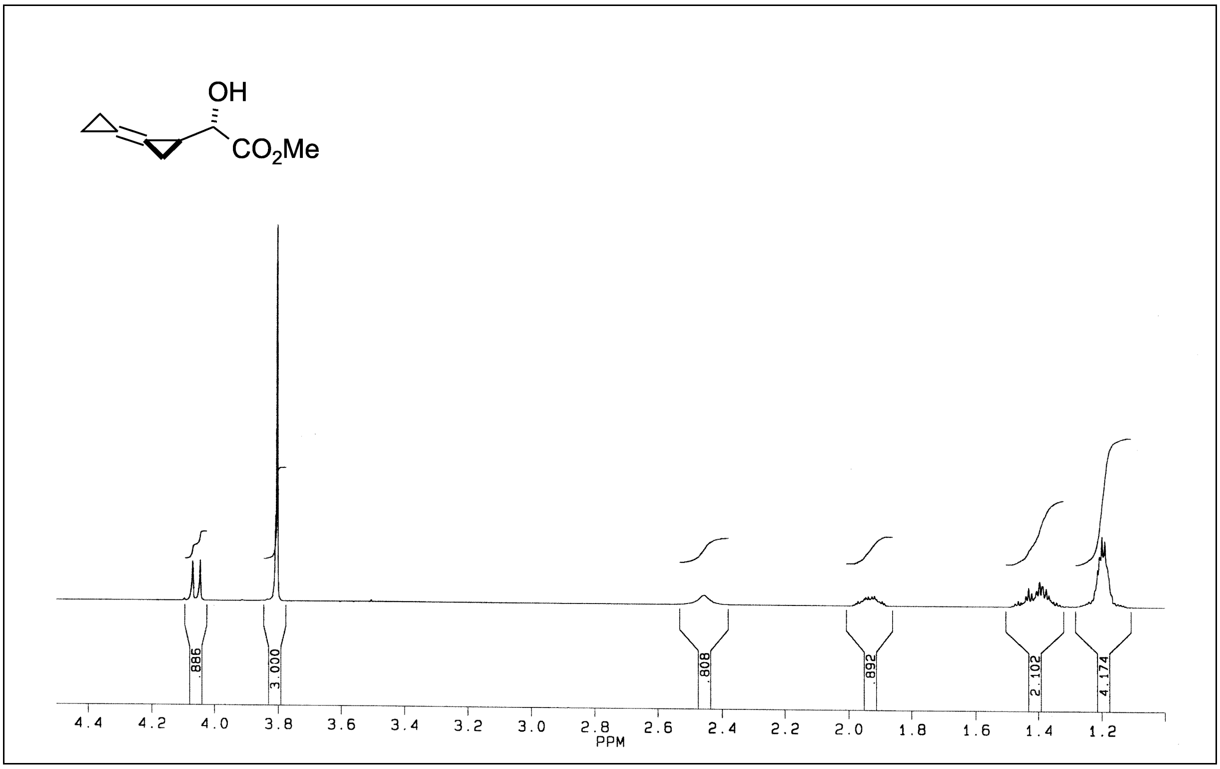
Methyl (S^*,R^*)-2-methylenecyclopropylhydroxyacetate (*syn*-**84**)



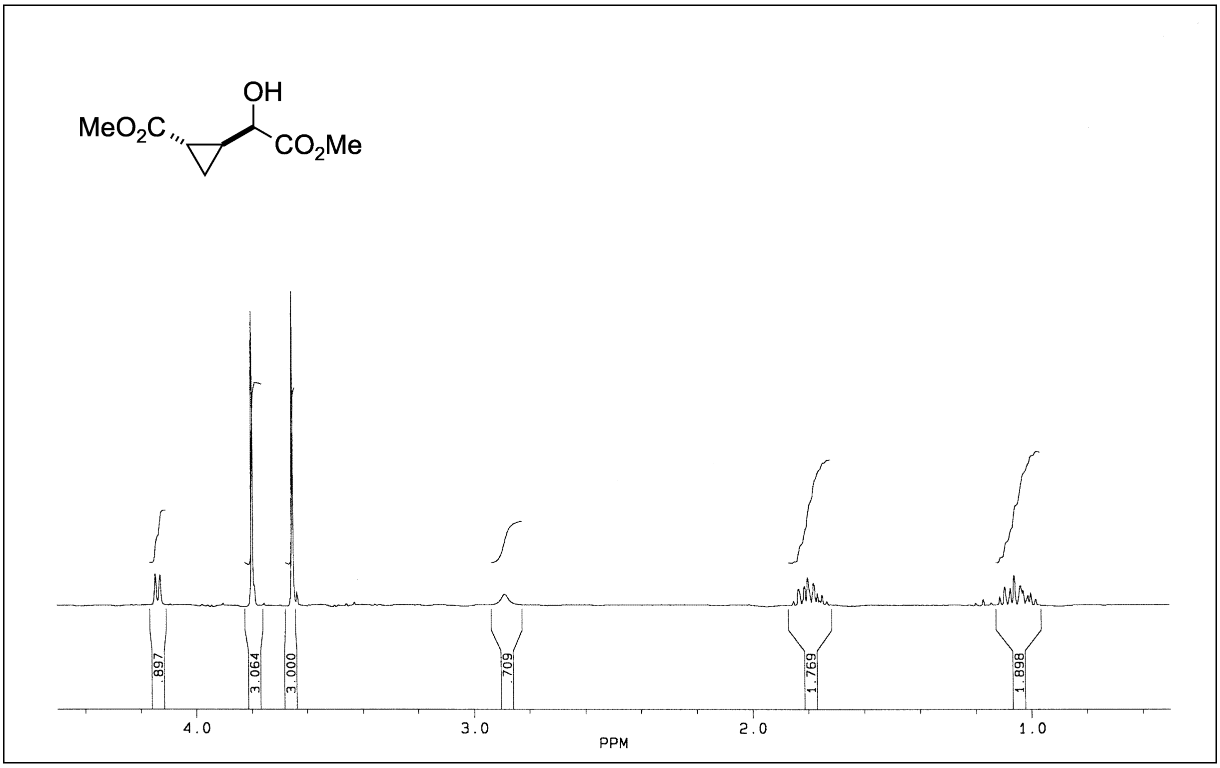
Methyl (S^*,S^*)-2-methylenecyclopropylhydroxyacetate (*anti*-**84**)



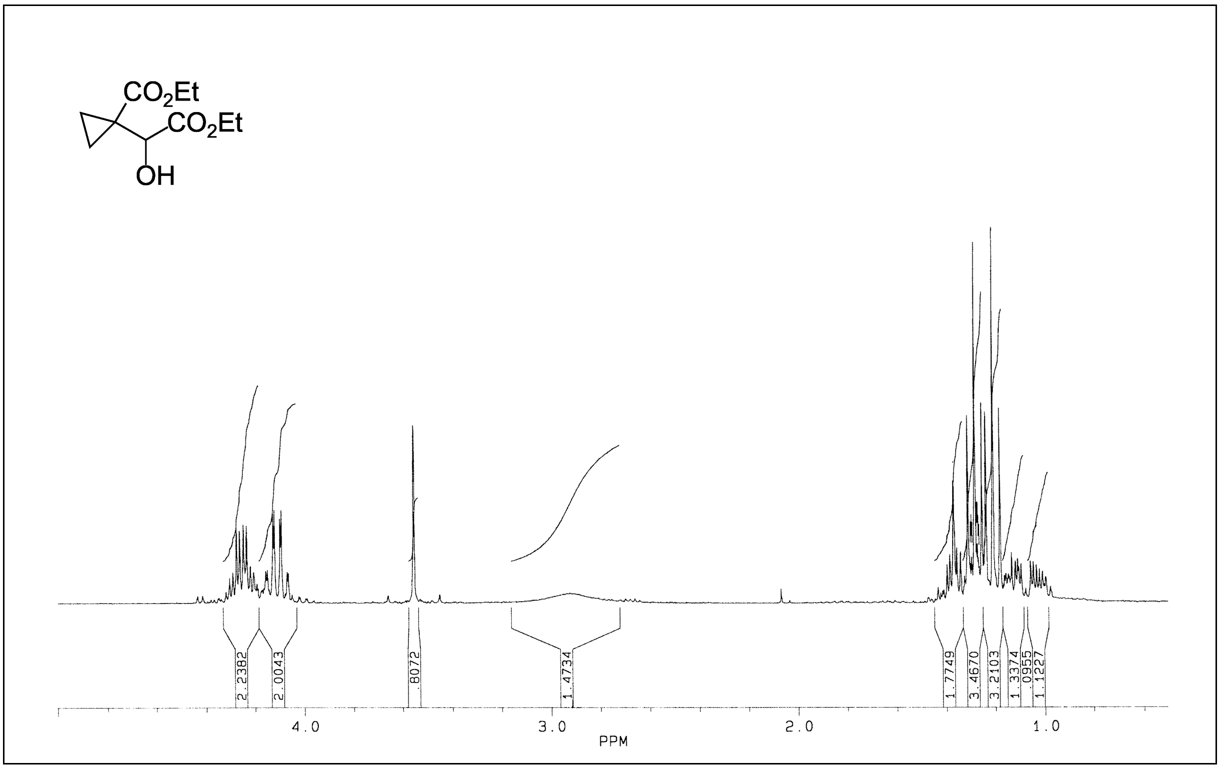
Methyl (S^*,R^*)-bicyclopropylidenylhydroxyacetate (*syn*-**85**)



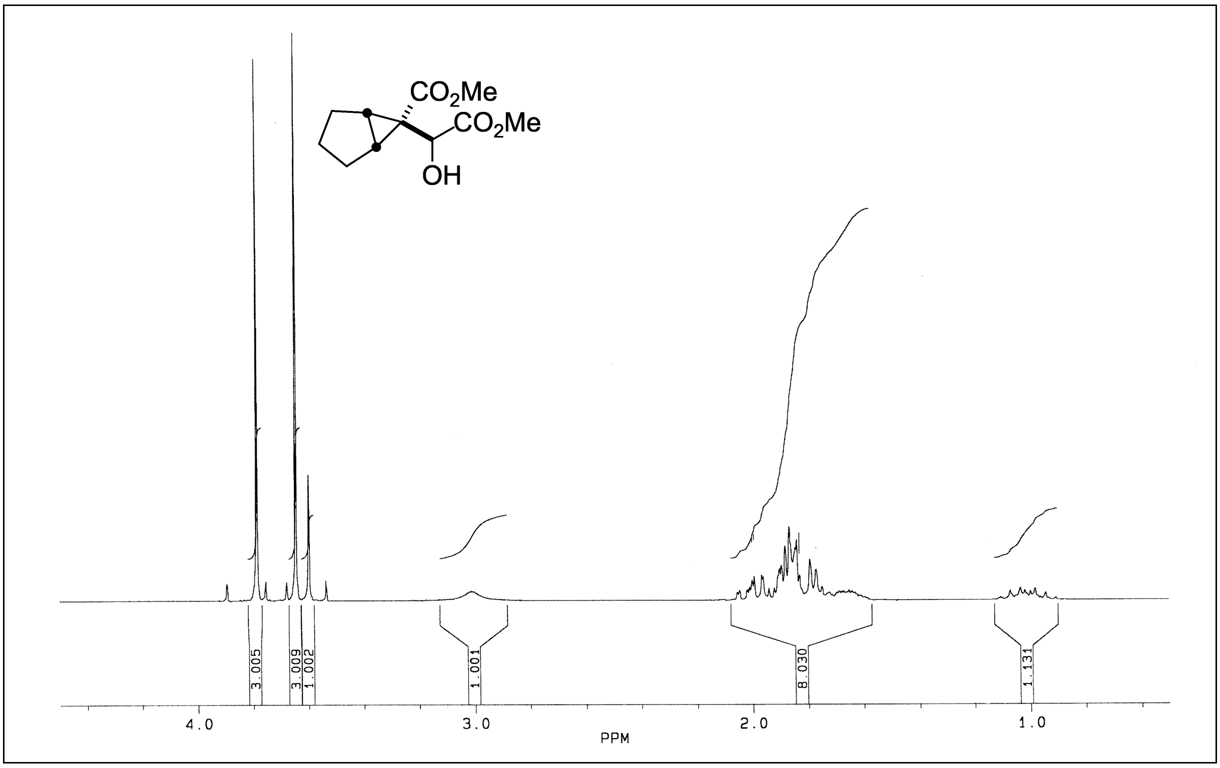
Methyl (S^*,S^*)-bicyclopropylidenylhydroxyacetate (*anti*-**85**)



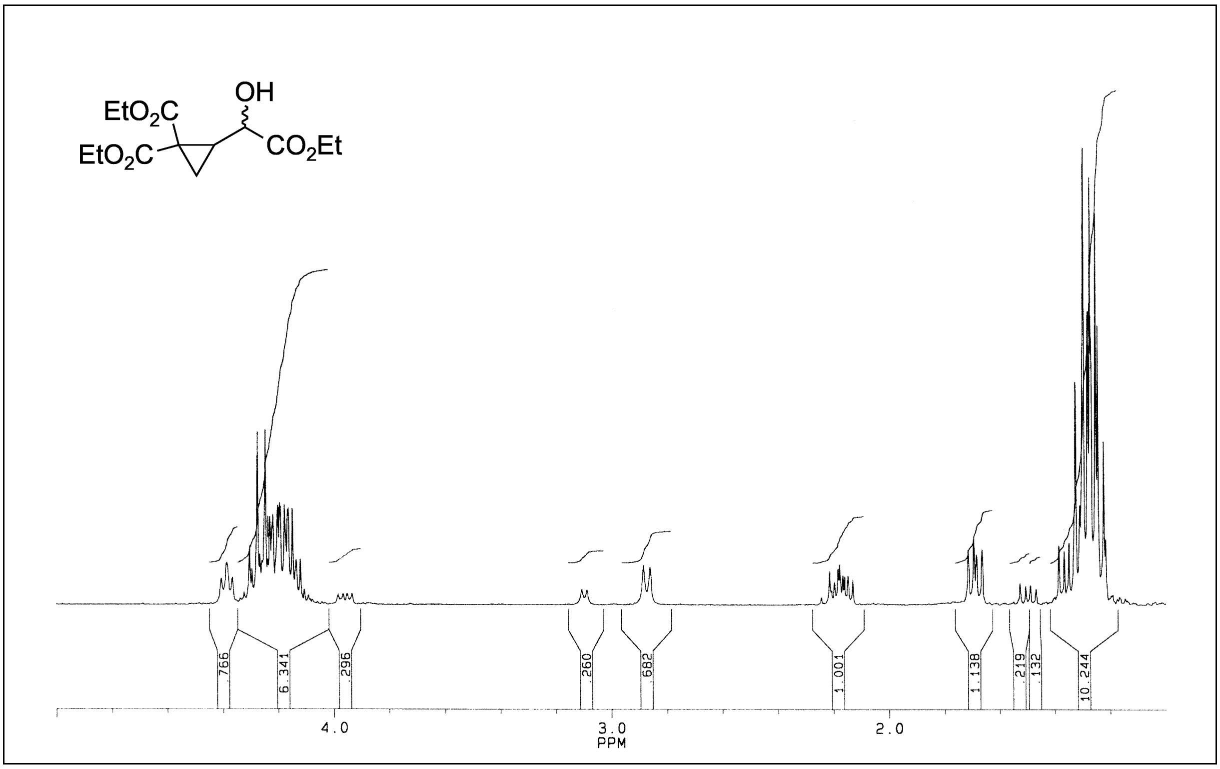
Methyl *trans*-(1-methoxycarbonylcycloprop-2-yl)hydoxyacetate (**86**), first diastereomer.



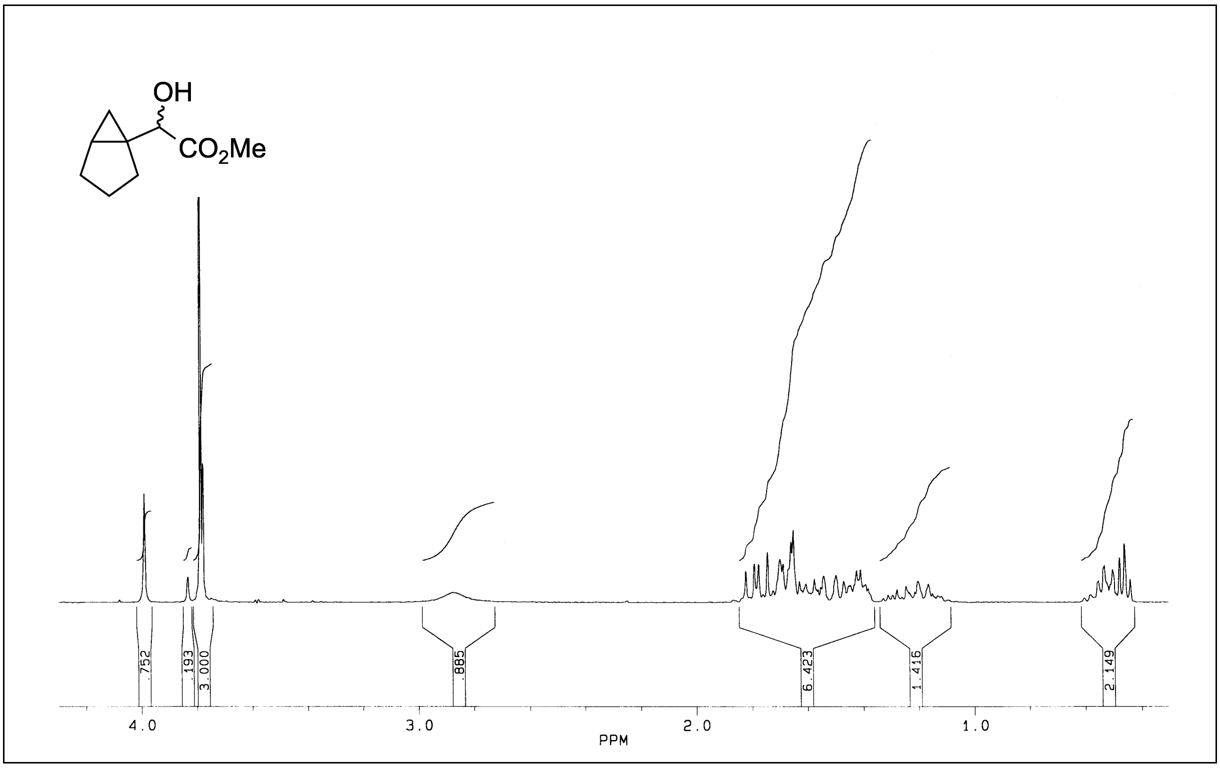
Ethyl (1-ethoxycarbonylcycloprop-1-yl)hydroxyacetate (**87**)



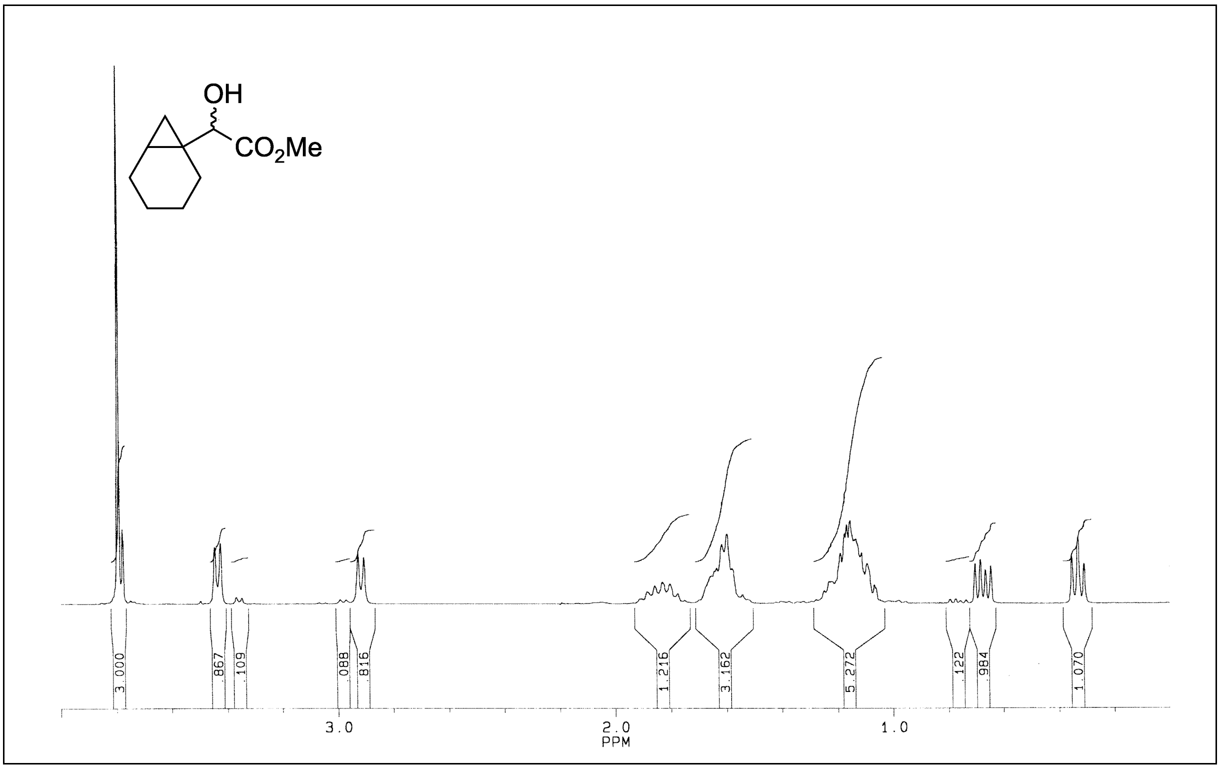
Methyl *exo*-(6-methoxycarbonylbicyclo[3.1.0]hex-6-yl)hydroxyacetate (**88**)



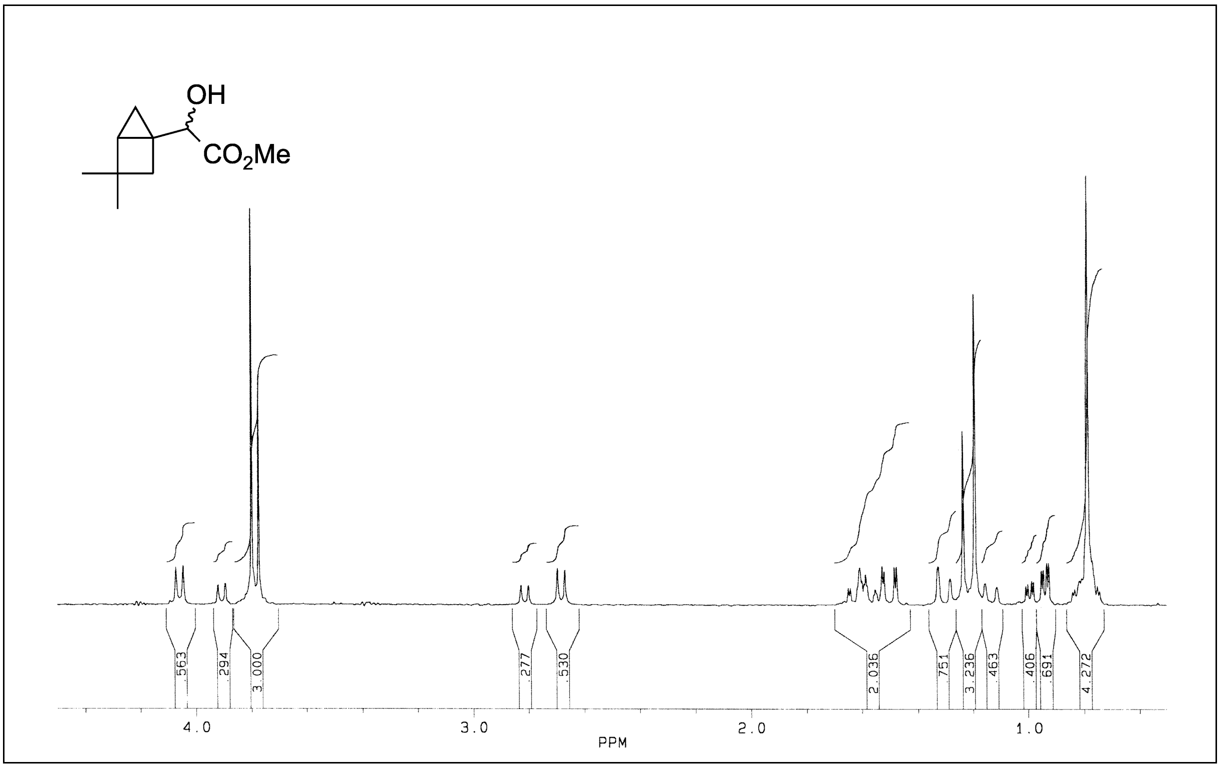
Ethyl [1,1-bis(ethoxycarbonyl)cycloprop-2-yl]hydroxyacetate (**89**)



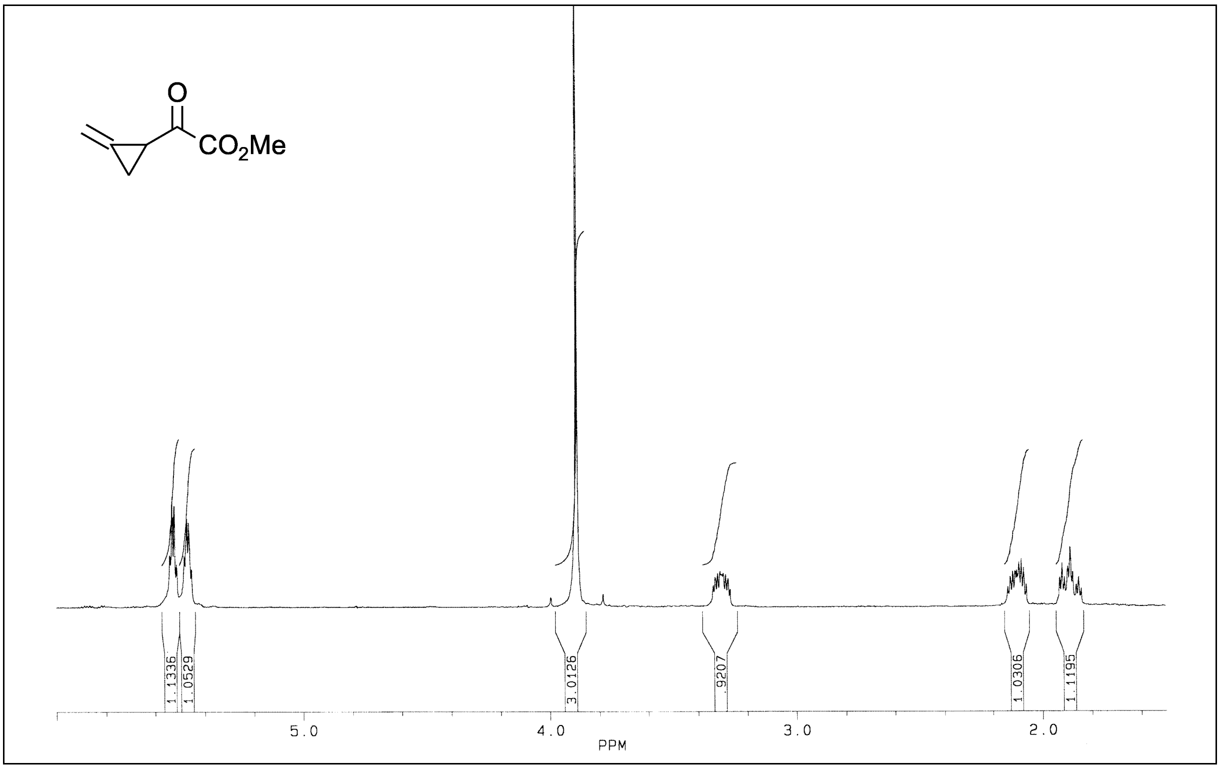
Methyl (bicyclo[3.1.0]hex-1-yl)hydroxyacetate (**91**)



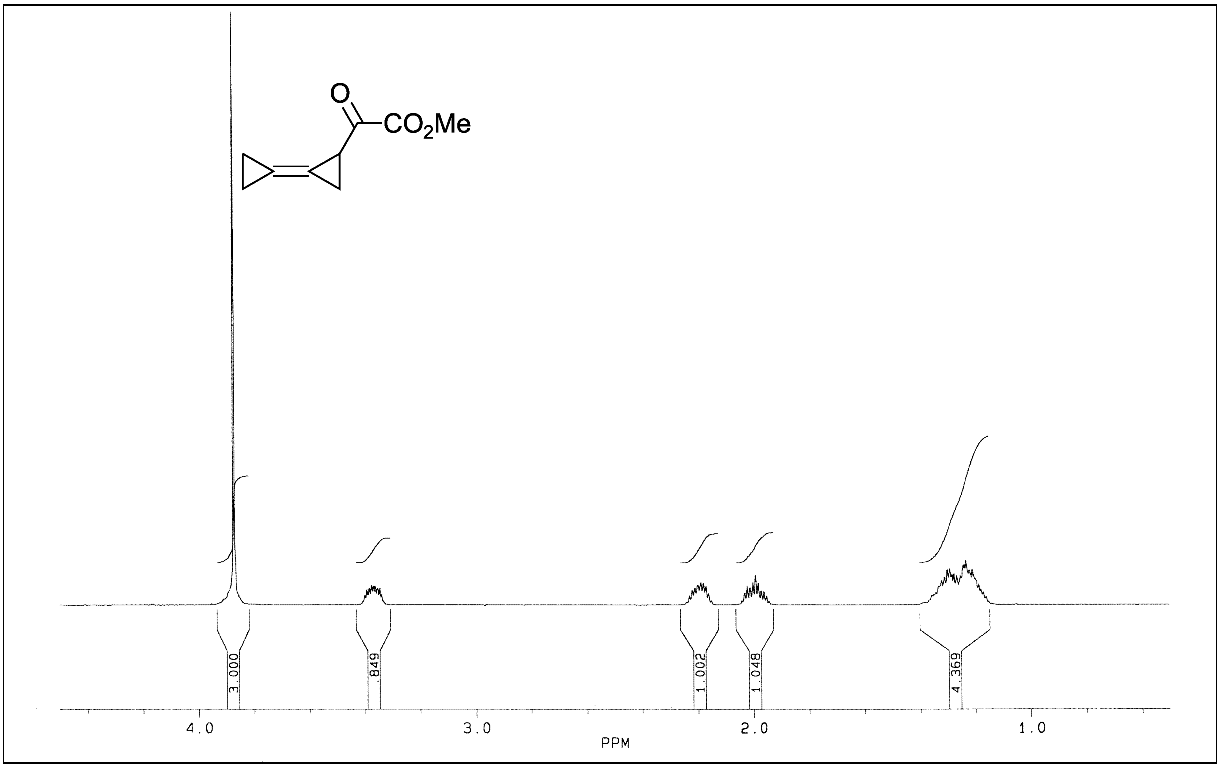
Methyl (bicyclo[4.1.0]hept-1-yl)hydroxyacetate (**92**)



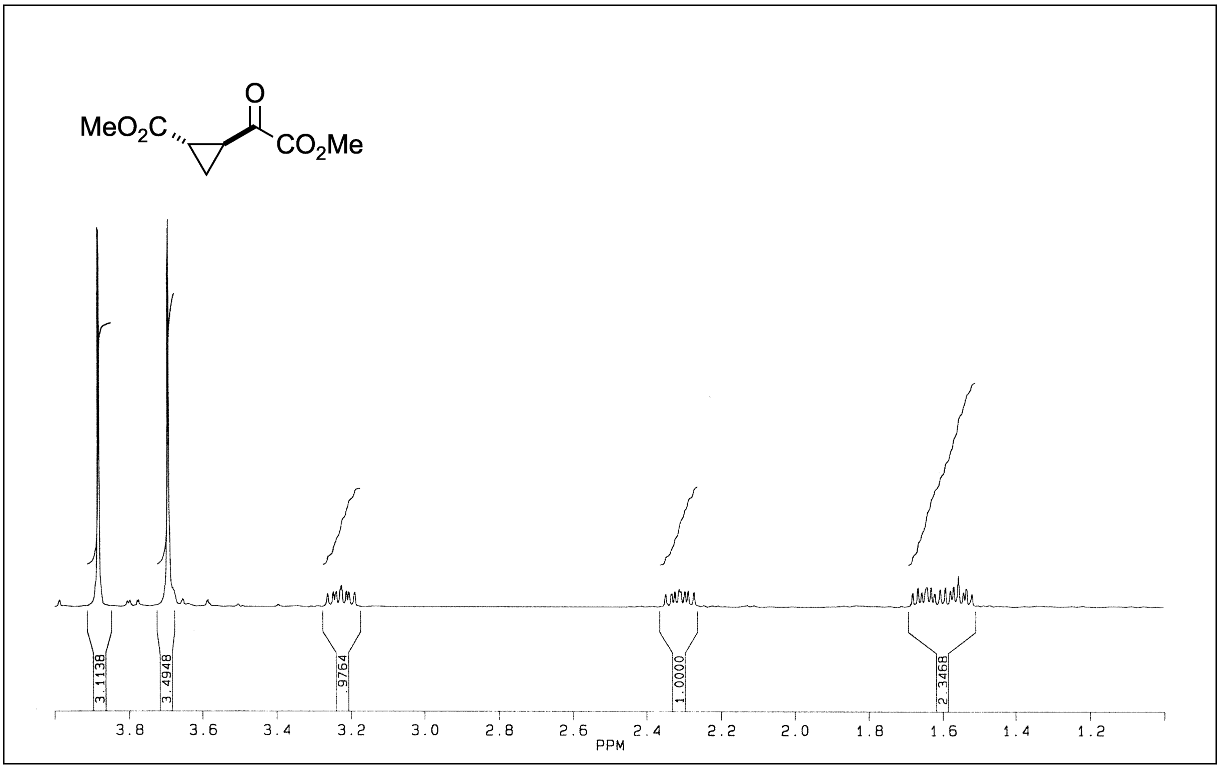
Methyl (3,3-dimethylbicyclo[2.1.0]pent-1-yl)hydroxyacetate (**93**)



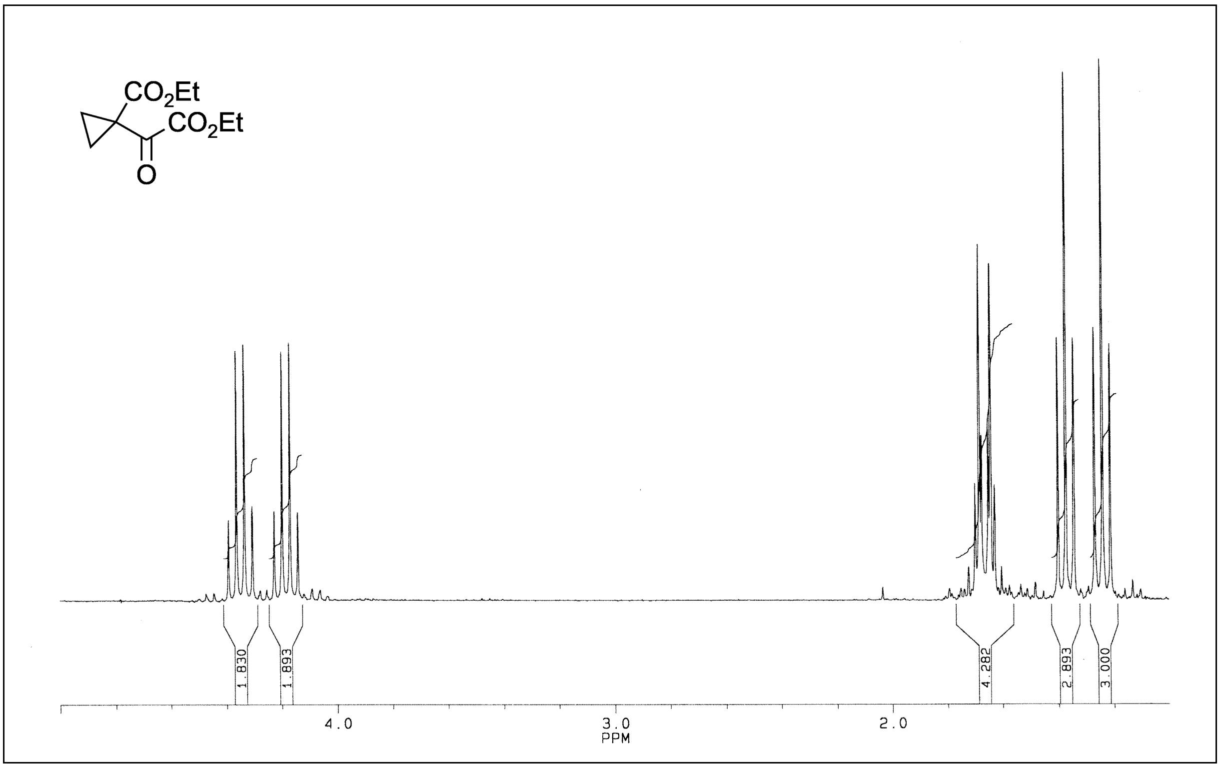
Methyl 2-methylenecyclopropyloxoacetate (**97**)



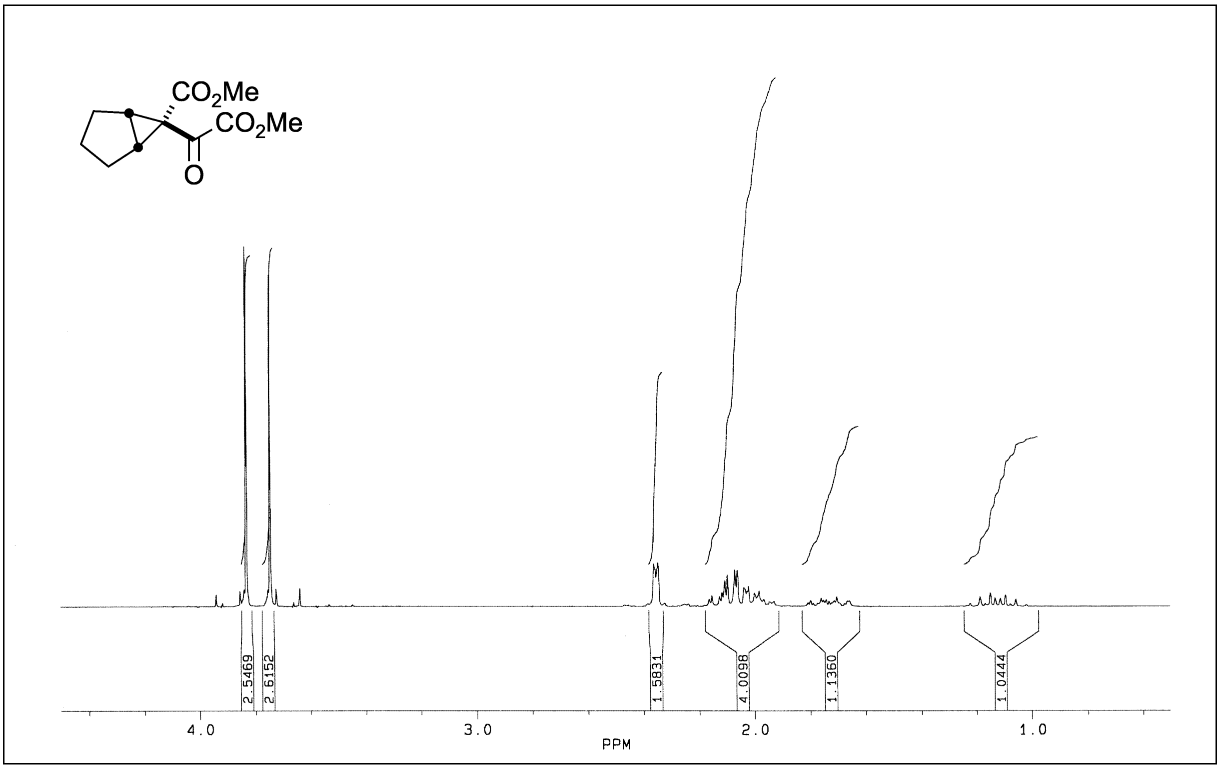
Methyl bicyclopropylidenyloxoacetate (**98**)



Methyl *trans*-(1-methoxycarbonylcycloprop-2-yl)oxoacetate (**99**)



Ethyl (1-ethoxycarbonylcycloprop-1-yl)oxoacetate (**100**)



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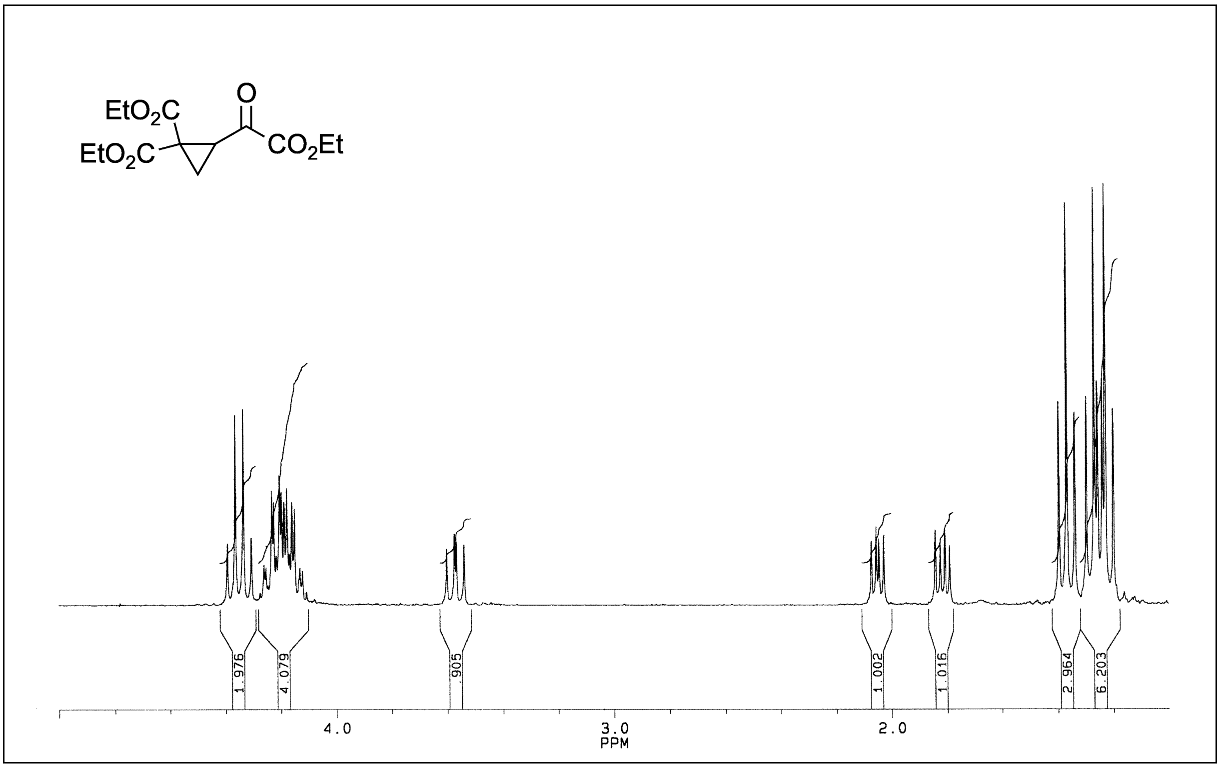
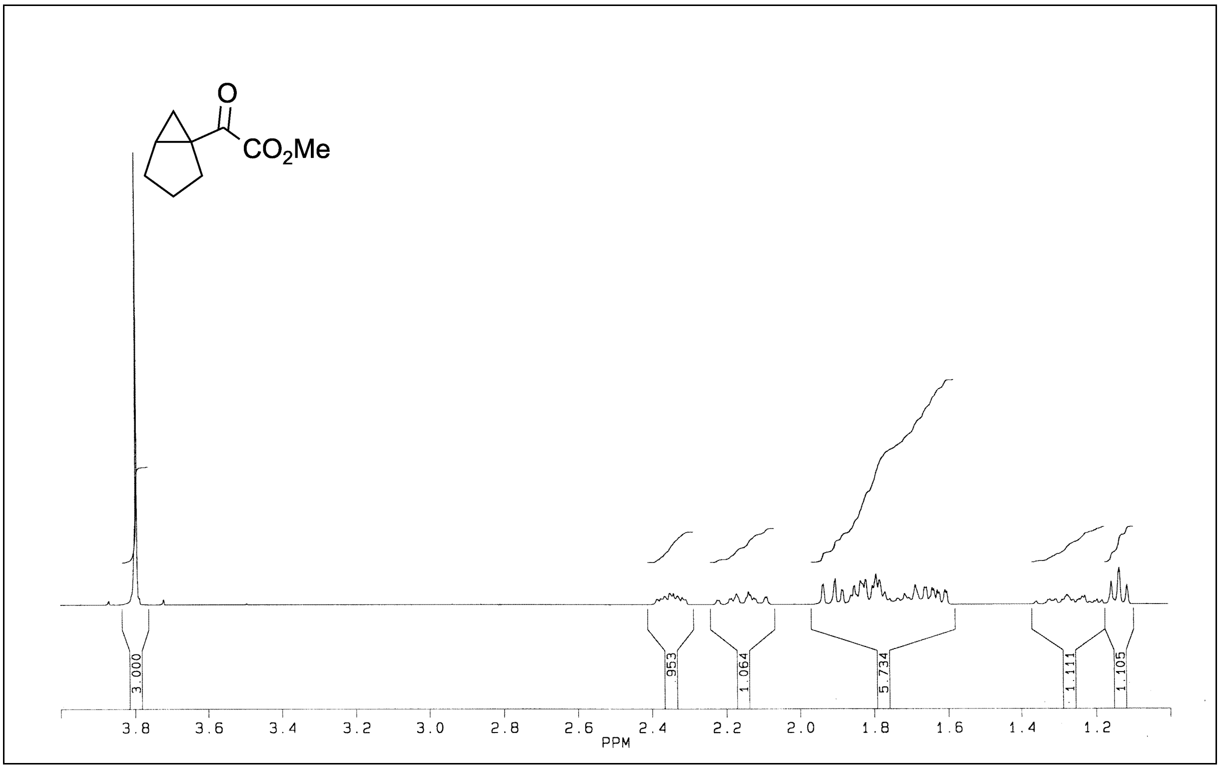
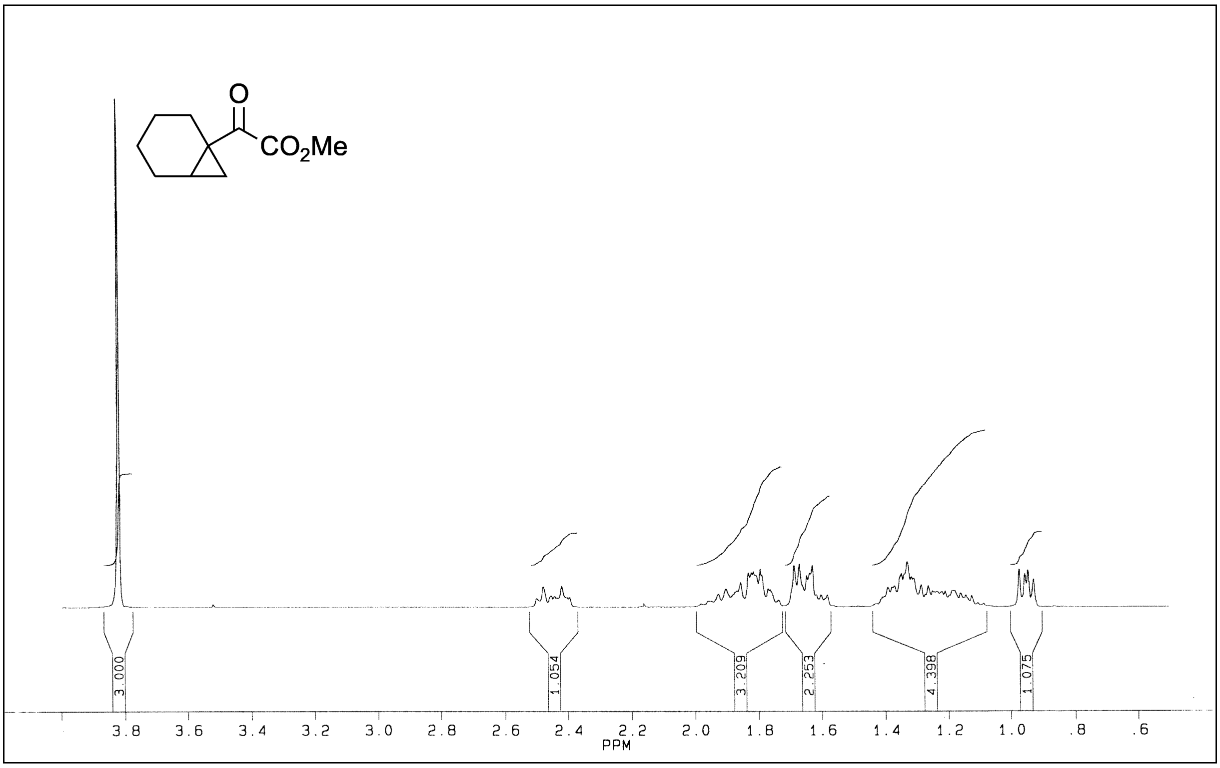


