One-pot, Two-step Queuing Cascades Involving a Heck Coupling, π-Allylpalladium Trapping and Diels-Alder Reaction

DISSERTATION

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Meinem Lehrer, Herrn Prof. A. de Meijere, möchte ich an dieser Stelle für die Überlassung des interessanten Themas, seine hilfreichen Anregungen, seine Diskussionsbereitschaft und die stete Unterstützung während der Anfertigung dieser Arbeit herzlich danken.

Knowledge should mean a full grasp of knowledge:
Knowledge means to know yourself, heart and soul.
If you have failed to understand yourself,
Then all of your reading has missed its call.

Dervish Yunus Emre
13th century

To

Seyhan and

Kadir Öztürk

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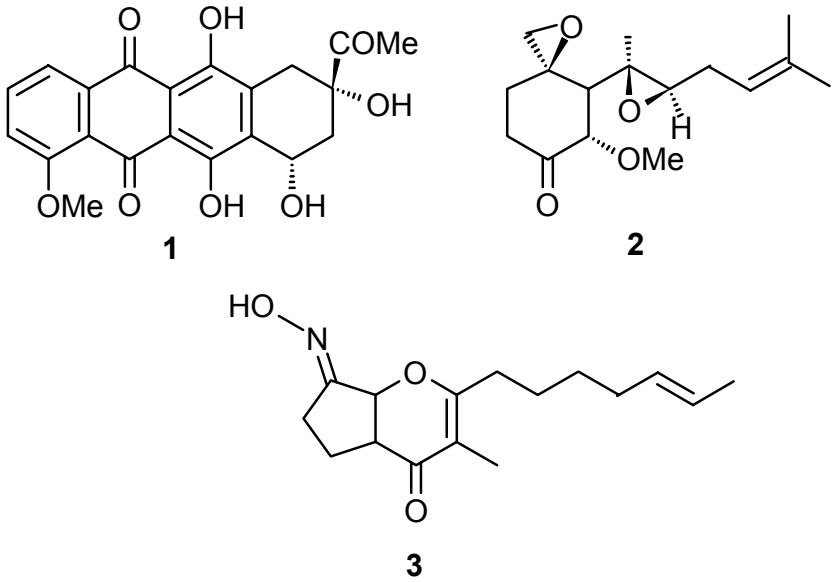
A. Introduction

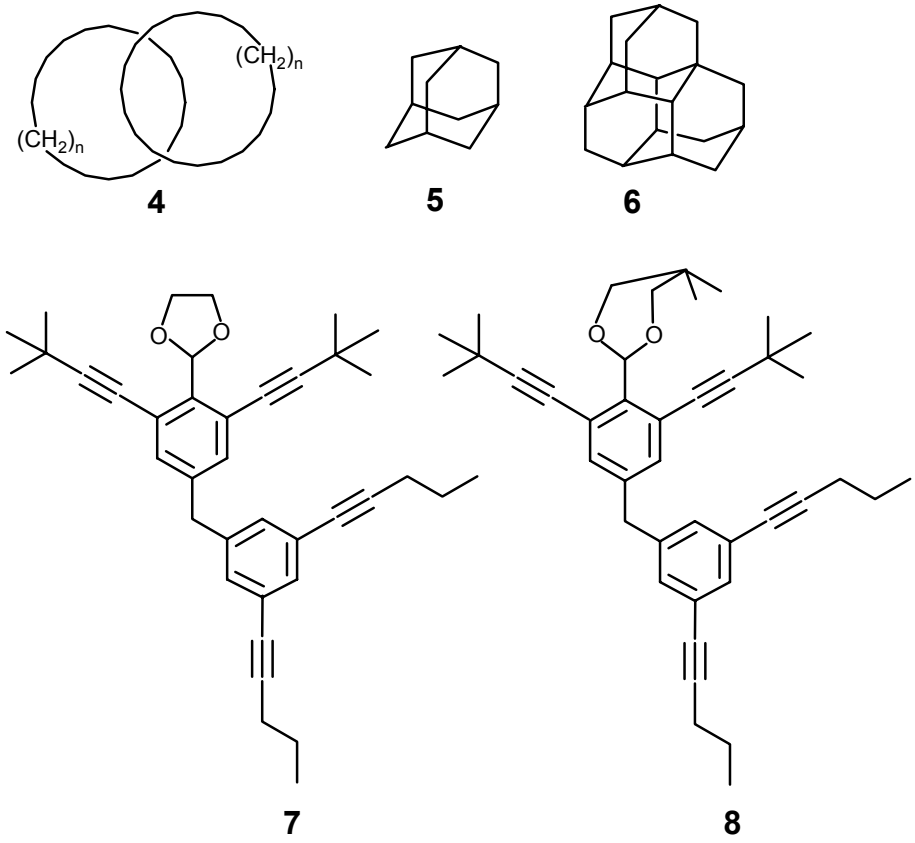
Initially, organic chemistry began like many other branches of the natural sciences with the investigation of natural products. However, it started to be accepted as an unambiguous and unique branch of science only after the artificial creation of its own material independently at the beginning of the last century. Emergence of this creative ability made organic chemistry a more distinguishable science which produces its own individual laws and utilizes them for its self-development. The creative potential of organic chemistry in contrast to many other branches of natural sciences resembles only that of the arts. Similar to those of colors or music notes, the unlimited capacity of carbon atoms to combine with each other as well as with other atoms allows for the creation of numberless structures, from the very simple to the complex each with its own unique appearance and chemical properties. The main goal of organic chemistry can be easily summarized as the synthesis of new molecules having specific functions which serve 'usefulness' to any part of life. In this respect, organic chemists have synthesized thousands of structurally diverse compounds which find numerous applications, particularly in medicine, agriculture and textile industry (Scheme 1).[1]



Scheme 1. Three examples of biologically active compounds: anti-tumor agent, Daunomycinone (**1**)[2]; antibiotic, (–)-Ovalicin (**2**)[3]; insecticide, Brevioxime (**3**).[4]

However, to evaluate the organic synthesis only in terms of 'usefulness' might not be realistic. On the other hand, a statement like the following "As the arts can be performed only for arts' sake, an organic synthesis can be also realized only for its own sake!" might be also quite pretentious. Some of the structurally fascinating compounds have been synthesized firstly for

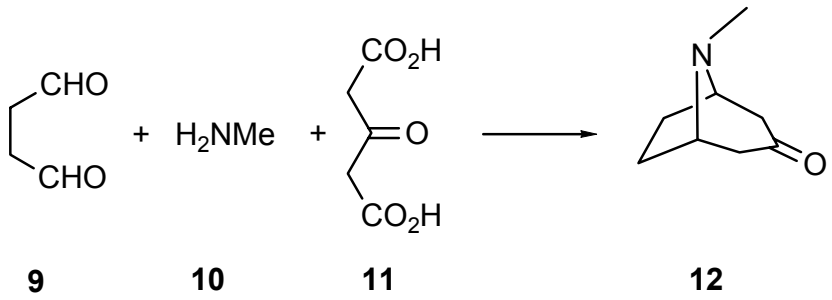
purely academic interest such as catenanes **4** (composition of interlocking carbon rings), adamantane **5** ('monomeric' building block of diamond) and its higher analogs (**6**) without expecting any applicable 'usefulness' (Scheme 2).[1] Nevertheless, we now are aware of catenane constitution of DNA in its replication process[5] and adamantane derivatives having antiviral activity.[6] One of the most interesting examples in this context has been recently demonstrated with the synthesis of several anthropomorphic molecules which are named as nanoputians (**7** and **8**), inspired by the Lilliputians in Swift's famous novel. 3-D animations of these man-shaped molecules are being utilized for educational purposes (Scheme 2).[7]



Scheme 2. Adamantane (**4**), Trimantane (**5**), Catenane (**6**) and NanoPutians (**7**, **8**)

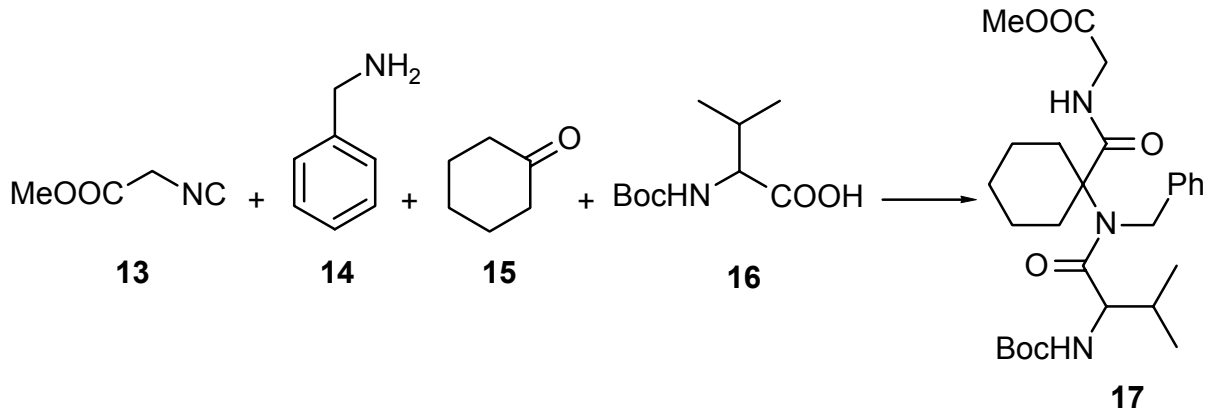
Today, modern synthetic organic chemistry not only deals with target of synthesis but also methods to reach it. The increasing interests in more complex structures enriched in chemo- or stereoselective respects require more elegant approaches which must be designated to give the most efficient results yet in the shortest time. In addition to this, they must be flexible protocols in terms of chemical diversity of ingredients to elaborate target molecules with a variety of slightly different substituent patterns. Any suggested methodology should also fulfill needs of modern synthesis from the standpoint of rising attentions in environmental issues. Under these

circumstances, traditional stepwise synthetic methods which, particularly, need several tedious individual steps for the construction of target molecules, are no longer desirable.[8] Actually, these modern requirements of organic synthesis were recognized about a century ago. One-pot synthesis of tropinone **12** starting from simple substrates – succindialdehyde **9**, methylamine **10** and acetonedicarboxylic acid **11** – can be shown as an one of the earliest examples of today's synthetic strategies (Scheme 3).[9]



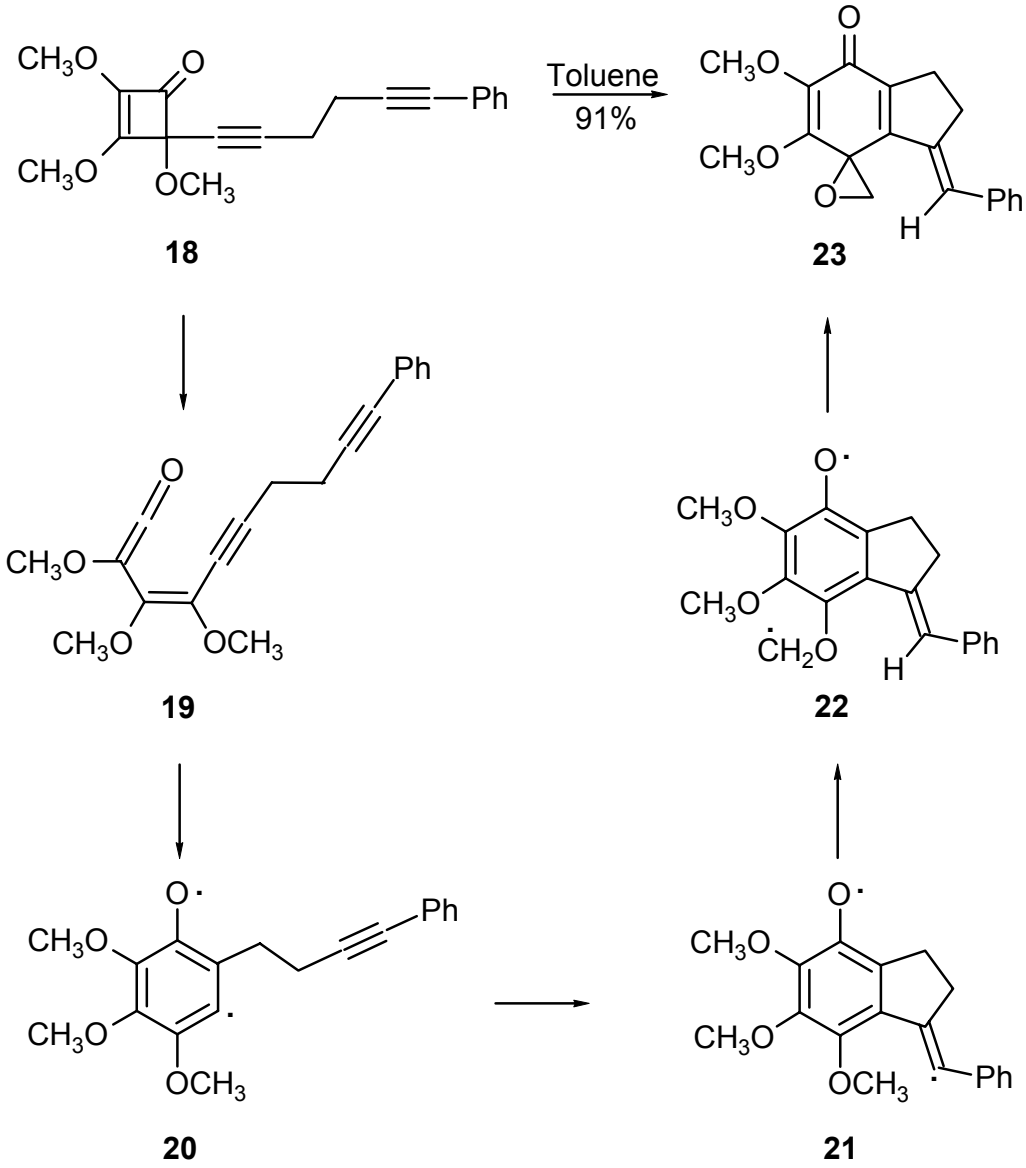
Scheme 3. One-pot synthesis of tropinone (**12**)

However, the idea of putting all starting materials in a one pot and carrying out the reaction without isolating the intermediates have started to appear as a distinctive methodology at the very beginning of the sixties. An important contribution to this concept came from isocyanide based chemistry by Ugi et al. So called four-component Ugi reaction (Ugi 4CR) have been emerged as direct access to peptides in a one step (Scheme 4).[10] Today, the Ugi reaction and its other variations play a major role in the synthesis of natural or non-natural biologically active compounds. This methodology has been improved with combination of Ugi 4CR with other reactions; some examples containing seven and more adducts have even been demonstrated.[11]



Scheme 4. An Ugi reaction

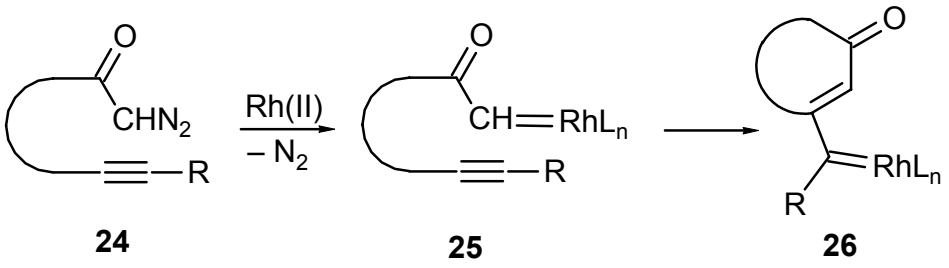
The reaction proceeding in a one-pot by combination of more than one individual step in a concurrent fashion can be generally defined as a domino or cascade reaction. By definition one-pot multicomponent reactions like the Ugi reaction above have to be accepted as a cascade reaction. However, not all cascade reactions do necessarily involve more than one component.[8] The formation of spiroepoxide **23** by termolysis of 4-alkynylcylobutenone **18** is one of the fascinating examples of such an unimolecular cascade reaction. After electrocyclic ring opening of cyclobutenone ring, rearrangement of occurring enynylketene **19** via diradicalic intermediates (**20**, **21** and **22**) makes this reaction possible in a high yield (Scheme 5).[12]



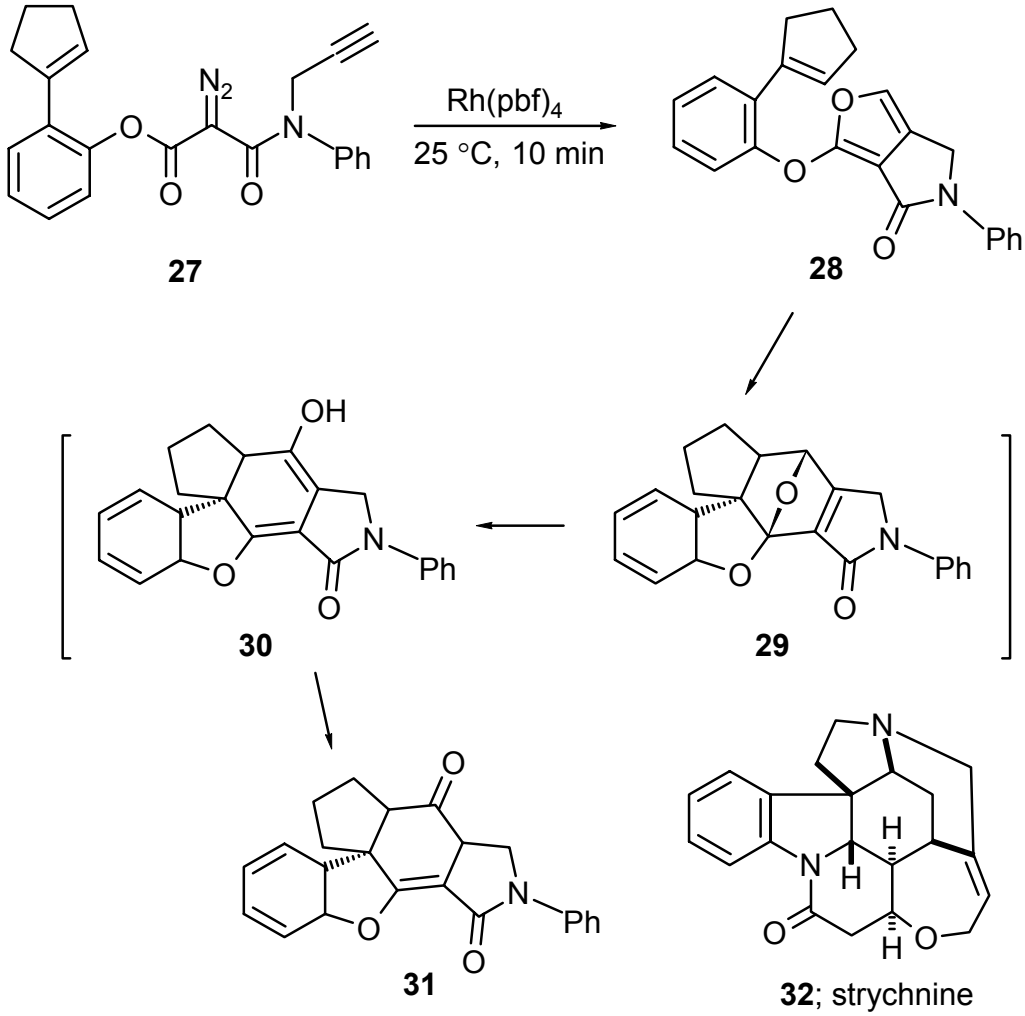
Scheme 5. An example of unimolecular cascade reaction.

In domino processes, even though in some cases individual steps might be performed separately (i.e., in a stepwise fashion), this is usually neither applicable nor preferable due to formation of unstable intermediates after each step[8]. Moreover, according to the strict definition by Tietze a domino reaction must be performed "under the same conditions without adding additional reagents and catalyst."[8a] Domino reactions can be classified with respect to mechanistic pathways of individual steps such as anionic-pericyclic or anionic-anionic. Among these, transition metal-catalyzed domino reactions occupy an important position, since diverse range of substrate toleration of transition metals and their unusual reactivity patterns to elaborate complex structures selectively match with expectations from a domino reaction[13]. Generally, transition metal catalyzed cascade reactions start with coordination of the metal species to carbon-carbon multiple bonds or oxidative addition of reactive bonds to the metal and subsequent insertion of various π-bonds to the metal complex. Occurring reactive σ-metal-carbon bond in these pathways can easily undergo reductive elimination or β-elimination processes. In order to perform sequential reactions in the presence of metal catalysts, these elimination processes must be blocked to transform the chemical information from one step to another. In the case of slow elimination processes, this transformation can be obtained by following insertion mechanisms or nucleophilic trapping of the intermediate metal-carbon complex. Furthermore, with an appropriate conditions and substrates lacking of available β-hydrogen for elimination are utilized for this purpose.[13c,d, 14]

Rhodium is one of the most commonly used metals for transition metal mediated cascade reactions.[13c,d,15] Recently, Rh(II)-catalyzed cyclization of acetylenic diaza carbonyl compounds has been developed as a general key strategy for the total synthesis of strychnine **32** (Scheme 7).[16] In the model study, treatment of catalytic amount rhodium(II) perfluorobutyrate with α-diazoamide **27** has initially afforded rhodium carbene complex like **25** in Scheme 6. This complex reacts immediately with alkyne moiety to generate the vinyl carbene intermediate **26**. Actually, many other transition metal reactions proceed via intermediates similar to **25** and **26** in Scheme 6. After electrocyclic ring closure and reductive elimination of rhodium complex to afford **26**, furan derivative **28** has been accomplished in 94% yield in a model study (Scheme 7). Subsequent intramolecular Diels-Alder reaction of furan **28** with cyclopentene moiety and opening of the oxybridge in intermediate **29** has furnished polycyclic structure **31**. This approach can be utilize for the construction of strychnine **32** after necessary modifications are made to the precursor **27**.



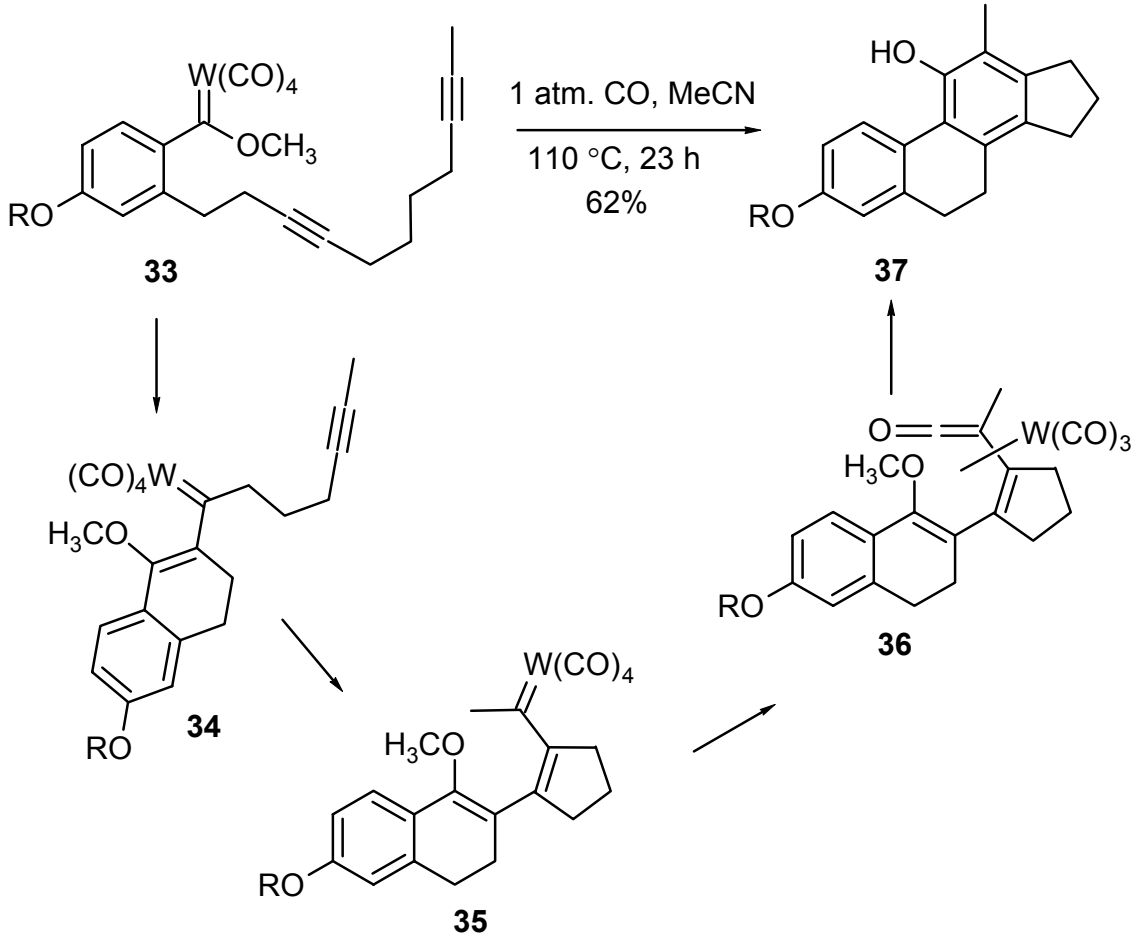
Scheme 6. The formation of rhodium vinyl carbene complex **26**



Scheme 7. Rh(II)-catalyzed cyclization of α-diazoamide **27** and the construction of polycyclic structure **31**; the model study for the synthesis of strychnine **32**.

Since their initial preparation in 1964,[17] Fischer carbene complexes have become one of the most useful tools in organic synthesis. In particular, α-β unsaturated Fischer carbenes (including aryl carbene complexes) have gained increasing attention since they undergo cycloadditions with alkynes to afford different ring systems such as phenols, cyclopentanones, indenes, furans and cyclobutenones under appropriate conditions. Fischer carbenes have found numerous applications in the construction of various structures, such as the promotion of sequential multi-cyclizations with acetylenes.[18]

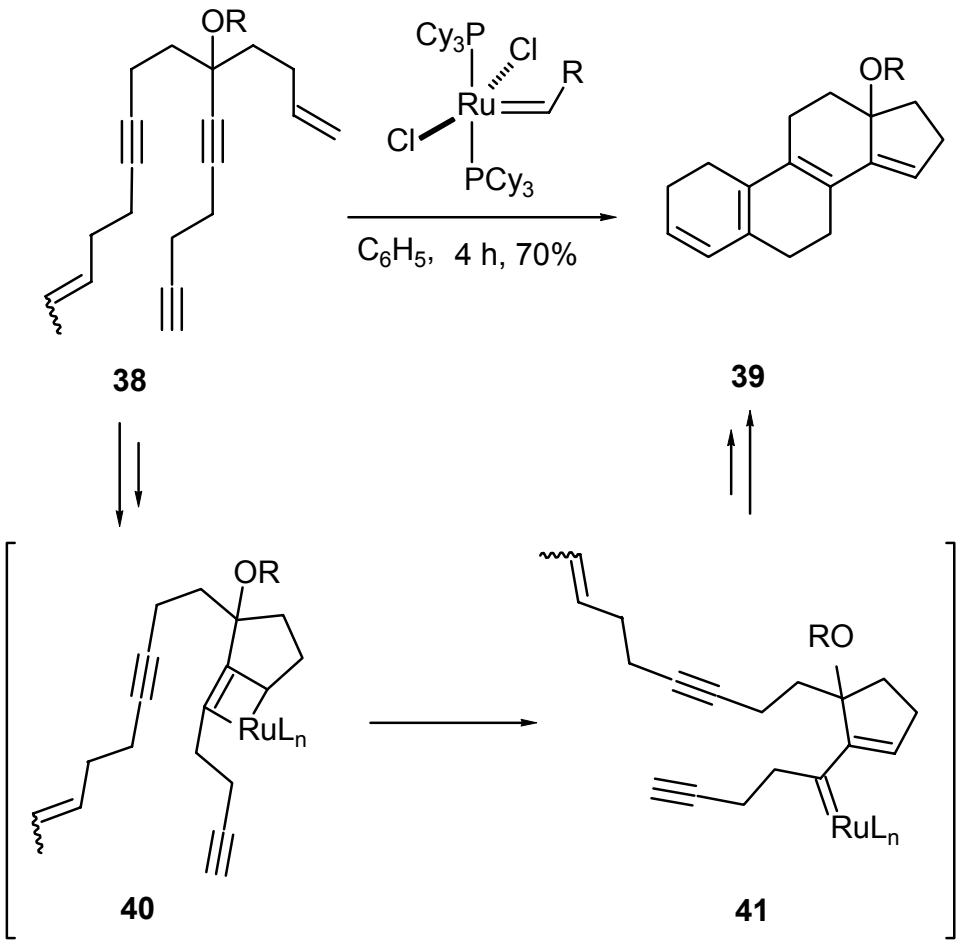
A striking example of metal assisted cascade reactions is the reaction performed by Fischer type tungsten carbene complex **33**. Two folds intramolecular annulation protocol with alkyne moieties has been used to produce a steroidal ring system **37**. After the first annulation, the generated second α-β unsaturated carbene complex **34** undergoes one more annulation with alkyne rest to afford the tetracyclic product **37** in 62% yield (Scheme 8).[19]



Scheme 8. The formation of stereoidal ring system **37** by α-β unsaturated Fischer type tungsten carbene complex **33** in a one-pot.

Ruthenium carbene complexes have emerged as valuable reagents in organic synthesis over the last two decades. They have been extensively utilized to couple diverse range of dienes or dienynes in a way to give unsaturated carbo- and heterocycles. This methodology now generally is referred to ring closing metathesis (RCM) reactions.[20] By designation of proper substrates, it is also possible to perform the ring closing metathesis in a concurrent fashion to obtain polycyclic structures.[21]

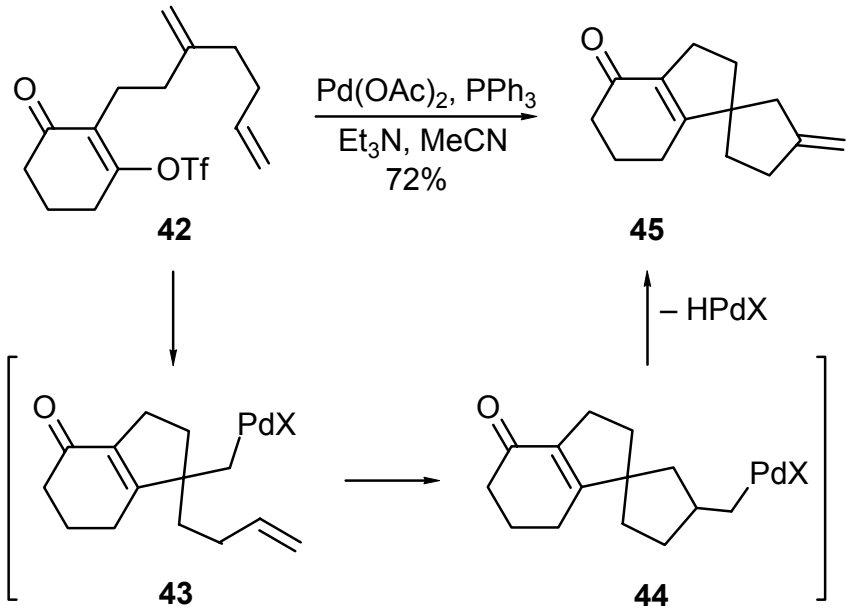
For instance, recently, the production of another stereoidal backbone **39** has been achieved by ruthenium mediated polycyclization of highly branched precursor **38**. The mechanism initiated with ruthenium alkylidene formation involves three subsequent intramolecular carbene-acetylene metatheses via metallacyclobutene and ruthenium carbene intermediates similar to **40** and **41** respectively (Scheme 9).[22]



Scheme 9. The construction of steroidal backbone **39** by ruthenium carbene complex; an example of sequential ring closing metathesis (RCM).

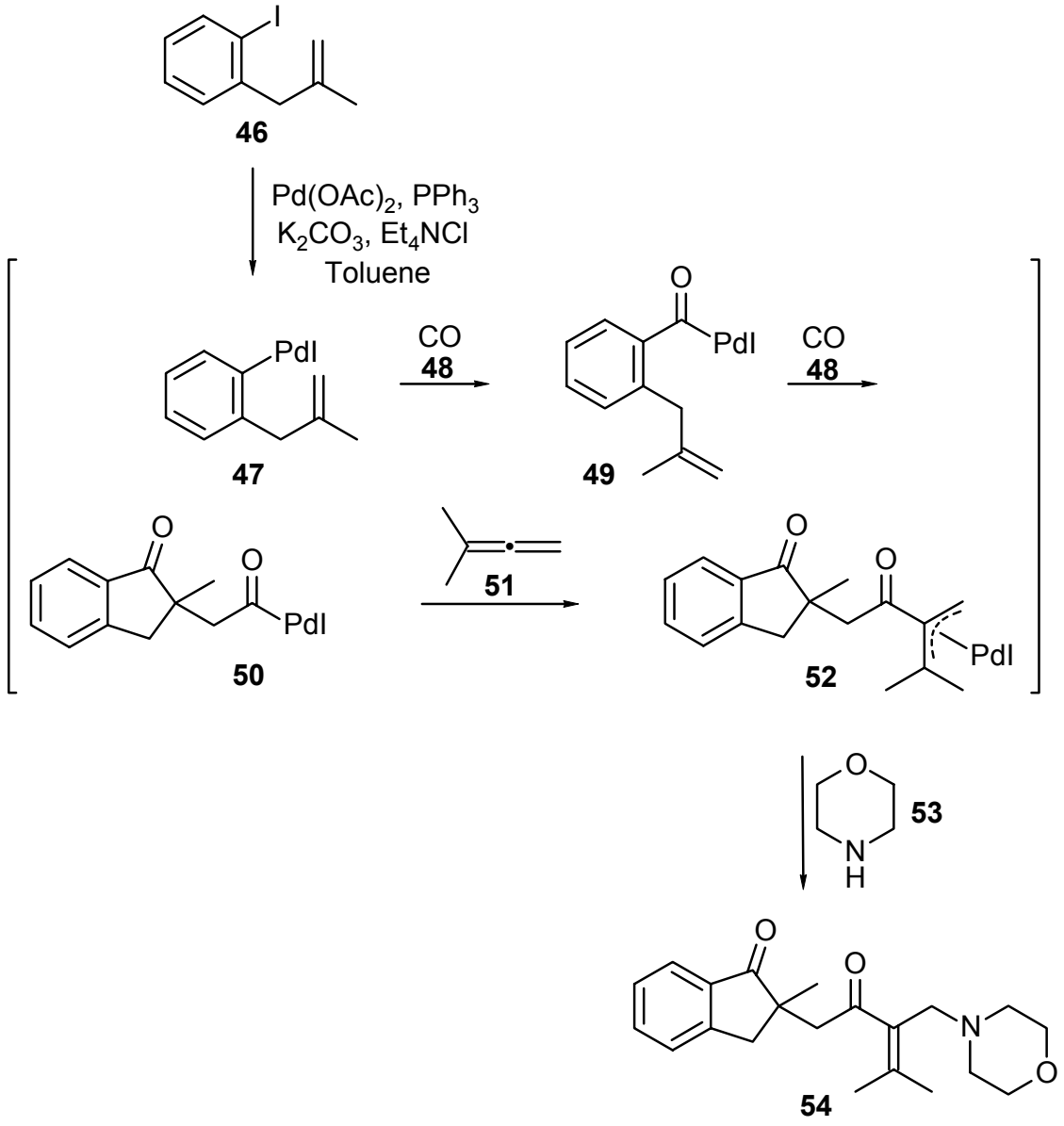
Palladium-catalyzed reactions are certainly one of the most deeply studied families of transition metal reactions. So called cross coupling reactions based on palladium catalysts have become a cornerstone in organic synthesis since they first emerged as a powerful methodology to build up a new bond between unsaturated carbon bonds about 25 years ago.[23] Today, palladium-catalyzed cross coupling reactions, particularly the Heck variant, provide both mechanistically and experimentally very well established protocols. The application area of these protocols ranges from synthesis of very simple substrates even to that of natural products.[23, 24]

Obviously, it is very beneficial to take palladium-catalyzed cross coupling reactions as part of a domino process in order to explore its potential by liberating advantages of these catalysts. Especially, when the Heck reaction is realized in intramolecular fashion, depending on the complexity of substrates, exceptional structural changes can be created in one operational step.[14a, 25] An impressive example of this has been recently demonstrated by Overman et al. Carbopalladation of the 1,1-disubstituted alkenyl unit as in conventional Heck cross coupling, yet in this case intramolecularly, affords the intermediate **43**. The lack of β-hydrogen in this intermediate suppresses the β-dehydropalladation. The first occurring alkylpalladium complex is trapped by insertion of alkenyl rest to form spirocyclic ring system **45** after the elimination of the second alkyl palladium complex with available β-hydrogen in the intermediate **44** (Scheme 10).[26]



Scheme 10. An example of intramolecular Heck reaction cascade by Overman et al. Synthesis of the spirocyclic ring system **45**

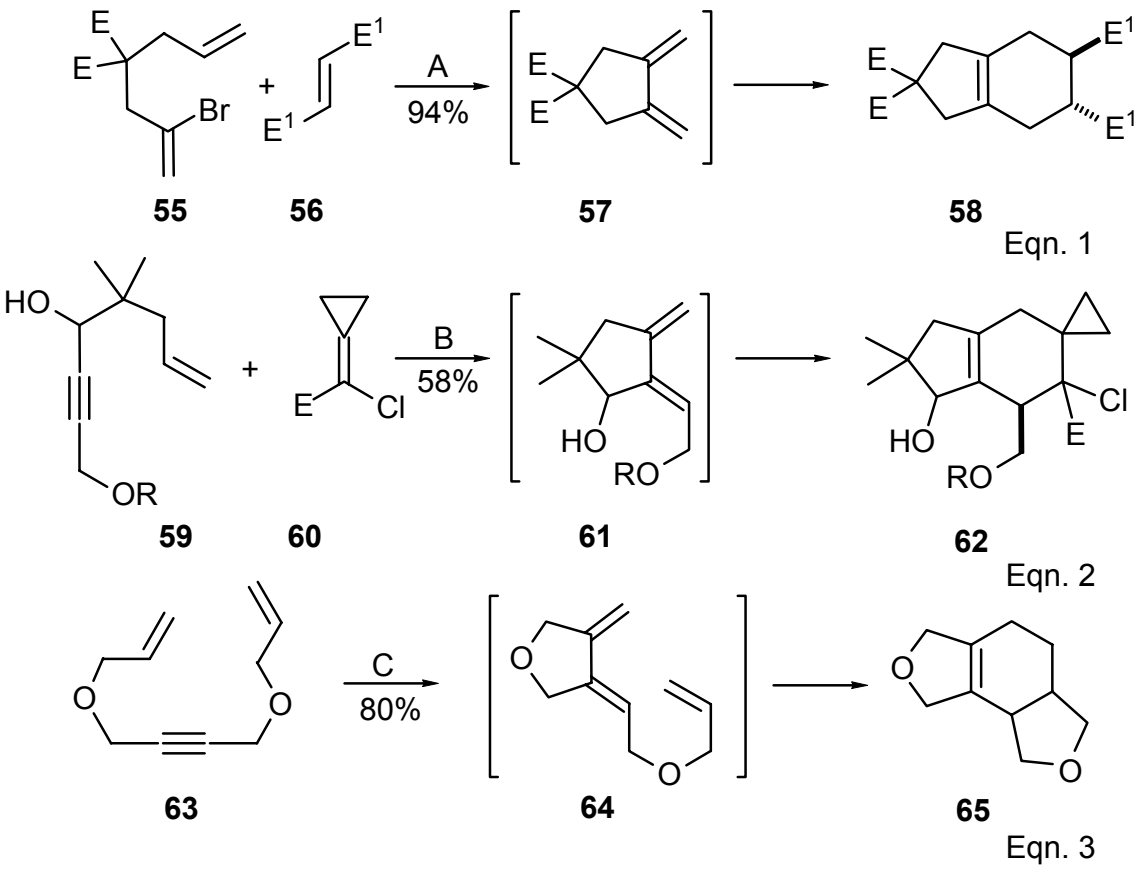
In addition to unimolecular cascades, the Heck reaction has been extensively utilized as a key step in multicomponent one-pot transformations.[24b, 25a] Grigg et al. has demonstrated an exciting example of multicomponent domino-Heck reaction involving four components and overall five sequential steps. In this example, the domino reaction initiating with oxidative addition of alkenyl iodide **46** onto palladium(0) goes on with two subsequent CO insertion, since insertion of CO is faster than that of allenes. The insertion of allene **51** in the fourth step generates π-allylpalladium intermediate **52** and nucleophilic trapping of this intermediate at the least substituted terminus gives the compound **54** in 78% yields (Scheme 11).[27]



Scheme 11. A multicomponent domino Heck reaction by Grigg et al.

In addition to these, domino reactions involving combinations of the Heck coupling with other types of palladium-catalyzed cross coupling processes such as Suziki and Stille as well as with classics of organic synthesis like aldol, Michael and Diels-Alder reactions have been also designated as well.[28]

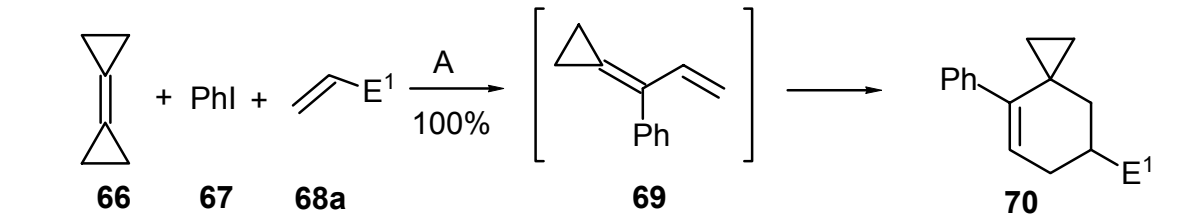
In recent years, a number of valuable examples of domino Heck-Diels-Alder reactions has been demonstrated by de Meijere et al (Scheme 12).[29] In these domino reactions, constructions of bi- and oligocycloc structures have been realized starting with synthesis of dienes (**57**, **61** and **64**) by an intramolecular Heck reaction (Equation 1)[29b] or palladium-catalyzed eneyne cycloisomerization (Equations 2 and 3).[30] Constructed dienes by these processes have been immediately trapped by dieneophiles present in the mixture from the beginning (one-pot, one-step protocol) or in two steps by addition of the dienophile right after the palladium-catalyzed process has been completed finally to give the ultimately desired cyclic structures.

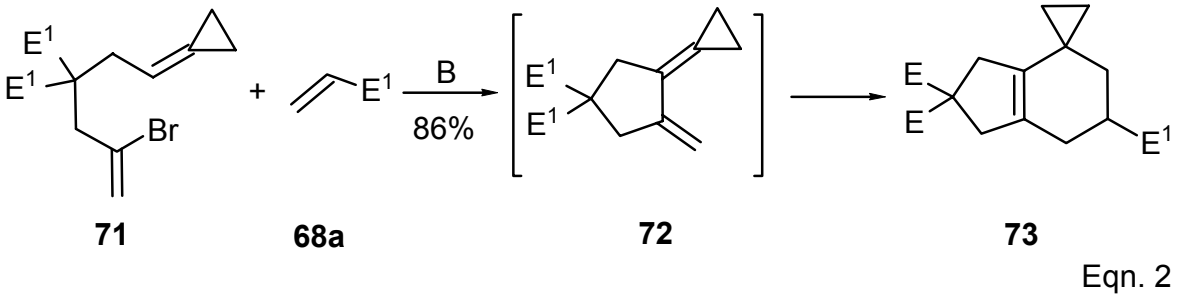


Scheme 12. Some examples of domino Heck-Diels-Alder reactions by de Meijere et al.
A: $Pd(OAc)_2$, PPh_3, Ag_2CO_3, MeCN, 90 °C, 48 h – B: $Pd(OAc)_2$, bbeda, C_6H_6, 70 °C, 48 h – C: $Pd(dba)_3.CHCl_3$, PPh_3, AcOH, C_6H_6, 80 °C, 100 min. – E = CO_2Me; E^1 = CO_2Et; R = TBDMS

Moreover, the Diels-Alder step has been carried out intramolecularly. For instance, the diene afforded by cycloisomerization of dieneyne **63** has produced the bisheterotricycle **65** in 80% yield under the conditions of the eneyne cycloisomerization via an intramolecular Diels-Alder reaction (Equation 3 in Scheme 12).[30b]

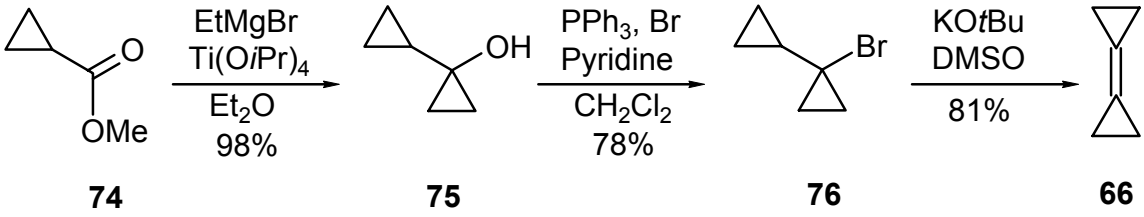
Heck-Diels-Alder cascades have been also performed to synthesize spiro[2.5]octene derivatives which constitute main core of various natural products such as the cytotoxic illudines, carcinogenic ptaquitosides or the antibiotic leaianafulvene.[31] Generally in such cascades, dienes having a cyclopropane ring at the methylene terminus have been achieved by a Heck reaction of alkenes bearing cyclopropane subunits and following Diels-Alder reactions of these dienes produce various spiro[2.5]octenes (Equations 1 and 2 in Scheme 13).[29a–d]





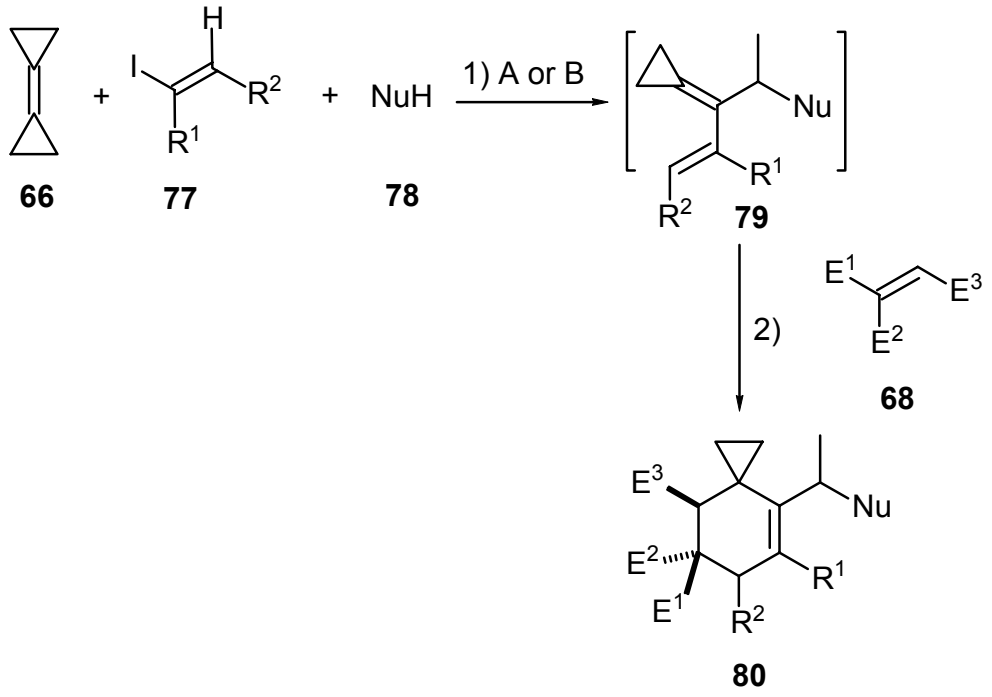
Scheme 13. Synthesis of spiro[2.5]octene derivatives (**70**, **73**) by domino Heck-Diels-Alder reactions. A: $Pd(OAc)_2$, PPh_3, K_2CO_3, Et_4NCl, MeCN, 80 °C, 48 h – B: $Pd(OAc)_2$, PPh_3, Ag_2CO_3, MeCN, 90 °C, 48 h – $E^1 = CO_2Me$

In this context, bicyclopropylidene (**66)** has appeared as one of the most ideal precursors readily available in preparative scales by three efficient steps starting from methyl cyclopropanecarboxylate **74** (Scheme 14).[32] Unlike the many other tetrasubstituted alkenes, bicyclopropylidene (**66**) exhibits high reactivity towards carbopalladations in the Heck reaction conditions even more rapidly than acrylates.[29a, b] As has been shown recently, bicyclopropylidene (**66**) reacts with wide range of aryl and alkyl halides in high yields. For example, one-pot reaction of bicyclopropylidene (**66**) with phenyl iodide **67** in the presence of methyl acrylate **68a** has afforded spiro[2.5]octene **70** in 100% yield in a single step (Equation 1 in Scheme 13).



Scheme 14. Synthesis of bicyclopropylidene (**66**) by de Meijere et al.

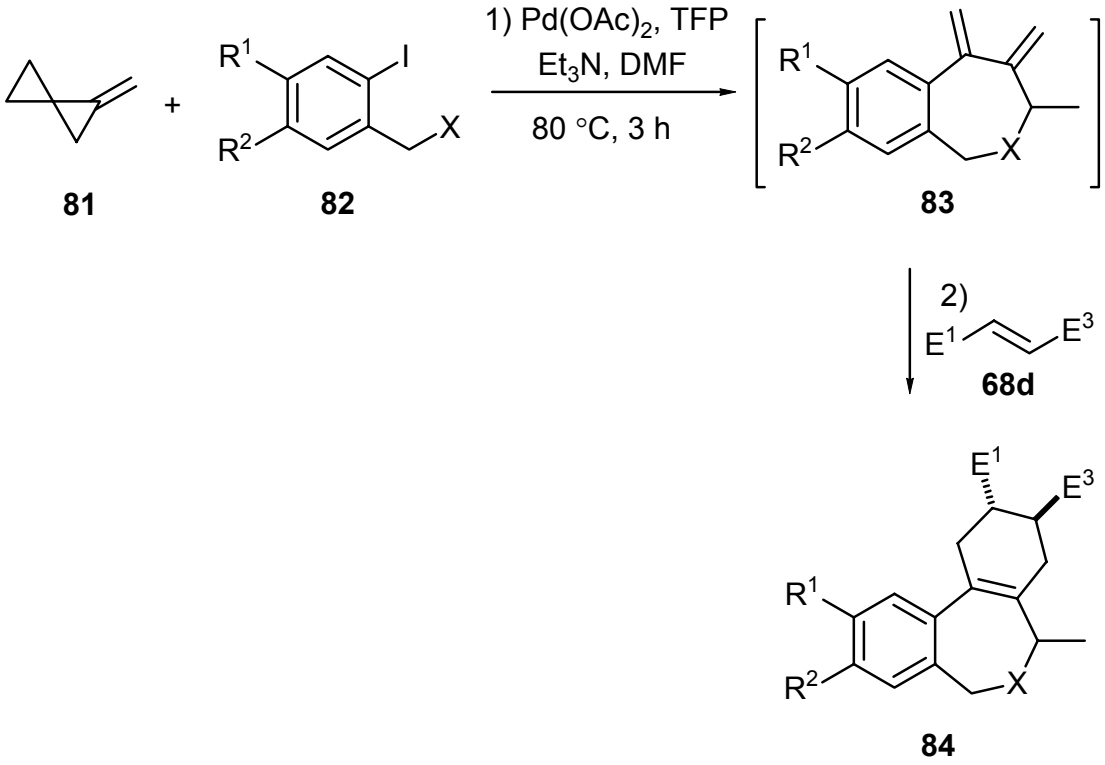
In this study, with the full details of the scope and limitations, a two step, one-pot queuing cascade with bicyclopropylidene (**66**) will be introduced as a novel access to spiro[2.5]octene derivatives having thoroughly different substituent patterns. This reaction constitutes the Heck coupling of bicyclopropylidene (**66**) with iodo alkenes **77**, trapping of π-allylpalladium intermediates with nucleophiles **78** and the subsequent Diels-Alder reaction of dienes **79** in the presence of various dienophiles **68** (Scheme 15).[33]



Scheme 15. A New one-pot, two-step four-component queuing cascade involving bicyclopropylidene (**66**), iodoalkenes **77**, nucleophiles **78** and dienophiles **68**; synthesis of spiro[2.5]octene derivatives **80**. A: $Pd(OAc)_2$, TFP, NEt_3, 2 h, 80 °C, DMF. – B: $Pd(OAc)_2$, TFP, K_2CO_3, Et_4NCl, 2 h, 80 °C, MeCN.