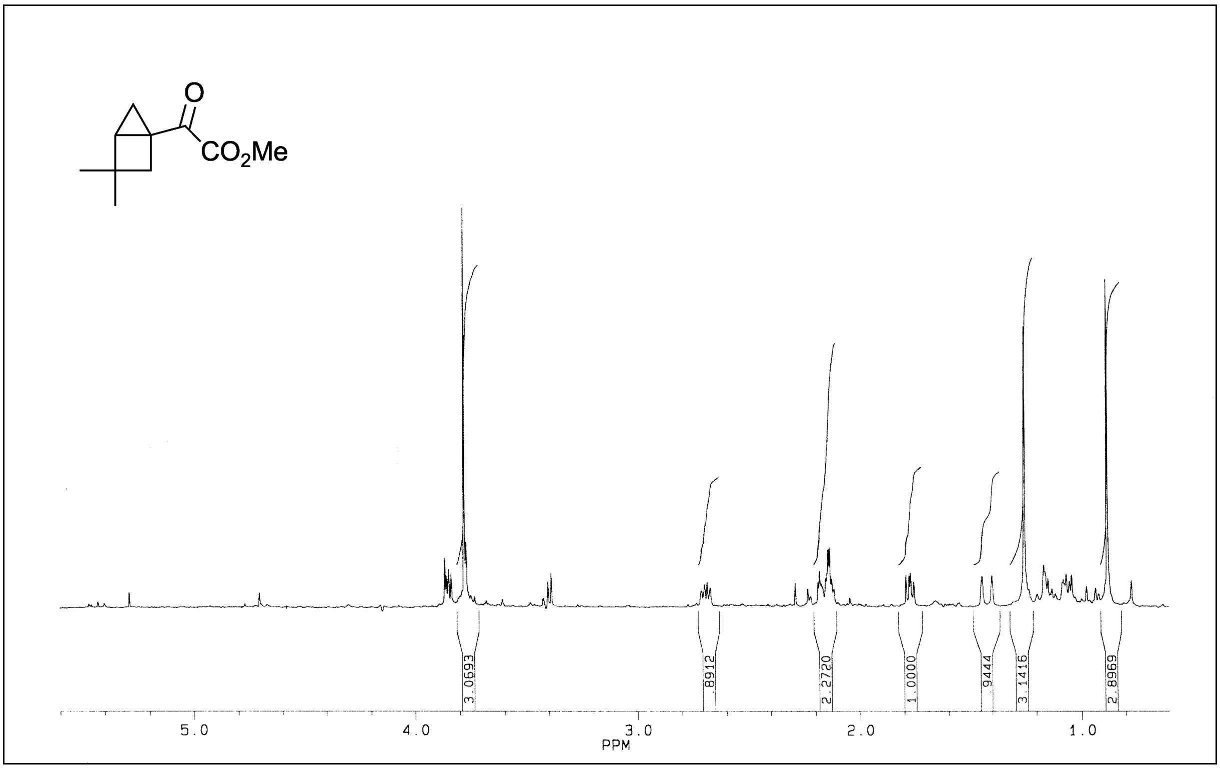
Ethyl [1,1-bis(ethoxycarbonyl)cycloprop-2-yl]oxoacetate (**102**)



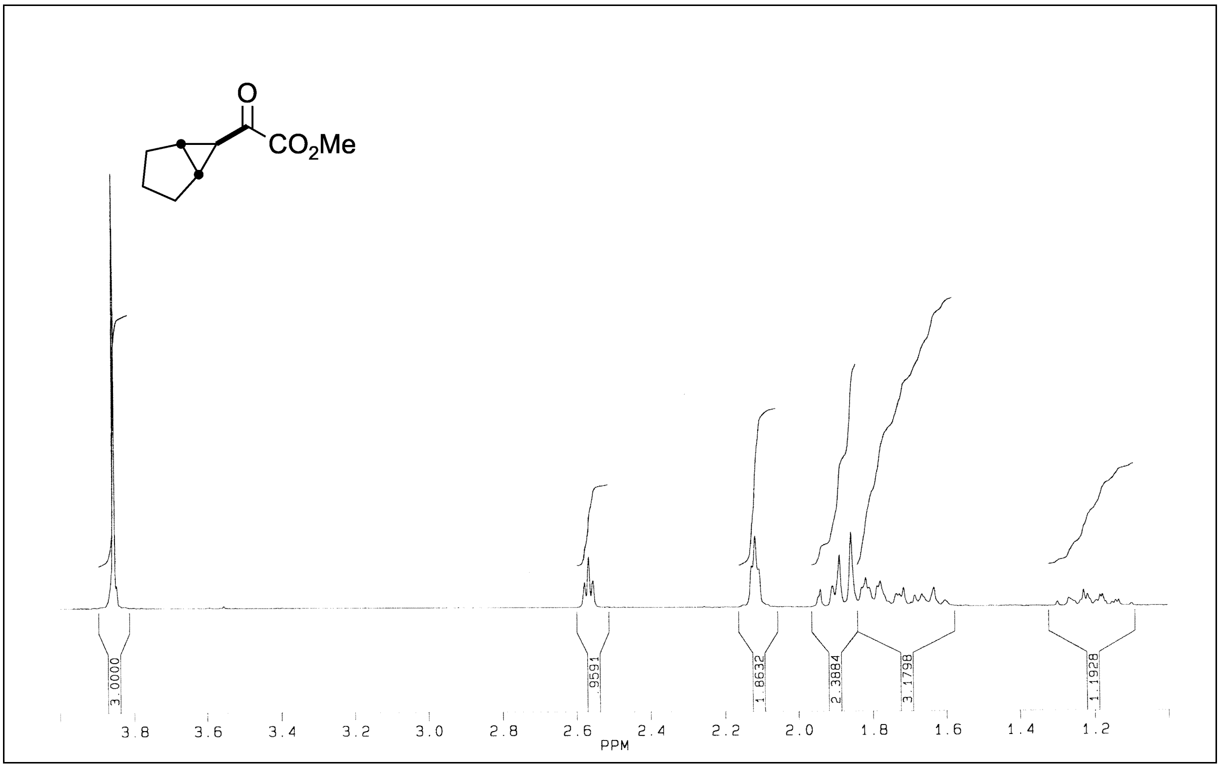
Methyl (bicyclo[3.1.0]hex-1-yl)oxoacetate (**103**)



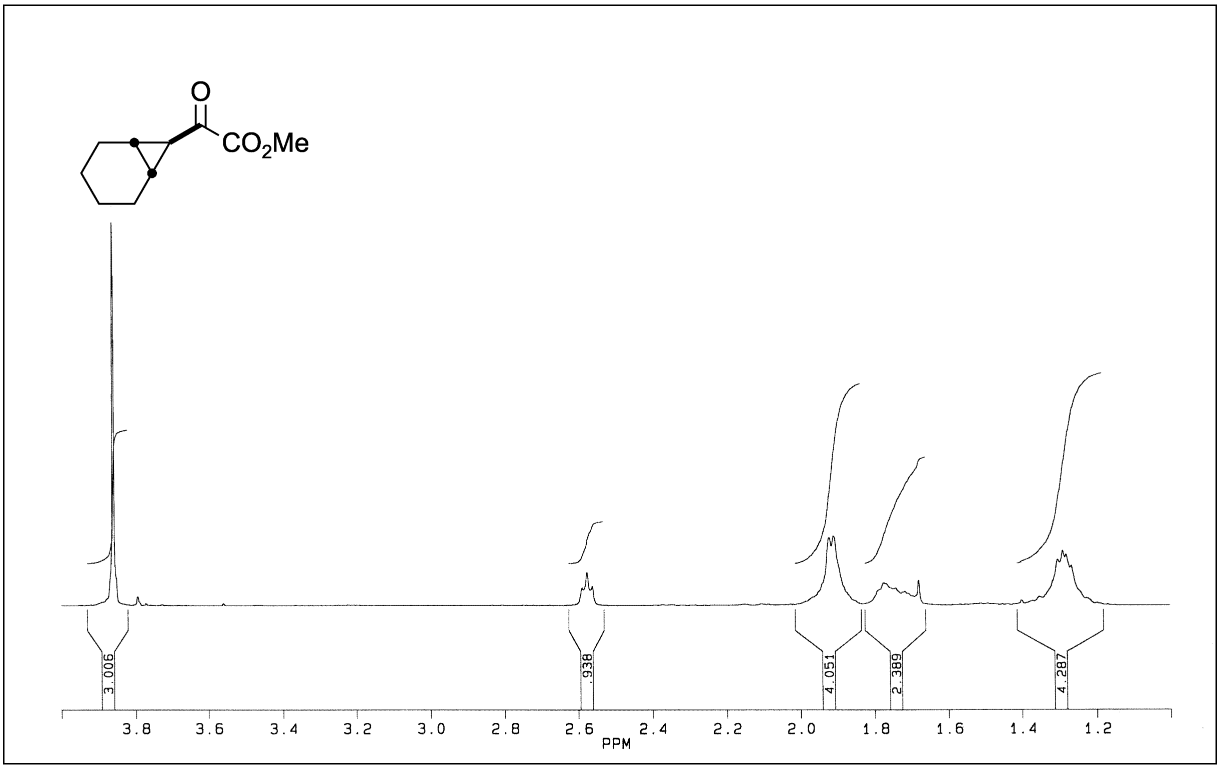
Methyl (bicyclo[4.1.0]hept-1-yl)oxoacetate (**104**)



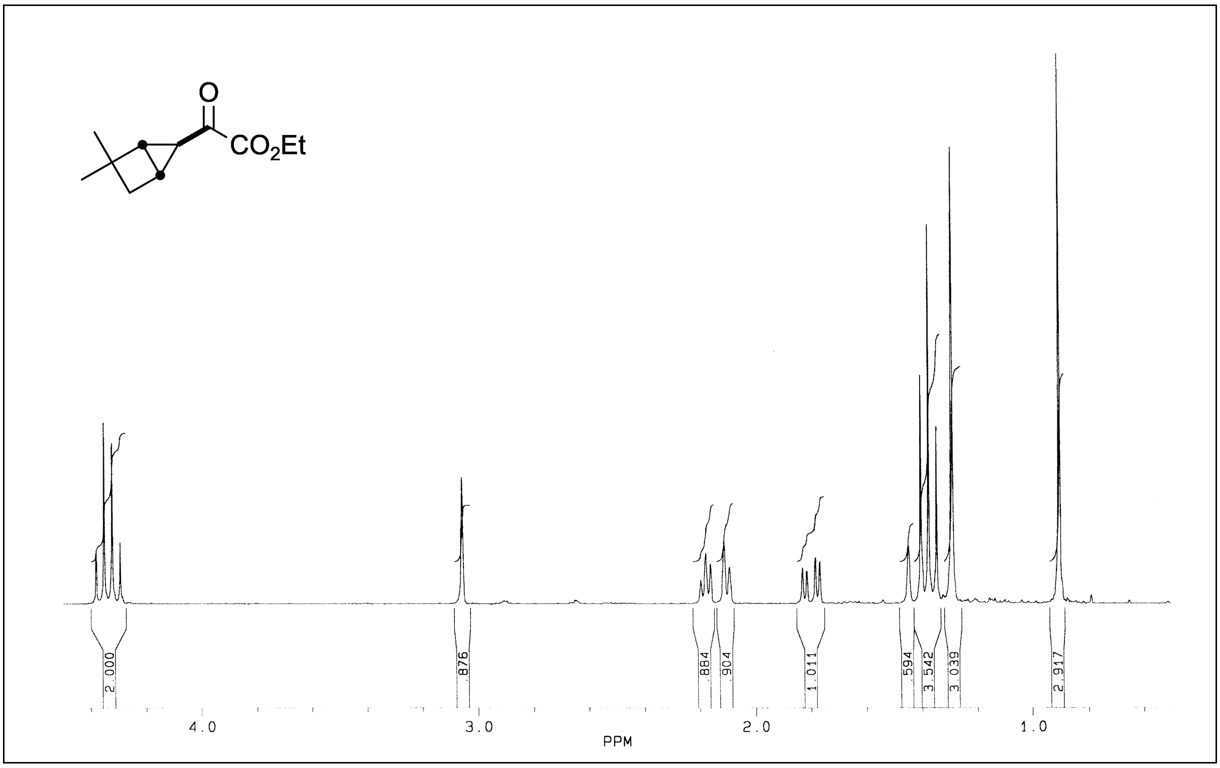
Methyl (3,3-dimethylbicyclo[2.1.0]pent-1-yl)oxoacetate (**105**) (reaction mixture)



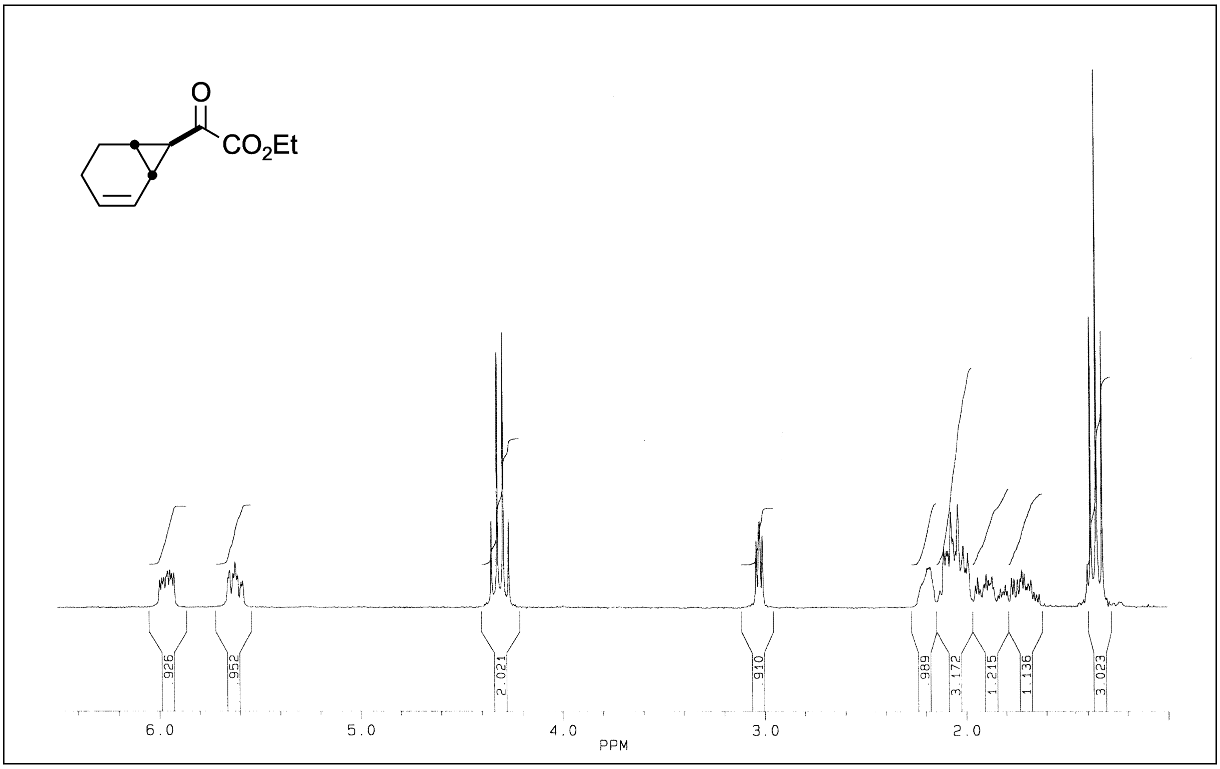
Methyl *exo*-(bicyclo[3.1.0]hex-6-yl)oxoacetate (**111**)



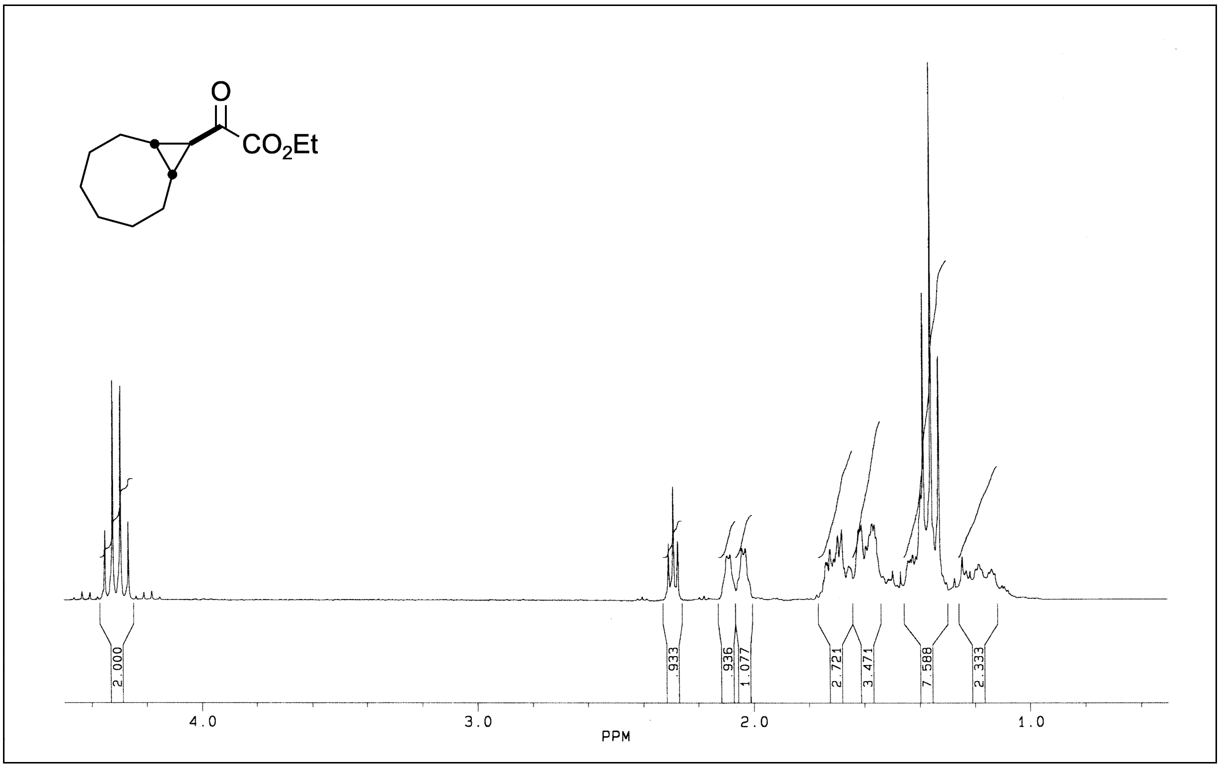
Methyl *exo*-(bicyclo[4.1.0]hept-7-yl)oxoacetate (**113**)



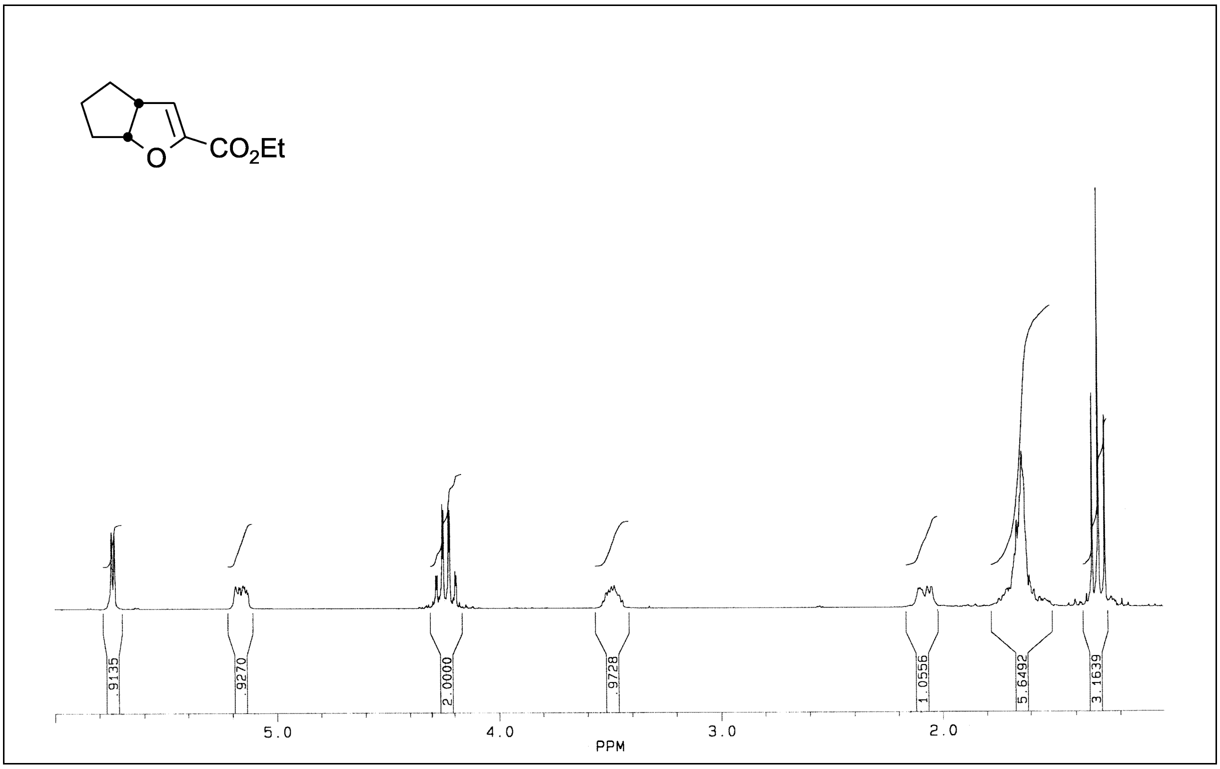
Ethyl *exo*-(2,2-dimethylbicyclo[2.1.0]pent-5-yl)oxoacetate (**115**)



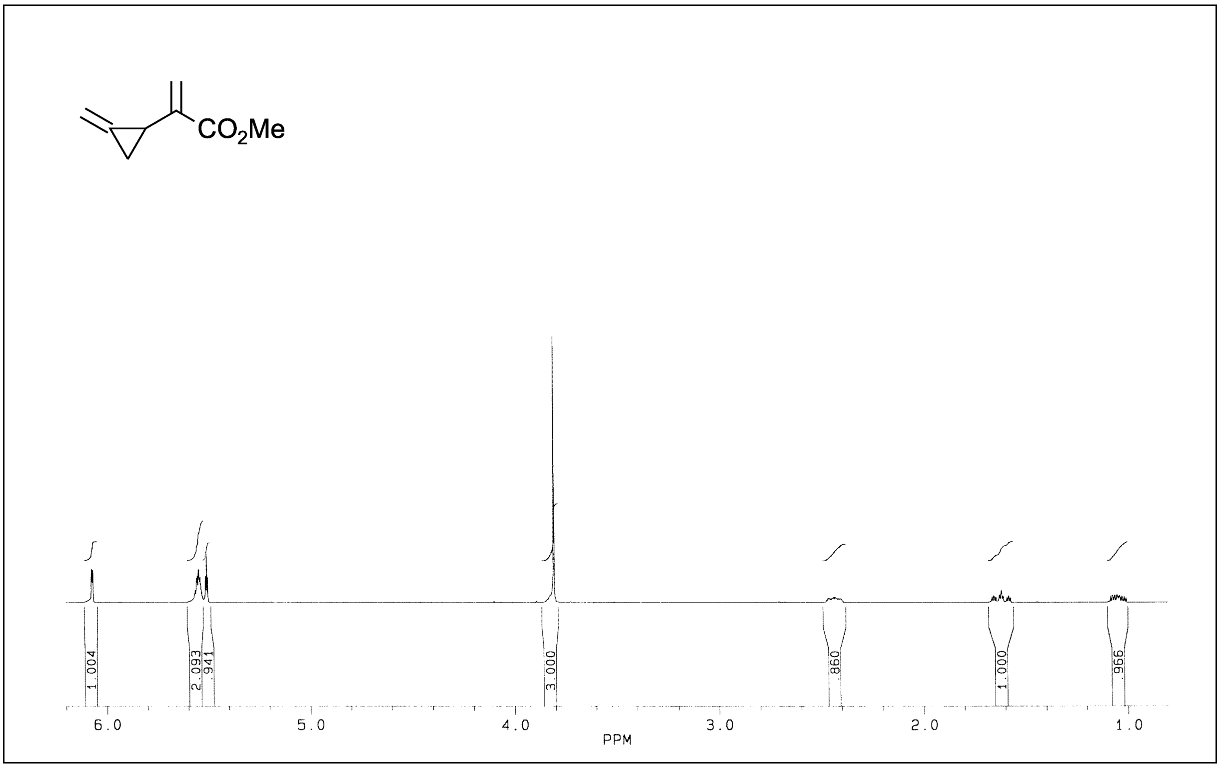
Ethyl *exo*-(bicyclo[4.1.0]hept-2-en-7-yl)oxoacetate (**116**)



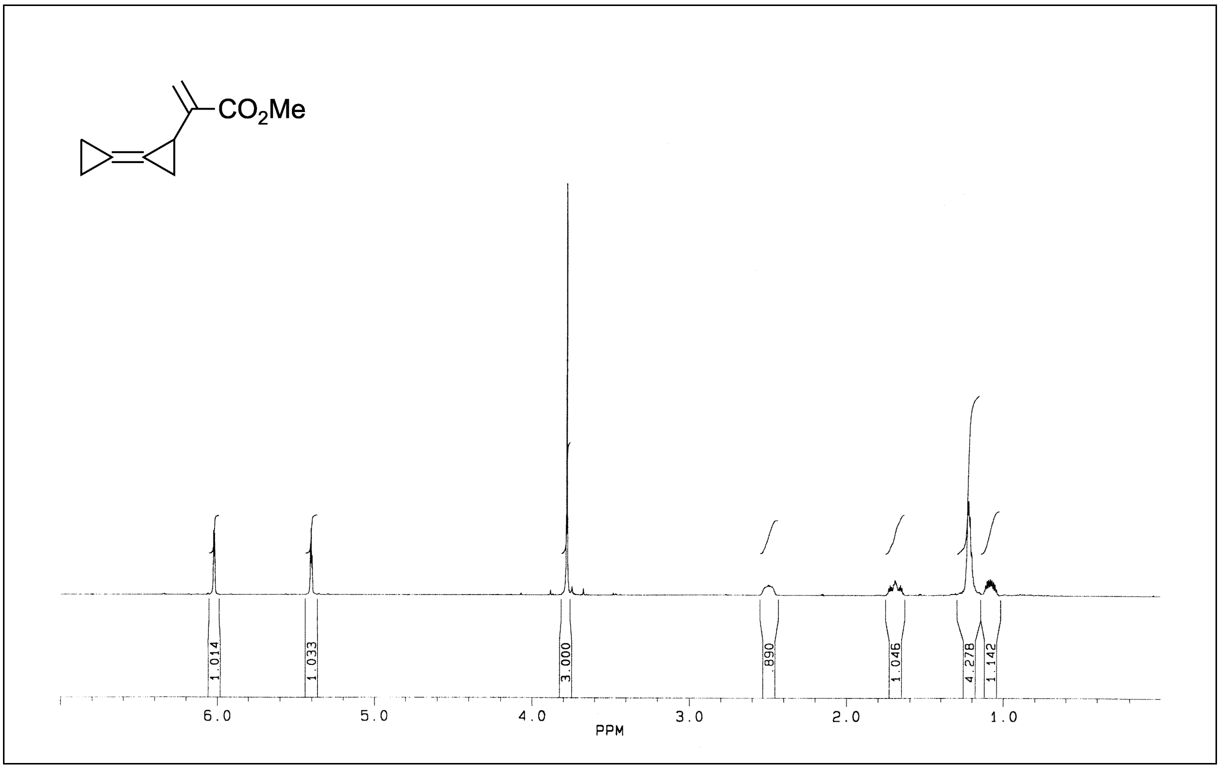
Ethyl *exo*-(bicyclo[6.1.0]non-9-yl)oxoacetate (**117**)



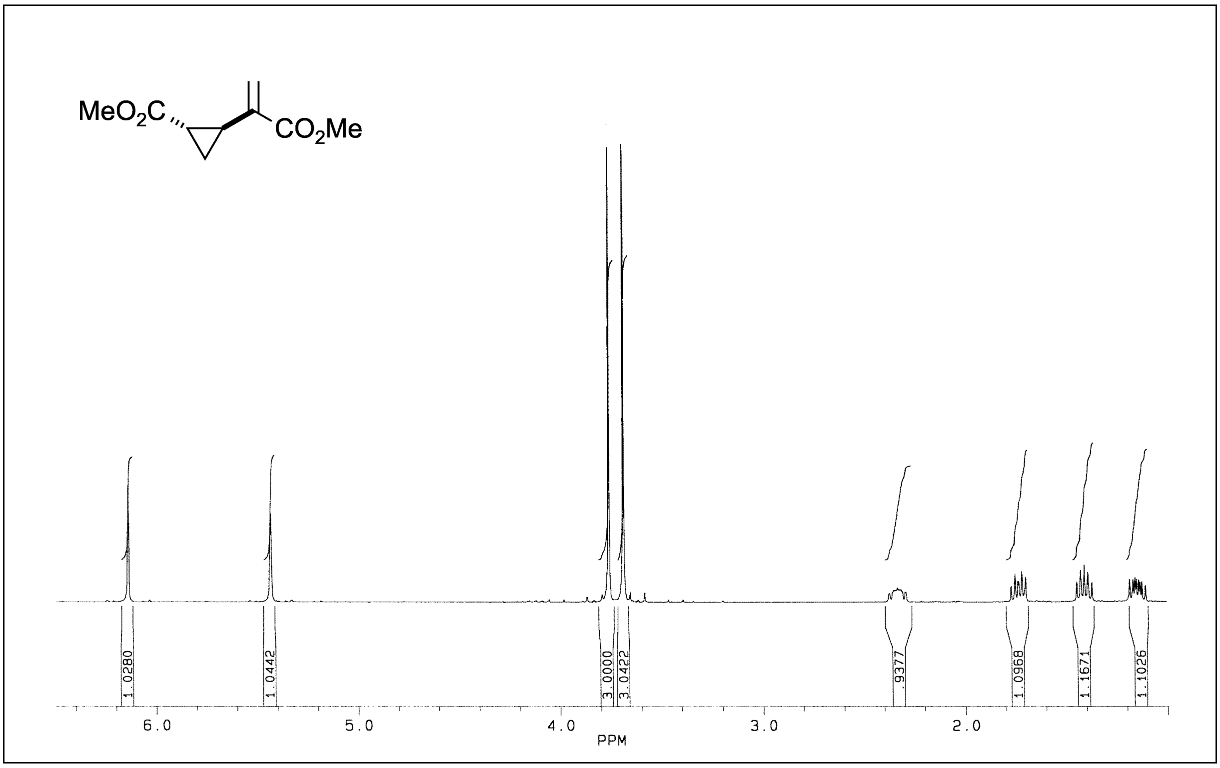
Ethyl 4,5,6,6a-tetrahydro-3a*H*-cyclopenta[b]furan-2-carboxylate (**120**)



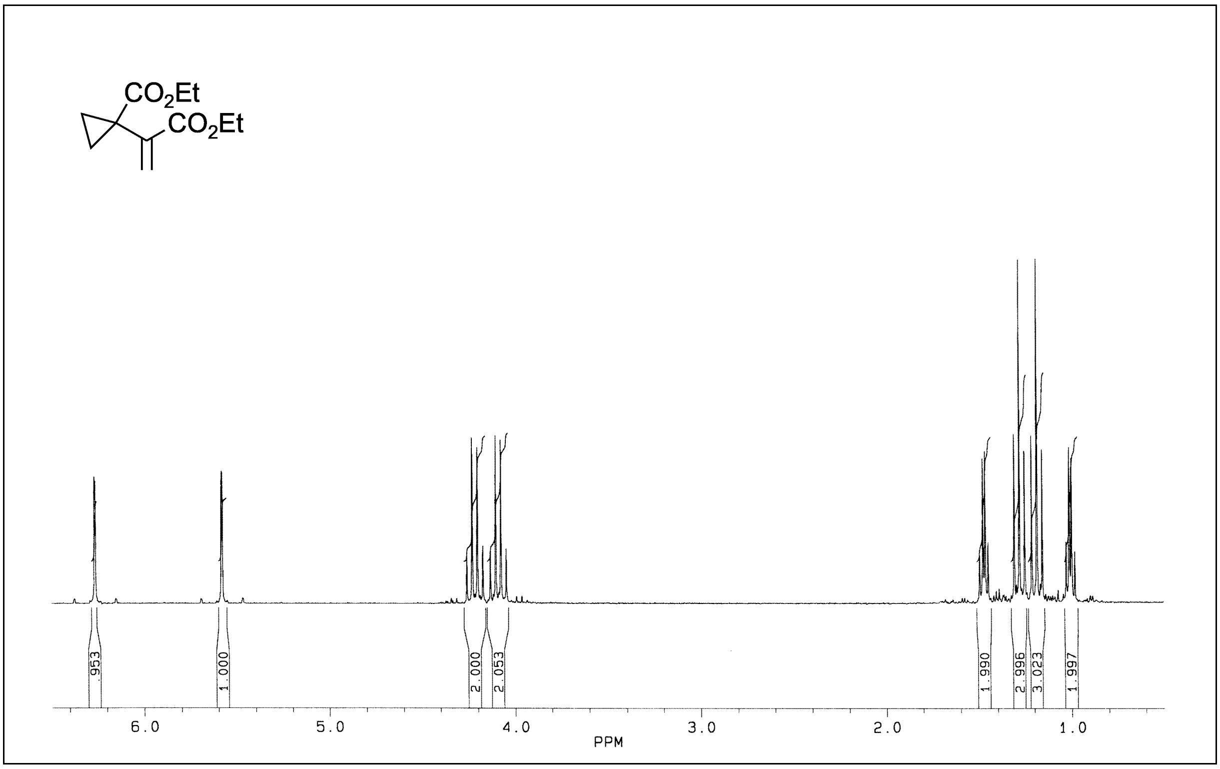
Methyl 2-(2-methylenecyclopropyl)propenoate (**123**)



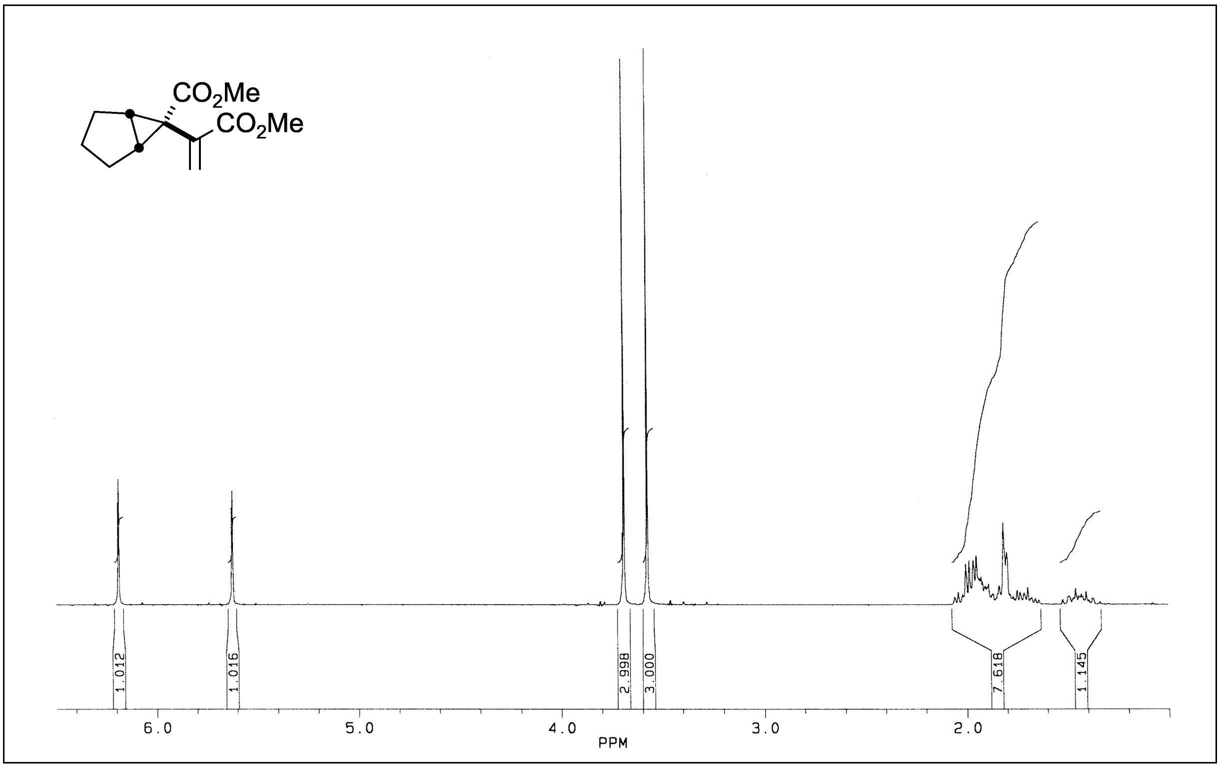
Methyl 2-bicyclopropylidenylpropenoate (**124**)



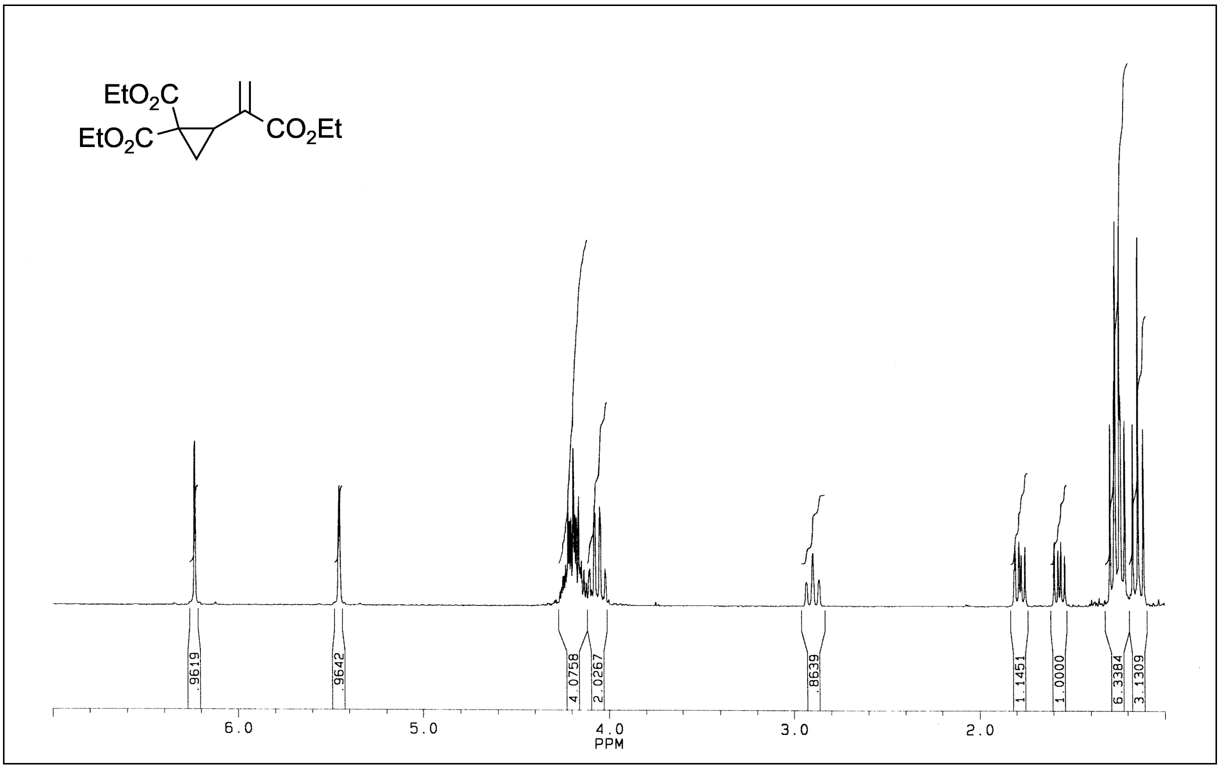
Methyl *trans*-2-(1-methoxycarbonylcycloprop-2-yl)propenoate (**126**)



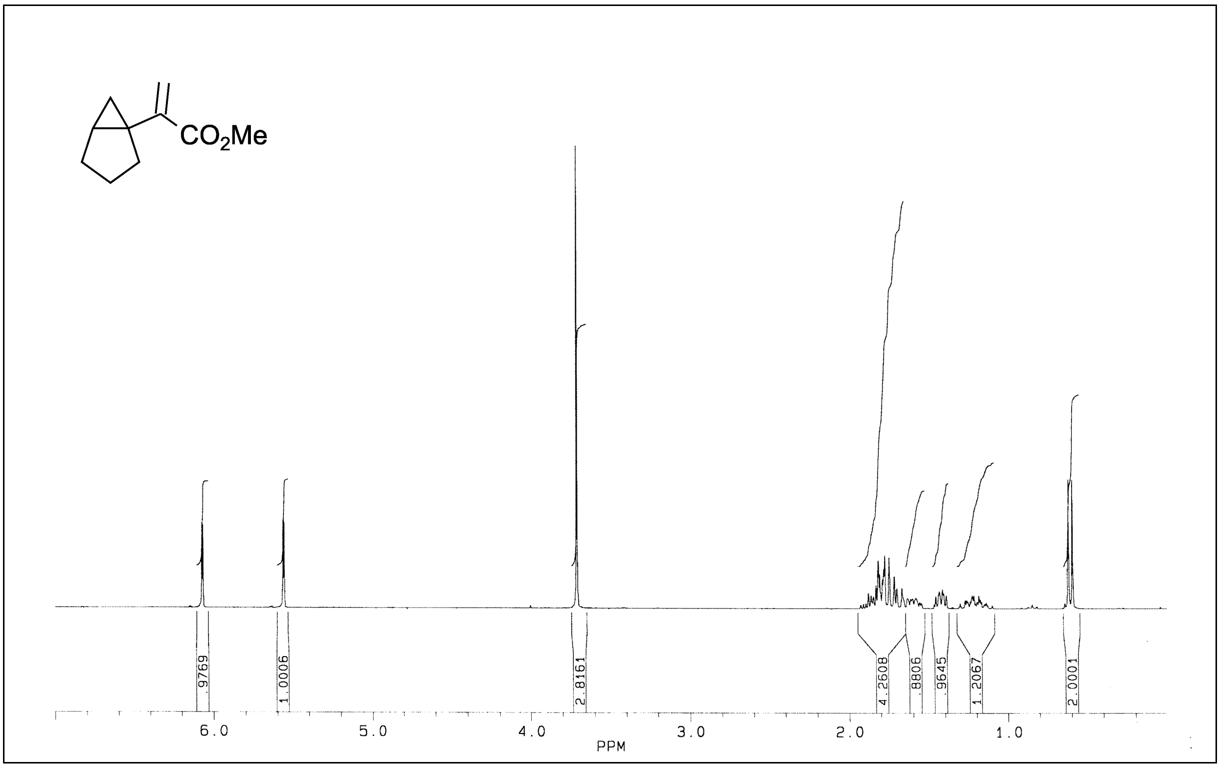
Ethyl 2-(1-ethoxycarbonylcycloprop-1-yl)propenoate (**127**)



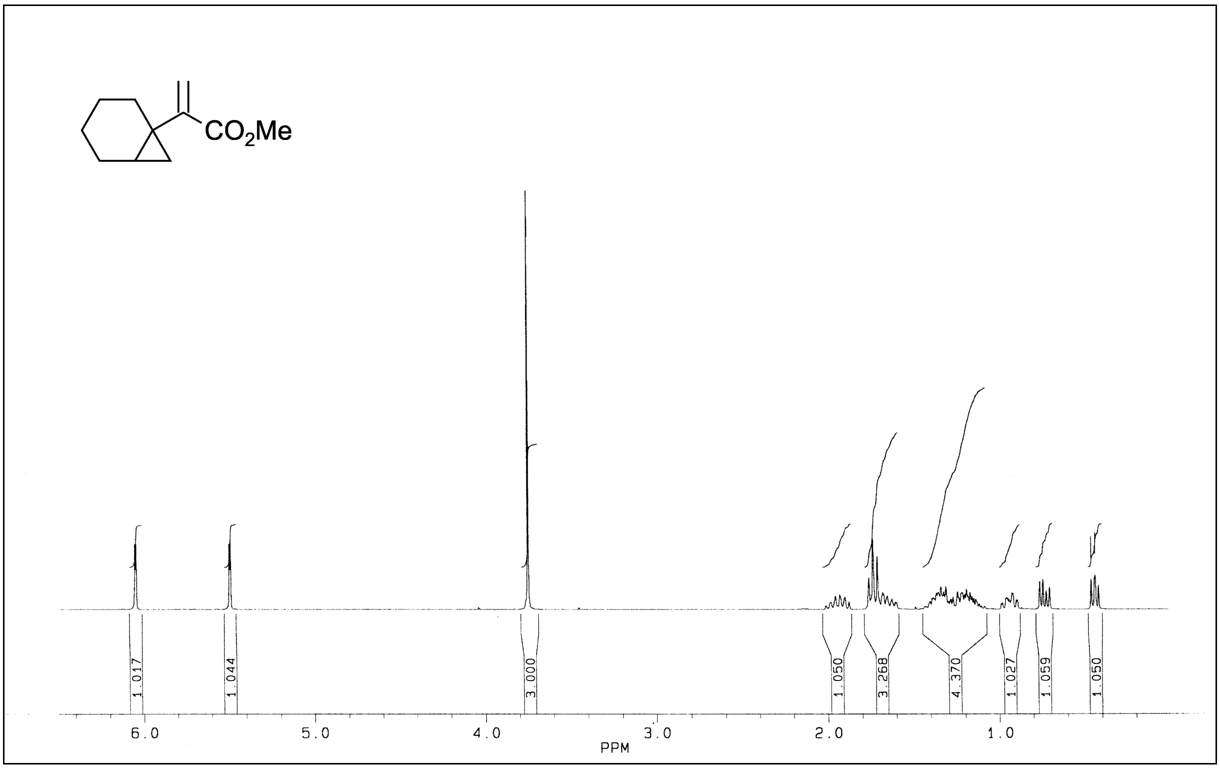
Methyl *exo*-2-(6-methoxycarbonylbicyclo[3.1.0]hex-6-yl)propenoate (**128**)