Moreover, some modifications performed on the domino Heck-Diels-Alder reaction with bicyclopropylidene (**66**) (equation 1 in Scheme 13) to enrich this already powerful methodology will be presented.

The last chapter of this study will focus on another one-pot yet three-component sequential reaction for the construction of heterocyclic fused ring systems **84** as depicted generally in Scheme 16. This reaction involves the Heck coupling of methylenespiropentane (**81**) with functionalized aryl iodides **82**, intramolecular trapping of respective π-allylpalladium complexes and subsequent Diels-Alder reactions of dienes like **83** with dimethyl fumarate **68d** (Scheme 16).



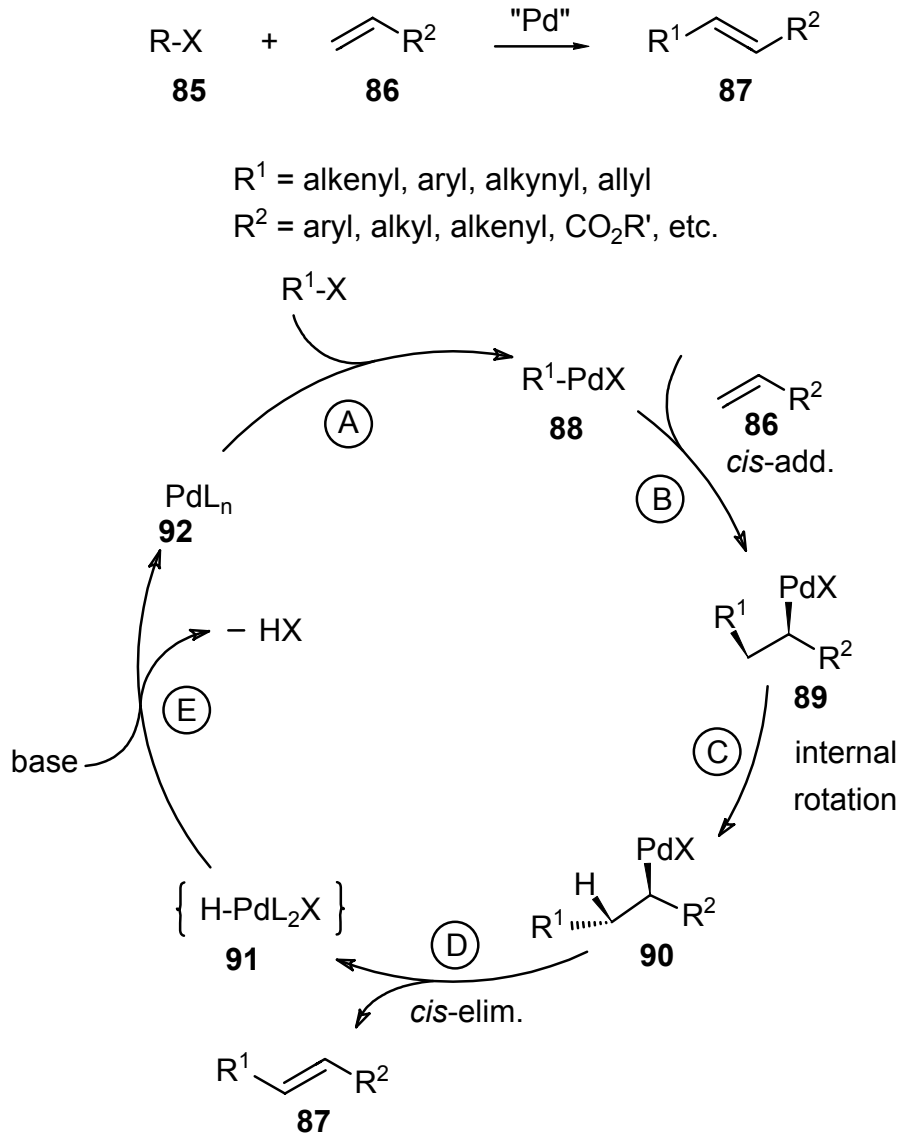
Scheme 16. A New one-pot, two-step three-component queuing cascade involving methylenespiropentene (**81**), functionalized aryliodides **82** and dimethyl fumarate **68d**; synthesis of heterocyclic fused ring systems **84**. – E^1, E^3 = CO_2Me

B. Main Part

1. Some Modifications on Domino Heck-Diels-Alder Reaction Involving Bicyclopropylidene

1.1. Introduction

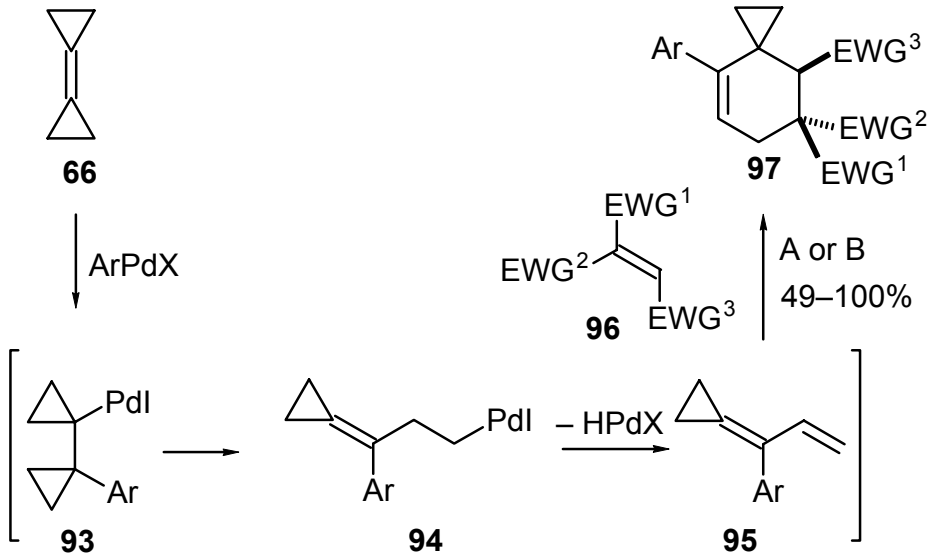
The starting step of all cascade reactions in this study is carbopalladation of the reactive double bond in substrates (i.e., bicyclopropylidene **66** and methylenespiropentane **81**) in Heck cross-coupling conditions. The Heck reaction can be very generally described as insertion of alkenes as well as alkynes into aryl- or alkenylpalladium species formed by oxidative addition of usually aryl- or alkenylhalides to a Pd(0) complex. Today, the Heck reaction is one of the most studied and versatile methods with an enlarging substrate spectrum for carbon-carbon bond formation ,particularly, between sp^2 carbons.[23]



Scheme 17. Mechanism of the Heck reaction.

The mechanism of the Heck reaction involves five main steps. The first step (A in Scheme 17) is oxidative addition of an aryl- or alkenylhalide to a coordinatively unsaturated 14-electron palladium(0) complex, giving a σ-alkenyl- or σ-arylpalladium(II) complex **88**. The next step (B in Scheme 17) is insertion of an unsaturated bond into σ-alkenyl- or σ-arylpalladium complex **88** (this term can be also referred to carbopalladation of an unsaturated bond by σ-alkenyl- or σ-arylpalladium complex **88**). This addition occurs in *syn* stereochemistry and generates a σ-(β-alkenyl)- or σ-(β-aryl)alkyl-palladium(II) complex **89**. Then in the third step (C in Scheme 17), internal rotation around the previous double bond occurs which provides the necessary synperiplanar oriented β-hydrogen with respect to the halopalladium moiety for the subsequent *syn*- β-hydride elimination. The β-H elimination (step D) produces the thermodynamically stable (*E*)-alkene **87** and the hydridopalladium halide **91** which undergoes reductive elimination in step E with the help of bases and regenerate active palladium complex **92**.[13a, 24a, 34]

Bicyclopropylidene (**66**) undergoes the Heck reaction with ring opening. After the initial carbopalladation of the highly strained double bond in bicyclopropylidene (**66**) by aryl or alkenylpalladium halides, opening of the cyclopropyl ring via a cyclopropylcarbinyl to homoallyl rearrangement affords the homoallylpalladium species **94**, which rapidly undergoes a β-hydride elimination to yield the diene **95** (Scheme 18).[29a–b]



Scheme 18. Recently developed three-component domino Heck-Diels-Alder reaction involving bicyclopropylidene (**66**). – A: $Pd(OAc)_2$, PPh_3, K_2CO_3, Et_4NCl, MeCN, 80 °C, 48 h. – B: $Pd(OAc)_2$, PPh_3, Et_3N, DMF, 80 °C, 48 h.

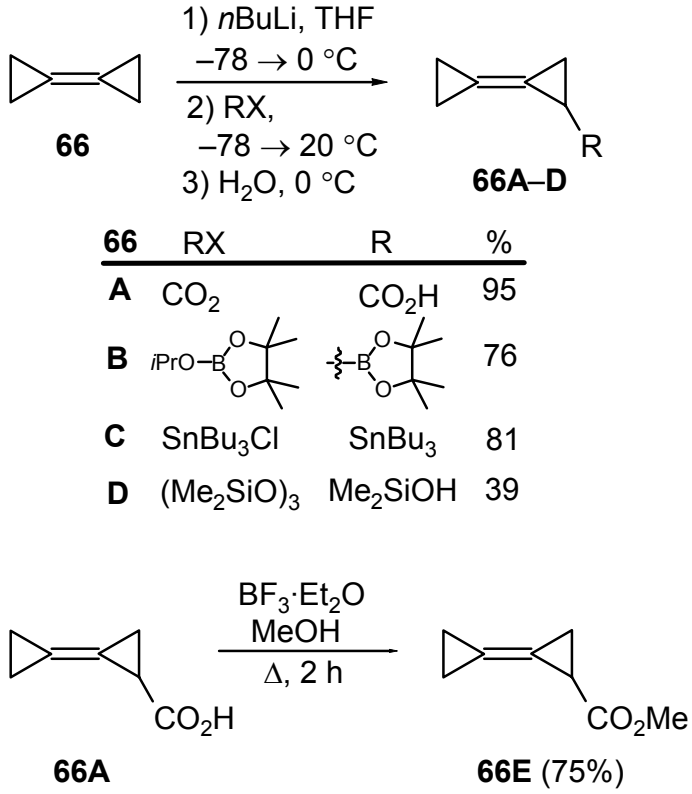
In domino Heck-Diels-Alder reaction with bicylopropylidene (**66**), in situ-formed allylidenecyclopropanes similar to **95** were allowed to react with dienophiles **96** present in the mixture from the beginning to produce spiro[2.5]octene derivatives **97**. Although 1,1-disubstituted dienes are known to be sluggish in the Diels-Alder reaction, allylidenecyclopropanes were found to undergo facile cycloaddition with various carbon dienophiles in moderate to very good yields. In the case of alkyl acrylates as dienophiles, only quasi-*meta* constituted spirooctenes were regioselectively obtained.

This domino Heck-Diels-Alder reaction was extensively studied and generalized for the preparation of spiro[2.5]octenes as a powerful methodology. It was widely explored by employing aryl- heteroaryl halides as well as variety of dienophiles. Furthermore, by using oligoiodoarenes via multiple Heck couplings with bicyclopropylidene (**66**) and following multifold Diels-Alder reaction even up to four spiro[2.5]octenes could be attached to the benzene ring in a single operation. The combinatorial potential of this process was demonstrated with the automated preparation of a structurally diverse set of spirooctene derivatives.[29b, 35]

*1.2. Domino Heck-Diels-Alder reaction with substituted bicyclopropylidenes (**66B–E**)*

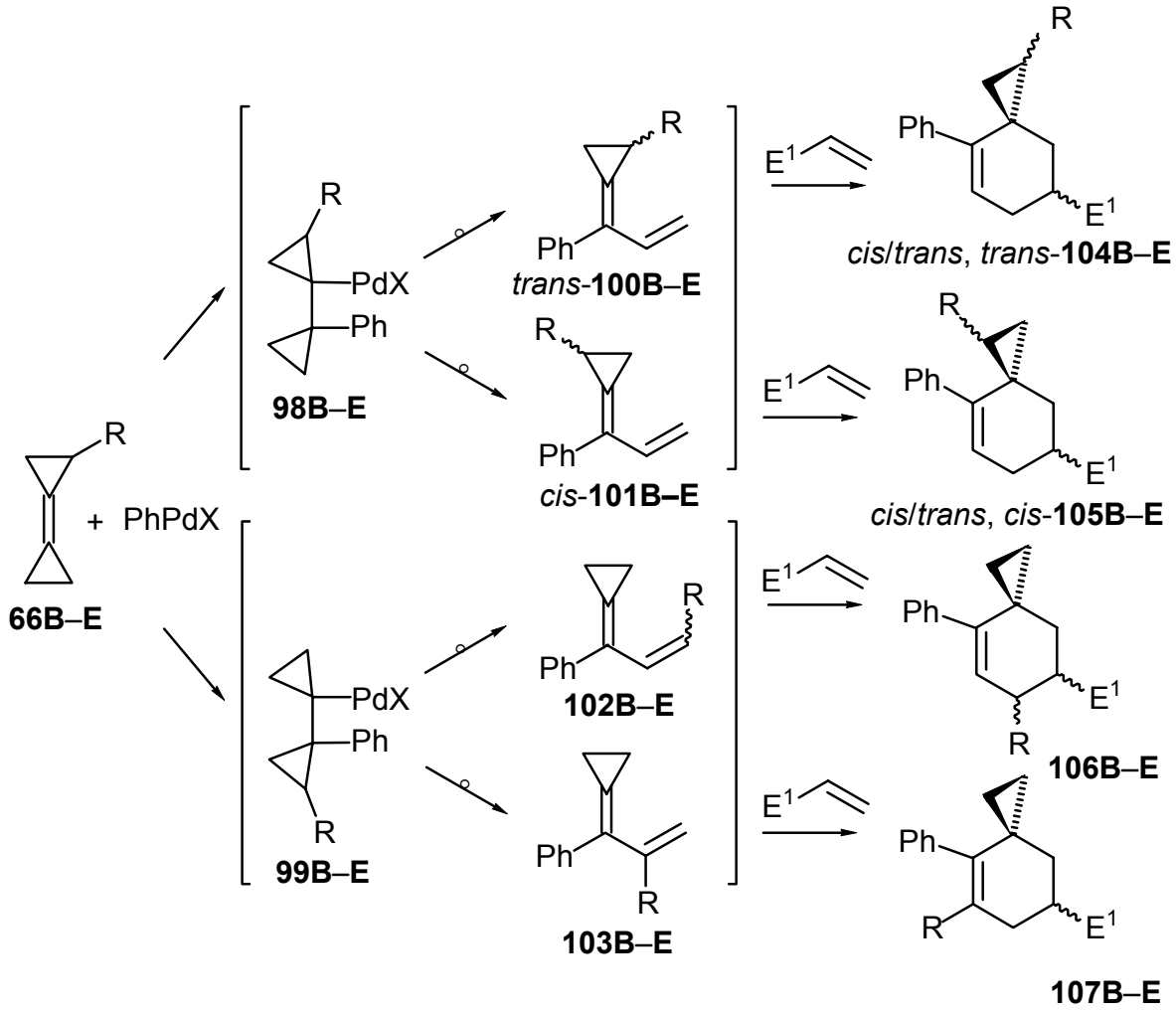
To enrich combinatorial potential of domino Heck-Diels-Alder reaction with bicyclopropylidene even further, substituted bicyclopropylidenes were also used.[29b, 35] However, to fill the gap in our understanding of the whole scope and limitations of this process, it must be deeply studied and supported by more accurate results. In this respect, final developments on domino Heck-Diels-Alder reaction with substituted bicyclopropylidenes (**66B–E**) are documented here.

Substituted bicyclopropylidenes are easily available by lithiation of bicyclopropylidene and subsequent addition of various electrophiles at low temperature.[36] In this study, five different mono-substituted bicyclopropylidenes (**66A–E**) were prepared according to known literature methods (Scheme 19).[36a–b] Except for **66A**, the other bicyclopropylidenes **66B–E** were utilized in the domino Heck-Diels-Alder process. Carboxylic acid substituted bicyclopropylidene **66A** was converted to methyl bicyclopropylidenecarboxylate **66E** applying the procedure of Seebach et al. (Scheme 19).[37]



Scheme 19. Preparation of mono-substituted bicyclopropylidene derivatives (**66A**–**E**)

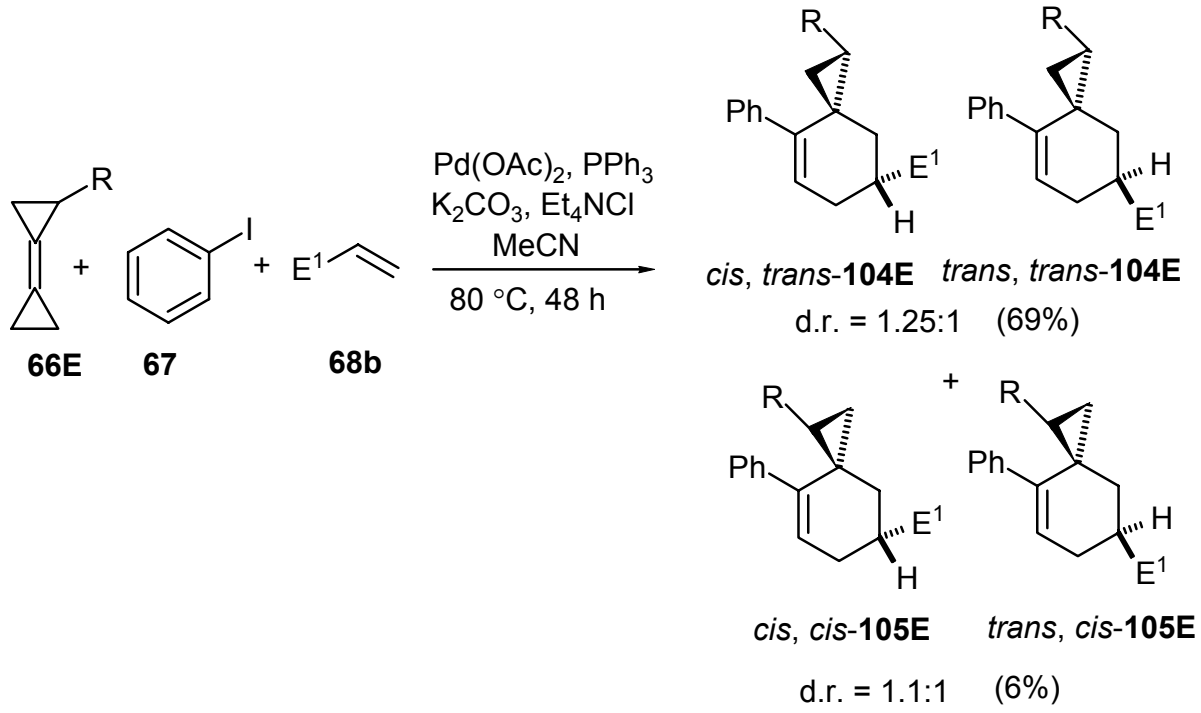
In the Heck reaction of a substituted bicyclopropylidene, with respect to the initial attack of arylpalladium species onto the double bond and subsequent opening of the substituted or the unsubstituted cyclopropane ring via a cyclopropylcarbinyl-homoallyl rearrangement up to four different regioisomeric dienes **100**–**103** are possible. In the intermediate **98**, opening of the unsubstituted cyclopropane moiety by cleavage of different proximal bonds of the ring produces regioisomers **100** and **101** called *trans* and *cis* respectively according to the positions of R and aryl rests in these dienes. Similarly, in the intermediate **99**, opening of the substituted cyclopropane ring by cleavage of different proximal bonds gives dienes **102** and **103**. Indeed, when the successive Diels-Alder reaction is taken into account, unless it is completely selective, regiodiastereomeric mixture of four spiro[2.5]octene derivatives **104**–**107** can appear at the same time (Scheme 20).[29b, 35]



Scheme 20. The mechanistic pathway for the formation of regioisomeric dienes **100**–**103** via carbopalladated intermediates **98** and **99** starting with monosubstituted bicyclopropylidenes **66B**–**E** and possible regiodiastereomeric mixture of spiro[2.5]octenes (**104**–**107**) after a Diels-Alder reaction.

Surprisingly, the one-pot domino Heck-Diels-Alder reaction of methyl bicyclopropylidene-carboxylate **66E** gave only regiodiastereomeric mixture of *cis*, *trans*-**104E** and *trans*, *trans*-**104E** together with *cis*, *cis*-**105E** and *trans*, *cis*-**105E** in 69% and 6% yields respectively (Scheme 21). (Spirooctenes were also called as *cis* or *trans* according to position of ester groups with respect to each other.) The configuration of both diastereomers *cis/trans*, *trans*-**104E** was rigorously proved by an X-ray crystal structure analysis (Figures 1 and 2). In both structures, the ester functionality on the cyclopropane ring is oriented towards the phenyl group which is perpendicular to the plane of the double bond due to steric interaction between its ortho hydrogens and the cyclopropane ring. Also the configuration of diastereomers *cis/trans*, *cis*-**105E** was proved by NOESY NMR measurements. Thus, this results showed that clearly the formation of intermediate **98E** is superior to that of intermediate **99E**. The primary reason

for the selectively formation of intermediate **98E** must be straightforward complexation of palladium species with heteroatoms of the ester group on cyclopropyl ring in the carbopalladation step (Scheme 21).[38]



Scheme 21. One-pot domino Heck-Diels-Alder reaction involving methyl bicyclopropylidene carboxylate (**66E**), iodo benzene **67** and *t*-butyl acrylate **68b**. – $E^1 = CO_2tBu$

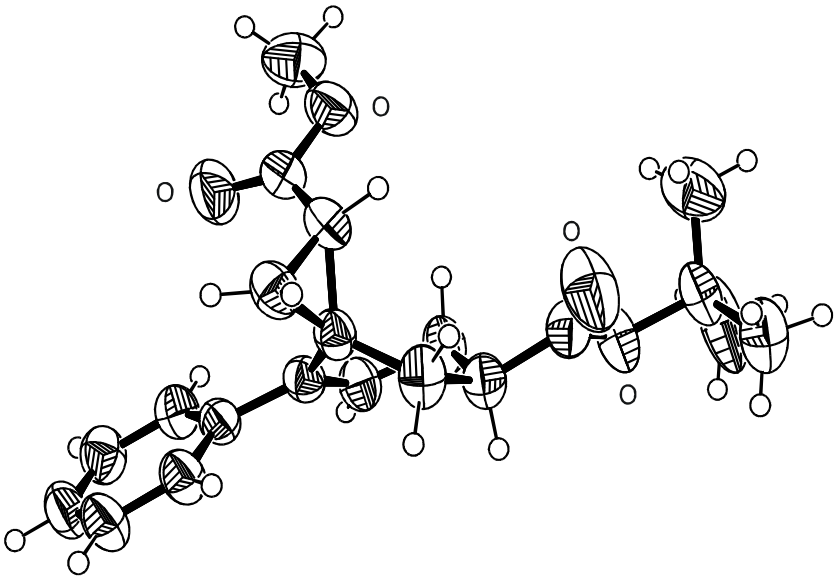


Figure 1. Structure of compound *cis*, *trans*-**104E** (major diastereomer) in the crystal.

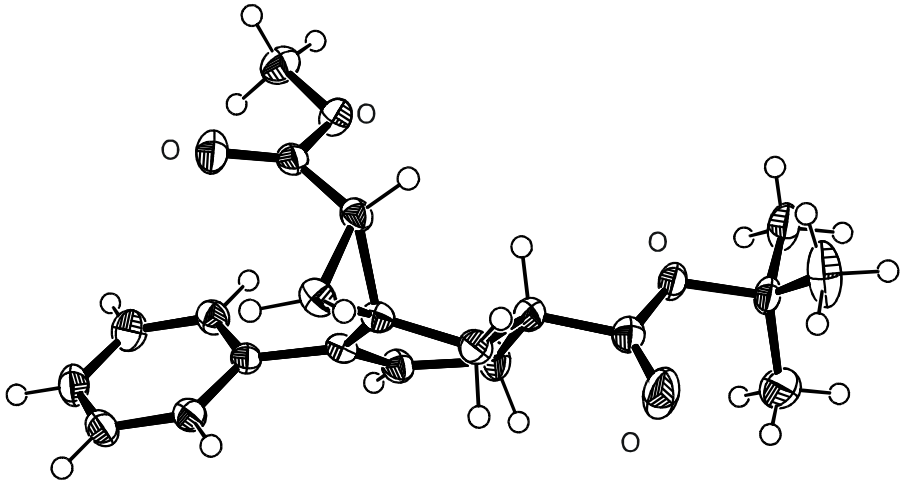


Figure 2. Structure of compound *trans*, *trans*-**104E** (minor diastereomer) in the crystal.

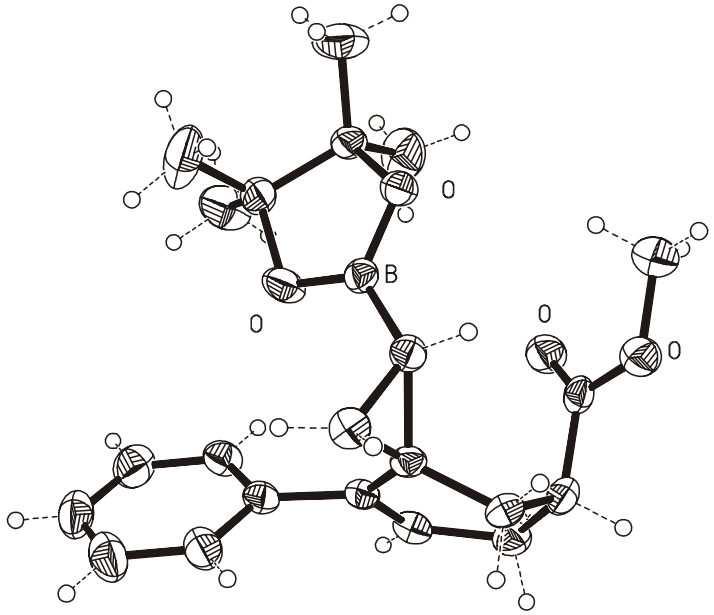
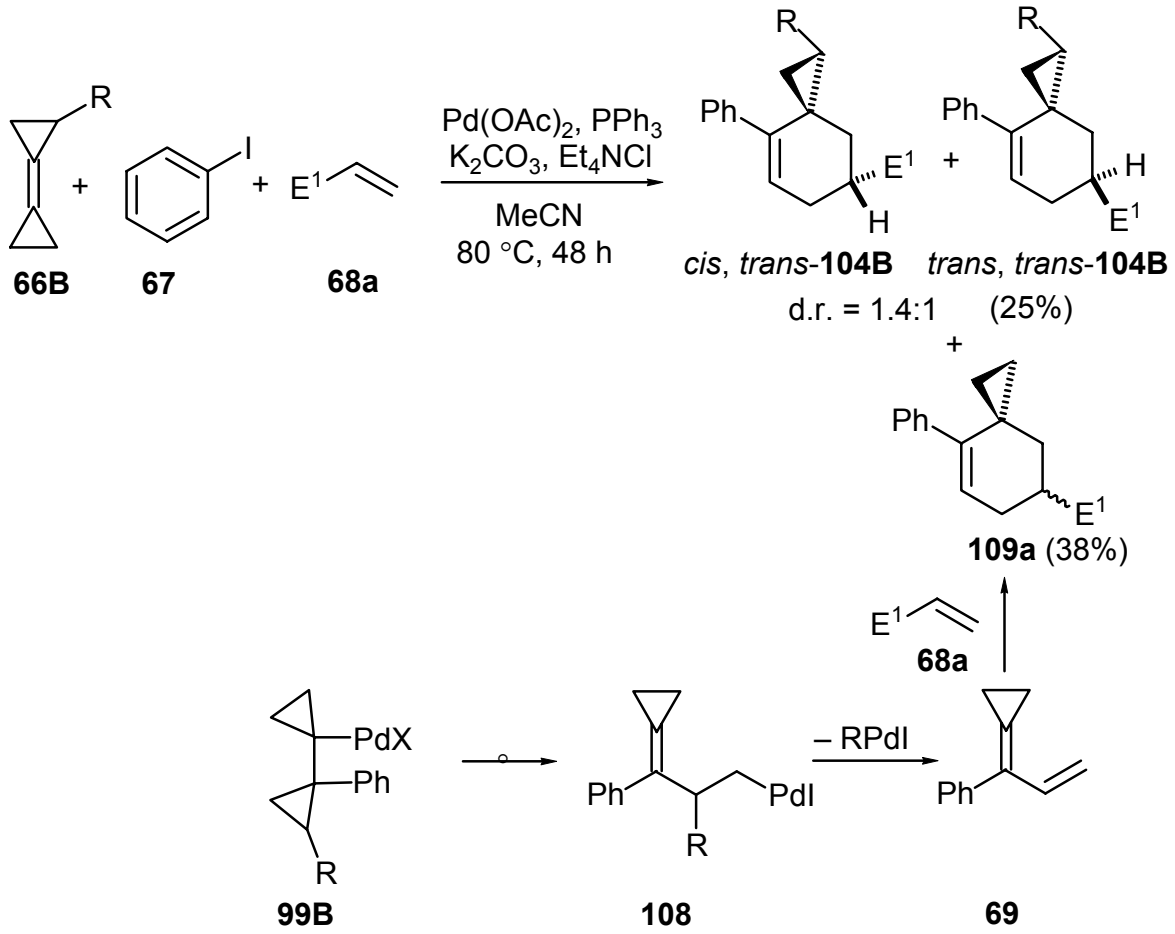


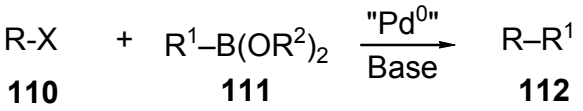
Figure 3. Structure of compound *cis*, *trans*-**104B** (major diastereomer) in the crystal.

However, the same reaction was performed with the sterically encumbered boranate substituted bicyclopropylidene **66B,** as a major product, spirooctene **109a** and mixture of diastereomers *cis/trans*, *trans*-**104B** were obtained in 38 % and 25% yields respectively (Scheme 22). The formation of product **109a** can be attributed to opening of the boranate substituted cyclopropane ring in intermediate **99B** affording homoallylpalladium species **108** that immediately undergo deboropalladation rather than dehydropalladation.[39] The exact configuration of diastereomers *cis/trans*, *trans*-**104B** was proved by NOESY NMR measurements and as well as by X-ray structure analysis of major diastereomer *cis*, *trans*-**104B** (Figure 3).



Scheme 22. One-pot domino Heck-Diels-Alder reaction involving boronate substituted bicyclopropylidene (**66B**), iodo benzene **67** and methyl acrylate **68a**. – $E^1 = CO_2Me$.

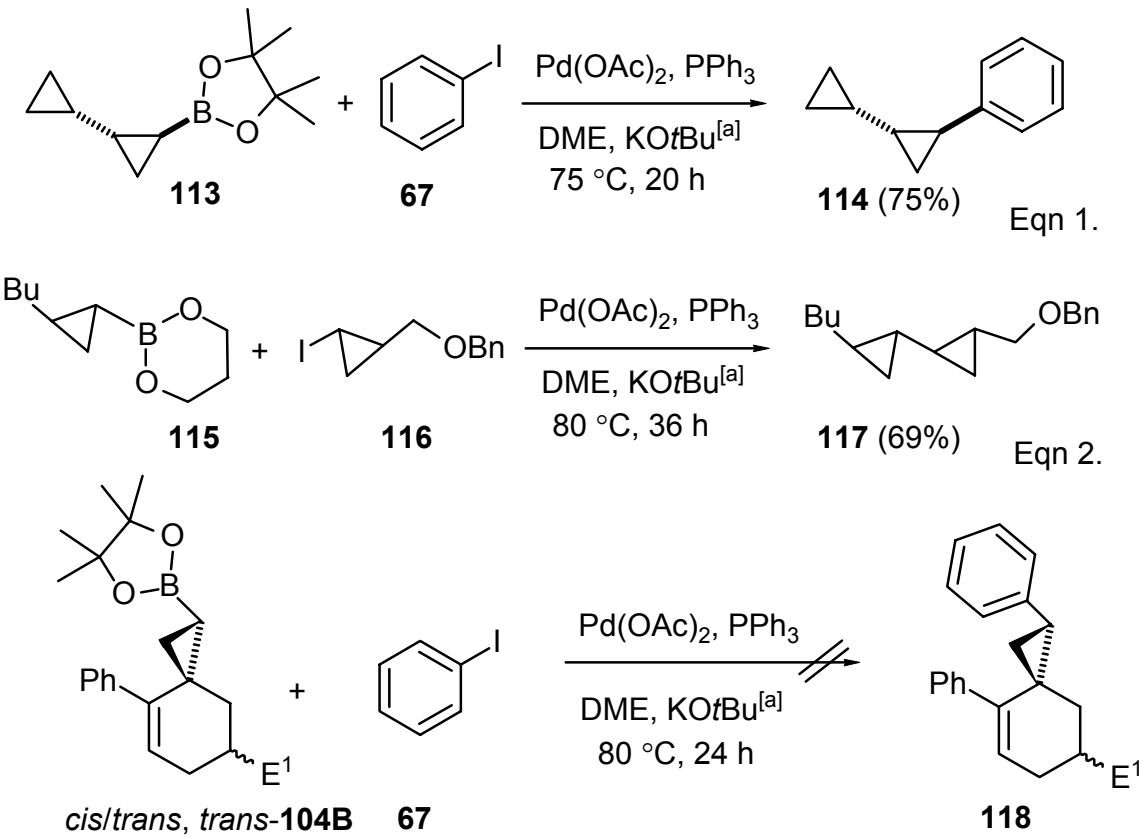
Moreover, isolated products *cis/trans*, *trans*-**104B** having boronate ester functionality on the cyclopropane ring are possible precursors for the Suziki-coupling. The Suziki reaction is one of the most utilized C–C bond forming cross-coupling reactions, which occurs in the presence of a base with a Pd^0 catalyst and involves transmetalation between R–Pd–X and organoboron compounds R^1–$B(OR^2)_2$ as a key step (Scheme 23).[40]



R = alkenyl, aryl, alkynyl; X = I, Br, Cl, OTf.
R^1 = aryl, alkyl, alkenyl,alkynyl
R^2 = H, alkyl, *c*-alkyl

Scheme 23. General representation of the Suziki reaction

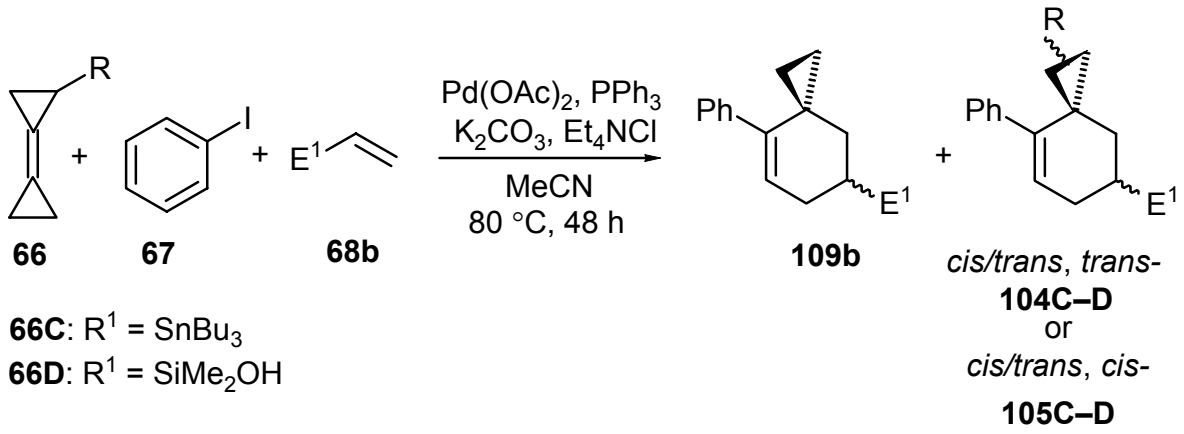
In this respect, spirooctenes *cis/trans*, *trans*-**104B** were further reacted with iodobenzene (**67**) in Suziki-coupling conditions. The coupling condition was selected from effective literature protocols in which cyclopropylboronate esters were coupled with aryl halides (equation 1) [36b, 41] and iodocylopropanes (equation 2)[42] in good yields (Scheme 24).



Scheme 24. Two recent examples of Suziki reaction with cyclopropylboronate esters **113** and **115** (equation 1, 2) and the reaction of boronate substituted spirooctenes *cis/trans*, *trans*-**104B** with iodo benzene **67** in the condition of equations 1 and 2. [a] 1 M solution of KO*t*Bu in *t*BuOH. – E^1 = CO_2Me.

However, in the same conditions the reaction of boronate substituted spirooctenes *cis/trans*, *trans*-**104B** with iodobenzene **67** did not give desired compound **118** and at the end of the reaction even the initial spirooctenes *cis/trans*, *trans*-**104B** could not be recovered.

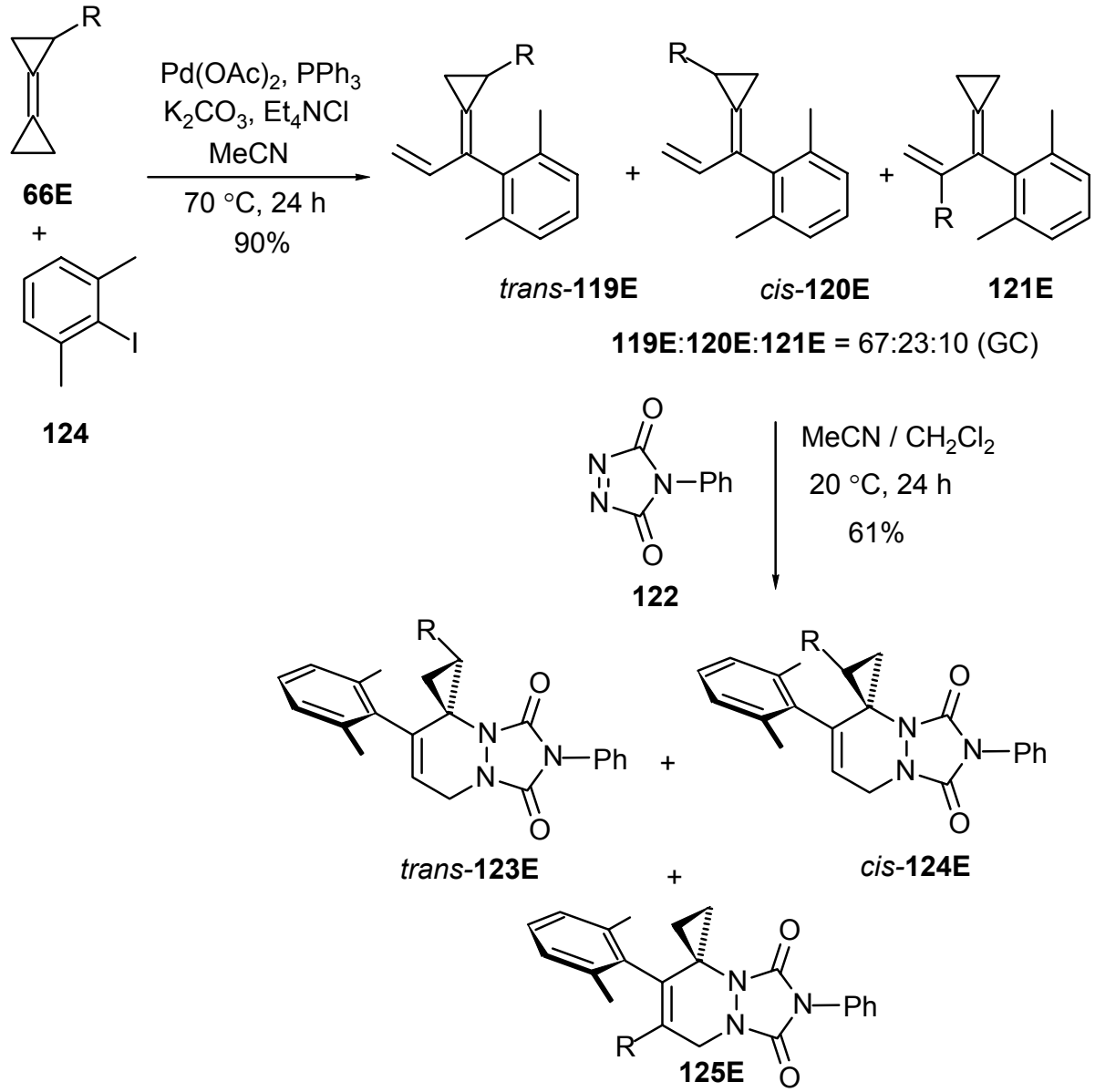
To realize the idea of using functionalized spiro[2.5]octenes as a precursor for the other types of cross-coupling reactions, the preparation of spirooctene derivatives having organostannane and organosilicon functionalities, starting with respective monosubstituted bicyclopropylidenes **66C** and **66D**, was also tried, since such spirooctene derivatives would be coupled with iodobenzene **67** by Stille and Hiyama cross-coupling reactions to yield compound **118**.[43] Unfortunately, domino Heck-Diels-Alder rections with bicylopropylidenes **66C** and **66D** were mainly produced structure **109b** in 49% and 25% yields respectively. Although, in both reactions, some amount of functionalized spirooctene derivatives *cis/trans*, *trans*-**104C–D** and/or *cis/trans*, *cis*-**105C–D** were observed, they could not be isolated and their exact configurations as well as their yields could not be determined (Scheme 25).



Scheme 25. One-pot domino Heck-Diels-Alder reactions involving substituted bicyclopropylidenes (**66C**–**D**), iodo benzene **67** and *t*-butyl acrylate **68b**. – $E^1 = CO_2tBu$

Furthermore, the preparation of spiro[2.5]octene derivatives having a substituent on the cyclopropane ring was also performed in two individual steps. For this purpose, the mixture of allylidenecyclopropane derivatives *trans*-**119E**, *cis*-**120E** and **121E** produced by the Heck reaction of methyl bicyclopropylidenecarboxylate **66E** with 2-iodo-1,3-dimethylbenzene **124** was allowed to react with dienophile *N*-phenyltriazolinedione **122** at room temperature for 24 h. The reaction produced expected regioisomeric mixture of spiro[2.5]octenes *trans*-**123E**, *cis*-**124E** and **125E** in 61% yield. The configuration of spirooctene derivatives *trans*-**123E** and *cis*-**124E** was confirmed by NOESY NMR measurements. The strong correlation of cyclopropyl proton adjacent to the ester functionality with one of the methyl groups of the aryl ring in the NOESY spectrum of *cis*-**124E** and correspondingly, the correlation of methylene

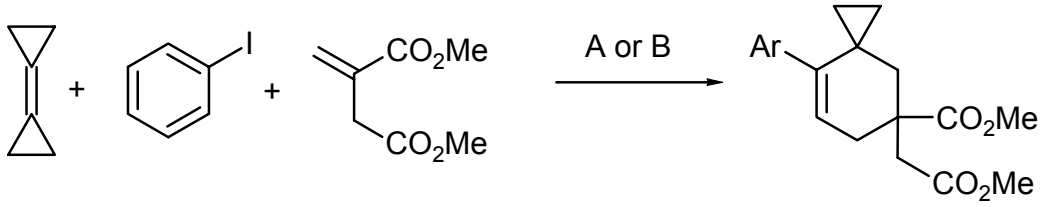
proton of cyclopropane ring in the spectrum of *trans*-**123E** with the same methyl substituent were accepted as proofs for the determination of these structures. Although in this reaction, the carbopalladated intermediate similar to **98E** was favorable, spirooctene **125E** via diene **121E** also appeared by opening of the substituted cyclopropyl ring in an intermediate resembling **99E**.



Scheme 26. The preparation of allylidenecyclopropanes *trans*-**119E**, *cis*-**120E** and **121E** by the Heck reaction of methyl bicyclopropylidenecarboxylate **66E** with 2-iodo-1,3-dimethylbenzene **124** and the formation of spiro[2.5]octenes *trans*-**123E**, *cis*-**124E**, **125E** by Diels-Alder reaction of allylidene-cyclopropanes *trans*-**119E**, *cis*-**120E**, **121E** with *N*-phenyltriazolinedione **122**.

*1.3. A modification on the spiro[2.5]octene derivative **127**: the effective construction of dispiroheterocyclic system **130**.*

It is known that some derivatives of itaconic acid such as mono- and diesters, amides and imides have fungicidal, herbicidal and insecticidal properties. Especially, *N*-arylitaconimides exhibits high activity as soil and foliage fungicides.[44] In domino Heck-Diels-Alder reaction with bicyclopropylidene (**66**), dimethyl ester of itaconic acid **126** was used as dienophile for the synthesis of spiro[2.5]octene derivative **127** (Scheme 27).[29b, 35]

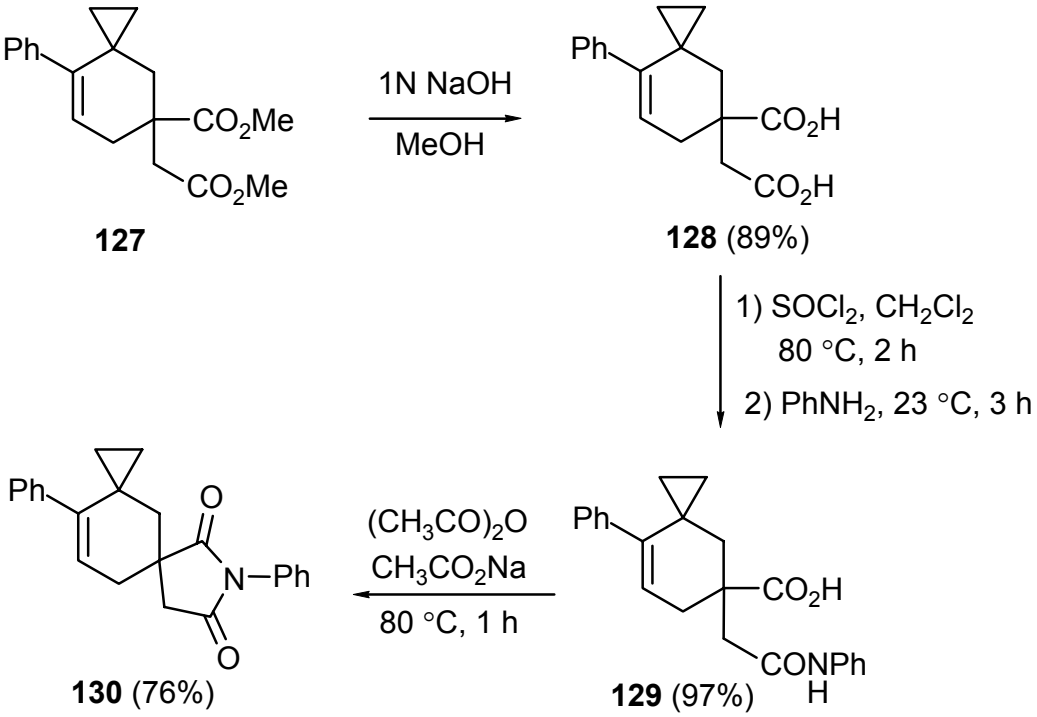


66 **67** **126** **127**

Entry	Reac. Conditions	Yield (%)[a]
1	B 80 C, 72 h	**47**
2	A 80 C, 48 h	**20**
3	A 120 C, 24 h	**29**
4	A 140 C, 36 h	**33**
5[b]	A 180 C, 48 h	**10**
6	A 140 C, 48 h	**10**
7[c]	A 80 C, 48 h 10 kbar	**72**

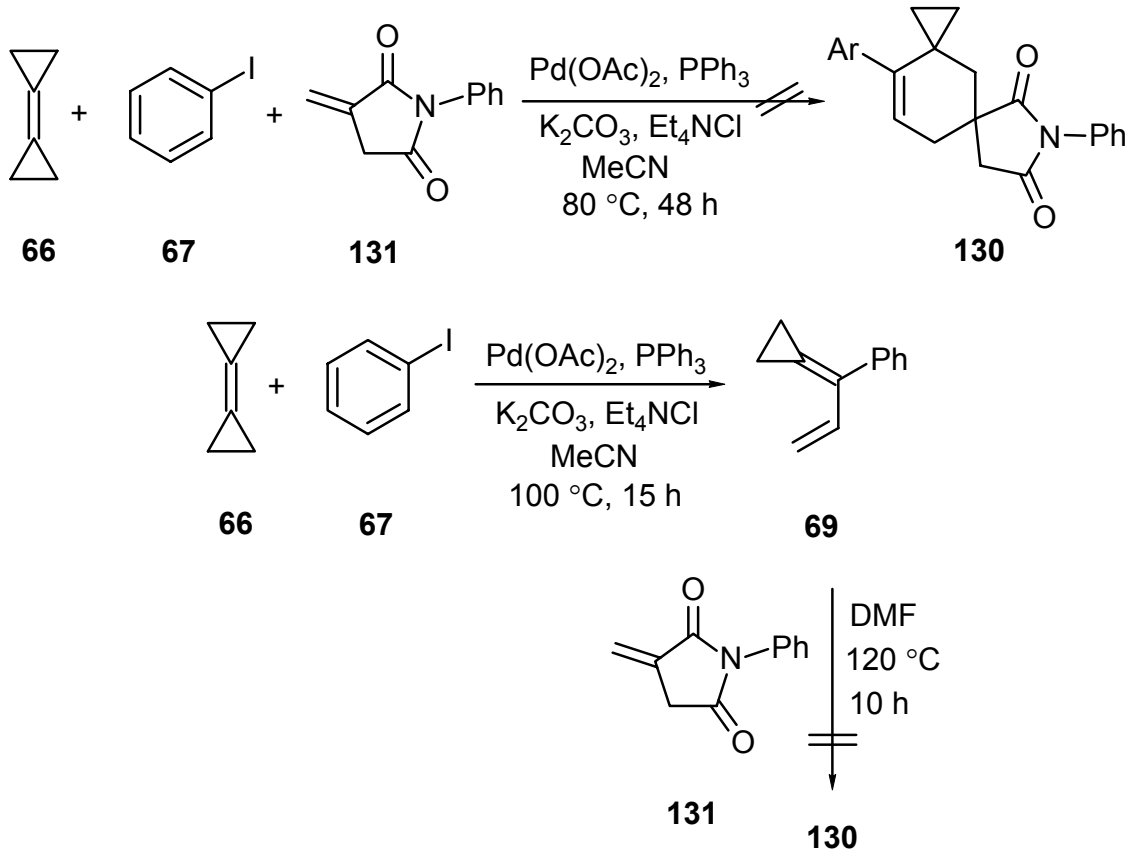
Scheme 27: The synthesis of spiro[2.5]octene **127**. – A: 5% mol $Pd(OAc)_2$, 15% mol PPh_3, Et_3N, DMF. – B: 5% mol $Pd(OAc)_2$, 15% mol PPh_3, K_2CO_3, Et_4NCl, MeCN. – [a]Isolated yield are given. – [b]NMP was used as solvent instead of DMF. –[c]4,5 ml DMF was used for 2.00 mmol bicyclopropylidene **66**, 1.00 mmol iodo benzene **67** and 2.00 mmol dienophile **126**.