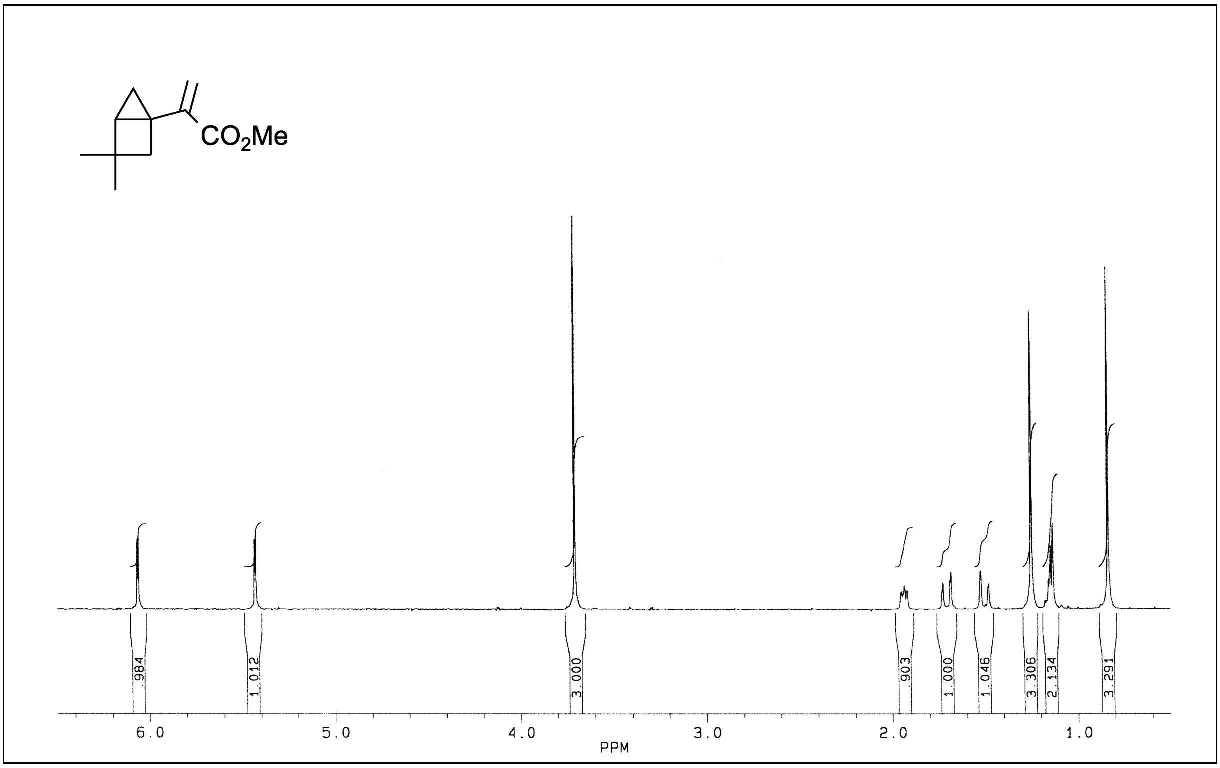
Ethyl 2-[1,1-bis(ethoxycarbonyl)cycloprop-2-yl]propenoate (**129**)



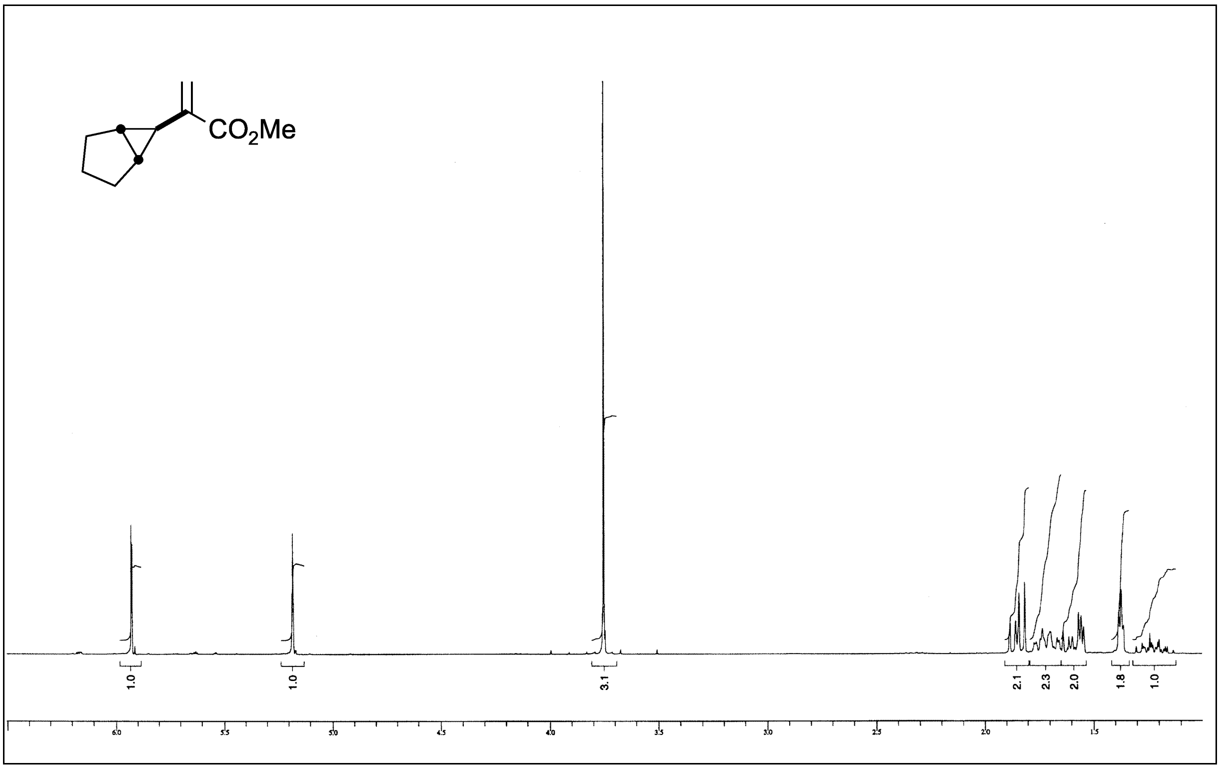
Methyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**130**)



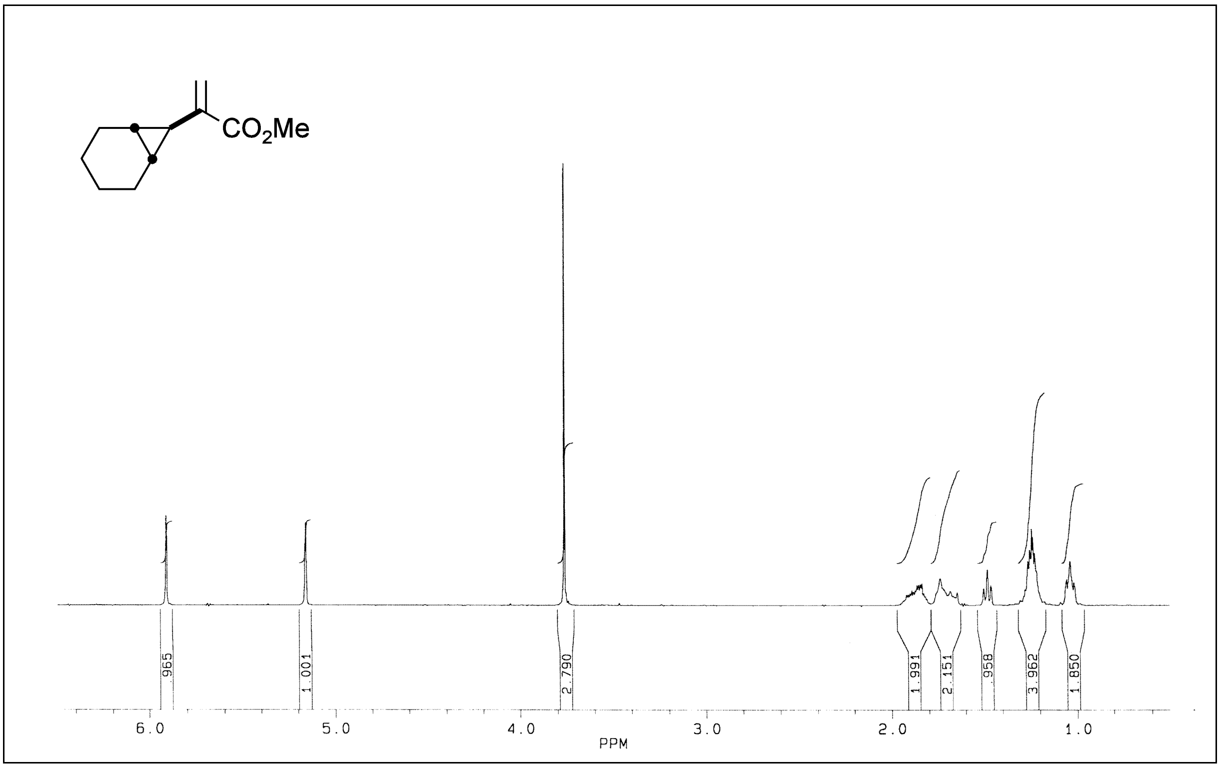
Methyl 2-(bicyclo[4.1.0]hept-1-yl)propenoate (**131**)



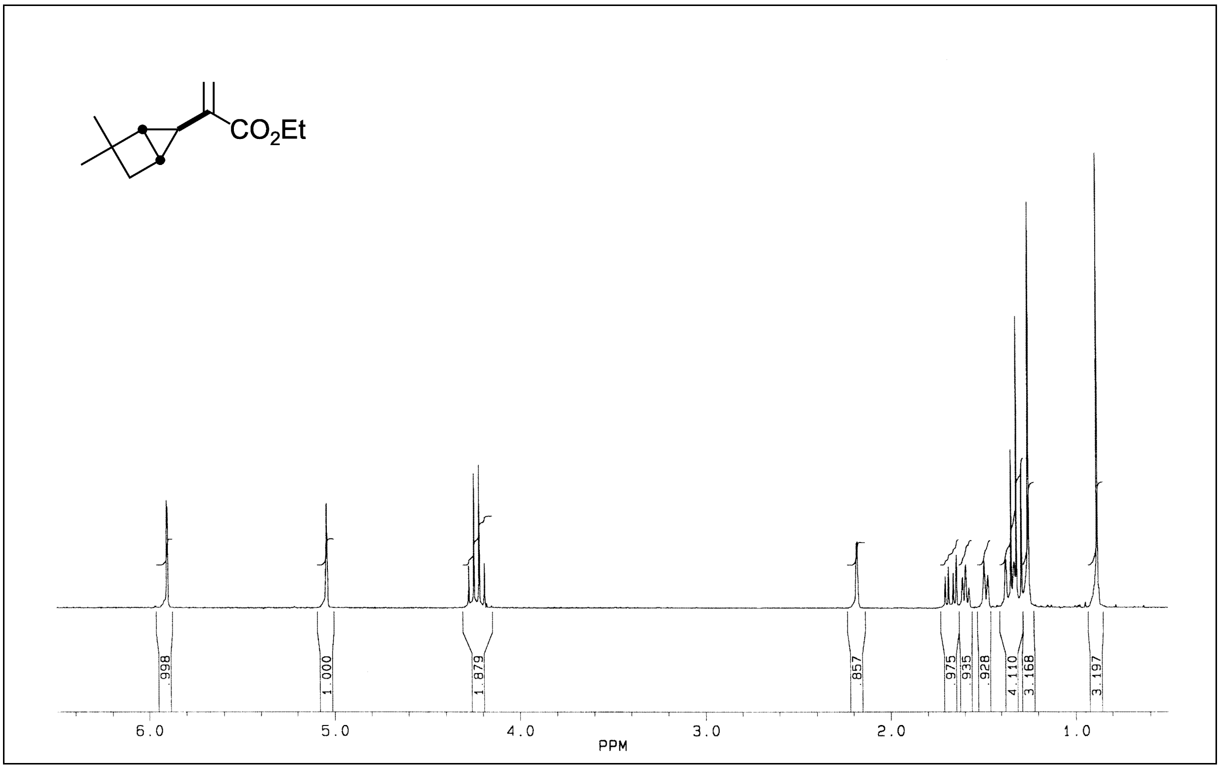
Methyl 2-(3,3-dimethylbicyclo[2.1.0]pent-1-yl)propenoate (**132**)



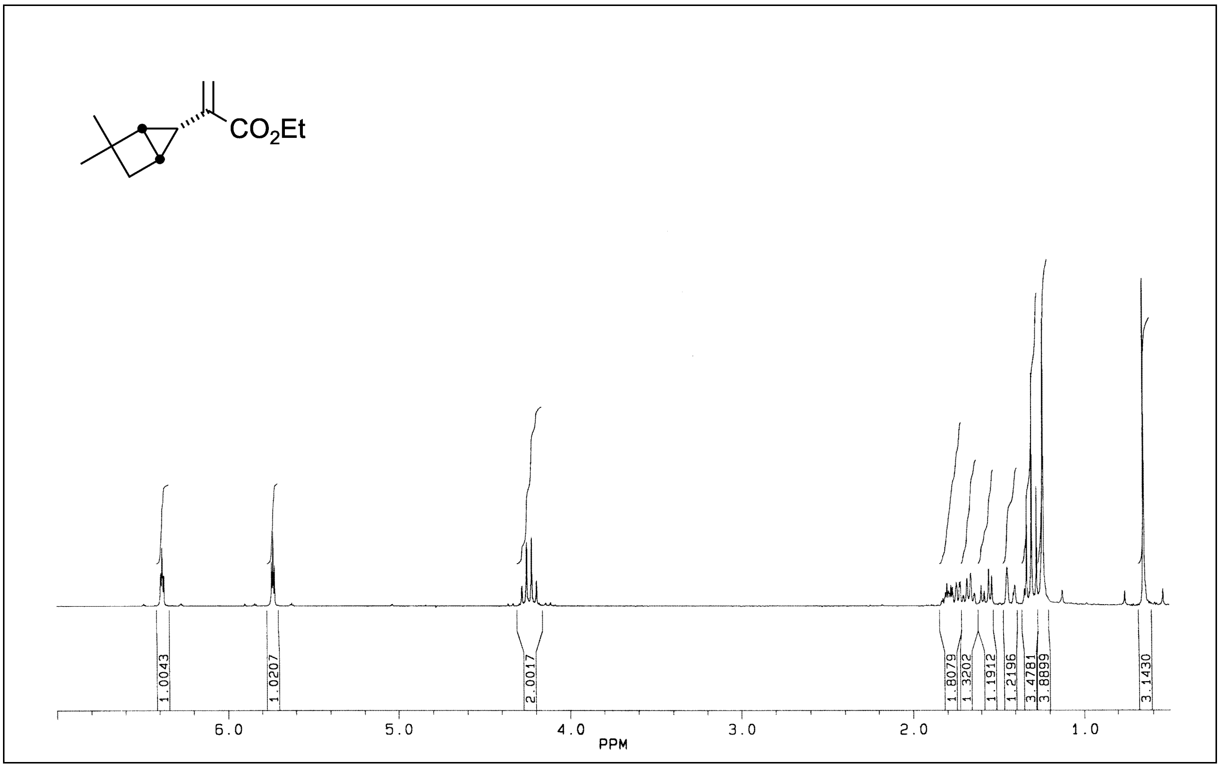
Methyl *exo*-2-(bicyclo[3.1.0]hex-6-yl)propenoate (**133**)



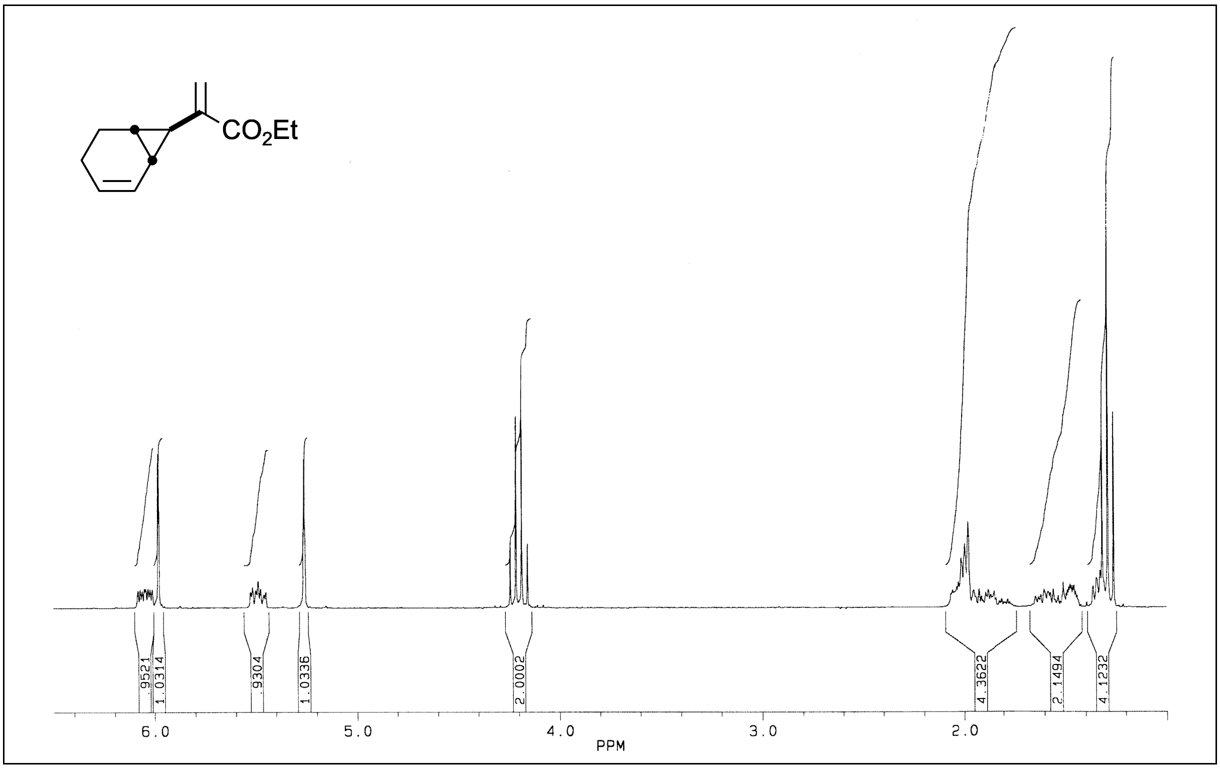
Methyl *exo*-2-(bicyclo[4.1.0]hept-7-yl)propenoate (**135**)



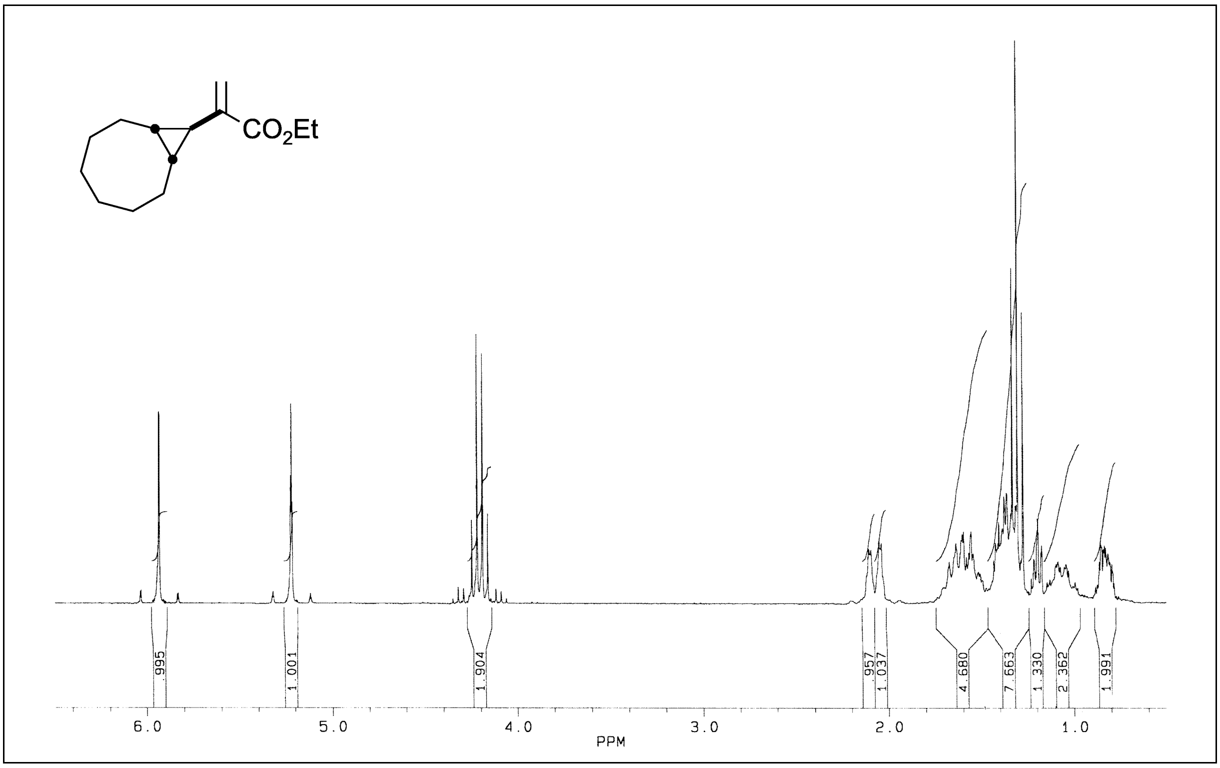
Ethyl *exo*-2-(2,2-dimethylbicyclo[2.1.0]pent-5-yl)propenoate (***exo*-137**)



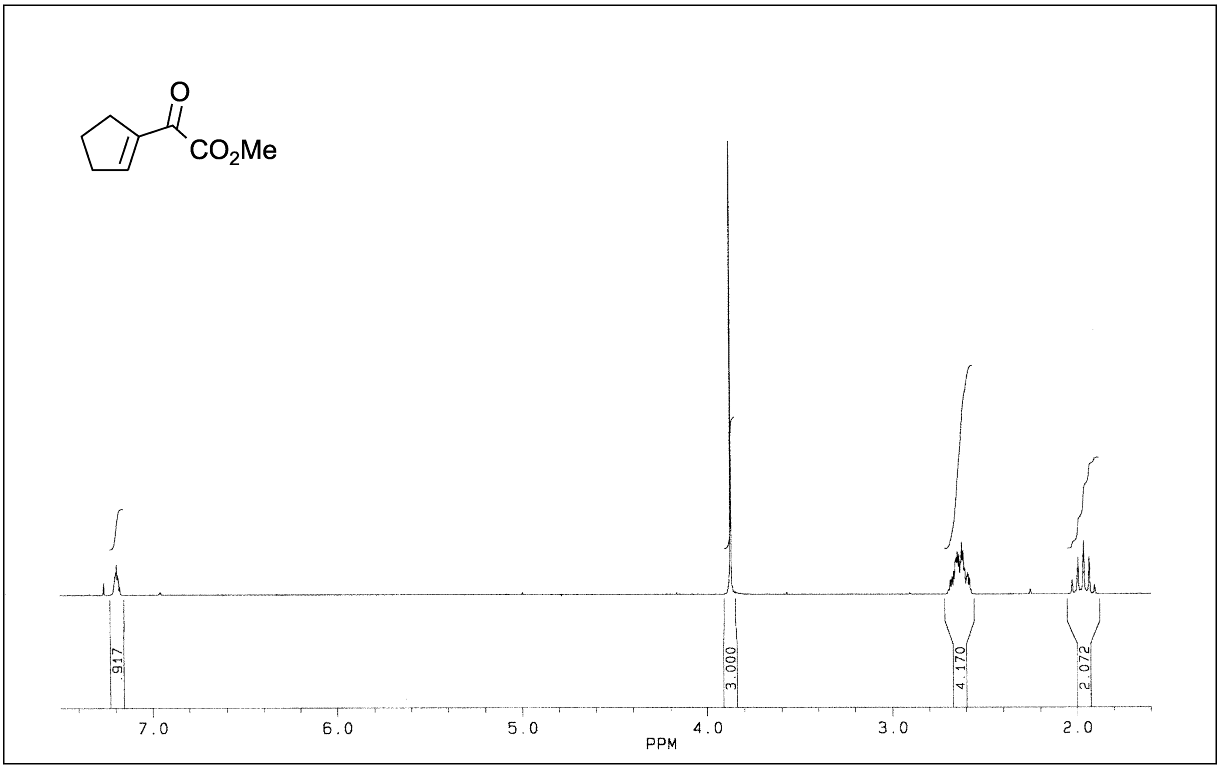
Ethyl *endo*-2-(2,2-dimethylbicyclo[2.1.0]pent-5-yl)propenoate (***endo*-137**)



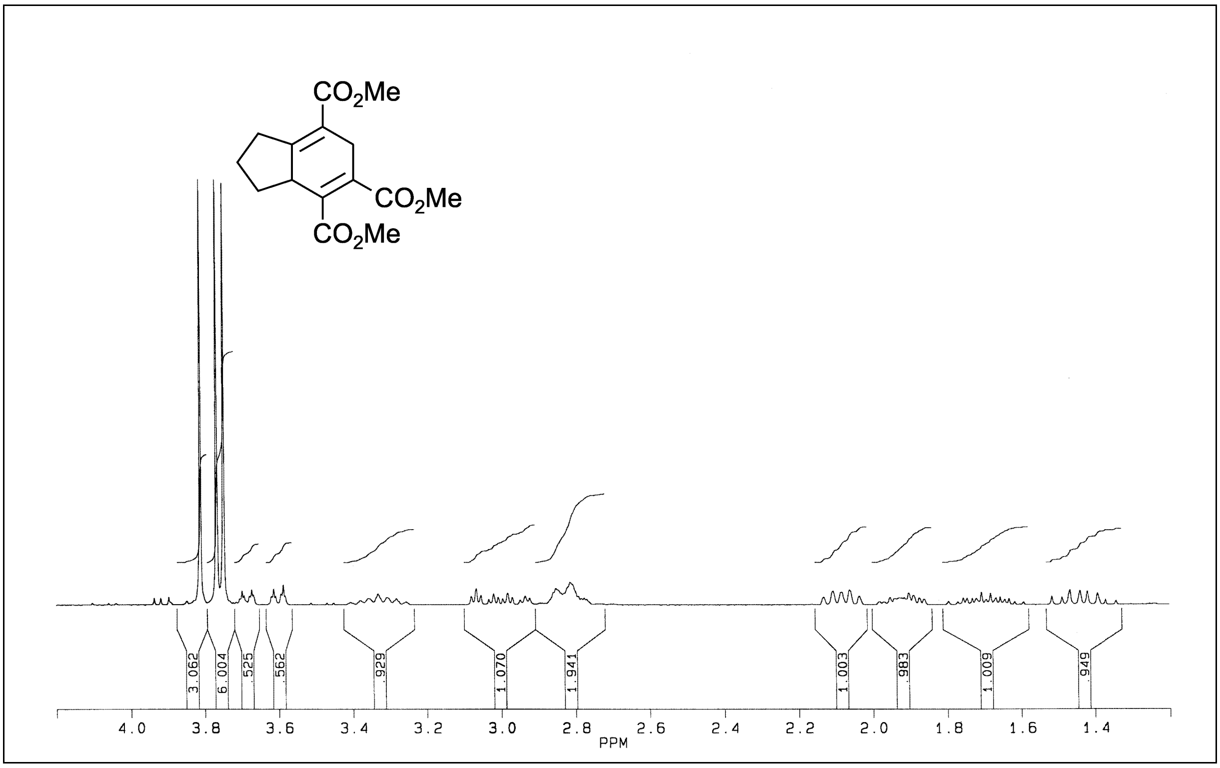
Ethyl *exo*-2-(bicyclo[4.1.0]hept-2-en-7-yl)propenoate (**138**)



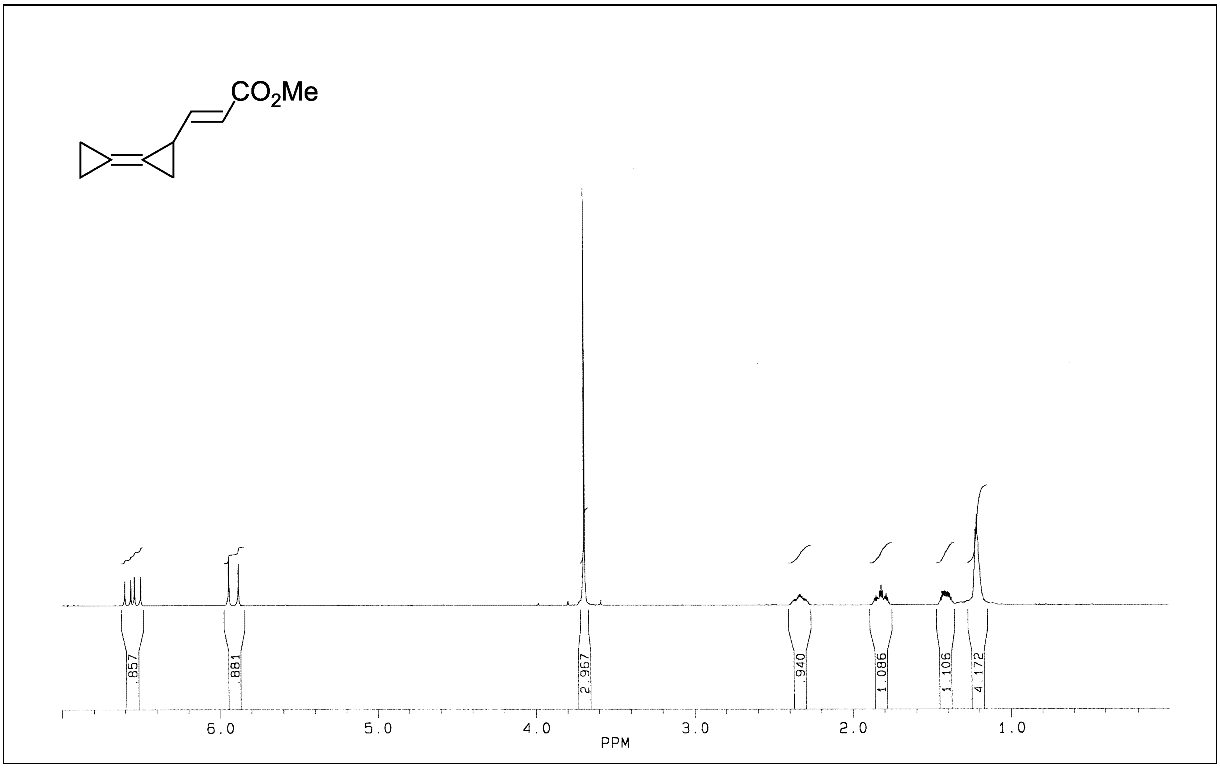
Ethyl *exo*-2-(bicyclo[6.1.0]non-9-yl)propenoate (**139**)



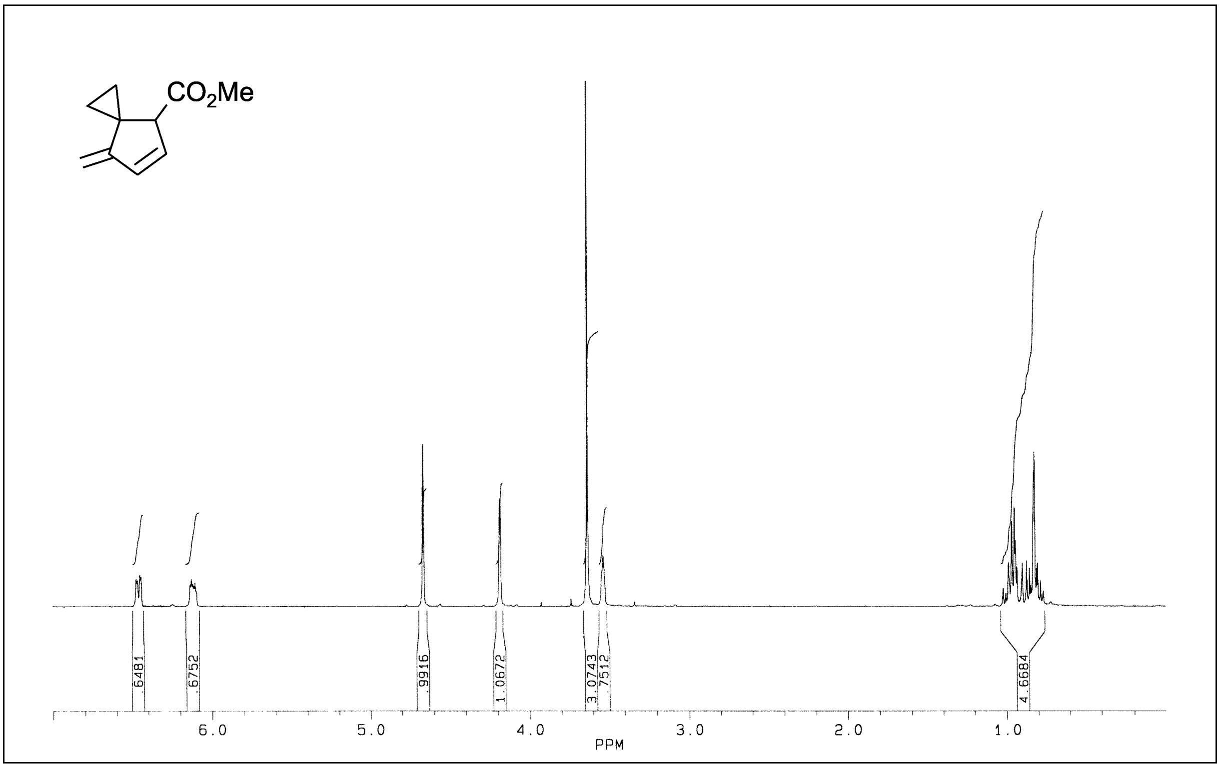
Methyl 2-(cyclopenten-1-yl)oxoacetate (**143**)



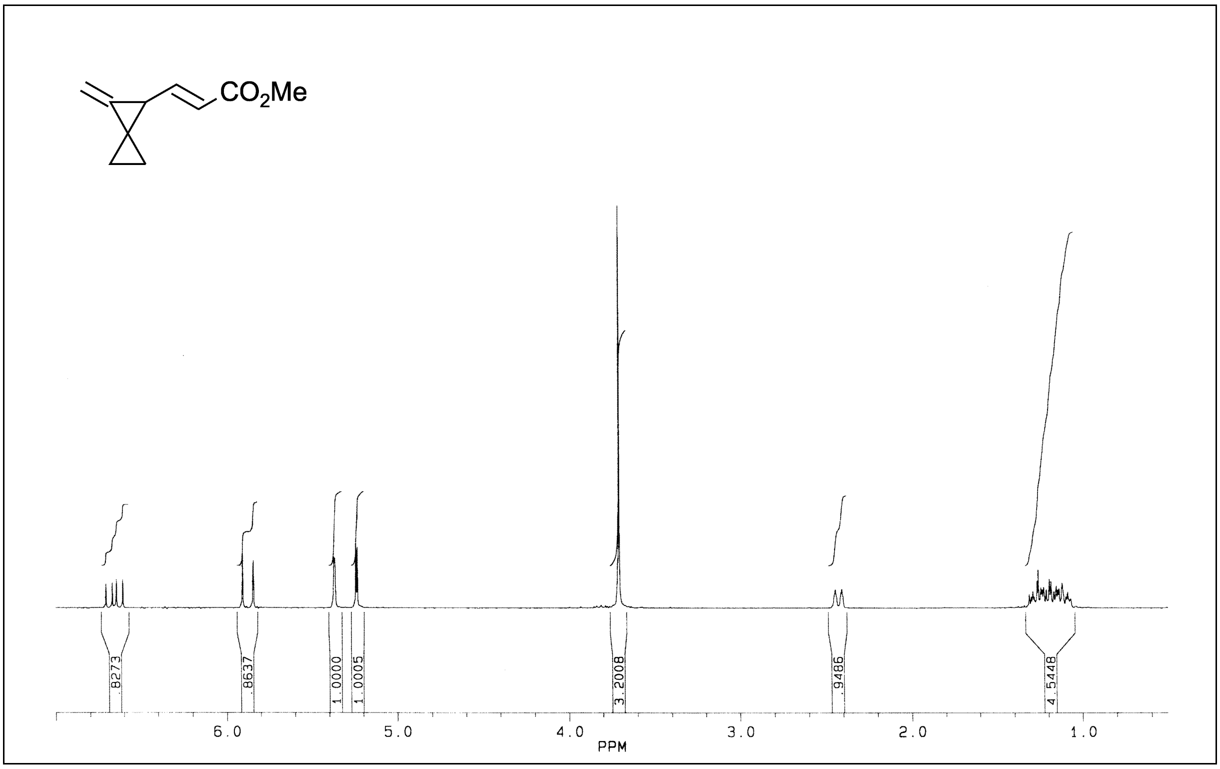
Trimethyl 2,3,3a,6-tetrahydro-1*H*-indene-4,5,7-tricarboxylate (**145**)



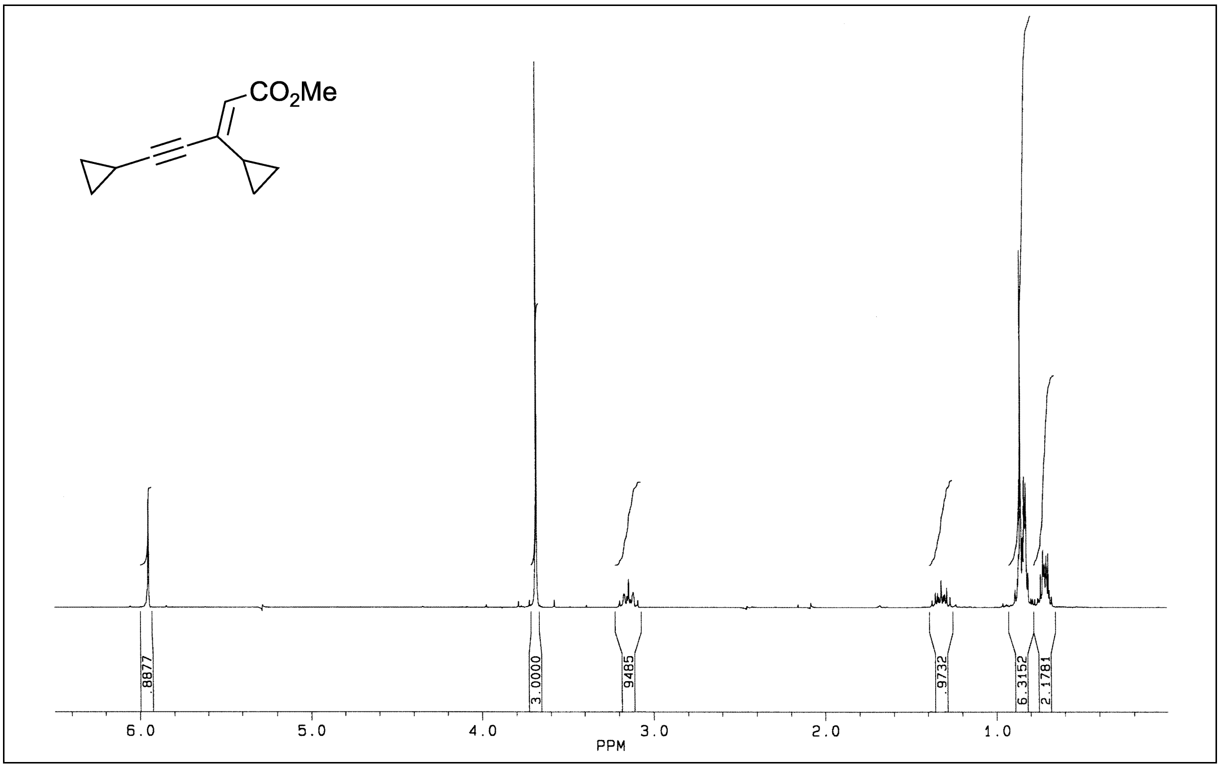
Methyl (*E*)-3-bicyclopropylidenylpropenoate (**146**)



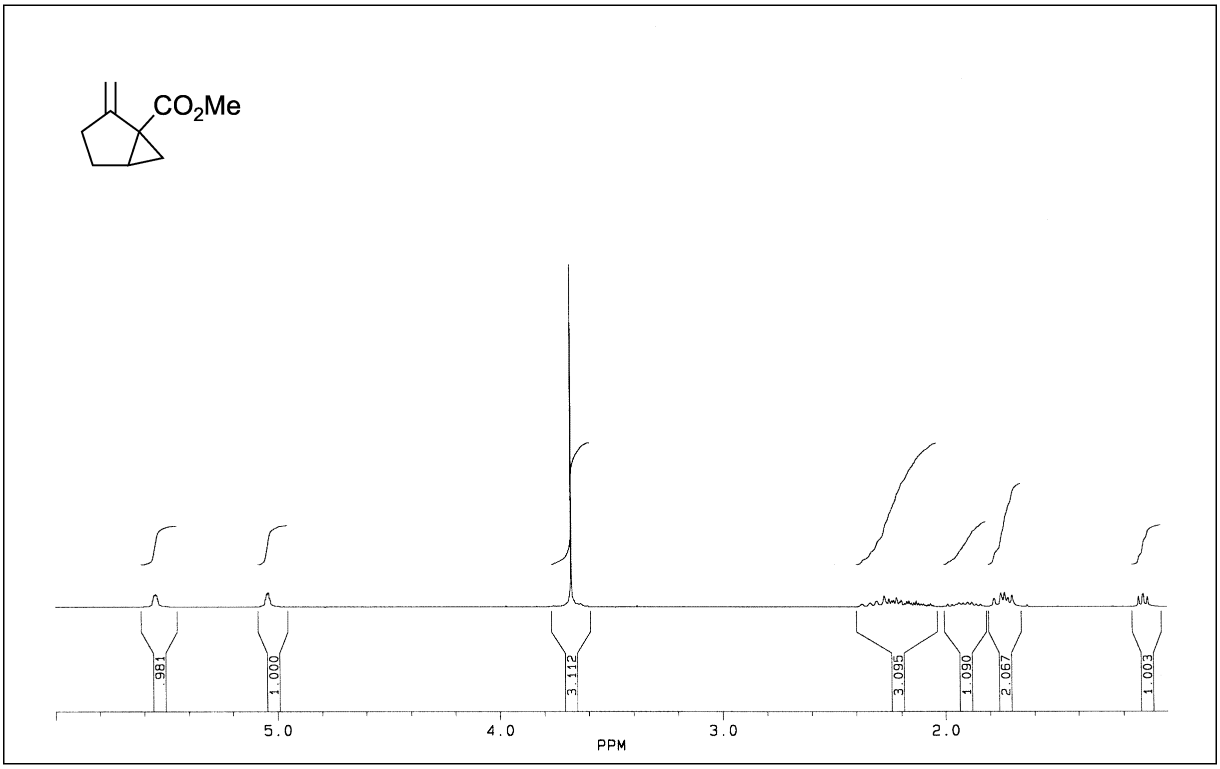
Methyl 7-methylenespiro[2.4]hept-5-ene-4-carboxylate (**147**)



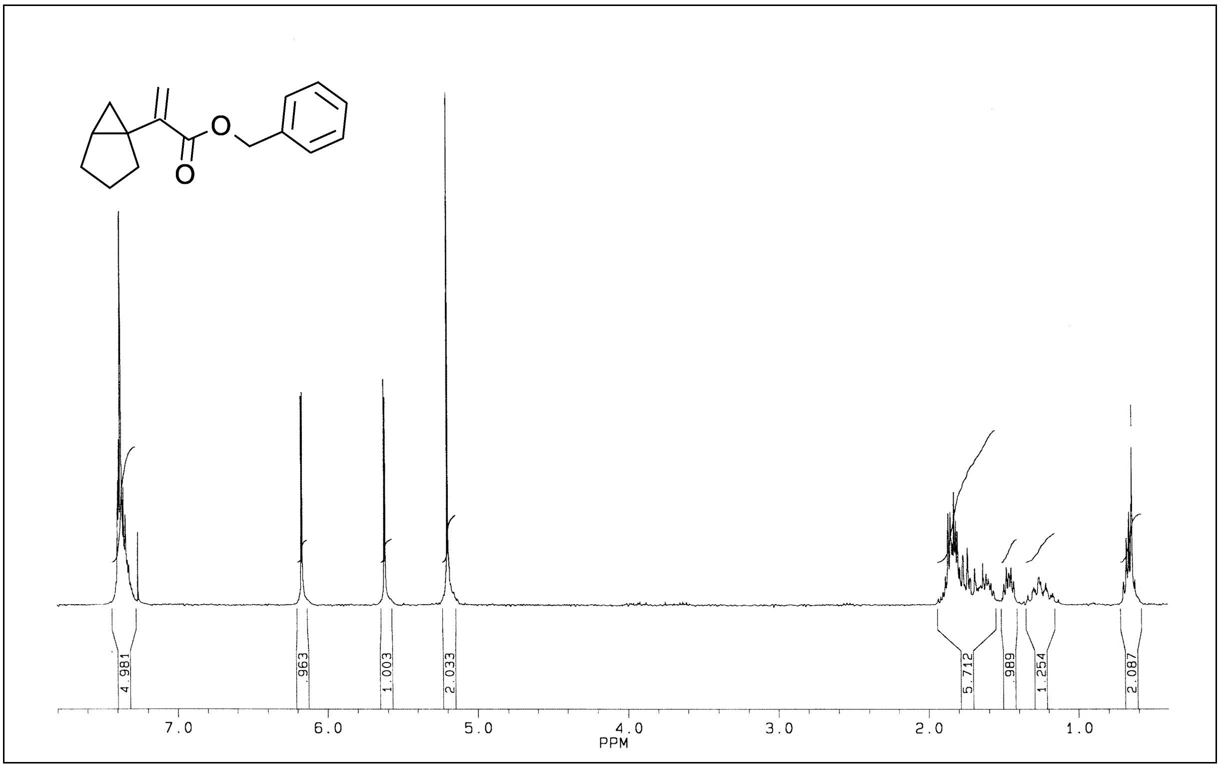
Methyl (*E*)-3-(2-methylenespiro[2.2]pent-1-yl)propenoate (**148**)