This suggested that the incorporation of the essential structural features of itaconic acid derivatives with a spirooctene skeleton might provide compounds with enhanced biological activity. Further synthetic manipulations on the diester moiety of spirooctene **127** would be useful to enrich substitution pattern of the main spirooctene frame in terms of combinatorial aspects as well. For these purposes, via series of transformation, the ester moiety was converted to *N*-phenylimide (Scheme 28). However, firstly, the yield of spiro[2.5]octene **127** had to be improved. Among several attempts, the best result was achieved in high pressure condition which accelerates the Heck coupling[45] as well as the Diels-Alder reaction [46] (Scheme 27).



Scheme 28. Three-step synthesis of dispirocyclic structure **130**.

By using already described literature procedures,[44a, 47] the convenient preparation of dispiro-heterocyclic structure **130** was performed in three steps in high yields. After basic hydrolysis of compound **127**, generated crude diacid structure **128** without further purification was transformed into amicacid containing spirooctene **129** by two subsequent operations. When the spirooctene **129** was heated at 80 ^{o}C for 1 h, desired structure **130** was readily isolated in 76% yield (Scheme 28).



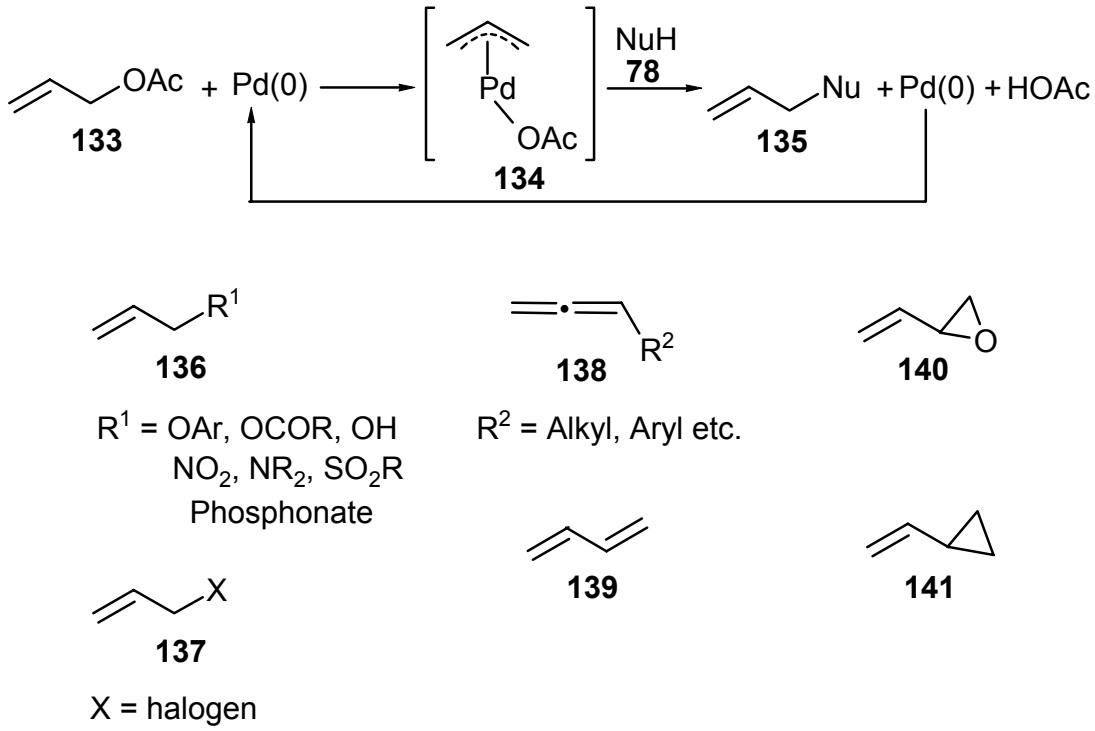
Scheme 29. Two attempts for the direct preparation of spiro[2.5]octene **130**.

Alternatively, direct preparation of **130** was also tried by using domino Heck-Diels-Alder methodology involving *N*-phenylitaconimide **131** as the dienophile in conditions similar to those which gave spiro[2.5]octene **127** in 47% yield. However, this reaction did not produce the desired spirooctene **130**. Heating the mixture of dienophile **131** and crude allylidenecylopropane derivative **69** generated by the Heck reaction of bicyclopropylidene **66** and iodobenzene **67**, at high temperature to promote the Diels-Alder reaction, did not also furnish the expected result (Scheme 29).

2. A Two-Step Four-Component Queuing Cascade Involving a Heck Coupling, π-Allylpalladium Trapping and Diels-Alder Reaction

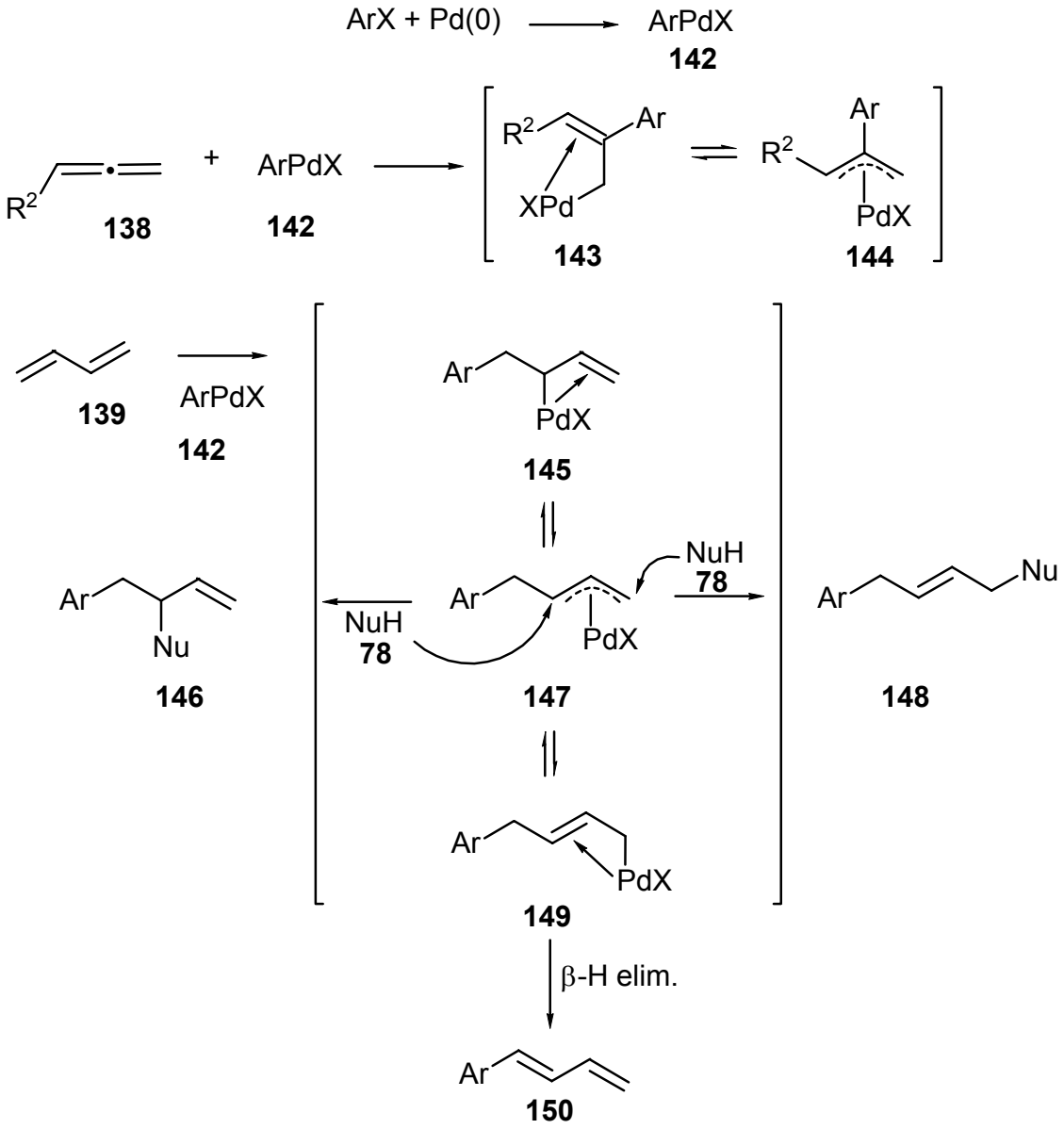
2.1. Introduction

Palladium-catalyzed reactions involving π-allylpalladium intermediates have emerged as one of the most useful applications in organic chemistry since these intermediates undergo different types of transformations. For instance, π-allylpalladium unit can be easily substituted with a variety of nucleophiles (Scheme 30). Indeed, this process is performed successfully in an asymmetric manner with highly selective chiral ligands. π-Allylpalladium complexes occur readily by both palladium(0) and palladium(II) catalysts in various substrates that contain at least one double bond (Scheme 30).[48] However, the Pd(II) catalyzed reaction of allylic substrates generates π-allylpalladium intermediates by consuming stoichiometric amount of Pd(II) salts.[48a, 49] Produced Pd(0) species should be re-oxidized to Pd(II) to make this reaction catalytic. For this purpose $CuCl_2$ and benzoquinone are extensively used.[50]



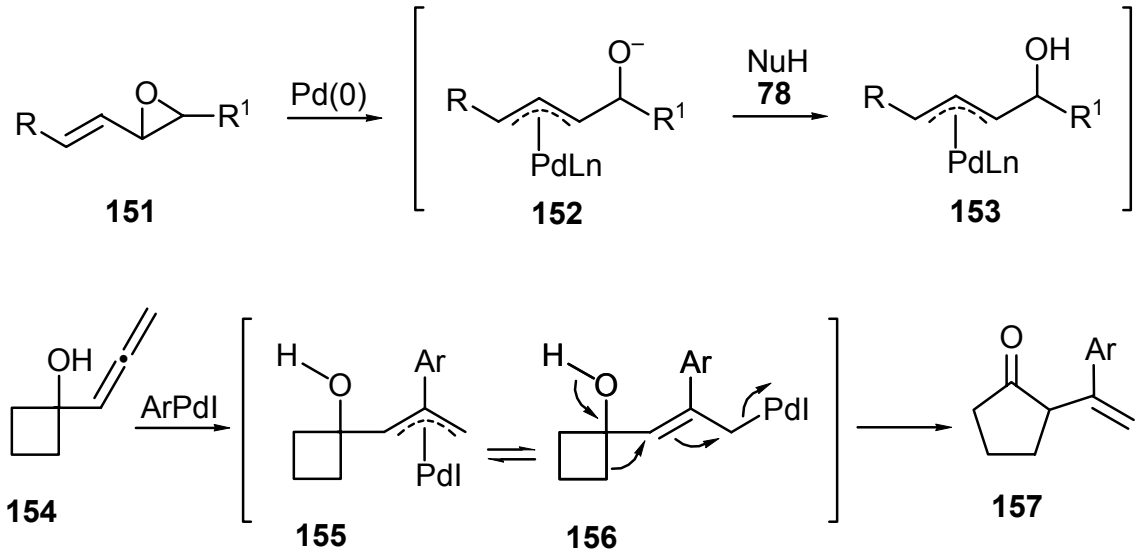
Scheme 30. An example of palladium(0) catalyzed allylic substitution via π-allylpalladium complex **134** and typical substrates **136**–**141** which can generate π-allylpalladium intermediates.

Allenes[51] **138** as well as conjugated dienes[52] **139** with aryl or alkenyl halides in the presence of Pd(0) catalysts produce also π-allylpalladium complexes **144** and **147** respectively (Scheme 31). Carbopalladation of these substrates by initially formed aryl- or alkenylpalladium species **142** gives a σ-allylpalladium complexes (**143**, **145)** which are expected to be in equilibrium with their canonical forms (i.e., π-allylpalladium complexes **144** and **147**). Generally, the reaction of π-allylpalladium species as **147** in scheme 31 with various nucleophiles can furnish two regioisomeric products **146** and **148** by attacking of a nucleophile to different terminus of the π-allylpalladium core. In the absence of nucleophiles, β-hydrogen elimination takes place to afford the coupling product **150**.



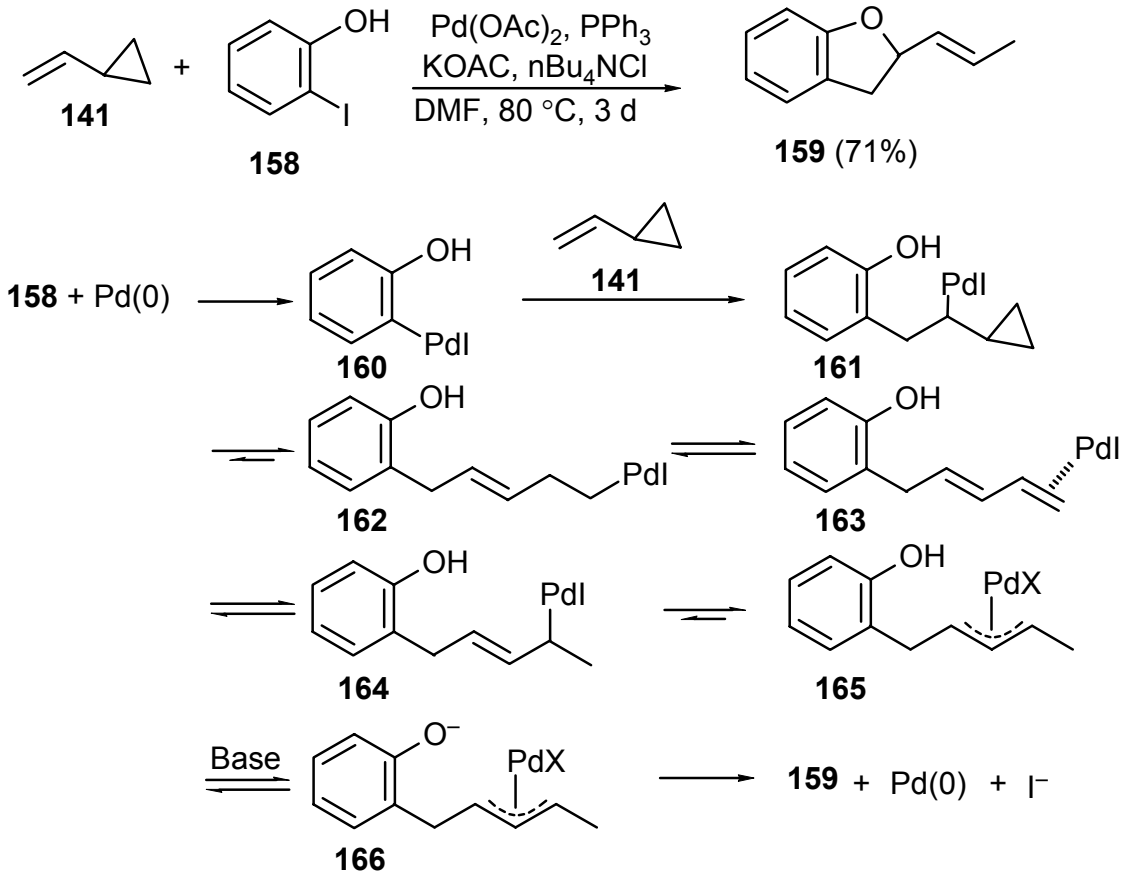
Scheme 31. Pd(0) catalyzed reaction of allene **138** and conjugated diene **139**; the formation of π-allylpalladium complexes **144** and **147**.

The formation of π-allylpalladium complexes in the reaction of strained building blocks usually goes together with a ring opening or a ring expansion process.[53] For instance, in the presence of Pd(0), alkenyloxirans **151** generates a π-allylpalladium complex **152** with the opening of the epoxy ring (Scheme 32).[54] The occurring alkoxide ion gains a proton from the nucleophile to form α-hydroxy-π-allylpalladium **153**. Correspondingly, the carbopalladation of allenylcyclobutanols **154** by initially formed arylpalladiumiodides affords first π-allylpalladium complex **155**; and following rearrangement, ring expansion processes produce cyclopentanone derivatives **157** (Scheme 32).[55]



Scheme 32. Palladium(0) catalyzed reactions of strained substrates **151** and **154**; the formation of π-allylpalladium intermediates **152** and **155**.

Recently, Larock et al. have demonstrated that palladium-catalyzed reaction of 2-iodophenol **158** with a vinyl cyclopropane **141** proceeds via an intermolecular trapping of π-allylpalladium intermediates **165**, **166** to furnish the heterocyclic product **159** (Scheme 33).[56] In this process, a typical carbopalladation of the carbon-carbon double bond in the alkene results in the immediate ring-opening of cyclopropylcarbinyl palladium species **161** to the corresponding homoallylpalladium complex **162**. Following β-hydride elimination and reverse regioselective addition of hydridopalladium species generate the key intermediate, π-allylpalladium complex **165**.

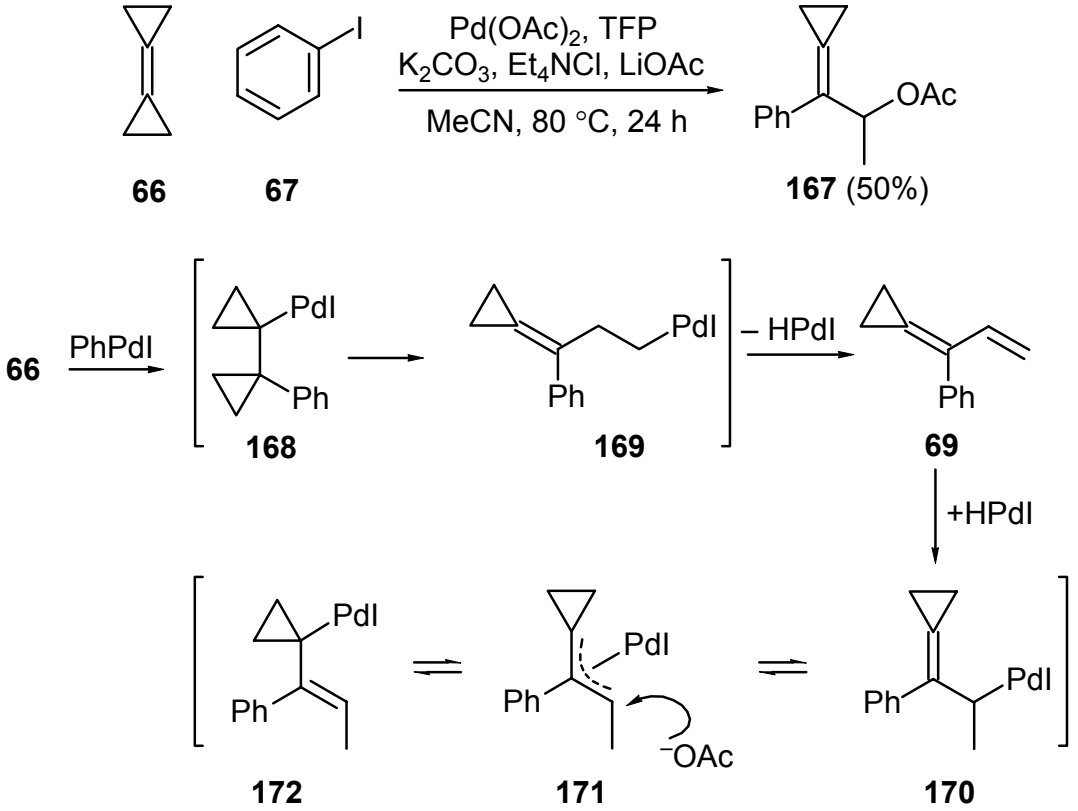


Scheme 33. The preparation of heterocyclic product **159** via intermolecular nucleophilic trapping of π-allylpalladium intermediates **166**.

*2.1.1. The formation of π-allylpalladium complexes in the palladium-catalyzed reaction of bicyclopropylidene (**66**) with arylhalides.*

In the course of detailed studies on the domino Heck-Diels-Alder reaction with bicyclopropylidene (**66**) by the isolation of the side product **167**, a second reaction mode was recognized.[57] The formation of the allylidenecylopropane **167** was attributed to an intermolecular nucleophilic trapping of the π-allylpalladium intermediate **171** at the sterically less hindered position by attacking of an acetate anion stemming from the catalyst precursor. Thus, in the absence of dienophiles and favored by the presence of tris(2-furyl)phosphane (TFP), which is known to retard β-hydride elimination,[58] **69** undergoes hydridopalladation with the reverse regioselectivity to form the σ-allylpalladium intermediate **170** in equilibrium with the π-allylpalladium complex **171**. By the additional source of LiOAc, the yield of the allylidenecylopropane was inceased to 50%. Moreover, this methodology was further developed using nitrogen, oxygen as well as carbon nucleophiles to prepare

allylidenecyclopropane derivatives of type **167**. Among them, the best results were achieved with amine nucleophiles in a few hours.[57]



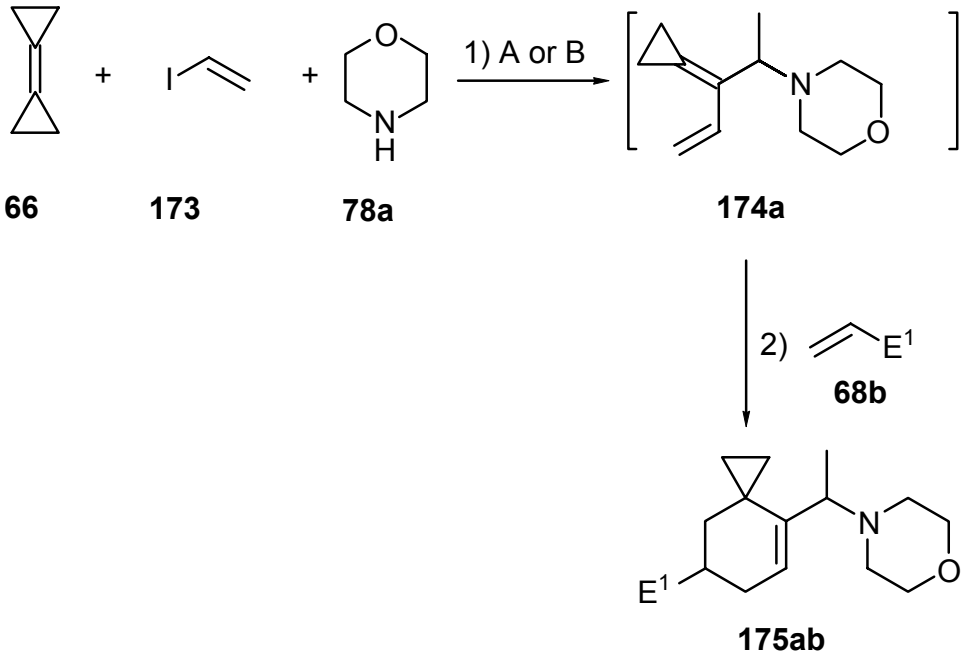
Scheme 34. The trapping of π-allylpalladium complex **171** with an acetate anion and the formation allylidenecyclopropane **167**; the Heck reaction of bicyclopropylidene (**66**) with iodo benzene **67** in the presence of TFP.

*2.2. One-pot, two-step, four-component queuing cascade of bicyclopropylidene (**66**) with iodoethene, amine nucleophiles (**78a**–**e**) and dienophiles (**68a**–**g**).*

In this study, a new dimension was added to the overall concept of bicyclopropylidene based cascade reactions via an extension of the second reaction mode into a four-component queuing cascade by coupling an alkenyl iodide with bicyclopropylidene (**66**) in the presence of TFP. After trapping of the formed π-allylpalladium intermediates with a nucleophile, this gave a conjugated diene, which was allowed to react with an added dienophile to furnish 8-(1'-aminoethyl) substituted spiro[2.5]oct-7-ene derivatives. Firstly, this cascade reaction was performed by coupling of bicyclopropylidene (**66**) with iodoethene (**173**) in the presence of

amine nucleophiles (**78**) in two different conditions and subsequent addition of various dienophiles. The results are summarized in Scheme 36 and Table 2.

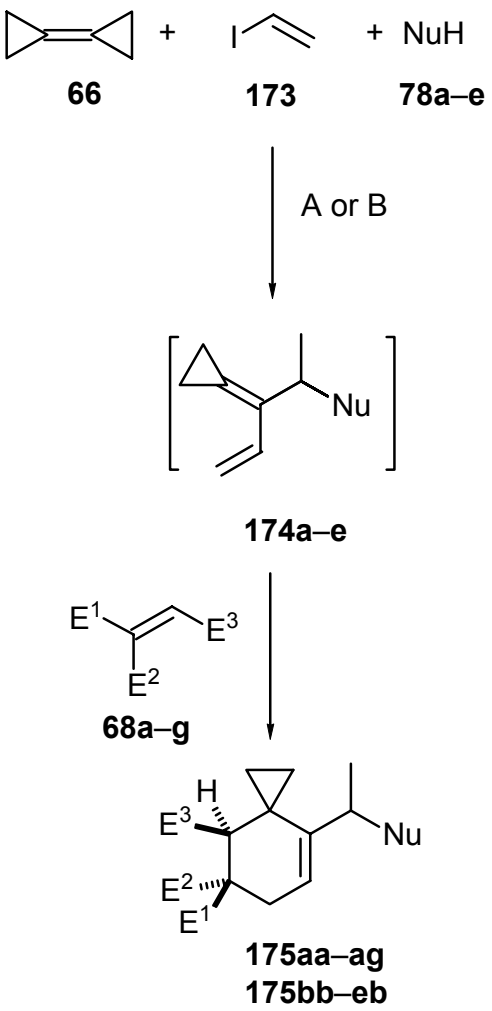
The palladium-catalyzed cross coupling with rearrangement and nucleophilic trapping cannot be carried out with the dienophile being present from the beginning, since a Michael addition of the nucleophile onto the dienophile would compete with the desired reaction. Therefore, at the beginning, it was decided to perform the reaction in two steps. In the light of the previous studies,[57, 59] for the first part of the reaction in which the formation of a conjugated diene takes place, two different rection conditions were utilized. The first one was typical Heck-coupling conditions, i.e. a mixture of $Pd(OAc)_2$ and NEt_3, yet in this case, necessarily using TFP as a ligand instead of PPh_3 in dimethylformamide. The second one generally referred to "Jeffery Conditions" was the palladium catalyst cocktail involving $Pd(OAc)_2$, TFP, K_2CO_3, and the phase transfer reagent Et_4NCl with solvent acetonitrile.[60] The application of these conditions in the presence of one equivalent of various amine nucleophiles at 80 °C for 2 h was enough to complete the coupling of bicyclopropylidene (**66**) with iodoethene **173** and trapping of π-allylpalladium intermediates to furnish reactive dienes, allylidenecyclopropanes, for the subsequent Diels-Alder step. A variety of reaction conditions was also examined by the addition of *tert*-butyl acrylate **68b** after 2 h into the model reaction of bicyclopropylidene **66**, iodoethene **173** and morpholine **78a** to find out the best condition for the second step (Scheme 35). To reach the maximum yield of the spiro[2.5]octene **175ab**, the reaction mixture had to be heated at 80 °C for 48 h after the first step (entries 4, 5 in Table 2). Since cyloaddition reactions take place more effectively in high concentrations, the amount of the solvent was reduced in some attempts (entries 2, 3 and 6). However, performing the reaction in 1 mL DMF for the conditions A and in 2 mL for the conditions B were ideal to obtain the highest yields. On the other hand, the reaction performed with only one equivalent bicyclopropylidene caused a sharp decrease in the yield of the spirooctene **175ab** (entry 9). Moreover, at elevated temperatures the reaction gave poorer yields, particularly in extended reaction times (entries 6, 7 and 8). Finally, to accelerate the Diels-Alder reaction, the Lewis acid $BF_3.Et_2O$ was also added with *tert*-butyl acrylate into the mixture.[61] After 12 h, this reaction did not gave the desired product **175ab** and the diene **174a** could not be observed (entry 10 in Table 1).



Scheme 35. The synthesis of spiro[2.5]octene **175ab**. – A: 5% mol $Pd(OAc)_2$, 10% mol TFP, Et_3N, DMF. – B: 5% mol $Pd(OAc)_2$, 10% mol TFP, K_2CO_3, Et_4NCl, MeCN. – E^1 = CO_2tBu, For details see Table 1.

Entry	Reaction Conditions[a]		Yield[b]	d.r.[c]
	Step 1	Step 2	(%)	
1	A, 1 mL DMF	80 °C, 12 h	19	–[d]
2	A, 0.5 mL DMF	80 °C, 48 h	53	1:1
3	A, 0.5 mL DMF	90 °C, 24 h	48	1:1
4	A, 1 mL DMF	80 °C, 48 h	66	1.3:1
5	B, 2 mL MeCN	80 °C, 48 h	64	1.3:1
6	A, 0.5 mL DMF	110 °C, 6 h	49	1.1:1
7	A, 1 mL DMF	110 °C, 6 h	53	1:1
8	A, 1 mL DMF	120 °C, 48 h	16	–[d]
9[e]	A, 1 mL DMF	80 °C, 48 h	34	1.1:1
10[f]	A, 1 mL DMF	23 °C, 48 h	–[g]	–

Table 1. Optimization of reaction conditions. – [a]4.00 mmol bicyclopropylidene **66**, 2.00 mmol iodoethene **173**, 2.00 mmol morpholine **78a** and 4.00 mmol *tert*-butyl acrylate **68b** were used. – [b]Isolated yield are given. – [c]Diastereomeric ratios were determined by integration of relevant ^1H NMR signals in the spectra of the crude products. – [d]Only one diastereomer was isolated. – [e]2.00 mmol bicyclopropylidene **66** was used. – [f]2.00 mmol $BF_3.Et_2O$ was added in the second step of the reaction.– [g]No product.



Scheme 36. A new one-pot, two-step four-component queuing cascade involving bicyclopropylidene (**66**), iodoethene (**173**), nucleophiles **78a**–**e** and dienophiles **68a**–**g**. A: $Pd(OAc)_2$, TFP, NEt_3, 2 h, 80 °C, DMF. – B: $Pd(OAc)_2$, TFP, K_2CO_3, Et_4NCl, 2 h, 80 °C, MeCN. For further details see Table 2.

With morpholine (**78a**) as a secondary amine, well known to be a good nucleophile,[62] the yields in this one-pot, two-step queuing cascade were generally good (39–66%). Exceptionally, reactions in which dienophiles **68f**–**g** were used did not yield expected products **175af**–**ag**. (Table 2). With piperidine (**78b**), pyrrolidine (**78c**), *N*-benzylpiperazine (**78d**), and *N*-*tert*-butoxycarbonylpiperazine (**78e**) in combination with **66**, **173** and the best yielding *tert*-butyl acrylate (**68b**), the cascade reaction gave the corresponding products **175bb**–**eb** mostly in moderate yield (21–49%). In all cases, the products from unsymmetrical dienophiles **68a**–**c** were only 5-substituted spiro[2.5]oct-7-ene derivatives as assigned on the basis of their NMR spectra. This is in agreement with the previously observed regioselectivities in Diels-Alder additions of acrylates to allylidenecyclopropanes.[29b, 63]

Nucleophile **78** NuH	Cond.	Dieno-Phile	E^1	E^2	E^3	Product	Yield (%)[a]	d.r.[b]
a Morpholine	B	**68a**	CO_2Me	H	H	**175aa**	65	1.1:1
a Morpholine	A	**68a**	CO_2Me	H	H	**175aa**	40	1.3:1
a Morpholine	A	**68b**	CO_2tBu	H	H	**175ab**	66	1.3:1
a Morpholine	B	**68b**	CO_2tBu	H	H	**175ab**	64	1.3:1
a Morpholine	B	**68c**	SO_2Ph	H	H	**175ac**	62	1.2:1
a Morpholine	A	**68c**	SO_2Ph	H	H	**175ac**	46	1.1:1
a Morpholine	B	**68d**	CO_2Me	H	CO_2Me	*cis/trans*-**175ad**	58	1.2:1
a Morpholine	B	**68e**	H	CO_2Me	CO_2Me	*cis/trans*-**175ad**	52	1.7:1
a Morpholine	A	**68d**	CO_2Me	H	CO_2Me	*cis/trans*-**175ad**	39	1.3:1
b Piperidine	A	**68b**	CO_2tBu	H	H	**175bb**	33	1:1
b Piperidine	B	**68b**	CO_2tBu	H	H	**175bb**	27	1:1
c Pyrrolidine	A	**68b**	CO_2tBu	H	H	**175cb**	29	1:1
c Pyrolidine	B	**68b**	CO_2tBu	H	H	**175cb**	21	1:1
d *N*-Bn-Piperazine	B	**68b**	CO_2tBu	H	H	**175db**	48	1.1:1
d *N*-Bn-Piperazine	A	**68b**	CO_2tBu	H	H	**175db**	44	1.4:1
e *N*-Boc-Piperazine	B	**68b**	CO_2tBu	H	H	**175eb**	49	1:1
e *N*-Boc-Piperazine	A	**68b**	CO_2tBu	H	H	**175eb**	39	1:1
a Morpholine	B	**68f**	CN	H	CN	**175af**	–	–
a Morpholine	A	**68f**	CN	H	CN	**175af**	trc.	–
a Morpholine	B	**68g**	SO_2Ph	H	SO_2Ph	**175ag**	–	–

Table 2. One-pot, two-step four-component queuing cascade involving bicyclopropylidene (**66**), iodoethene **173**, nucleophiles **78a**–**e**, dienophiles **68a**–**g** (see Scheme 36). [a]Isolated yields are given. – [b]Diastereomeric ratios were determined by integration of relevant ^{1}H NMR signals in the spectra of the crude products.

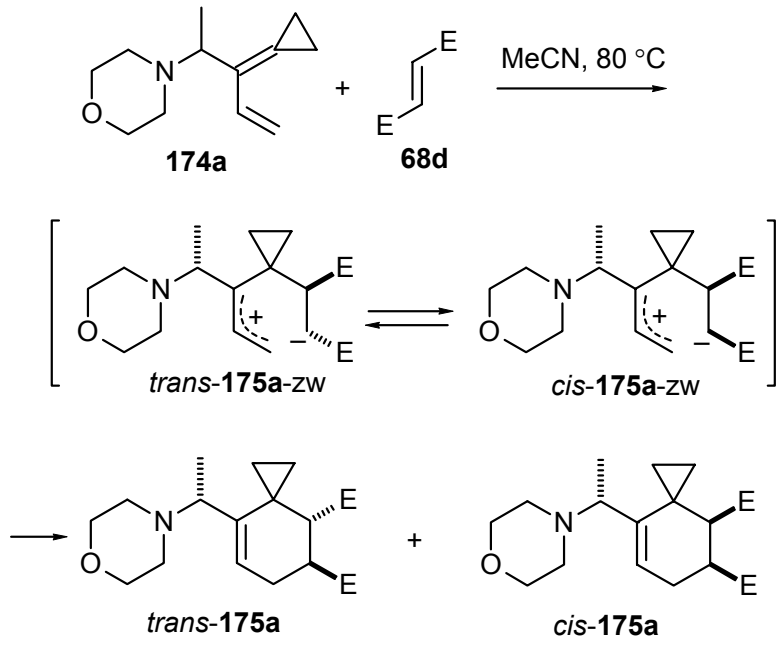
The reaction with dimethyl fumarate **68d** and dimethyl maleate **68e** both gave mixtures of dimethyl *cis*- and *trans*-spiro[2.5]octenedicarboxylates (*cis*- *and trans*-**175ad**) in slightly different ratios (Table 2), irrespective of the conditions (A or B in Scheme 36) used. Control experiments confirmed that simple heating in dimethylformamide at 80 °C causes **68e** to isomerize to **68d**, (50% conversion after 1.5 h, ~98% conversion after 6 h), whereas heating of **68e** in acetonitrile at 80 °C did not lead to any isomerization even after 24 h.

Attention was then turned to the reaction of isolated diene **174a** with dimethyl maleate (**68e**) to explain the formation of the *trans*-spirooctenedicarboxylate *trans*-**175ad** along with *cis*-**175ad** under conditions B (i.e., in acetonitrile), since isomerization of **68e** to **68d** during the course of the Heck reaction is well known.[64] In other words, in the absence of the catalyst ingredients, *cis*-**175ad** would be expected as a single product if the cycloaddition of dimethyl maleate (**68e**) to the 1,3-diene **174a** occurred in a concerted mode. Surprisingly, however, the reaction of a fourfold excess of dimethyl maleate (**68e**) with diene **174a** in acetonitrile at 80 °C after 24 h again gave virtually the same mixture of *cis*- *and trans*-**175ad** in a ratio of 1.4:1 in quantitave yield (based on the diene **174a**) along with a 3:1 mixture of **68d** and **68e**.

The reaction of **174a** with a twofold excess of **68e** was also performed in deuterated acetonitrile and monitored by NMR spectroscopy. After 1 h, some dimethyl fumarate (**68d**) was detectable, but none of the cycloadduct *cis*- or *trans*-**175ad** from the diene **174a**. The concentration of **68d** continued to increase until the formation of *cis*- and *trans*-**175ad** set in. Thus, the second order rate of the cycloaddition of **68d** to **174a** at the given temperature becomes comparable to that of the first order or pseudo-first order rate of isomerization of **68e** to **68d** only when the concentration of **68d** has reached a certain level (almost one third of that of **68e** after 7 h). It is well known that dimethyl fumarate (**68d**) is more reactive as a dienophile than dimethyl maleate (**68e**) by a factor of about 82.[65] Most probably, the diene **174a**, which is a tertiary amine, catalyzes the isomerization of **68e** to **68d**. Indeed, in a control experiment, *N*-allylmorpholine as a model for **174a** was shown to cause this isomerization.

Altogether these results imply that the cycloaddition of dimethyl fumarate (**68d**) to **174a** must proceed in two steps through the zwitterionic intermediate *trans*-**175a**-zw, just as has been suggested for the reaction of (1'-arylallylidene)cyclopropanes with **68d** and **68e** (Scheme 3).[29b] Rather than undergoing immediate cyclization, the initial zwitterion *trans*-**175a**-zw by internal rotation can go to *cis*-**175a**-zw and then cyclize to furnish the cycloadduct of dimethyl maleate (**68e**). Since only two diastereomers were obtained from both **68d** and **68e**, the stereocenter present in the diene **174a** most probably controls the approach of the dienophile **68d** in such a

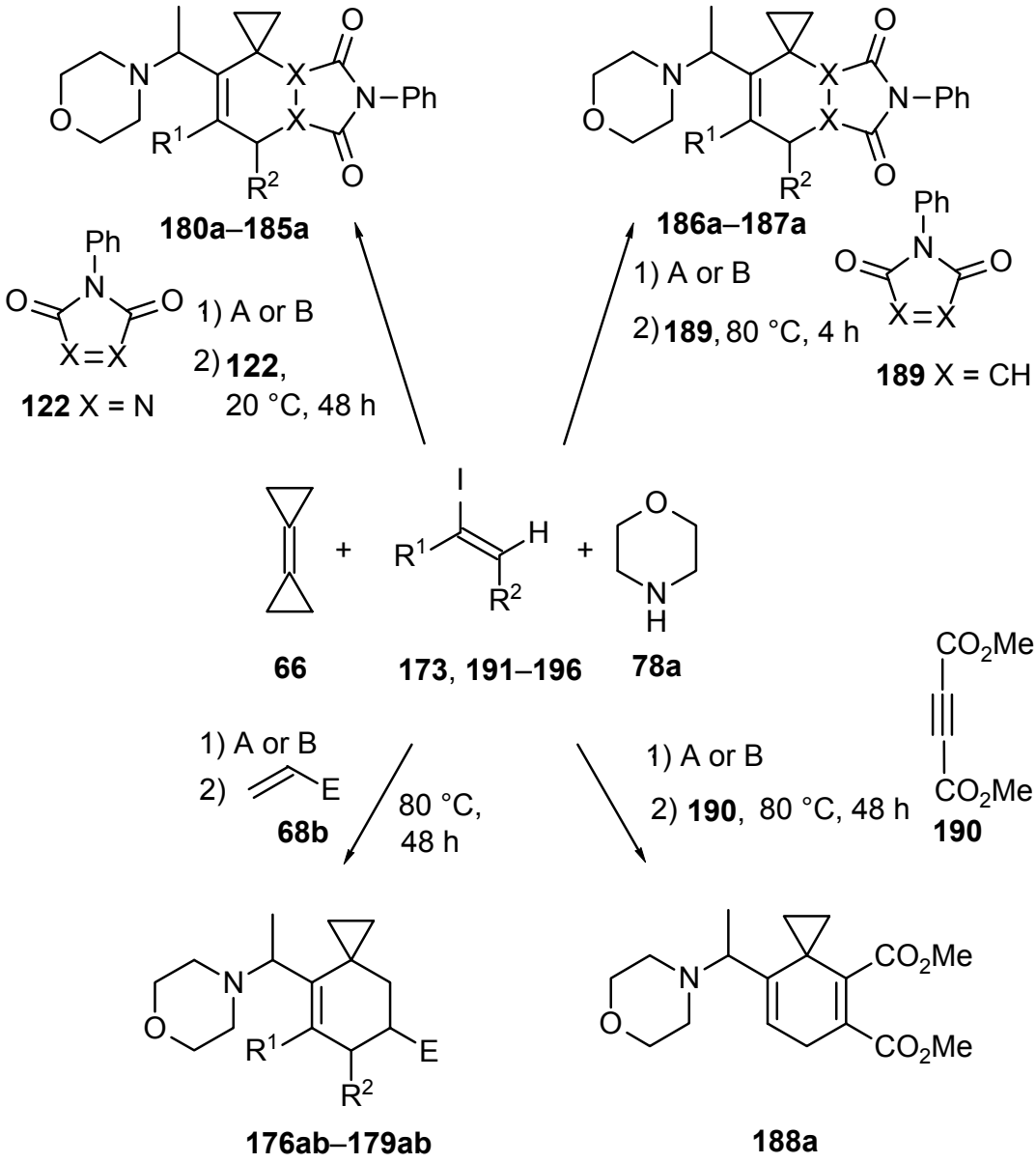
way as to only form the zwitterion *trans*-**175a**-zw as shown, and this undergoes rotation only to *cis*-**175a**-zw or ring closure to *trans*-**175a**.



Scheme 37. Rationalizing the formation of both diastereomeric cycloadducts *trans*-**175a** and *cis*-**175a** from the allylidenecyclopropane **174a** and dimethyl fumarate (**68d**). E = CO_2Me.

*2.3. One-pot, two-step, four-component queuing cascade of bicyclopropylidene (**66**) with iodoalkene derivatives, morpholine (**78a**) and dienophiles (**68a–g**).*

The complexity of the product structure was further increased by the use of heteroatom-containing dienophiles **122** and **189** with various substituted vinyl iodides **191**–**196** (Scheme 38 and Table 3), which were prepared according to published procedures. In most of these cases, however, the yields were only moderate and, in general, lower than with iodoethene (**173**). In the reactions of α-iodostyrene (**191)** (entries 3, 5 and 17 in Table 3) and 5-(1-iodovinyl)benzo[1,3]dioxole **192** (entry 2 in Table 2), more than one equivalent of morpholine had to be added, and the reaction mixture with the palladium catalyst had to be heated for more than two hours to drive the first section of the sequential reaction to completion. Indeed, when the reactions of iodoalkenes **191** and **192** were carried out with sterically encumbered dienophiles such as *tert*-butyl acrylate (**68b**) (entries 3, 4 in Table 3), prolonged reaction times and higher temperatures than 80 °C were necessary for the Diels-Alder reaction in the second step to be successful.



Scheme 38. One-pot, two-step four-component queuing cascade involving bicyclopropylidene (**66**), iodoalkenes **173** and **191**–**196**, morpholine **78a** and dienophiles **68b**, **122**, **189** and **190**. A: $Pd(OAc)_2$, TFP, NEt_3, 80 °C, 48 h, DMF. – B: $Pd(OAc)_2$, TFP, K_2CO_3, Et_4NCl, 80 °C, 48h, MeCN. E = CO_2tBu, For details see Table 3.

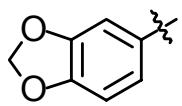
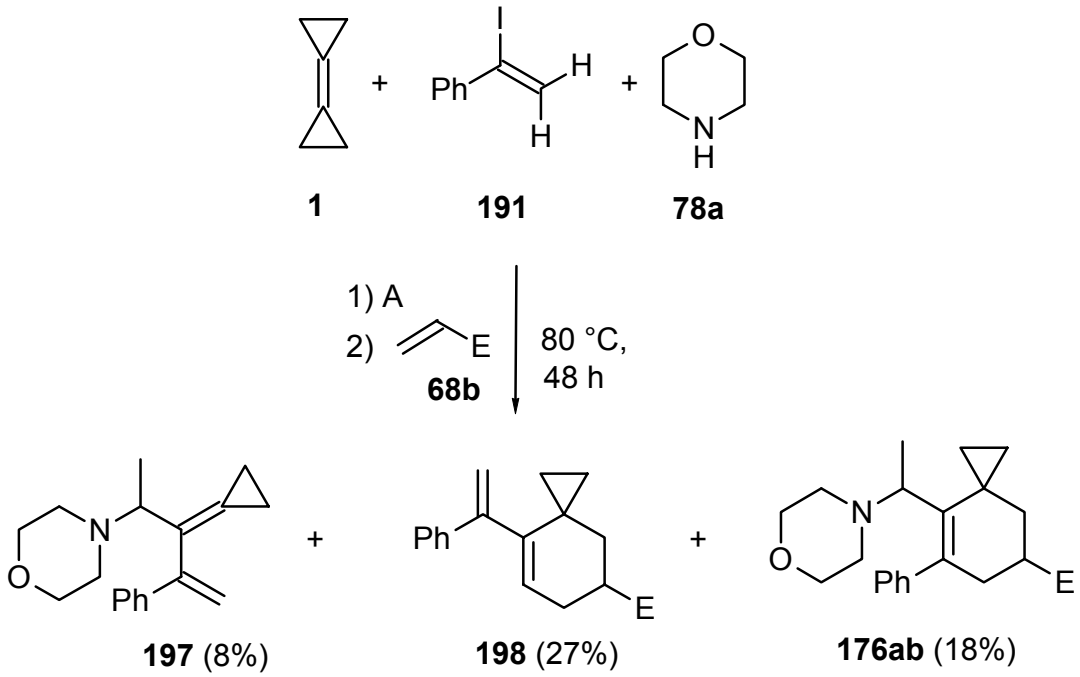
Entry	Cond.	Time [h]	Alkenyl Iodide	R^1	R^2	Dieno-phile	Product	Yield[a] (%)	d.r.[b]
1	A	2	**191**	Ph	H	**68b**	**176ab**	18	1:1
2	A	4	**191**	Ph	H	**68b**	**176ab**	23	1:1
3	B[c,d]	3	**191**	Ph	H	**68b**	**176ab**	36	1.1:1
4	B[c,d]	3	**192**		H	**68b**	**177ab**	44	1.2:1
5	B	3.5	**193**	$[(CH_2)_2NCH_2]$ Bn		**68b**	**178ab**	10	–[e]
6	B[f]	3.5	**193**	$[(CH_2)_2NCH_2]$ Bn		**68b**	**178ab**	26	2.5:1[e]
7[g]	B	3.5	**194**	$–(CH_2)_4–$		**68b**	**179ab**	–	–
8	B[f]	3.5	**194**	$–(CH_2)_4–$		**68b**	**179ab**	25	1:1
9	A[h]	5	**194**	$–(CH_2)_4–$		**122**	**180a**	33	4.6:1
10	B	3	**193**	$[(CH_2)_2NCH_2]$ Bn		**122**	**181a**	17	–[e]
11	A	3	**195**	H	2-thienyl	**122**	**182a**	26	1:1
12	A	2	**196**	H	Ph	**122**	**183a**	35	1.4:1
13	B	2	**196**	H	Ph	**122**	**183a**	32	1.4:1
14	B	2	**173**	H	H	**122**	**184a**	50	–[e]
15	B[d]	3	**191**	Ph	H	**122**	**185a**	35	–[e]
16	A	2	**173**	H	H	**189**	**186a**	40	1:1
17	A[d]	3	**191**	Ph	H	**189**	**187a**	40	1.18:1
18	B[i]	2	**173**	H	H	**190**	**188a**	30	–[e]
19	A	2	**173**	H	H	**190**	**188a**	24	–[e]

Table 3. One-pot, two-step four-component queuing cascade involving bicyclopropylidene (**66**), iodoalkenes **173** and **191**–**196**, morpholine **78a** and dienophiles **68b**, **122**, **189** and **190**. (see Scheme 38). [a] Isolated yields are given. – [b] Diastereomeric ratios were determined by integration of relevant ^{1}H NMR signals in the spectra of the crude products. – [c] 100 °C, 65 h for the second step. – [d] 1.5 equiv. of morpholine (**78a**) used in the first step.– [e] Only one diastereomer was isolated. – [f] 1.2 equiv. of morpholine (**78a**) used in the first step. – [g] Products could not be isolated. – [h] 100 °C for the first step. [i] 80 °C, 4 h for the second step.