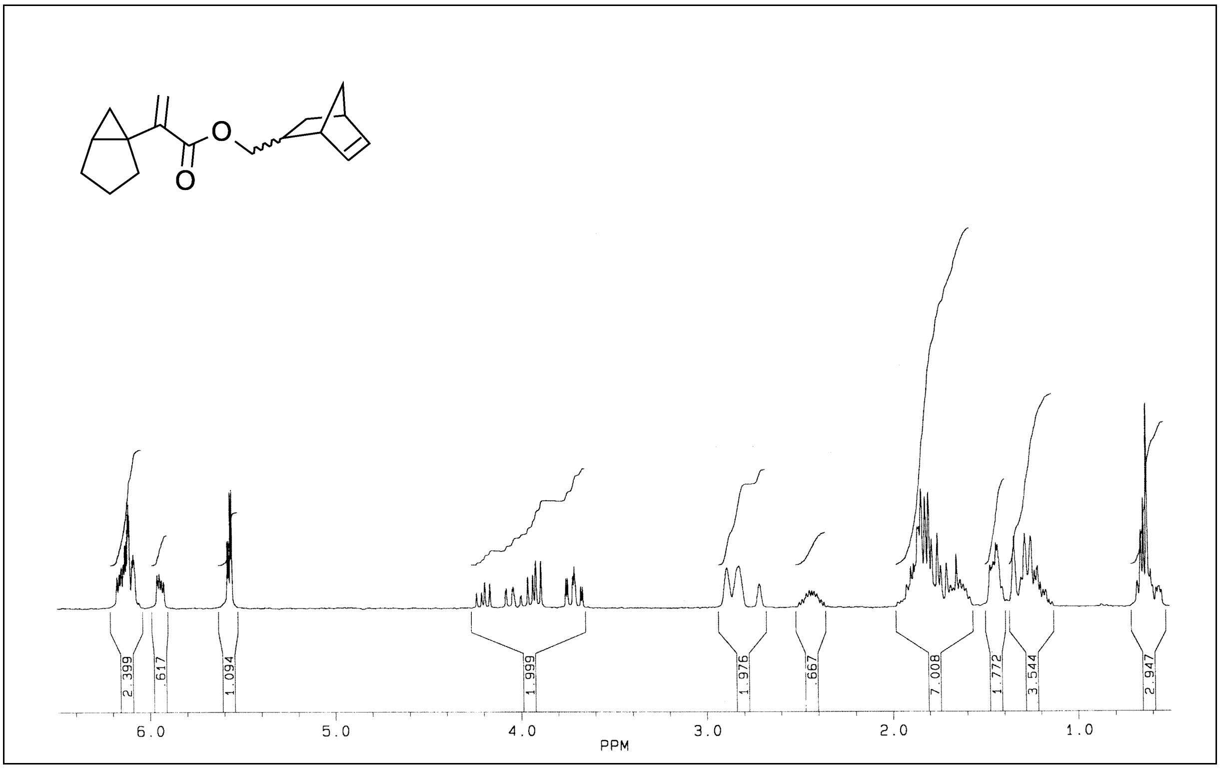
Methyl (2*E*)-3,5-dicyclopropylpent-2-en-4-ynoate (**152**)



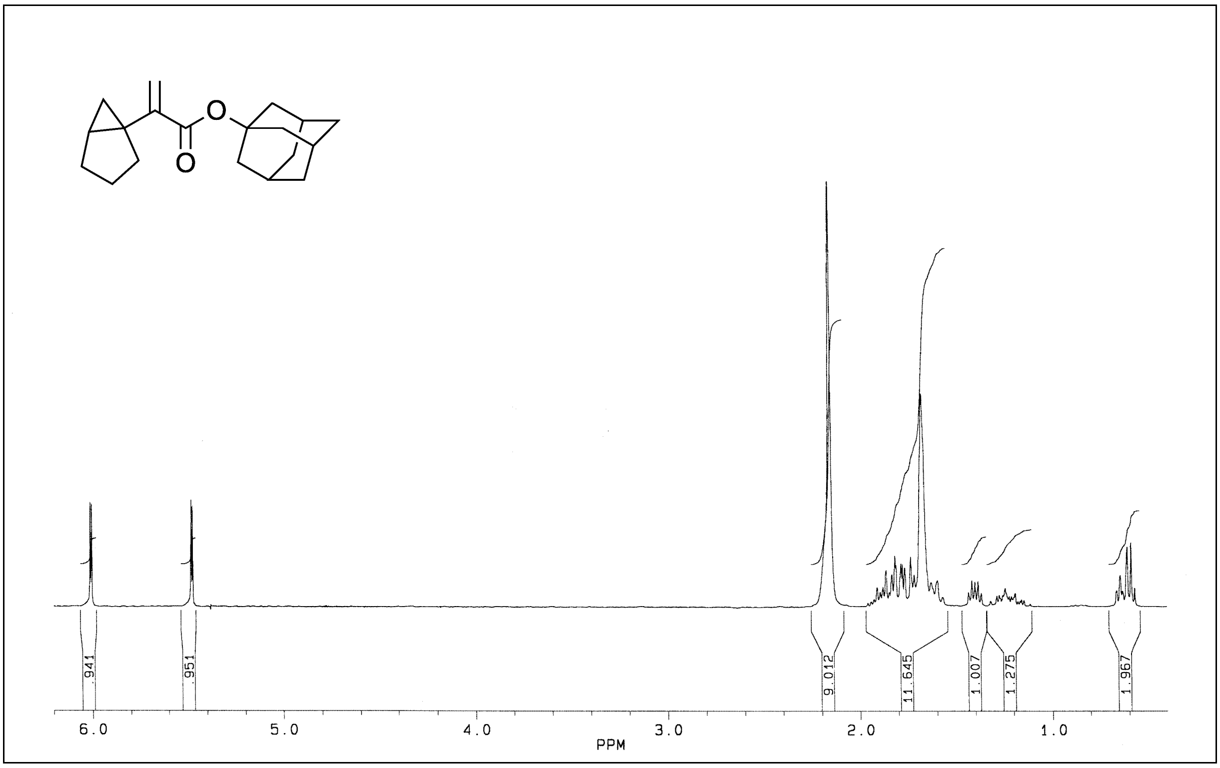
Methyl 2-methylenebicyclo[3.1.0]hexane-1-carboxylate (**156**)



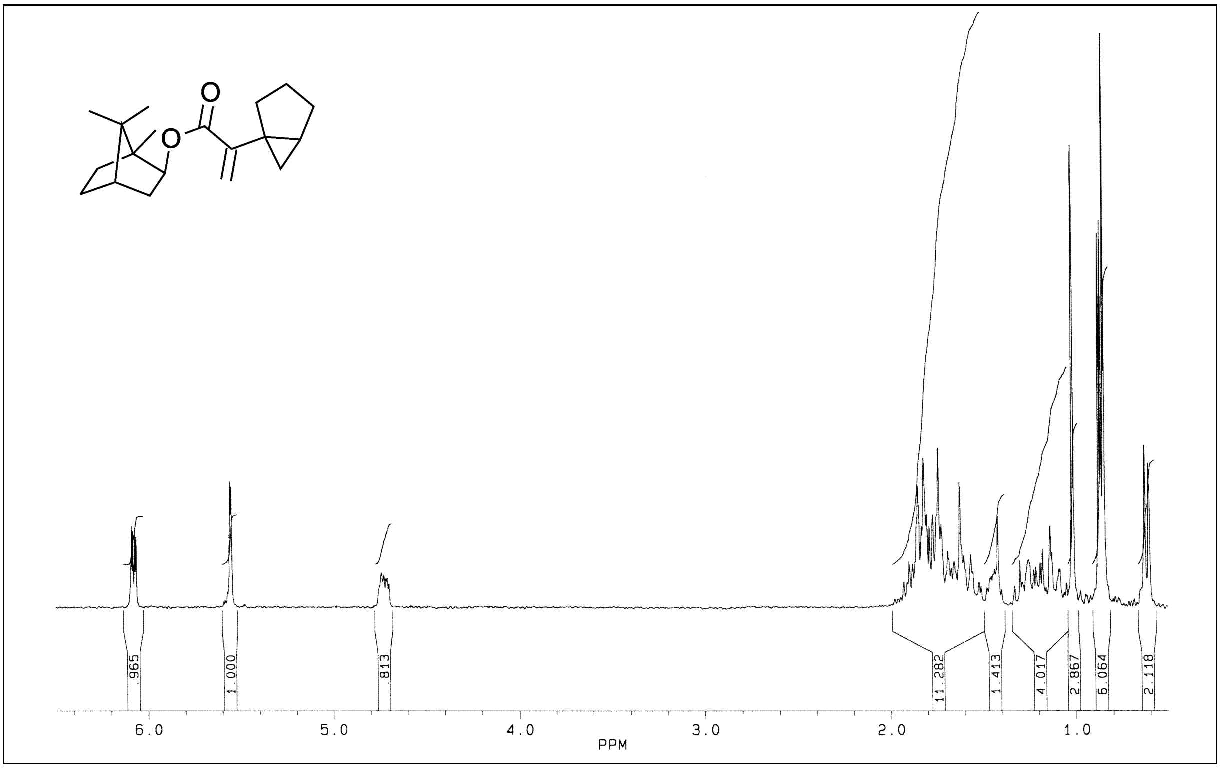
Benzyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**168**)



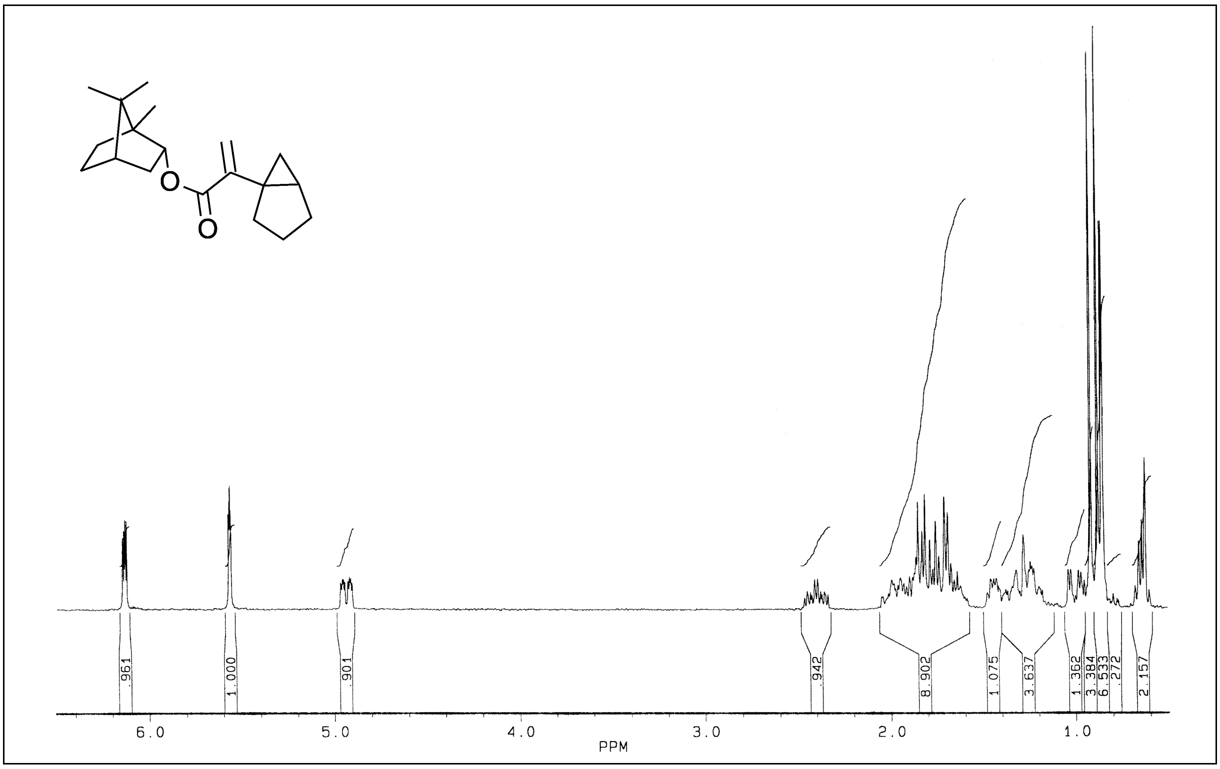
(Bicyclo[2.2.1]hept-5-en-2-yl)methyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**169**)



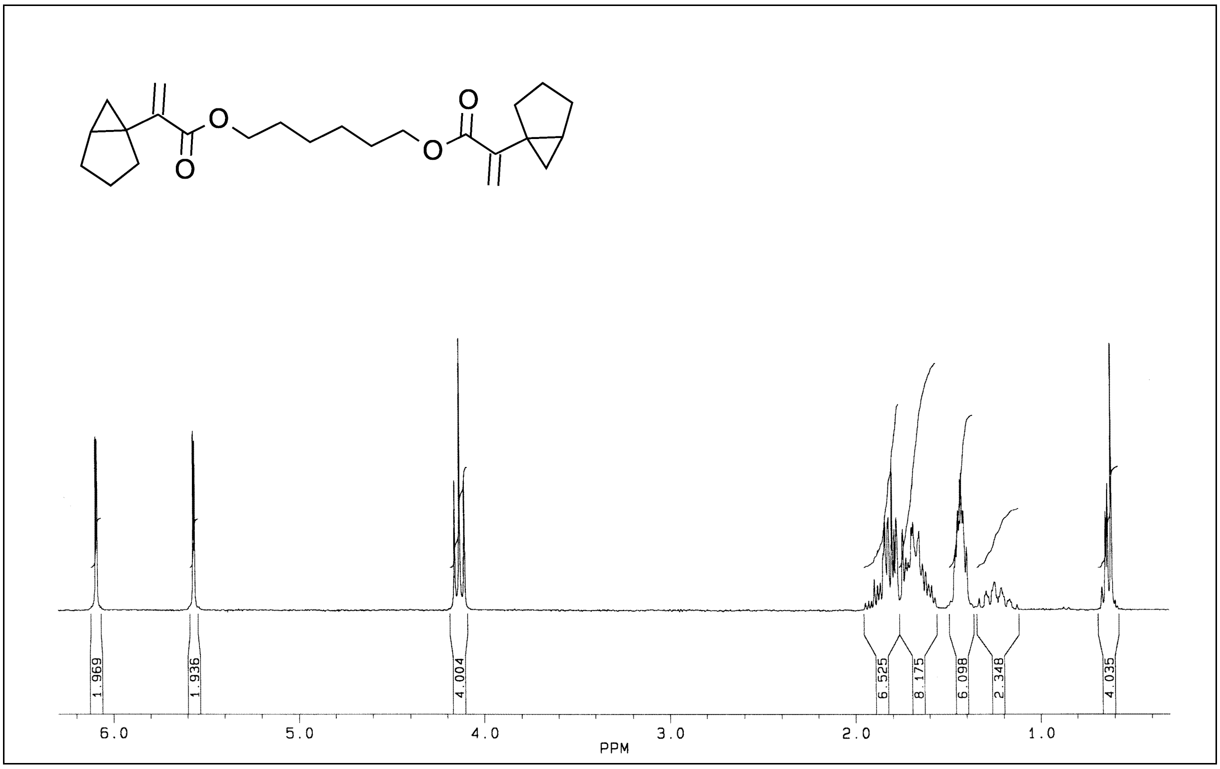
Adamant-1-yl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**170**)



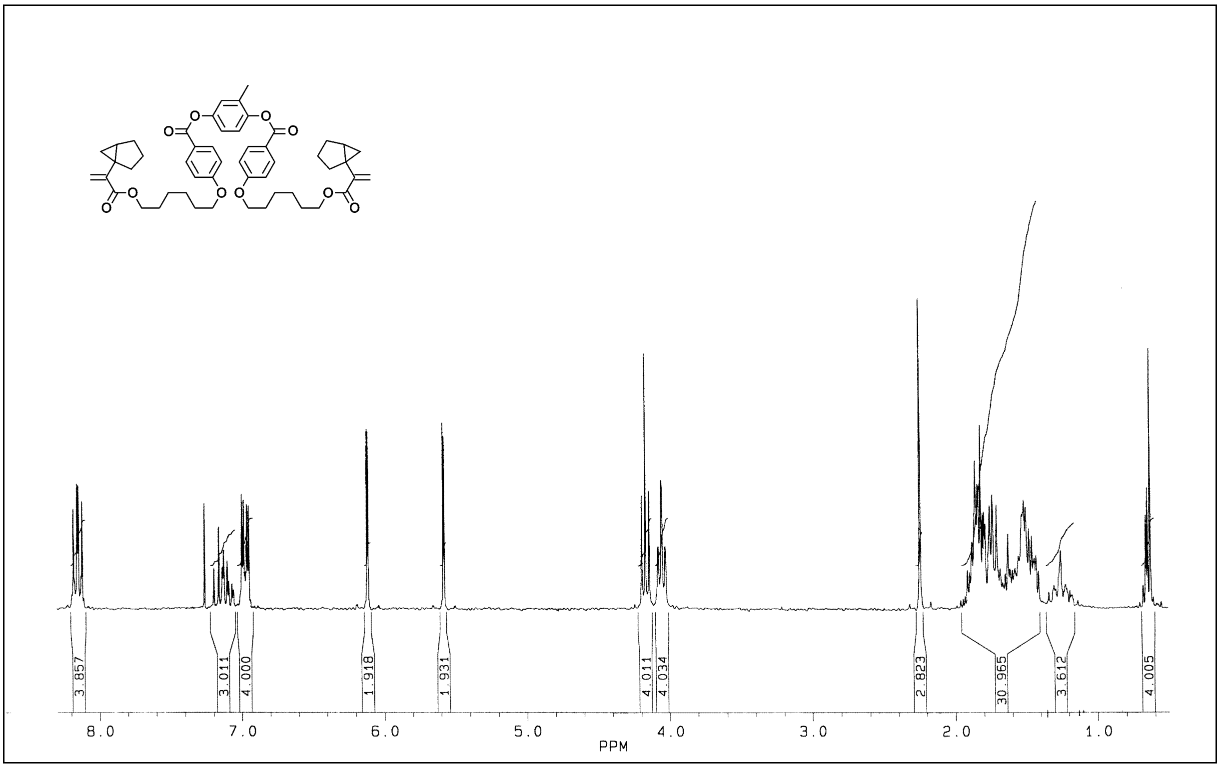
(*1R,S,2'S*)-*exo*-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**171**)



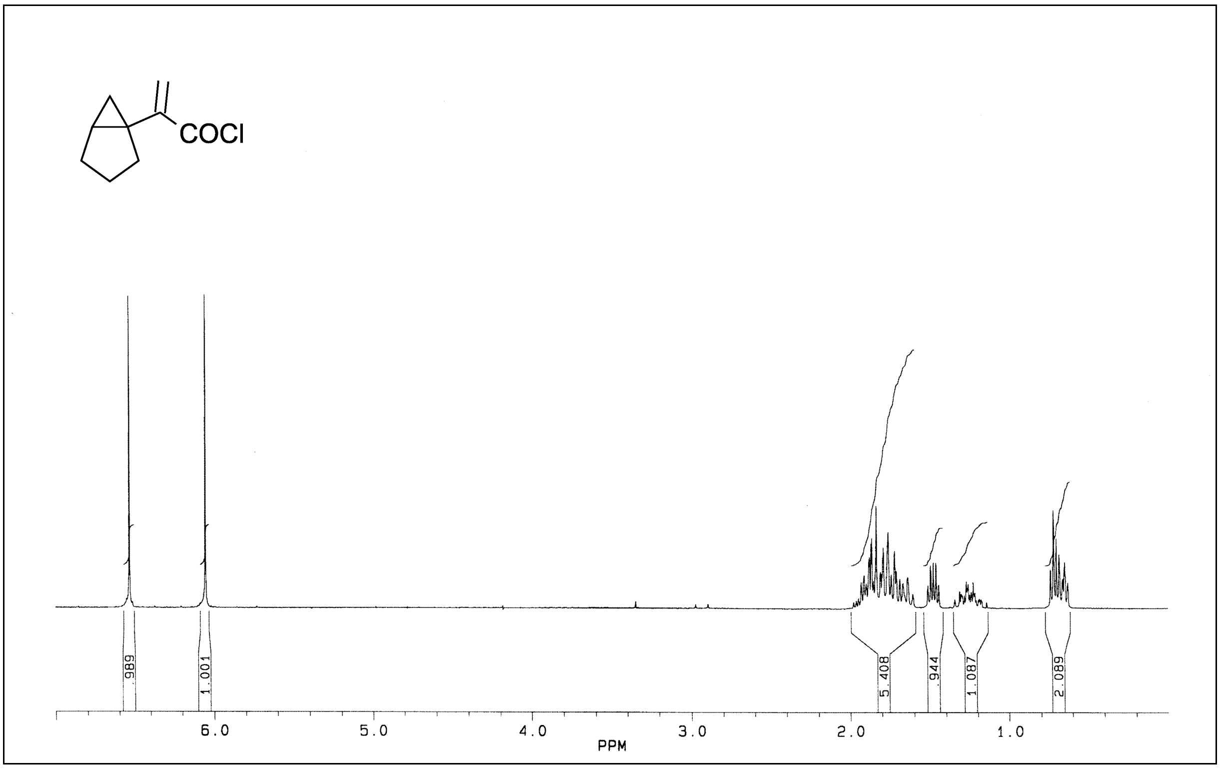
(*1R,S,2'R*)-*endo*-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl 2-(bicyclo[3.1.0]hex-1-yl)propenoate(**172**)



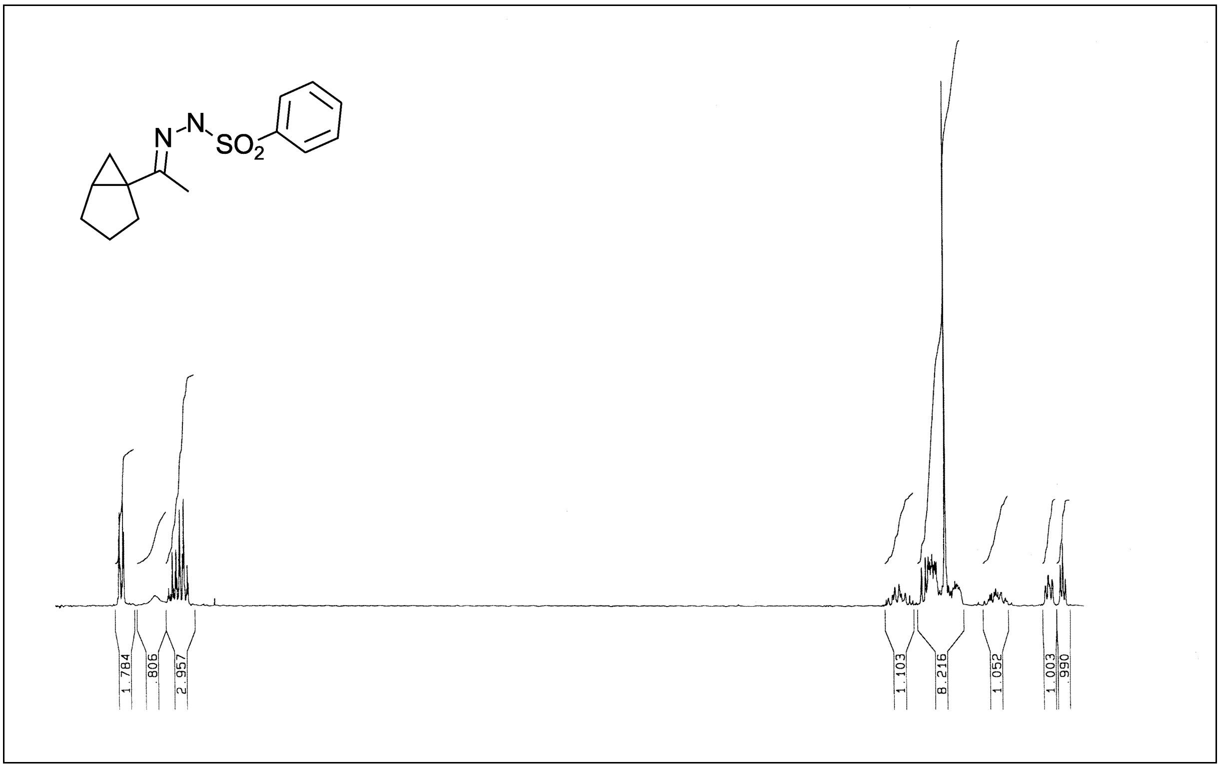
1,6-bis[2-(Bicyclo[3.1.0]hex-1-yl)propenoyloxy]hexane (**174**)



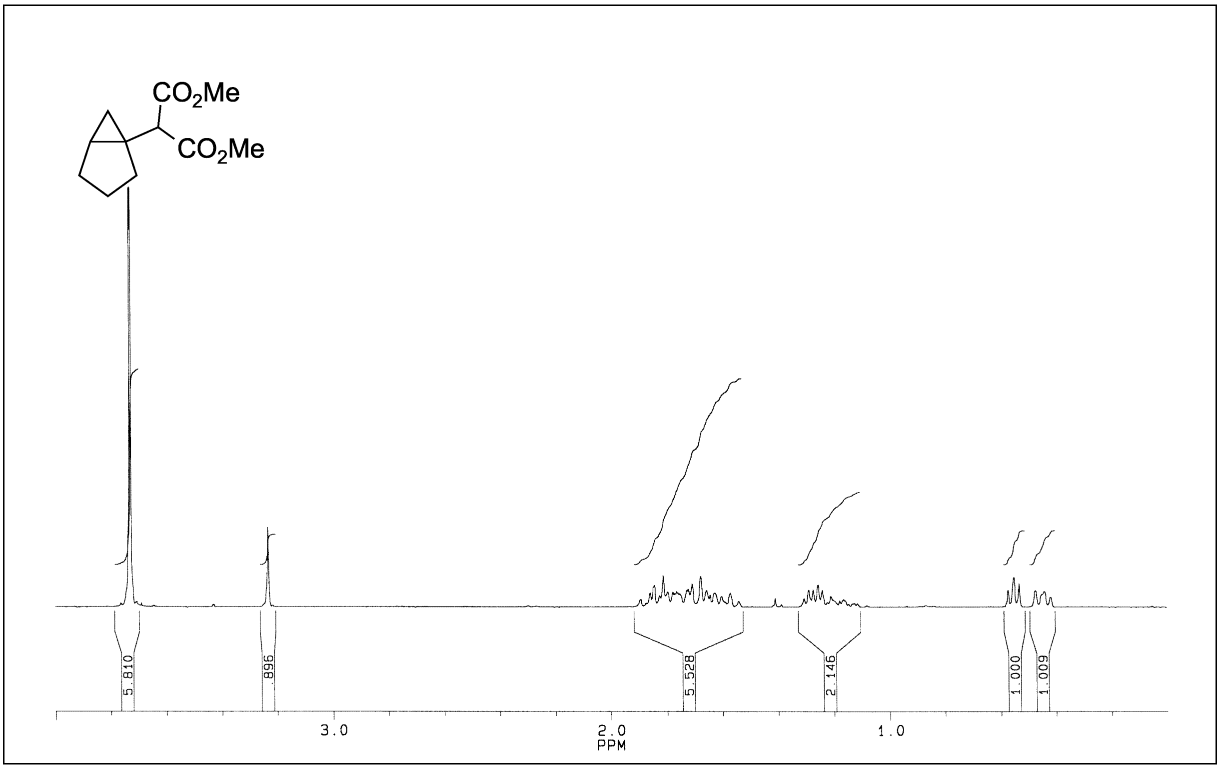
1,4-di-{4-[6-(2-(Bicyclo[3.1.0]hex-1-yl)propenoyloxy)hexyloxy]phenylcarbonyloxy}-2-methylbenzene (**175**)



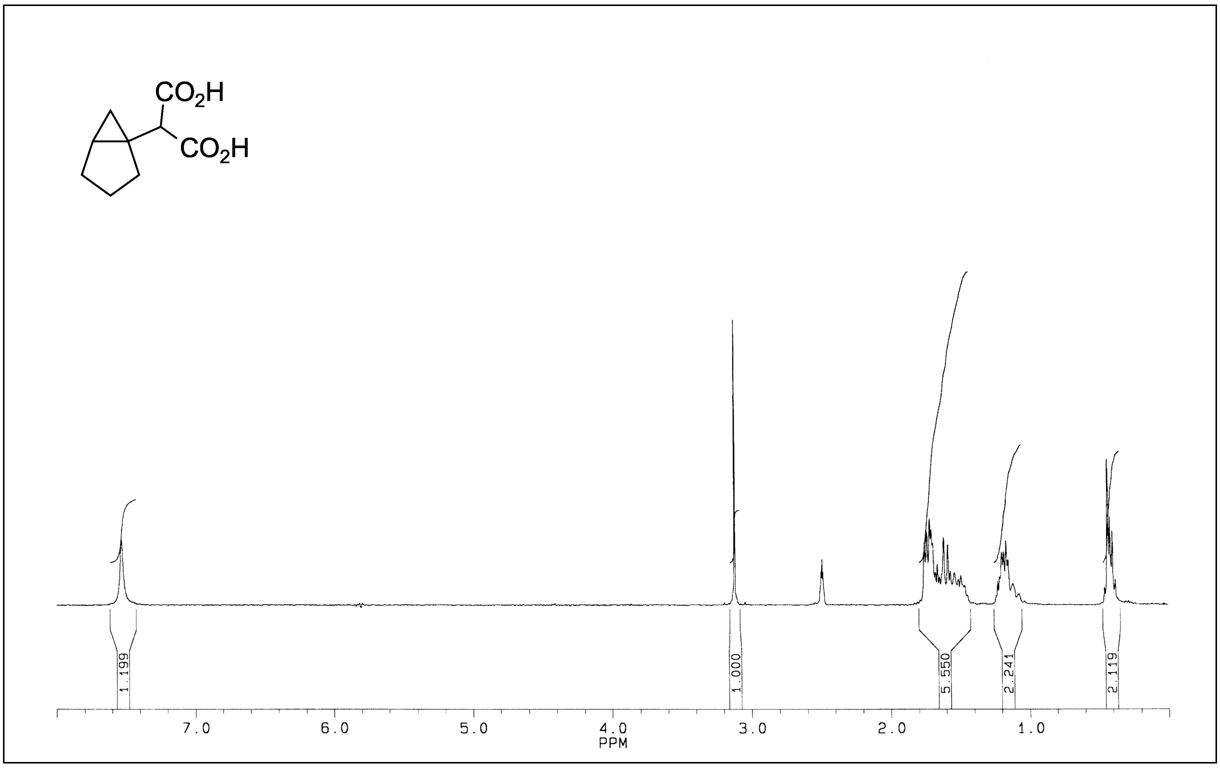
2-(Bicyclo[3.1.0]hex-1-yl)propenoyl chloride (**176**)



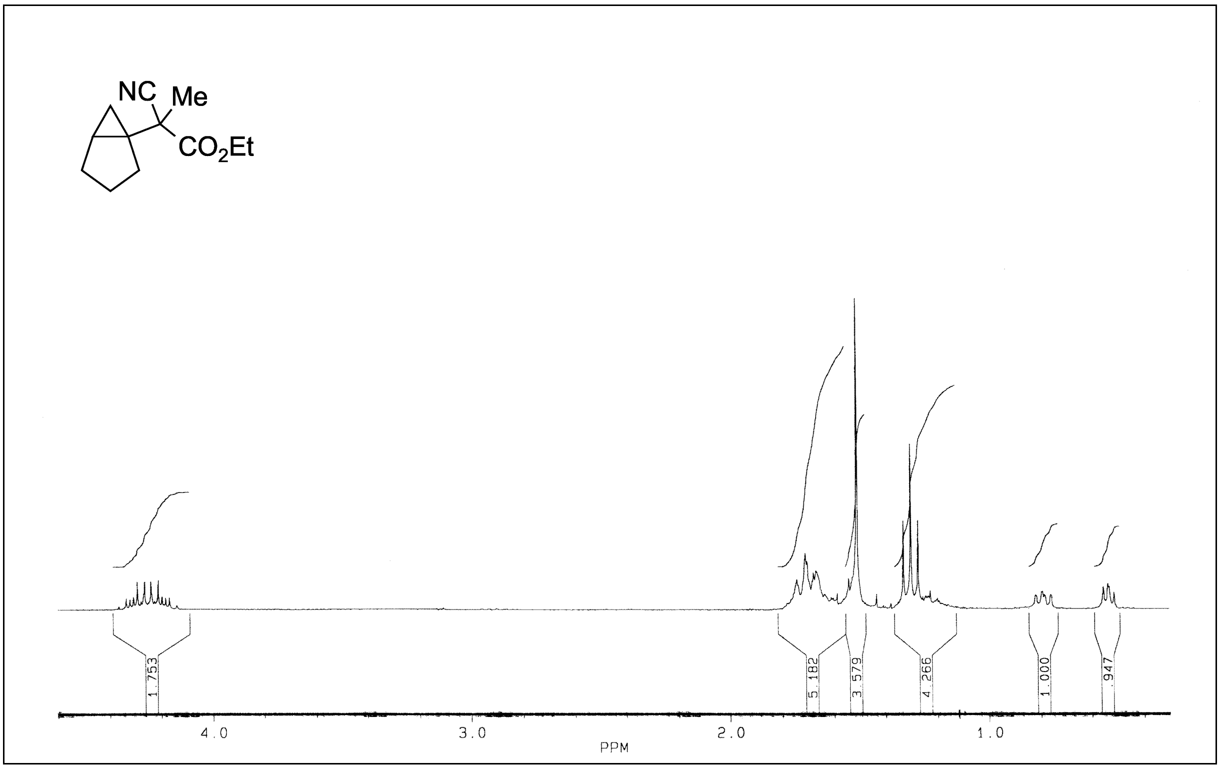
N'-[(*1E*)-1-Bicyclo[3.1.0]hex-1-ylethylidene]benzenesulfonohydrazide (**183**)



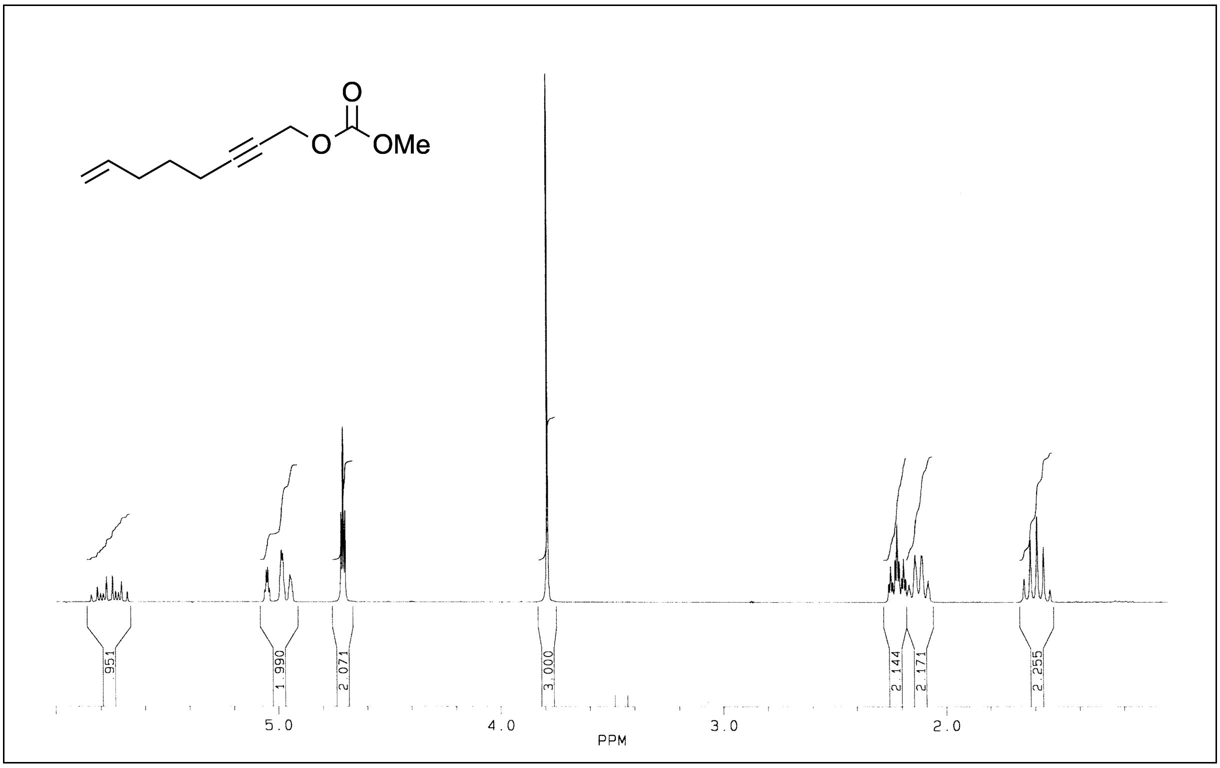
Dimethyl 2-(bicyclo[3.1.0]hex-1-yl)malonate (**189**)



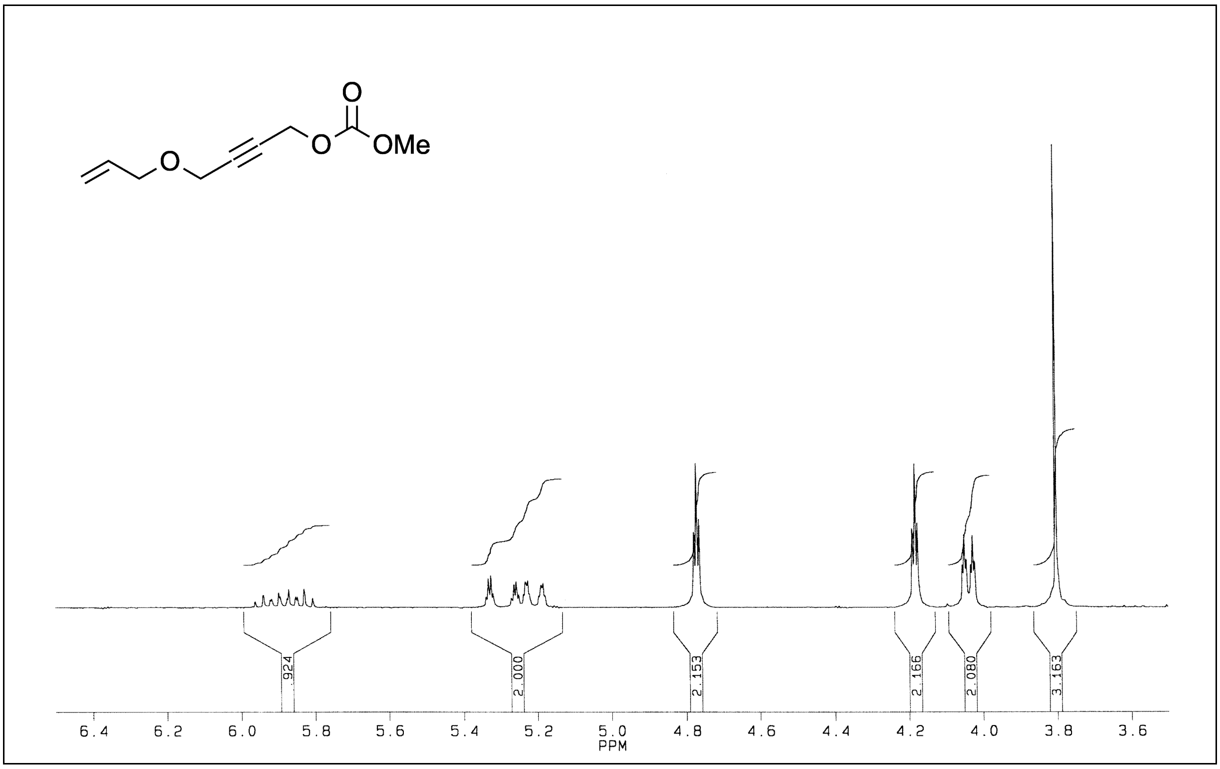
2-(Bicyclo[3.1.0]hex-1-yl)malonic acid (**191**)



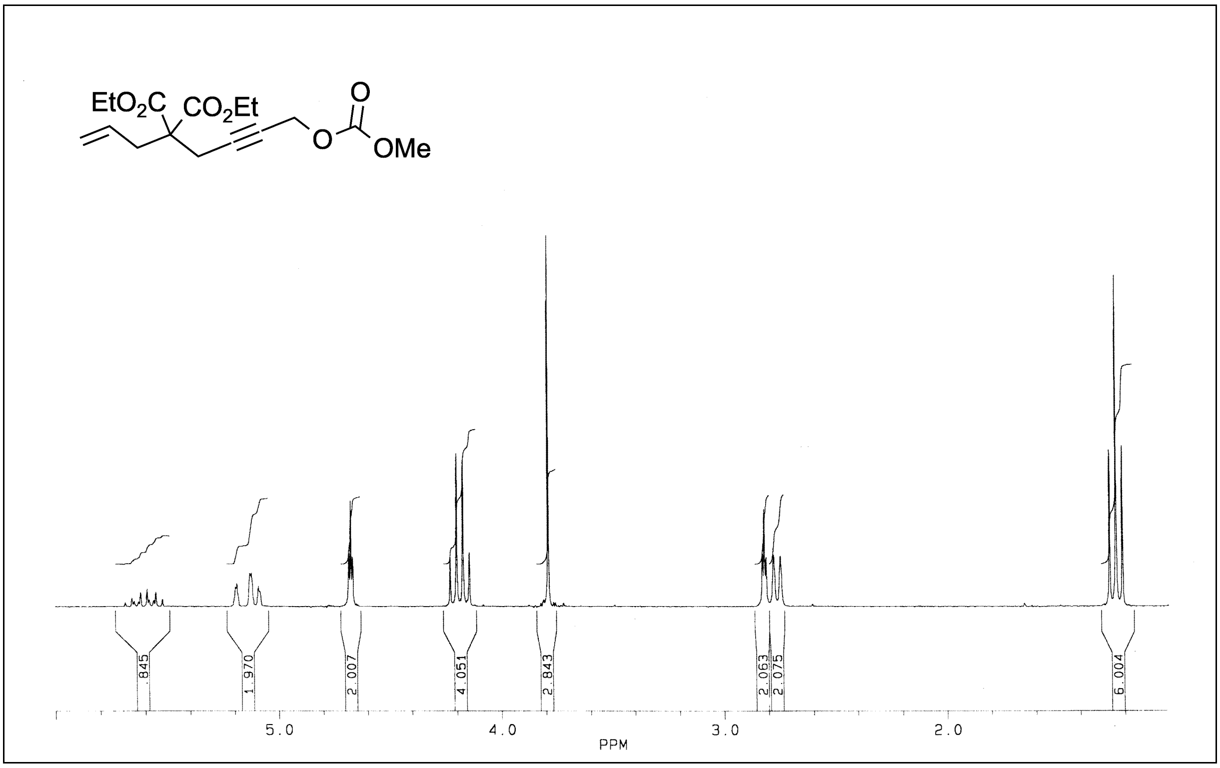
Ethyl 2-cyano-2-(bicyclo[3.1.0]hex-1-yl) propanoate (**195**), first diastereomer



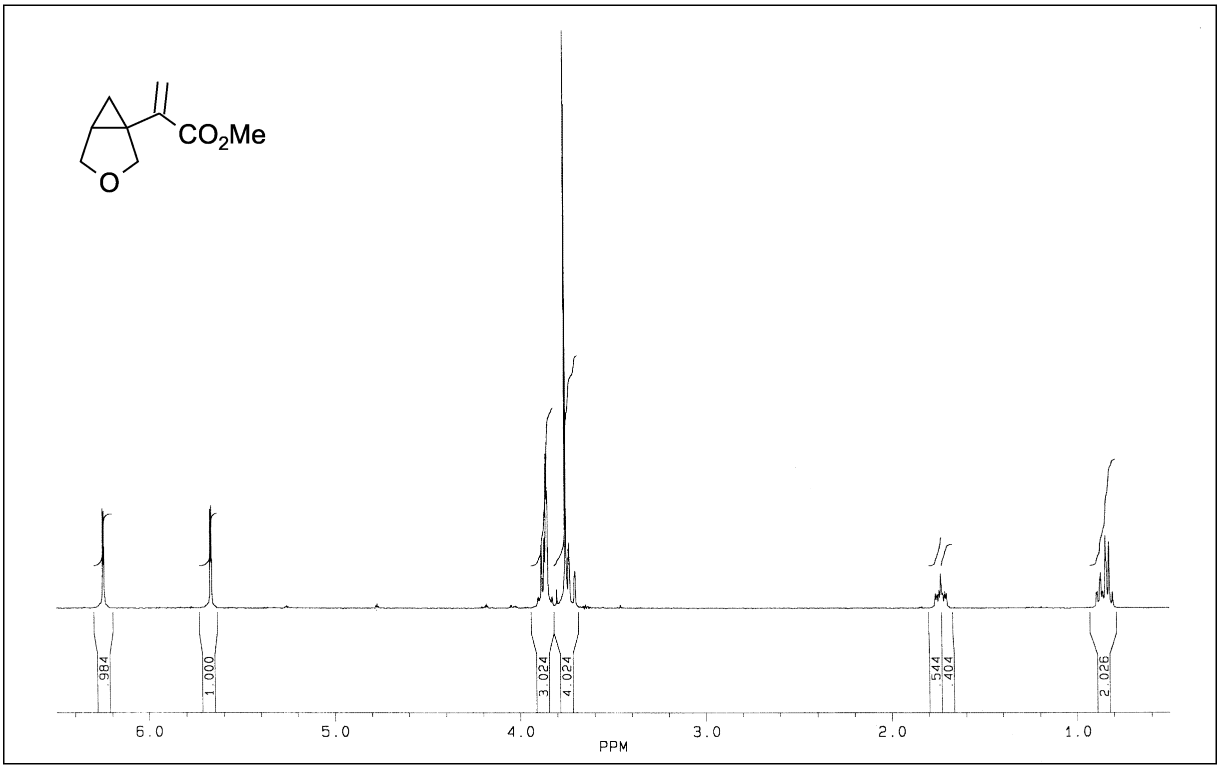
Methyl (oct-7-en-2-ynyl)carbonate (**196**)



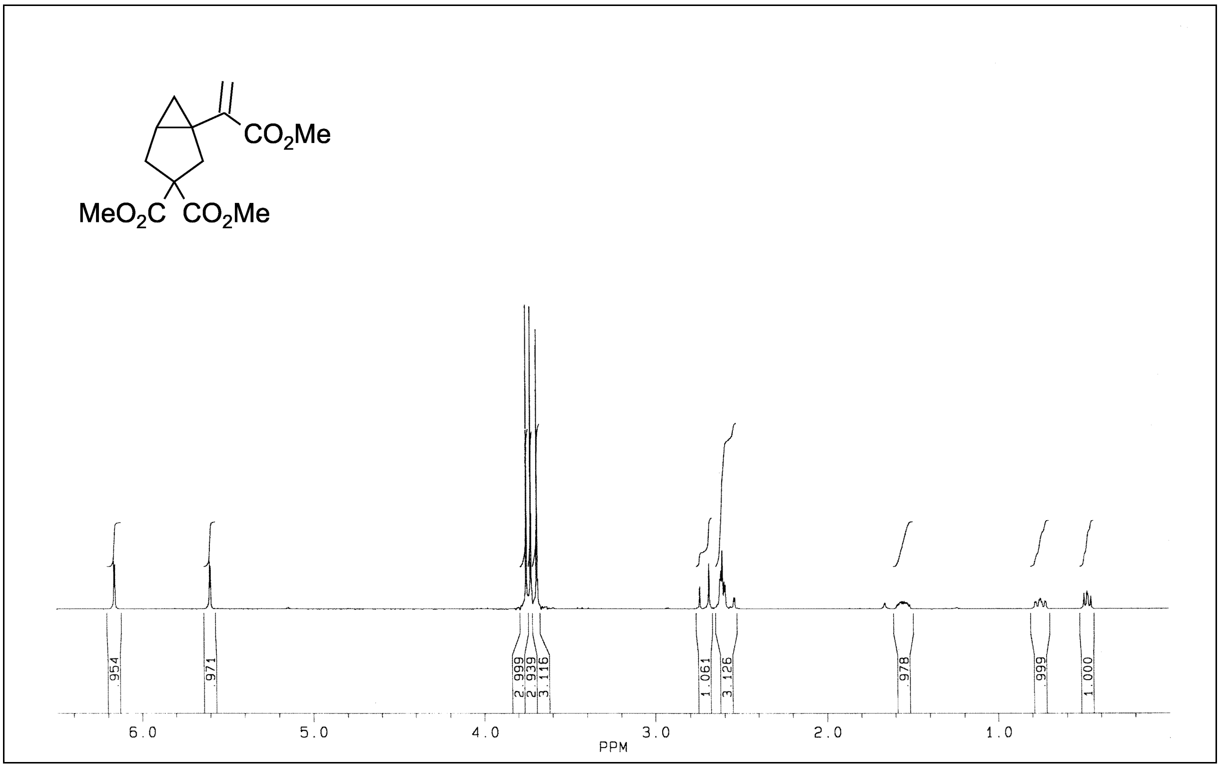
Methyl (5-oxa-oct-7-en-2-ynyl)carbonate (**201**)



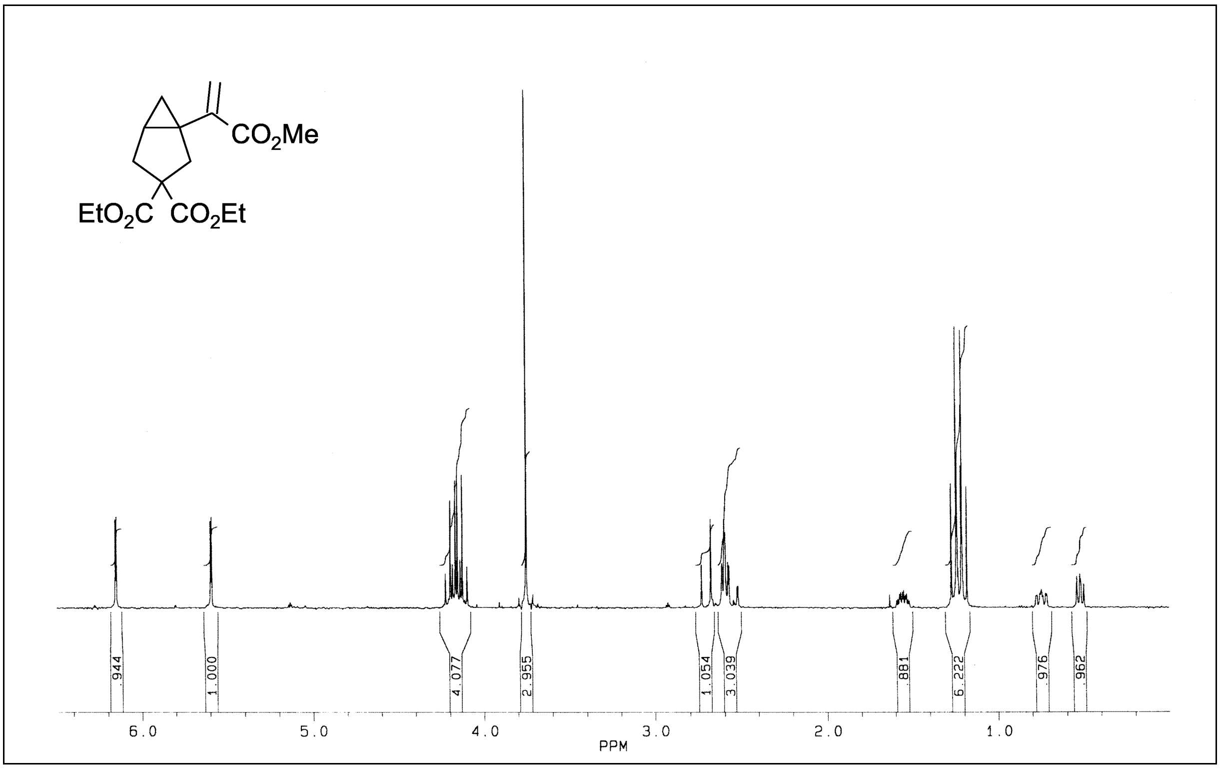
Methyl [5,5-bis(ethoxycarbonyl)oct-7-en-2-ynyl]carbonate (**206**)



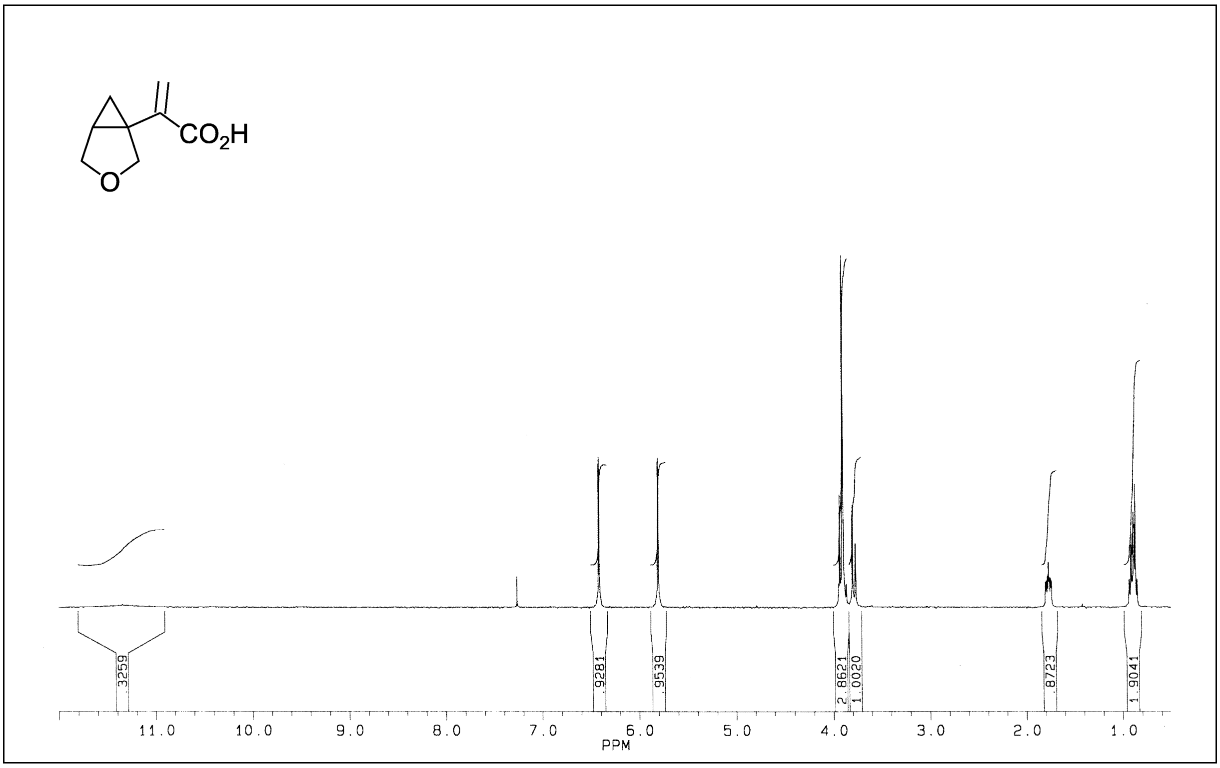
Methyl 2-(3-oxa-bicyclo[3.1.0]hex-1-yl)propenoate (**207**)



Methyl 2-{3,3-bis(methoxycarbonyl)bicyclo[3.1.0]hex-1-yl}propenoate (**208**)

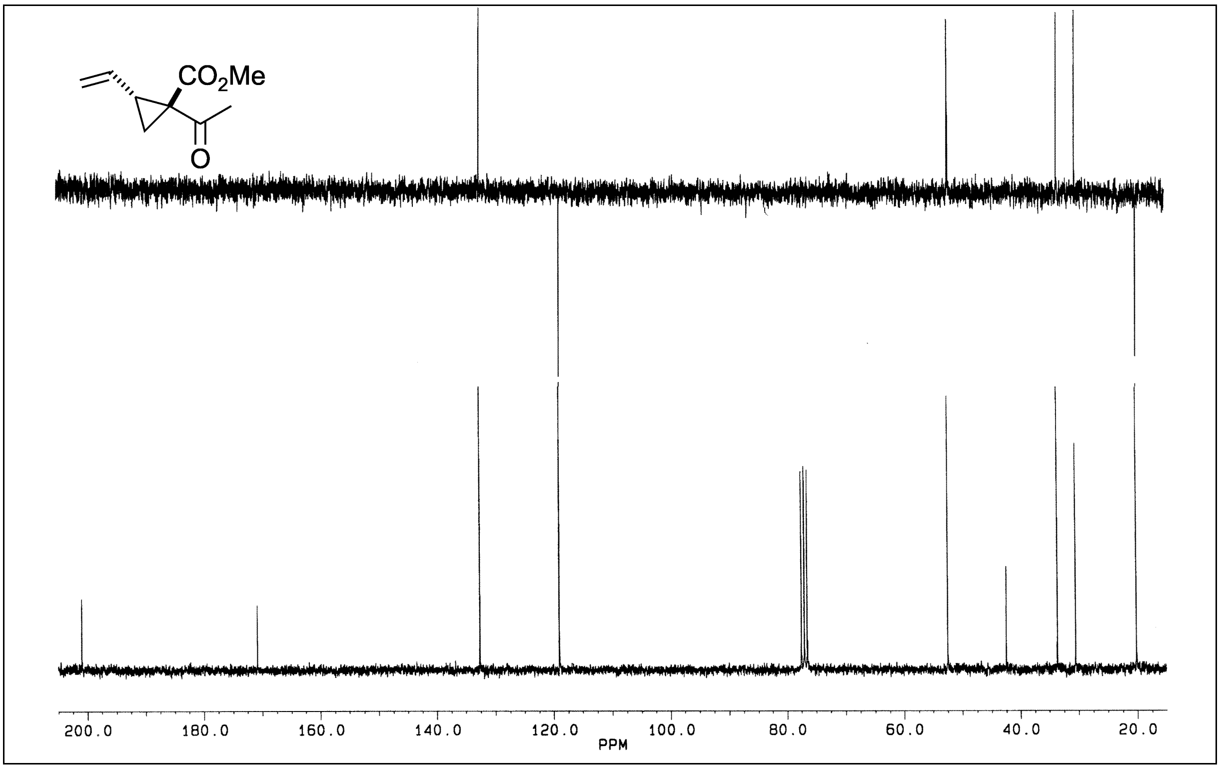


Methyl 2-{3,3-bis(ethoxycarbonyl)bicyclo[3.1.0]hex-1-yl}propenoate (**209**)

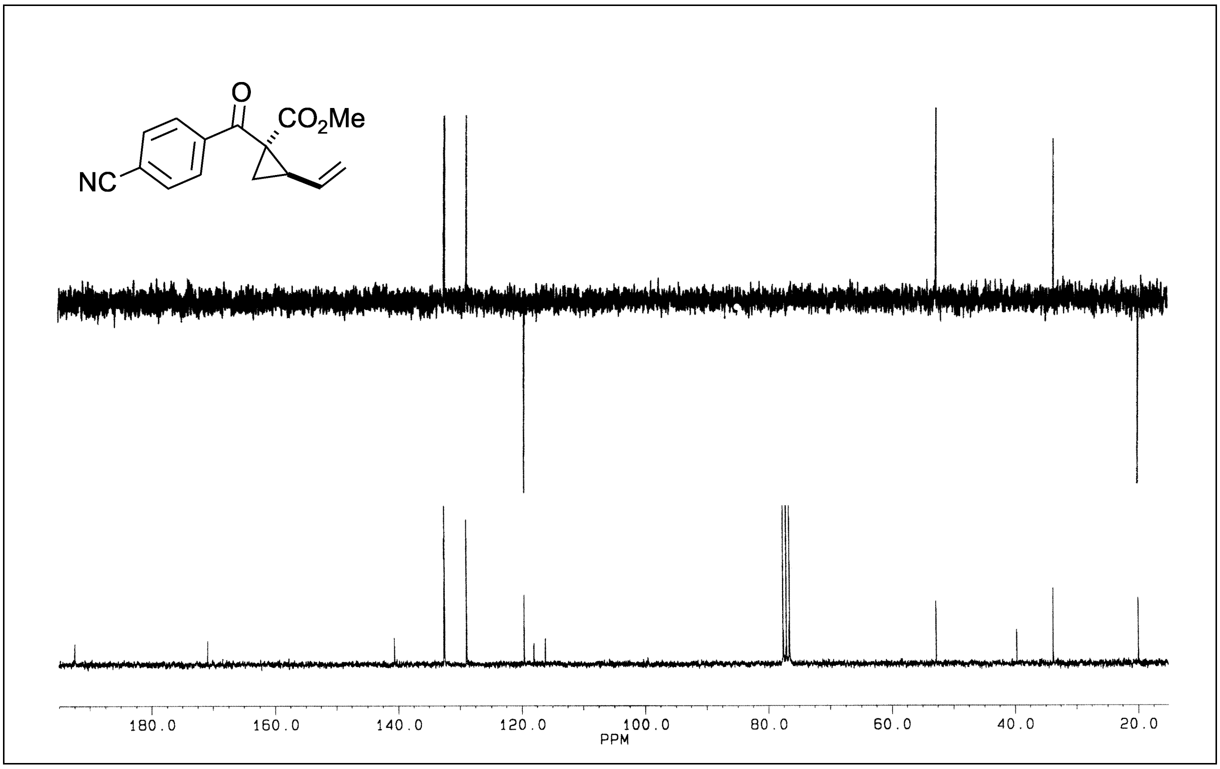


2-(3-Oxa-bicyclo[3.1.0]hex-1-yl)propenoic acid (**211**)

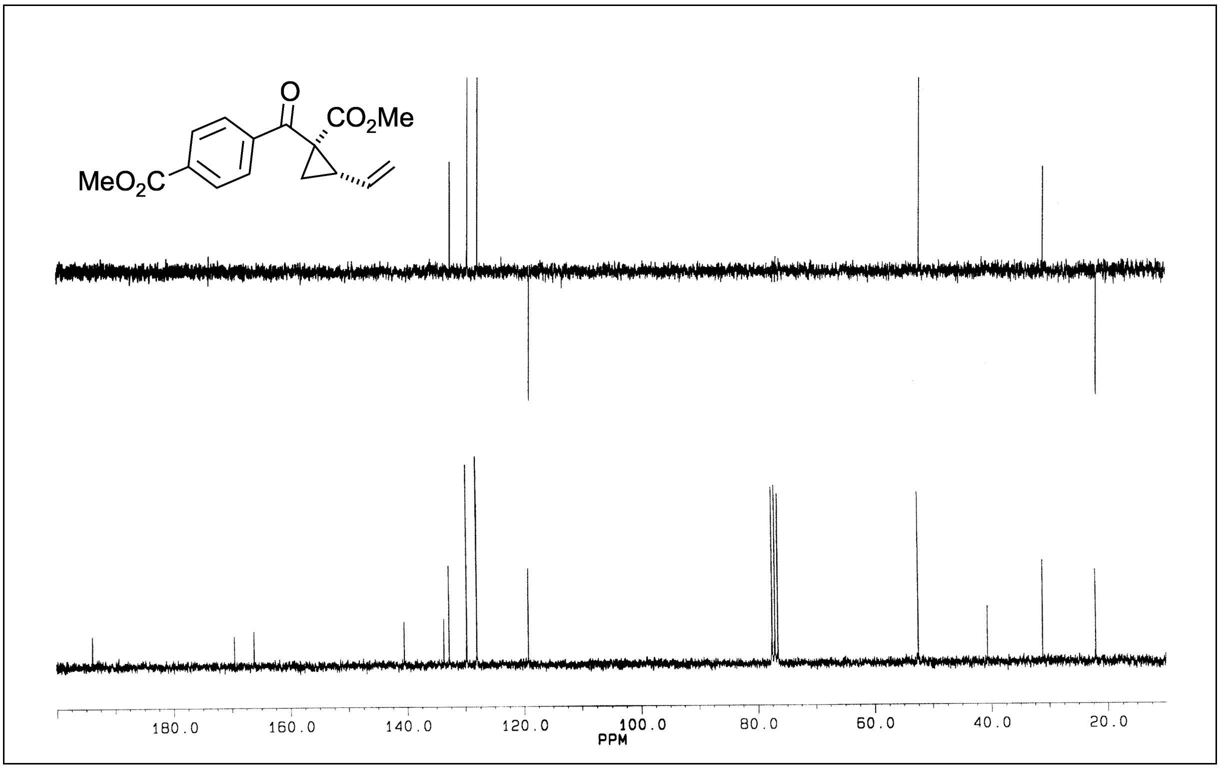
2. ^{13}C-NMR spectra



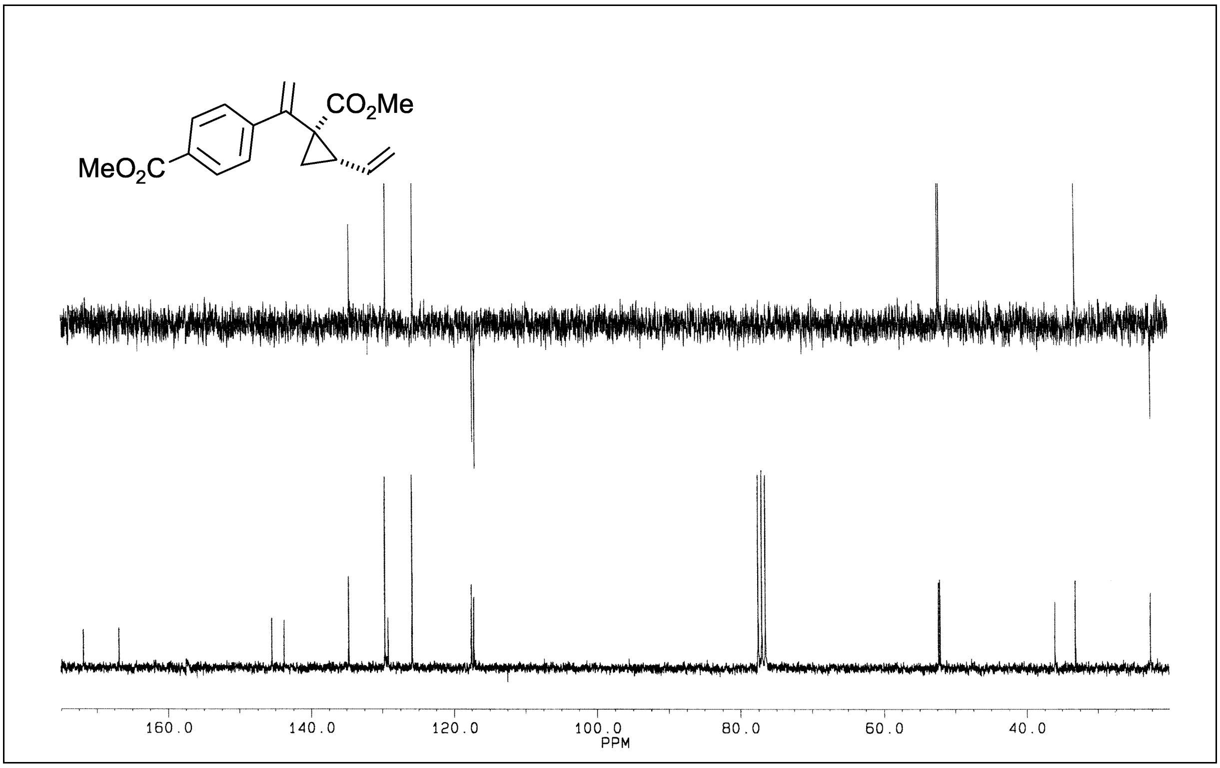
(*E*)-Methyl 1-acetyl-2-ethenylcyclopropanecarboxylate (***E*-23**)



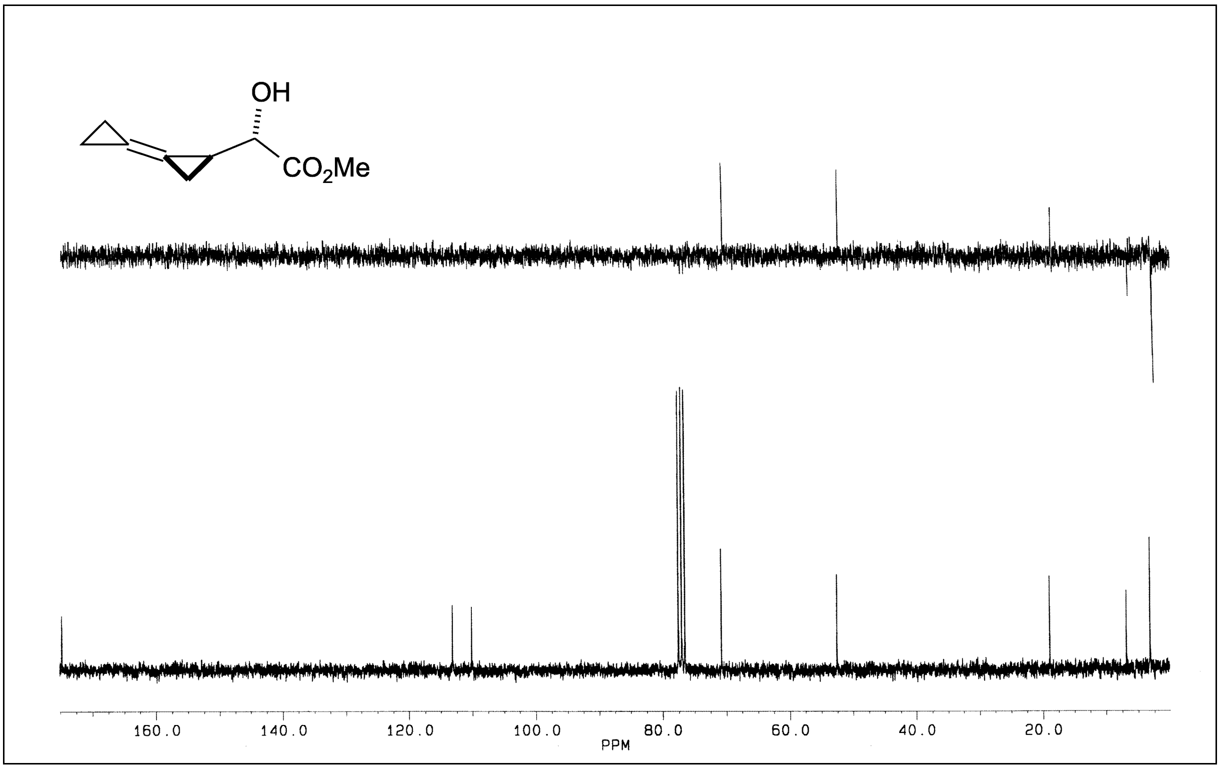
(*E*)-Methyl 1-(4-cyanophenyl)carbonyl-2-ethenylcyclopropanecarboxylate (***E*-24**)



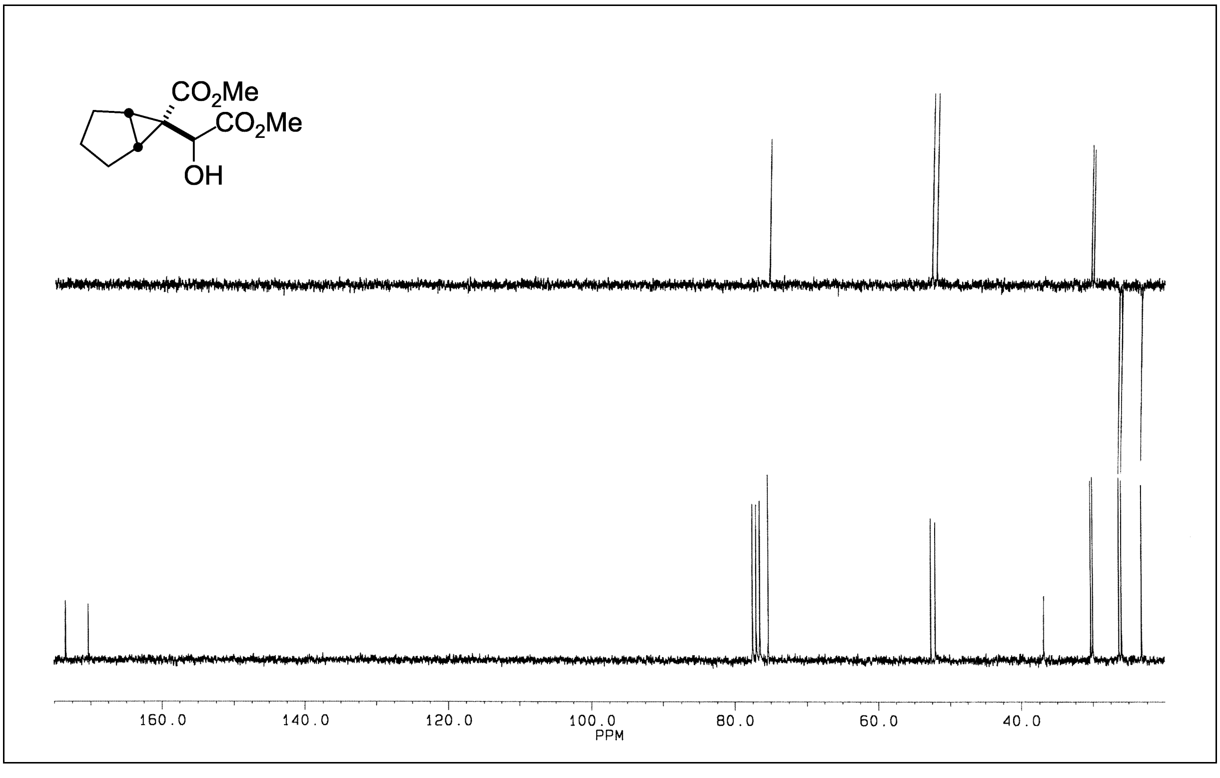
(*Z*)-Methyl 1-(4-methoxycarbonylphenyl)carbonyl-2-ethenylcyclopropanecarboxylate (***Z*-25**)



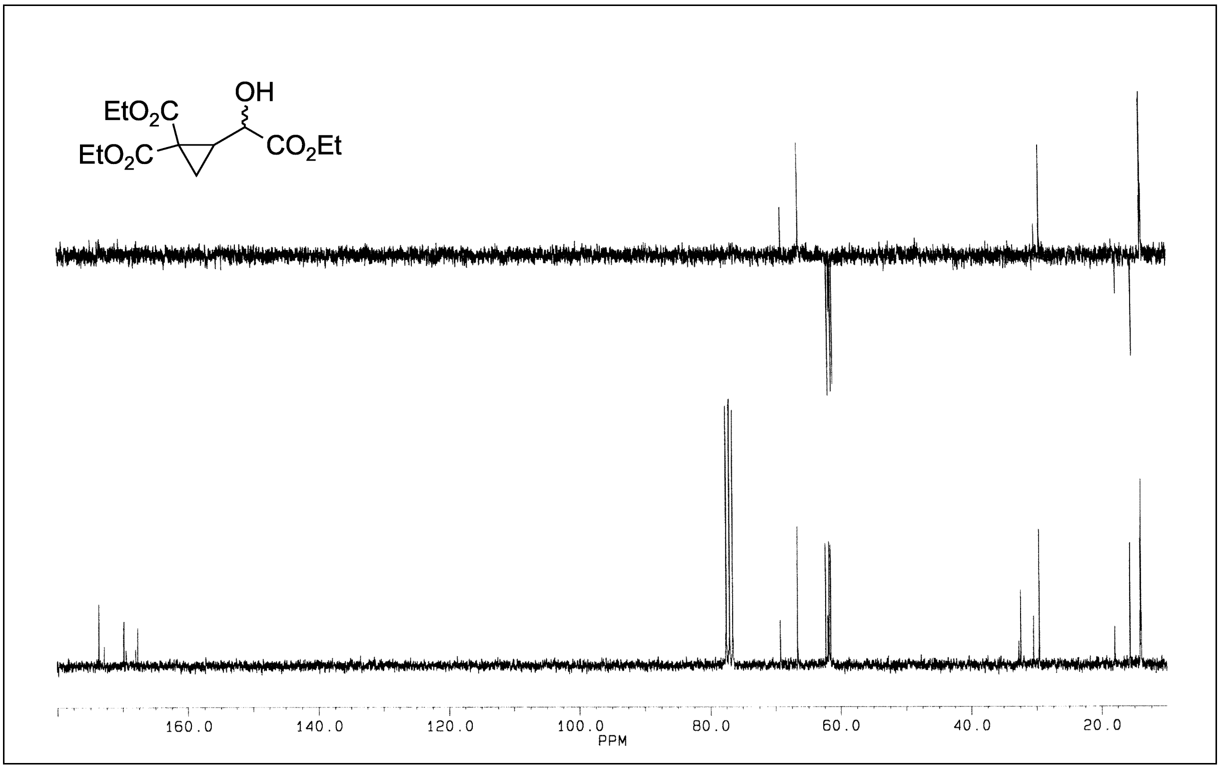
(*Z*)-Methyl 1-[1-(4-methoxycarbonylphenyl)ethen-1-yl]-2-ethenylcyclopropanecarboxylate (***Z*-26**)



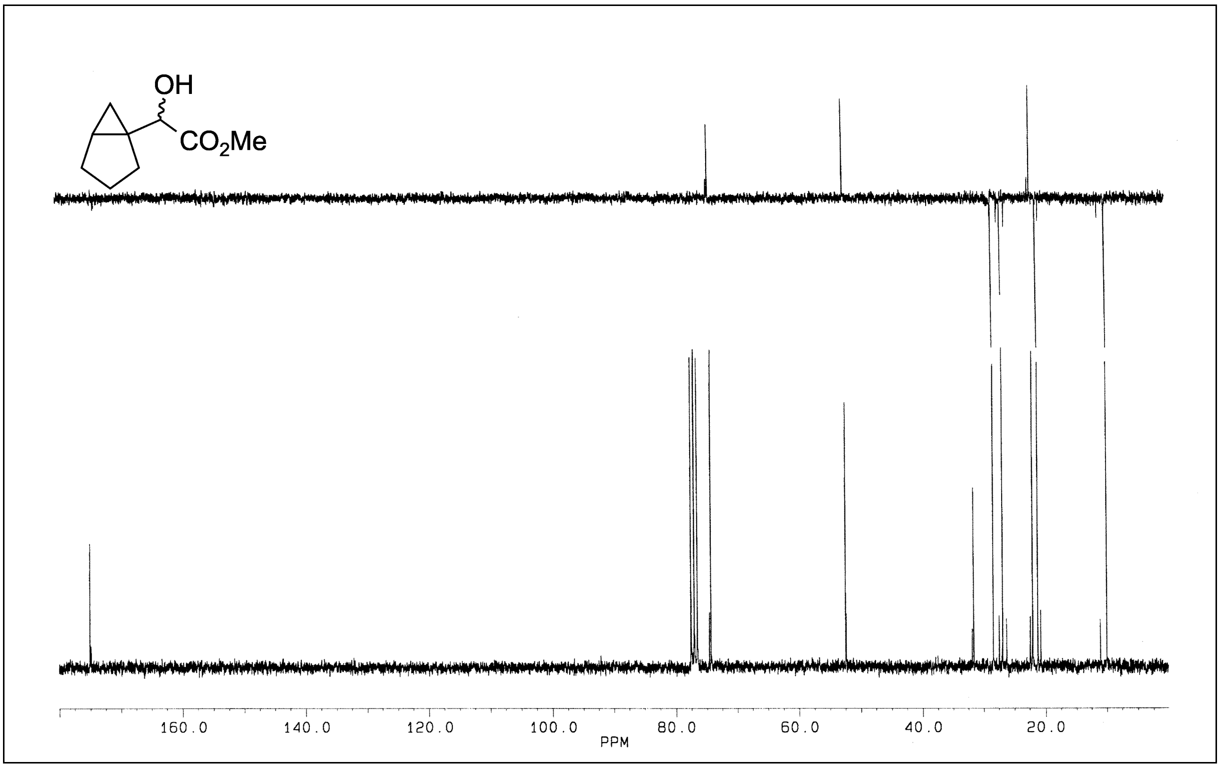
Methyl (S^*,S^*)-bicyclopropylidenylhydroxyacetate (***anti*-85**)



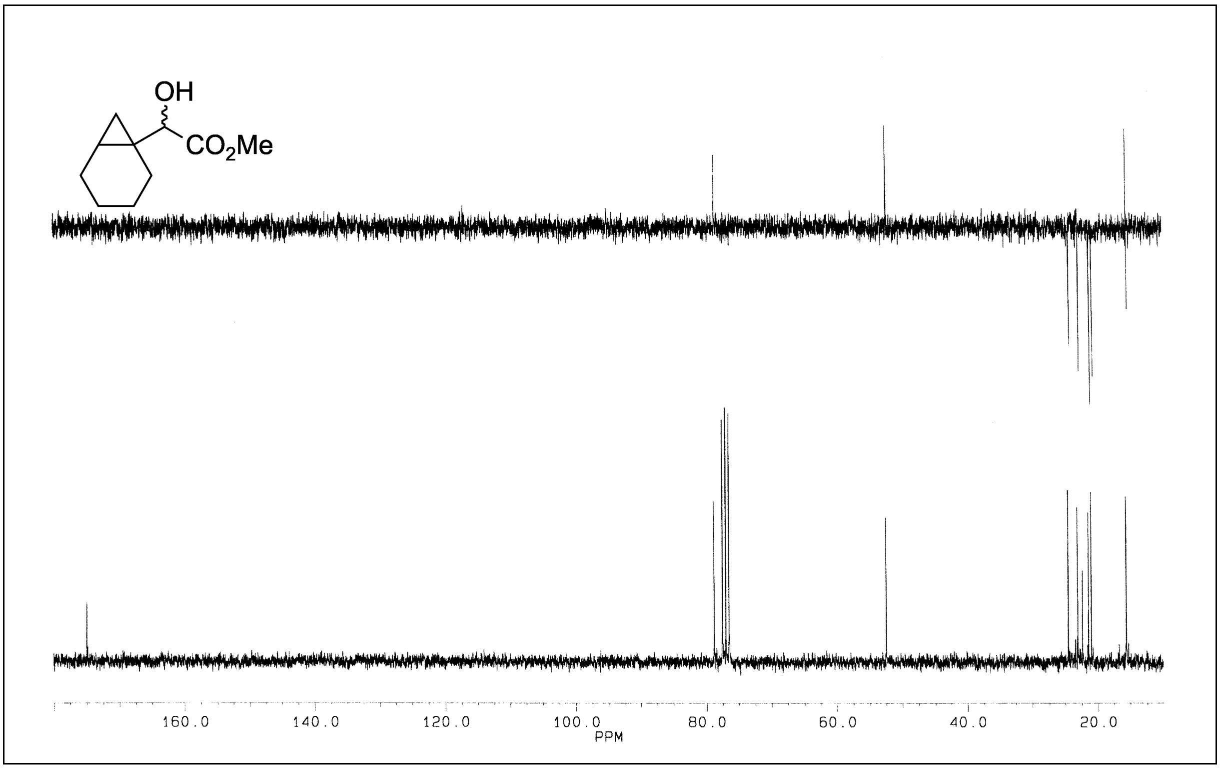
Methyl *exo*-(6-methoxycarbonylbicyclo[3.1.0]hex-6-yl)hydroxyacetate (**88**)



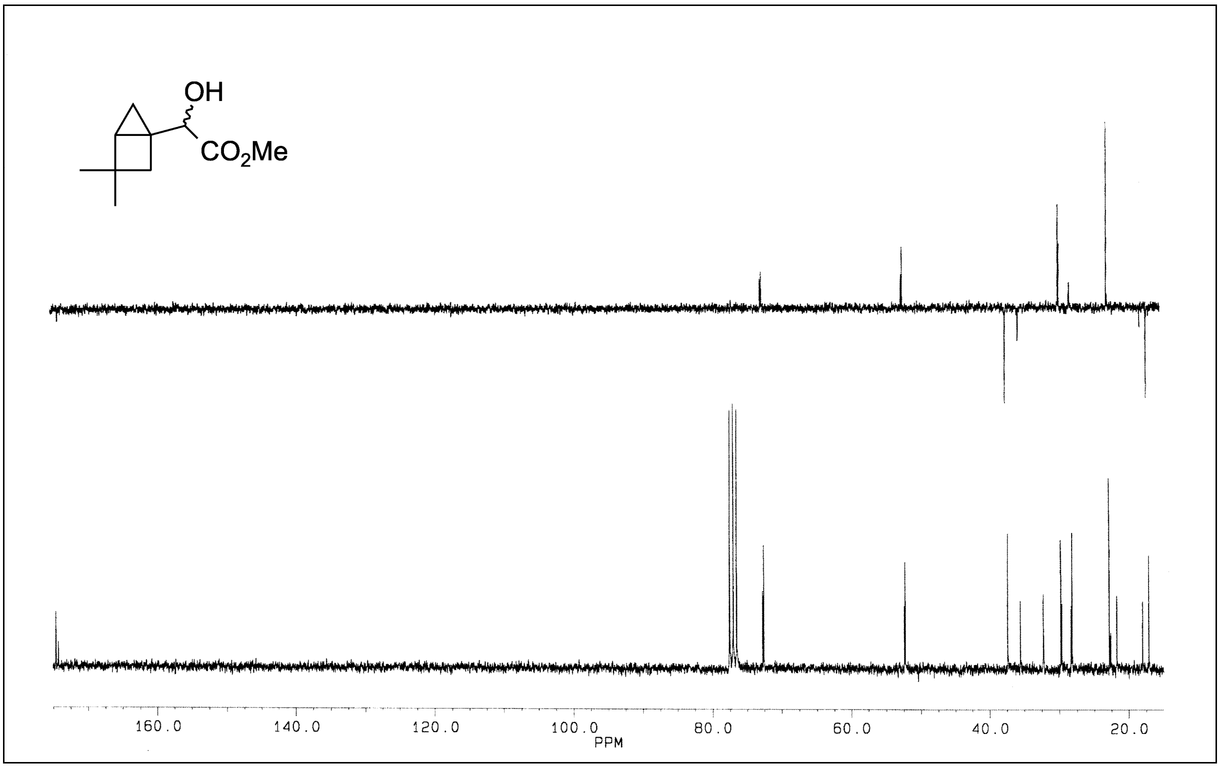
Ethyl [1,1-bis(ethoxycarbonyl)cycloprop-2-yl]hydroxyacetate (**89**)



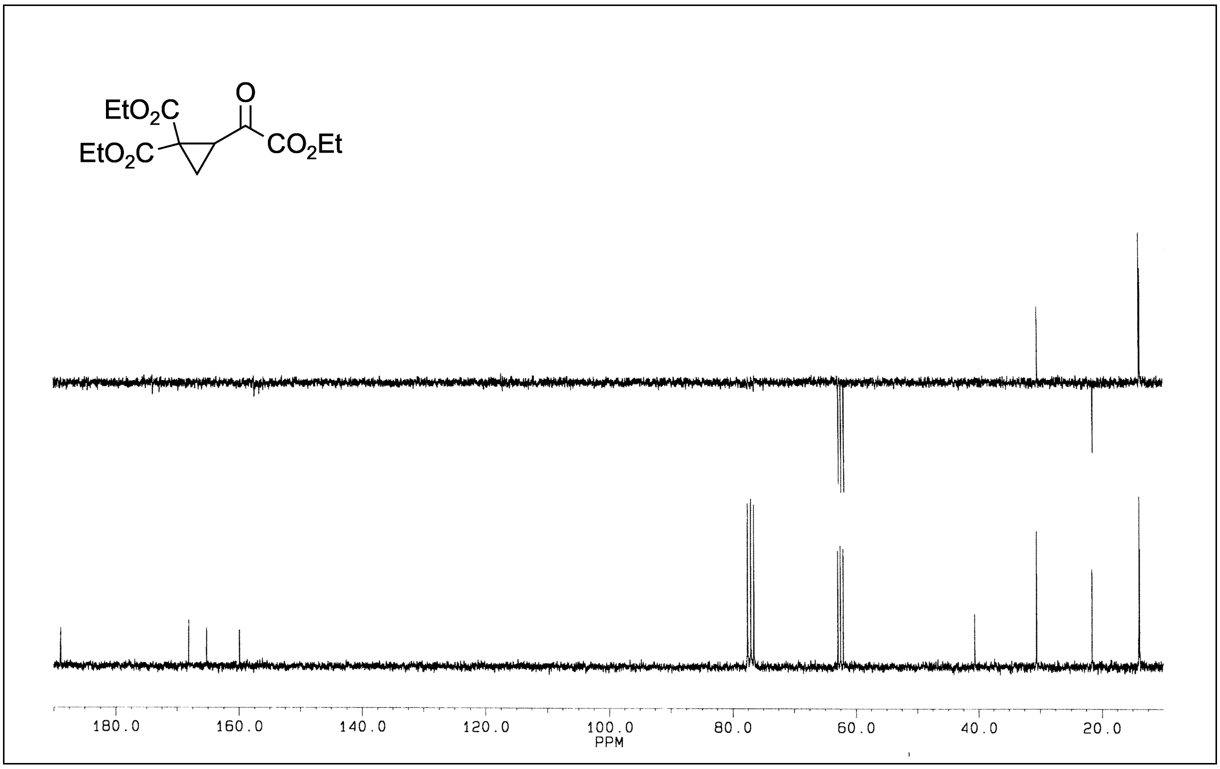
Methyl (bicyclo[3.1.0]hex-1-yl)hydroxyacetate (**91**)



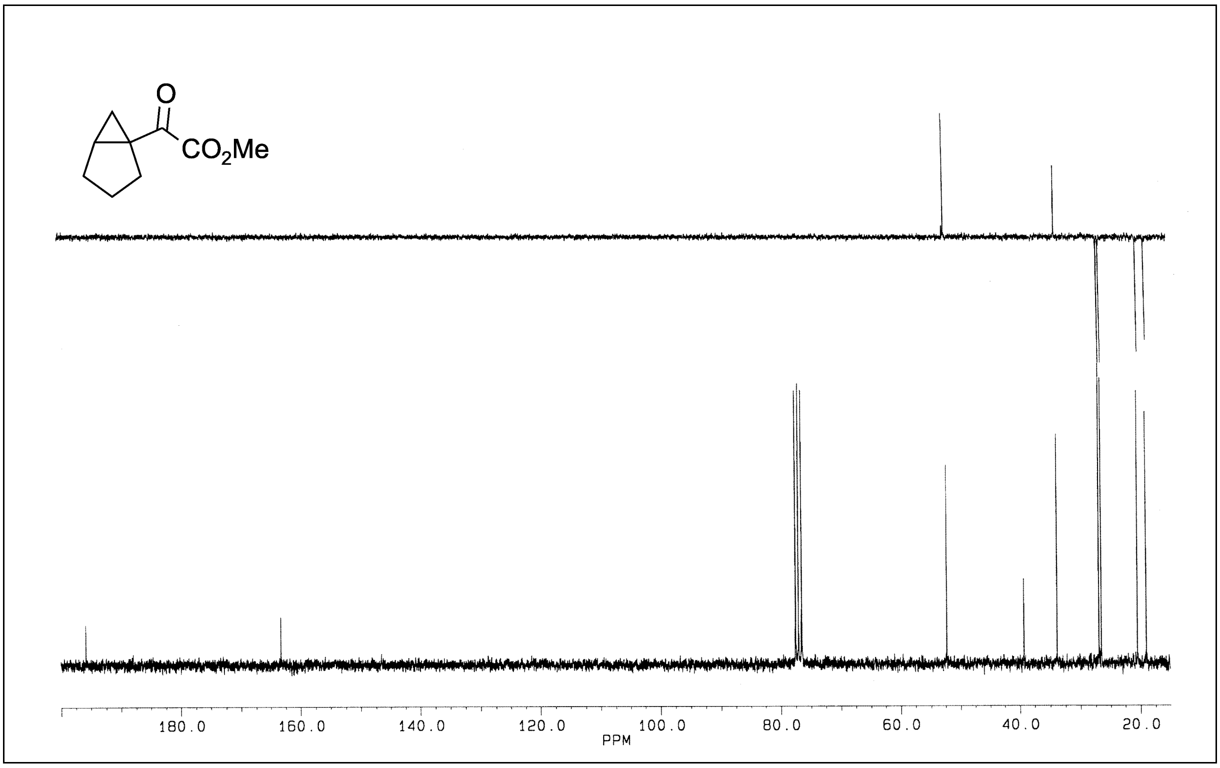
Methyl (bicyclo[4.1.0]hept-1-yl)hydroxyacetate (**92**)



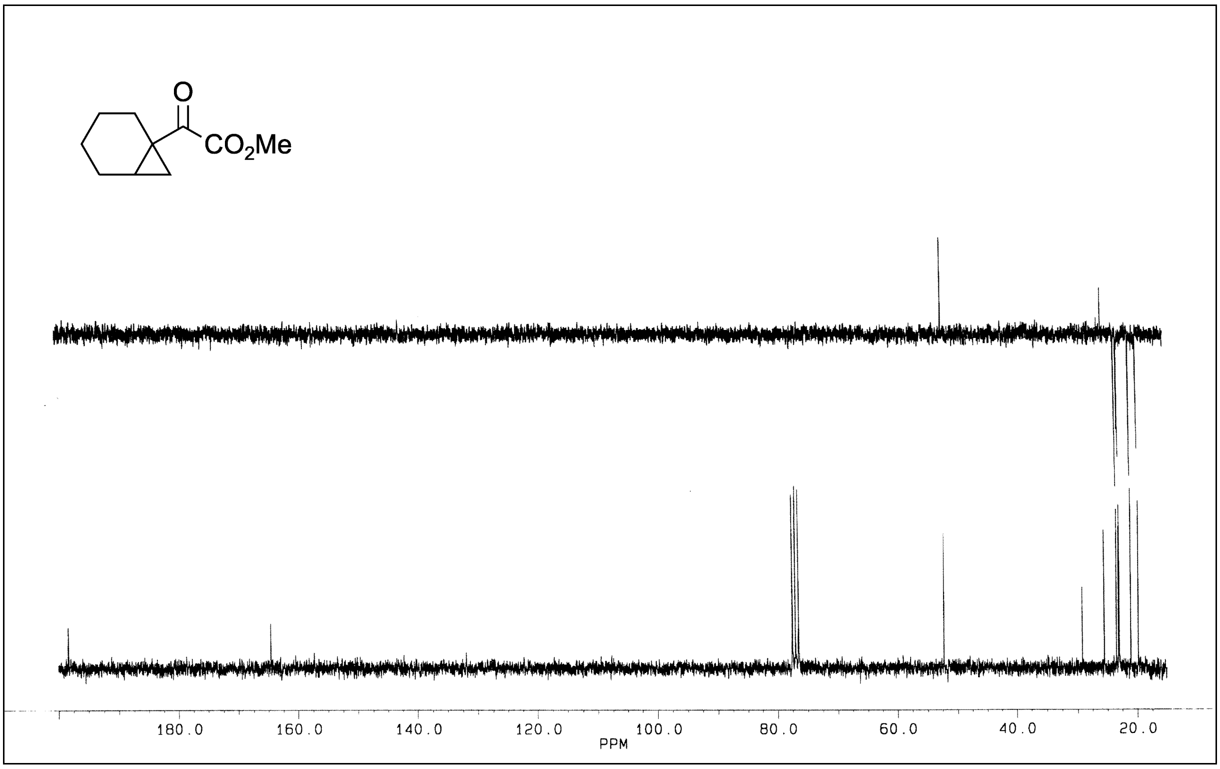
Methyl (3,3-dimethylbicyclo[2.1.0]pent-1-yl)hydroxyacetate (**93**)