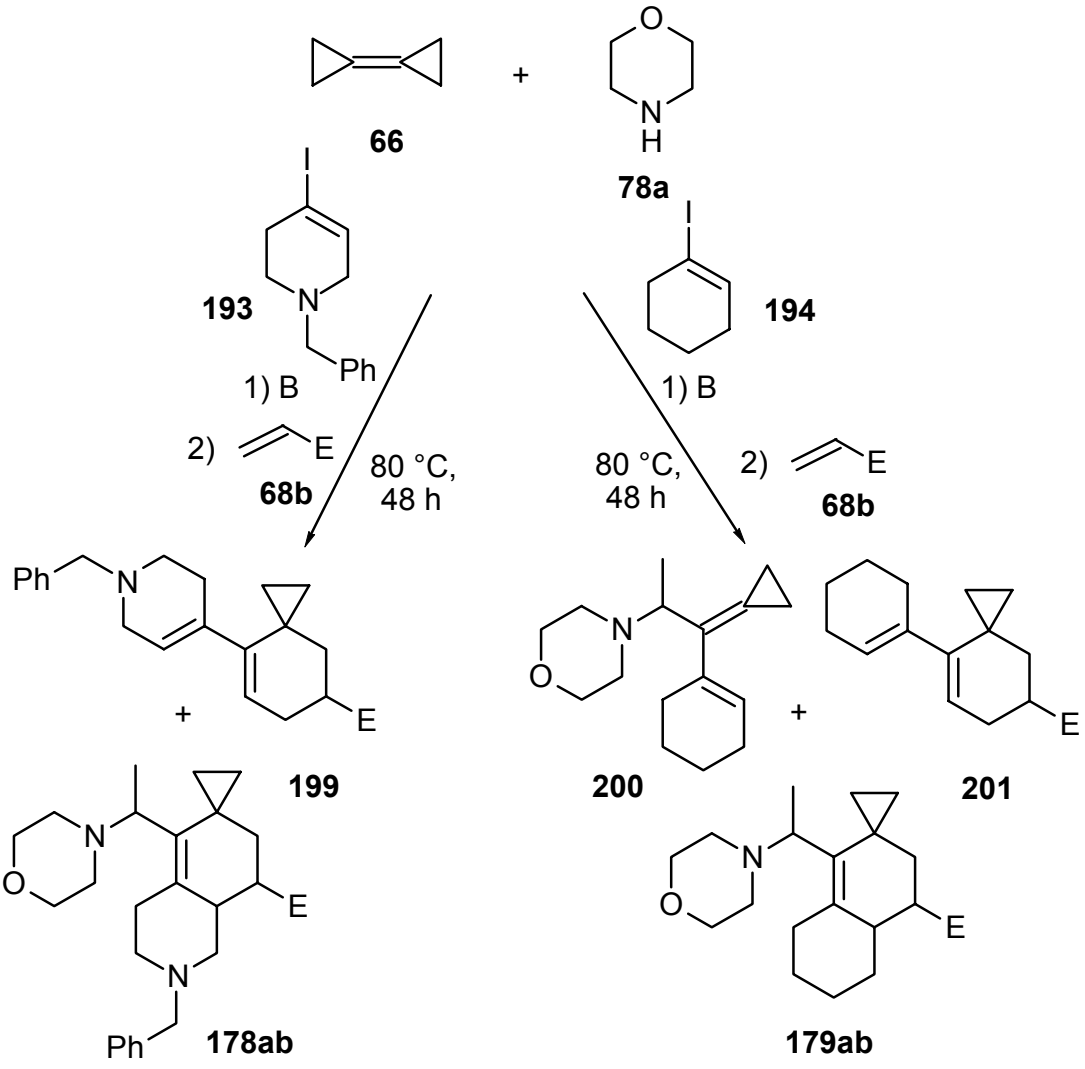
For example, the reaction of α-iodostyrene (**191**) with **66** and one equivalent of morpholine (**78a**) under the usual conditions (80 °C, 2 h for the first step and 80 °C, 48 h for the second step) yielded the diene **197** (8%) and the styryl[2.5]spirooctene derivative **198** (27%) along with the expected product **176ab** (18%) (entry 1 in Table 3, Scheme 39). Although, the yield of the spirooctene **176ab** was increased to 23% by prolongation of the reaction time to 4 h, structures **197** and **198** still existed in the reaction mixture (entry 2 in Table 3). Formation of the by-product **197** and **198** could only be eliminated by applying 1.5 equivalents of **78a** in the first step and prolonged heating (65 h) at elevated temperature (100 °C) for the second step (entry 3 in Table 3).



Scheme 39. The reaction of α-iodostyrene (**191**) with **66** and one equivalent of morpholine (**78a**) under the usual conditions; formation of the by-product **197** and **198**. – A: $Pd(OAc)_2$, TFP, NEt_3, 80 °C, DMF. – E = CO_2tBu, For details see Table 3.

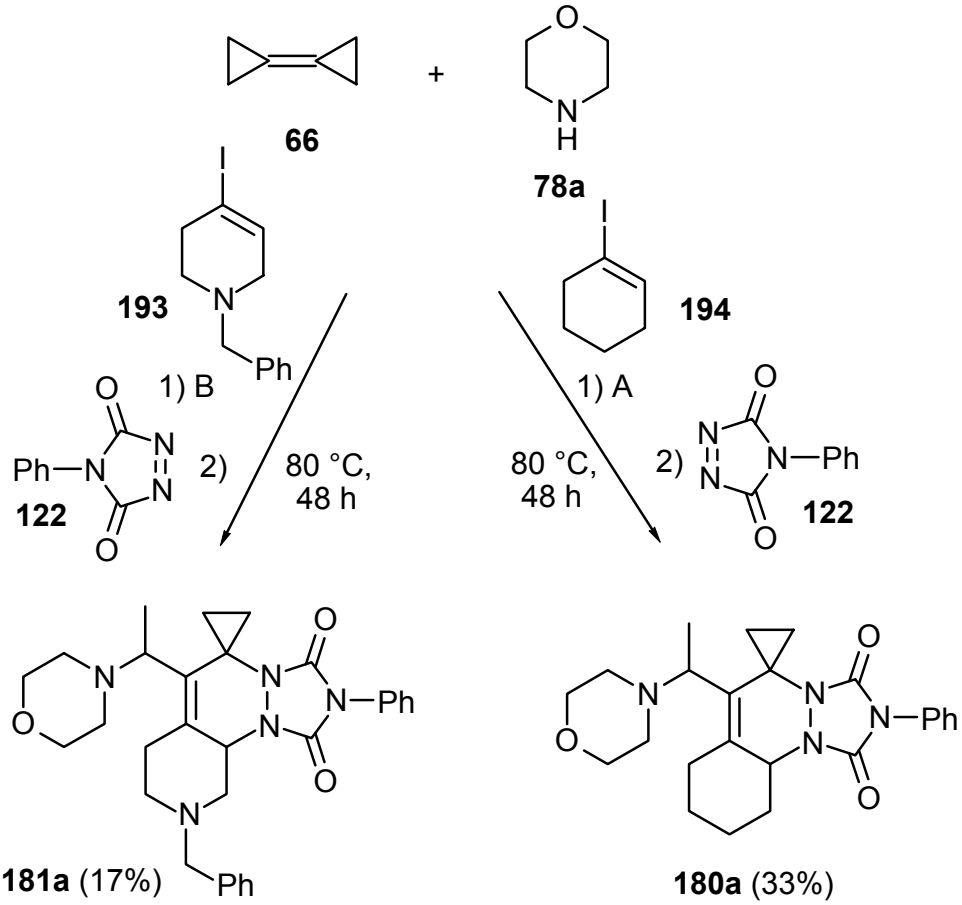
Similarly, when iodocyclohexene (**194**), with **66** and one equivalent of morpholine (**78a**) were heated at 80 °C for 3.5 h in the first step and for a further 48 h after the dienophile **68b** was added, the by-product **200** and **201** have been observed along with diastereomeric mixture of desired product **179ab**. However, these structures could not be isolated and diastereomeric ratio of the **179ab** could not be determined (entry 7 in Table 3 and Scheme 40). In the same conditions, by applying 1.2 equivalents morpholine, formation of **200** and **201** could be eliminated. Although, in the reaction mixture, two diastereomers were observed, only one of

them could be isolated in 25% yield (entry 8 in Table 3 and Scheme 40). Correspondingly, the reaction of *N*-benzyl-4-iodotetrahydropyridine **193** with bicyclopropylidene (**66**) in one equivalent morpholine (**78a**) gave both structures **199** and **178ab** in 12% and 10% yields respectively (entry 5 in Table 3 and Scheme 40). When the reaction was performed again with 1.2 equivalents morpholine, only desired product **178ab** appeared as mixture of diastereomers. Unfortunately, only one of them could be isolated in 26% yield (entry 6 in Table 3 and Scheme 40). Interestingly, however, in the case of (*E*)-1-iodo-2-phenylethene (**196**) (entries 12 and 13 in Table 3) 2 h without using more than one equivalent of morpholine were enough to complete the first step of the reaction.



Scheme 40. The reaction of *N*-benzyl-4-iodotetrahydropyridine (**193**) and iodocyclohexene (**194**), with **66** and one equivalent of morpholine (**78a**); formation of the by-product **199**, **200** and **201**. – B: $Pd(OAc)_2$, TFP, K_2CO_3, Et_4NCl, 80 °C, MeCN. E = CO_2tBu, For details see Table 3.

Yet, even spirocyclopropanated heterooligocyclic systems **180a** and **181a** (entries 9 and 10 in Table 3) were accessible by the use of iodocyclohexene **194** and *N*-benzyl-4-iodotetrahydropyridine **193**, respectively. For the first step of the sequential reaction of iodocyclohexene (**194**), the mixture had to be heated for an exceptionally long time, i.e. for 5 h at 100 °C, to reach the maximum yield, whereas the reactions of other iodoalkenes gave lower yields when the temperature for the first steps exceeded 80 °C. The configuration of the major diastereomer **180a** was rigorously proved by an X-ray crystal structure analysis (Figure 4).



Scheme 41. The preparation of spirocyclopropanated heterooligocyclic systems **180a** and **181a**. A: $Pd(OAc)_2$, TFP, NEt_3, 100 °C, 5 h, DMF. – B: $Pd(OAc)_2$, TFP, K_2CO_3, Et_4NCl, 80 °C, 3 h, MeCN. For details see Table 3.

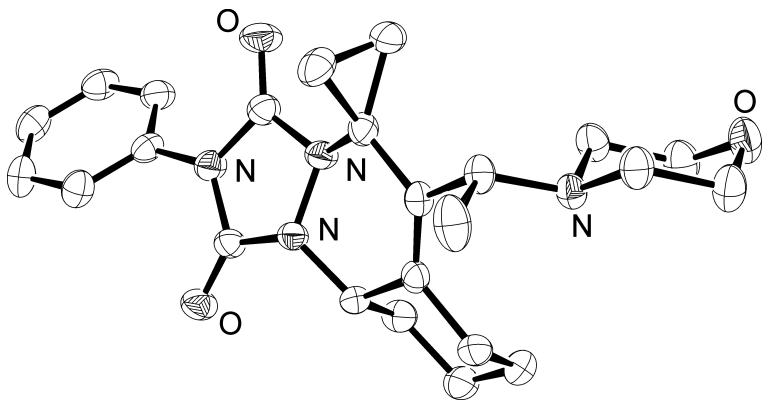


Figure 4. Structure of compound **180a** in the crystal.[66]

A heterocyclic substituent could also be attached to the spirooctene core as in **182a** by means of 2-(2-iodovinyl)thiophene **195** in the cross-coupling step (entry 11 in Table 3). Furthermore, heteroatoms could be incorporated in the spirooctene moiety of the Diels-Alder products by employing the highly reactive dienophile *N*-phenyltriazolinedione (PTAD) **122** as in structures **183a** and **184a** (entries 12, 13 and 14 in Table 3). The spirooctene **184a** was obtained in 50% yield and its configuration could be rigorously proved by an X-ray crystal structure analysis (Figure 5). Whereas with *N*-phenylmaleimide (**189**) the cycloaddition could be completed at 80 °C in 4 h, the reaction with **122** gave better yields when carried out at 20 °C for prolonged times (up to 2 d).

Furthermore, the reaction of **66** with (*E*)-1-Benzyl-3-iodomethylenepiperidine (**202**) in the presence of 1.2 equivalents morpholine (**78a**) at 80 ^{o}C for 3.5 h gave only the spirooctene **203** in 20% yield after addition of dienophile **68b** and heating of the mixture for another 60 h at the same temperature. Interestingly, when this procedure was repeated with 1.5 equivalents of morpholine in longer reaction times (4 h for the first step and 72 h for the second one), again only **203** was obtained in 26 % yield. In spite of high concentration of nucleophile (**78a)** in the reaction mixture, the intermediate diene **204** and desired product **205** could not be observed (Scheme 42).

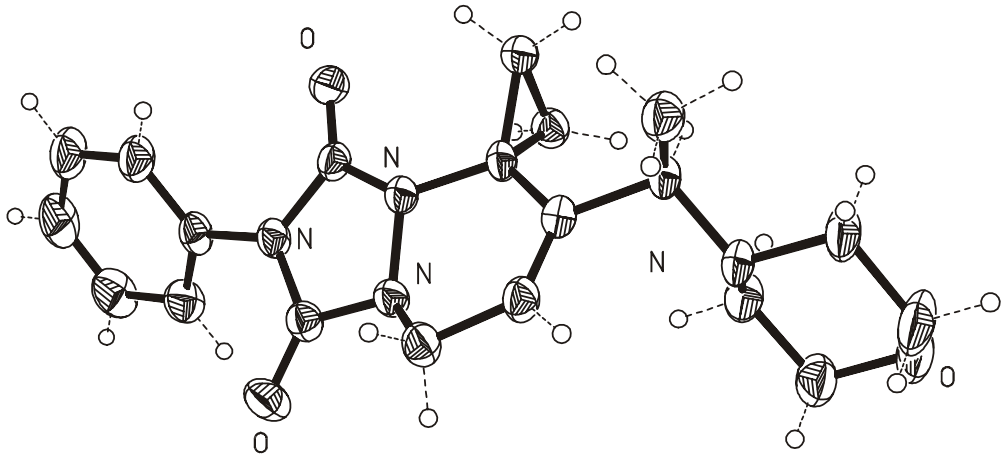
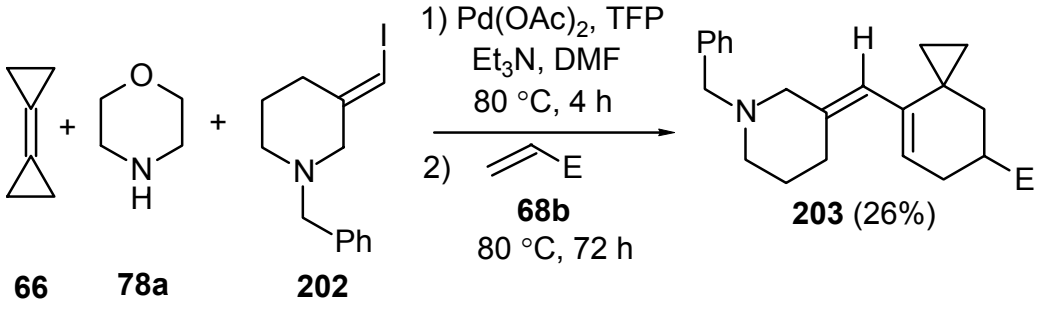
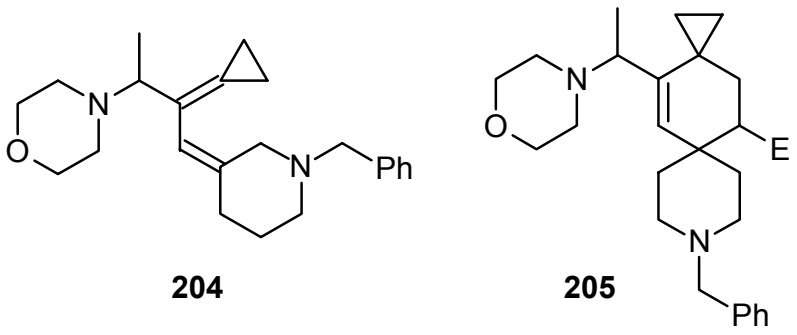


Figure 5. Structure of compound **184a** in the crystal.

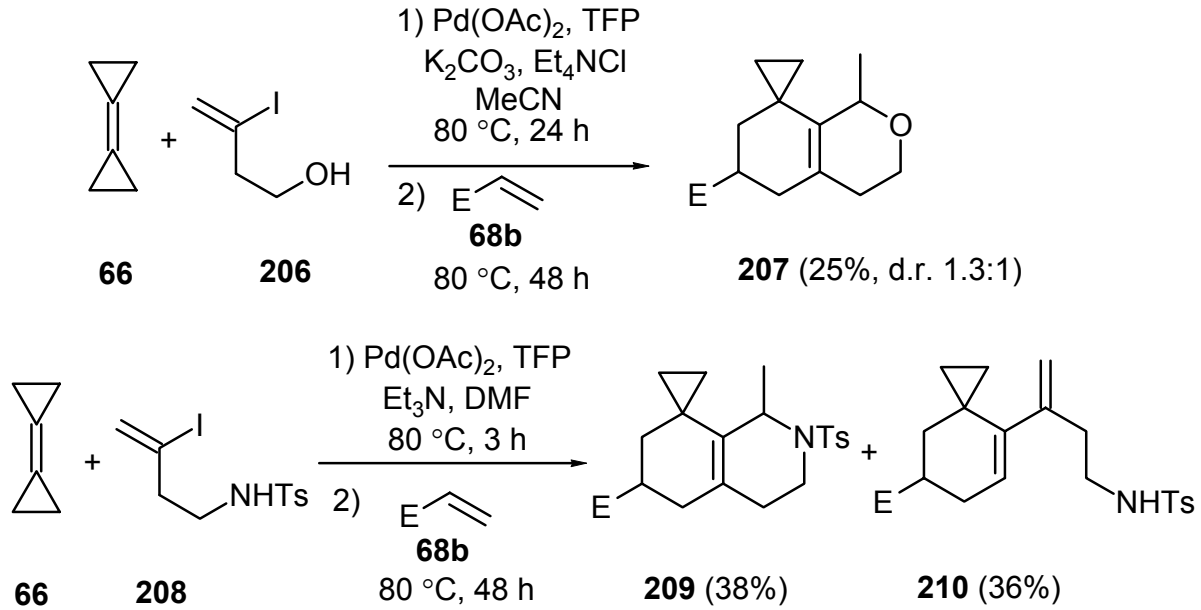




Scheme 42. The reaction of (E)-1-Benzyl-3-iodomethylenepiperidine (**202**) with **66** in the presence of 1.5 equivalents of morpholine (**78a**); formation of the spiro[2.5]octane **203**. – E = CO_2*t*Bu

*2.4. An inter-intra-intermolecular queuing cascade involving bicyclopropylidene **66**, a functionalized iodoalkene and a dienophile*

To extend the scope of this cascade reaction even further, functionalized vinyl iodides **206** and **208** were employed to provide, by intramolecular π-allylpalladium trapping in the first step after the cross-coupling and rearrangement, spirocyclopropanated heterobicycles **207**, **209**, albeit in moderate yields only (at best 25 and 38%, respectively) (Scheme 43).[67] Although this is not a four-component reaction, this inter-intra-intermolecular queuing cascade proceeds by the same number of individual steps and with formation of the same number of carbon-carbon and carbon-heteroatom bonds (altogether four) as the four-component cascades discussed above. Interestingly, the iodohomoallyl alcohol **206** gave the best results under conditions B in acetonitrile with potassium carbonate and the phase transfer agent (Et_4NCl) (entry 7 in Table 4), whereas the *N*-tosylhomoallylamine **208** gave the best yield of 38% under conditions A ($Pd(OAc)_2$, TFP, NEt_3, DMF, 80 °C, 3 h) (entry 3 in Table 5) and the product **209** was obtained as a single diastereomer along with the tosylaminobutenylspiro[2.5]octenecarboxylate **210** resulting from β-hydride elimination in the intermediate of type **169** as in Scheme 34 and immediate Diels-Alder addition of **68b**. The configuration of **209** was also rigorously proved by an X-ray crystal structure analysis (Figure 6) All attempts to suppress the formation of **210** by increasing the reaction temperature or the time were unsuccessful.



Scheme 43. An inter-intra-intermolecular queuing cascade involving bicyclopropylidene (**66**), a functionalized iodoalkene **206**, **208** and a dienophile **68b**. – E = CO_2tBu

Entry	Reaction Conditions[a]		Yield[b]	d.r.[c]
	Step 1	Step 2	(%)	
1	A, 1 mL DMF 80 °C, 3 h	80 °C, 48h	6	1:1
2	A, 1 mL DMF 80 °C, 24 h	80 °C, 48 h	10	1:1
3	B, 1 mL MeCN 80 °C, 24 h	80 °C, 48 h	18	1.2:1
4	B, 1 mL DMF 100 °C, 24 h	100 °C, 24 h	–[d]	–
5[e]	B, 1 mL MeCN 80 °C, 24 h	80 °C, 48 h	11	1.1:1
6	B, 2 mL DMA 100 °C, 24 h	100 °C, 24 h	–[d]	–
7	B, 2 mL MeCN 80 °C, 24 h	80 °C, 48 h	25	1.3:1
8	B, 2 mL MeCN 80 °C, 48 h	80 °C, 48 h	17	1.1:1

Table 4. Optimization of the reaction conditions for the cascade involving bicyclopropylidene (**66**), a functionalized iodoalkene **206** and a dienophile **68b**. – [a] 4.00 mmol bicyclopropylidene **66**, 2.00 mmol iodoalkene **206** and 4.00 mmol *tert*-butyl acrylate **68b** were used. – [b] Isolated yield are given. – [c] Diastereomeric ratios were determined by integration of relevant ^{1}H NMR signals in the spectra of the crude products. – [d] No product. – [e] 5% mol $Pd(dba)_2$ was used. – A: 5% mol $Pd(OAc)_2$, 10% mol TFP, Et_3N. – B: 5% mol $Pd(OAc)_2$, 10% mol TFP, K_2CO_3, Et_4NCl.

Entry	Reaction Conditions[a]		Products[b]	
	Step 1	Step 2	**209**(%)	**210**(%)
1	B, 2 mL MeCN 80 °C, 3 h	80 °C, 48 h	8	–[c]
2	B, 2 mL MeCN 80 °C, 24 h	80 °C, 48 h	13	–[c]
3	A, 1 mL DMF 80 °C, 3 h	80 °C, 48 h	38	36
4	A, 1 mL DMF 80 °C, 24 h	80 °C, 48 h	17	24
5	A, 2 mL DMF 100 °C, 24 h	100 °C, 16 h	28	18
6	A, 2 mL DMF 120 °C, 2 h	100 °C, 16 h	18	17

Table 5. Optimization of the reaction conditions for the cascade involving bicyclopropylidene (**66**), a functionalized iodoalkene **208** and a dienophile **68b**. – [a] 4.00 mmol bicyclopropylidene **66**, 2.00 mmol iodoalkene **208** and 4.00 mmol *tert*-butyl acrylate **68b** were used. – [b] Isolated yield are given. – [c] No product. – A: 5% mol $Pd(OAc)_2$, 10% mol TFP, Et_3N. – B: 5% mol $Pd(OAc)_2$, 10% mol TFP, K_2CO_3, Et_4NCl.

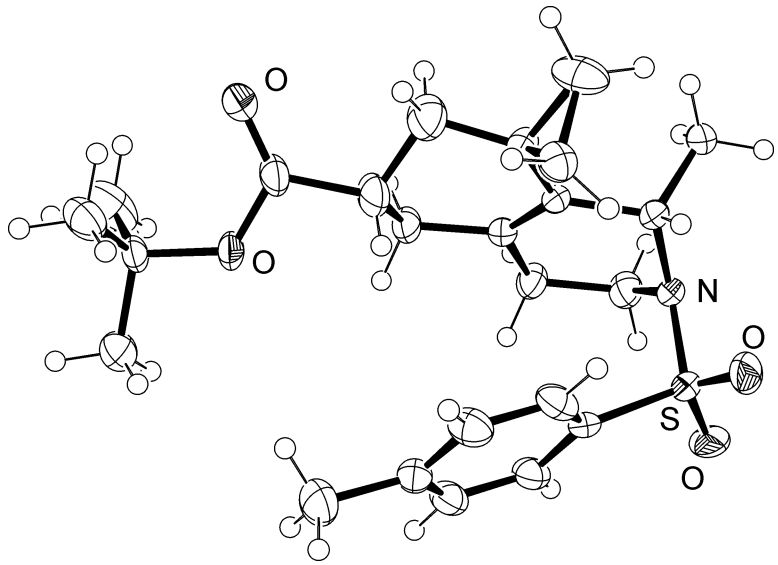
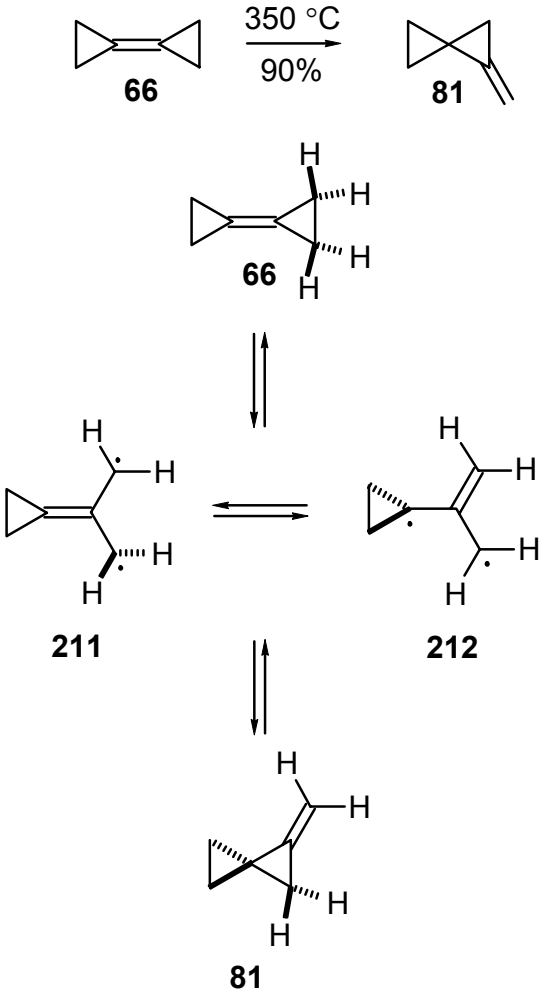


Figure 6. Structure of compound **209** in the crystal.[66]

3. Two-Step Queuing Cascade Reactions with Methylenespiropentane Involving a Heck Coupling, π-Allylpalladium Trapping and Diels-Alder Reaction

3.1. Introduction

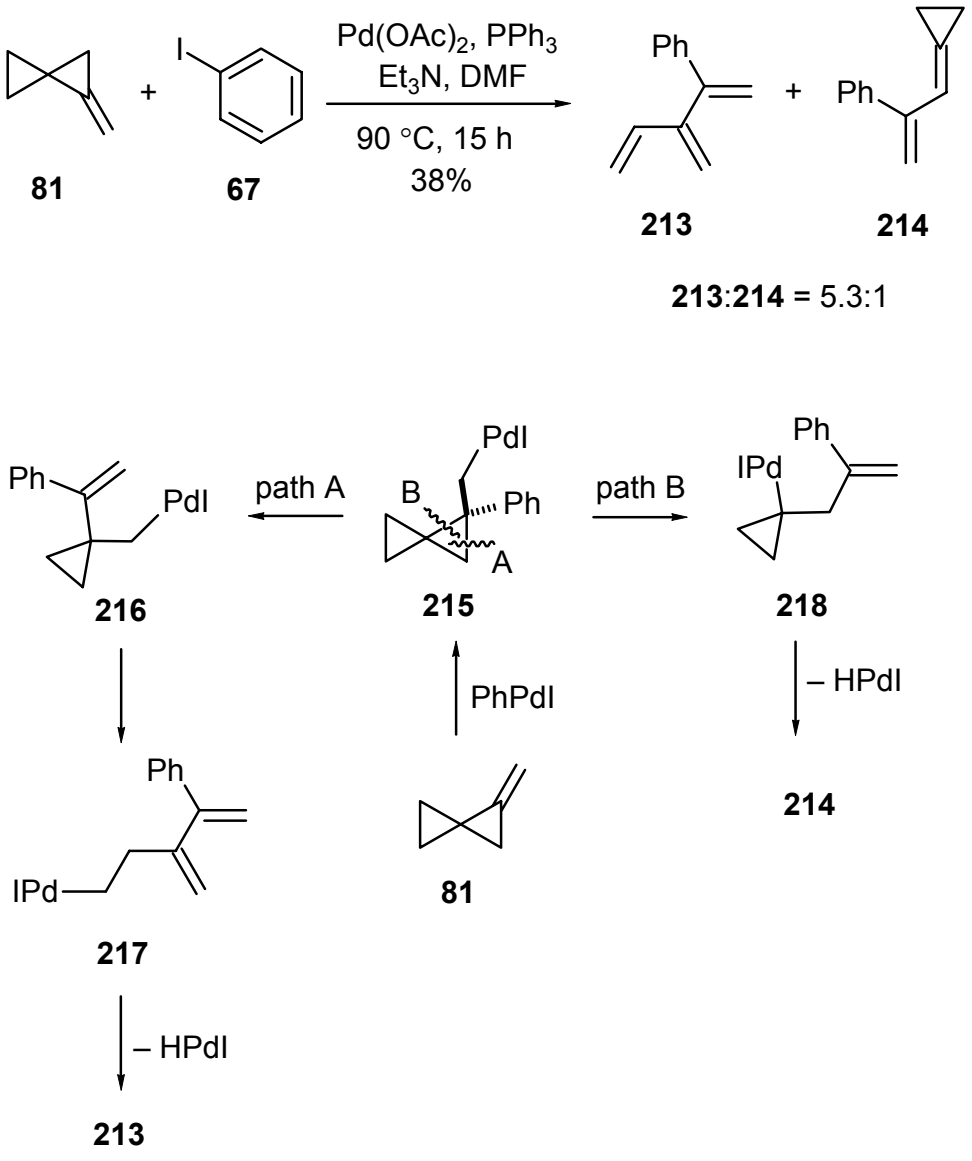
Another highly strained building block, methylenespiropentane (**81**), is easily available in preparative quantities by rearrangement of bicyclopropylidene (**66**) at 350 °C in a flow system (Scheme 44).[68]



Scheme 44. The thermal rearrangement of bicyclopropylidene (**66**) to methylenespiropentane (**81**) in the gas phase.

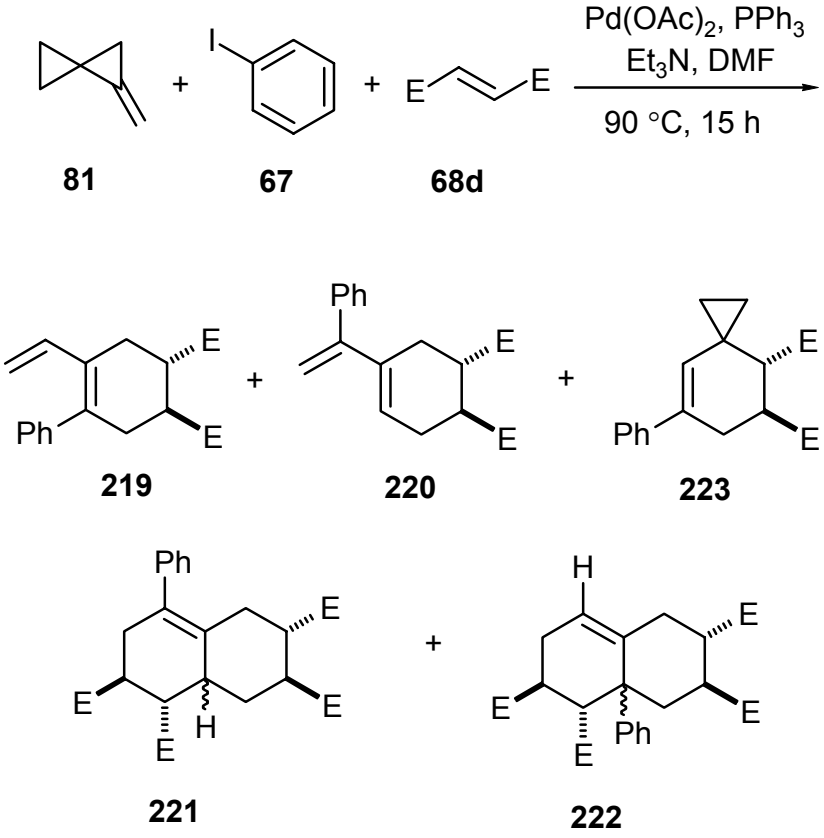
Since the strain energy of methylenespiropentane (**81**) (74.6 kcal/mol) is only 2.8 kcal/mol lower than that of bicyclopropylidene (**66**)[69], methylenespiropentane (**81**) is expected to undergo similar types of carbopalladation reactions as bicyclopropylidene (**66**) does, which include the immediate opening of strained cyclopropyl rings after the carbopalladation process.

In this respect, previous studies have demonstrated that the coupling of methylenespiropentane (**81**) with iodobenzene **67** in the usual Heck conditions ($Pd(OAc)_2$, PPh_3, Et_3N) in DMF gave the mixture of cross-conjugated triene **213** and allylidenecyclopropane derivatives **214**[70]. A reasonable mechanism that accounts for the formation of products **213** and **214** involves firstly cleavage of two different proximal bonds (A and B) in cyclopropane ring adjacent to the carbopalladated former exomethylene in the intermediate **215**. The complex **216** occurred in path A undergoes one more cyclopropyl-carbinyl to homoallyl rearrangement affording the homoallyl palladium species **217**, which yields the conjugated triene **213** after a β-hydride elimination. On the other hand, the homoallylpalladium complex **218** arising from cleavage of the proximal bond B, undergoes immediately a β-hydride elimination to produce the diene **214** (Scheme 45).



Scheme 45. The Heck reaction of methylenespiropentane (**81**) with iodobenzene **67**.

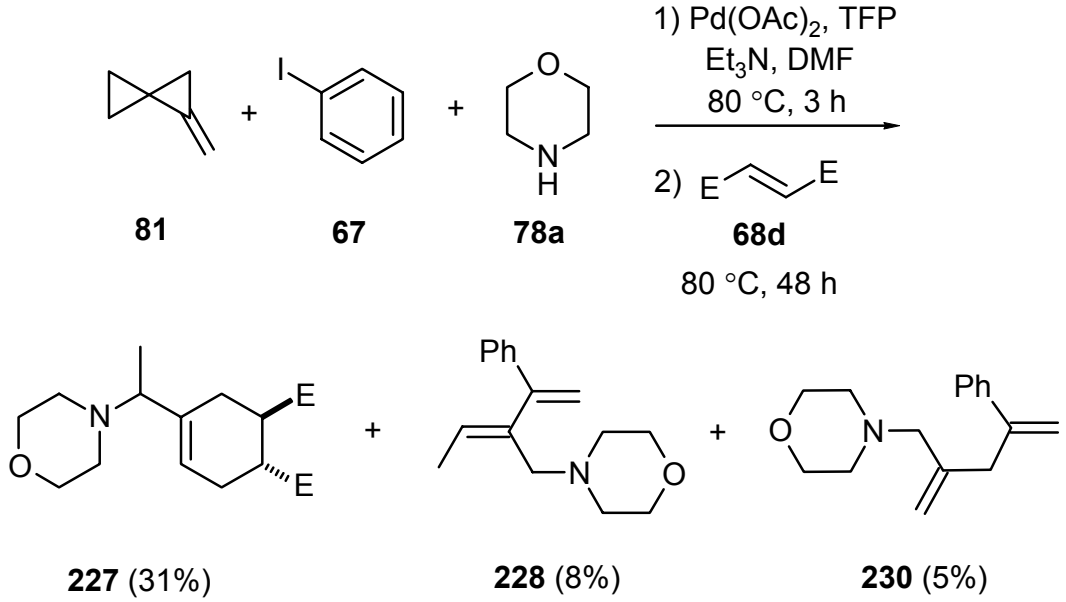
Moreover, when the coupling of methylenespiropentane (**81**) with iodobenzene **67** was performed in the presence of a dienophile such as dimethylfumarate **68d** (i.e., a domino Heck-Diels-Alder reaction with methylenespiropentane (**81**), the reaction yielded the mixture of mono- and transmissive cycloaddition products (**219**–**222**)[71] of the conjugated triene **213** along with the spirooctene **223** arising from allylidenecyclopropane **214**. However, this domino process could not be further investigated due to formation of several isomeric mixtures in low yields.



Scheme 46. The domino Heck-Diels-Alder reaction involving methylenespiropentane (**81**), iodobenzene **67**, dimethyl fumarate **68d**. – E = CO_2Me

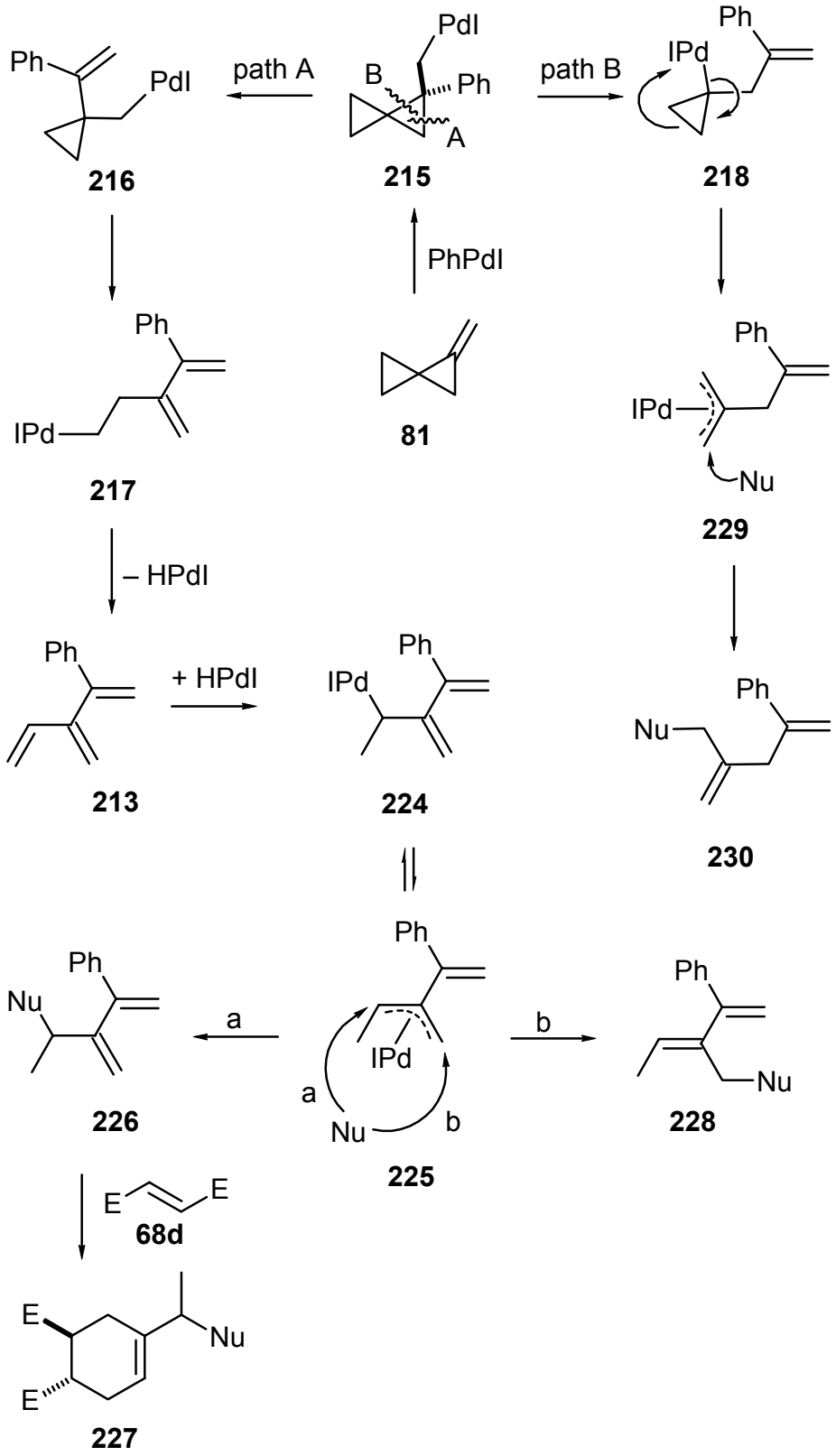
*3.2. A two-step, four-component queuing cascade with methylenespiropentane (**81**) involving nucleophilic trapping of π-Allylpalladium intermediates.*

In this study, the utility of methylenespiropentane (**81**) in cascade reactions was significantly enhanced by carrying out the carbopalladation in the presence of tris(2-furyl)phosphane (TFP) which stimulates the formation of π-allylpalladium complexes. These complexes were successfully trapped as in the four-component, two-step cascade involving morpholine **78a** as a nucleophile (Scheme 47).



Scheme 47. A new one-pot, two-step four component queuing cascade involving methylenespiropentane (**81**), iodobenzene **67**, morpholine **78a** and dimethyl fumarate. – E = CO_2Me

In the corresponding mechanism (Scheme 48), the π-allylpalladium complex **225** must be formed after a β-hydride elimination and readdition of the hydridopalladium species via a σ-allylpalladium intermediate **224** and trapped with morpholine **78a** from two different terminuses affording dienes **226** and **228**. Subsequently, the diene **226** undergoes a cycloaddition with dimethyl fumarate **68d** to yield cyclohexene derivative **227**. On the other hand, the formation of the π-allylpalladium complex **229** most probably is originated from distal C–C bond cleavage of the cyclopropane ring in the intermediate **218** and trapped by morpholine **78a** to give the compound **230**.



Scheme 48. The mechanism for the formation of dienes **226**, **228** and **230** via trapping of π-allylpalladium intermediates **225** and **229**. – NuH = Morpholine (**78a**). – E = CO_2Me

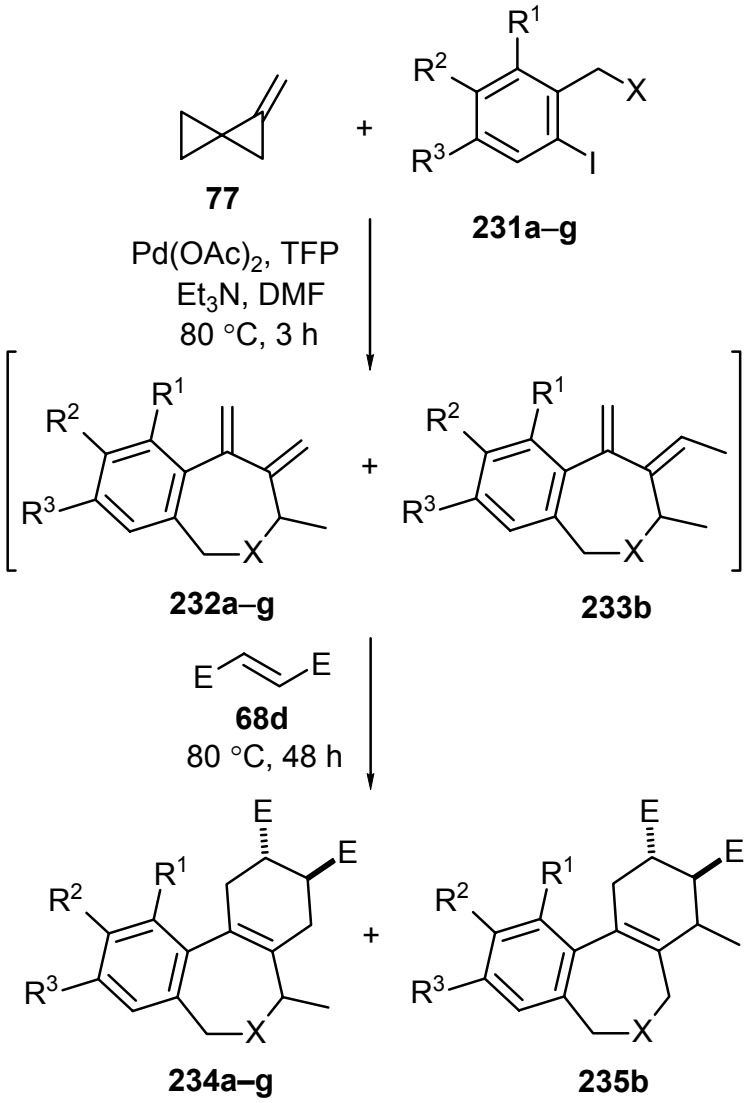
Even though, in this reaction the yield was not high enough, the concept of novel cascades involving methylenespiropentane (**81**) proved to be feasible with limited numbers of products. Another important outcome of the reaction constitutes selectively formation of the diene **226** having appropriate configuration for the consecutive Diels-Alder reaction.

*3.3. A two-step, three-component queuing cascade with methylenespiropentane (**81**) involving intramolecular nucleophilic trapping of π-Allylpalladium intermediates; a direct access to benzoxepine and benzoazepine derivatives.*

Taking these results into account, functionalized aryl iodides (**231a**–**g)** were coupled with methylenespiropentane (**81**) with a typical palladium catalyst cocktail (e.g. $Pd(OAc)_2$, TFP, NEt_3) at 80 ^oC for 3 h to provide intermolecular π-allylpalladium trapping, which furnish a cyclization in the first step and yields various heterocycles with respect to the identity of aryl iodides. A dienophile (dimethyl fumarate, **68d**) added right after cross coupling with rearrangement and nucleophilic trapping processes gave final structures (**234a**–**g** and **235b)** in low yields by building a cyclohexene ring on intermediate dienes (**232a**–**g** and **233b)**. Related results are summarized in Scheme 49 and in Table 6.

Inspiring by successful literature protocols utilized for palladium-catalyzed annulations involving an intramolecular trapping of π-allylpalladium intermediates,[72] numerous reaction conditions were tried to improve the yield of this cascade reaction. All attempts for this purpose were performed with a model reaction involving methylenespiropentane (**81**), o-iodobenzyl alcohol **231a** and dimethyl fumarate **68d**.

Since the nature of the base is one of the most critical factors for the success of palladium-catalyzed annulation reactions,[72a] the optimization work was mainly focused on this issue. Attempts were rather disappointing in the conditions having a phase transfer agents (Et_4NCl or nBu_4NCl) with various acetate and carbonate bases (NaOAc, KOAc, K_2CO_3, Ag_2CO_3, Cs_2CO_3). Moreover, amine bases such as Et_3N and $EtN(iPr)_2$ were utilized with or without phase transfer catalysis. Among them, conditions having only Et_3N gave more reasonable yields. However, these conditions never furnished better yields than 22 %. Although $Pd(OAc)_2$ is known as very effective catalyst for these type of annulation reactions,[72a] $Pd(dba)_2$ and $Pd_2(dba)_3$ were also tried in some cases. Also all efforts to tune the reaction temperature or the time for both steps could not increase the yield.



Scheme 49. A two-step, three component queuing cascade involving methylenespiropentane (**81**), functionalized iodoarenes (**231a**–**g**) and dimethyl fumarate **68d**.

Entry	Aryl Iodide	R^1	R^2	R^3	X	Product	Yield[a] (%)	d.r.[b]
1	**231a**	H	H	H	OH	**234a**	22	1:1
2	**231b**	H	H	H	HNPh	**234-235b**	27	1.6:1
3	**231c**	H	OCH_3	OCH_3	OH	**234c**	18	1.6:1
4	**231d**	H	$–OCH_2O–$		OH	**234d**	21	1:1
5	**231e**	H	$–OCH_2O–$		HNPh	**234e**	20	1.5:1
6	**231f**	H	$–O(CH_2)_2O–$		OH	**234f**	23	1.1:1
7	**231g**	$–OCH_2O–$		H	OH	**234g**	29	1.1:1

Table 6. [a] Isolated yield are given. – [b] Diastereomeric ratios were determined by integration of relevant ^{1}H NMR signals in the spectra of the crude products.

The new three-component, two-step cascade involving an intramolecular trapping of π-allylpalladium intermediates was highly selective. Oligoheterocycles **234a**–**g** mainly arised from dienes of type **232a**–**g**. Only in one case (entry 2 in Table 6), the benzoazepine derivative **235b** bearing the methyl substituent on the cyclohexene moiety was isolated in 5% yield. Like the formation of diene **228** in Scheme 48, the formation of benzoazepine **235b** must be initiated with attacking of the amine to the other terminus of the corresponding π-allylpalladium intermediate. Thus, the intermediately formed diene **233b** via this pathway gave **235b** by undergoing immediate Diels-Alder reaction with dimethyl fumarate **68d** in the second step.

The reaction was also selective with respect to employed functionalized aryl iodides. *o*-Iodo benzylic alcohols and amines (**231a**–**g**) gave successfully corresponding benzoxepine and benzoazepine derivatives (**234a**–**g**), whereas attempts with *o*-iodoaniline **236** and 2-iodo-phenetyl alcohol **238** to obtain structures involving six and eight membered heterocycles (**237** and **239**, respectively) were not successful. On the other hand, the reaction performed with *o*-iodo benzoic acid **240** produced a seven membered lactone derivative **241**, albeit in only 8% yield (Scheme 50). Despite having generally low yields (18–29%), this cascade reaction produced valuable fused heterocycles (**234a**–**g**), commonly found in the framework of numerous natural and synthetic biologically active compounds.[73] Moreover, one of the benzoxepine derivatives (**234g**) was strictly proved by X-ray structure analysis (Figure 7).

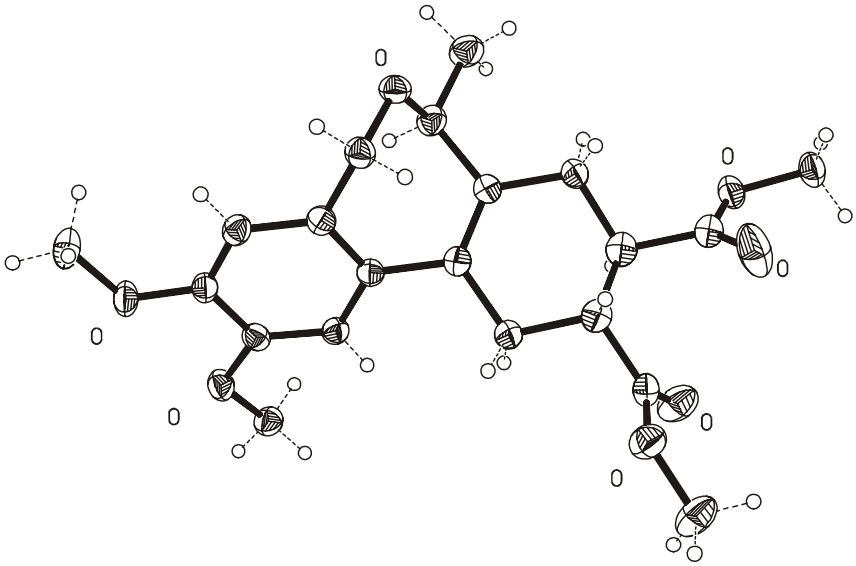
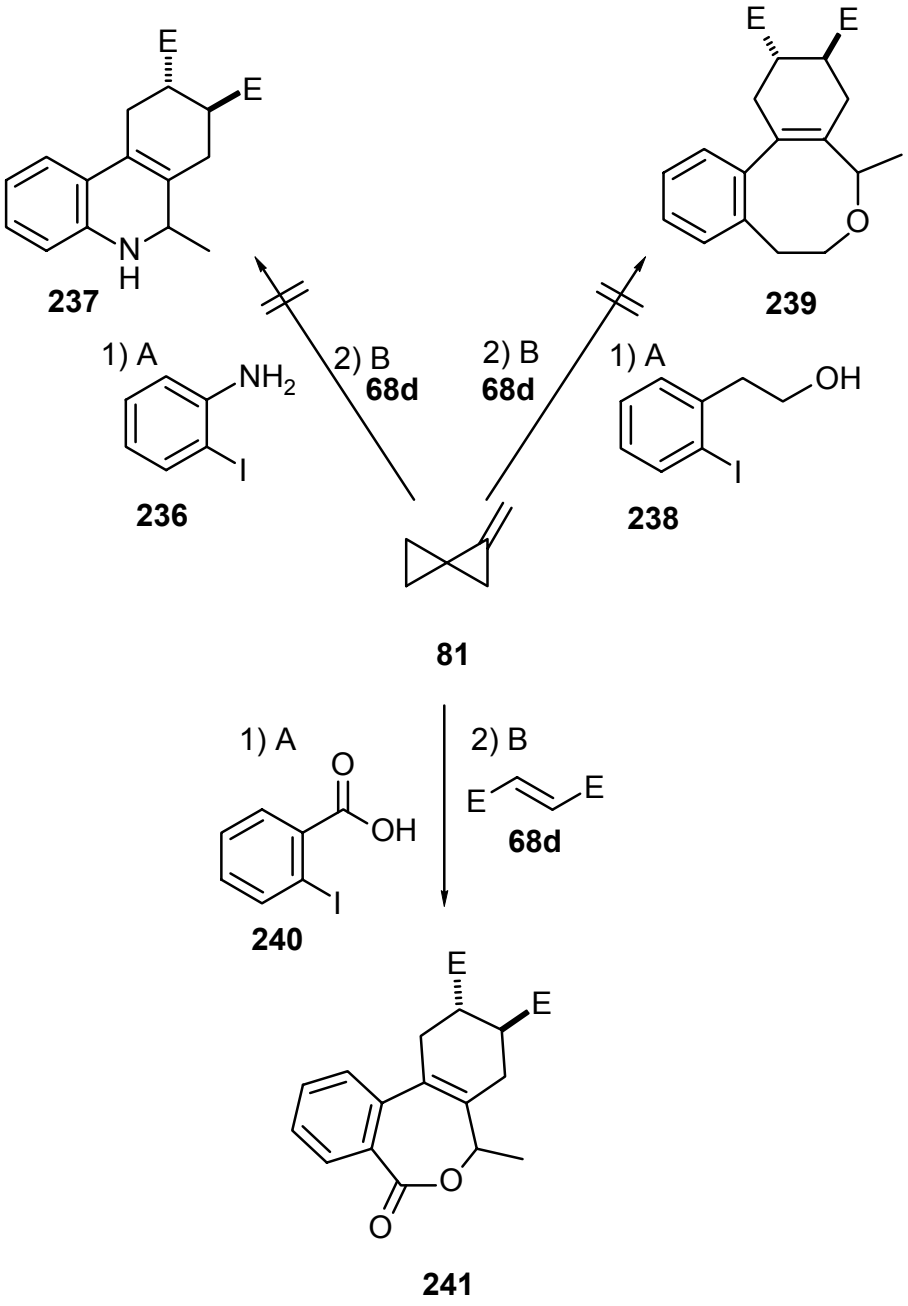


Figure 7. Structure of compound **234c** (major diastereomer) in the crystal.

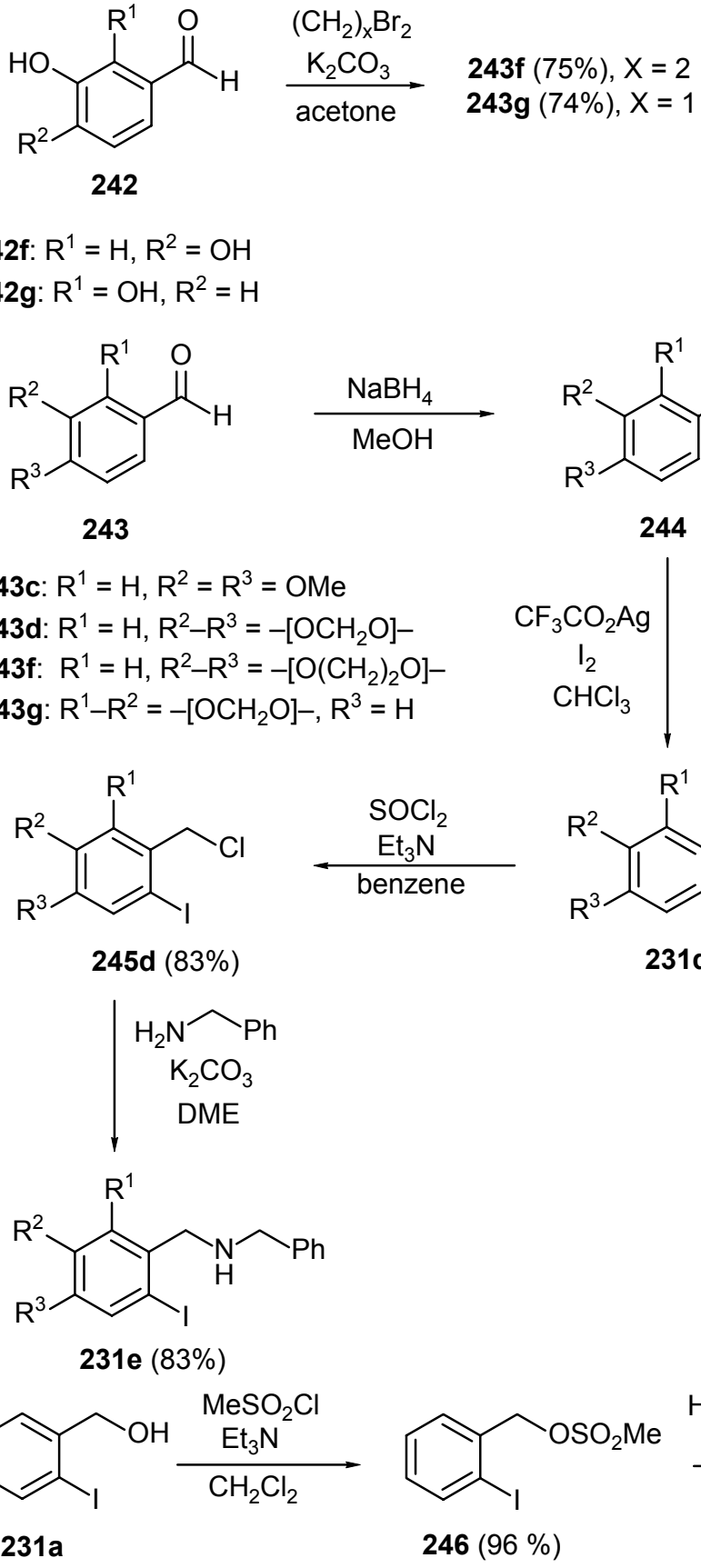


Scheme 50. Attempts for the synthesis of six and eight membered heterocycles (**237** and **239**) and the preparation of seven membered lactone derivative **241**.

*3.4. Preparation of functionalized aryl iodides (**231b–g**)*

Functionalized aryl iodides were prepared starting with corresponding aldehydes by following reduction and iodination processes (Scheme 51). Aldehydes **243f** and **243g** were obtained from commercially available respective catechol derivatives **242f–g** in a single operation. Reduction of aldehydes **243c–d** and **243f–g** by $NaBH_4$ in dry MeOH produced benzyl alcohol derivatives **244c–d** and **244f–g** in quantitative amounts. Subsequently, selective iodination was performed by CF_3CO_2Ag and I_2 couple to yield *o*-iodobenzylic alcohols **231c–d** and **231f–g**. Yields were generally very high for this process, only **231g** was obtained in moderate yield (60%). Iodoarenes having benzylamine functionality (**231b** and **231e**) were achieved easily by application of two different protocols on structures **231a** and **231d.** Interestingly, the reaction of *o*-iodobenzylic alcohol **231d** with methanesulfonyl chloride in the presence of Et_3N did not give desired mesylate. The o-iodobenzylic amine **231e** could be obtained via chlorination of alcohol **231d** in 83% yield.

Iodoarenes, particularly those involving dioxole moiety are considerably important, since dioxole subunits take place in the structure of natural and non-natural biologically active compounds.[74] In this respect, benzoxepine and benzoazepine derivatives together with dioxole subunits might offer new perspectives for the preparation of structures that possess pharmacological properties.



Scheme 51. Prepartion of functionalized aryl iodides **231b**–**g**

C. Experimental

1. General

1.1. Physical and spectroscopic measurements

NMR spectra were recorded with a Varian Mercury 200 (200 MHz for ^{1}H and 50.3 MHz for ^{13}C), a Bruker AM 250 (250 MHz for ^{1}H and 62.9 MHz for ^{13}C NMR), a Varian UNITY-300 (300 MHz for ^{1}H and 75.5 MHz for ^{13}C NMR) or a Varian Inova 600 (600 MHz for ^{1}H and 151 MHz for ^{13}C NMR) instruments. Chemical shifts δ were given in ppm relative to residual peaks of deuterated solvents and coupling constants, *J*, were given in Hertz. The following abbreviations are used to describe spin multiplicities in ^{1}H NMR spectra: s = singlet; bs = broad singlet; d = doublet; t = triplet; q = quartet; dd = doublet of doublets; ddd = doublet of doublet of doublets; dt = doublet of triplets; dq = doublet of quartets; m = multiplets. Multiplicities in ^{13}C NMR spectra were determined by DEPT (Distortionless Enhancement by Polarization Transfer): + = primary or tertiary (positive DEPT signal), − = secondary (negative DEPT Signal), C_{quat} = quaternary carbon atoms] or APT (Attached Proton Test) measurements. HMQC (Heteronuclear Multiple Quantum Coherence) spectra were also measured. IR spectra were recorded on a Bruker IFS 66 spectrometer and measured as KBr pellets or as oils between KBr plates. Low resolution mass spectra (EI at 70 eV or DCI with NH_3) were obtained on a Finnigan MAT 95 spectrometer. High resolution mass spectra (HRMS) were obtained on a Finnigan MAT 95 spectrometer by preselected-ion peak matching at $R \approx 10000$ to be within ±2 ppm of the exact masses. Elemental analyses were carried out by the Mikroanalytisches Laboratorium des Instituts für Organische und Biomolekulare Chemie der Universität Göttingen. Chromatographic separations were performed with Merck Silica 60 (200−400 or 70−230 mesh). The dimensions of the columns are given as "diameter × height of the silica gel column". TLC was performed with Macherey-Nagel TLC Alugram® Sil G/UV 254 plates, detection was under UV light at 254 nm and development with MOPS reagent (10% molybdophosphoric acid in ethanol). Melting points were obtained with a Büchi apparatus according to Dr. Totto1i; values are uncorrected.

1.2. Reagents and solvents

All reagents were used as purchased from commercial suppliers without further purification unless otherwise indicated. Acetonitrile was dried over P_2O_5, DMF and CH_2Cl_2 were distilled

from CaH_2. Ether and THF were freshly destilled from sodium/benzophenone ketyl. Solvents for column chromotography, ethyl acetate and light petroleum were distilled in a rotatory evaporator.

1.3. Preparation of known compounds

The following compounds were prepared according to known literature methods: bicyclopropylidene (**66**)[32], methyl bicyclopropylidenecarboxylate (**66E**)[36a], 2-(1',1''-bicyclopropylidene-2'-yl)-4,4,5,5,-tetramethyl-1,3-dioxa-2-borolan (**66B**)[36b], 2-(Tributylstannyl)bicyclopropylidene (**66C**)[36b], *N*-phenylitaconimide (**131**)[44a], *N*-allylmorpholine[75], iodoethene (**173**)[76], 1-benzyl-4-iodo-1,2,3,6-tetrahydropyridine (**193**)[77], (1-iodovinyl)benzene (**191**)[78], 5-(1-iodovinyl)benzo[1,3]dioxole (**192**)[78], 1-iodo-cyclohexene (**194**)[78], 2-(2-iodovinyl)thiophene (**195**)[79], (*E*)-1-iodo-2-phenylethene (**196**)[80], (*E*)-1-Benzyl-3-iodo methylenepiperidine (**202**)[77], 3-iodobut-3-en-1-ol (**206**)[81], *N*-(3-iodobut-3-enyl)-4-methylbenzenesulfonamide (**208**)[82], N-phenyltriazolinedione (**122**)[83], 5-[(1-diethoxyphosphinyl)oxo-vinyl]-benzo[1,3]dioxole[84], methylenespiropentane (**81**)[68], 2,3-dihydrobenzo[1,4]dioxine-6-carbaldehyde (**243f**)[85], benzo[1,3]dioxole-4-carbaldehyde (**243g**)[85], (3,4-dimethoxy-phenyl)-methanol (**244c**)[86], piperonylic alcohol (**244d**)[87], (2,3-dihydrobenzo[1,4]dioxin-6-yl)-methanol (**244f**)[88], benzo[1,3]dioxol-4-yl-methanol (**244g**)[88], 2-iodo-4,5-dimethoxybenzyl alcohol (**231c**)[89], (6-iodo-benzo[1,3]dioxol-5-yl)-methanol (**231d**)[90], (5-iodo-benzo[1,3]dioxol-4-yl)-methanol (**231g**)[88], 5-chloromethyl-6-iodo-benzo[1,3]dioxole (**245d**)[91], methanesulfonic acid 2-iodo-benzylester (**246**)[92], benzyl-(2-iodobenzyl)amine (**231b**)[77], 2-(2-iodo-phenyl)-ethanol (**238**)[93]

2. Procedures, spectroscopic and physical identifications of new compounds

*2.1. Domino Heck-Diels-Alder reaction with substituted bicyclopropylidenes (**66A-D**)*

*2.1.1. General procedure for the one-pot, one-step Heck-Diels-Alder reaction involving a mono-substituted bicyclopropylidene (**66A-D**), an iodoarene, a dienophile (**GP-1**)*

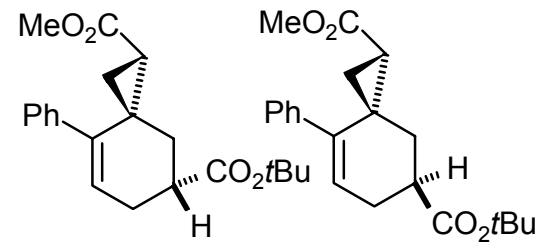
A screw-cap Pyrex bottle was charged with anhydrous acetonitrile (2 mL), K_2CO_3 (2 equivalent) and Et_4NCl (1 equivalent). Argon was bubbled through the mixture for 5 min, $Pd(OAc)_2$ (5 mol%), and triphenylphosphane (15 mol%) were added, and the mixture was stirred once more for an additional 5 min with argon bubbling through, before the respective

iodoarene (1 equivalent), mono-substituted bicyclopropylidene (**66A-D**) (2 equivalent) and respective dienophile (2 equivalent) were added. The bottle was tightly closed, and the mixture was stirred for the given period of time at the stated temperature. After cooling to room temperature, the reaction mixture was taken up in 20 mL of diethyl ether. The solution was washed with water (2 × 20 mL), the aqueous phase was extracted with diethyl ether (2 × 20 mL), and the combined organic phases were dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator, the residue was subjected to chromatography on silica gel.

2.1.2. Synthesis of spirooctenes

5-tert-Butyl-1-methyl 8-phenylspiro[2.5]oct-7-ene-1,5-dicarboxylate (*cis*/*trans*, *trans*-104E) and (*cis/trans, cis*-105E)

According to GP-1, $Pd(OAc)_2$ (20.3 mg, 90 µmol), triphenylphophane (71.3 mg, 271 µmol), K_2CO_3 (500 mg, 3.62 mmol), Et_4NCl (300 mg, 1.81 mmol), iodobenzene (**67**, 369 mg, 1.81 mmol), methyl bicyclopropylidenecarboxylate (**66E**, 500 mg, 3.62 mmol) and *tert*-butyl acrylate (**68b**, 464 mg, 3.62 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 10:1) to yield *cis*/*trans*, *trans*-**104E** (427.5 mg, 69%, colorless solid) as a mixture of two diastereomers (ratio 1.25:1 according to NMR) and *cis*/*trans*, *cis*-**105E** (37 mg, 6%, yellowish oil) as a mixture of two diastereomers (ratio 1.1:1). Diastereomers *cis*/*trans*, *trans*-**104E** have been partially separated from each other as crystals by slow evaporation of solvents of two-phase 1:1 ethyl acetate/diethyl ether solution of these compounds.

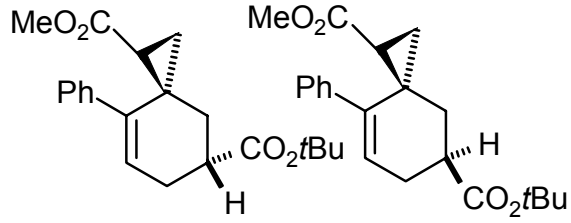


cis, *trans*-**104E** *trans*, *trans*-**104E**

Major diastereomer (*cis*, *trans*-**104E**): R_f = 0.37 (light petroleum/ethyl acetate 10:1); IR (KBr): $\tilde{\nu}$ = 3064, 3027, 2997, 2977, 2956, 2919, 2876, 1732, 1723, 1495, 1481, 1440, 1389, 1370, 1351, 1320, 1280, 1265, 1226, 1212, 1194, 1169, 1068, 1048, 946, 892, 846, 757, 696 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.19 (dd, *J* = 5.2, 8.3 Hz, 1 H, *c*Pr-H), 1.49 [s, 9 H, $C(CH_3)_3$], 1.58 (t, *J* = 5.6 Hz, 1 H, *c*Pr-H), 1.74–2.13 (*AB system*, δ_A = 2.08, δ_B = 1.78, J_A = 7.9, 13.5 Hz, J_B = 5.3, 13.5 Hz, 2 H, 4-H or 6-H), 1.97–2.03 (m, 1 H, *c*Pr-H), 2.47–2.53 (m, 2 H, 4-H or 6-H), 2.64–2.75 (m, 1 H, 5-H), 3.36 (s, 3 H, OCH_3), 5.94 (t, *J* = 4.7 Hz, 1 H, 7-H), 7.13–7.32 (m, 5 H, Ph);

^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 18.27 (–, *c*Pr-C), 27.49 (–, C-4 or C-6), 28.07 [+, $C(CH_3)_3$], 29.39 (+, *c*Pr-C), 29.62 (C_{quat}, *c*Pr-C), 37.42 (–, C-4 or C-6), 40.03 (+, C-5), 51.25 (+, OCH_3), 80.50 [C_{quat}, $C(CH_3)_3$], 126.52 (+, Ph), 127.56 (+, 2 × Ph), 127.62 (+, 2 × Ph), 129.30 (+, C-7), 140.96 (C_{quat}), 141.70 (C_{quat}), 170.88 (C_{quat}, C=O), 174.53 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 342 (11) [M^+], 327 (4) [$M^+ - CH_3$], 311 (6), 286 (26), 240 (48), 226 (46), 209 (17), 181 (100), 167 (22), 154 (11), 57 (26); elemental analysis* calcd (%) for $C_{21}H_{26}O_4$ (342.4): C 73.66, H 7.65; found: C 73.56, H 7.43.

Minor diastereomer (*trans*, *trans*-**104E**): R_f = 0.37 (light petroleum/ethyl acetate 10:1); IR (KBr): $\tilde{\nu}$ = 3080, 3027, 2996, 2978, 2955, 2927, 2867, 1733, 1723, 1494, 1481, 1437, 1387, 1370, 1351, 1318, 1280, 1258, 1226, 1212, 1192, 1170, 1068, 947, 893, 846, 829, 756, 697 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.29–1.36 (m, 2 H, *c*Pr-H, 4-H or 6-H), 1.46 [s, 9 H, $C(CH_3)_3$], 1.63–1.68 (m, 1 H, *c*Pr-H), 1.76–1.81 (m, 1 H, *c*Pr-H), 2.23 (t, *J* = 12.7 Hz, 1 H, 4-H or 6-H), 2.39–2.67 (m, 2 H, 4-H or 6-H), 2.89–3.03 (m, 1 H, 5-H), 3.34 (s, 3 H, OCH_3), 5.76 (t, *J* = 3.8 Hz, 1 H, 7-H), 7.06–7.10 (m, 2 H, Ph), 7.20–7.31 (m, 3 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.92 (–, *c*Pr-C), 28.06 [+, $C(CH_3)_3$], 29.0 (–, C-4 or C-6), 30.38 (C_{quat}, *c*Pr-C), 30.50 (+, *c*Pr-C), 38.80 (–, C-4 or C-6), 40.37 (+, C-5), 51.32 (+, OCH_3), 80.38 [C_{quat}, $C(CH_3)_3$], 126.39 (+, C-7), 127.40 (+, 2 ×Ph), 128.07 (+, 2 ×Ph), 130.16 (+, Ph), 138.97 (C_{quat}), 141.59 (C_{quat}), 170.90 (C_{quat}, C=O), 174.34 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 342 (4) [M^+], 286 (22), 240 (42), 226 (44), 181 (100), 167 (24), 154 (16), 115 (9), 57 (82), 41 (39); elemental analysis* calcd (%) for $C_{21}H_{26}O_4$ (342.4): C 73.66, H 7.65; found: C 73.56, H 7.43. Elemental analysis was carried out for the mixture of diastereomers.

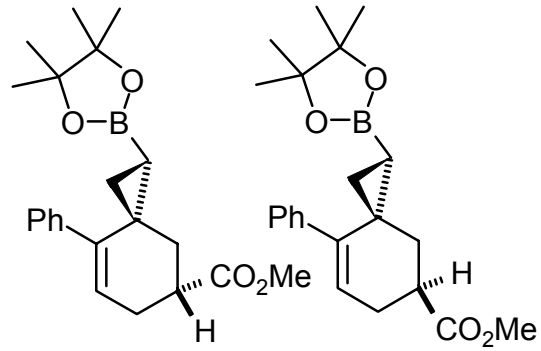


cis, *cis*-**105E** *trans*, *cis*-**105E**

cis/*trans*, *cis*-**105E**:* R_f = 0.46 (light petroleum/ethyl acetate 10:1); IR (Film): $\tilde{\nu}$ = 3079, 3056, 3003, 2977, 2951, 2931, 2846, 1729, 1492, 1479, 1441, 1392, 1368, 1335, 1316, 1258, 1212, 1192, 1170, 1152, 1070, 990, 904, 849, 829, 764, 705 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.93–0.97 (m, 1 H, *c*Pr-H), 1.13 (dd, *J* = 4.9, 8.1 Hz, 1 H, *c*Pr-H), 1.19 (dd, *J* = 4.6, 6.0 Hz, 1 H, *c*Pr-H), 1.28–1.32 (m, 1 H, *c*Pr-H), 1.43 [s, 9 H, $C(CH_3)_3$], 1.44 [s, 9 H, $C(CH_3)_3$], 1.55–1.60 (m, 1 H, *c*Pr-H), 1.75 (dd, *J* = 6.0, 8.3 Hz, 1 H, *c*Pr-H), 1.89–2.19 (m, 4 H, 4-H or 6-H), 2.34–2.44 (m, 4 H, 4-H or 6-H), 2.48–2.60 (m, 1 H, 5-H), 2.68–2.78 (m, 1 H, 5-H), 3.65 (s, 3 H, OCH_3), 3.67 (s, 3 H, OCH_3), 5.59–5.64 (m, 2 H, 2 × 7-H), 6.99–7.04 (m, 4 H, Ph), 7.19–7.29 (m, 6 H, Ph); ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 17.80 (–, *c*Pr-C), 18.59 (–, *c*Pr-C), 24.65 (+, 2 × *c*Pr-C),

28.03 [+, 2 × $C(CH_3)_3$], 28.32 (–, C-4 or C-6), 28.60 (–, C-4 or C-6), 29.25 (C_{quat}, *c*Pr-C), 29.90 (–, C-4 or C-6), 30.06 (C_{quat}, *c*Pr-C), 30.99 (–, C-4 or C-6), 40.24 (+, C-5), 40.43 (+, C-5), 51.68 (+, OCH_3), 51.72 (+, OCH_3), 80.09 [C_{quat}, $C(CH_3)_3$], 80.21 [C_{quat}, $C(CH_3)_3$], 126.48 (+, C-7), 126.81 (+, C-7), 126.94 (+, Ph), 126.99 (+, Ph), 127.71 (+, 2 × Ph), 127.77 (+, 2 × Ph), 129.34 (+, 2 × Ph), 129.42 (+, 2 × Ph), 139.07 (C_{quat}), 139.48 (C_{quat}), 140.66 (C_{quat}), 140.87 (C_{quat}), 171.87 (C_{quat}, C=O), 172.09 (C_{quat}, C=O), 174.25 (C_{quat}, C=O), 175.50 (C_{quat}, C=O); MS (DCI), *m/z* (%): 702.7 (12) [$2M + NH_4^+$], 360 (100) [$M + NH_4^+$], 343 (14) [$M + H^+$] 304 (61); HRMS-ESI for $C_{21}H_{26}O_4$ (342.43): [$M + H$]$^+$ 343.19047, calcd. 343.19039; [M + Na]$^+$ 365.17244, calcd. 365.17233. *For all measurements pure mixture of diastereomers *cis*/*trans*, *cis*-**105E** was used.

Methyl 8-phenyl-1-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)spiro[2.5]oct-7-ene-5-carboxylate (*cis*/*trans*, *trans*-104B), Methyl 8-phenylspiro[2.5]oct-7-ene-5-carboxylate (109a): According to GP-A, $Pd(OAc)_2$ (19.3 mg, 85 μmol), triphenylphophane (67 mg, 254 μmol), K_2CO_3 (470 mg, 3.40 mmol), Et_4NCl (281.5 mg, 1.70 mmol), iodobenzene (**173**, 347 mg, 1.70 mmol), 2-(1',1''-Bicyclopropyliden-2'-yl)-4,4,5,5,-tetramethyl-1,3-dioxa-2-borolan (**66B**, 700 mg, 3.40 mmol) and methyl acrylate (**68a**, 293 mg, 3.40 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 10:1) to yield *cis*/*trans*, *trans*-**104B** (156.5 mg, 25%, yellowish oil) as a mixture of two diastereomers (ratio 1.4:1 according to NMR) and ***109a** (156 mg, 38%, yellowish oil). Diastereomer *cis*, *trans*-**104B** has been crystallized by slow evaporation of solvents of two-phase 1:1 ethyl acetate/diethyl ether solution of this compound. *For the spectroscopic identification of compound **109a** see: references 29b and 35a.



cis, *trans*-**104B** *trans*, *trans*-**104B**

Major diastereomer (*cis*, *trans*-**104B**): R_f = 0.18 (light petroleum/ethyl acetate 10:1); IR (KBr): $\tilde{\nu}$ = 3075, 2979, 2924, 2882, 2827, 1737, 1632, 1599, 1492, 1421, 1389, 1379, 1381, 1359, 1334, 1261, 1233, 1190, 1171, 1142, 1073, 1045, 1001, 973, 959, 914, 903, 867, 844, 812, 757, 702 cm^{-1}; ^{1}H NMR (300 MHz, C_6D_6): δ = 0.14 (dd, *J* = 7.7, 10.0 Hz, 1 H, *c*Pr-H), 0.90 (s, 6 H, 2 × CH_3), 0.92 (s, 6 H, 2 × CH_3), 0.97 (dd, *J* = 4.1, 10.2 Hz, 1 H, *c*Pr-H), 1.28

(dd, J = 3.8, 12.4 Hz, 1 H, 4-H), 1.52 (dd, J = 4.2, 7.6 Hz, 1 H, *c*Pr-H), 2.31 (t, J = 12.2 Hz, 1 H, 4-H), 2.42–2.64 (m, 2 H, 6-H), 3.04–3.15 (m, 1 H, 5-H), 3.33 (s, 3 H, OCH_3), 5.62 (t, J = 3.8 Hz, 1 H, 7-H), 7.09–7.25 (m, 5 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT)*: δ = 18.44 (–, *c*Pr-C), 24.35 (+, 2 × CH_3), 25.03 (+, 2 × CH_3), 26.96 (C_{quat}, *c*Pr-C), 28.78 (–, C-6), 39.73 (+, C-5), 40.69 (–, C-4), 51.57 (+, OCH_3), 82.76 (2 × C_{quat}), 126.09 (+, Ph), 127.08 (+, 2 × Ph), 127.67 (+, C-7), 128.84 (+, 2 × Ph), 141.08 (C_{quat}), 142.24 (C_{quat}), 175.93 (C_{quat}, C=O). * Peaks belong to C-2 could not be observed because of ^{13}C-$^{10/11}$B coupling. MS (70 eV, EI), *m/z* (%): 368 (25) [M^+], 308 (10), 268 (26), 240 (60), 213 (21), 180 (100), 167 (38), 153 (19), 115 (16), 101 (30), 85 (65), 55 (18), 41 (22); elemental analysis calcd (%) for $C_{21}H_{26}O_4$ (342.4): C 71.75, H 7.94; found: C 71.46, H 7.68.

Minor diastereomer (*trans*, *trans*-**104B**): R_f = 0.21 (light petroleum/ethyl acetate 10:1); IR (Film): $\tilde{\nu}$ = 3079, 3054, 3026, 2998, 2977, 2929, 2857, 1738, 1599, 1492, 1437, 1407, 1373, 1330, 1256, 1230, 1196, 1171, 1143, 1115, 1016, 963, 907, 857, 760, 704 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.22–0.25 (m, 1 H, *c*Pr-H), 0.96–0.99 (m, 1 H, *c*Pr-H), 1.03 (s, 6 H, 2 × CH_3), 1.07 (s, 6 H, 2 × CH_3), 1.20 (dd, J = 3.9, 7.5 Hz, 1 H, *c*Pr-H), 1.80 (dd, J = 5.8, 13.4 Hz, 1 H, 4-H), 2.17 (dd, J = 6.4, 12.9 Hz, 1 H, 4-H), 2.48–2.54 (m, 1 H, 6-H), 2.62–2.68 (m, 1 H, 6-H), 2.83–2.89 (m, 1 H, 5-H), 3.76 (s, 3 H, OCH_3), 5.80 (t, J = 4.4 Hz, 1 H, 7-H), 7.20–7.29 (m, 5 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT)*: δ = 16.66 (–, *c*Pr-C), 24.42 (+, 2 × CH_3), 25.12 (+, 2 × CH_3), 25.84 (C_{quat}, *c*Pr-C), 27.61 (–, C-6), 39.44 (+, C-5), 39.55 (–, C-4), 51.78 (+, OCH_3), 82.70 (2 × C_{quat}), 126.19 (+, Ph), 127.30 (+, 2 × Ph), 128.08 (+, C-7), 128.54 (+, 2 × Ph), 141.40 (C_{quat}), 143.58 (C_{quat}), 175.72 (C_{quat}, C=O). * Peaks belong to C-2 could not be observed because of ^{13}C-$^{10/11}$B coupling. MS (70 eV, EI), *m/z* (%): 368 (36) [M^+], 336 (10), 308 (12), 268 (35), 240 (64), 224 (27), 205 (39), 181 (100), 167 (43), 154 (20), 141 (17), 115 (18), 85 (72), 69 (29), 55 (44); $C_{22}H_{29}BO_4$ (368.29): calcd. 368.2159 (correct HRMS).

*2.1.2.1. An attempt for the synthesis of tert-Butyl 8-phenyl-1-(tributylstannyl) spiro[2.5]oct-7-ene-5-carboxylate (cis/trans, trans-**104C**) and/or (cis/trans, cis-**105C**)*

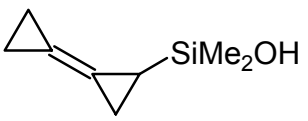
According to GP-1, $Pd(OAc)_2$ (15.2 mg, 67 µmol), triphenylphophane (53.2 mg, 202 µmol), K_2CO_3 (374.4 mg, 2.7 mmol), Et_4NCl (250 mg, 1.35 mmol), iodobenzene (**67**, 276 mg, 1.35 mmol), 2-(Tributylstannyl)bicyclopropylidene (**66C**, 1 g, 2.7 mmol) and *tert*-butyl acrylate (**68b**, 347 mg, 2.7 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl

acetate, 14:1) to yield mixture of *cis*/*trans*, *trans*-**104D** and/or *cis*/*trans*, *cis*-**105D*** along with some amount of unidentified compounds (33 mg, yellowish oil) and ***tert-Butyl 8-phenylspiro[2.5]oct-7-ene-5-carboxylate (109b)** (187 mg. 49%, yellowish oil). *These spirooctenes could not be isolated purely and their exact configurations could not be determined. For the spectroscopic identification of compound **109b** see: references 29b and 35a.

*2.1.2.2. An attempt for the synthesis of tert-Butyl 1-(hydroxydimethylsilanyl)-8-phenylspiro[2.5]oct-7-ene-5-carboxylate (cis/trans, trans-**104D**) and/or (cis/trans, cis-**105D**)*

According to GP-1, $Pd(OAc)_2$ (18.2 mg, 80 μmol), triphenylphophane (64 mg, 243 μmol), K_2CO_3 (448 mg, 3.24 mmol), Et_4NCl (300 mg, 1.62 mmol), iodobenzene (**67**, 330 mg, 1.62 mmol), bicyclopropyliden-2-yl-dimethylsilanol (**66D**, 500 mg, 3.24 mmol) and *tert*-butyl acrylate (415 mg, 3.24 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 14:1) to yield mixture of *cis*/*trans*, *trans*-**104D** and/or *cis*/*trans*, *cis*-**105D*** along with some amount of unidentified compounds (214 mg, colorless oil) and ***tert*-Butyl 8-phenylspiro[2.5]oct-7-ene-5-carboxylate** (**109b**) (116 mg. 25%, yellowish oil). *These spirooctenes could not be isolated purely and their exact configurations could not be determined. For the spectroscopic identification of compound **109b** see: references 29b and 35a.

*2.2. The synthesis of Bicyclopropyliden-2-yl-dimethylsilanol (**66D**).*

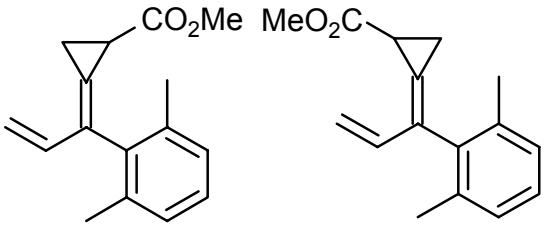


To an solution of *n*Buli (5.25 mL, 2.5 M in Hexane) in 15 mL anhydrous THF at –30 °C Bicyclopropylidene (**66**) (1 g, 12.5 mmol) in 2 mL anhydrous THF was added dropwise with a syringe. After stirring 1 h at 0 °C, the reaction mixture was quenched at –78 °C by slow addition of Hexamethylcyclotrisiloxane (0.92 g, 4.125 mmol) in 5 mL anhydrous THF and stirred at –78 °C for 1 h and at room temperature for 2 h. After cooling to –78 °C, 10 % HCl (10 mL) was added into the mixture and allowed to warm to room temperature. The mixture was poured into 100 mL ether and extracted. The organic phase was dried ($MgSO_4$) and concentrated in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g,

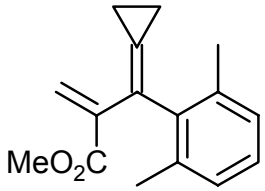
3 × 30 cm, light petroleum/ethyl acetate, 10:1) to yield **66D** (0.75 g, 39%, colorless oil). IR (film): $\tilde{\nu}$ = 3282, 3050, 2979, 2958, 1270, 1251, 1192, 1075, 998, 954, 904, 862, 840, 819, 777, 686 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.06 (s, 3 H, CH_3), 0.10 (s, 3 H, CH_3), 0.72–0.80 (m, 1 H, *c*Pr-H), 1.22–1.09 (m, 5 H, *c*Pr-H), 1.34–1.41 (m, 1 H, *c*Pr-H), 2.03 (br.s, 1 H, OH); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = –1.53 (+, CH_3), –1.07 (+, CH_3), 2.86 (–, *c*Pr-C), 3.33 (–, *c*Pr-C), 5.15 (+, *c*Pr-C), 5.85 (–, *c*Pr-C), 107.56 (C_{quat}), 112.43(C_{quat}); MS (DCI), *m/z* (%): 172.1 (100) [$M + NH_4^+$], 155 (37) [$M + H^+$], 109 (13).

*2.3. Preparation of allylidenecyclopropanes trans-**119E**, cis-**120E** and **121E****

Methyl 2-[1-(2,6-dimethylphenyl)allylidene]cyclopropanecarboxylate [*trans*-119E, *cis*-120E] and Methyl 2-[cyclopropylidene-(2,6-dimethylphenyl)-methyl]acrylate (121E):



trans-**119E** *cis*-**120E**



121E

According to GP-1, $Pd(OAc)_2$ (55 mg, 250 µmol), triphenylphophane (200 mg, 750 µmol), K_2CO_3 (1382 mg, 10.0 mmol), Et_4NCl (828 mg, 5.0 mmol), 2-iodo-1,3-dimethylbenzene (**124**, 1160 mg, 5.00 mmol), methyl bicyclopropylidenecarboxylate (**66E**, 1382 mg, 10.0 mmol) were stirred in anhydrous MeCN (6 mL) at 70 °C for 24 h. After cooling to room temperature, the reaction mixture was taken up in 60 mL of diethyl ether. The solution was washed with water (2 × 40 mL), the aqueous phase was extracted with diethyl ether (2 × 40 mL), and the combined organic phases were dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator, the residue was subjected to chromatography on silica gel (250 g, 5 × 40 cm, light petroleum/ethyl acetate, 12:1) to yield *trans*-**119E**, *cis*-**120E**, and **121E** (1090 mg, 90%, yellowish oil) as a mixture of three regioisomers (ratio 67:23:10 according to GC). For all spectral analysis, pure mixture of these regioisomers have been used. In ^1H and ^{13}C NMR spectra of the mixture, individual data for every single structure have been demonstrated by structure numbers (**119E**, **120E** and **121E**) whenever this is possible.* Preparation of these compounds was firstly performed by Daniel Frank. Full spectroscopic idendification of compounds firstly has been given in this study. Bp. = 0.1 Torr, 112 °C; R_f = 0.26 (light petroleum/ethyl acetate 12:1); IR (Film): $\tilde{\nu}$ = 3088, 3005, 2951, 2921, 2857, 1734, 1608, 1582, 1464, 1436, 1412, 1378, 1346, 1291, 1261,

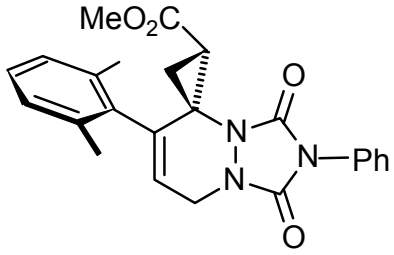
1233, 1195, 1169, 1138, 1112, 1079, 1049, 1030, 988, 970, 944, 911, 863, 812, 771, 736, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ = 0.96–1.00 (m, 2 H, *c*Pr-H)**[121E]**, 1.30–1.33 (m, 2 H, *c*Pr-H)**[121E]**, 1.61–1.63 (m, 2 H, *c*Pr-H)**[119E]**, 1.75 (dd, *J* = 4.0, 79.8 Hz, 1 H, *c*Pr-H)**[119E]**, 2.00–2.03 (m, 2 H, *c*Pr-H)**[120E]**, 2.04 (s, 3 H, Ar-CH_3)**[120E]**, 2.05 (s, 3 H, Ar-CH_3)**[120E]**, 2.09 (s, 3 H, Ar-CH_3)**[119E]**, 2.12 (s, 6 H, 2 × Ar-CH_3)**[121E]**, 2.15 (s, 3 H, Ar-CH_3)**[119E]**, 2.52 (d, *J* = 4.0 Hz, 1 H, *c*Pr-H)**[120E]**, 2.54 (d, *J* = 4.1 Hz, 1 H, *c*Pr-H)**[119E]**, 3.52 (s, 3 H, OCH_3)**[120E]**, 3.72 (s, 3 H, OCH_3)**[119E]**, 3.82 (s, 3 H, OCH_3)**[121E]**, 4.71 (d, *J* = 17.3 Hz, 1 H, vinyl-H)**[119E]**, 4.73 (d, *J* = 17.3 Hz, 1 H, vinyl-H)**[120E]**, 4.90 (s, 1 H, vinyl-H)**[121E]**, 5.05 (d, *J* = 10.4 Hz, 1 H, vinyl-H)**[119E]**, 5.09 (d, *J* = 10.6 Hz, 1 H, vinyl-H)**[120E]**, 5.53 (s, 1 H, vinyl-H)**[121E]**, 6.60 (dd, *J* =10.3, 17.3 Hz, 1 H, vinyl-H)**[120E]**, 6.72 (dd, *J* =10.4, 17.3 Hz, 1 H, vinyl-H)**[119E]**, 6.98–7.14 (m, 9 H, Ar)**[119-121E]**; ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 2.44 (–, *c*Pr-C)**[121Ea]**, 5.02 (–, *c*Pr-C)**[121E]**, 11.61 (–, *c*Pr-C)**[120E]**, 11.73 (–, *c*Pr-C)**[119E]**, 17.68 (–, *c*Pr-C)**[120E]**, 17.82 (–, *c*Pr-C)**[119E]**, 19.14 (+, 2 × Ar-CH_3)**[121E]**, 19.31 (+, 2 × Ar-CH_3)**[119E]**, 19.58 (+, 2 × Ar-CH_3)**[119E]**, 51.50 (+, OCH_3)**[120E]**, 51.74 (+, OCH_3)**[121E]**, 51.80 (+, OCH_3)**[119E]**, 115.5 (–, vinyl-C)**[119E]**, 115.8 (–, vinyl-C)**[120E]**, 118.5 (–, vinyl-C)**[121E]**, 124.48 (C_{quat})**[120E]**, 125.01 (C_{quat})**[121E]**, 125.07 (C_{quat})**[119E]**, 126.9 (+, 3 × Ar-C), 127.0 (+, Ar-C), 127.02 (+, 2 × Ar-C), 127.13 (+, Ar-C), 127.16 (+, 2 × Ar-C), 127.43 (C_{quat})**[121E]**, 128.44 (2 × C_{quat})**[121E]**, 130.21 (C_{quat})**[119E]**, 130.58 (C_{quat})**[120E]**, 135.38 (+, vinyl-C)**[119E]**, 135.7 (+, vinyl-C)**[120E]**, 135.9 (C_{quat})**[120E]**, 136.2 (C_{quat})**[119E]**, 136.4 (C_{quat})**[120E]**, 136.48 (C_{quat})**[119E]**, 136.65 (C_{quat})**[120E]**, 136.98 (C_{quat})**[119E]**, 138.16 (C_{quat})**[121E]**, 141.50 (C_{quat})**[121E]**, 169.22 (C_{quat}, C=O)**[121E]**, 171.73 (C_{quat}, C=O)**[120E]**, 172.30 (C_{quat}, C=O)**[119E]**; MS (70 eV, EI), *m/z* (%): 242 (80) [M^+], 227 (20), [$M^+ - CH_3$], 210 (22), 195 (20), 183 (85), 167 (100), 153 (33), 128 (14), 115 (8); elemental analysis calcd (%) for $C_{16}H_{18}O_2$ (242.3): C 79.31, H 7.49; found: C 79.24, H 7.37.

*2.4. Hetero-Diels-Alder reaction of allylidenecyclopropanes trans-**119E**, cis-**120E** and **121E** with N-phenyltriazolinedione (**122**)*

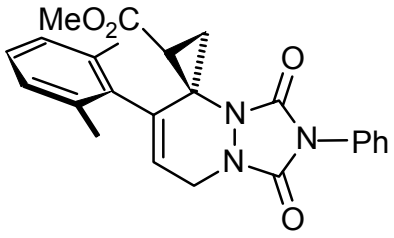
Methyl 6'-(2,6-dimethylphenyl)-2'-phenylspiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo [1,2-a]pyridazine]-1',3'-dione-1-carboxylate [*trans*-123E, *cis*-124E] and Methyl 6'-(2,6-dimethylphenyl)-2'-phenylspiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo [1,2-a]pyridazine]-1',3'-dione-7'-carboxylate (125E):

The mixture of allylidenecyclopropanes (**119–121E**) (242 mg, 1.00 mmol) and dienophile *N*-phenyltriazolinedione **122 (**350 mg, 2.00 mmol) was stirred in anhydrous MeCN (2 mL) and 1 ml CH_2Cl_2 at 20 °C for 24 h. After then, the reaction mixture was taken up in 50 mL of CH_2Cl_2. The solution was washed with water (2 × 20 mL), the aqueous phase was extracted with diethyl ether (2 × 20 mL), and the combined organic phases were dried ($MgSO_4$). After

removal of the solvent in a rotatory evaporator, the residue was subjected to chromatography on silica gel (100g, 3 × 30 cm, light petroleum/ethyl acetate, 1:1) to yield *trans*-**123E**, *cis*-**124E** [R_f = 0.72 (light petroleum/ethyl acetate 1:1)] and **125E** [R_f = 0.61 (light petroleum/ethyl acetate 1:1)] (255 mg, 61%, yellowish oily solid) as a mixture of three regioisomers (ratio 7.1:1:1.4 according to crude NMR).



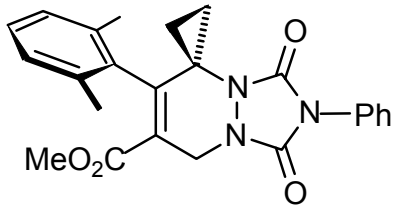
trans-**123E**



cis-**124E**

trans-**123E***: ^{1}H NMR (300 MHz, $CDCl_3$): δ =1.70 (dd, *J* = 6.9, 8.7 Hz, 1 H, *c*Pr-H), 2.12 (s, 3 H, Ar-CH_3), 2.31 (s, 3 H, Ar-CH_3), 2.41 (t, *J* = 9.23 Hz, 1 H, *c*Pr-H), 3.21 (dd, *J* = 6.9, 9.8 Hz, 1 H, *c*Pr-H), 3.53 (s, 3 H, OCH_3), 4.31–4.63 (AB-system, δ_A = 4.60, δ_B = 4.35, J_A = 3.7, 17.3 Hz, J_B = 3.4, 17.3 Hz, 2 H, a-H), 5.89 (t, *J* = 3.43 Hz, 1 H, b-H), 7.02–7.16 (m, 3 H, Ar), 7.34–7.48 (m, 5 H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = 16.68 (–, *c*Pr-C), 20.63 (+, Ar-CH_3), 20.82 (+, Ar-CH_3), 30.07 (+, *c*Pr-C), 44.76 (–, C-a), 48.30 (C_{quat}, *c*Pr-C), 52.11 (+, OCH_3), 124.68 (+, C-b), 125.54 (+), 127.52 (+), 127.67 (+), 127.90 (+), 128.34 (+), 129.12 (+), 130.76 (C_{quat}), 135.34 (C_{quat}), 135.71 (C_{quat}), 136.81 (2 × C_{quat}), 149.44 (C_{quat}, C=O), 152.37 (C_{quat}, C=O), 168.14 (C_{quat}, C=O). *cis*-**124E***: ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.25–1.28 (m, 1 H, *c*Pr-H), 1.82 (dd, *J* = 7.5, 10.0 Hz, 1 H, *c*Pr-H), 2.25 (s, 3 H, Ar-CH_3), 2.33 (s, 3 H, Ar-CH_3), 3.39 (t, *J* = 7.14 Hz, 1 H, *c*Pr-H), 3.66 (s, 3 H, OCH_3), 4.23–4.60 (AB-system, δ_A = 4.56, δ_B = 4.27, J_A = 4.4, 16.8 Hz, J_B = 2.4, 16.8 Hz, 2 H, a-H), 5.77 (dd, *J* = 2.6, 3.9 Hz, 1 H, b-H), 7.01–7.17 (m, 3 H, Ar), 7.33–7.58 (m, 5 H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = 17.07 (–, *c*Pr-C), 19.94 (+, Ar-CH_3), 20.32 (+, Ar-CH_3), 25.39 (+, *c*Pr-C), 46.85 (–, C-a), 46.30 (C_{quat}, *c*Pr-C), 52.20 (+, OCH_3), 121.36 (+, C-b), 126.23 (+), 127.58 (+), 128.09 (+), 128.31 (+), 129.08 (2 × +), 131.24 (+), 133.28 (C_{quat}), 136.18 (C_{quat}), 136.76 (C_{quat}), 137.59 (C_{quat}), 149.88 (C_{quat}, C=O), 154.91 (C_{quat}, C=O), 170.04 (C_{quat}, C=O). IR (KBr): $\tilde{\nu}$ = 3116, 3065, 2994, 2951, 2923, 2853, 1768, 1736, 1703, 1494, 1453, 1423, 1376, 1356, 1294, 1260, 1201, 1181, 1166, 1143, 805, 768, 754, 711, 692 cm^{-1}; MS (70 eV, EI), *m/z* (%): 417 (100) [M^+], 402 (12), [$M^+ - CH_3$], 385 (18), 370 (5), 357 (6), 342 (10), 330 (25), 240 (16), 211 (26), 181 (11), 167 (25), 154 (18), 128 (25), 91 (17), 55 (14); elemental analysis calcd (%) for $C_{24}H_{23}N_3O_4$ (417.5): C 69.05, H 5.55, N 10.07; found: C 68.83, H 5.79, N 9.89.

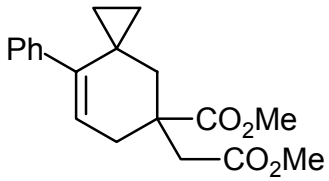
IR, EI mass and elemental analysis were carried out for the mixture of regioisomers *trans*-**123E** and *cis*-**124E**.



125E: ^{1}H NMR (300 MHz, $CDCl_3$, 50 °C): δ = 0.86–0.90 (m, 2 H, *c*Pr-H), 2.08–2.13 (m, 2 H, *c*Pr-H), 2.18 (s, 6 H, 2 × Ar-CH_3), 3.51 (s, 3 H, OCH_3), 4.62 (s, 2 H, a-H), 7.0–7.52 (m, 8 H, Ar, Ph); ^{13}C NMR (50.2 MHz, $CDCl_3$, DEPT): δ = 12.45 (–, 2 × *c*Pr-C), 19.91 (+, 2 × Ar-CH_3), 43.28 (C_{quat}, *c*Pr-C), 45.11 (–, C-a), 51.79 (+, OCH_3), 120.9 (C_{quat}), 122.1 (C_{quat}), 125.7 (+), 127.4 (+), 128.2 (+), 128.3 (+), 129.1 (+), 129.2 (+), 131.2 (C_{quat}), 132.9 (C_{quat}), 135.8 (C_{quat}), 148.4 (C_{quat}), 150.4 (C_{quat}, C=O), 153.1 (C_{quat}, C=O), 164.2 (C_{quat}, C=O); IR (KBr): $\tilde{\nu}$ = 3066, 3020, 2951, 2923, 2851, 1779, 1734, 1711, 1634, 1621, 1597, 1564, 1507, 1415, 1344, 1276, 1230, 1166, 1028, 765, 712, 688 cm^{-1}; MS (70 eV, EI), *m/z* (%): 417 (38) [M^+], 402 (18), [M^+ – CH_3], 358 (5), 269 (5), 212 (16), 181 (14), 167 (19), 128 (17), 119 (18), 93 (100), 77 (19), 65 (12); HRMS-ESI for $C_{24}H_{23}N_3O_4$ (417.5): [M + H]$^+$ 418.17619, calcd. 418.17613.