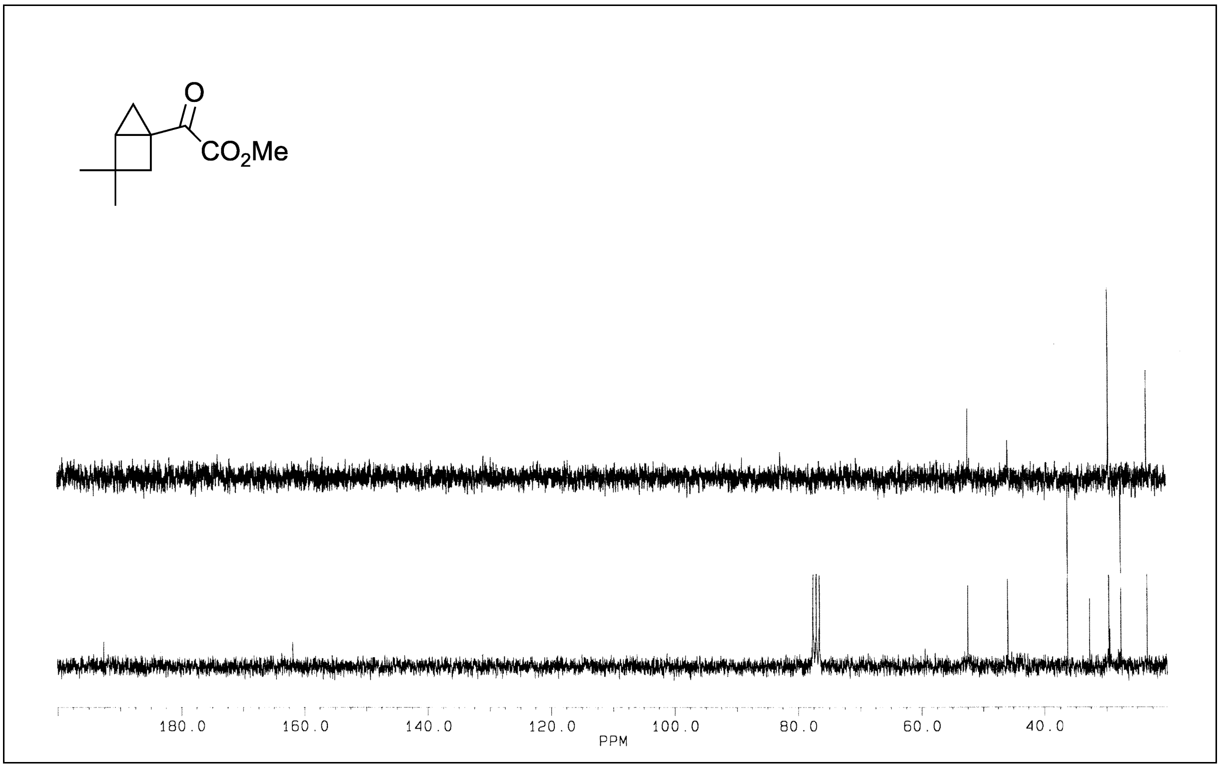
Ethyl [1,1-bis(ethoxycarbonyl)cycloprop-2-yl]oxoacetate (**102**)



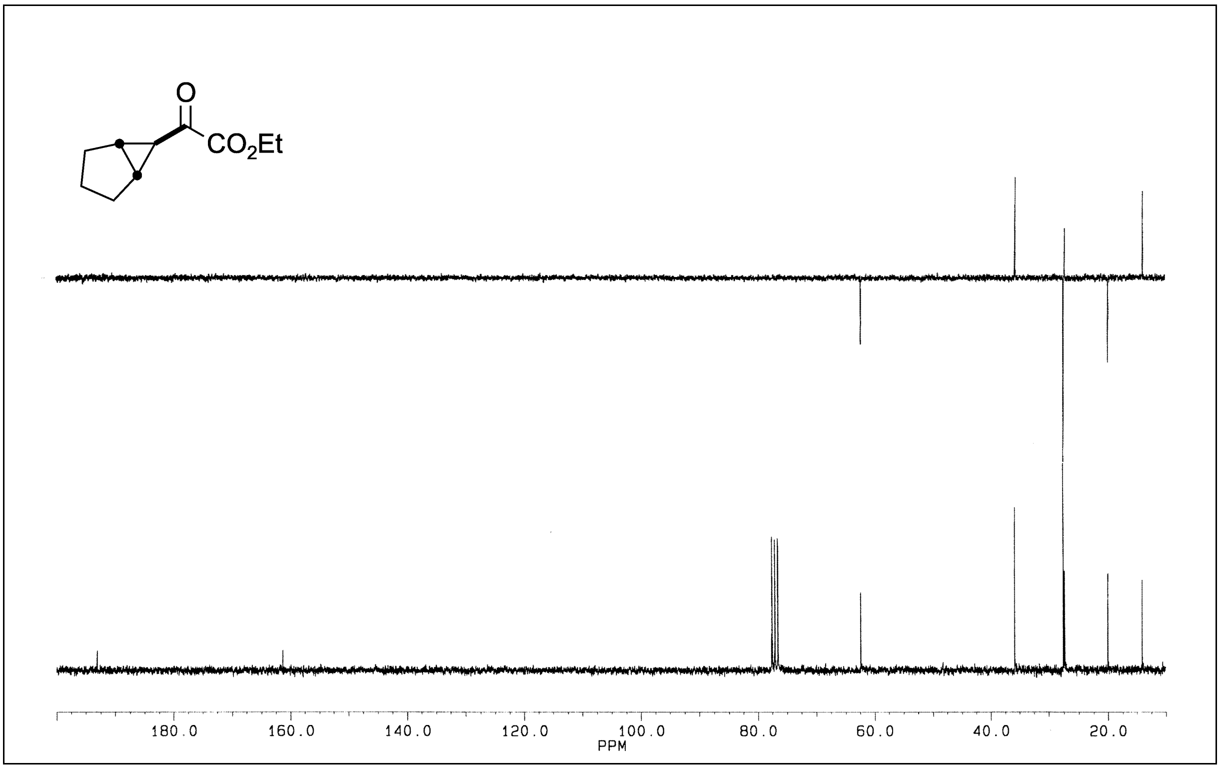
Methyl (bicyclo[3.1.0]hex-1-yl)oxoacetate (**103**)



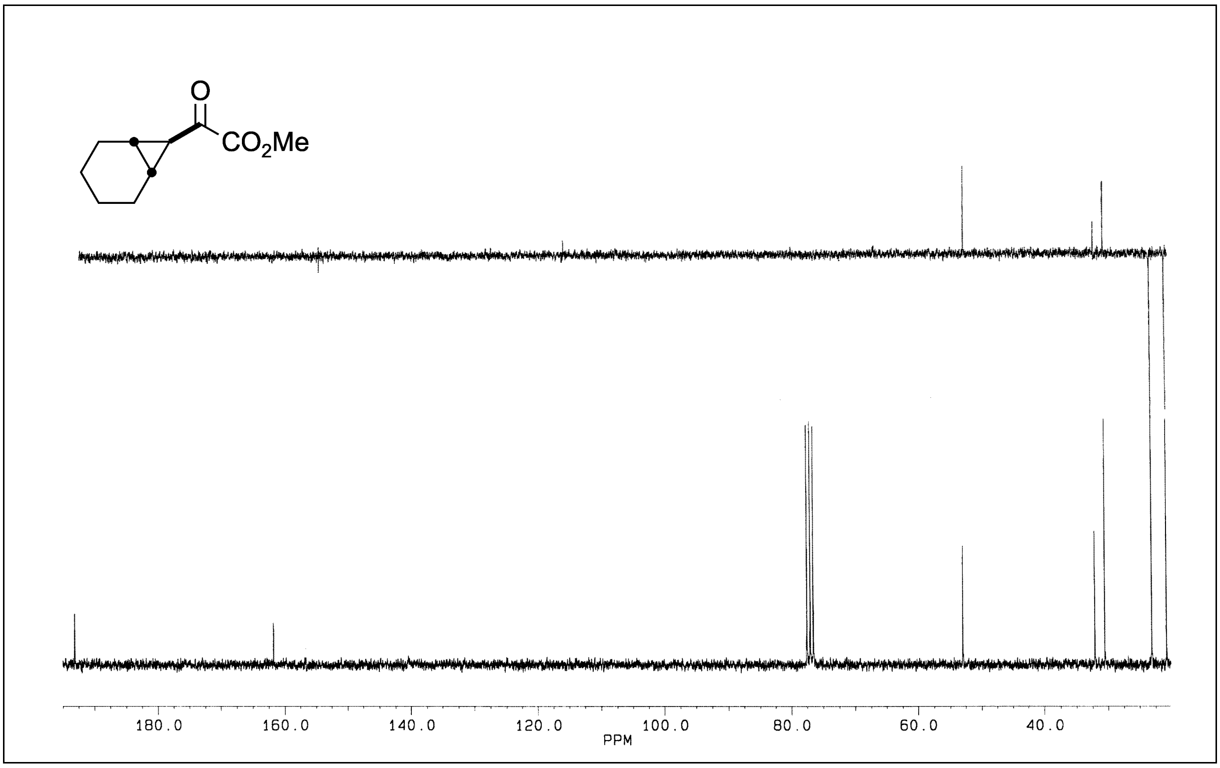
Methyl (bicyclo[4.1.0]hept-1-yl)oxoacetate (**104**)



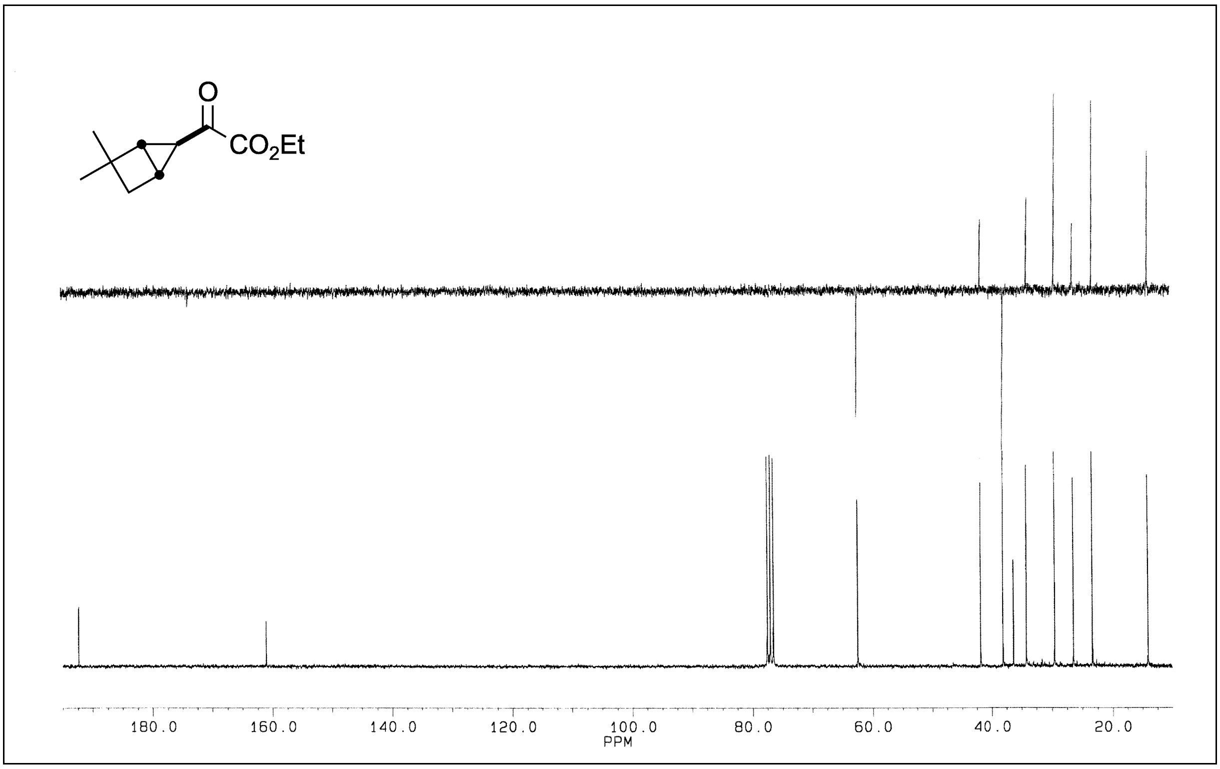
Methyl (3,3-dimethylbicyclo[2.1.0]pent-1-yl)oxoacetate (**105**) (reaction mixture)



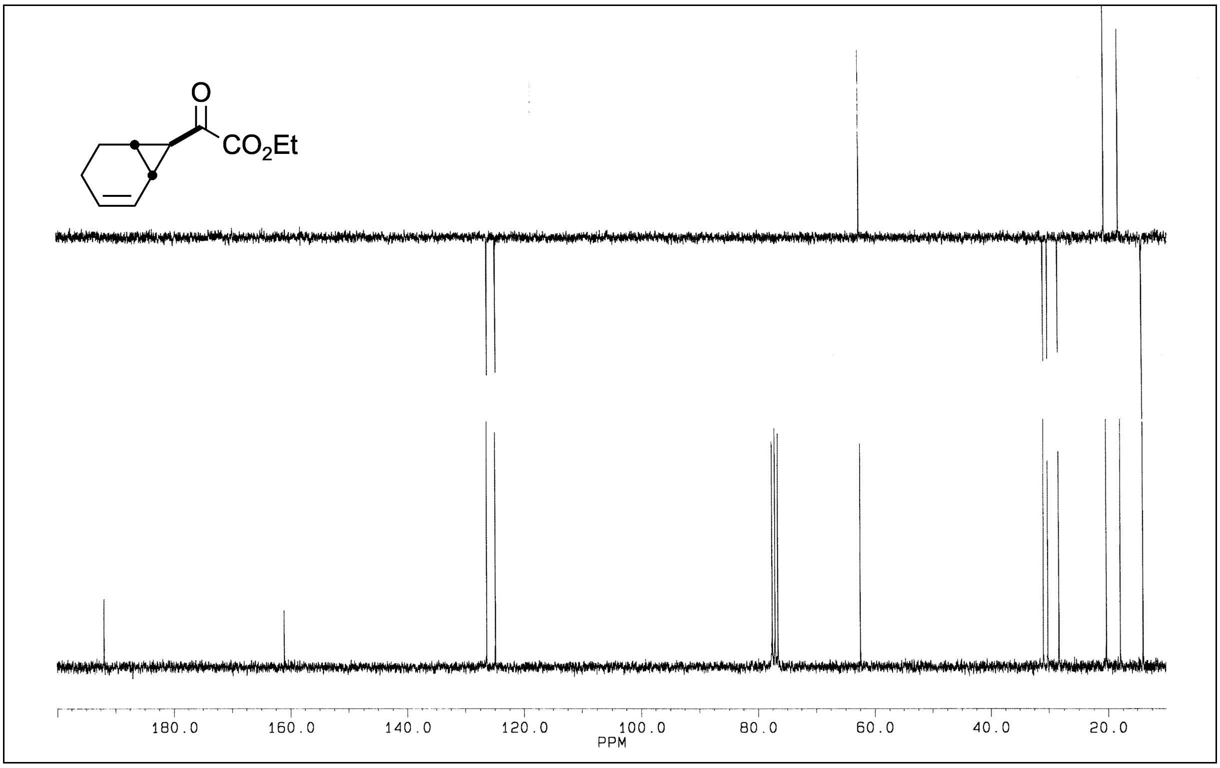
Ethyl *exo*-(bicyclo[3.1.0]hex-6-yl)oxoacetate (**112**)



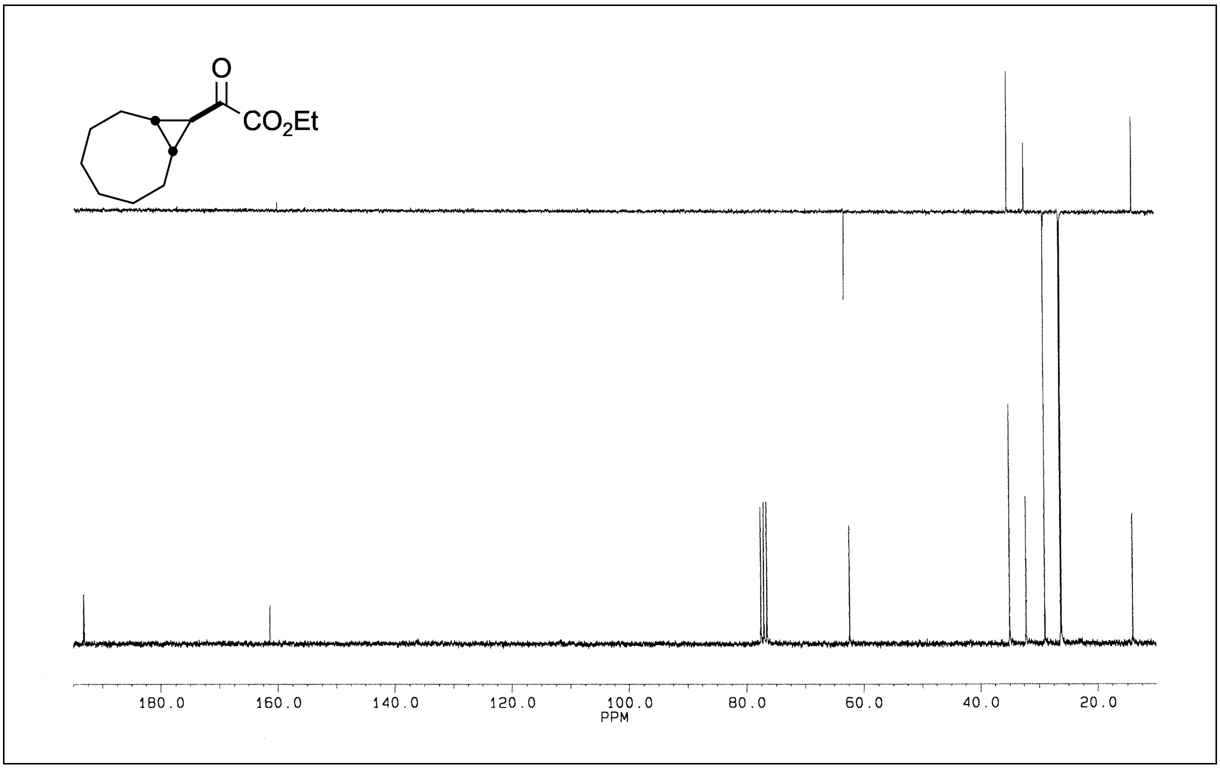
Methyl *exo*-(bicyclo[4.1.0]hept-7-yl)oxoacetate (**113**)



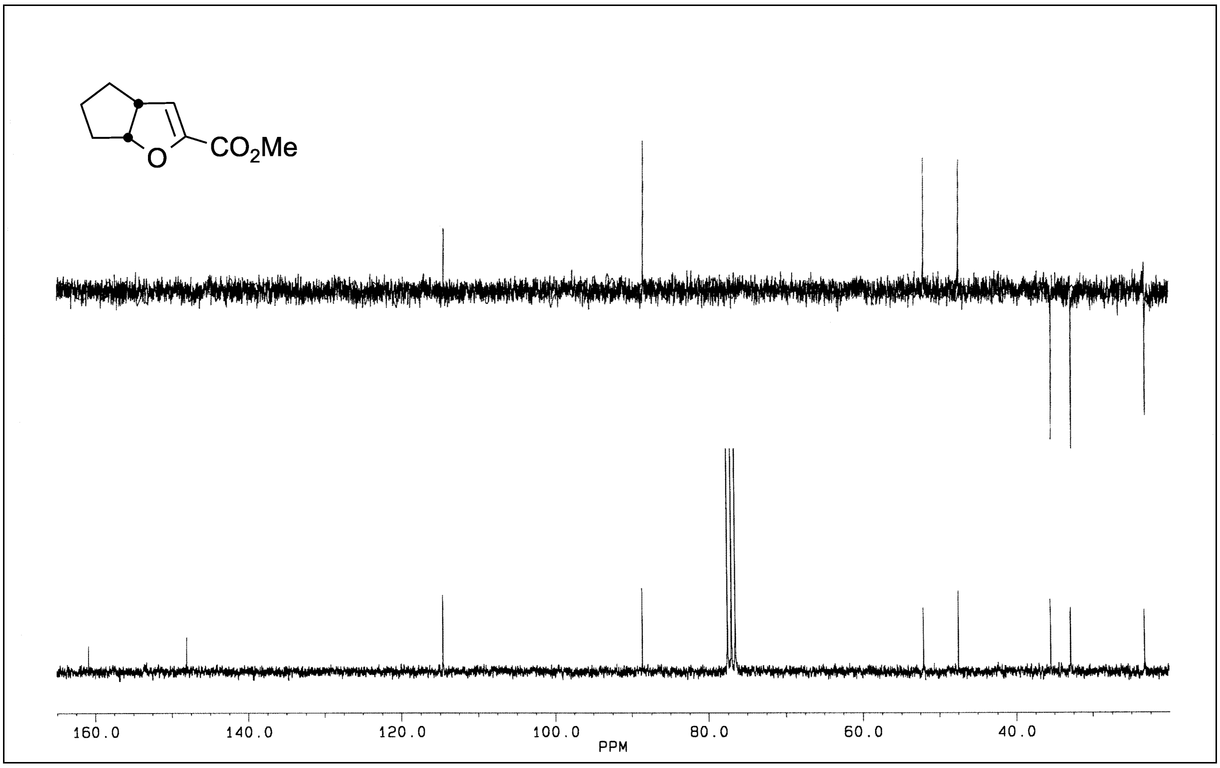
Ethyl *exo*-(2,2-dimethylbicyclo[2.1.0]pent-5-yl)oxoacetate (***exo*-115**)



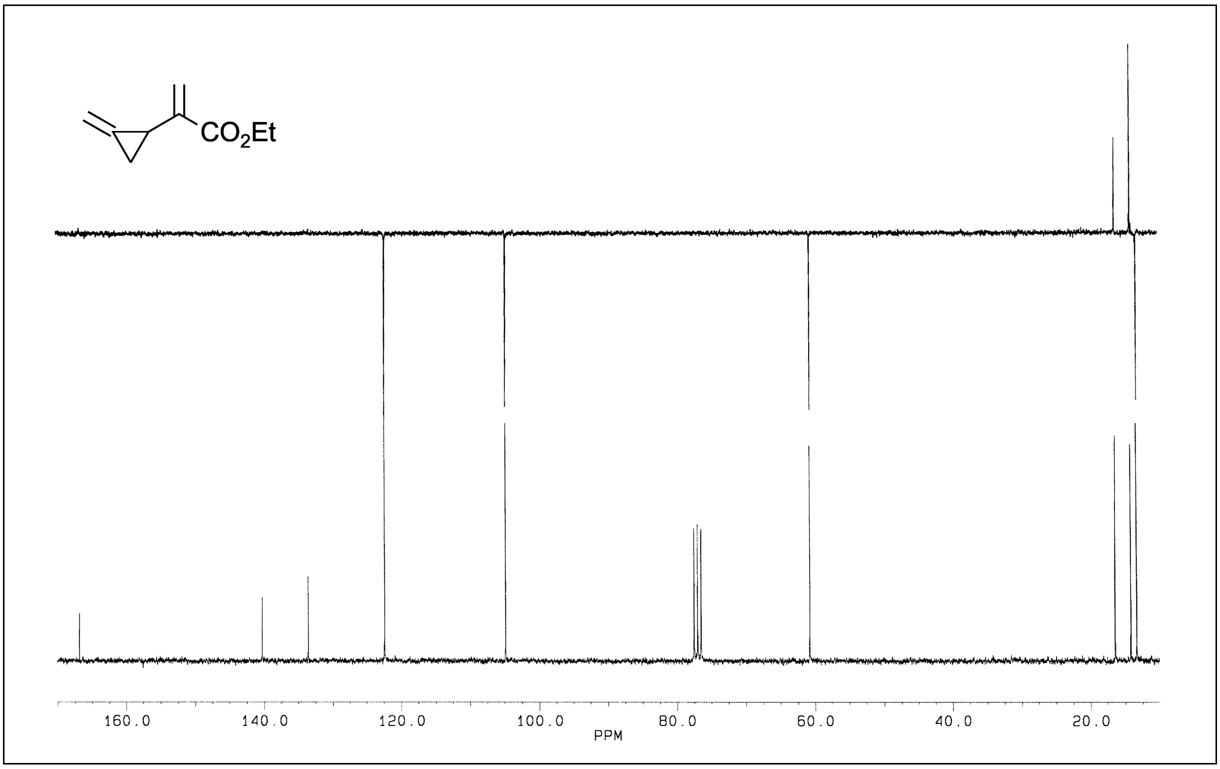
Ethyl *exo*-(bicyclo[4.1.0]hept-2-en-7-yl)oxoacetate (**116**)



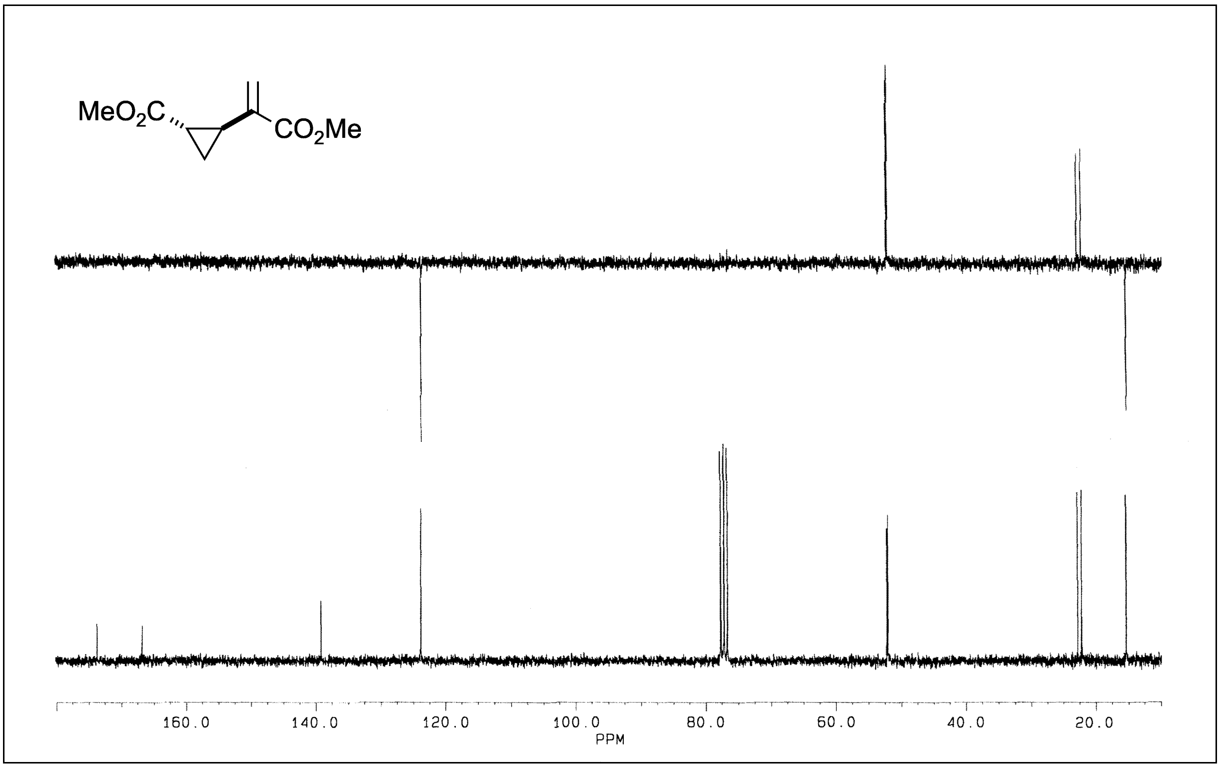
Ethyl *exo*-(bicyclo[6.1.0]non-9-yl)oxoacetate (**117**)



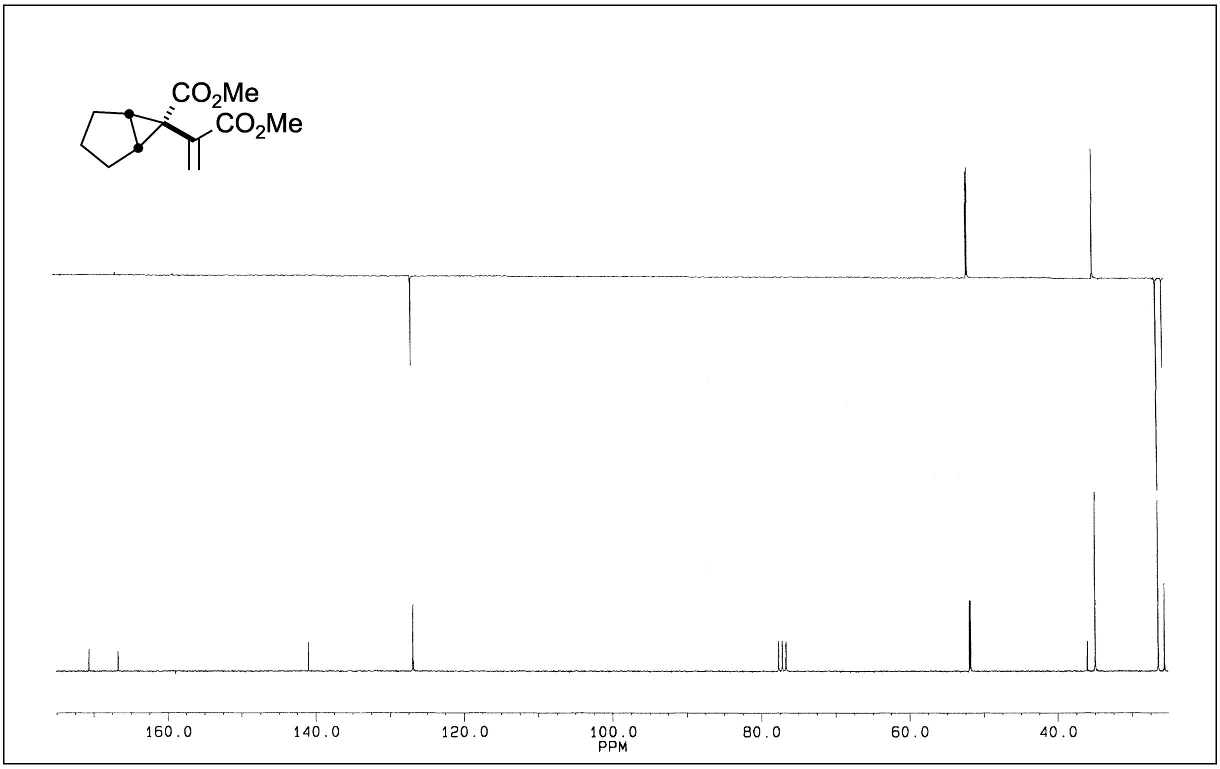
Methyl 4,5,6,6a-tetrahydro-3a*H*-cyclopenta[b]furan-2-carboxylate (**119**)



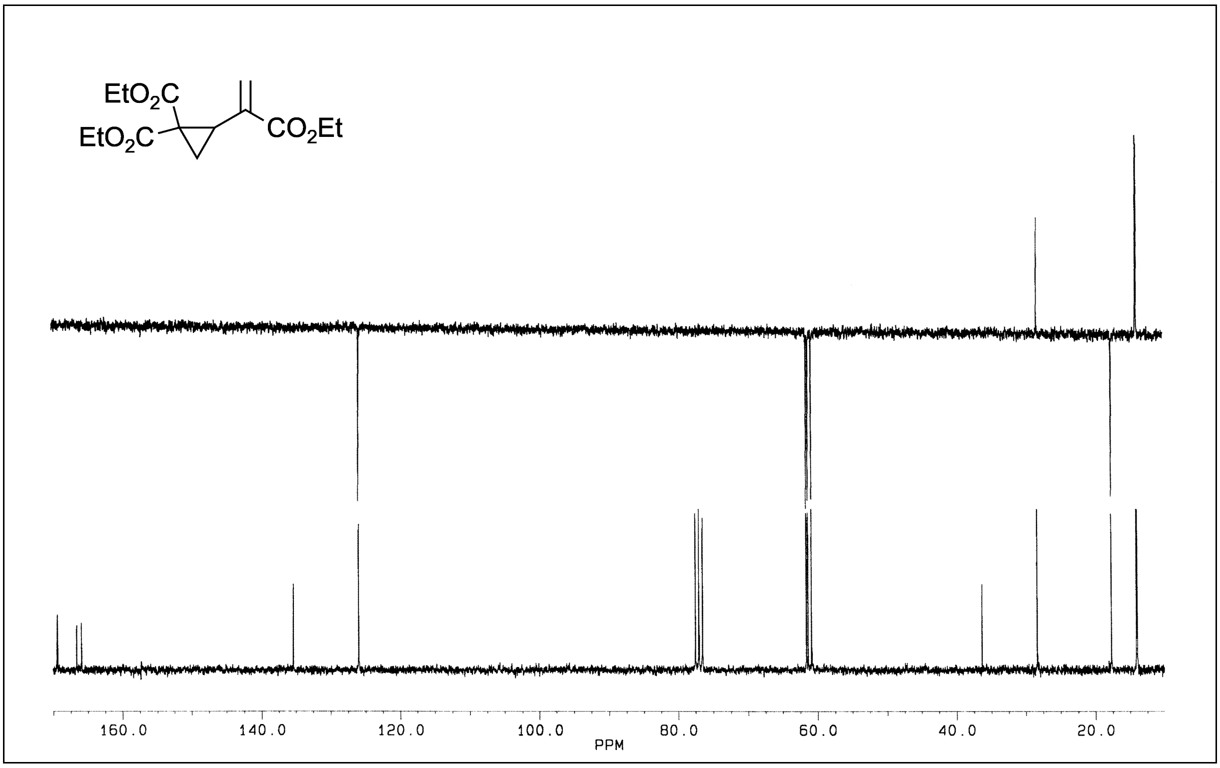
Ethyl 2-(2-methylenecyclopropyl)propenoate (**141**)



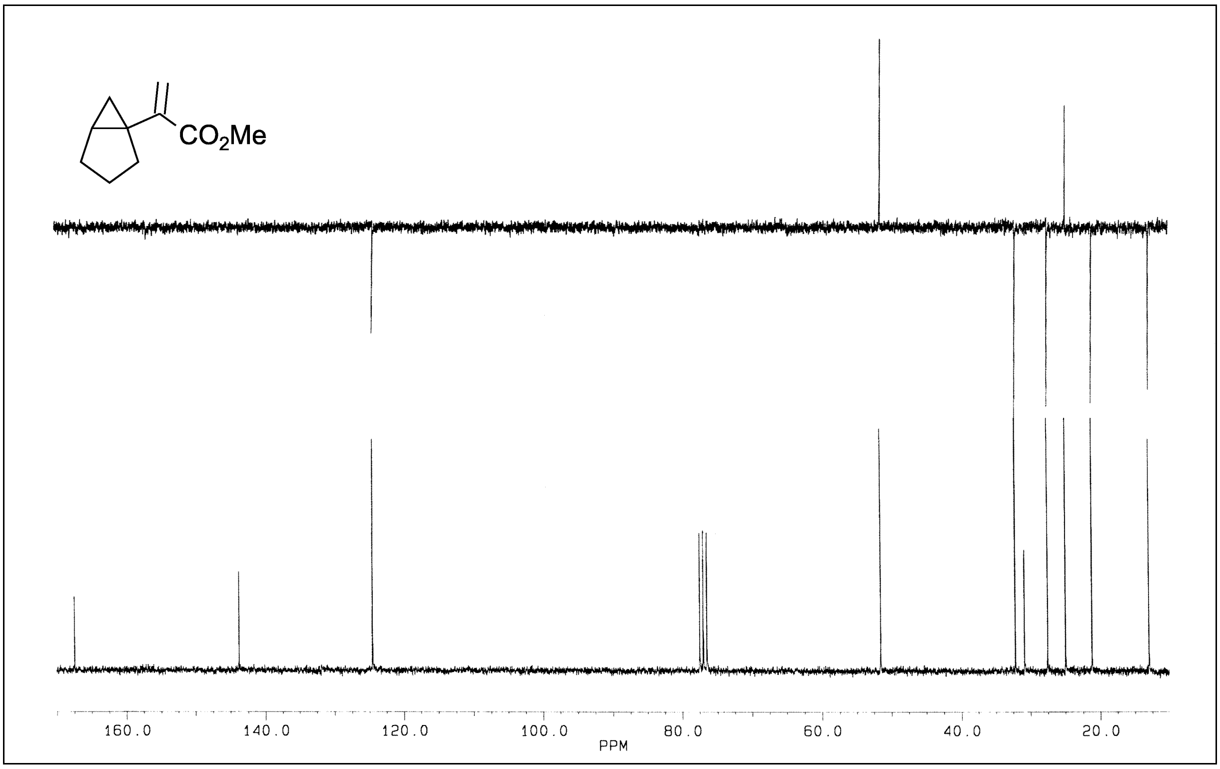
Methyl *trans*-2-(1-methoxycarbonylcycloprop-2-yl)propenoate (**126**)



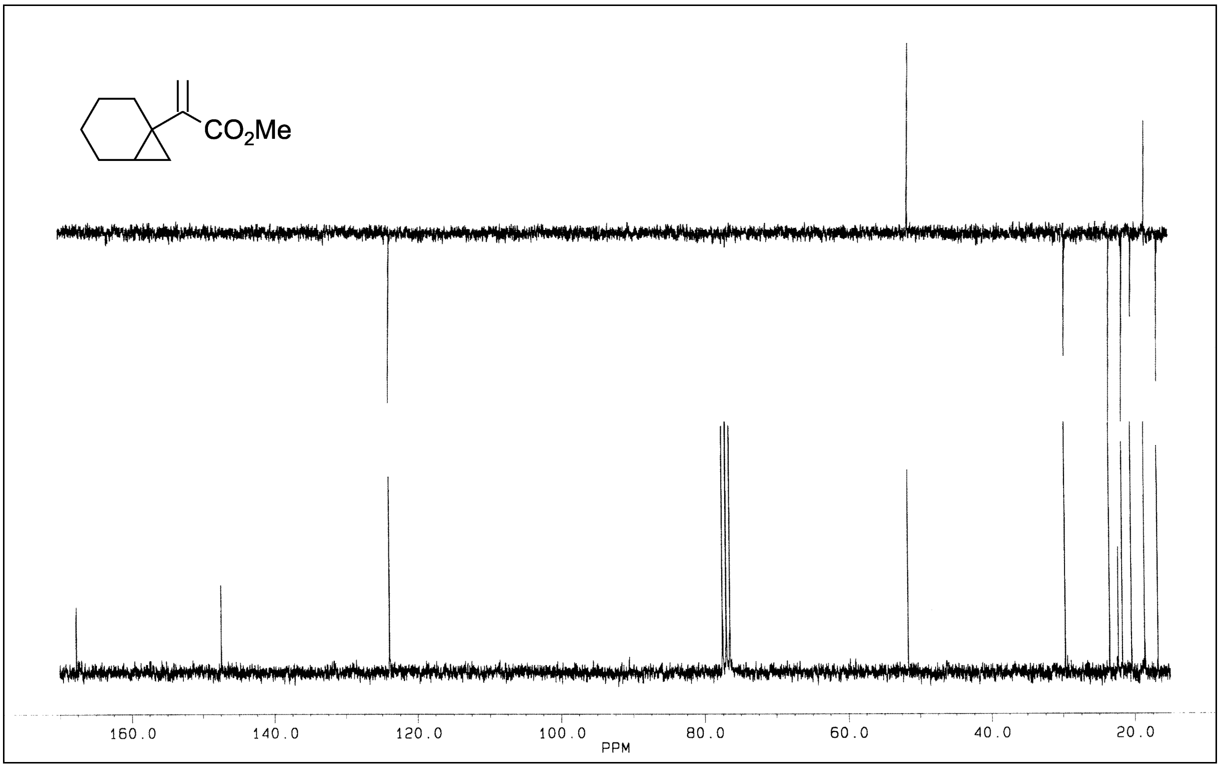
Methyl 2-(6-methoxycarbonylbicyclo[3.1.0]hex-6-yl)propenoate (**128**)



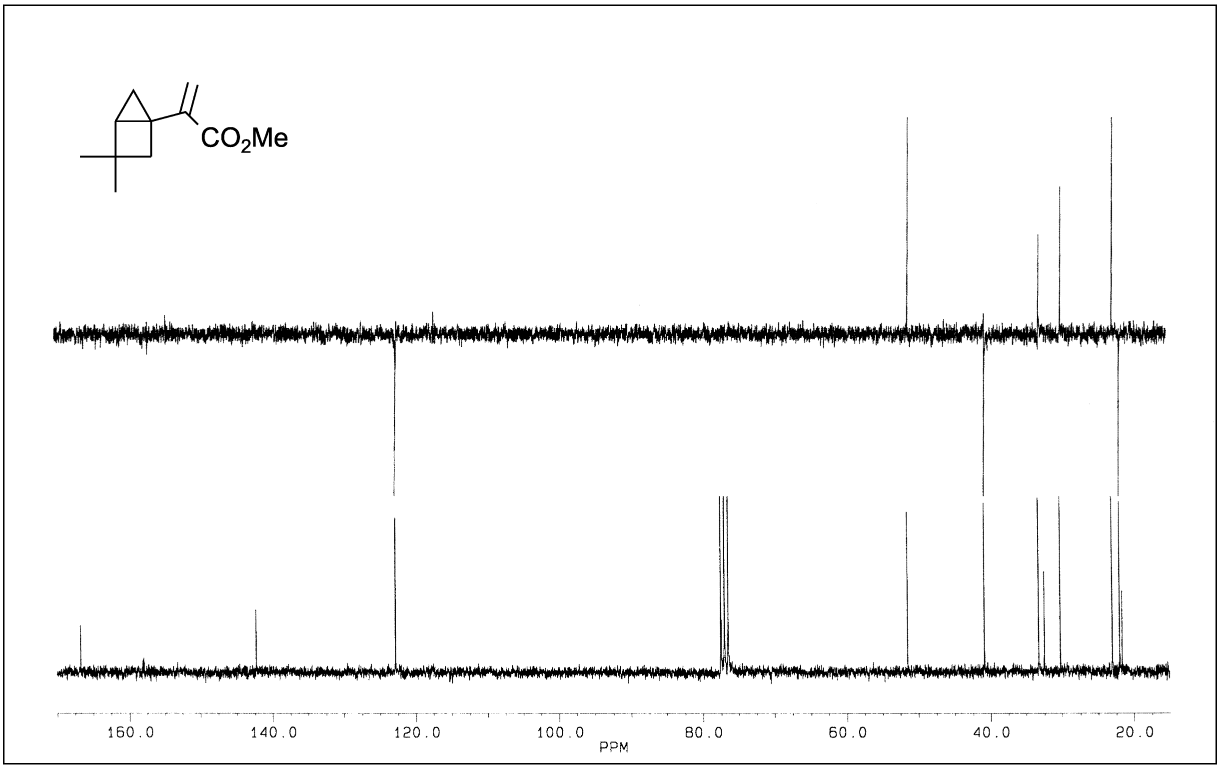
Ethyl 2-[1,1-bis(ethoxycarbonyl)cycloprop-2-yl]propenoate (**129**)



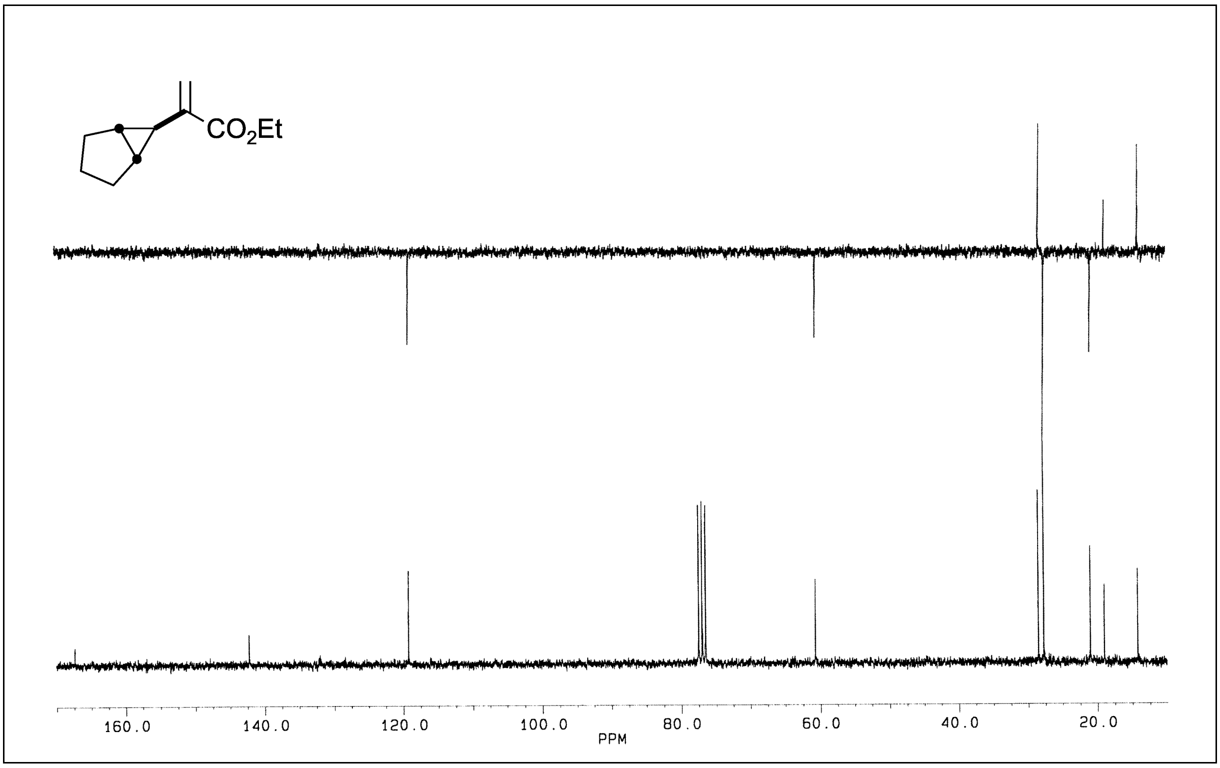
Methyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**130**)



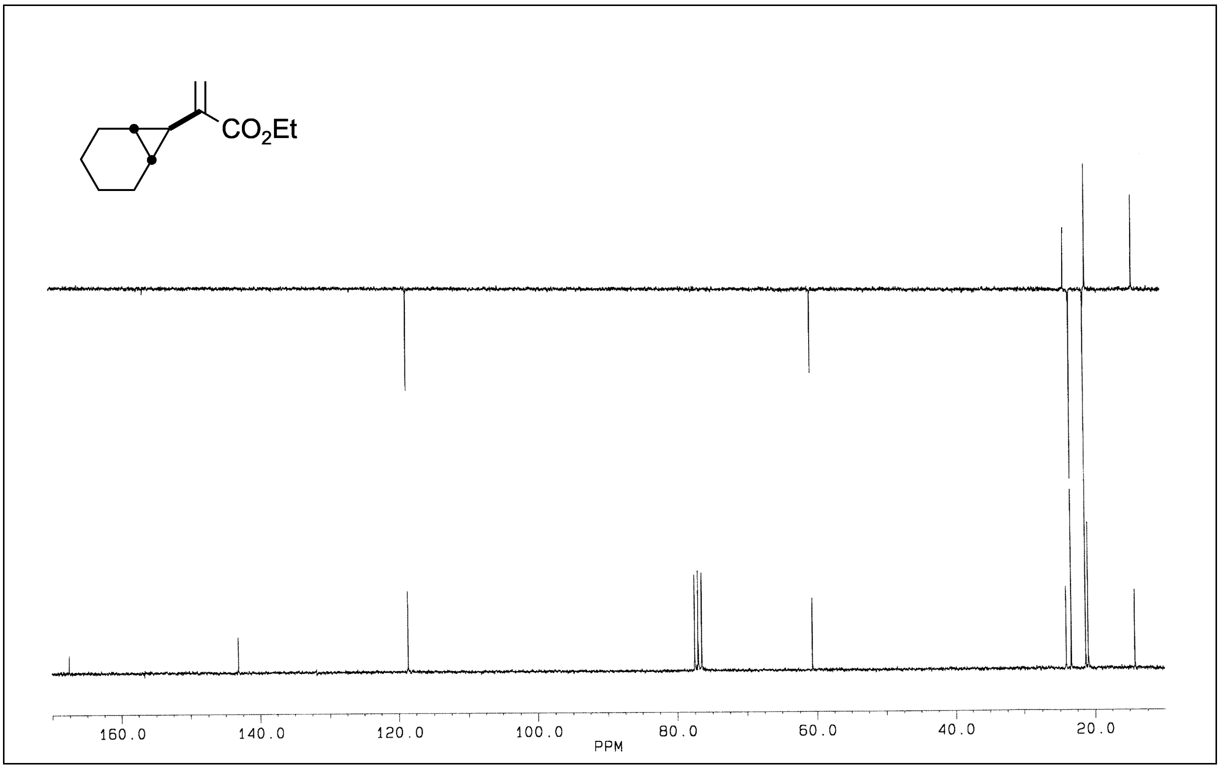
Methyl 2-(bicyclo[4.1.0]hept-1-yl)propenoate (**131**)