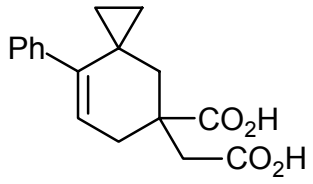
*2.5. A modification on the spiro[2.5]octene derivative **127***

Methyl 8-phenyl-5-(methoxycarbonylmethyl)spiro[2.5]oct-7-ene-5-carboxylate (**127**):



A sealable Teflon tube with anhydrous DMF (4.5 mL) was charged under argon with $Pd(OAc)_2$ (11.2 mg, 49.9 μmol) and PPh_3 (39.3 mg, 150 μmol). Argon was bubbled through the mixture for 5 min and the mixture was treated with iodo benzene (**67**, 204 mg, 1.00 mmol) and itaconic acid dimethyl ester (**126**, 316 mg, 2.00 mmol), bicyclopropylidene (**66**, 160 mg, 2.00 mmol). After heating at 80 °C for 48 h at 10 kbar, the solution was cooled to ambient temperature, added to water (50 mL) and extracted with diethyl ether (5 × 20 mL). The combined organic phases were washed with water (4 × 10 mL), NaCl solution (10 mL) and being dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator the residue (578 mg) was subjected to chromatography on silica gel (column 3 × 30 cm, pentane/diethyl ether 10:1) yielded **127** as a colorless oil (228 mg, 72%). For the spectroscopic identification of this compound see: references 29b or 35.

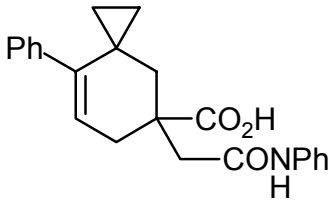
5-Carboxymethyl-8-phenylspiro[2.5]oct-7-ene-5-carboxylic acid (**128**):



Spirooctene **127** (0.819 g, 2.6 mmol) was heated in the mixture of 80 mL 1N NaOH and 40 mL MeOH under reflux for 6 h. After solution was cooled to ambient temperature, it was carefully acidified with 2N HCl and then added into 100 ml ethyl acetate. The solution was washed with brine (3 × 30 mL). The separated organic phase was dried ($MgSO_4$) and evaporated under vacuum in a rotatory evaporator. The remaining white solid (**128**, 0,663 g, 89%) was used without further purification for the next step.

IR (KBr): $\tilde{\nu}$ = 3189, 2937, 2646, 1734, 1704, 1491, 1441, 1409, 1379, 1343, 1271, 1256, 1239, 1171, 1129, 1059, 1024, 991, 915, 824, 760, 702, 685 cm^{-1}; ^1H NMR (300 MHz, d_6-acetone): δ = 0.43–0.57 (m, 4 H, *c*Pr-H), 1.73 (dd, *J* = 1.5, 13.4 Hz, 1 H, 4-H or 6-H), 2.23 (d, *J* = 13.9 Hz, 1 H, 4-H or 6-H), 2.35 (ddd, *J* = 1.5, 5.0, 17.8 Hz, 1 H, 4-H or 6-H), 2.76 (dd, *J* = 2.7, 17.7 Hz, 1 H, 4-H or 6-H), 2.81–3.04 (AB-system, δ_A = 3.0, δ_B = 2.84, J_{AB} = 17.1 Hz, 2 H, C*H*$_2$COOH), 5.47 (dd, *J* = 2.7, 4.6 Hz, 1 H, 7-H), 7.04–7.07 (m, 2 H, Ph), 7.23–7.31 (m, 3 H, Ph), 9.6–11.2 (b.s, 2 H, OH); ^{13}C NMR (75.5 MHz, d_6-acetone, DEPT): δ = 10.26 (–, *c*Pr-C), 12.58 (–, *c*Pr-C), 18.80 (C_{quat}, *c*Pr-C), 34.35 (–, C-4 or C-6), 39.59 (–, *C*H_2COOH), 41.51 (–, C-4 or C-6), 43.96 (C_{quat}, C-5), 123.79 (+, C-7), 127.5 (+, Ph), 128.3 (+, 2 × Ph), 130.2 (+, 2 × Ph), 141.0 (C_{quat}), 142.9 (C_{quat}), 172.2 (C_{quat}, C=O), 177.3 (C_{quat}, C=O); MS (DCI), *m/z* (%): 304 (54) [*M* + NH_4^+], 303 (56), 286 (100) [*M* – H_2O + NH_4^+], 242 (22), 197 (16), 134 (19).

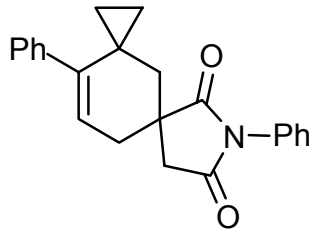
8-Phenyl-5-phenylcarbomoylmethylspiro[2.5]oct-7-ene-5-carboxylic acid (**129**):



The mixture of **128** (710 mg, 2.48 mmol) and $SOCl_2$ (0.189 mL, 2.6 mmol) in 10 mL CH_2Cl_2 was heated at 80 °C for 2 h. During this time the acid **128** dissolved and a brown solution appeared. Then, to this solution (ice-cold), aniline (0.45 mL, 4.96 mmol) was added dropwise and obtained mixture was stirred at room temperature for 3 h. After then, all material was dissolved in 150 mL CH_2Cl_2 and 150 mL Et_2O and washed with brine (3 × 20 mL). The separated organic phase was dried (Na_2SO_4) and evaporated under vacuum in a rotatory evaporator. The remaining brown solid (**129**, 875 mg, 97%) was used without further purification for the next step. IR (KBr): $\tilde{\nu}$ = 3.287, 3081, 2942, 2913, 1733, 1649, 1598, 1549, 1498, 1446, 1422, 1393, 1364, 1319, 1257, 1211, 1192, 1072, 1056, 1025, 987, 976, 822, 755, 701, 692 cm^{-1}; ^1H NMR (300 MHz, d_6-acetone): δ = 0.43–0.59 (m, 4 H, *c*Pr-H), 1.79 (dd, *J* = 1.5, 13.3 Hz, 1 H, 4-H or 6-H), 2.24 (d, *J* = 13.7 Hz, 1 H, 4-H or 6-H), 2.40 (ddd, *J* = 1.9, 4.8, 17.9 Hz, 1 H, 4-H or 6-H), 2.78 (dd, *J* = 2.8, 17.9 Hz, 1 H, 4-H or 6-H), 2.93–3.14 (AB-system, δ_A = 3.11, δ_B = 2.96, J_{AB} = 15.6 Hz, 2

H, C*H*$_2$CONPh), 5.49 (dd, *J* = 3.1, 4.9 Hz, 1 H, 7-H), 7.00–7.07 (m, 3 H, Ph), 7.22–7.30 (m, 5 H, Ph), 7.61–7.64 (m, 2 H, Ph); ^{13}C NMR (62.9 MHz, d-DMSO, DEPT): δ = 9.85 (–, *c*Pr-C), 11.97 (–, *c*Pr-C), 18.13 (C_{quat}, *c*Pr-C), 33.45 (–, C-4 or C-6), 41.47(–, C-4 or C-6), 42.99 (–, *C*H$_2$CONPh), 119.1 (+, 2 × Ph), 122.9 (+, C-7), 123.2 (+, Ph), 126.7 (+, Ph), 127.6 (+, 2 × Ph), 128.7 (+, 2 × Ph), 129.0 (+, 2 × Ph), 139.3 (C_{quat}), 139.9 (C_{quat}), 141.6 (C_{quat}), 169.5 (C_{quat}, C=O), 177.2 (C_{quat}, C=O).

7,12-Diphenyl-7-azadispiro[2.1.4.3]dodec-11-ene-6,8-dione (**130**):



The mixture of **129** (778 mg, 2.15 mmol), acetic anhydride (2 mL, 21.5 mmol) and sodium acetate (177 mg, 2.15 mmol) was heated at 80 °C for 1 h. After heating, the solution was cooled to ambient temperature, added to water (50 mL) and extracted with ethyl acetate (2 × 100 mL). The combined organic phases were washed with brine (4 × 20 mL) and dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator the residue was subjected to chromatography on silica gel (100g, 3 × 30 cm, light petroleum/ethyl acetate, 6:1) yielded **130** as a colorless solid (562 mg, 76%).

R_f = 0.33 (light petroleum/ethyl acetate 6:1), IR (KBr): $\tilde{\nu}$ = 2915, 1775, 1706, 1593, 1492, 1454, 1396, 1288, 1196, 1166, 1072, 1018, 989, 972, 912, 991, 843, 827, 752, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.38–0.42 (m, 1 H, *c*Pr-H), 0.51–0.63 (m, 3 H, *c*Pr-H), 1.18 (dd, *J* = 2.3, 13.3 Hz, 1 H, 4-H or 6-H), 2.17 (ddd, *J* = 2.4, 5.6, 17.2 Hz, 1 H, 4-H or 6-H), 2.63 (d, *J* = 13.2 Hz, 1 H, 4-H or 6-H), 2.83 (dd, *J* = 2.1, 17.1 Hz, 1 H, 4-H or 6-H), 2.73–3.13 (AB-system, δ_A = 3.07, δ_B = 2.74, J_{AB} = 18.6 Hz, 2 H, C*H*$_2$CONPh), 5.49 (dd, *J* = 2.2, 5.6 Hz, 1 H, 7-H), 6.95–6.97 (m, 2 H, Ph), 7.16–7.25 (m, 5 H, Ph), 7.29–7.33 (m, 1 H, Ph), 7.38–7.41 (m, 2 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 8.78 (–, *c*Pr-C), 13.71 (–, *c*Pr-C), 18.19 (C_{quat}, *c*Pr-C), 35.11 (–, C-4 or C-6), 40.14 (–, *C*H$_2$CONPh), 40.89 (–, C-4 or C-6), 44.12 (C_{quat}, C-5), 121.73 (+, C-7), 126.40 (+, 2 × Ph), 126.9 (+, Ph), 127.6 (+, 2 × Ph), 128.5 (+, Ph), 129.1 (+, 2 × Ph), 129.2 (+, 2 × Ph), 131.9 (C_{quat}), 139.5 (C_{quat}), 143.7 (C_{quat}), 175.4 (C_{quat}, C=O), 181.4 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 343 (100) [M^+], 314 (7), 209 (46), 188 (16), 167 (19), 156 (14), 141 (12), 128 (7); $C_{23}H_{21}NO_2$ (343.42): calcd. 343.1572 (correct HRMS).

*2.5.1. Two attempts for the direct preparation of spiro[2.5]octene **130**.*

1) A screw-cap Pyrex bottle was charged with anhydrous acetonitrile (2 mL), K_2CO_3 (556 mg, 4.00 mmol) and Et_4NCl (332 mg, 2.00 mmol). Argon was bubbled through the mixture for 5 min, $Pd(OAc)_2$ (22.4 mg, 5 mol%), and triphenylphosphane (78.7 mg, 15 mol%) were added, and the mixture was stirred once more for an additional 5 min with argon bubbling through, before iodobenzene (**67**, 408 mg, 2.00 mmol), bicyclopropylidene (**66**, 320 mg, 4.00 mmol) and *N*-phenylitaconimide (**131**, 749 mg, 4.00 mmol) were added. The bottle was tightly closed, and the mixture was stirred at 80 °C for 48 h. After cooling to room temperature, the reaction mixture was taken up in 20 mL of diethyl ether. The solution was washed with water (2 × 20 mL), the aqueous phase was extracted with diethyl ether (2 × 20 mL), and the combined organic phases were dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator, the residue was subjected to chromatography on silica gel (100g, 3 × 30 cm, light petroleum/ethyl acetate, 6:1). Separated fractions could not be identified and desired product **130** could not be observed.

2) A screw-cap Pyrex bottle was charged with anhydrous acetonitrile (2 mL), K_2CO_3 (556 mg, 4.00 mmol) and Et_4NCl (332 mg, 2.00 mmol). Argon was bubbled through the mixture for 5 min, $Pd(OAc)_2$ (22.4 mg, 5 mol%), and triphenylphosphane (78.7 mg, 15 mol%) were added, and the mixture was stirred once more for an additional 5 min with argon bubbling through, before iodobenzene (**67**, 408 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were added. The bottle was tightly closed, and the mixture was stirred at 100 °C for 15 h. After cooling to room temperature, the reaction mixture was taken up in 20 mL of diethyl ether. The solution was washed with water (20 mL), the aqueous phase was extracted with diethyl ether (2 × 20 mL), and the combined organic phases were dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator, the residue was dissolved in 1 mL DMF and taken into a screw-cap Pyrex bottle. After addition of *N*-phenylitaconimide (**131**, 749 mg, 4.00 mmol), the mixture stirred at 120 °C for 10 h. After cooling to room temperature, the solvent was removed in a rotatory evaporator. The residue was subjected to chromatography on silica gel (100g, 3 × 30 cm, light petroleum/ethyl acetate, 6:1). Separated fractions could not be identified and desired product **130** could not be observed. Only 390 mg *N*-phenylitaconimide (**131**) was recovered.

*2.6. A two-step four-component queuing cascade with bicyclopropylidene (**66**)*

*2.6.1. General procedure for the one-pot, two-step queuing cascade involving bicyclopropylidene (**66**) an iodoalkene, a secondary amine **78** and a dienophile under conditions A (GP-A):*

Palladium acetate (22.4 mg, 100 µmol, 5 mol%) and tri-2-furylphosphine (46.4 mg, 200 µmol, 10 mol%), were suspended in anhydrous DMF (1 mL) in a screw-cap pyrex bottle. Argon was bubbled through the mixture for 5 min, and then the respective amine (2.00 mmol or 2.50 mmol), triethylamine (202 mg, 2.00 mmol), iodoalkene (2.00 mmol) and bicyclopropylidene (**66**) (320 mg, 4.00 mmol) were added. After having stirred the mixture for the given time at the stated temperature the bottle was cooled to ambient temperature, the respective dienophile (4.00 mmol) was added, (*N*-phenyltriazolinedione was added to the ice-cooled mixture), and then the mixture was stirred for an additional time as stated at the given temperature in a preheated oil bath. After cooling to room temperature, the reaction mixture was taken up in 20 mL of diethyl ether. The solution was washed with water (2 × 20 mL). The aqueous phase was extracted with diethyl ether (2 × 20 mL). The combined organic phases were dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator, the residue was subjected to chromatography on silica gel.

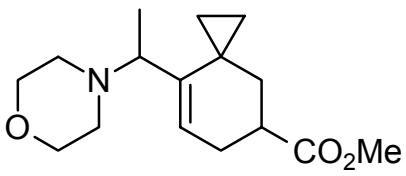
*2.6.2. General procedure for the one-pot, two-step queuing cascade involving bicyclopropylidene (**66**) an iodoalkene, a secondary amine **78** and a dienophile under conditions B (GP-B):*

A screw-cap Pyrex bottle was charged with anhydrous acetonitrile (2 mL), K_2CO_3 (556 mg, 4.00 mmol) and Et_4NCl (332 mg, 2.00 mmol). Argon was bubbled through the mixture for 5 min, $Pd(OAc)_2$ (22.4 mg, 100 µmol, 5 mol%), and tri-2-furylphosphine (46.4 mg, 200 µmol, 10 mol%) were added, and the mixture was stirred once more for an additional 5 min with argon bubbling through, before the respective iodoalkene (2.00 mmol), the nucleophile (2.00 mmol or 2.50 mmol) and bicyclopropylidene (**66**) (320 mg, 4.00 mmol) were added. The bottle was tightly closed, and the mixture was stirred for the given period of time at the stated temperature. After the bottle was cooled to ambient temperature, the respective dienophile (4.00 mmol) was added, (*N*-phenyltriazolinedione was added to the ice-cooled mixture), and then the mixture was stirred for the additional time at the given temperature in a preheated oil bath. After cooling to room temperature, the reaction mixture was taken up in 20 mL of diethyl ether. The solution was washed with water (2 × 20 mL), the aqueous phase was extracted with diethyl ether (2 × 20 mL), and the combined organic phases were dried ($MgSO_4$). After

removal of the solvent in a rotatory evaporator, the residue was subjected to chromatography on silica gel.

*2.6.3. Synthesis of spiro[2.5]octenes (**175aa–ad** and **175bb–eb**)*

Methyl 8-(1-morpholin-4-ylethyl)spiro[2.5]oct-7-ene-5-carboxylate (175aa):



1) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. After cooling the mixture to room temperature methyl acrylate (**68a**, 344 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **175aa** (363 mg, 65%, yellowish oil) as a mixture of two diastereomers (ratio 1.1:1 according to NMR).

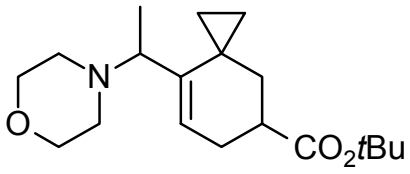
2) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 2 h. After cooling the mixture to room temperature, methyl acrylate (**68a**, 344 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **175aa** (223 mg, 40%, yellowish oil) as a mixture of two diastereomers (ratio 1.3:1 according to NMR).

Major diastereomer: R_f = 0.27 (light petroleum/ethyl acetate, 3:1); IR (film): $\tilde{\nu}$ = 3076, 2973, 2851, 2809, 1738, 1653, 1456, 1329, 1160, 1120, 911, 866 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.32–0.39 (m, 1 H, *c*Pr-H), 0.47–0.54 (m, 1 H, *c*Pr-H), 0.77–0.95 (m, 2 H, *c*Pr-H), 1.02 (d, *J* = 6.23 Hz, 3 H, CH_3), 1.24 (ddd, *J* = 12.75, 2.72, 1.2 Hz, 1 H, 4- or 6-H), 2.03 (ddd, *J* = 12.5, 12.5, 1.7 Hz, 1 H, 4- or 6-H), 2.12 (q, *J* = 6.23 Hz, 1 H, 1'-H), 2.29–2.45 (m, 6 H, CH_2NCH_2, 4- or 6-H), 2.67–2.80 (m, 1 H, 5-H), 3.63–3.69 (m, 4 H, CH_2OCH_2), 3.66 (s, 3 H; OCH_3), 5.77 (dd, *J* = 4.4, 2.9 Hz, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.74 (–, *c*Pr-C), 13.23 (–, *c*Pr-C), 17.78 (+, CH_3), 19.47 (C_{quat}, *c*Pr-C), 28.34 (–, C-4 or -6), 38.56 (–, C-4 or -6

), 39.29 (+, C-5), 50.74 (–, CH_2NCH_2), 51.56 (+, OCH_3), 59.17 (+, C-1'), 67.20 (–, CH_2OCH_2), 124.8 (+, C-7), 140.73 (C_{quat}, C-8), 176.09 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 279 (29) [M^+], 264 (100) [$M^+ - CH_3$], 250 (11) [$M^+ - C_2H_5$], 133 (21), 114 (86), 91 (24), 86 (12); $C_{16}H_{25}NO_3$ (279.38): calcd. 279.1834 (correct HRMS); elemental analysis calcd (%) for $C_{16}H_{25}NO_3$: C 68.79, H 9.02; found: C 68.63, H 9.10.

Minor diastereomer: R_f = 0.23 (light petroleum/ethyl acetate, 3:1); IR (film): $\tilde{\nu}$ = 3079, 2952, 2851, 2805, 1740, 1650, 1457, 1257, 1194, 1172, 945, 861 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.35–0.51 (m, 2 H, *c*Pr-H), 0.59–0.66 (m, 1 H, *c*Pr-H), 1.03 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.02–1.14 (m, 1 H, *c*Pr-H), 1.48 (dd, *J* = 12.8, 3.1, Hz, 1 H, 4- or 6-H), 1.90 (dd, *J* = 10.2, 13 Hz, 1 H, 4- or 6-H), 2.20 (q, *J* = 6.8 Hz, 1 H, 1'-H), 2.32–2.48 (m, 6H, CH_2NCH_2, 4- or 6-H), 2.69–2.80 (m, 1 H, 5-H), 3.63–3.71 (m, 4 H, CH_2OCH_2), 3.66 (s, 3 H, OCH_3), 5.71 (t, *J* = 3.8 Hz, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 11.75 (–, *c*Pr-C), 12.39 (–, *c*Pr-C), 16.99 (+, CH_3), 18.51 (C_{quat}, *c*Pr-C), 27.80 (–, C-4 or -6), 38.16 (–, C-4 or -6), 38.72 (+, C-5), 50.38 (–, CH_2NCH_2), 51.42 (+, OCH_3), 58.51 (+, C-1'), 67.24 (–, CH_2OCH_2), 121.4 (+, C-7), 143.67 (C_{quat}, C-8), 175.84 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 279 (26) [M^+], 264 (100) [$M^+ - CH_3$], 250 (16) [$M^+ - C_2H_5$], 133 (19), 114 (94), 91 (22), 86 (16); $C_{16}H_{25}NO_3$ (279.38): calcd. 279.1834 (correct HRMS).

***tert*-Butyl 8-(1-morpholin-4-ylethyl)spiro[2.5]oct-7-ene-5-carboxylate (175ab):**



1) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 2 h. After cooling the mixture to room temperature, *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **175ab** (426 mg, 66%, yellowish oil) as a mixture of two diastereomers (ratio 1.3:1 according to NMR).

2) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. After cooling the mixture to

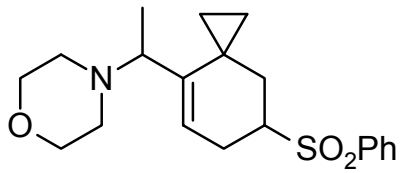
room temperature *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **175ab** (413 mg, 64%, yellowish oil) as a mixture of two diastereomers (ratio 1.3:1 according to NMR).

Major diastereomer: R_f = 0.34 (light petroleum/ethyl acetate, 3:1); IR (film): $\tilde{\nu}$ = 3077, 2977, 2851, 2809, 2689, 1731, 1455, 1367, 1339,1253, 1150, 1119, 942, 855 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.32–0.39 (m, 1 H, *c*Pr-H), 0.47–0.54 (m, 1 H, *c*Pr-H), 0.77–0.92 (m, 2 H, *c*Pr-H), 1.02 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.19 (ddd, *J* = 12.4, 2.7, 1.2 Hz, 1 H, 4- or 6- H), 1.43 [s, 9 H, $C(CH_3)_3$], 1.98 (t, *J* = 12.7 Hz, 1 H, 4- or 6-H), 2.09 (q, *J* = 6.4 Hz, 1 H, 1'-H), 2.27–2.42 (m, 6 H, CH_2NCH_2, 4- or 6-H), 2.53–2.68 (m, 1 H, 5-H), 3.65 (t, *J* = 4.4 Hz, 4 H, CH_2OCH_2), 5.76 (t, *J* = 3.6 Hz, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.75 (–, *c*Pr-C), 13.16 (–, *c*Pr-C), 17.87 (+, CH_3), 19.45 (C_{quat}, *c*Pr-C), 28.00 [+, $C(CH_3)_3$], 28.53 (–, C-4 or -6), 38.51 (–, C-4 or -6), 40.32 (+, C-5), 50.75 (–, CH_2NCH_2), 59.11 (+, C-1'), 67.15 (–, CH_2OCH_2), 79.78 [C_{quat}, $C(CH_3)_3$], 120.7 (+, C-7), 140.64 (C_{quat}, C-8), 174.98 (C_{quat}, C=O); MS (70 eV, EI) *m/z* (%): 321 (46) [M^+], 306 (68) [$M^+ - CH_3$], 250 (60) [$M^+ - C_2H_5$], 133 (30), 114 (100), 100 (22), 86 (20); elemental analysis calcd (%) for $C_{19}H_{31}NO_3$ (321.5): C 70.99, H 9.72; found: C 70.78, H 9.52.

Minor diastereomer: R_f = 0.29 (light petroleum/ethyl acetate, 3:1); IR (film): $\tilde{\nu}$ = 3079, 2977, 2851, 2804, 2689, 1730, 1454, 1367, 1329, 1256, 1150, 1119, 945, 863 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.35–0.42 (m, 1 H, *c*Pr-H), 0.46–0.54 (m, 1 H, *c*Pr-H), 0.57–0.64 (m, 1 H, *c*Pr-H), 1.03 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.08–1.17 (m, 1 H, *c*Pr-H), 1.43 [s, 10 H, $C(CH_3)_3$, 4- or 6-H*], 1.87 (t, *J* = 12.9 Hz, 1 H, 4- or 6-H), 2.20 (q, *J* = 6.5 Hz, 1 H 1'-H), 2.31 –2.42 (m, 6 H, CH_2NCH_2, 4- or 6-H), 2.57–2.68 (m, 1 H, 5-H), 3.64 (t, *J* = 4.6 Hz, 4 H, CH_2OCH_2), 5.71 (t, *J* = 3.6 Hz, 1 H, 7-H). *The peak of this proton sits under the broad singlet of the *tert*-butyl group, thus the spin coupling constant of this proton could not be determined. This proton correlates clearly with the carbon peak at 38.14 ppm in the HMQC spectrum.^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.13 (–, *c*Pr-C), 12.43 (–, *c*Pr-C), 17.15 (+, CH_3), 18.63 (C_{quat}, *c*Pr-C), 28.01 [+, $C(CH_3)_3$], 28.01 (–, C-4 or -6), 38.14 (–, C-4 or -6), 39.85 (+, C-5), 50.47 (–, CH_2NCH_2), 58.58 (+, C-1'), 67.17 (–, CH_2OCH_2), 79.88 [C_{quat}, $C(CH_3)_3$], 120.68 (+, C-7), 140.58 (C_{quat}, C-8), 174.81 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 321 (49) [M^+], 306 (94) [$M^+ - CH_3$], 250 (80) [$M^+ - C_2H_5$], 133 (30), 114 (100), 100 (26), 86 (22); elemental analysis calcd

(%) for $C_{19}H_{31}NO_3$: C 70.99, H 9.72; found: C 70.72, H 9.98. $C_{19}H_{31}NO_3$ (321.46): calcd. 321.2304 (correct HRMS).

4-[1-(7-Benzenesulfonylspiro[2.5]oct-4-en-4-yl)-ethyl]-morpholine (175ac):



1) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. After cooling the mixture to room temperature phenyl vinyl sulfone (**68c**, 672 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 1:1) to yield **175ac** (450 mg, 62%, yellowish oil) as a mixture of two diastereomers (ratio 1.2:1 according to NMR).

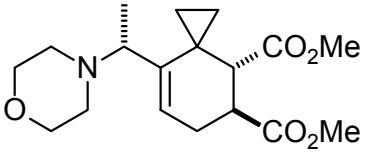
2) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 2 h. After cooling the mixture to room temperature, phenyl vinyl sulfone (**68c**, 672 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100g, 3 × 30 cm, light petroleum/ethyl acetate 1:1) to yield **175ac** (334 mg, 46%, yellowish oil) as a mixture of two diastereomers (ratio 1.1:1 according to NMR).

Major diastereomer: R_f = 0.45 (light petroleum/ethyl acetate, 1:1); IR (KBr): $\tilde{\nu}$ = 3064, 2972, 2955, 2856, 2814, 1448, 1311 (S=O), 1275 (S=O), 1152 (S=O), 1116 (S=O), 1023, 938, 861, 726 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.30–0.39 (m, 1 H, *c*Pr-H), 0.52–0.62 (m, 1 H, *c*Pr-H), 0.74–0.84 (m, 1 H, *c*Pr-H), 0.92–1.00 (m, 1 H, *c*Pr-H), 0.99 (d, *J* = 6.3 Hz, 3 H, CH_3), 1.38 (ddd, *J* = 12.4, 2.7, 1.2 Hz, 1 H, 6- or 8-H), 2.04–2.17 (m, 2 H, 1'-H, 6- or 8-H), 2.29–2.41 (m, 6 H, CH_2NCH_2, 6- or 8-H), 3.28–3.45 (m, 1 H, 7-H), 3.65 (t, *J* = 4.56 Hz, 4 H, CH_2OCH_2), 5.72 (t, *J* = 3.8 Hz, 1 H, 5-H), 7.52–7.70 (m, 3 H, Ph), 7.86–7.90 (m, 2 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.74 (–, *c*Pr-C), 13.37 (–, *c*Pr-C), 17.34 (+, CH_3), 19.49 (C_{quat}, *c*Pr-C), 25.57 (–, C-6 or -8), 34.67 (–, C-6 or -8), 50.46 (–, CH_2NCH_2), 59.00 (+, C-1'), 59.77 (+,

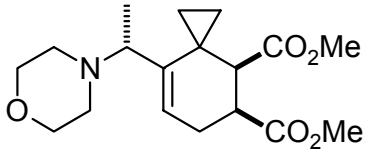
C-7), 66.99 (–, CH_2OCH_2), 118.60 (+, C-5), 128.71 (+, Ph-C), 128.99 (+, Ph-C), 133.56 (+, Ph-C), 137.02 (C_{quat}), 141.18 (C_{quat}); MS (70 eV, EI), *m/z* (%): 361 (11) [M^+], 346 (38) [M^+ – CH_3], 204 (35), 117 (28), 114 (100), 91 (33); elemental analysis calcd (%) for $C_{20}H_{27}NO_3S$ (361.5): C 66.45, H 7.53; found: C 66.24, H 7.61.

Minor diastereomer: R_f = 0.38 (light petroleum/ethyl acetate, 1:1); IR (film): $\tilde{\nu}$ = 3057, 2967, 2858, 2812, 1447, 1306 (S=O), 1273 (S=O), 1147 (S=O), 1114 (S=O), 944, 751, 725 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.24–0.38 (m, 1 H, *c*Pr-H), 0.45–0.55 (m, 2 H, *c*Pr-H), 0.92 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.17–1.23 (m, 1H, *c*Pr-H), 1.33 (ddd, *J* = 12.7, 2.7, 1.4 Hz, 1 H, 6- or 8-H), 2.04 (t, *J* = 12.1 Hz, 1 H, 6- or 8-H), 2.16–2.45 (m, 7 H, CH_2NCH_2, 1'-H, 6- or 8-H), 3.20–3.36 (m, 1 H, 7-H), 3.54 (t, *J* = 4.6 Hz, 4 H, CH_2OCH_2), 5.72 (dd, *J* = 5.5, 4.9 Hz, 1 H, 5-H), 7.44–7.63 (m, 3 H, Ph), 7.77–7.82 (m, 2 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 11.83 (–, *c*Pr-C), 13.85 (–, *c*Pr-C), 16.31 (+, CH_3), 19.06 (C_{quat}, *c*Pr-C), 25.65 (–, C-6 or -8), 34.36 (–, C-8 or -6), 50.19 (–, CH_2NCH_2), 58.56 (+, C-1'), 59.67 (+, C-7), 67.25 (–, CH_2OCH_2), 120.09 (+, C-5), 128.82 (+, Ph-C), 129.13 (+, Ph-C), 133.68 (+, Ph-C), 137.23 (C_{quat}), 141.61 (C_{quat}); MS (70 eV, EI), *m/z* (%): 361 (13) [M^+], 346 (47) [M^+ – CH_3], 204 (42), 117 (37), 114 (100), 91 (33) 77 (61); elemental analysis calcd. (%) for $C_{20}H_{27}NO_3S$ (361.5): C 66.45, H 7.53; found: C 66.21, H 7.62.

4,5-dimethyl 8-(1-morpholin-4-ylethyl)spiro[2.5]oct-7-ene-carboxylate (*cis-/trans*-175ad):



trans-**175a**



cis-**175a**

1) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL), at 80 °C for 2 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying over $MgSO_4$, the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 1:1) to yield *cis-/trans*-**175ad** (391.7 mg, 58%, yellowish oil) as a mixture of two diastereomers (ratio 1.2:1 according to NMR).

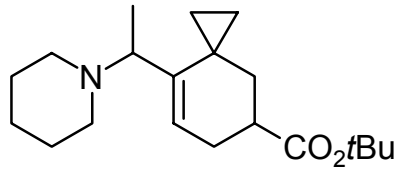
2) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 2 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100g, 3 × 30 cm, light petroleum/ethyl acetate 1:1) to yield **175ad** (263 mg, 39%, yellowish oil) as a mixture of two diastereomers (ratio 1.3:1 according to NMR).

3) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL), at 80 °C for 2 h. After cooling the mixture to room temperature, dimethyl maleate (**68e**, 576 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying over $MgSO_4$, the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 1:1) to yield *cis-/trans*-**175ad** (351 mg, 52%, yellowish oil) as a mixture of two diastereomers (ratio 1.7:1 according to NMR).

Major and minor diastereomers*: R_f = 0.27 (light petroleum/ethyl acetate, 3:1); IR (film): $\tilde{\nu}$ = 3083, 2953, 2850, 2809, 2691, 1739, 1466, 1349, 1265, 1197, 1172, 1119, 1021, 945, 918, 864 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.43–0.50 (m, 1 H, *c*Pr-H), 0.59–0.68 (m, 3 H, *c*Pr-H), 0.70–0.81 (m, 2 H, *c*Pr-H), 0.93–0.99 (m, 2 H, *c*Pr-H), 1.04 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.04 (d, *J* = 6.5 Hz, 3 H, CH_3), 2.08 (q, *J* = 6.7 Hz, 1 H, 1'-H), 2.19–2.52 (m, 13 H, 2 × (CH_2NCH_2), 2 × 6-H, 1'-H), 2.58 (d, *J* = 4.3 Hz, 1 H, 4-H), 2.82 (d, *J* = 7.3 Hz, 1 H, 4-H), 3.12 (q, *J* = 7.0 Hz, 1 H, 5-H), 3.21–3.26 (m, 1 H, 5-H), 3.62–3.68 (m, 8 H, 2 × CH_2OCH_2), 3.65 (s, 3 H, OCH_3), 3.67 (s, 9 H, 3 × OCH_3), 5.75 (q, *J* = 3.5 Hz, 2 H, 2 × 7-H); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = 9.77 (–, *c*Pr-C), 9.86 (–, *c*Pr-C), 10.65 (–, *c*Pr-C), 11.61 (–, *c*Pr-C), 16.95 (+, CH_3), 17.22 (+, CH_3), 18.61 (C_{quat}, *c*Pr-C), 19.29 (C_{quat}, *c*Pr-C), 24.51 (–, C-6), 26.51 (–, C-6), 40.56 (+, C-5), 41.33 (+, C-5), 49.77 (+, C-4), 50.52 (–, CH_2NCH_2), 50.66 (–, CH_2NCH_2), 50.77 (+, C-4), 51.59 (+, 4 × OCH_3), 58.93 (+, C-1'), 59.56 (+, C-1'), 67.22 (–, 2 × CH_2OCH_2), 120.04 (+, C-7), 121.09 (+, C-7), 138.76 (C_{quat}, C-8), 139.65 (C_{quat}, C-8), 173.11 (C_{quat}, C=O), 173.24 (C_{quat}, C=O), 174.04 (C_{quat}, C=O), 174.72 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 337 (10) [M^+], 322 (47) [M^+ – CH_3], 262 (5), 191 (11), 131 (24), 114 (100), 91 (24) 59 (26);

elemental analysis calcd (%) for $C_{18}H_{27}NO_5$ (337.4): C 64.07, H 8.07; found: C 64.26, H 7.86. *Proton and carbon chemical shifts were given for both diastereomers together because ^{1}H NMR and ^{13}C NMR spectra were not proper to classify all of the peaks for major and minor diastereomers. IR, EI mass and elemental analysis were carried out for the mixture of diastereomers.

***tert*-Butyl 8-(1-piperidin-4-ylethyl)spiro[2.5]oct-7-ene-5-carboxylate (175bb):**



1) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), piperidine (**78b**, 170.3 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**1**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 2 h. After cooling the mixture to room temperature *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 1:1) to yield **175bb** (209 mg, 33%, yellowish oil) as a mixture of two diastereomers (ratio 1:1 according to NMR).

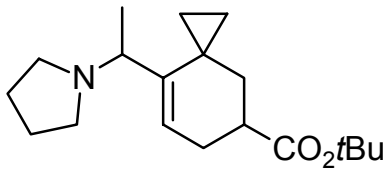
2) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), piperidine (**78b**, 170.3 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. After cooling the mixture to room temperature *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 1:1) to yield **175bb** (171 mg, 27%, yellowish oil) as a mixture of two diastereomers (ratio 1.1:1 according to NMR).

Diastereomer I: R_f = 0.28 (light petroleum/ethyl acetate, 1:1); IR (film): $\tilde{\nu}$ = 3075, 2975, 2932, 2852, 2793, 2747, 1729, 1456, 1391, 1367, 1320, 1255, 1153, 1060, 932, 851 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.29–0.34 (m, 1 H, *c*Pr-H), 0.45–0.49 (m, 1 H, *c*Pr-H), 0.82–0.91 (m, 2 H, *c*Pr-H), 0.99 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.13–1.19 (m, 1 H, 4- or 6-H), 1.36–1.51 (m, 6 H, piperidine), 1.43 [s, 9 H, $C(CH_3)_3$], 1.98 (t, *J* = 11.9 Hz, 1 H, 4- or 6-H), 2.19–2.45 (m, 7 H, 4- or 6-H, piperidine, 1'-H), 2.58 – 2.71 (m, 1 H, 5-H), 5.68 – 5.71 (m, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.77 (–, *c*Pr-C), 13.70 (–, *c*Pr-C), 16.41 (+, CH_3), 19.91 (C_{quat},

*c*Pr-C), 24.75 (–, piperidine), 26.19 (–, piperidine), 28.02 [+, $C(CH_3)_3$], 28.64 (–, C-4 or -6), 38.79 (–, C-4 or -6), 40.41 (+, C-5), 50.91 (–, piperidine), 59.49 (+, C-1'), 79.71 [C_{quat}, $C(CH_3)_3$], 120.29 (+, C-7), 141.16 (C_{quat}, C-8), 175.21 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 319 (18) [M^+], 304 (58) [$M^+ - CH_3$], 248 (60), 234 (12), 112 (100), 84 (26); elemental analysis calcd (%) for $C_{20}H_{33}NO_2$ (319.5): C 75.19, H 10.41; found: C 74.97, H 10.66.

Diastereomer II: R_f = 0.18 (light petroleum/ethyl acetate 1:1); IR (film): $\tilde{\nu}$ = 3078, 2975, 2932, 2852, 2790, 2748, 1729, 1456, 1391, 1367, 1332, 1257, 1153, 1117, 933, 850 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.27–0.34 (m, 1 H, *c*Pr-H), 0.40–0.48 (m, 1 H, *c*Pr-H), 0.51–0.58 (m, 1 H, *c*Pr-H), 0.98 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.09–1.19 (m, 1 H, *c*Pr-H), 1.29–1.51 (m, 7 H, 4- or 6-H, piperidine), 1.37 [s, 9 H, $C(CH_3)_3$], 1.79–1.89 (m, 1 H, 4- or 6-H), 2.18–2.40 (m, 7 H, 4- or 6-H, piperidine, 1'-H), 2.51–2.63 (m, 1 H, 5-H), 5.68 (d, *J* = 3.9 Hz, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.24 (–, *c*Pr-C), 12.60 (–, *c*Pr-C), 16.36 (C_{quat}, *c*Pr-C), 18.76 (+, CH_3), 24.62 (–, piperidine), 26.12 (–, piperidine), 27.94 [+, $C(CH_3)_3$], 28.09 (–, C-4 or -6), 38.25 (–, C-4 or -6), 39.92 (+, C-5), 50.75 (–, piperidine), 58.76 (+, C-1'), 79.68 [C_{quat}, $C(CH_3)_3$], 121.45 (+, C-7), 141.00 (C_{quat}, C-8), 174.87 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 319 (18) [M^+], 304 (58) [$M^+ - CH_3$], 248 (60), 234 (12), 112 (100), 84 (26); elemental analysis calcd (%) for $C_{20}H_{33}NO_2$ (319.5): C 75.19, H 10.41; found: C 74.97, H 10.66.

***tert*-Butyl 8-(1-pyrrolidin-4-ylethyl)spiro[2.5]oct-7-ene-5-carboxylate (175cb):**



1) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), pyrrolidine (**78c**, 142 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 2 h. After cooling the mixture to room temperature *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate/methanol 3:1:1) to yield **175cb** (176 mg, 29%, yellowish oil) as a mixture of two diastereomers (ratio 1:1 according to NMR).

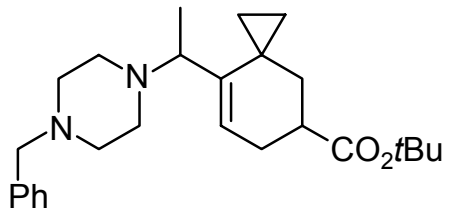
2) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), pyrrolidine (**78c**, 142 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. After cooling the mixture to

room temperature *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate/methanol 3:1:1) to yield **175cb** (127 mg, 21%, yellowish oil) as a mixture of two diastereomers (ratio 1:1 according to NMR).

Diastereomer I: R_f = 0.33 (light petroleum/ethyl acetate/methanol, 3:1:1); IR (film): $\tilde{\nu}$ = 3075, 2971, 2932, 2875, 2776, 2712, 1728, 1478, 1457, 1256, 1152, 985, 850 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 0.34–0.38 (m, 1 H, *c*Pr-H), 0.46–0.49 (m, 1 H, *c*Pr-H), 0.62–0.66 (m, 1 H, *c*Pr-H), 0.80–0.84 (m, 1 H, *c*Pr-H), 1.07 (d, *J* = 6.2 Hz, 3 H, CH_3), 1.14–1.17 (m, 1 H, 4- or 6-H), 1.39 [s, 9 H, $C(CH_3)_3$], 1.66–1.71 (m, 4 H, pyrrolidine), 1.81 (q, *J* = 6.11 Hz, 1 H, 1'-H), 1.96 (td, *J* = 1.8, 12.5 Hz, 1 H, 4- or 6-H), 2.21 (ddd, *J* = 17.5, 11.5, 2.5 Hz, 1 H, 4- or 6-H), 2.33–2.38 (m, 3 H, 4- or 6-H, pyrrolidine), 2.42–2.44 (m, 2 H, pyrrolidine), 2.55–2.60 (m, 1 H, 5-H), 5.79 (dd, *J* = 2.4, 4.9 Hz, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.59 (–, *c*Pr-C), 13.17 (–, *c*Pr-C), 18.66 (C_{quat}, *c*Pr-C), 22.72 (+, CH_3), 23.35 (–, pyrrolidine), 28.04 [+, $C(CH_3)_3$], 28.55 (–, C-4 or -6), 38.30 (–, C-4 or -6), 40.43 (+, C-5), 52.66 (–, pyrrolidine), 59.31 (+, C-1'), 79.78 [C_{quat}, $C(CH_3)_3$], 119.74 (+, C-7), 142.42 (C_{quat}, C-8), 175.16 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 305 (20) [M^+], 290 (56) [$M^+ - CH_3$], 234 (44), 220 (10), 98 (100), 70 (22); elemental analysis calcd (%) for $C_{19}H_{31}NO_2$ (305.5): C 74.71, H 10.23; found: C 74.41, H 10.01.

Diastereomer II: R_f = 0.25 (light petroleum/ethyl acetate/methanol, 3:1:1); IR (film): $\tilde{\nu}$ = 3078, 2971, 2875, 2776, 2710, 1728, 1478, 1457, 1391, 1367, 1256, 1054, 947, 850 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.36–0.42 (m, 1 H, *c*Pr-H), 0.44–0.51 (m, 1 H, *c*Pr-H), 0.55–0.61 (m, 1 H, *c*Pr-H), 0.96–1.03 (m, 1 H, *c*Pr-H), 1.07 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.40–1.47 (m, 1 H, 4- or 6-H), 1.41 [s, 9 H, $C(CH_3)_3$], 1.67–1.71 (m, 4 H, pyrrolidine), 1.82–1.89 (m, 1' H, 4- or 6-H), 1.98 (q, *J* = 6.4 Hz, 1 H, 1'-H), 2.27–2.34 (m, 2 H, 4- or 6-H), 2.43–2.54 (m, 4 H, pyrrolidine), 2.54–2.63 (m, 1 H, 5-H), 5.79 (t, *J* = 4.0 Hz, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.11 (–, *c*Pr-C), 12.27 (–, *c*Pr-C), 18.42 (C_{quat}, *c*Pr-C), 22.64 (+, CH_3), 23.33 (–, pyrrolidine), 28.03 [+, $C(CH_3)_3$], 38.07 (–, C-4 or -6), 39.88 (+, C-5), 52.67 (–, pyrrolidine), 58.19 (+, C-1'), 79.80 [C_{quat}, $C(CH_3)_3$], 120.97 (+, C-7), 142.54 (C_{quat}, C-8), 174.86 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 305 (4) [M^+], 290 (24) [$M^+ - CH_3$], 234 (28), 220 (12), 98 (100), 70 (35), 57 (30), 41 (18); elemental analysis calcd (%) for $C_{19}H_{31}NO_2$ (305.5): C 74.71, H 10.23; found: C 74.41, H 10.01.

***tert*-Butyl 8-[1-(4-benzylpiperazin-1-yl)ethyl]spiro[2.5]oct-7-ene-5-carboxylate (175db):**



1) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), *N*-benzylpiperazine (**78d**, 352.5 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. After cooling the mixture to room temperature *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **175db** (395 mg, 48%, yellowish oil) as a mixture of two diastereomers (ratio 1.1:1 according to NMR).

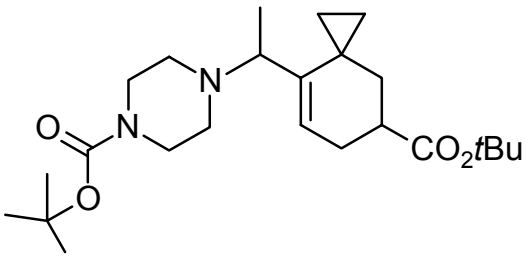
2) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), *N*-benzylpiperazine (**78d**, 352.5 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 2 h. After cooling the mixture to room temperature *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **175db** (362 mg, 44%, yellowish oil) as a mixture of two diastereomers (ratio 1.4:1 according to NMR).

Major diastereomer: R_f = 0.39 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 3063, 2975, 2932, 2808, 2689, 1727, 1495, 1391, 1367, 1330, 1258, 1153, 1013, 910, 849, 823, 734 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.33–0.40 (m, 1 H, *c*Pr-H), 0.45–0.52 (m, 1 H, *c*Pr-H), 0.56–0.64 (m, 1 H, *c*Pr-H), 1.03 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.11–1.18 (m, 1 H, *c*Pr-H), 1.36–1.43 (m, 1 H, 4- or 6-H), 1.43 [s, 9 H, $C(CH_3)_3$], 1.88 (t, *J* = 11.6 Hz, 1 H, 4- or 6-H), 2.09 (q, *J* = 6.2 Hz, 1 H, 1'-H), 2.31–2.42 (m, 10 H, piperazine, 4- or 6-H), 2.56–2.67 (m, 1 H, 5-H), 3.48 (s, 2 H, Bn), 5.68 (t, *J* = 3.8 Hz, 1 H, 7-H), 7.21–7.30 (m, 5 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.11 (–, *c*Pr-C), 12.61 (–, *c*Pr-C), 17.37 (+, CH_3), 18.73 (C_{quat}, *c*Pr-C), 28.03 [+, $C(CH_3)_3$], 28.12 (–, C-4 or -6), 38.30 (–, C-4 or -6), 39.99 (+, C-5), 49.81 (–, piperazine), 53.51 (–, piperazine), 58.23 (+, C-1'), 63.10 (–, Bn), 79.77 [C_{quat}, $C(CH_3)_3$], 121.5 (+, C-7), 126.87 (+, Ph-C), 128.08 (+, Ph-C), 129.21 (+, Ph-C), 138.21 (C_{quat}), 141.16 (C_{quat}), 174.88 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 410 (26) [M^+], 395 (6) [$M^+ - CH_3$], 203 (10),

175 (100), 91 (42); elemental analysis calcd (%) for $C_{26}H_{38}N_2O_2$ (410.6): C 76.06, H 9.33; found: C 75.81, H 9.14.

Minor diastereomer: R_f = 0.55 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 3063, 3026 2974, 2931, 2807, 1727, 1495, 1455, 1391, 1367, 1318, 1256, 1150, 1013, 906, 849, 825, 736 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.29–0.35 (m, 1 H, *c*Pr-H), 0.47–0.52 (m, 1 H, *c*Pr-H), 0.80–0.89 (m, 2 H, *c*Pr-H), 1.02 (d, *J* = 6.4 Hz, 3 H, CH_3), 1.15–1.21 (m, 1 H, 4- or 6-H), 1.43 [s, 9 H, $C(CH_3)_3$], 1.98 (t, *J* = 12.30 Hz, 1 H, 4- or 6-H), 2.17 (q, *J* = 6.42 Hz, 1 H, 1'-H), 2.24–2.56 (m, 10 H, piperazine, 4- or 6-H), 2.56–2.68 (m, 1 H, 5-H), 3.48 (s, 2 H, Bn), 5.73 (t, *J* = 3.8 Hz, 1 H, 7-H); 7.21–7.30 (m, 5 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.79 (–, *c*Pr-C), 13.38 (–, *c*Pr-C), 17.71 (+, CH_3), 19.62 (C_{quat}, *c*Pr-C), 28.05 [+, $C(CH_3)_3$], 28.59 (–, C-4 or -6), 38.68 (–, C-4 or -6), 40.41 (+, C-5), 49.99 (–, piperazine), 53.43 (–, piperazine), 58.88 (+, C-1'), 63.09 (–, Bn), 79.76 [C_{quat}, $C(CH_3)_3$], 120.48 (+, C-7), 126.88 (+, Ph-C), 128.09 (+, Ph-C), 129.18 (+, Ph-C), 138.22 (C_{quat}), 141.04 (C_{quat}), 175.09 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 410 (36) [M^+], 395 (8) [$M^+ - CH_3$], 337 (19), 203 (14), 175 (100), 91 (35); elemental analysis calcd (%) for $C_{26}H_{38}N_2O_2$ (410.6): C 76.06, H 9.33; found: C 75.81, H 9.14.

***tert*-Butyl 4-[1-(7-*tert*-butoxycarbonylspiro[2.5]oct-4-en-4-yl)ethyl]piperazinecarboxylate (175eb):**



1) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), *N*-Boc-piperazine (**78e**, 372 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL), at 80 °C for 2 h. After cooling the mixture to room temperature, *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **175eb** (410.7 mg, 49%, yellowish oil) as a mixture of two diastereomers (ratio 1:1 according to NMR).

2) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), *N*-Boc-piperazine (**78e**, 372 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in

anhydrous DMF (1 mL), at 80 °C for 2 h. After cooling the mixture to room temperature *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **175eb** (327 mg, 39%, yellowish oil) as a mixture of two diastereomers (ratio 1.4:1 according to NMR).

Diastereomer I: R_f = 0.54 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 3076, 2976, 2931, 2814, 1727, 1698, 1455, 1422, 1366, 1291, 1248, 1170, 1003, 923, 733 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.31–0.38 (m, 1 H, *c*Pr-H), 0.47–0.54 (m, 1 H, *c*Pr-H), 0.77–0.92 (m, 2 H, *c*Pr-H), 1.02 (d, *J* = 6.4 Hz, 3 H, CH_3), 1.16–1.21 (m, 1 H, 4- or 6-H), 1.43 [s, 9 H, $C(CH_3)_3$], 1.44 [s, 9 H, $C(CH_3)_3$], 1.98 (t, *J* = 12.3 Hz, 1 H, 4- or 6-H), 2.18 (q, *J* = 6.3 Hz, 1 H, 1'-H), 2.25–2.38 (m, 6 H; piperazine, 4- or 6-H), 2.57–2.69 (m, 1 H, 5-H), 3.35 (t, *J* = 4.8 Hz, 4 H, piperazine), 5.75 (dd, *J* = 2.7, 4.6 Hz, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.65 (–, *c*Pr-C), 13.19 (–, *c*Pr-C), 17.22 (+, CH_3), 19.46 (C_{quat}, *c*Pr-C), 27.85 [+, $C(CH_3)_3$], 28.21 [+, $C(CH_3)_3$], 28.39 (–, C-4 or -6), 38.41 (–, C-4 or -6), 40.13 (+, C-5), 43.19 (–, piperazine)*, 49.59 (–, piperazine), 58.60 (+, C-1'), 79.08 [C_{quat}, $C(CH_3)_3$], 79.58 [C_{quat}, $C(CH_3)_3$], 120.63 (+, C-7), 140.59 (C_{quat}), 154.51 (C_{quat}, C=O). 174.79 (C_{quat}, C=O); *It appears as a multiplet of low intensity. This carbon correlates clearly with the triplet at 3.35 ppm in the HMQC spectrum. MS (70 eV, EI), *m/z* (%): 420 (3) [M^+], 397 (8), 284 (17), 213 (52), 157 (100), 57 (48), 41 (14); elemental analysis calcd (%) for $C_{24}H_{40}N_2O_4$ (420.6): C 68.54, H 9.59; found: C 68.30, H 9.42.

Diastereomer II: R_f = 0.48 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 3078, 2975, 2931, 2811, 2756, 1727, 1699, 1455, 1422, 1366, 1291, 1248, 1167, 1003, 923, 733 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.34–0.42 (m, 1 H, *c*Pr-H), 0.46–0.54 (m, 1 H, *c*Pr-H), 0.56–0.64 (m, 1 H, *c*Pr-H), 1.02 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.08–1.21 (m, 1 H, *c*Pr-H), 1.38–1.44 (m, 1 H, 4- or 6-H), 1.43 [s, 9 H, $C(CH_3)_3$], 1.44 [s, 9 H, $C(CH_3)_3$], 1.88 (dd, *J* = 10.7, 12.8 Hz, 1 H, 4- or 6-H), 2.22–2.43 (m, 7 H, piperazine, 4- or 6-H, 1'-H), 2.57–2.69 (m, 1 H, 5-H), 3.35 (t, *J* = 4.9 Hz, 4 H, piperazine), 5.68 (t, *J* = 3.8 Hz, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.10 (–, *c*Pr-C), 12.39 (–, *c*Pr-C), 16.43 (+, CH_3), 18.51 (C_{quat}, *c*Pr-C), 27.89 [+, $C(CH_3)_3$], 27.89 (–, C-4 or -6), 28.27 [+, $C(CH_3)_3$], 38.09 (–, C-4 or -6), 39.75 (+, C-5), 43.58 (–, piperazine)*, 49.32 (–, piperazine), 59.74 (+, C-1'), 79.14 [C_{quat}, $C(CH_3)_3$], 79.69 [C_{quat}, $C(CH_3)_3$], 121.65 (+, C-7), 140.58 (C_{quat}), 154.61 (C_{quat}, C=O), 174.64 (C_{quat}, C=O). *It appears as a multiplet of low intensity. This carbon correlates clearly with the triplet at 3.35 ppm in the

HMQC spectrum. MS (70 eV, EI), *m/z* (%): 420 (13) [M^+], 405 (18) [$M^+ - CH_3$], 293 (22), 279 (10), 213 (18), 157 (32), 133 (50), 57 (100), 41 (34); elemental analysis calcd (%) for $C_{24}H_{40}N_2O_4$ (420.6): C 68.54, H 9.59; found: C 68.30, H 9.42.

*2.6.4. Attempts for the synthesis of spiro[2.5]octenes **175af–ag***

8-(1-morpholin-4-ylethyl)spiro[2.5]oct-7-ene-4,5-dicarbonitrile (175af):

1) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. After cooling the mixture to room temperature *trans*-2-butenedinitrile (**68f**, 312 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1). Separated fractions could not be identified and desired product **175af** could not be observed.

2) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 2 h. After cooling the mixture to room temperature, *trans*-2-butenedinitrile (**68f**, 312 mg, 4.00 mmol) added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100g, 3 × 30 cm, light petroleum/ethyl acetate 3:1). Separated fractions could not be identified and desired product **175af** could not be observed.

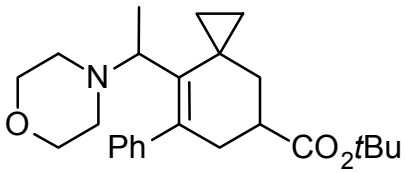
4-[1-(7,8-Bis-benzenesulfonylspiro[2.5]oct-4-en-4-yl)-ethyl]-morpholine (175ag):

1) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. After cooling the mixture to room temperature *trans*-1,2-Bis-(phenylsulfonyl)ethylene (**68g**, 1.23 g, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed. The residue was subjected to column chromatography on

silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1). Separated fractions could not be identified and desired product **175ag** could not be observed.

*2.6.5. Synthesis of spiro[2.5]octenes (**176ab–179ab**)*

***tert*-Butyl 8-(1-morpholin-4-ylethyl)-7-phenylspiro[2.5]oct-7-ene-5-carboxylate (176ab):**



1) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 μmol), tri-2-furylphosphine (46.4 mg, 200 μmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 261 mg, 3.00 mmol), (1-iodovinyl)benzene (**191**, 460 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 100 °C for 65 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 10:1) to yield **176ab** (286 mg, 36%, yellowish oil) as a mixture of two diastereomers (ratio 1.1:1 according to NMR).

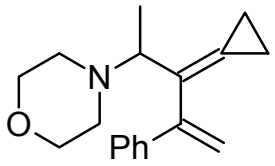
Major diastereomer: R_f = 0.48 (light petroleum/ethyl acetate, 10:1); IR (film): $\tilde{\nu}$ = 3003, 2980, 2951, 2853, 2803, 1723, 1450, 1263, 1149, 1113, 943, 849, 705 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.29–0.36 (m, 1 H, *c*Pr-H), 0.59–0.66 (m, 1 H, *c*Pr-H), 0.83–0.95 (m, 1 H, *c*Pr-H), 1.05–1.13 (m, 1 H, 4- or 6-H), 1.11 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.41 (s, 9 H, $C(CH_3)_3$), 1.63–1.70 (m, 1 H, *c*Pr-H), 2.02–2.37 (m, 5 H, CH_2NCH_2, 4- or 6-H), 2.37–2.59 (m, 2 H, 4- or 6-H), 2.75–2.93 (m, 2 H, 5-H, 1-H), 3.57 (t, *J* = 4.1 Hz, 4 H, CH_2OCH_2), 7.05 (d, *J* = 9.1 Hz, 2 H, Ph), 7.19–7.34 (m, 3 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.78 (–, *c*Pr-C), 14.83 (–, *c*Pr-C), 18.04 (+, CH_3), 19.14 (C_{quat}, *c*Pr-C), 28.02 [+, $C(CH_3)_3$], 36.85 (–, C-4 or -6), 40.35 (–, C-4 or -6), 40.99 (+, C-5), 51.86 (–, CH_2NCH_2), 61.86 (+, C-1'), 67.00 (–, CH_2OCH_2), 79.98 [C_{quat}, $C(CH_3)_3$], 126.12 (+, Ph-C), 128.09 (+, Ph-C), 128.17 (+, Ph-C), 135.69 (C_{quat}), 136.43 (C_{quat}), 144.11 (C_{quat}), 174.77 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 397 (30) [M^+], 382 (8) [$M^+ - CH_3$], 254 (36), 209 (31), 114 (100), 100 (26), 57 (39); elemental analysis calcd (%) for $C_{25}H_{35}NO_3$ (397.6): C 75.53, H 8.87; found: C 75.59, H 8.64

Minor diastereomer: R_f = 0.44 (light petroleum/ethyl acetate 10:1); IR (film): $\tilde{\nu}$ = 3077, 2975, 2851, 2806, 1726, 1450, 1367, 1265, 1151, 1122, 943, 864, 703 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.37–0.45 (m, 1 H, *c*Pr-H), 0.54–0.62 (m, 1 H, *c*Pr-H), 1.00 (d, *J* = 7.1 Hz, 3 H, CH_3), 1.02–1.09 (m, 1 H, *c*Pr-H), 1.32 (dd, *J* = 12.7, 3.6 Hz, 1 H, 4- or 6-H), 1.43 [s, 9 H,

$C(CH_3)_3$], 1.83–1.98 (m, 2 H, 4- or 6-H, *c*Pr-H), 2.22 (br.s, 4 H, CH_2NCH_2), 1.83–1.98 (m, 2 H, 4- or 6-H), 2.73–2.88 (m, 2 H, 5-H, 1-H), 3.55 (t, J = 4.6 Hz, 4 H, CH_2OCH_2), 7.04 (d, J = 8.1 Hz, 2 H, Ph), 7.18–7.33 (m, 3 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.07 (–, *c*Pr-C), 14.13 (–, *c*Pr-C), 18.78 (C_{quat}, *c*Pr-C), 19.07 (+, CH_3), 27.97 [+, $C(CH_3)_3$], 36.56 (–, C-4 or -6), 39.69 (–, C-4 or -6), 40.56 (+, C-5), 51.55 (–, CH_2NCH_2), 61.11 (+, C-1'), 67.06 (–, CH_2OCH_2), 79.93 [C_{quat}, $C(CH_3)_3$], 125.91 (+, Ph-C), 127.98 (+, Ph-C), 128.17 (+, Ph-C), 135.63 (C_{quat}), 136.66 (C_{quat}), 144.35 (C_{quat}), 174.65 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 397 (22) [M^+], 382 (8) [$M^+ - CH_3$], 254 (32), 209 (28), 114 (100), 100 (25), 57 (30); elemental analysis calcd (%) for $C_{25}H_{35}NO_3$ (397.6): C 75.53, H 8.87; found: C 75.57, H 8.56.

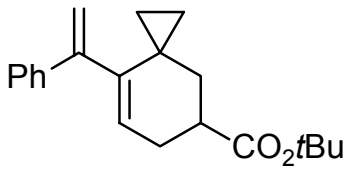
2) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), (1-iodovinyl)benzene (**191**, 460 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 2 h. After cooling the mixture to room temperature, *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 10:1) to yield **176ab** (142.5 mg, 18%, yellowish oil) as a mixture of two diastereomers (ratio 1:1 according to NMR), **197** (45.6 mg, 8%, yellowish oil) and **198** (170 mg, 27%, yellowish oil).

4-(2-Cyclopropylidene-1-methyl-3-phenyl-but-3-enyl)-morpholine (197):



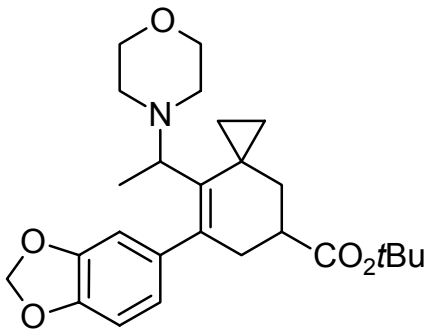
R_f = 0.33 (light petroleum/ethyl acetate, 10:1); IR (film): $\tilde{\nu}$ = 3078, 3052, 2972, 2851, 2807, 1724, 1597, 1492, 1445, 1265, 1118, 1009, 942, 777, 701 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.76 (t, J = 7.8 Hz, 2 H, *c*Pr-H), 1.18 (t, J = 7.8 Hz, 2 H, *c*Pr-H), 1.28 (d, J = 7.1 Hz, 3 H, CH_3), 2.38–2.55 (m, 4 H, CH_2NCH_2), 3.39 (q, J = 6.7 Hz, 1 H, 1-H), 3.65 (t, J = 4.7 Hz, 4 H, CH_2OCH_2), 5.25 (d, J = 1.9 Hz, 1 H, vinyl), 5.60 (d, J = 1.88 Hz, 1 H, vinyl), 7.21–7.32 (m, 5 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 2.98 (–, *c*Pr-C), 3.82 (–, *c*Pr-C), 14.70 (+, CH_3), 50.04 (–, CH_2NCH_2), 63.22 (+, C-1), 67.34 (–, CH_2OCH_2), 114.04 (–, vinyl), 125.49(C_{quat}), 126.66 (+, Ph-C), 127.56 (+, Ph-C), 127.80 (+, Ph-C), 129.78 (C_{quat}), 142.56 (C_{quat}), 149.51 (C_{quat}); MS (70 eV, EI) *m/z* (%): 269 (18) [M^+], 268 (37), 183 (4) [M^+ – morpholinyl], 114 (100)

***tert*-Butyl 8-(1-phenylvinyl)spiro[2.5]oct-7-ene-5-carboxylate (198)**:



R_f = 0.76 (light petroleum/ethyl acetate, 10:1); IR (film): $\tilde{\nu}$ = 3081, 2977, 2931, 1726, 1367, 1255, 1152, 903, 780 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.29–0.61 (m, 4 H, *c*Pr-H), 1.37 (dd, *J* = 2.9, 13.1 Hz, 1 H, 4- or 6-H), 1.46 [s, 9 H, $C(CH_3)_3$], 2.09 (t, *J* = 12.2 Hz, 1 H, 4- or 6-H), 2.47 (dd, *J* = 3.7, 7.9 Hz, 2 H, 4- or 6-H), 2.71–2.86 (m, 1 H, 5-H), 4.94 (d, *J* = 1.8 Hz, 1 H, vinyl), 5.42 (d, *J* = 1.8 Hz, 1 H, vinyl), 5.65 (t, *J* = 3.8 Hz, 1 H, 7-H), 7.23–7.32 (m, 3 H, Ph), 7.37–7.41 (m, 2 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 12.80 (–, *c*Pr-C), 13.69 (–, *c*Pr-C), 19.44 (C_{quat}, *c*Pr-C), 28.07 [+, $C(CH_3)_3$], 28.47 (–, C-4 or -6), 37.29 (–, C-4 or -6), 40.37 (+, C-5), 79.97 [C_{quat}, $C(CH_3)_3$], 114.22 (–, vinyl), 124.82 (+, C-7), 126.04 (+, Ph-C), 127.48 (+, Ph-C), 128.22 (+, Ph-C), 140.16 (C_{quat}), 142.22 (C_{quat}), 147.56 (C_{quat}), 174.88 (C_{quat}, C=O); MS (70 eV, EI) *m/z* (%): 310 (3) [M^+], 254 (60), 209 (41), 181 (30), 167 (39), 115 (19), 103 (32), 91 (46), 77 (27), 57 (100), 41 (52).

***tert*-Butyl 7-(benzo[1,3]dioxol-5-yl)-8-(1-morpholin-4-ylethyl)spiro[2.5]oct-7-ene-5-carboxylate (177ab):**



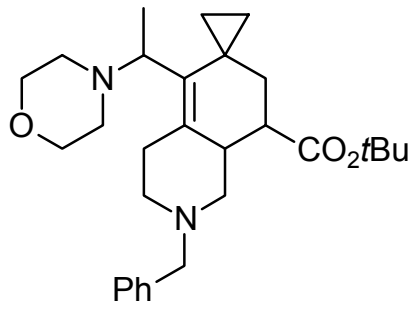
According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 μmol), tri-2-furylphosphine (46.4 mg, 200 μmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 261 mg, 3.00 mmol), 5-(1-iodovinyl)benzo[1,3]dioxole (**192**, 548.1 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL), at 80 °C for 3 h. After cooling the mixture to room temperature, *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and then the mixture was heated with stirring at 100 °C for an additional 65 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 4:1) to yield **177ab** (386 mg, 44%, yellowish oil) as a mixture of two diastereomers (ratio 1.2:1 according to NMR).

Major diastereomer: R_f = 0.44 (light petroleum/ethyl acetate 4:1); IR (KBr): $\tilde{\nu}$ = 2976, 2952, 2806, 1726, 1606, 1485, 1452, 1433, 1367, 1266, 1238, 1211, 1152, 1121, 1039, 939, 810 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.27–0.34 (m, 1 H, *c*Pr-H), 0.57–0.65 (m, 1 H, *c*Pr-H), 0.78–0.95 (m, 1 H, *c*Pr-H), 1.05 (dd, *J* = 12.7, 3.3 Hz, 1 H, 4- or 6-H), 1.11 (d, *J* = 7.0 Hz, 3 H,

CH_3), 1.41 [s, 9 H, $C(CH_3)_3$], 1.62–1.69 (m, 1 H, *c*Pr-H), 2.03 (td, *J* = 12.0, 2.0 Hz, 1 H, 4- or 6-H), 2.22 (br.s, 4 H, CH_2NCH_2), 2.34–2.55 (m, 2 H, 4- or 6-H), 2.77–2.89 (m, 2 H, 5-H, 1-H), 3.57 (br.s, 4 H, CH_2OCH_2), 5.94–5.96 (m, 2 H, OCH_2O), 6.47 (dd, *J* = 7.8, 1.7 Hz, 1 H, Ph), 6.53 (d, *J* = 1.6 Hz, 1 H, Ph), 6.76 (d, *J* = 7.6 Hz, 1 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.69 (–, *c*Pr-C), 14.78 (–, *c*Pr-C), 17.96 (+, CH_3), 19.04 (C_{quat}, *c*Pr-C), 27.93 [+, $C(CH_3)_3$], 36.81 (–, C-4 or -6), 40.18 (–, C-4 or -6), 40.84 (+, C-5), 51.80 (–, CH_2NCH_2), 61.77 (+, C-1), 66.89 (–, CH_2OCH_2), 79.86 [C_{quat}, $C(CH_3)_3$], 100.72 (–, OCH_2O), 108.05 (+, Ph-C), 108.59 (+, Ph-C), 120.94 (+, Ph-C), 135.79 (C_{quat}, Ph-C), 136.05 (C_{quat}, Ph-C), 137.70 (C_{quat}, Ph-C), 145.69 (C_{quat}), 147.27 (C_{quat}), 174.64 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 441 (12) [M^+], 426 (5) [$M^+ - CH_3$], 298 (56), 131 (22), 114 (95), 100 (28), 57 (100), 41 (45); elemental analysis calcd (%) for $C_{26}H_{35}NO_5$ (441,6): C 70.72, H 7.99; found: C 70.55, H 7.72.

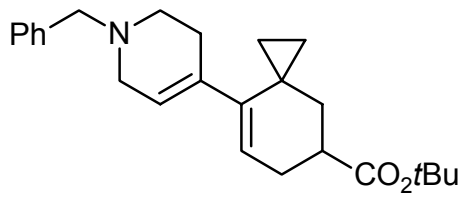
Minor diastereomer: R_f = 0.39 (light petroleum/ethyl acetate 4:1); IR (KBr): $\tilde{\nu}$ = 3077, 2975, 2852, 2805, 1725, 1505, 1485, 1433, 1367, 1239, 1150, 1121, 1039, 938, 810 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.36–0.44 (m, 1 H, *c*Pr-H), 0.53–0.61 (m, 1 H, *c*Pr-H), 0.77–0.90 (m, 1 H, *c*Pr-H), 0.99 (d, *J* = 6.9 Hz, 3 H, CH_3), 1.30 (dd, *J* = 12.7, 3.6 Hz, 1 H, 4- or 6-H), 1.43 [s, 9 H, $C(CH_3)_3$], 1.85–1.94 (m, 2 H, *c*Pr-H, 4- or 6-H), 2.24 (br.s, 4 H, CH_2NCH_2), 2.35–2.58 (m, 2 H, 4- or 6-H), 2.72–2.89 (m, 2 H, 5-H, 1-H), 3.58 (t, *J* = 4.3 Hz 4 H, CH_2OCH_2), 5.92–5.97 (m, 2 H, OCH_2O), 6.48 (dd, *J* = 8.1, 1.0 Hz, 1 H, Ph), 6.54 (d, *J* = 1.5 Hz, 1 H, Ph), 6.76 (d, *J* = 8.0 Hz, 1 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.14 (–, *c*Pr-C), 14.17 (–, *c*Pr-C), 18.76 (+, CH_3), 19.03 (C_{quat}, *c*Pr-C), 27.97 [+, $C(CH_3)_3$], 36.55 (–, C-4 or -6), 37.67 (–, C-4 or -6), 40.51 (+, C-5), 51.59 (–, CH_2NCH_2), 61.18 (+, C-1), 67.12 (–, CH_2OCH_2), 79.98 [C_{quat}, $C(CH_3)_3$], 100.74 (–, OCH_2O), 107.98 (+, Ph-C), 108.80 (+, Ph-C), 121.14 (+, Ph-C), 136.07 (C_{quat}, 2 × Ph-C), 138.06 (C_{quat}, Ph-C), 145.62 (C_{quat}), 147.24 (C_{quat}), 174.67 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 441 (29) [M^+], 426 (14) [$M^+ - CH_3$], 298 (100), 253 (17), 131 (14), 114 (42), 100 (13), 57 (22), 41 (5); elemental analysis calcd (%) for $C_{26}H_{35}NO_5$ (441.6): C 70.72, H 7.99; found: C 70.55, H 7.72

***tert*-Butyl 2'-benzyl-5'-(1-Morpholin-4-ylethyl)-1',2',3',4',6',7',8',8a'-octahydrospiro [cyclopropane-1,6'(7'*H*)-isoquinoline]- 8'-carboxylate (178ab):**



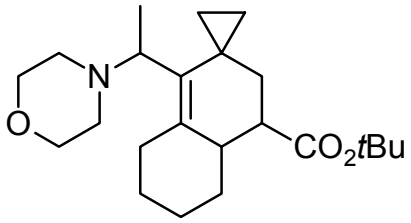
According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 209 mg, 2.40 mmol), 1-benzyl-4-iodo-1,2,3,6-tetrahydropyridine (**193**, 600 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL), at 80 °C for 3.5 h., *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added to the mixture, and then it was stirred at 80 °C for an additional 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **178ab** (242.6 mg, 26%, colorless solid). The reaction gave actually mixture of two diastereomers (ratio 2.5:1 according to NMR). However, only major diastereomer could be isolated. R_f = 0.42 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 3082, 2977, 2852, 2796, 1725, 1496, 1453, 1395, 1368, 1321, 1272, 1147, 1120, 1056, 1027, 983, 947, 916, 864, 846, 821, 741, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.38 (bs., 2 H, *c*Pr-H), 0.62–0.65 (m, 1 H, *c*Pr-H), 0.77–0.83 (m, 1 H, *c*Pr-H), 1.10 (d, J = 6.8 Hz, 3 H, CH_3), 1.26 [s, 9 H, $C(CH_3)_3$], 1.53 (t, J = 11.1 Hz, 1 H), 1.79–1.90 (m, 3 H), 1.95–2.04 (m, 1 H), 1.12–2.21 (m, 1 H), 2.34 (bs., 4 H, CH_2NCH_2), 2.57 (dt, J = 4.2, 10.6 Hz, 1 H), 2.85–2.90 (m, 1 H), 2.95–3.00 (m, 1 H), 3.32–3.58 (AB system: δ_A = 3.56, δ_B = 3.35, J_{AB} = 13.0 Hz, 2 H, Bn), 3.62 (t, J = 4.11 Hz, 4 H, CH_2OCH_2), 3.64–3.94 (m, 1 H), 7.16–7.32 (m, 5 H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = 10.06 (–, *c*Pr-C), 11.85 (–, *c*Pr-C), 17.36 (+, CH_3), 19.65 (C_{quat}, *c*Pr-C), 27.78 [+, $C(CH_3)_3$], 29.34 (–), 30.54 (–), 41.55 (+, *C*H), 45.56 (+, *C*H), 51.71 (–, CH_2NCH_2), 54.07 (–), 58.10 (+, *C*H), 59.49 (–), 62.78 (–, Bn), 67.15 (–, CH_2OCH_2), 80.03 [C_{quat}, $C(CH_3)_3$], 126.76 (+, Ph), 128.05 (+, 2 × Ph), 128.94 (+, 2 × Ph), 131.33 (C_{quat}), 132.60 (C_{quat}), 138.45 (C_{quat}), 174.52 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 466 (30) [M^+], 379 (78), 323 (54), 288 (15), 232 (18), 159 (14), 134 (28), 114 (25); 91 (100), 57 (29), 42 (12); elemental analysis calcd (%) for $C_{29}H_{24}N_2O_3$ (466.7): C 74.64, H 9.07; found: C 74.63, H 8.95.

***tert*-Butyl 8-(1-Benzyl-5'-1,2,3,6-tetrahydropyridin-4-yl)-spiro[2.5]oct-7-ene-5-carboxylate (199):**



According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 μmol), tri-2-furylphosphine (46.4 mg, 200 μmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), 1-benzyl-4-iodo-1,2,3,6-tetrahydropyridine (**193**, 600 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL), at 80 °C for 3.5 h., *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added to the mixture, and then it was stirred at 80 °C for an additional 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **178ab** (93.3 mg, 10%, colorless solid) and **199** (91 mg, 12%, yellowish oil) R_f = 0.5 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 3061, 3024, 2977, 2932, 2795, 2745, 1726, 1493, 1455, 1390, 1368, 1329, 1280, 1268, 1150, 1173, 1017, 984, 962, 904, 845, 742 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.33–0.38 (m, 1 H, *c*Pr-H), 0.47–0.58 (m, 2 H, *c*Pr-H), 0.68–0.73 (m, 1 H, *c*Pr-H), 1.26–1.31 (m, 1 H), 1.41 [s, 9 H, $C(CH_3)_3$], 1.97 (t, *J* = 12.1 Hz, 1 H), 2.04–2.09 (m, 2 H), 2.26–2.32 (m, 2 H), 2.35–2.43 (m, 1 H), 2.53–2.61 (m, 1 H), 2.62–2.69 (m, 1 H, 5-H), 2.82–3.03 (m, 2 H), 3.54 (d, *J* = 1.7 Hz, 2 H, pyridine), 5.16–5.19 (m, 1 H, C*H*), 5.40–5.42 (m, 1 H, C*H*), 7.19–7.32 (m, 5 H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = 11.90 (–, *c*Pr-C), 13.59 (–, *c*Pr-C), 18.89 (C_{quat}, *c*Pr-C), 28.02 [+, $C(CH_3)_3$], 28.35 (–), 31.60 (–), 37.22 (–), 40.35 (+, C-5), 49.52 (–), 52.50 (–), 62.59 (–, pyridine), 79.82 [C_{quat}, $C(CH_3)_3$], 121.60 (+, *C*H), 122.14 (+, *C*H), 126.95 (+, Ph), 128.13 (+, 2 × Ph), 129.11 (+, 2 × Ph), 136.36 (C_{quat}), 138.10 (C_{quat}), 143.35 (C_{quat}), 174.95 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 379 (199) [M^+], 322 (35), 306 (4), 278 (10), 172 (10), 91 (97), 57 (20); elemental analysis calcd (%) for $C_{25}H_{33}NO_2$ (379.6): C 79.11, H 8.76; found: C 79.21, H 8.63.

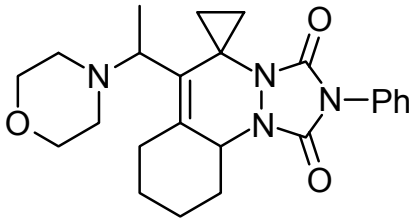
tert-Butyl 1'-(1-Morpholin-4-ylethyl)-4',4a',5',6',7',8'-hexahydrospiro[cyclopropane-1,2'(3'*H*)-naphthalene]- 4'-carboxylate (179ab):



According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 209 mg, 2.40 mmol), 1-iodo-cyclohexene (**194**, 416 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL), at 80 °C for 3.5 h., *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added to the mixture, and then it was stirred at 80 °C for an additional 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **179ab** (188 mg, 25%, yellowish oil). The reaction gave actually mixture of two diastereomers (ratio 1:1 according to NMR). However, only one diastereomer could be isolated. R_f = 0.45 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 3076, 2922, 2853, 2801, 2686, 1726, 1479, 1455, 1430, 1391, 1367, 1322, 1270, 1150, 1123, 1049, 1027, 994, 978, 951, 864, 843, 802, 793 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.36 (bs., 2 H, *c*Pr-H), 0.60–0.63 (m, 1 H, *c*Pr-H), 0.69–0.83 (m, 1 H, *c*Pr-H), 096 (dd, *J* = 2.3, 12.4 Hz, 2 H), 1.09 (d, *J* = 6.9 Hz, 3 H, CH_3), 1.40 [s, 9 H, $C(CH_3)_3$], 1.30–1.49 (m, 1 H), 1.61–1.77 (m, 5 H, $2CH_2$ + CH), 1.83–1.90 (m, 2 H), 2.16–2.34 (m, 6 H, CH_2NCH_2 + 2× CH), 3.63(t, *J* = 4.38 Hz, 4 H, CH_2OCH_2), 3.84–3.88 (m, 1 H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.31 (–, *c*Pr-C), 11.62 (–, *c*Pr-C), 17.36 (+, CH_3), 19.79 (C_{quat}, *c*Pr-C), 26.19 (–), 26.51 (–), 28.05 [+, $C(CH_3)_3$], 30.45 (–), 34.60 (–), 39.06 (–), 42.03 (+, *C*H), 48.59 (+, *C*H), 51.87 (–, CH_2NCH_2), 58.39 (+, *C*H), 62.28 (–, CH_2OCH_2), 79.85 [C_{quat}, $C(CH_3)_3$], 130.13 (C_{quat}), 135.65 (C_{quat}), 175.34 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 375 (20) [M^+], 232 (100), 203 (38), 187 (55), 145 (30), 114 (22), 88 (14), 57 (20); elemental analysis calcd (%) for $C_{23}H_{37}NO_3$ (375.6): C 73.56, H 9.93; found: C 73.55, H 9.64.

*2.6.6. Synthesis of spiro[2.5]octenes (**180a–188a**)*

6'-[1-Morpholin-4-ylethyl]-2'-phenylspiro[cyclopropane-1,5'(10a'*H*)-5',7',8',9',10',10a'-hexahydro-[1,2,4]triazolo[1,2-a]cinnoline]-1,3-dione (180a):



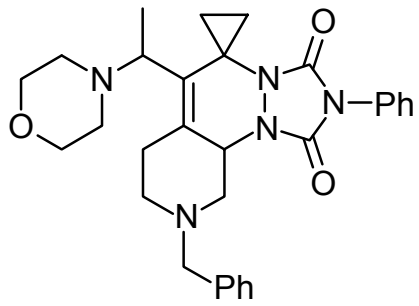
According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 μmol), tri-2-furylphosphine (46.4 mg, 200 μmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), 1-iodo-cyclohexene (**194**, 416 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 5 h. *N*-Phenyltriazolinedione (**122**, 700 mg, 4.00 mmol) was added to the ice-cooled mixture, and then it was stirred again at room temperature for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **180a** (280 mg, 33%, colorless solid) as a mixture of two diastereomers (ratio 4.6:1 according to NMR).

Major diastereomer: m.p. 151 °C, R_f = 0.446 (light petroleum/ethyl acetate, 3:1); IR (KBr): $\tilde{\nu}$ = 3033, 2961, 2926, 2856, 1762, 1709, 1504, 1459, 1415, 1301, 1270, 1128, 1117, 1069, 1033, 866, 765 cm^{-1}; ^1H NMR (300 MHz, $C_2D_2Cl_4$, 100 °C): δ = 1.22–1.36 (m, 1 H, *c*Pr-H), 1.28 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.37–1.48 (m, 1 H, *c*Pr-H), 1.51–1.67 (m, 1 H, cychex), 1.75 (dt, *J* = 3.6, 13.1 Hz, 1 H, cychex), 1.88–2.00 (m, 5 H, *c*Pr-H, cychex), 2.06–2.14 (m, 1 H, *c*Pr-H), 2.47–2.54 (m, 1 H, 1-H), 2.49 (t, *J* = 4.4 Hz, 4 H, CH_2NCH_2), 2.65–2.71 (m, 1 H, cychex), 3.71 (t, *J* = 4.7 Hz, 4 H, CH_2OCH_2), 3.77 (br.s, 1 H, cychex), 4.23 (dd, *J* = 4.2, 10.8 Hz, 1 H, cychex), 7.35–7.52 (m, 5 H, Ph); ^{13}C NMR (75.5 MHz, $C_2D_2Cl_4$, 100 °C, DEPT): δ = 10.03 (–, *c*Pr-C), 10.48 (–, *c*Pr-C), 18.04 (+, CH_3), 24.28 (–, cychex), 26.80 (–, cychex), 29.91 (–, cychex), 31.99 (–, cychex), 40.88 (C_{quat}, *c*Pr-C), 51.88 (–, CH_2NCH_2), 57.68 (+, C-1), 58.66 (+, cychex), 66.79 (–, CH_2OCH_2), 125.46 (+, Ph-C), 127.66 (+, Ph-C), 127.85 (C_{quat}), 128.62 (+, Ph-C), 131.36 (C_{quat}), 133.92 (C_{quat}), 149.51 (C_{quat}, C=O), 151.98 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 422 (54) [M^+], 393 (16), 337 (22), 336 (100), 217 (16), 114 (14), 100 (42); elemental analysis calcd (%) for $C_{24}H_{30}N_4O_3$ (422.5): C 68.22, H 7.16; found: C 67.91, H 7.07.

Minor diastereomer: R_f = 0.108 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 3071, 2932, 2853, 1772, 1714, 1546, 1504, 1413, 1295, 1264, 1130, 1117, 1029, 985, 766 cm^{-1} ;^1H NMR (300 MHz, $CDCl_3$): δ = 0.60–0.67 (m, 1 H, *c*Pr-H), 0.70–0.77 (m, 1 H, *c*Pr-H), 0.82–0.89 (m, 1 H, *c*Pr-H), 0.99–1.06 (m, 1 H, *c*Pr-H), 1.13–1.29 (m, 1 H, cychex), 1.36 (d, *J* = 6.3 Hz, 3 H,

CH_3), 1.46 (td, *J* = 3.2, 12.0 Hz, 1 H, cychex), 1.57 (tt, *J* = 3.5, 13.0 Hz, 1 H, cychex), 1.71 (td, *J* = 3.5, 13.7 Hz, 1 H, cychex), 1.82–1.86 (m, 2 H, cychex), 2.56 (t, *J* = 4.6 Hz, 4 H, CH_2NCH_2), 2.98–3.03 (m, 1 H, cychex), 3.25 (d, *J* = 13.60Hz, 1 H, cychex), 3.58 (q, *J* = 3.9 Hz, 4 H, CH_2OCH_2), 4.17 (dd, *J* = 4.1, 11.2 Hz, cychex), 4.67 (q, *J* = 6.3 Hz, 1 H, 1-H), 7.29 – 7.34 (m, 1 H, Ph), 7.46–7.51 (m, 4 H, Ph); ^{13}C NMR (75.478 MHz, $CDCl_3$, DEPT): δ = 11.25 (–, *c*Pr-C), 13.51 (–, *c*Pr-C), 19.87 (+, CH_3), 23.83 (–, cychex), 27.25 (–, cychex), 30.26 (–, cychex), 34.44 (–, cychex), 44.07 (C_{quat}, *c*Pr-C), 49.66 (–, CH_2NCH_2), 51.37 (+, C-1), 58.39 (+, cychex), 67.30 (–, CH_2OCH_2), 125.37 (+, Ph-C), 126.99 (C_{quat}), 127.80 (+, Ph-C), 128.95 (+, Ph-C), 131.33 (C_{quat}), 136.57 (C_{quat}), 149.67 (C_{quat}, C=O), 152.78 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 422 (79) [M^+], 407 (11) [$M^+ - CH_3$], 336 (55), 261 (18), 247 (30), 246 (100), 232 (27), 218 (24), 178 (20), 119 (39), 91 (42), 77 (20), 41 (22) for $C_{24}H_{30}N_4O_3$ (422.53); HRMS (EI):calcd 422.2318 (correct HRMS).

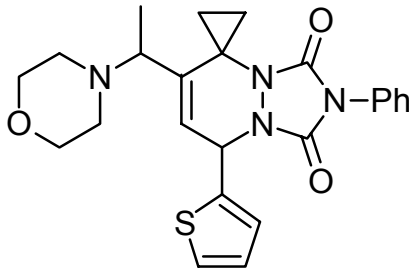
6'-[1-morpholin-4-ylethyl]-9'-(*N*)-benzyl-2'-phenylspiro[cyclopropane-1,5'(10a'*H*)-5',7',8',9',10',10a'-hexahydro-[1,2,4]triazolo[1,2-a]cinnoline]-1,3-dione (181a):



According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 μmol), tri-2-furylphosphine (46.4 mg, 200 μmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), 1-benzyl-4-iodo-1,2,3,6-tetrahydropyridine (**193**, 600 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL), at 80 °C for 3 h. *N*-Phenyltriazolinedione (**122**, 700 mg, 4.00 mmol) was added to the ice-cooled mixture, and then it was stirred at room temperature for an additional 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **181a** (180 mg, 17%, colorless oil), R_f = 0.17 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 3028, 2956, 2850, 2798, 1770, 1713, 1503, 1456, 1412, 1361, 1265, 1120, 1071, 1029, 936, 863, 736, 739 cm^{-1}; ^{1}H NMR (300 MHz, $C_2D_2Cl_4$, 100 °C): δ = 1.24–1.33 (m, 1 H, *c*Pr-H), 1.29 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.36–1.43 (m, 1 H, *c*Pr-H), 1.79–1.87 (m, 1 H, *c*Pr-H), 2.02–2.15 (m, 2 H, tetrahydropyridine), 2.24 (t, *J* = 10.3 Hz, 1 H, tetrahydropyridine), 2.29–2.35 (m, 1 H, *c*Pr-H), 2.39–2.51 (m, 1 H, 1-H), 2.47 (q, *J* = 4.3 Hz, 4 H, CH_2NCH_2), 2.94–2.99 (m, 1 H, tetrahydropyridine), 3.56–3.78 (AB system: δ_A = 3.6, δ_B = 3.8, J_{AB} = 13.3 Hz, 2 H, Bn), 3.56–3.78 (1 H, tetrahydropyridine)*, 3.68 (t, *J* = 4.6 Hz, 4 H, CH_2OCH_2), 3.98–4.02 (m,

1 H, tetrahydropyridine), 4.47 (dd, J = 4.4, 9.9 Hz, 1 H, tetrahydropyridine), 7.28–7.48 (m, 10 H, Ph); * The peak of this proton sits under the peaks of the AB system, thus the spin couplings of this proton could not be determined. This proton correlates clearly with the carbon peak at 28.49 ppm in the HMQC spectrum. ^{13}C NMR (75.5 MHz, $C_2D_2Cl_4$, 100 °C, DEPT): δ = 9.40 (–, *c*Pr-C), 10.67 (–, *c*Pr-C), 17.85 (+, CH_3), 28.49 (–, tetrahydropyridine), 40.74 (C_{quat}, *c*Pr-C), 51.80 (–, CH_2NCH_2), 52.61 (–, tetrahydropyridine), 57.06 (+, tetrahydropyridine), 57.32 (–, tetrahydropyridine), 57.71 (+, C-1), 61.61 (–, Bn), 66.70 (–, CH_2OCH_2), 125.52 (+, Ph), 126.86 (+, Ph), 127.77 (+, Ph), 127.98 (+, Ph), 128.53 (+, Ph), 128.66 (+, Ph), 128.81 (C_{quat}), 130.99 (C_{quat}), 131.19 (C_{quat}), 137.72 (C_{quat}), 149.24 (C_{quat}, C=O), 152.27 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 513 (34) [M^+], 427 (26) [M^+ – morpholinyl], 397 (9), 307 (6), 134 (46), 100 (46), 91 (100), 42 (14); elemental analysis calcd (%) for $C_{30}H_{35}N_5O_3$ (513.6): C 70.15, H 6.87; found: C 69.98, H 6.71.

6'-(1-Morpholin-4-ylethyl)-2'-phenyl-8'-(thiophen-2-yl)spiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo[1,2-a]pyridazine]-1',3'-dione (182a):



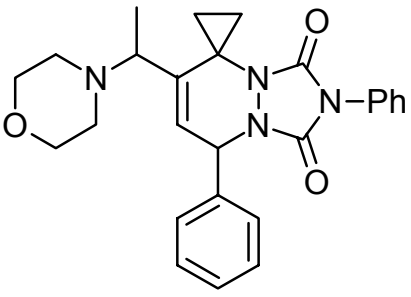
According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), 2-(2-iodovinyl)thiophene (**195**, 472 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. *N*-Phenyltriazolinedione (**122**, 700 mg, 4.00 mmol) was added to the ice-cooled mixture, and then it was stirred again at room temperature for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **182a** (232 mg, 26%, colorless solid) as a mixture of two diastereomers (ratio 1:1 according to NMR).

Diastereomer I: m.p. 160 °C, R_f = 0.15 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 3102, 3088, 2963, 2859, 2815, 1769, 1715, 1502, 1409, 1310, 1165, 1116, 767, 731 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.14–1.21 (m, 1 H, *c*Pr-H), 1.19 (d, J = 6.8 Hz, 3 H, CH_3), 1.59–1.74 (m, 2 H, *c*Pr-H), 2.46–2.64 (m, 6 H, *c*Pr-H, CH_2NCH_2, 1-H), 3.70 (t, J = 4.6 Hz, 4 H, CH_2OCH_2), 5.88 (d, J = 5.2 Hz, 1 H, 8'-H), 6.17 (d, J = 5.2 Hz, 1 H, 7'-H), 6.99 (dd, J = 3.6, 5.1 Hz, 1 H, thiophene), 7.21 (d, J = 3.8 Hz, 1 H, thiophene), 7.27–7.42 (m, 6 H, Ph,

thiophene); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.36 (–, *c*Pr-C), 11.32 (–, *c*Pr-C), 16.08 (+, CH_3), 41.85 (C_{quat}, *c*Pr-C), 50.14 (–, CH_2NCH_2), 53.57 (–, C-8'), 57.28 (+, C-1), 67.07 (–, CH_2OCH_2), 121.17 (+, C-7'), 125.45 (+, Ph), 126.38 (+, thiophene), 126.93 (+, thiophene), 127.87 (+, Ph or thiophene), 128.01 (+, Ph or thiophene), 128.87 (+, Ph), 130.76 (C_{quat}), 138.93 (C_{quat}), 139.48 (C_{quat}), 149.94 (C_{quat}, C=O), 152.08 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 450 (27) [M^+], 364 (100) [M^+ – morpholine], 348 (8), 173 (17), 114 (30), 100 (90); elemental analysis calcd (%) for $C_{24}H_{26}N_4O_3S$ (450.6): C 63.98, H 5.82, N 12.43; found: C 63.76, H 5.71, N 12.68.

Diastereomer II: m.p. 122 °C, R_f = 0.15 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 3108, 3062, 2963, 2858, 2796, 1775, 1714, 1502, 1411, 1112, 766, 713 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.17–1.44 (m, 3 H, *c*Pr-H), 1.25 (d, *J* = 6.4 Hz, 3 H, CH_3), 2.32 (q, *J* = 6.4 Hz, 1 H, 1-H), 2.47 (br.s, 4 H, *c*Pr-H, CH_2NCH_2), 2.81–2.90 (m, 1 H, *c*Pr-H), 3.69 (t, *J* = 4.5 Hz, 4 H, CH_2OCH_2), 5.89 (d, *J* = 5.0 Hz, 1 H, 8'-H), 6.29 (d, *J* = 4.86 Hz, 1 H, 7'-H), 6.98 (dd, *J* = 3.5, 5.1 Hz, 1 H, thiophene), 7.19 (d, *J* = 3.4 Hz, 1 H, thiophene), 7.27–7.42 (m, 6 H, Ph, thiophene); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 9.37 (–, *c*Pr-C), 11.56 (–, *c*Pr-C), 18.22 (+, CH_3), 41.92 (C_{quat}, *c*Pr-C), 50.76 (–, CH_2NCH_2), 53.19 (–, C-8'), 58.27 (+, C-1), 67.04 (–, CH_2OCH_2), 120.19 (+, C-7'), 125.47 (+, Ph), 126.49 (+, Ph or thiophene), 126.83 (+, thiophene), 127.76 (+, thiophene), 128.06 (+, Ph or thiophene), 128.91 (+, Ph), 130.75 (C_{quat}), 138.75 (C_{quat}), 139.31 (C_{quat}), 150.45 (C_{quat}, C=O), 152.15 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 450 (9) [M^+], 363 (32) [M^+ – morpholine – H], 348 (4), [M^+ – morpholine – H – CH_3], 173 (11), 114 (36), 100 (100); elemental analysis calcd (%) for $C_{24}H_{26}N_4O_3S$(450.6): C 63.98, H 5.82; found: C 63.90, H 6.06.

6'-(1-Morpholin-4-ylethyl)-2',8'-diphenylspiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo-[1,2-a]pyridazine]-1',3'-dione (183a):



According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), (*E*)-1-iodo-2-phenylethene (**196**, 460 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL), at 80 °C for 2 h. *N*-phenyltriazolinedione (**122**, 700 mg, 4.00 mmol) was added to the ice-cooled mixture and then it was stirred at room temperature for an additional 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected

to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 1:1) to yield **183a** (310 mg, 35%, colorless solid) as a mixture of two diastereomers (ratio 1.4:1 according to NMR).

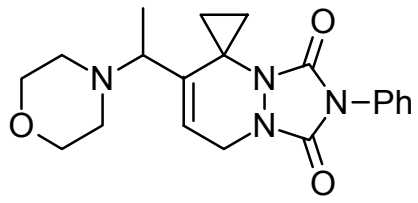
2) According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 μmol), tri-2-furylphosphine (46.4 mg, 200 μmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), (*E*)-1-iodo-2-phenylethene (**196**, 460 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL), at 80 °C for 2 h. *N*-Phenyltriazolinedione (**122**, 700 mg, 4.00 mmol) was added to the ice-cooled mixture, and then it was stirred at room temperature for an additional 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 1:1) to yield **183a** (283 mg, 32%, colorless oil) as a mixture of two diastereomers (ratio 1.4:1 according to NMR).

Major diastereomer: m.p. 171 °C, R_f = 0.47 (light petroleum/ethyl acetate 1:1); IR (KBr): $\tilde{\nu}$ = 3106, 3058, 3026, 2977, 2857, 2818, 1763, 1706, 1506, 1411, 1290, 1174, 1112, 768 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.18 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.21–1.31 (m, 1 H, *c*Pr-H), 1.55–1.65 (m, 1 H, *c*Pr-H), 1.90–2.00 (m, 1 H, *c*Pr-H), 2.32–2.65 (m, 6 H, *c*Pr-H, CH_2NCH_2, 1-H), 3.66 (t, *J* = 4.6 Hz, 4 H, CH_2OCH_2), 5.54 (d, *J* = 4.6 Hz, 1 H, 8'-H), 5.99 (d, *J* = 4.7 Hz, 1 H, 7'-H), 7.25–7.44 (m, 10 H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = 10.96 (–, *c*Pr-C), 11.33 (–, *c*Pr-C), 15.02 (+, CH_3), 41.54 (C_{quat}, *c*Pr-C), 49.86 (–, CH_2NCH_2), 57.92 (+, C-1), 58.98 (–, C-8'), 67.00 (–, CH_2OCH_2), 121.82 (+, C-7'), 125.39 (+, Ph-C), 127.90 (+, Ph-C), 127.98 (+, Ph-C), 128.57 (+, Ph-C), 128.64 (+, Ph-C), 128.82(+, Ph-C), 130.85 (C_{quat}), 137.07 (C_{quat}), 137.80 (C_{quat}), 149.68 (C_{quat}, C=O), 151.83 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 444 (11) [M^+], 358 (46) [M^+ – morpholinyl], 167 (12), 114 (26), 100 (100) 91 (14); elemental analysis calcd (%) for $C_{26}H_{28}N_4O_3$ (444.5): C 70.25, H 6.35; found: C 70.54, H 6.26.

Minor diastereomer: m.p. 170 °C, R_f = 0.47 (light petroleum/ethyl acetate, 1:1); IR (KBr): $\tilde{\nu}$ = 3065, 2962, 2854, 2811, 1769, 1711, 1502, 1414, 1301, 1265, 1116, 765 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.24 (d, *J* = 6.3 Hz, 3 H, CH_3), 1.31–1.39 (m, 2 H, *c*Pr-H), 1.43–1.51 (m, 1 H, *c*Pr-H), 2.36–2.49 (m, 5 H, CH_2NCH_2, 1-H), 2.74–2.82 (m, 1 H, *c*Pr-H), 3.69 (t, *J* = 4.4 Hz, 4 H, CH_2OCH_2), 5.60 (d, *J* = 4.9 Hz, 1 H, 8'-H), 6.15 (d, *J* = 5.0 Hz, 1 H, 7'-H), 7.29–7.44 (m, 10 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 9.61 (–, *c*Pr-C), 11.59 (–, *c*Pr-C), 17.83 (+, CH_3), 41.97 (C_{quat}, *c*Pr-C), 50.61 (–, CH_2NCH_2), 58.18 (+, C-1), 58.29 (–, C-8'), 67.09 (–, CH_2OCH_2), 120.47 (+, C-7'), 125.43 (+, Ph-C), 128.00 (+, Ph-C), 128.43 (+, Ph-C), 128.59 (+, Ph-C), 128.72(+, Ph-C), 128.89 (+, Ph-C), 130.81 (C_{quat}), 134.48 (C_{quat}), 138.44 (C_{quat}), 150.56

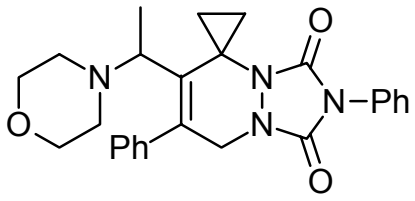
(C_{quat}, C=O), 151.60 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 444 (25) [M^+], 358 (80) [M^+ – morpholinyl], 357 (94), 167 (14), 119 (15), 114 (26), 100 (100), 91 (16); elemental analysis calcd (%) for $C_{26}H_{28}N_4O_3$ (444.5): C 70.25, H 6.35; found: C 70.43, H 6.07.