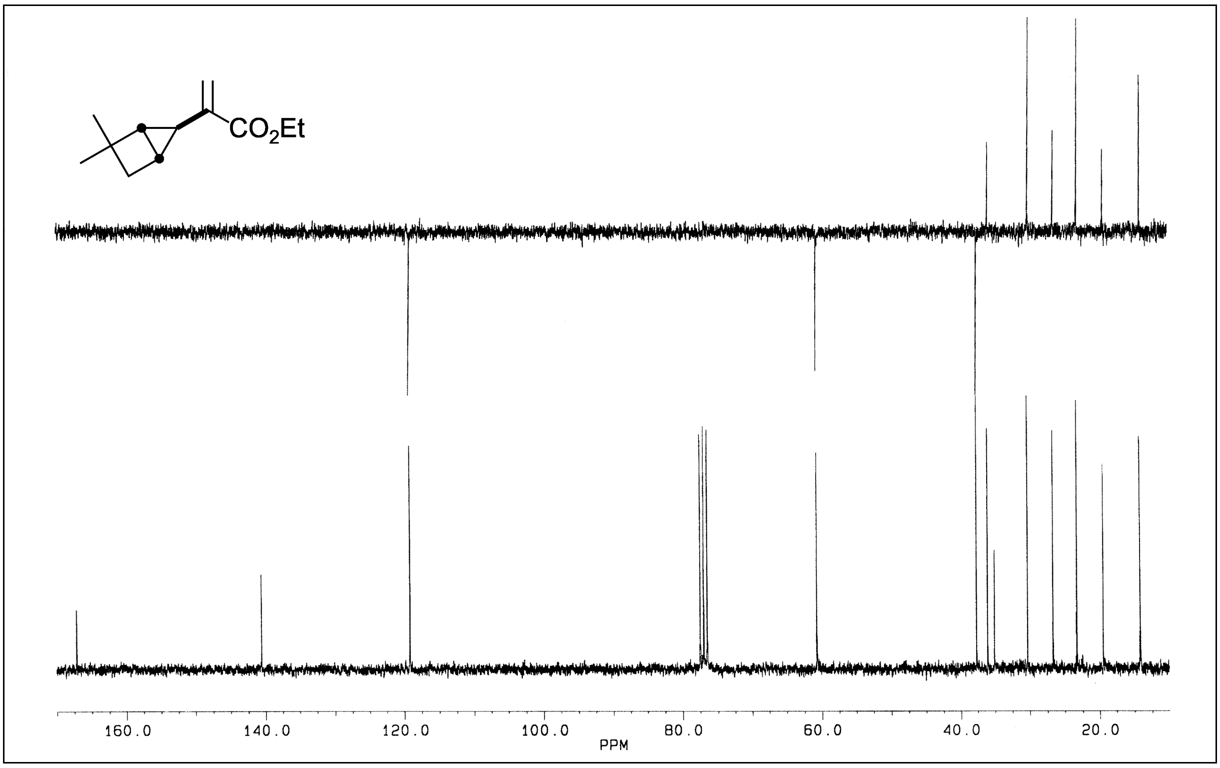
Methyl 2-(3,3-dimethylbicyclo[2.1.0]pent-1-yl)propenoate (**132**)



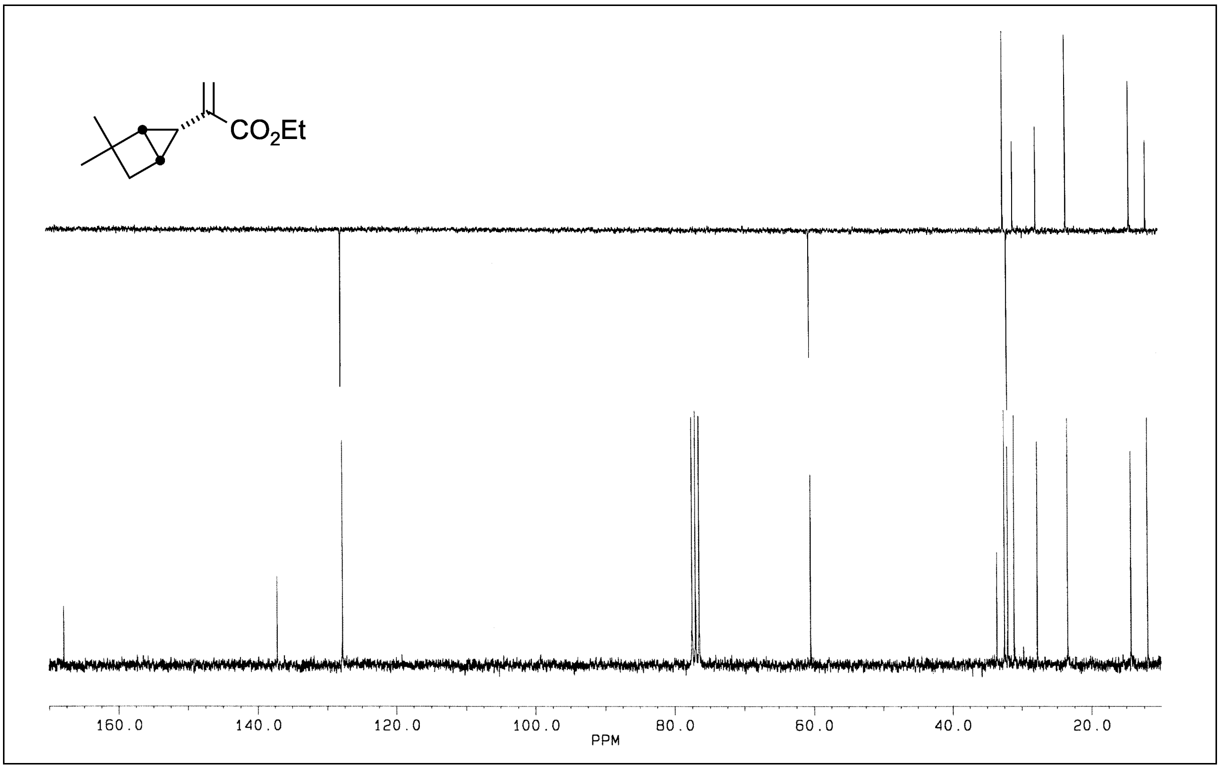
Ethyl *exo*-2-(bicyclo[3.1.0]hex-6-yl)propenoate (**134**)



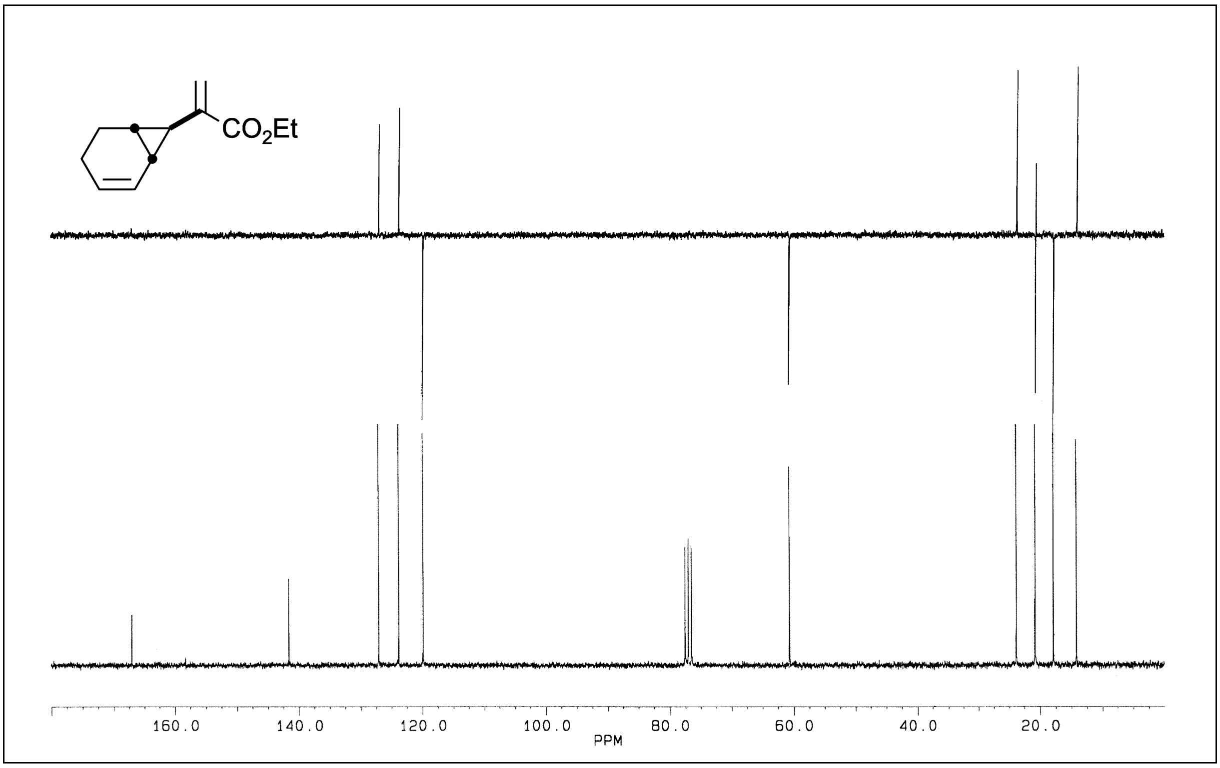
Ethyl *exo*-2-(bicyclo[4.1.0]hept-7-yl)propenoate (**136**)



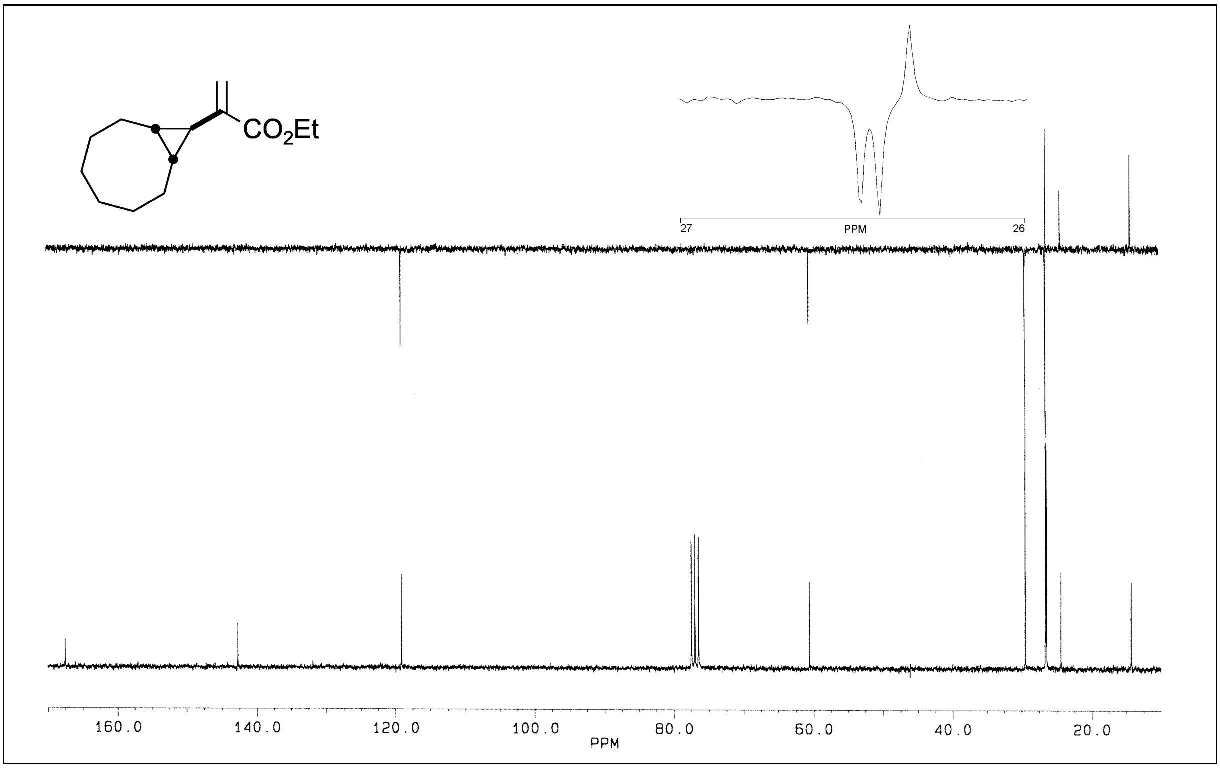
Ethyl *exo*-2-(2,2-dimethylbicyclo[2.1.0]pent-5-yl)propenoate (***exo*-137**)



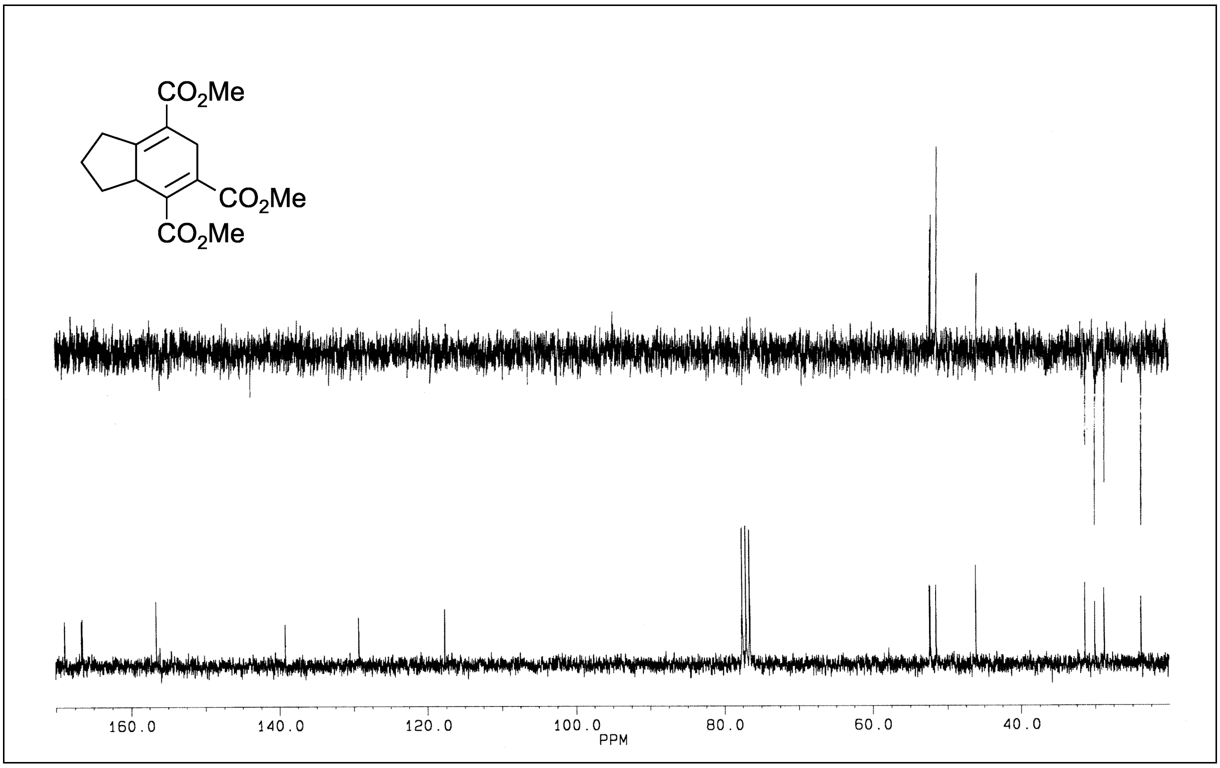
Ethyl *endo*-2-(2,2-dimethylbicyclo[2.1.0]pent-5-yl)propenoate (***endo*-137**)



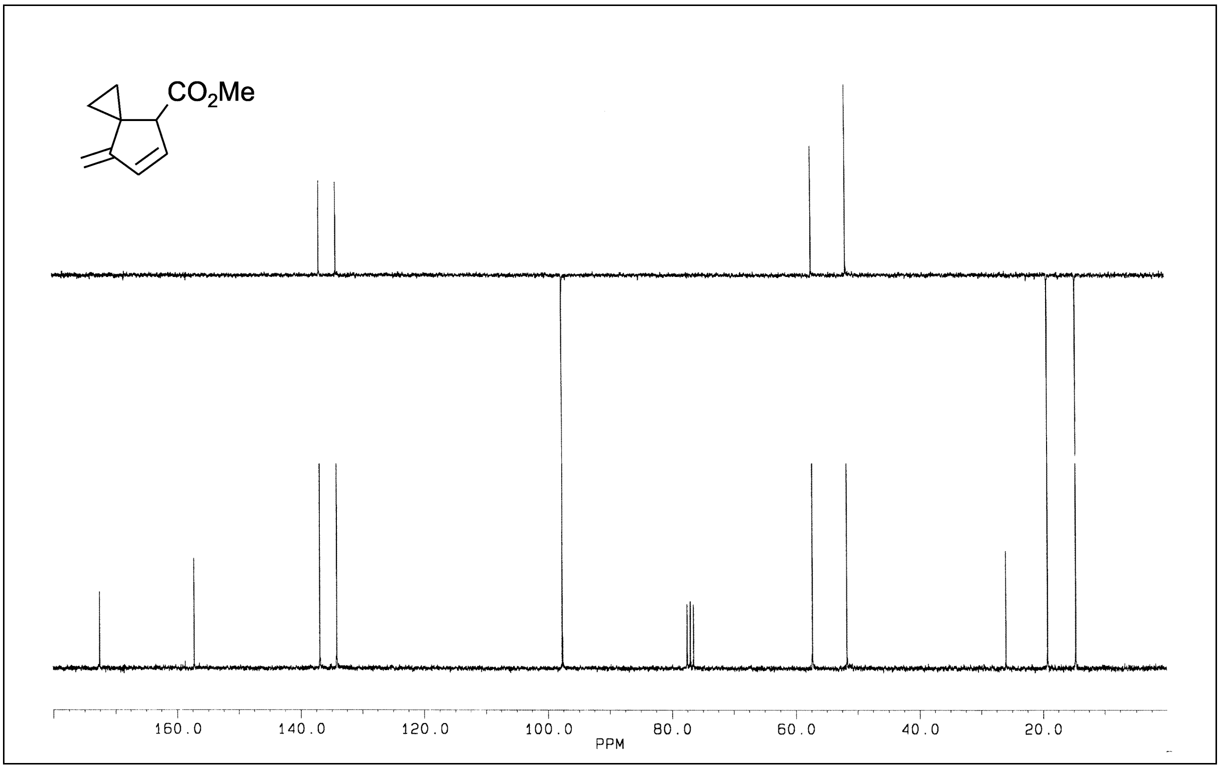
Ethyl *exo*-2-(bicyclo[4.1.0]hept-2-en-7-yl)propenoate (**138**)



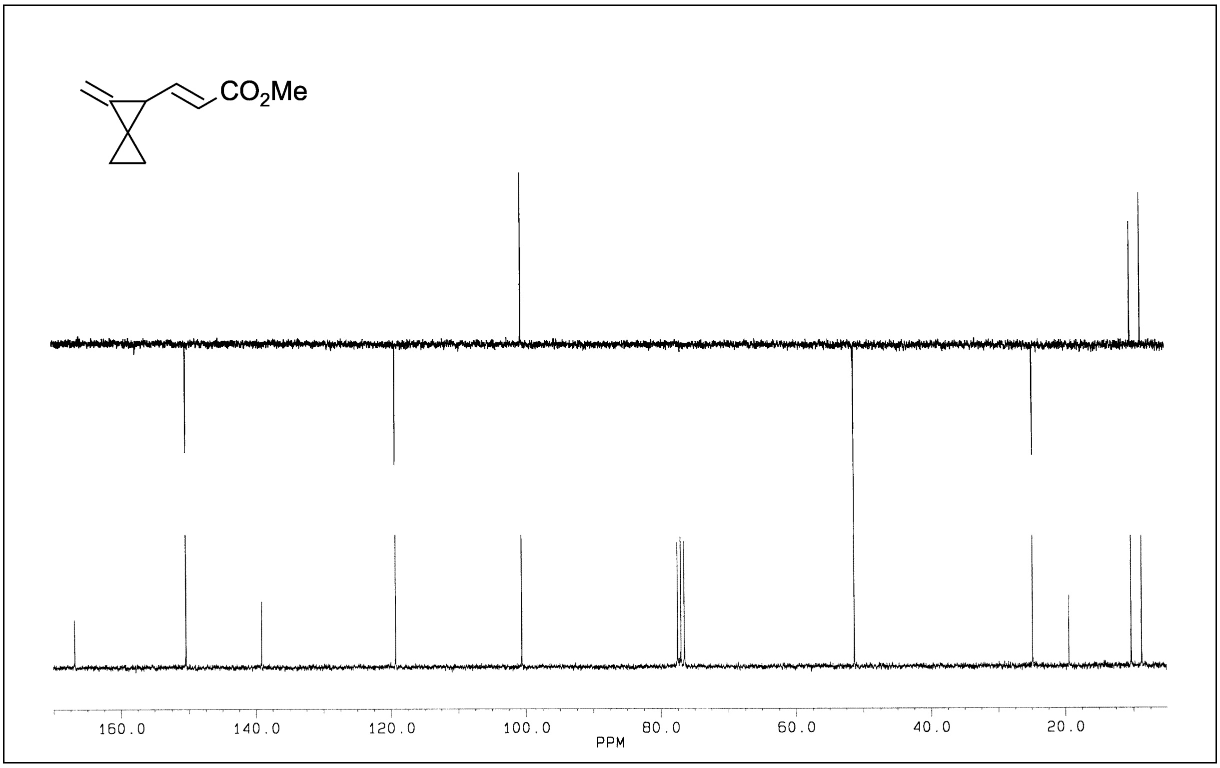
Ethyl *exo*-2-(bicyclo[6.1.0]non-9-yl)propenoate (**139**)



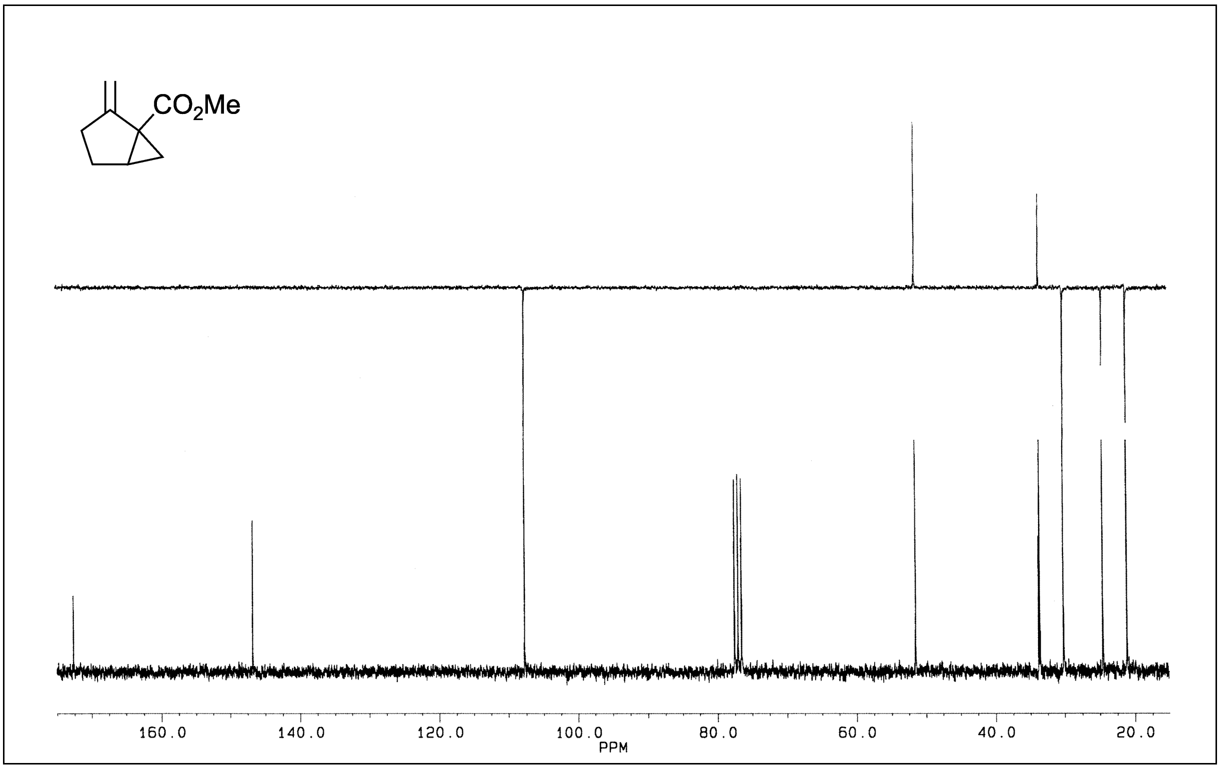
Trimethyl 2,3,3a,6-tetrahydro-1*H*-indene-4,5,7-tricarboxylate (**145**)



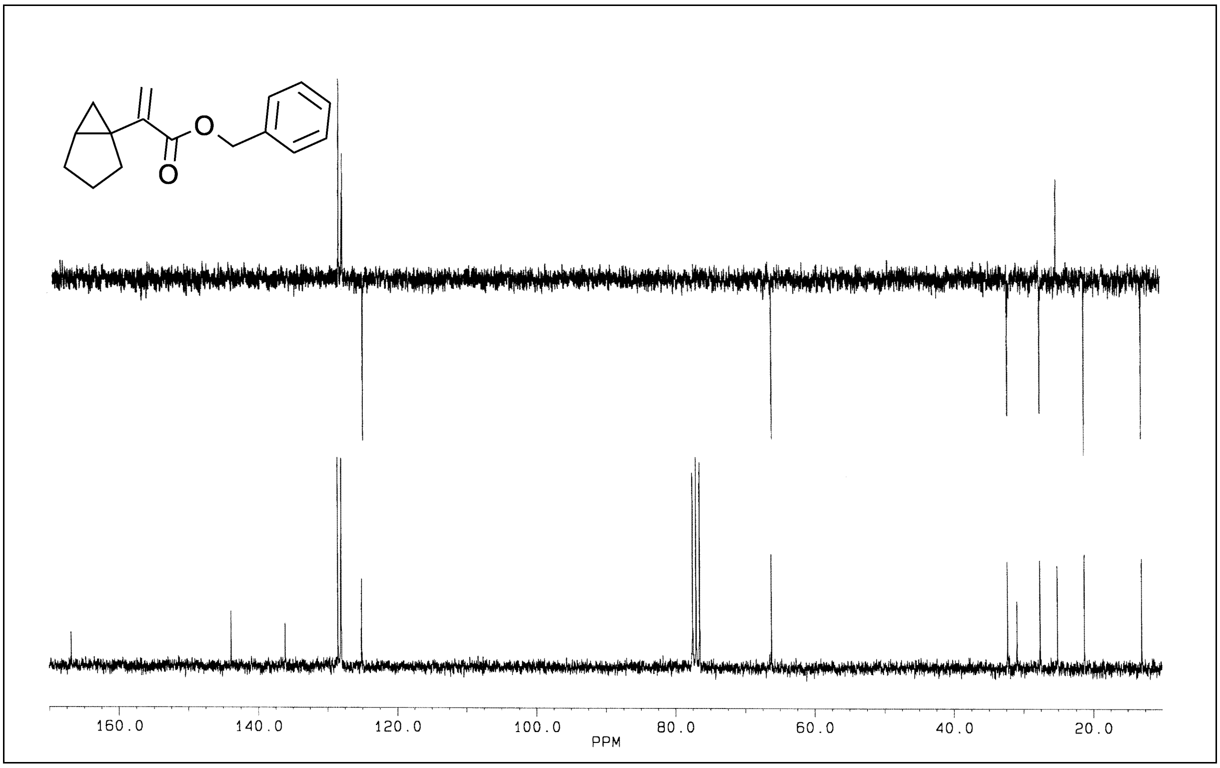
Methyl 7-methylenespiro[2.4]hept-5-ene-4-carboxylate (**147**)



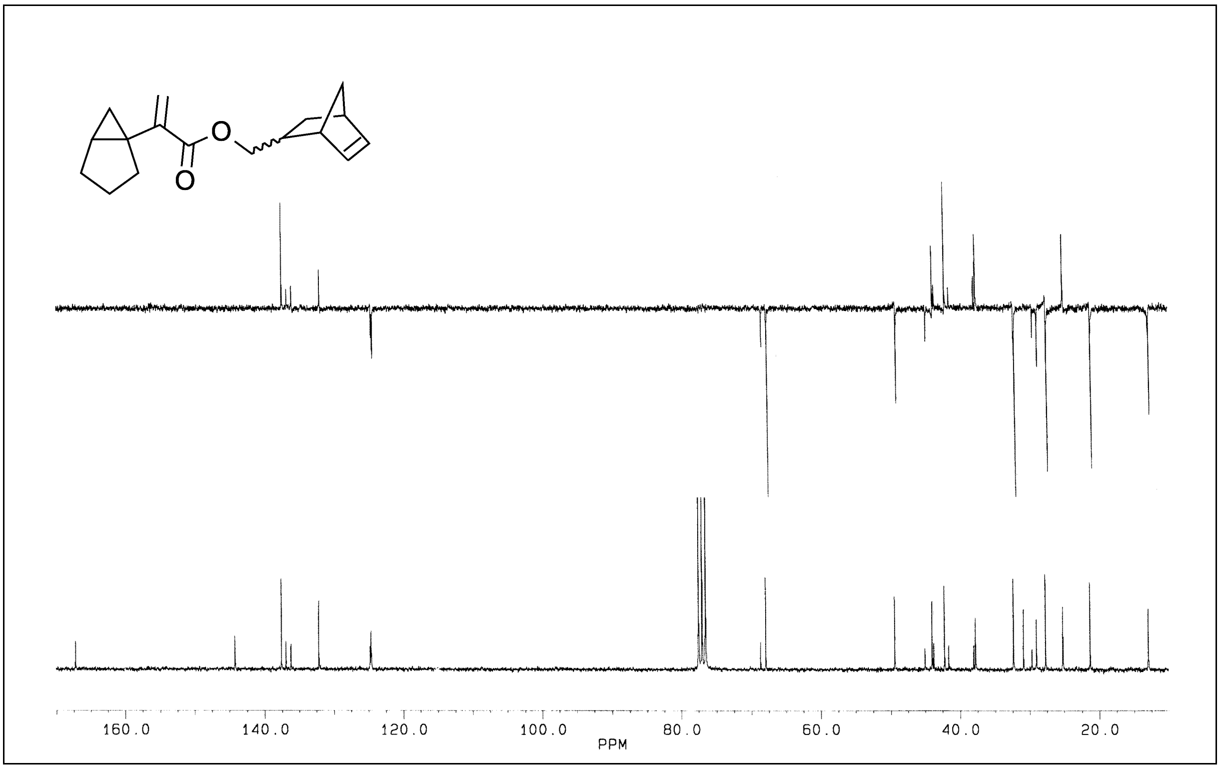
Methyl (E)-3-(2-methylenespiro[2.2]pent-1-yl)propenoate (**148**)



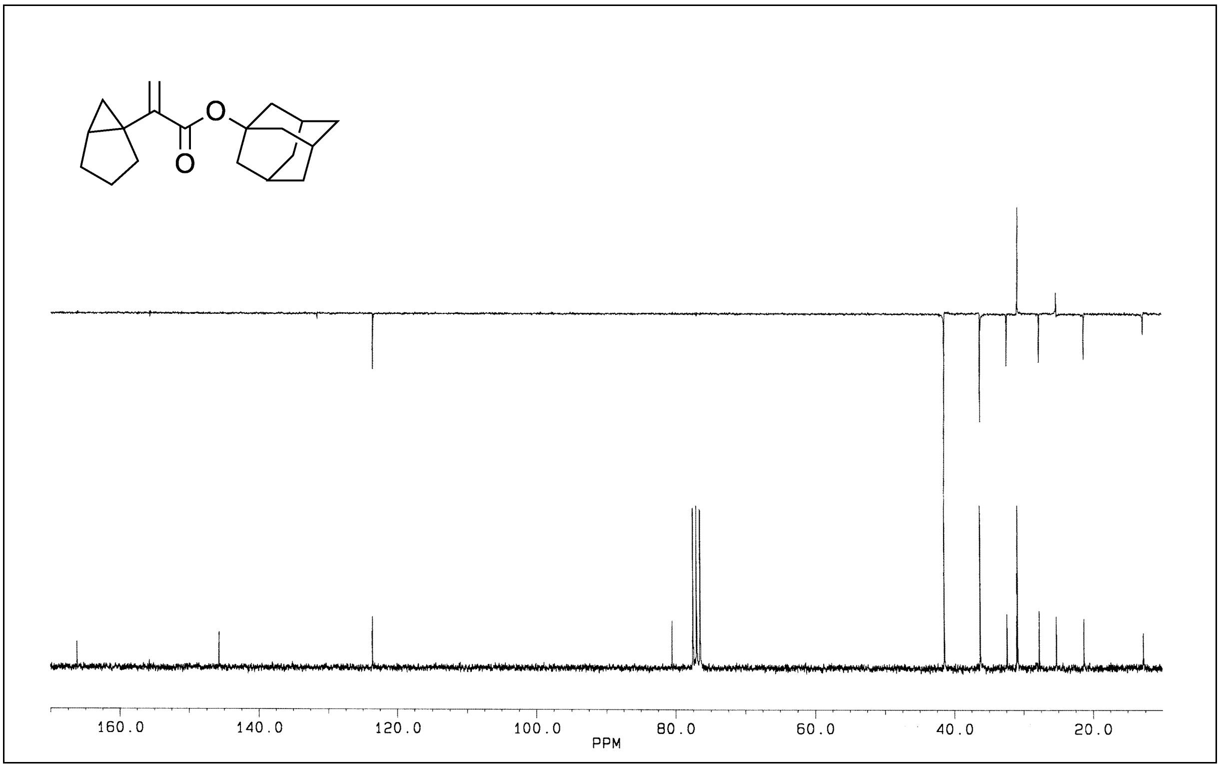
Methyl 2-methylenebicyclo[3.1.0]hexane-1-carboxylate (**156**)



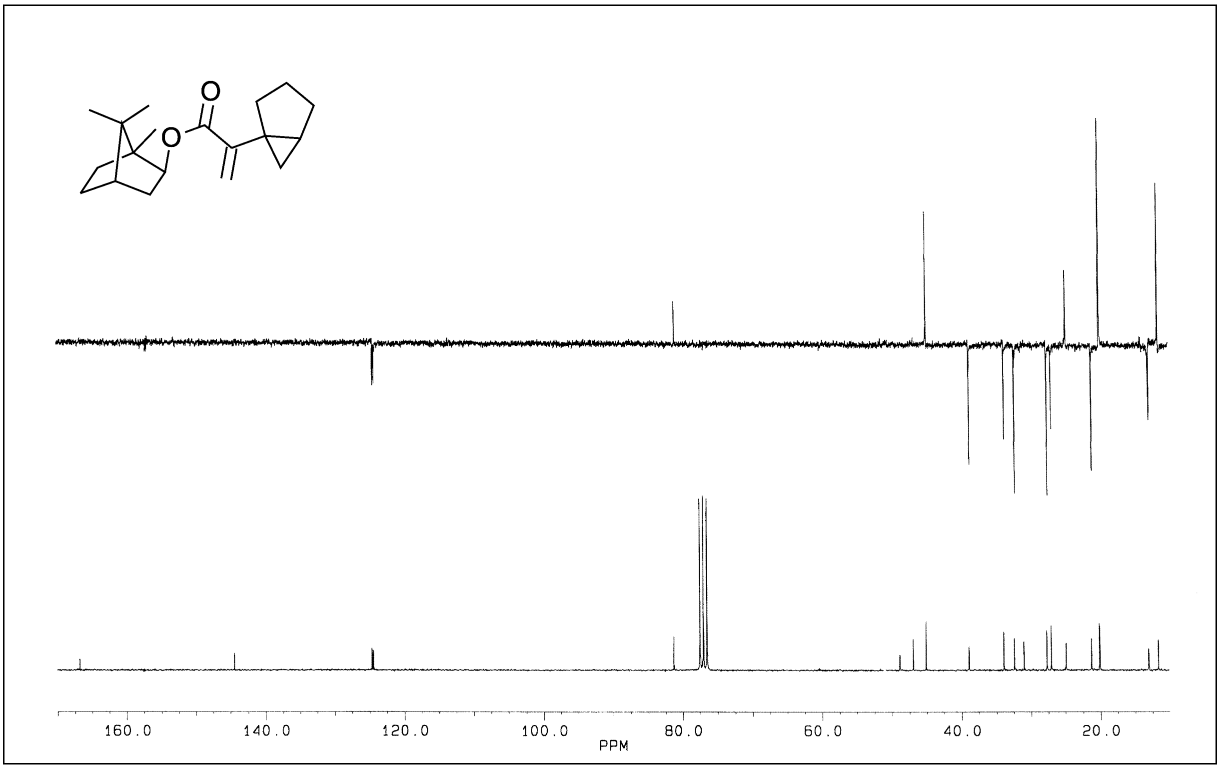
Benzyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**168**)



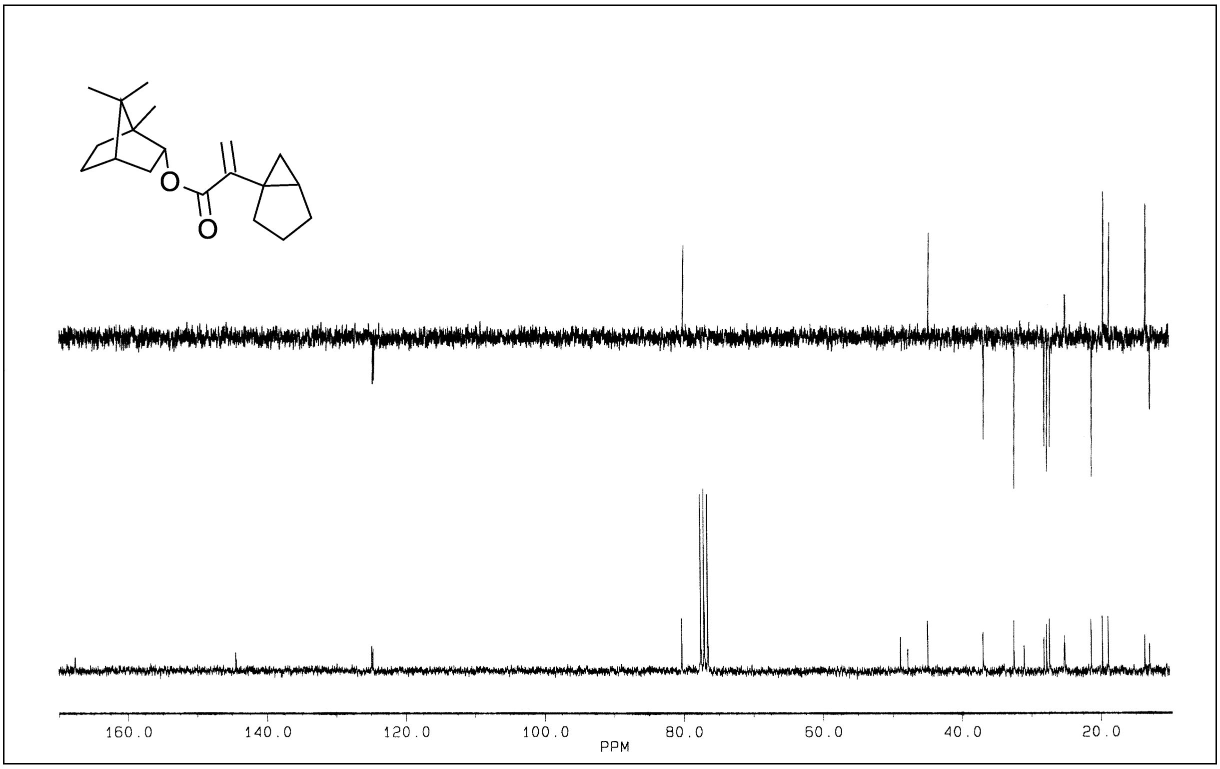
(Bicyclo[2.2.1]hept-5-en-2-yl)methyl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**169**)



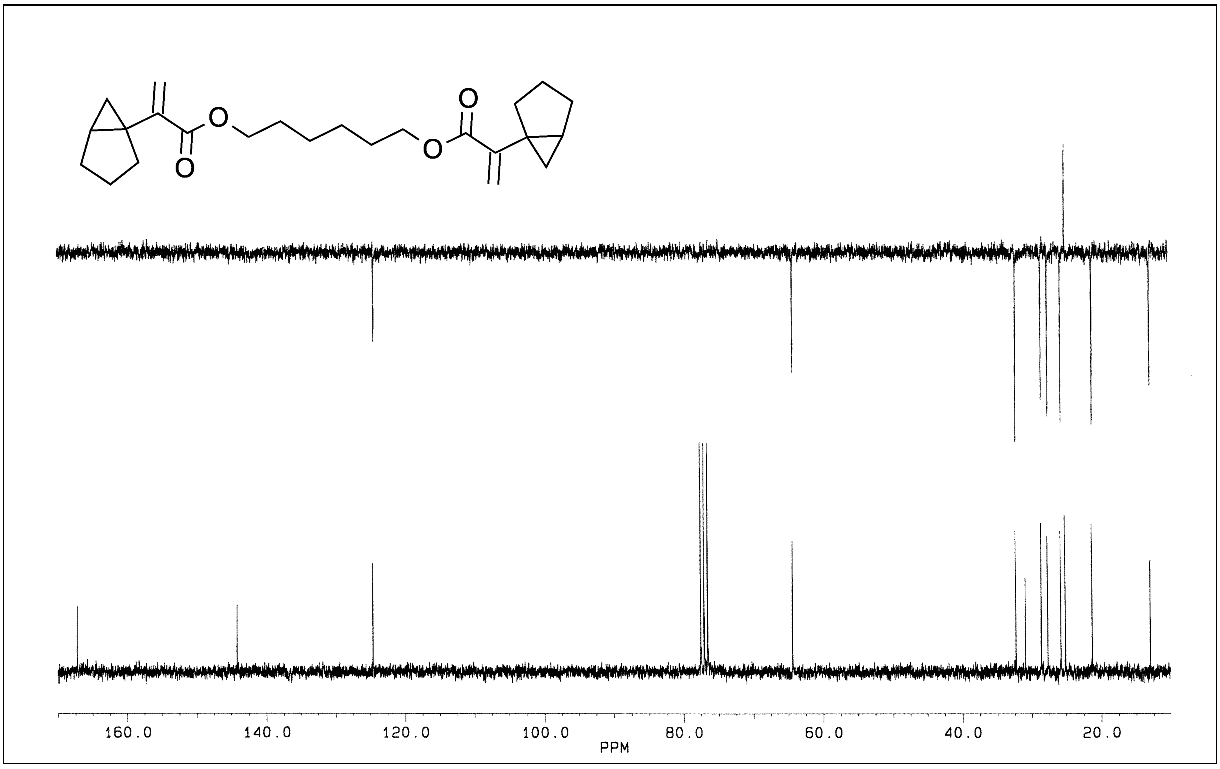
Adamant-1-yl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**170**)



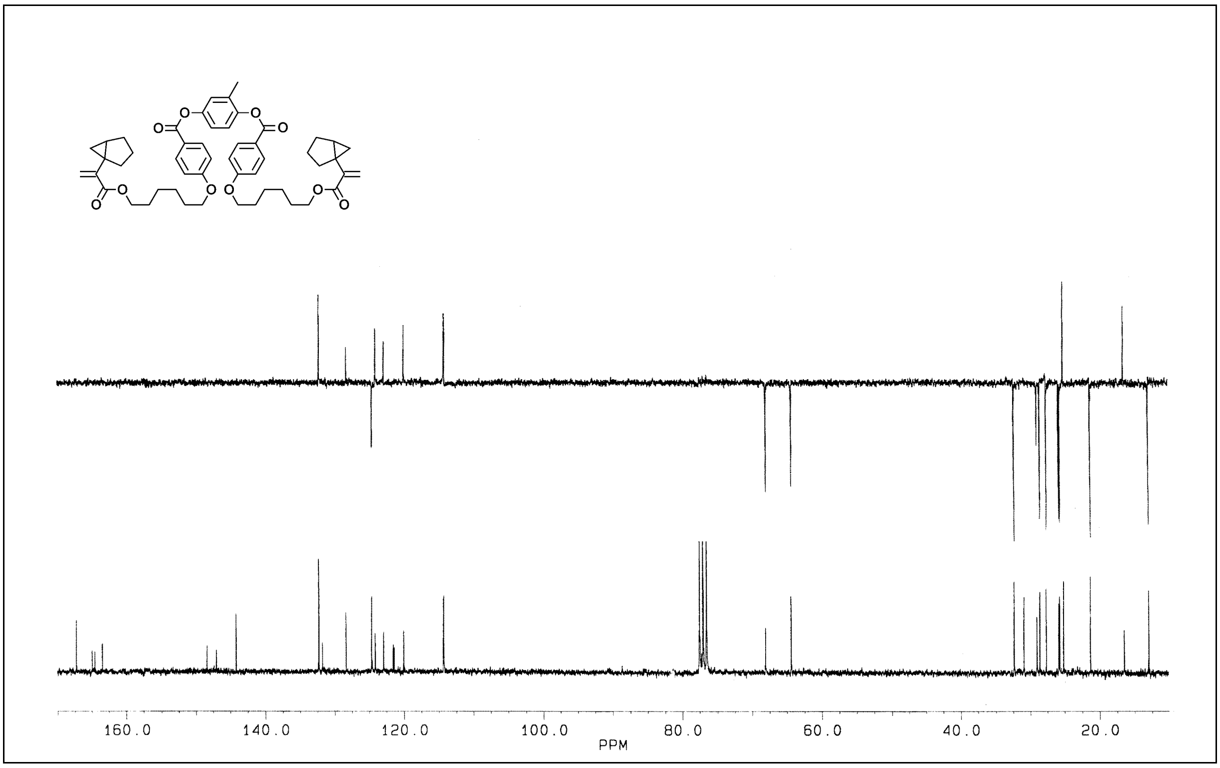
(*1R,S,2'S*)-*exo*-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**171**)



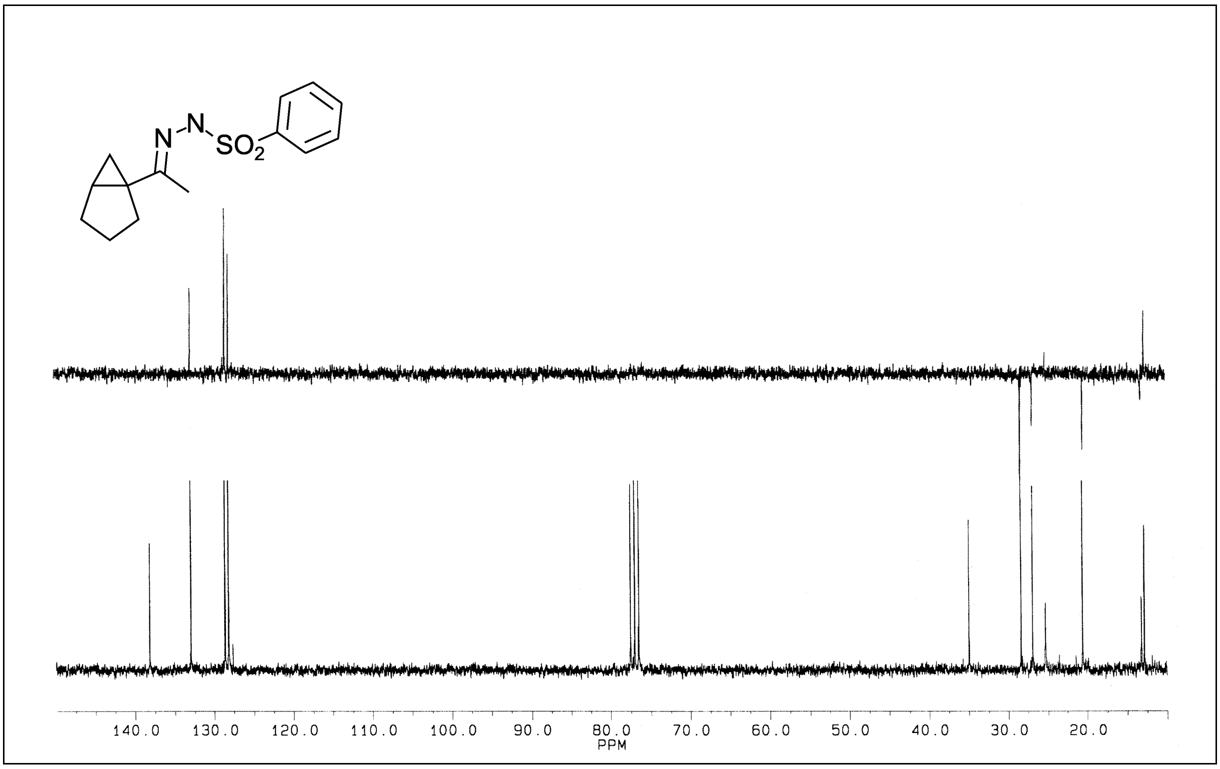
(*1R,S,2'R*)-*endo*-1,7,7-Trimethylbicyclo[2.2.1]hept-2-yl 2-(bicyclo[3.1.0]hex-1-yl)propenoate (**172**)



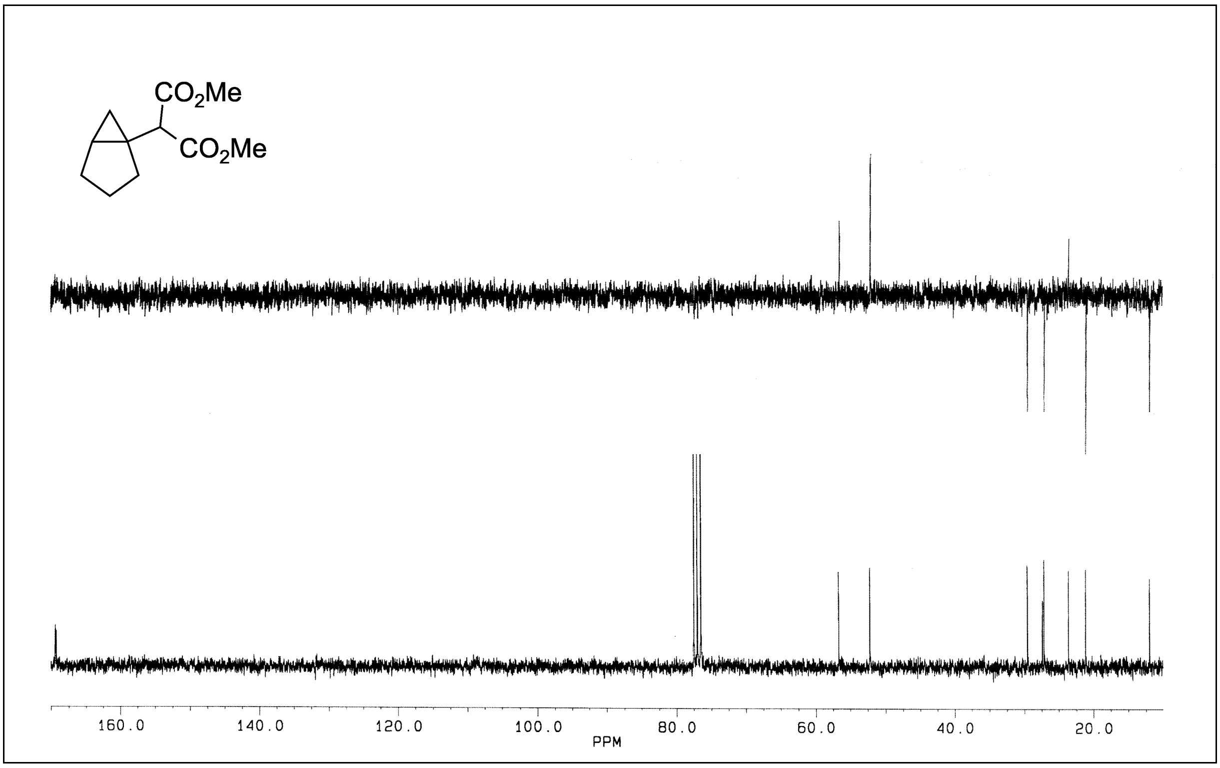
1,6-bis{2-(Bicyclo[3.1.0]hex-1-yl)propenoyloxy}hexane (**174**)



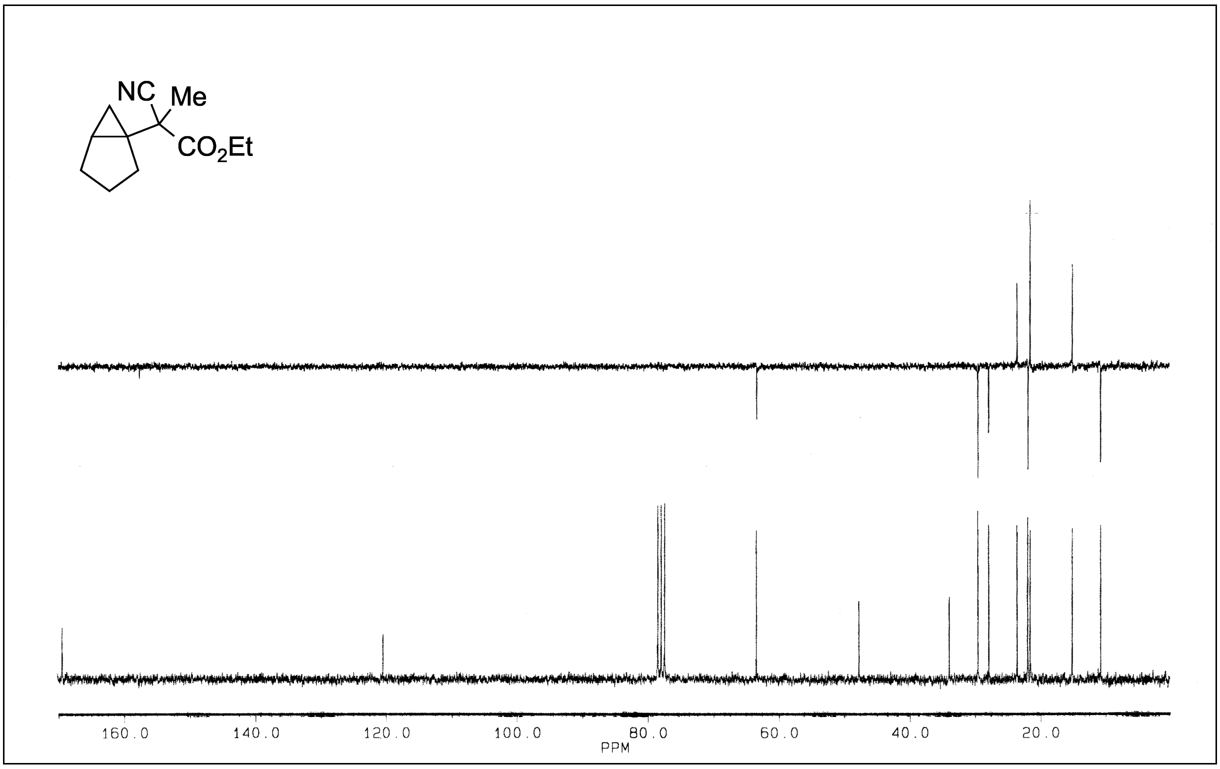
1,4-di-{4-[6-(2-(Bicyclo[3.1.0]hex-1-yl)propenoyloxy)hexyloxy]phenylcarbonyloxy}-2-methylbenzene (**175**)



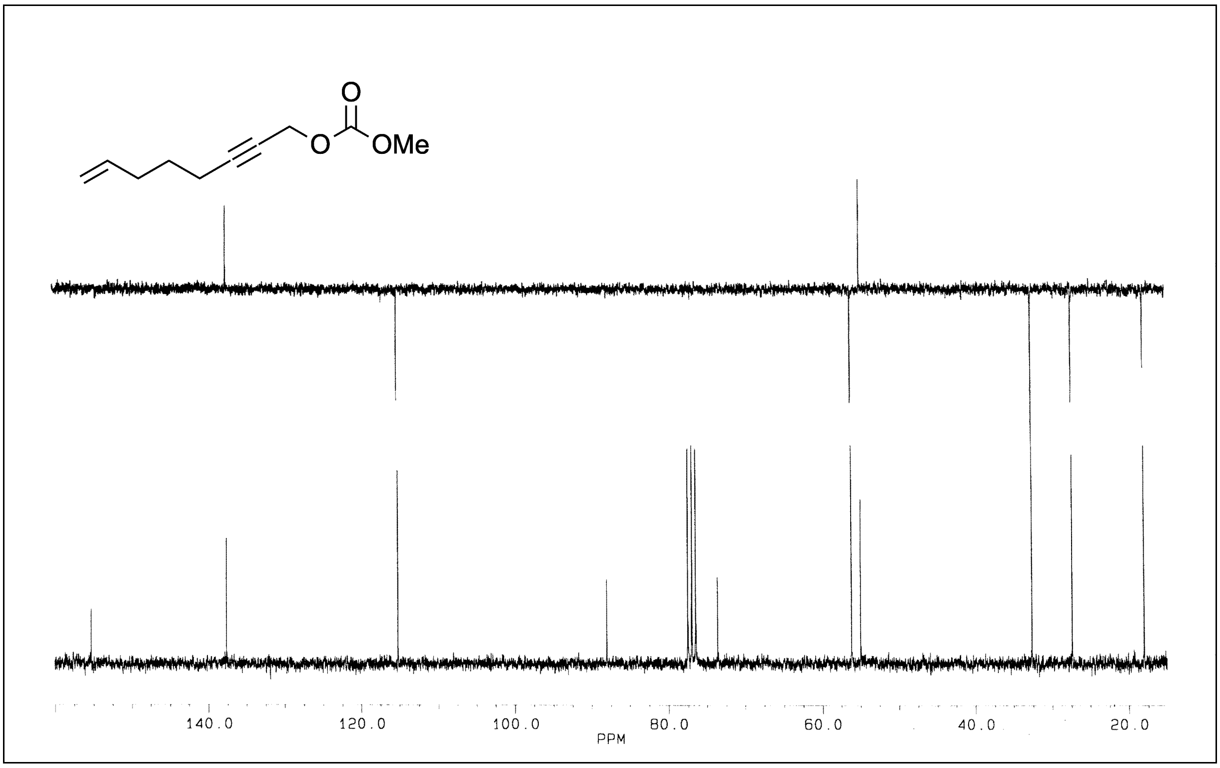
N'-[(*1E*)-1-Bicyclo[3.1.0]hex-1-ylethylidene]benzenesulfonohydrazide (**183**)



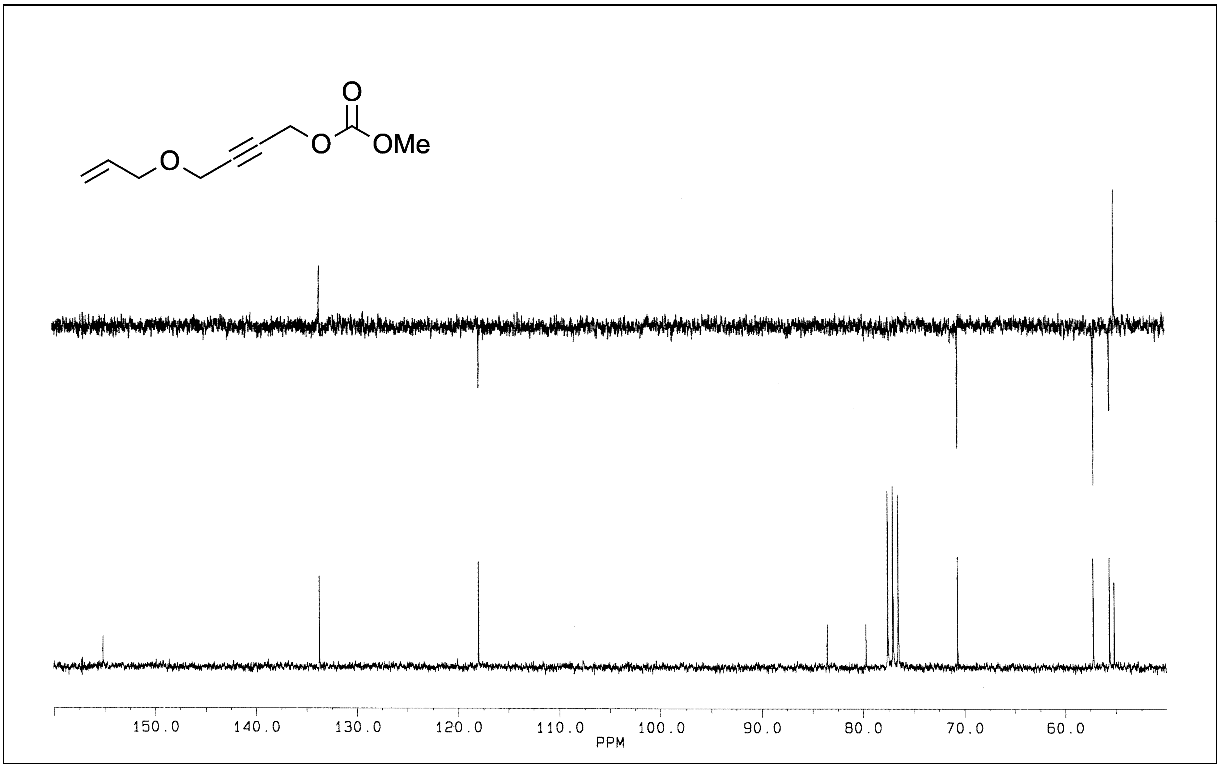
Dimethyl 2-(bicyclo[3.1.0]hexen-1-yl)malonate (**189**)



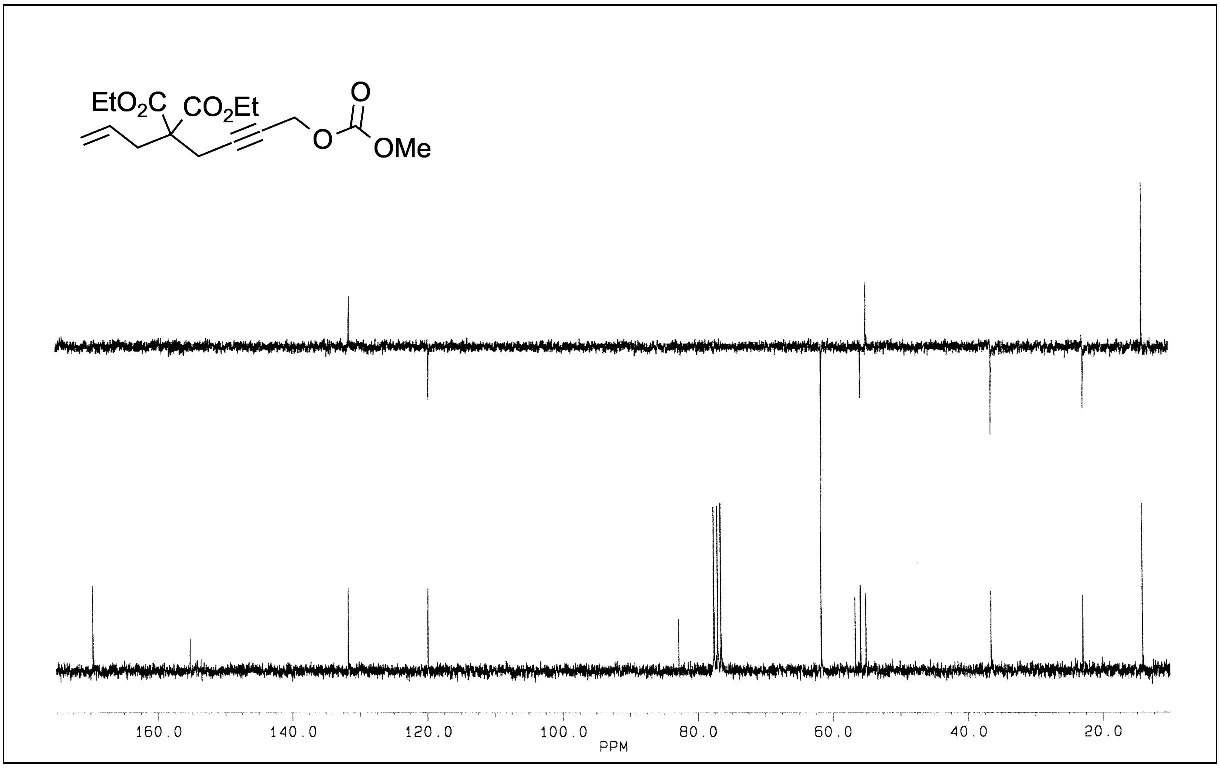
Ethyl 2-cyano-2-(bicyclo[3.1.0]hex-1-yl) propanoate (**195**), first diastereomer



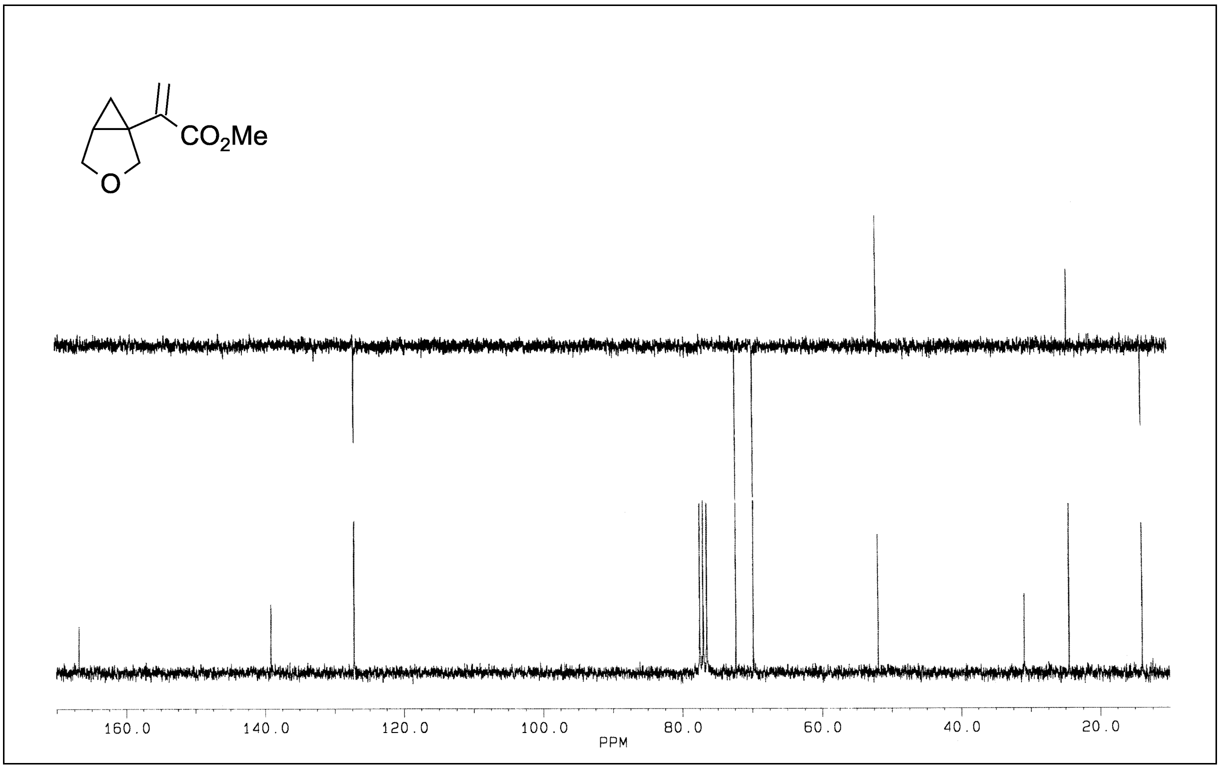
Methyl (oct-7-en-2-ynyl)carbonate (**196**)



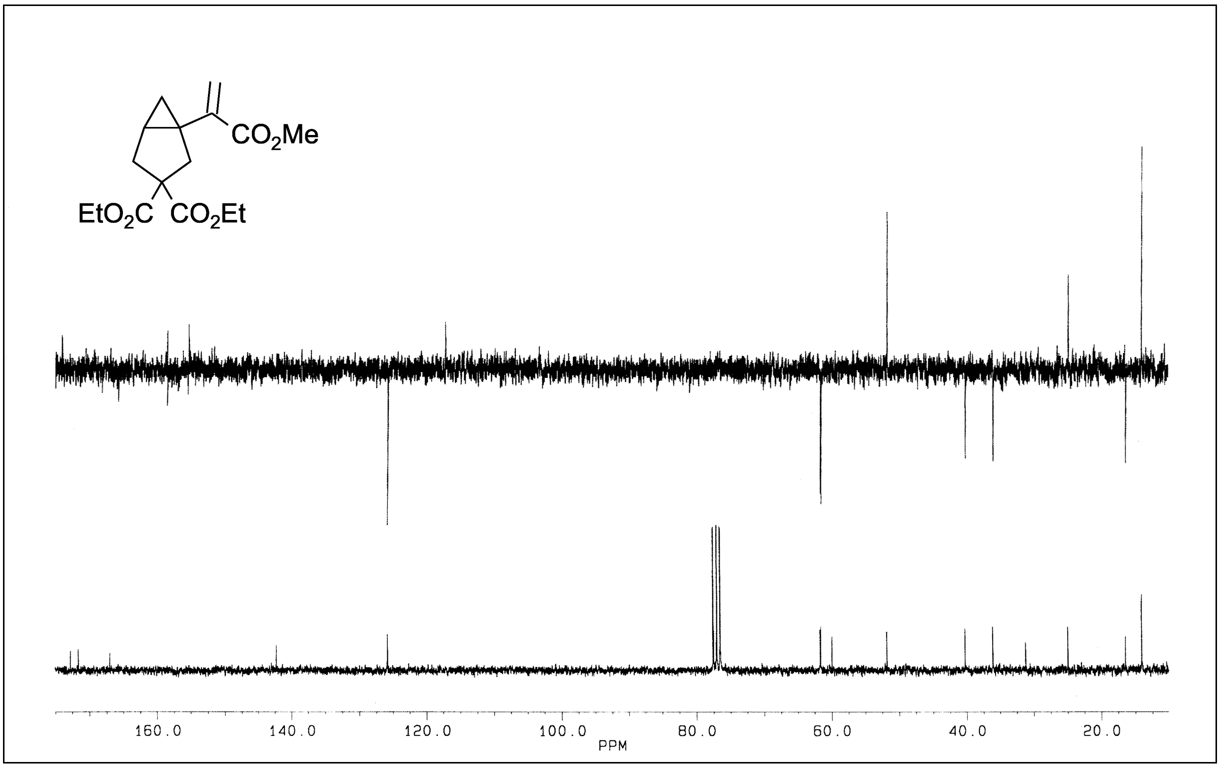
Methyl (5-oxa-oct-7-en-2-ynyl)carbonate (**201**)



Methyl [5,5-bis(ethoxycarbonyl)oct-7-en-2-ynyl]carbonate (**206**)



Methyl 2-(3-oxa-bicyclo[3.1.0]hex-1-yl)propenoate (**207**)



Methyl 2-{3,3-bis(ethoxycarbonyl)bicyclo[3.1.0]hex-1-yl}propenoate (**209**)

G. CRYSTAL DATA

1. *exo*-6-(Methoxycarbonyl)bicyclo[3.1.0]hexane-6-carboxylic acid (72)

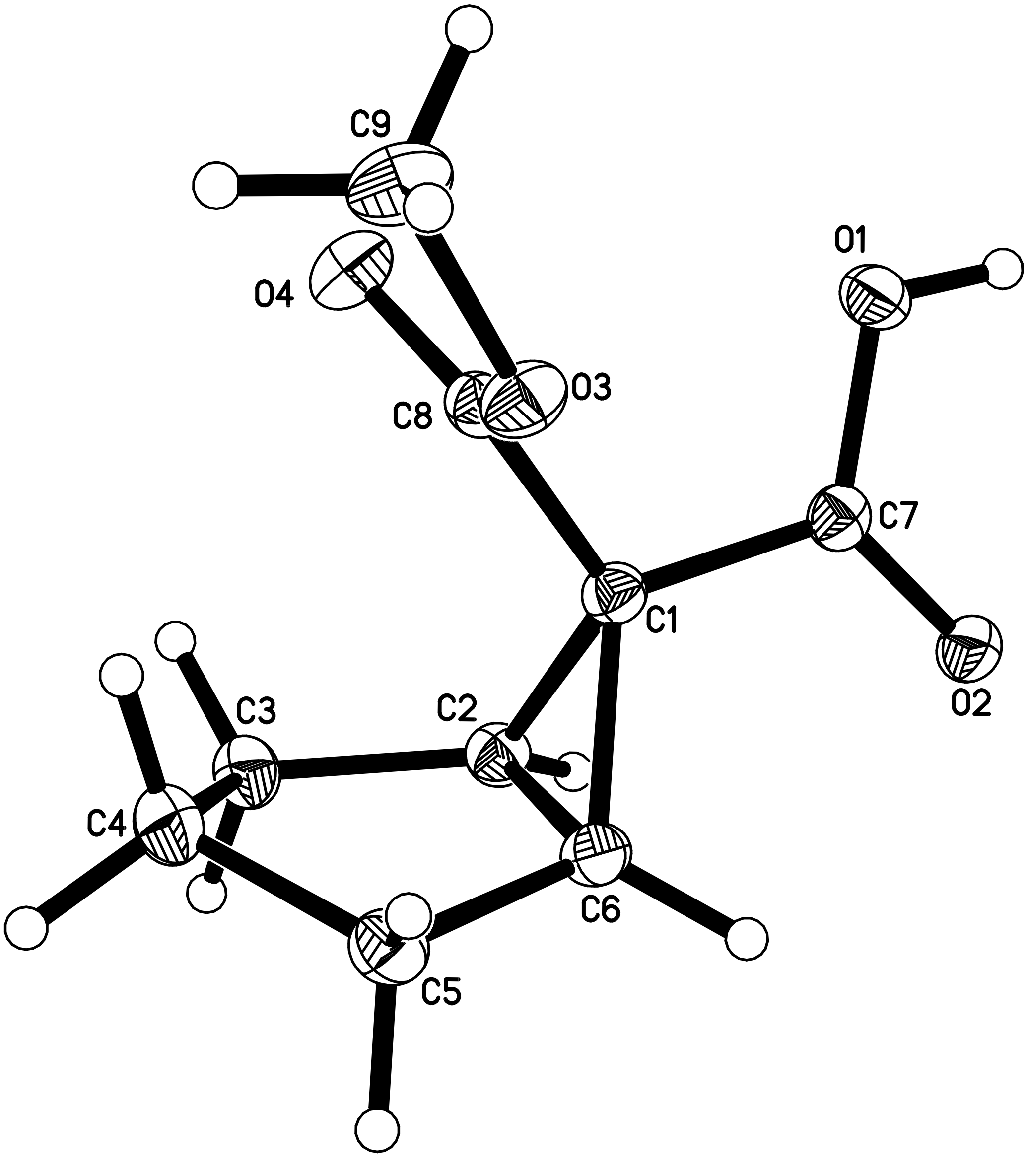


Table 1. Crystal data and structure refinement for **72**.

Empirical formula	$C_9H_{12}O_4$
Formula weight	184.19
Temperature	120(2) K
Wavelength	0.71073 Å
Crystal system	Monoclinic

Space group	$P2_1/n$	
Unit cell dimensions	a = 9.1290(2) Å	α = 90°
	b = 8.7002(2) Å	β = 109.28(1)°
	c = 11.6958(3) Å	γ = 90°
Volume	876.82(4) Å^3	
Z	4	
Density (calculated)	1.395 Mg/m^3	
Absorption coefficient	0.110 mm^{-1}	
F(000)	392	
Crystal size	0.20 × 0.12 × 0.10 mm^3	
θ-range for data collection	2.47 to 28.99°	
Index ranges	–12<=h<=12, –11<=k<=11, –15<=l<=15	
Reflections collected	7793	
Independent reflections	2315 [R_{int} = 0.0259]	
Completeness to θ = 28.99°	99.1%	
Absorption correction	Not applied	
Max. and min. transmission	0.9891 and 0.9783	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2315 / 0 / 166	
Goodness-of-fit on F^2	1.057	
Final R indices [I>2sigma(I)]	R_1 = 0.0357, wR_2 = 0.0930	
R indices (all data)	R_1 = 0.0414, wR_2 = 0.0961	
Largest diff. peak and hole	0.395 and –0.220 eÅ^{-3}	

Table 2. Atomic coordinates (× 10^4) and equivalent isotropic displacement parameters (Å^2 × 10^3) for **72**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
O(1)	5693(1)	8181(1)	678(1)	19(1)
O(2)	4334(1)	10082(1)	1156(1)	18(1)
O(3)	4849(1)	5378(1)	2168(1)	18(1)
O(4)	7327(1)	6176(1)	2935(1)	21(1)
C(1)	5260(1)	8022(1)	2545(1)	14(1)
C(2)	5719(1)	9084(1)	3653(1)	16(1)
C(3)	6568(1)	8367(1)	4873(1)	19(1)
C(4)	5584(1)	6963(1)	4971(1)	21(1)
C(5)	3919(1)	7318(1)	4130(1)	20(1)
C(6)	4104(1)	8433(1)	3191(1)	16(1)
C(7)	5043(1)	8858(1)	1394(1)	15(1)
C(8)	5958(1)	6448(1)	2592(1)	15(1)
C(9)	5434(1)	3841(1)	2092(1)	24(1)

Table 3.Anisotropic displacement parameters (Å^2 × 10^3) for **72**. The anisotropic displacement

factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + \ldots + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	26(1)	18(1)	16(1)	2(1)	10(1)	4(1)
O(2)	19(1)	17(1)	18(1)	4(1)	7(1)	4(1)
O(3)	17(1)	14(1)	23(1)	–3(1)	6(1)	0(1)
O(4)	17(1)	18(1)	29(1)	2(1)	7(1)	2(1)
C(1)	15(1)	13(1)	16(1)	0(1)	6(1)	1(1)
C(2)	17(1)	14(1)	16(1)	–1(1)	6(1)	0(1)
C(3)	20(1)	22(1)	16(1)	0(1)	4(1)	0(1)
C(4)	23(1)	22(1)	19(1)	5(1)	8(1)	1(1)
C(5)	20(1)	20(1)	21(1)	2(1)	9(1)	–1(1)
C(6)	15(1)	16(1)	18(1)	0(1)	7(1)	1(1)
C(7)	13(1)	15(1)	15(1)	–1(1)	3(1)	–1(1)
C(8)	17(1)	14(1)	14(1)	1(1)	7(1)	0(1)
C(9)	25(1)	14(1)	32(1)	–5(1)	11(1)	1(1)

Table 4. Selected bond lengths [Å] and angles [°] for **72**.

O(1)-C(7)	1.315(1)	C(1)-C(7)	1.485(1)	C(2)-C(3)	1.514(1)
O(2)-C(7)	1.229(1)	C(1)-C(8)	1.504(1)	C(3)-C(4)	1.543(1)
O(3)-C(8)	1.343(1)	C(1)-C(6)	1.528(1)	C(4)-C(5)	1.545(1)
O(3)-C(9)	1.453(1)	C(1)-C(2)	1.533(1)	C(5)-C(6)	1.517(1)
O(4)-C(8)	1.203(1)	C(2)-C(6)	1.503(1)		

C(7)-O(1)-H(1O)	108.3(11)	C(3)-C(4)-C(5)	105.58(8)
C(8)-O(3)-C(9)	114.41(8)	C(6)-C(5)-C(4)	105.54(8)
C(7)-C(1)-C(8)	114.02(8)	C(2)-C(6)-C(5)	108.11(8)
C(7)-C(1)-C(6)	115.24(8)	C(2)-C(6)-C(1)	60.73(6)
C(8)-C(1)-C(6)	123.24(8)	C(5)-C(6)-C(1)	117.93(8)
C(7)-C(1)-C(2)	112.89(8)	O(2)-C(7)-O(1)	123.98(9)
C(8)-C(1)-C(2)	121.55(8)	O(2)-C(7)-C(1)	122.12(9)
C(6)-C(1)-C(2)	58.82(6)	O(1)-C(7)-C(1)	113.89(8)
C(6)-C(2)-C(3)	108.67(8)	O(4)-C(8)-O(3)	124.06(9)
C(6)-C(2)-C(1)	60.45(6)	O(4)-C(8)-C(1)	124.87(9)
C(3)-C(2)-C(1)	117.42(8)	O(3)-C(8)-C(1)	111.05(8)
C(2)-C(3)-C(4)	105.48(8)		

Table 5. Hydrogen coordinates (× 10^4) and isotropic displacement parameters ($Å^2$ × 10^3) for **72**.

Atom	x	y	z	U(eq)
H(1O)	5571(19)	8779(19)	41(18)	45(4)
H(2)	5925(13)	10142(14)	3498(12)	17(3)
H(31)	6611(15)	9116(16)	5507(14)	28(3)
H(32)	7641(16)	8085(14)	4976(12)	22(3)
H(41)	5621(16)	6776(17)	5811(14)	32(4)
H(42)	5989(14)	6017(15)	4717(12)	21(3)
H(51)	3315(15)	7849(14)	4607(12)	23(3)
H(52)	3327(15)	6383(15)	3752(12)	24(3)
H(6)	3215(15)	9056(15)	2706(12)	21(3)
H(91)	6165(16)	3547(17)	2865(14)	29(4)
H(92)	4548(16)	3188(17)	1882(13)	31(4)
H(93)	5964(15)	3841(15)	1523(13)	25(3)

Table 6. Torsion angles [°] for **72**.

C(7)-C(1)-C(2)-C(6)	106.59(9)	C(8)-C(1)-C(6)-C(5)	13.46(14)
C(8)-C(1)-C(2)-C(6)	–112.35(10)	C(2)-C(1)-C(6)-C(5)	–96.09(10)
C(7)-C(1)-C(2)-C(3)	–156.50(8)	C(8)-C(1)-C(7)-O(2)	171.84(8)
C(8)-C(1)-C(2)-C(3)	–15.43(12)	C(6)-C(1)-C(7)-O(2)	20.96(13)
C(6)-C(1)-C(2)-C(3)	96.91(9)	C(2)-C(1)-C(7)-O(2)	–44.06(12)
C(6)-C(2)-C(3)-C(4)	14.87(10)	C(8)-C(1)-C(7)-O(1)	–9.08(12)
C(1)-C(2)-C(3)-C(4)	–50.85(11)	C(6)-C(1)-C(7)-O(1)	–159.95(8)
C(2)-C(3)-C(4)-C(5)	–24.63(11)	C(2)-C(1)-C(7)-O(1)	135.02(8)
C(3)-C(4)-C(5)-C(6)	25.21(11)	C(9)-O(3)-C(8)-O(4)	–3.02(14)
C(3)-C(2)-C(6)-C(5)	0.89(11)	C(9)-O(3)-C(8)-C(1)	175.28(9)
C(1)-C(2)-C(6)-C(5)	112.44(9)	C(7)-C(1)-C(8)-O(4)	88.30(12)
C(3)-C(2)-C(6)-C(1)	–111.55(9)	C(6)-C(1)-C(8)-O(4)	–123.46(11)
C(4)-C(5)-C(6)-C(2)	–16.28(10)	C(2)-C(1)-C(8)-O(4)	–52.36(13)
C(4)-C(5)-C(6)-C(1)	49.59(12)	C(7)-C(1)-C(8)-O(3)	–89.98(10)
C(7)-C(1)-C(6)-C(2)	–102.56(9)	C(6)-C(1)-C(8)-O(3)	58.26(12)
C(8)-C(1)-C(6)-C(2)	109.55(10)	C(2)-C(1)-C(8)-O(3)	129.35(9)
C(7)-C(1)-C(6)-C(5)	161.35(9)		

Table 7. Hydrogen bonds for **72** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...O(2)#1	0.885(19)	1.74(2)	2.6175(11)	170.4(16)

Symmetry transformations used to generate equivalent atoms: #1 –x+1, –y+2, –z

2. Methyl (R^*,S^*)-2-methylenecyclopropylhydroxyacetate (84).

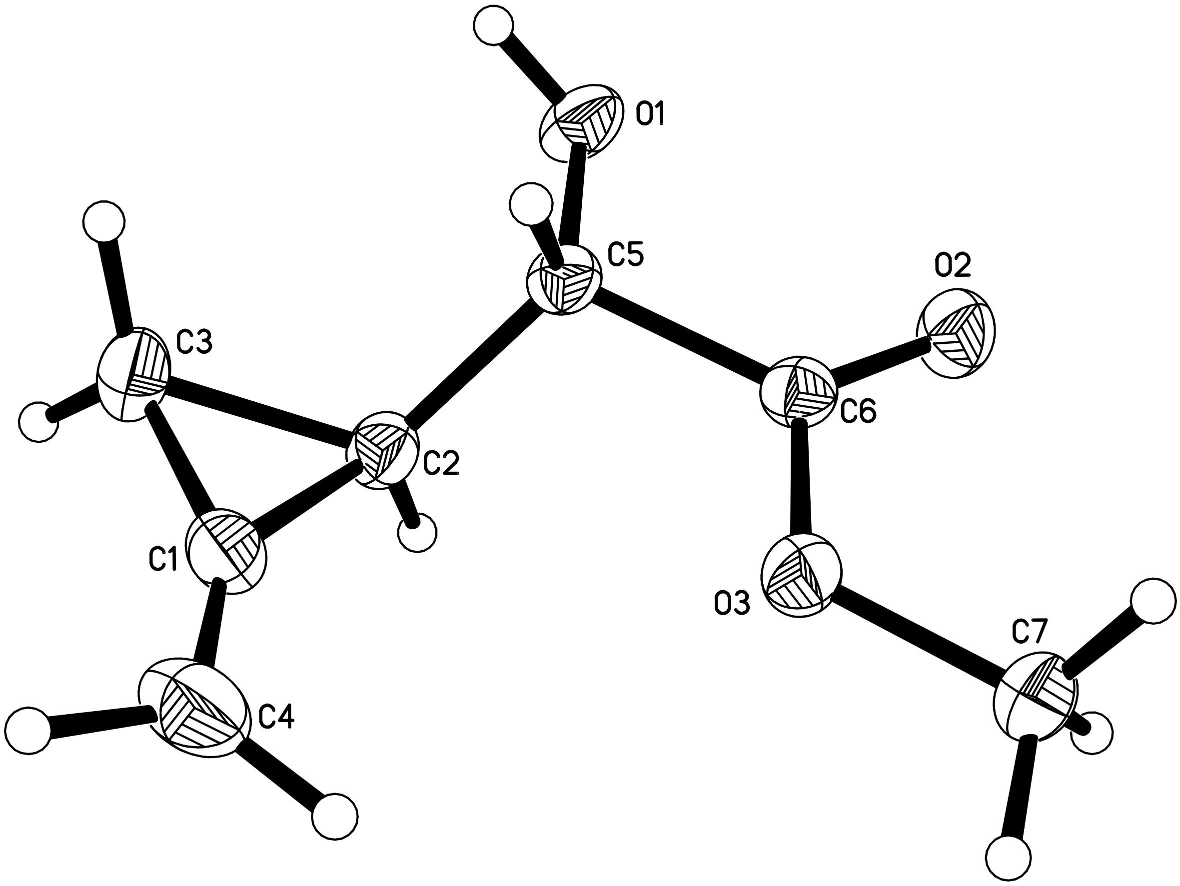


Table 1. Crystal data and structure refinement for **84**.

Empirical formula	$C_7 H_{10} O_3$	
Formula weight	142.15	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 7.2608(2) Å	α = 90°.
	b = 5.0643(2) Å	β = 92.89(1)°.
	c = 19.9397(6) Å	γ = 90°.
Volume	732.27(4) $Å^3$	
Z	4	
Density (calculated)	1.289 Mg/m^3	
Absorption coefficient	0.101 mm^{-1}	

F(000)	304
Crystal size	0.64 x 0.22 x 0.12 mm^3
θ-range for data collection	2.05 to 29.49°.
Index ranges	–10<=h<=9, –6<=k<=7, –27<=l<=27
Reflections collected	7561
Independent reflections	2017 [R_{int} = 0.0167]
Completeness to θ = 29.49°	99.7%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9880 and 0.9384
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2017 / 0 / 131
Goodness-of-fit on F^2	1.030
Final R indices [$I>2\sigma(I)$]	R_1 = 0.0346, wR_2 = 0.0999
R indices (all data)	R_1 = 0.0374, wR_2 = 0.1035
Largest diff. peak and hole	0.326 and –0.297 eÅ^{-3}

Table 2. Atomic coordinates (× 10^4) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **84**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
O(1)	278(1)	6625(1)	2231(1)	26(1)
O(2)	3283(1)	9580(1)	2231(1)	27(1)
O(3)	4506(1)	7101(1)	1430(1)	24(1)
C(1)	1526(1)	3216(2)	683(1)	26(1)
C(2)	883(1)	5414(2)	1088(1)	22(1)
C(3)	–327(1)	2971(2)	935(1)	30(1)
C(4)	2889(2)	2172(2)	365(1)	36(1)
C(5)	1645(1)	5730(1)	1805(1)	19(1)
C(6)	3217(1)	7718(2)	1855(1)	19(1)
C(7)	6119(1)	8784(2)	1462(1)	29(1)

Table 3. Bond lengths [Å] and angles [°] for **84**.

O(1)-C(5)	1.4133(9)	C(1)-C(3)	1.465(1)
O(2)-C(6)	1.204(1)	C(1)-C(2)	1.465(1)
O(3)-C(6)	1.3311(9)	C(2)-C(5)	1.516(1)
O(3)-C(7)	1.447(1)	C(2)-C(3)	1.539(1)
C(1)-C(4)	1.313(1)		

C(6)-O(3)-C(7)	115.29(7)	C(1)-C(3)-C(2)	58.31(6)
C(4)-C(1)-C(3)	149.20(9)	O(1)-C(5)-C(2)	111.54(6)
C(4)-C(1)-C(2)	147.23(9)	O(1)-C(5)-C(6)	107.19(6)
C(3)-C(1)-C(2)	63.37(6)	C(2)-C(5)-C(6)	111.61(6)
C(1)-C(2)-C(5)	119.26(7)	O(2)-C(6)-O(3)	124.93(7)
C(1)-C(2)-C(3)	58.32(6)	O(2)-C(6)-C(5)	124.42(7)
C(5)-C(2)-C(3)	116.68(7)	O(3)-C(6)-C(5)	110.64(6)

Table 4. Anisotropic displacement parameters ($Å^2 \times 10^3$) for **84**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2}U^{11} + \ldots + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	29(1)	20(1)	32(1)	–3(1)	14(1)	–3(1)
O(2)	29(1)	21(1)	30(1)	–6(1)	4(1)	–3(1)
O(3)	20(1)	29(1)	24(1)	–4(1)	4(1)	–4(1)
C(1)	35(1)	23(1)	20(1)	–1(1)	–1(1)	–3(1)
C(2)	23(1)	19(1)	23(1)	1(1)	0(1)	–2(1)
C(3)	32(1)	27(1)	32(1)	–1(1)	–2(1)	–10(1)
C(4)	50(1)	33(1)	25(1)	–4(1)	6(1)	3(1)
C(5)	23(1)	16(1)	20(1)	0(1)	4(1)	–1(1)
C(6)	21(1)	18(1)	19(1)	2(1)	1(1)	1(1)
C(7)	21(1)	39(1)	28(1)	0(1)	2(1)	–7(1)

Table 5. Hydrogen coordinates ($\times 10^4$) and isotropic displacement parameters ($Å^2 \times 10^3$) for **84**.

Atom	x	y	z	U(eq)
H(1O)	–230(20)	5290(30)	2360(7)	45(4)
H(2)	465(16)	7070(30)	873(6)	30(3)
H(31)	–516(17)	1810(30)	1300(7)	34(3)
H(32)	–1359(19)	3150(30)	627(7)	41(3)
H(41)	2780(20)	470(30)	157(7)	47(4)
H(42)	4020(20)	3160(30)	320(7)	52(4)
H(5)	2174(15)	4060(20)	1959(5)	21(2)
H(71)	5820(20)	10610(30)	1420(7)	45(4)
H(72)	6800(20)	8340(30)	1071(7)	43(4)
H(73)	6820(20)	8450(30)	1860(7)	45(4)

Table 6. Torsion angles [°] for **84**.

C(4)-C(1)-C(2)-C(5)	–70.12(17)	C(3)-C(2)-C(5)-C(6)	163.98(7)
C(3)-C(1)-C(2)-C(5)	105.01(8)	C(7)-O(3)-C(6)-O(2)	2.91(12)
C(4)-C(1)-C(2)-C(3)	–175.13(17)	C(7)-O(3)-C(6)-C(5)	–176.69(6)
C(4)-C(1)-C(3)-C(2)	174.85(17)	O(1)-C(5)-C(6)-O(2)	4.73(10)
C(5)-C(2)-C(3)-C(1)	–109.43(8)	C(2)-C(5)-C(6)-O(2)	127.13(8)
C(1)-C(2)-C(5)-O(1)	–143.05(7)	O(1)-C(5)-C(6)-O(3)	–175.67(6)
C(3)-C(2)-C(5)-O(1)	–76.14(9)	C(2)-C(5)-C(6)-O(3)	–53.26(8)
C(1)-C(2)-C(5)-C(6)	97.07(8)		

Table 7. Hydrogen bonds for **84** [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
O(1)-H(1O)...O(1)#1	0.819(17)	2.027(16)	2.7873(5)	154.1(15)

Symmetry transformations used to generate equivalent atoms: #1 -x,y-1/2,-z+1/2

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