6'-(1-Morpholin-4-ylethyl)-2'-phenylspiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo[1,2-a]pyridazine]-1',3'-dione (184a):



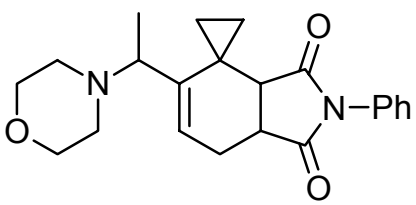
According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 μmol), tri-2-furylphosphine (46.4 mg, 200 μmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. *N*-Phenyltriazolinedione (**122**, 700 mg, 4.00 mmol) was added to the ice-cooled mixture, and then it was stirred at room temperature for an additional 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, CH_2Cl_2/ethyl acetate, 1:1) to yield **184a** (367.2 mg, 50%, colorless solid), m.p. 130 °C, R_f = 0.25 (CH_2Cl_2/ethyl acetate 1:1); IR (KBr): $\tilde{\nu}$ = 2962, 2953, 2852, 2813, 1771, 1709, 1699, 1504, 1421, 1313, 1268, 1142, 1123, 916, 860, 767 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.17 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.18–1.26 (m, 1 H, *c*Pr-H), 1.34–1.43 (m, 1 H, *c*Pr-H), 1.69–1.78 (m, 1 H, *c*Pr-H), 2.31–2.52 (m, 6 H, *c*Pr-H, CH_2NCH_2, 1-H), 3.68 (t, *J* = 4.6 Hz, 4 H, CH_2OCH_2), 4.18–4.40 (m, 2 H, 8'-H), 6.01 (t, *J* = 6.6 Hz, 1 H, 7'-H), 7.32–7.46 (m, 5 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 9.76 (–, *c*Pr-C), 11.58 (–, *c*Pr-C), 15.91 (+, CH_3), 41.36 (C_{quat}, *c*Pr-C), 44.28 (–, C-8'), 49.94 (–, CH_2NCH_2) 58.20 (+, C-1), 66.93 (–, CH_2OCH_2), 116.49 (+, C-7'), 125.29 (+, Ph), 127.92 (+, Ph), 128.87 (+, Ph), 130.83 (C_{quat}), 138.72 (C_{quat}), 149.66 (C_{quat}, C=O), 152.62 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 368 (20) [M^+], 281 (100) [M^+ – morpholine], 266 (6) [M^+ – morpholine – CH_3], 178 (16), 114 (10), 100 (64); elemental analysis calcd (%) for $C_{20}H_{24}N_4O_3$ (368.4): C 65.20, H 6.57; found: C 64.90, H 6.25.

6'-(1-Morpholin-4-ylethyl)-2',7'-diphenylspiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo-[1,2-a]pyridazine]-1',3'-dione (185a):



According to GP-B, $Pd(OAc)_2$ (22.4mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 261 mg, 3.00 mmol), (1-iodovinyl)benzene (**191**, 460 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 3 h. *N*-Phenyltriazolinedione (**122**, 700 mg, 4.00 mmol) was added to the ice-cooled mixture and then it was stirred at room temperature for an additional 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 3:1) to yield **185a** (311 mg, 35%, colorless solid), m.p. 70 °C, R_f = 0.30 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 3050, 2956, 2850, 2805, 1772, 1713, 1598, 1503, 1407, 1265, 1143, 1119, 942, 863 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.25 (d, *J* = 7.0 Hz, 3 H, CH_3), 1.29–1.37 (m, 1 H, *c*Pr-H), 1.53–1.62 (m, 1 H, *c*Pr-H), 2.14–2.22 (m, 2 H, *c*Pr-H), 2.30 (br.s, 4 H, CH_2NCH_2), 3.08 (q, *J* = 6.7 Hz, 1 H, 1-H), 3.61 (t, *J* = 4.4 Hz, 4 H, CH_2OCH_2), 4.50 (s, 2 H, 8'-H), 7.10–7.14 (m, 2 H, Ph), 7.33–7.42 (m, 4 H, Ph), 7.45–7.50 (m, 4 H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = 11.77 (–, *c*Pr-C), 13.69 (–, *c*Pr-C), 17.51 (+, CH_3), 38.24 (C_{quat}, *c*Pr-C), 48.67 (–, C-8'), 51.50 (–, CH_2NCH_2), 59.79 (+, C-1), 66.77 (–, CH_2OCH_2), 125.33 (+, Ph-C), 127.63 (+, Ph-C), 127.89 (+, Ph-C), 128.56 (+, Ph-C), 128.88 (+, Ph-C), 131.22 (C_{quat}), 133.44 (C_{quat}), 136.70 (C_{quat}), 137.78 (C_{quat}), 150.39 (C_{quat}, C=O), 152.97 (C_{quat}, C=O); MS (70 eV, EI) *m/z* (%): 444 (22) [M^+], 357 (52) [M^+ – morpholinyl], 254 (7), 167 (16), 114 (27), 100 (100); elemental analysis calcd (%) for $C_{26}H_{28}N_4O_3$ (444.5): C 70.25, H 6.35, N 12.60; found: C 69.98, H 6.52, N 12.42.

5-[1'-(Morpholin-4''-yl)ethyl]-2-phenylspiro[cyclopropane-1',4-(3a,4,7,7a-tetrahydroiso-indole)]-1,3-dione (186a):



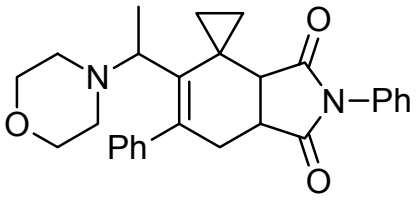
According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 2 h. After cooling the mixture to room temperature, 1-phenyl-pyrrole-2,5-dione (**189**, 693 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 4 h. After work-up and

drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 1:1) to yield **186a** (290 mg, 40%, yellow solid) as a mixture of two diastereomers (ratio 1:1 according to NMR).

Diastereomer I: m.p. 127 °C, R_f = 0.42 (light petroleum/ethyl acetate 1:1); IR (KBr): $\tilde{\nu}$ = 3087, 3022, 2955, 2906, 2847, 2809, 1708, 1595, 1494, 1456, 1435, 1368, 1298, 1183, 1170, 1135, 1111, 855, 759 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.30–0.34 (m, 1 H, *c*Pr-H), 0.72–0.80 (m, 1 H, *c*Pr-H), 1.58 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.20–1.26 (m, 1 H, *c*Pr-H), 1.75–1.83 (m, 1 H, *c*Pr-H), 2.21–2.47 (m, 6 H, CH_2NCH_2, 3a-H, 7-H), 2.65 (q, *J* = 6.7 Hz, 1 H, 1'-H), 2.81 (ddd, *J* = 2.0, 7.2, 14.8 Hz, 1 H, 7-H), 3.29–3.36 (m, 1 H, 7a-H), 3.50 (t, *J* = 4.6 Hz, 4 H, CH_2OCH_2), 5.85 (dd, *J* = 2.9, 6.9 Hz, 1 H, 6-H), 7.18–7.21 (m, 2 H, Ph), 7.32–7.45 (m, 3 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 7.65 (–, *c*Pr-C), 13.04 (–, *c*Pr-C), 15.04 (+, CH_3), 20.05 (C_{quat}, *c*Pr-C), 24.19 (–, C-7), 41.59 (+, C-3a), 50.19 (+, C-7a), 50.57 (–, CH_2NCH_2), 64.02 (+, C-1'), 66.96 (–, CH_2OCH_2), 125.95 (+, Ph-C, C-6), 128.26 (+, Ph), 128.88 (+, Ph-C), 131.89 (C_{quat}), 144.11 (C_{quat}), 177.07 (C_{quat}, C=O), 178.88 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 366 (46) [M^+], 351 (93) [M^+ – CH_3], 152 (6), 133 (8), 117 (18), 114 (100), 91 (16), 86 (27); elemental analysis calcd (%) for $C_{22}H_{26}N_2O_3$ (366.5): C 72.11, H 7.15; found: C 71.96, H 7.02.

Diastereomer II: m.p. 140 °C, R_f = 0.38 (light petroleum/ethyl acetate 1:1); IR (KBr): $\tilde{\nu}$ = 3064, 2965, 2891, 2846, 2815, 1773, 1702, 1597, 1500, 1455, 1435, 1390, 1301, 1189, 1172, 1115, 1040, 944, 923, 754 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.35–0.43 (m, 1 H, *c*Pr-H), 0.79–0.87 (m, 1 H, *c*Pr-H), 0.98 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.06–1,18 (m, 1 H, *c*Pr-H), 1.47–1.55 (m, 1 H, *c*Pr-H), 2.31–2.50 (m, 6 H, CH_2NCH_2, 3a-H, 7-H), 2.80–2.92 (m, 2 H, 1'-H, 7-H), 3.32–3.40 (m, 1 H, 7a-H), 3.52–3.63 (m, 4 H, CH_2OCH_2), 5.93 (br.s, 1 H, 6-H), 7.13–7.17 (m, 2 H, Ph), 7.34–7.45 (m, 3 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 6.71 (–, *c*Pr-C), 11.87 (+, CH_3), 12.73 (–, *c*Pr-C), 22.29 (C_{quat}, *c*Pr-C), 24.56 (–, C-7), 41.60 (+, C-7a), 49.16 (–, CH_2NCH_2), 50.05 (+, C-3a), 60.80 (+, C-1'), 67.28 (–, CH_2OCH_2), 123.30 (+, C-6), 126.33 (+, Ph-C), 128.49 (+, Ph-C), 129.05 (+, Ph-C), 131.98 (C_{quat}), 143.59 (C_{quat}), 177.74 (C_{quat}, C=O), 178.96 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 366 (25) [M^+], 351 (77) [M^+ – CH_3], 133 (6), 114 (100), 86 (16); elemental analysis calcd (%) for $C_{22}H_{26}N_2O_3$ (366.5): C 72.11, H 7.15; found: C 71.96, H 7.02.

5-(1'-(Morpholin-4''-yl)ethyl)-2,6-diphenylspiro[cyclopropane-1',4-(3a,4,7,7a-tetrahydroisoindole)]-1,3-dione (187a):



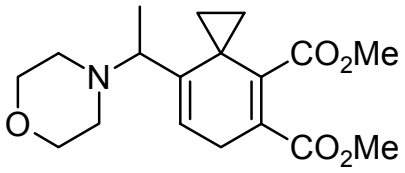
According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), (1-iodo-vinyl)-benzene (**191**, 460 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 2 h. After cooling the mixture to room temperature, 1-Phenyl-2,5-dihydropyrrole-2,5-dione (**189**, 693 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 4 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **187a** (353 mg, 40%, colorless solid) as a mixture of two diastereomers (ratio 1.18:1 according to NMR).

Major diastereomer: m.p. 165 °C, R_f = 0.18 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 2969, 2847, 2802, 1777, 1713, 1597, 1493, 1388, 1185, 1115, 862 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.41–0.49 (m, 1 H, *c*Pr-H), 0.78–0.86 (m, 1 H, *c*Pr-H), 1.15 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.21–1.28 (m, 1 H, *c*Pr-H), 2.17 (br.s, 4 H, CH_2NCH_2), 2.31 (d, *J* = 9.2 Hz, 1 H, 3a-H), 2.41–2.49 (m, 1 H, *c*Pr-H), 2.95–2.98 (m, 2 H, 7-H), 3.08 (q, *J* = 7.0 Hz, 1 H, 1'-H), 3.42–3.49 (m, 1 H, 7a-H), 3.55 (t, *J* = 4.45 Hz, 4 H, CH_2OCH_2), 6.94–6.97 (m, 2 H, Ph), 7.22–7.52 (m, 8 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 8.44 (–, *c*Pr-C), 13.47 (–, *c*Pr-C), 16.75 (+, CH_3), 21.33 (C_{quat}, *c*Pr-C), 31.72 (–, C-7), 42.07 (+, C-7a), 51.11 (+, C-3a), 51.42 (–, CH_2NCH_2), 59.89 (+, C-1'), 67.01 (–, CH_2OCH_2), 126.11 (+, Ph), 126.66 (+, Ph), 127.58 (+, Ph), 128.26 (+, Ph), 128.43 (+, Ph), 129.15 (+, Ph), 131.99 (C_{quat}), 138.10 (C_{quat}), 139.28 (C_{quat}), 141.69 (C_{quat}), 177.43 (C_{quat}, C=O), 178.44 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 442 (35) [M^+], 427 (33) [M^+ – CH_3], 355 (20) [M^+ – morpholinyl – H], 209 (14), 165 (15), 114 (100), 88 (10); elemental analysis calcd (%) for $C_{28}H_{30}N_2O_3$ (442.6): C 75.99, H 6.83; found: C 75.70, H 7.03.

Minor diastereomer: m.p. 168 °C, R_f = 0.22 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 3077, 3051, 2965, 2852, 2791, 1779, 1709, 1596, 1492, 1390, 1181, 1151, 1120, 1113, 861 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.41–0.49 (m, 2 H, *c*Pr-H), 1.08 (d, *J* = 7.4 Hz, 3 H, CH_3), 1.21–1.29 (m, 1 H, *c*Pr-H), 1.61 (q, *J* = 7.1 Hz, 1 H, *c*Pr-H), 2.12 (br.s, 4 H, CH_2NCH_2), 2.53 (d, *J* = 9.2 Hz, 1 H, 3a-H), 2.83–2.99 (m, 2 H, 7-H) 3.05 (q, *J* = 7.0 Hz, 1 H, 1'-H), 3.28–3.46 (m, 5 H, CH_2OCH_2, 7a-H), 7.05–7.07 (m, 2 H, Ph), 7.24–7.49 (m, 8 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 9.28 (–, *c*Pr-C), 12.94 (–, *c*Pr-C), 17.53 (+, CH_3), 21.10 (C_{quat},

*c*Pr-C), 32.11 (–, C-7), 42.40 (+, C-7a), 49.71 (+, C-3a), 51.45 (–, CH_2NCH_2), 60.62 (+, C-1'), 66.84 (–, CH_2OCH_2), 126.07 (+, Ph-C), 126.59 (+, Ph-C), 127.75 (+, Ph-C), 128.17 (+, Ph-C), 128.46 (+, Ph-C), 129.07 (+, Ph-C), 131.82 (C_{quat}), 138.98 (C_{quat}), 139.27 (C_{quat}), 141.98 (C_{quat}), 177.60 (C_{quat}, C=O), 178.57 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 442 (34) [M^+], 427 (66) [M^+ – CH_3], 355 (30) [M^+ – morpholinyl – H], 208 (16), 165 (15), 114 (100), 88 (16); elemental analysis calcd (%) for $C_{28}H_{30}N_2O_3$ (442.6):C 75.99, H 6.83; found: C 75.70, H 6.90.

Dimethyl 8-(1-morpholin-4-ylethyl)spiro[2.5]octa-4,7-diene-4,5-dicarboxylate (188a):



According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (2 mL) at 80 °C for 2 h. After cooling the mixture to room temperature dimethyl acetylenedicarboxylate (**190**, 568 mg, 4.00 mmol) was added, and then the mixture was heated again with stirring at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 1:1) to yield **188a** (200 mg, 30%, yellowish oil).

2) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 174 mg, 2.00 mmol), iodoethene (**173**, 308 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 2 h. After cooling the mixture to room temperature, dimethyl acetylenedicarboxylate (**190**, 568 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 1:1) to yield **188a** (160 mg, 24%, yellowish oil).

R_f = 0.5 (light petroleum/ethyl acetate, 1:1), IR (film): $\tilde{\nu}$ = 3056, 2953, 2895, 2857, 2824, 1733, 1630, 1587, 1436, 1371, 1266, 1162, 1118, 1033, 737, 704 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.00–1.15 (m, 3 H, *c*Pr-H), 1.06 (d, *J* = 6.7 Hz, 3 H, CH_3), 1.25–1.35 (m, 1 H, *c*Pr-H), 2.22 (q, *J* = 6.5 Hz, 1H, 1-H), 2.35–2.50 (m, 4 H, CH_2NCH_2), 3.15 (d, *J* = 3.6 Hz, 2 H, 6-H), 3.65 (t, *J* = 4.5 Hz, 4 H, CH_2OCH_2), 3.72 (s, 3 H, OCH_3), 3.78 (s, 3 H, OCH_3), 5.85 (t, *J* = 3.7 Hz, 1 H, 7-H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 13.46 (–, *c*Pr-C), 14.15 (–, *c*Pr-C), 17.14 (+, CH_3), 22.21 (C_{quat}, *c*Pr-C), 26.51 (–, C-6), 50.31 (–, CH_2NCH_2), 51.93 (+, OCH_3), 52.13 (+, OCH_3), 57.91 (+, C-1), 67.10 (–, CH_2OCH_2), 119.91 (+, C-7), 124.75 (C_{quat}), 136.82

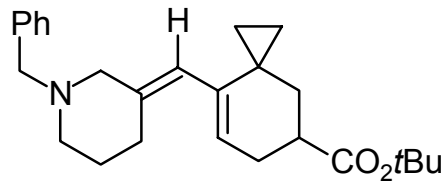
(C_{quat}), 146.69 (C_{quat}), 165.78 (C_{quat}, C=O), 168.46 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 335 (41) [M^+], 334 (100) [M^+ – H], 320 (12), 276 (16), 216 (13), 189 (17), 157 (11), 114 (26), 100 (34); elemental analysis calcd (%) for $C_{18}H_{25}NO_5$ (335.4): C 64.46, H 7.51; found: C 64.19, H 7.76.

*2.6.7. An attempt for the synthesis of tert-Butyl 8-Benzyl-13-(1-morpholin-4-ylethyl)-8-azadisipiro[2.2.5.2]tridec-12-ene-5-carboxylate (**205**)*

1) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 209 mg, 2.40 mmol), (*E*)- 1-Benzyl-3-iodomethylenepiperidine (**202**, 626 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3.5 h. After cooling the mixture to room temperature, *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 60 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 1:1). In isolated fractions, desired compound **205** could not be observed. The reaction gave only the spirooctene **203** (157 mg, 20%, yellowish oil).

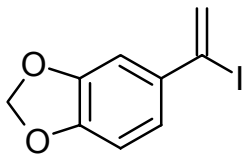
2) According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), morpholine (**78a**, 261 mg, 3.00 mmol), (*E*)- 1-Benzyl-3-iodomethylenepiperidine (**202**, 626 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 4 h. After cooling the mixture to room temperature, *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 72 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 1:1). In isolated fractions, desired compound **205** could not be observed. The reaction gave only the spirooctene **203** (204 mg, 20%, yellowish oil).

***tert*-Butyl 8-(1-benzyl-piperidin-3-ylidenemethyl)-spiro[2.5]oct-7-ene-5-carboxylate (203):**



IR (film): $\tilde{\nu}$ = 3063, 3026, 2976, 2932, 2793, 2744, 1726, 1494, 1454, 1391, 1367, 1314, 1287, 1258, 1151, 1170, 1019, 986, 968, 904, 848, 739, 699 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.29–0.37 (m, 1 H, *c*Pr-H), 0.38–0.46 (m, 1 H, *c*Pr-H), 0.54–0.60 (m, 1 H, *c*Pr-H), 0.79–0.85 (m, 1 H, *c*Pr-H), 1.34–1.39 (m, 1 H, 4- or 6-H), 1.42 [s, 9 H, $C(CH_3)_3$], 1.52–1.63 (m, 2 H), 1.93–2.02 (m, 1 H, 4- or 6-H), 2.19 (t, *J* = 5.8 Hz, 2 H, pyridine), 2.31–2.36 (m, 2 H), 2.49 (t, *J* = 5.5 Hz, 2 H, pyridine), 2.59–2.69 (m, 1 H, 5-H), 2.85 (s, 2 H, pyridine), 3.51(s, 2 H, Bn), 5.29 (bs., 1 H, C*H*), 5.38–5.41 (m, 1 H, 7-H), 7.29–7.31 (m, 1 H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = 10.98 (–, *c*Pr-C), 12.56 (–, *c*Pr-C), 19.81 (C_{quat}, *c*Pr-C), 25.93 (–), 27.50 (–, pyridine), 27.99 [+, $C(CH_3)_3$], 28.36 (–), 36.99 (–, C-4 or -6), 40.22 (+, C-5), 53.86 (–, pyridine), 61.48 (–, pyridine), 62.58 (–, Bn), 79.80 [C_{quat}, $C(CH_3)_3$], 120.99 (+, *C*H), 123.1 (+, C-7), 126.8 (+, Ph), 128.0 (+, 2 × Ph), 129.1 (+, 2 × Ph), 136.98 (C_{quat}), 138.02 (C_{quat}), 138.58 (C_{quat}), 174.85 (C_{quat}, C=O); MS (70 eV, EI) *m/z* (%): 393 (40) [M^+], 337 (25), 320 (9), 172 (38), 91 (100), 57 (17); elemental analysis calcd (%) for $C_{26}H_{35}NO_2$ (393.6): C 79.35, H 8.96; found: C 78.90, H 8.78.

*2.7. Preparation of 5-(1-Iodovinyl)benzo[1,3]dioxole (**192**)*



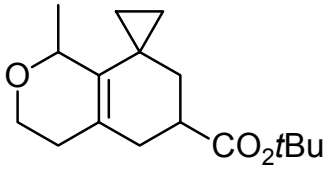
To an ice-cold solution of 5-[(1-diethoxyphosphinyl)oxo-vinyl]-benzo[1,3]dioxole* (2 g, 6.66 mmol) in anhydrous CH_2Cl_2 (20 mL) was added Me_3SiI (2.85 mL, 20.0 mmol) dropwise with a syringe. After stirring 15 min at 0 °C, the reaction mixture was quenched by addition of saturated $NaHCO_3$ (20 mL) and saturated Na_2SO_3 (20 mL) solutions. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated. The vinyl iodide was purified by column chromatography using *n*-pentane as an eluent. **192** was isolated as a very sensitive pink oil (1.092 g, 60%) and immediately used after isolation. * This precursor was prepared according to a known procedure from the corresponding ketone and directly used for the preparation of **192** without further purification.

^1H NMR (250 MHz, $CDCl_3$) δ = 5.98 (s, 2 H, OCH_2O), 6.35 (d, *J* = 1.4 Hz, 1 H, vinyl), 6.71–6.75 (m, 1 H, vinyl), 7.01–7.05 (m, 3 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 101.36

(–), 106.68 (C_{quat}), 107.49 (+, Ph), 108.16 (+, Ph-C), 122.13 (+, Ph-C), 126.13 (–), 135.84 (C_{quat}), 147.16 (C_{quat}), 147.93 (C_{quat}).

*2.8. An inter-intra-intermolecular queuing cascade involving bicyclopropylidene (**66**) a functionalized iodoalkene (**206**, **208**)*

2-Methyl-8-*tert*-butoxycarbonylspiro[cyclopropane-1',10-(3-oxabicyclo[4.4.0]dec-1(6)-ene)] (207):



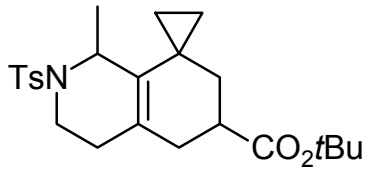
According to GP-B, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), K_2CO_3 (556 mg, 4.00 mmol), Et_4NCl (332 mg, 2.00 mmol), 3-iodobut-3-en-1-ol (**206**, 396 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous MeCN (4 mL) at 80 °C for 24 h. After cooling the mixture to room temperature, *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and then the mixture was heated with stirring at 80 °C for an additional 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate, 4:1) to yield **207** (140 mg, 25%, yellowish oil) as a mixture of two diastereomers (ratio 1.3:1 according to NMR).

Major and minor diastereomers*: R_f = 0.56 (light petroleum/ethyl acetate, 4:1); IR (film): $\tilde{\nu}$ = 3081, 2977, 2932, 1726, 1452, 1392, 1367, 1318, 1259, 1153, 1107, 1036, 984, 850 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.34–0.72 (m, 6 H, *c*Pr-H), 0.76–0.89 (m, 2 H, *c*Pr-H), 1.11 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.15–1.23 (m, 2 H), 1.28 (d, *J* = 6.4 Hz, 3 H, CH_3), 1.44 [s, 18 H, 2 × $C(CH_3)_3$], 1.69–2.27 (m, 10 H), 2.68–2.82 (m, 2 H), 3.58–3.78 (m, 3 H), 3.80–3.99 (m, 3 H); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.23 (–, *c*Pr-C), 11.87 (–, *c*Pr-C), 13.08 (–, *c*Pr-C), 13.43 (–, *c*Pr-C), 18.37 (C_{quat}, *c*Pr-C), 19.03 (C_{quat}, *c*Pr-C), 19.80 (+, CH_3), 20.58 (+, CH_3), 28.02 [+, 2 × $C(CH_3)_3$], 29.09 (–), 30.08 (–), 32.69 (–), 33.54 (–), 38.06 (–), 39.32 (–), 40.13 (+), 40.43 (+), 57.45 (–), 54.49 (–), 66.13 (+), 68.77 (+), 79.99 [C_{quat}, 2 × $C(CH_3)_3$], 124.40 (C_{quat}), 127.22 (C_{quat}), 132.29 (C_{quat}), 133.58 (C_{quat}), 174.68 (C_{quat}, C=O), 174.79 (C_{quat}, C=O); MS (DCI), *m/z* (%): 296 (100) [$M + NH_4^+$], 279 (2) [$M + H^+$], 240 (73), 232 (20); elemental analysis calcd (%) for $C_{17}H_{26}O_3$ (278.4): C 73.35, H 9.41; found: C 73.59, H 9.41. *Proton and carbon chemical shifts are given in one series for both diastereomers together because ^1H NMR and ^{13}C NMR spectra were not appropriate to classify all of the peaks for major and minor

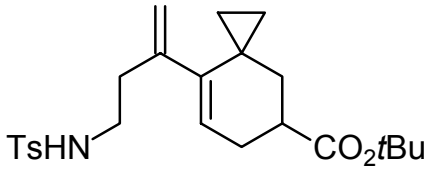
diastereomers. IR, DCI mass and elemental analysis were carried out for the mixture of diastereomers.

2-Methyl-3-(toluene-4-sulfonyl)-8-*tert*-butoxycarbonylspiro[cyclopropane-1',10-(3-aza-bicyclo[4.4.0]dec-1(6)-ene)](209) and 2,2-Dimethylpropionic acid 8-[1-methylene-3-toluene-4-sulfonylamino)-propyl]spiro[2.5]oct-7-en-5-yl ester (210) :

According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), *N*-(3-iodobut-3-enyl)-4-methylbenzenesulfonamide (**208**, 702.4 mg, 2.00 mmol) and bicyclopropylidene (**66**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (2 mL), at 80 °C for 3 h. After cooling the mixture to room temperature *tert*-butyl acrylate (**68b**, 512 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 4:1) to yield **209** (328 mg, 38%, colorless solid) and **210** (311 mg, 36%, yellowish oil).



209: m.p. 110 °C, R_f = 0.35 (light petroleum/ethyl acetate 4:1); IR (KBr): $\tilde{\nu}$ = 3097, 3072, 3002, 2978, 2909, 2869, 2829, 1716, 1597, 1448, 1433, 1372, 1367, 1338, 1263, 1158, 1089, 1033, 942, 815, 694 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 0.36–0.44 (m, 1H, *c*Pr-H), 0.49–0.67 (m, 2 H, *c*Pr-H), 0.80–0.89 (m, 1 H, *c*Pr-H), 1.05–1.11 (m, 1H), 1.18 (d, *J* = 6.5 Hz, 3 H, CH_3), 1.42 [s, 9 H, $C(CH_3)_3$], 1.63–1.98 (m, 4 H), 2.03–2.18 (m, 1 H), 2.41 (s, 1 H, CH_3), 2.47–2.59 (m, 1 H), 3.26–3.38 (m, 1 H), 3.63–3.79 (m, 2 H), 7.25 (d, *J* = 7.8 Hz, 2 H, Ph), 7.65 (d, *J* = 8.3 Hz, 2 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 11.91 (–, *c*Pr-C), 13.17 (–, *c*Pr-C), 18.75 (C_{quat}, *c*Pr-C), 20.21 (+, CH_3), 21.10 (+, CH_3), 28.01 [+, $C(CH_3)_3$], 28.25 (–), 33.09 (–), 37.42 (–), 38.15 (–), 40.47 (+), 46.93 (+), 79.52 [C_{quat}, $C(CH_3)_3$], 125.59 (C_{quat}), 127.45 (+, Ph-C), 129.42 (+, Ph-C), 132.62 (C_{quat}), 139.07 (C_{quat}), 142.67 (C_{quat}), 174.13 (C_{quat}, C=O); MS (70 eV, EI), *m/z* (%): 431 (4) [M^+], 416 (4) [$M^+ - CH_3$], 375 (6), 361 (17), 360 (100), 220 (26), 204 (10), 174 (18), 133 (11), 105 (15), 91 (66), 57 (52), 41 (24); elemental analysis calcd (%) for $C_{24}H_{33}NO_4S$ (431.6): C 66.79, H 7.71; found: C 66.68, H 7.50.



210: R_f = 0.31 (light petroleum/ethyl acetate 4:1); IR (film): $\tilde{\nu}$ = 3275 (N–H), 3080, 3003, 2976, 2924, 2872, 1728 (C=O), 1599, 1457, 1421, 1392, 1367, 1337, 1257, 1167, 1095, 985, 903, 847, 814, 667 cm^{-1}; ^1H

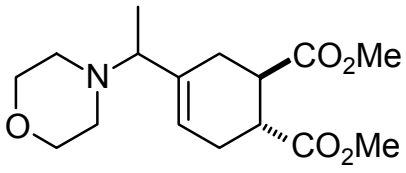
NMR (300 MHz, $CDCl_3$): δ = 0.20–0.28 (m, 1H, *c*Pr-H), 0.37–0.44 (m, 2 H, *c*Pr-H), 0.46–0.57 (m, 1H, *c*Pr-H), 1.14–1.20 (m, 1H), 1.35 [s, 9 H, $C(CH_3)_3$], 1.80 (t, *J* = 12.1 Hz, 1 H), 2.02–2.09 (m, 2 H), 2.11–2.18 (m, 2 H), 2.34 (s, 3 H, CH_3), 2.48–2.58 (m, 1 H, 5-H), 2.77–2.99 (m, 2 H), 4.27 (t, *J* = 5.9 Hz, 1 H), 4.53 (d, *J* = 2.7 Hz, 1 H, vinyl), 4.66 (br.s, 1 H, vinyl), 5.00–5.03 (m, 1 H, 7-H), 7.23 (d, *J* = 8.0 Hz, 2 H, Ph), 7.68 (d, *J* = 8.0 Hz, 2 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 11.71 (–, *c*Pr-C), 13.12 (–, *c*Pr-C), 18.43 (C_{quat}, *c*Pr-C), 21.26 (+, CH_3), 27.81 (–)*, 27.81 [+, $C(CH_3)_3$], 36.50 (–), 36.81 (–), 39.94 (+, C-5), 40.82 (–), 79.78 [C_{quat}, $C(CH_3)_3$], 115.14 (–, vinyl), 122.46 (+, C-7), 126.91 (+, Ph-C), 129.44 (+, Ph-C), 136.56 (C_{quat}), 141.52 (C_{quat}), 143.08 (C_{quat}), 144.14 (C_{quat}), 174.50 (C_{quat}, C=O). *The peak of this carbon sits under the broad singlet of the *tert*-butyl group. This carbon peak correlates clearly with the multiplet between 2.11–2.18 ppm in the HMQC spectrum. MS (ESI, MeOH) *m/z* (%): 885 (100) $[2M + Na]^+$, 454 (63) $[M + Na]^+$; HRMS (ESI) calcd. for $C_{24}H_{33}NO_4S$ $[M + H]^+$ 432.22031; found 432.22036

*2.9. Two-step queuing cascade reactions with methylenespiropentane (**81**)*

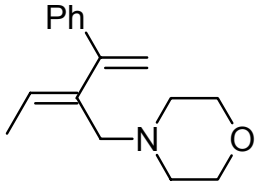
*2.9.1. The one-pot, two-step queuing cascade involving methylenespiropentane (**81**) iodobenzene **67**, morpholine **78a** and dimethyl fumarate **68d**.*

1,2-dimethyl 4-(1-morpholin-4-ylethyl)-5-phenyl-cyclohex-4-ene-carboxylate (227), 4-[2-(1-Phenylvinyl)-but-2-enyl]-morpholine (228), 4-(2-Methylene-4-phenyl-pent-4-enyl)-morpholine (230):

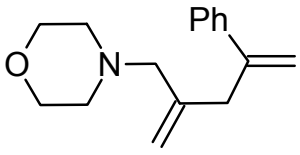
Palladium acetate (22.4 mg, 100 µmol, 5 mol%) and tri-2-furylphosphine (46.4 mg, 200 µmol, 10 mol%), were suspended in anhydrous DMF (1 mL) in a screw-cap pyrex bottle. Argon was bubbled through the mixture for 5 min, and then the morpholine (**78a**, 174 mg, 2.00 mmol), triethylamine (202 mg, 2.00 mmol), iodobenzene (**67**, 408 mg, 2.00 mmol) and methylenespiropentane (**81**) (320 mg, 4.00 mmol) were added. After having stirred the mixture at 80 °C, for 3 h the bottle was cooled to ambient temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, then the mixture was stirred at 80 °C, for 48 h in a preheated oil bath. After cooling to room temperature, the reaction mixture was taken up in 20 mL of diethyl ether. The solution was washed with water (2 × 20 mL). The aqueous phase was extracted with diethyl ether (2 × 20 mL). The combined organic phases were dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator, the residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate,1:1) to yield **227** (240 mg, 31%, colorless oil), **228** (39 mg, 8%, colorless oil) and **230** (25 mg, 5%, colorless oil).



227: R_f = 0.61 (light petroleum/ethyl acetate 1:1); IR (film): $\tilde{\nu}$ = 3054, 3020, 2952, 2849, 2805, 2688, 1734, 1600, 1492, 1437, 1379, 1346, 1331, 1297, 1259, 1221, 1162, 1117, 1070, 1004, 911, 864, 798, 771, 744, 704 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 0.97 (d, J = 6.8 Hz, 3 H, CH_3), 2.10–2.30 (m, 4 H, CH_2NCH_2), 2.34–2.40 (m, 1 H, 3-H or 6-H), 2.49–2.58 (m, 1 H, 3-H or 6-H), 2.67–2.91 (AB system: δ_A = 2.89, δ_B = 2.70, J_{AB} = 13.0 Hz, 2 H, 3-H or 6-H), 2.96–3.12 (m, 3 H, 3× C*H*), 3.56–3.61 (m, 4 H, CH_2OCH_2), 3.63 (s, 3 H, OCH_3), 3.69 (s, 3 H, OCH_3), 6.95–6.99 (m, 2 H, Ph), 7.17–7.29 (m, 3 H, Ph); ^{13}C NMR (75.5 MHz, $CDCl_3$, DEPT): δ = 15.66 (+, CH_3), 31.01 (+, *C*H), 35.80 (–, C-3 or C-6), 36.75 (+, *C*H), 46.08 (+, *C*H), 51.65 (+, OCH_3), 51.79 (+, OCH_3), 53.22 (–, CH_2NCH_2), 57.89 (–, C-3 or C-6), 60.82 (–, CH_2OCH_2), 126.61 (+, Ph), 128.00 (+, 2 × Ph), 128.13 (+, 2 × Ph), 133.69 (C_{quat}), 133.41 (C_{quat}), 141.70 (C_{quat}), 174.06 (C_{quat}, C=O), 175.86 (C_{quat}, C=O); MS (70 eV, EI), m/z (%): 387 (100) [M^+], 356 (8), 328 (10), 268 (8), 241 (14), 181 (40), 100 (12); elemental analysis calcd (%) for $C_{22}H_{29}NO_5$ (387.5): C 68.20, H 7.54; found: C 67.97, H 7.69.



228: R_f = 0.71 (light petroleum/ethyl acetate 1:1); IR (film): $\tilde{\nu}$ = 3056, 3023, 2954, 2850, 2804, 2759, 1737, 1496, 1458, 1437, 1411, 1381, 1349, 1329, 1298, 1206, 1223, 1197, 1162, 1117, 1066, 1004, 982, 915, 864, 801, 771, 742, 706 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.68 (d, J = 6.8 Hz, 3 H, CH_3), 2.38 (t, J = 4.6 Hz, 4 H, CH_2NCH_2), 2.91 (s, 2 H), 3.65 (t, J = 4.7 Hz, 4 H, CH_2OCH_2), 5.05 (d, J = 1.6 Hz, 1 H, vinyl-H), 5.58 (d, J = 1.6 Hz, 1 H, vinyl-H), 5.78 (q, J = 6.8 Hz, 1 H, vinyl-H), 7.17–7.39 (m, 5 H, Ph); ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 14.56 (+, CH_3), 53.39 (–, CH_2NCH_2), 64.47 (–, CH_2), 66.99 (–, CH_2OCH_2), 114.78 (–, vinyl-C), 125.83 (+, vinyl-C), 126.41 (+, 2 × Ph), 127.36 (+, Ph), 128.20 (+, 2 × Ph), 137.59 (C_{quat}), 139.79 (C_{quat}), 146.76 (C_{quat}); MS (70 eV, EI), m/z (%): 243 (48) [M^+], 228 (8), 198 (8), 143 (8), 128 (9), 115 (8), 100 (100), 56 (10).



230: R_f = 0.60 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 3081, 3023, 2958, 2912, 2853, 2805, 1739, 1701, 1650, 1626, 1574, 1495, 1453, 1346, 1329, 1290, 1268, 1243, 1118, 1071, 1035, 1012, 965, 867, 779, 733, 705 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 2.35 (t, J = 4.3 Hz, 4 H, CH_2NCH_2), 2.86 (s, 2 H), 3.30 (s, 2 H), 3.70 (t, J = 4.7 Hz, 4 H, CH_2OCH_2), 4.94 (d, J = 15 Hz, 2 H, vinyl-H), 5.14 (s, 1 H, vinyl-H), 5.45 (d, J = 1.6 Hz, 1 H, vinyl-H), 7.24–7.34 (m, 3 H, Ph), 7.44–7.48 (m, 2 H, Ph); ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 40.01 (–, CH_2), 53.56 (–, CH_2NCH_2), 63.94 (–, CH_2), 67.13 (–, CH_2OCH_2), 114.55

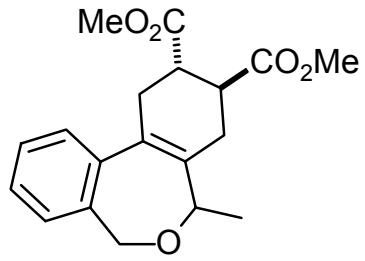
(–, vinyl-C), 114.81 (–, vinyl-C), 126.12 (+, 2 × Ph), 127.31 (+, Ph), 128.08 (+, 2 × Ph), 140.98 (C_{quat}), 143.70 (C_{quat}), 145.65 (C_{quat}); MS (70 eV, EI), m/z (%): 243 (74) [M^+], 228 (15), 213 (10), 198 (13), 184 (8), 143 (23), 138 (46), 115 (20), 100 (100), 95 (18), 77 (12), 56 (14).

2.9.2. *The one-pot, two-step queuing cascade involving methylenespiropentane (**81**) functionalized iodoarenes **231a–g**, **240** and dimethyl fumarate **68d**.*

2.9.2.1. General procudere (GP)

Palladium acetate (22.4 mg, 100 µmol, 5 mol%) and tri-2-furylphosphine (46.4 mg, 200 µmol, 10 mol%), were suspended in anhydrous DMF (1 mL) in a screw-cap pyrex bottle. Argon was bubbled through the mixture for 5 min, and then triethylamine (202 mg, 2.00 mmol), the respective iodoarene (**231a**–**g**, 2.00 mmol) and methylenespiropentane (**81**) (320 mg, 4.00 mmol) were added. After having stirred the mixture for the given time at the stated temperature the bottle was cooled to ambient temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and then the mixture was stirred for an additional time as stated at the given temperature in a preheated oil bath. After cooling to room temperature, the reaction mixture was taken up in 20 mL of diethyl ether. The solution was washed with water (2 × 20 mL). The aqueous phase was extracted with diethyl ether (2 × 20 mL). The combined organic phases were dried ($MgSO_4$). After removal of the solvent in a rotatory evaporator, the residue was subjected to chromatography on silica gel.

2,3-Dimethyl 5-methyl-1,2,3,4,5,7-hexahydro-dibenzo[c,e]oxepine-dicarboxylate (234a) :

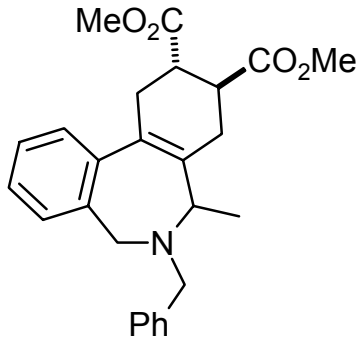


According to GP, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), 2-iodobenzyl alcohol (**231a**, 468 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **234a** (145 mg, 22%, colorless solid) as a mixture of two diastereomers (ratio 1:1 according to NMR). R_f = 0.32 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 2953, 2857,

1735, 1487, 1437, 1381, 1333, 1246, 1198, 1176, 1083, 1036, 914, 843, 755 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.16 (d, *J* = 6.9 Hz, 3 H, CH_3), 1.17 (d, *J* = 6.1 Hz, 3 H, CH_3), 2.19–2.49 (m, 2 H, 1-H or 4-H), 2.54–2.65 (m, 3 H, 1-H or 4-H), 2.79–3.13 [m, 7 H, 2 × (2-H + 3-H), 1-H or 4-H], 3.68 (s, 9 H, 3 × OCH_3), 3.71 (s, 3 H, OCH_3), 3.76–3.89 (m, 2 H, 2 × 5-H), 4.17 (d, *J* = 12.5 Hz, 1 H, 7-H), 4.21 (d, *J* = 12.5 Hz, 1 H, 7-H), 4.37 (d, *J* = 3.1 Hz, 1 H, 7-H), 4.41 (d, *J* = 3.1 Hz, 1 H, 7-H), 7.19–7.37 (m, 8 H, Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 16.22 (+, CH_3), 16.63 (+, CH_3), 26.99 (–, C-1 or C-4), 28.07 (–, C-1 or C-4), 30.39 (–, C-1 or C-4), 31.20 (–, C-1 or C-4), 40.92 (+, C-2 or C-3), 40.93 (+, C-2 or C-3), 41.55 (+, C-2 or C-3), 41.78 (+, C-2 or C-3), 52.00 (+, 2 × OCH_3), 52.04 (+, 2 × OCH_3), 67.72 (–, C-7), 67.77 (–, C-7), 69.51 (+, C-5), 70.17 (+, C-5), 125.19 (+, Ar), 125.55 (+, Ar), 127.59 (+, Ar), 127.89 (+, Ar), 128.23 (+, Ar), 128.25 (+, Ar), 128.88 (+, Ar), 129.27 (+, Ar), 132.38 (C_{quat}), 132.84 (C_{quat}), 133.60 (C_{quat}), 134.26 (C_{quat}), 136.04 (C_{quat}), 136.45 (C_{quat}), 140.80 (C_{quat}), 141.94 (C_{quat}), 174.49 (C_{quat}, C=O), 174.53 (C_{quat}, C=O), 174.77 (C_{quat}, C=O), 175.11 (C_{quat}, C=O); MS (70 eV, EI), m/z (%): 330 (30) [M^+], 315 (11) [$M^+ - CH_3$], 299 (17), 270 (22), 252 (70), 227 (38), 211 (18), 195 (22), 193 (66), 167 (100), 165 (34), 105 (34), 84 (85), 79 (38), 53 (24), 43 (38); elemental analysis calcd (%) for $C_{19}H_{22}O_5$ (330.4): C 69.07, H 6.71; found: C 68.77, H 6.56. Proton and carbon chemical shifts are given in one series for both diastereomers together because ^1H NMR and ^{13}C NMR spectra were not appropriate to classify all of the peaks for each diastereomers. IR, EI mass and elemental analysis were carried out for the mixture of diastereomers.

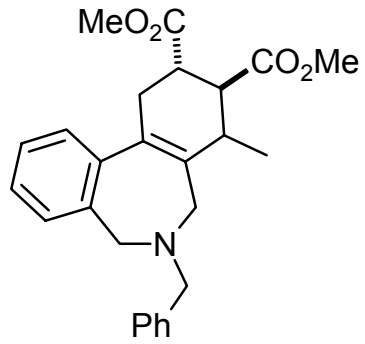
2,3-Dimethyl 6-benzyl-5-methyl-2,3,4,5,6,7-hexahydro-1H-dibenzo[c,e]azepinedicarboxylate (234b) and 2,3-Dimethyl 6-benzyl-5-methyl-2,3,4,5,6,7-hexahydro-1H-dibenzo [c,e]azepinedicarboxylate (235b)

According to GP, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), benzyl-(2-iodobenzyl)amine (**231b**, 646 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 1:1) to yield **234b** (186 mg, 22%, colorless oil) as a mixture of two diastereomers (ratio 1.6:1 according to NMR) and **235b** (43 mg, 5% colorless oil).



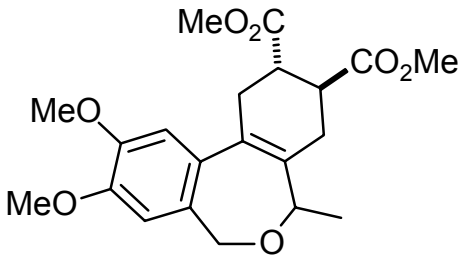
Major diastereomer (234b): R_f = 0.54 (light petroleum/ethyl acetate 1:1); *IR (film): $\tilde{\nu}$ = 3064, 3037, 2991, 2895, 2798, 1734, 1726, 1455, 1437, 1373, 1325, 1300, 1242, 1202, 1175, 1154, 1130, 1088, 1067, 1029, 1007, 911, 877, 836, 807, 755, 734, 701 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.13 (d, J = 6.8 Hz, 3 H, CH_3), 2.33–2.45 (m, 2 H, 1-H or 4-H), 2.73–2.80 (m, 1 H, 1-H or 4-H), 2.88–3.02 [m, 4 H, 1-H or 4-H, 2-H, 3-H, 5-H], 3.24–3.38 (AB system: δ_A = 3.35, δ_B = 3.27, J_{AB} = 12.2 Hz, 2 H, Bn), 3.58 (s, 2 H, 7-H), 3.71 (s, 3 H, OCH_3), 3.75 (s, 3 H, OCH_3), 7.14–7.41 (m, 9 H, Ar, Ph); ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 16.26 (+, CH_3), 30.79 (–, C-1 or C-4), 31.63 (–, C-1 or C-4), 41.81 (+, C-2 or C-3), 41.89 (+, C-2 or C-3), 52.03 (+, OCH_3), 52.06 (+, OCH_3), 54.81 (–, Bn), 55.63 (–, C-7), 56.72 (+, C-5), 125.50 (+, Ar), 126.88 (+, Ar), 127.10 (+, Ar), 127.37 (+, Ar), 128.36 (+, 2 × Ph), 128.98 (+, 2 × Ph), 129.73 (+, Ph), 133.26 (C_{quat}), 133.54 (C_{quat}), 135.54 (C_{quat}), 140.01 (C_{quat}), 141.04 (C_{quat}), 175.04 (C_{quat}, C=O), 175.40 (C_{quat}, C=O); *MS (70 eV, EI), m/z (%): 419 (8) [M^+], 404 (100) [$M^+ - CH_3$], 388 (5), 91 (40); *elemental analysis calcd (%) for $C_{26}H_{29}NO_4$ (419.5): C 74.44, H 6.97; found: C 74.21, H 6.72.

Minor diastereomer (234b): R_f = 0.49 (light petroleum/ethyl acetate 1:1); ^1H NMR (300 MHz, $CDCl_3$): δ = 1.00 (d, J = 6.7 Hz, 3 H, CH_3), 2.45–2.75 (m, 2 H, 1-H + 4-H), 3.05–3.16 (m, 3 H, 2-H, 3-H, 5-H], 3.20–3.37 (AB system: δ_A = 3.35, δ_B = 3.22, J_{AB} = 11.1 Hz, 2 H, Bn), 3.51–3.86 (AB system: δ_A = 3.83, δ_B = 3.54, J_{AB} = 13.1 Hz, 2 H, 7-H), 3.72 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 7.17–7.41 (m, 9 H, Ar, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 17.92 (+, CH_3), 30.57 (–, C-1 or C-4), 31.13 (–, C-1 or C-4), 41.28 (+, C-2 or C-3), 41.32 (+, C-2 or C-3), 52.07 (+, 2 × OCH_3), 55.95 (–, Bn), 57.10 (+, C-5), 57.45 (–, C-7), 125.05 (+, Ar), 126.89 (+, Ar), 127.03 (+, Ar), 127.39 (+, Ar), 128.30 (+, 2 × Ph), 128.87 (+, 2 × Ph), 129.42 (+, Ph), 131.45 (C_{quat}), 132.95 (C_{quat}), 136.00 (C_{quat}), 139.83 (C_{quat}), 142.01 (C_{quat}), 174.79 (C_{quat}, C=O), 174.86 (C_{quat}, C=O). *IR, EI mass and elemental analysis were carried out for the mixture of diastereomers.



235b: IR (film): $\tilde{\nu}$ = 3061, 3025, 2950, 2799, 1734, 1495, 1436, 1362, 1265, 1198, 1174, 1121, 1063, 1027, 912, 848, 755, 736, 700, 668 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.30 (d, *J* = 7.1 Hz, 3 H, CH_3), 2.33 (d, *J* = 11.0 Hz, 1 H, 5-H), 2.40–2.50 (m, 1 H, 1-H), 2.59–2.67 (m, 2 H, 2-H or 3-H and 4-H), 2.80 (d, *J* = 11.1 Hz, 1 H, 5-H), 2.93 (dd, *J* = 4.8, 17.0 Hz, 1 H, 1-H), 3.03–3.12 (m, 1 H, 2-H or 3-H), 3.35–3.49 (m, 2 H, Bn or 7-H), 3.69 (s, 3 H, OCH_3), 3.73 (s, 3 H, OCH_3), 3.63–3.77 (m, 2 H, Bn or 7-H), 7.19–7.36 (m, 9 H, Ar, Ph); ^{13}C NMR (50.3 MHz, $CDCl_3$, DEPT): δ = 19.22 (+, CH_3), 30.80 (–, C-1), 38.21 (+, C-2 or C-3), 42.54 (+, C-2 or C-3), 50.40 (+, C-4), 51.90 (+, OCH_3), 51.97 (+, OCH_3), 52.90 (–, C-5), 55.50 (–, Bn or C-7), 59.71 (–, Bn or C-7), 125.70 (+, Ar), 126.94 (+, 2 × Ar), 127.30 (+, Ar), 128.24 (+, 2 × Ph), 128.81 (+, 2 × Ph), 129.92 (+, Ph), 132.99 (C_{quat}), 134.94 (C_{quat}), 135.94 (C_{quat}), 139.31 (C_{quat}), 141.00 (C_{quat}), 174.53 (C_{quat}, C=O), 175.34 (C_{quat}, C=O); MS (70 eV, EI), m/z (%): 419 (42) [M^+], 388 (8), 327 (16), 318 (12), 268 (14), 220 (20), 192 (23), 182 (34), 165 (32), 150 (22), 105 (83), 91 (100), 84 (78), 59 (54), 45 (35); HRMS-ESI for $C_{26}H_{29}NO_4$ (419.53): [*M* + H]$^+$ 420.21705, calcd. 420.21693.

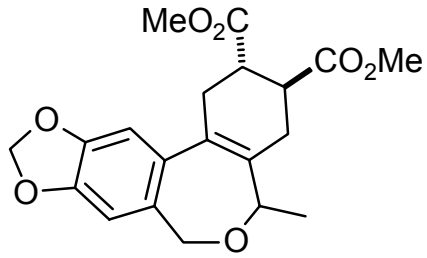
2,3-Dimethyl 9,10-dimethoxy-5-methyl-1,2,3,4,5,7-hexahydro-dibenzo[c,e]oxepine-dicarboxylate (234c) :



According to GP, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), 2-iodo-4,5-dimethoxybenzyl alcohol (**231c**, 588 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **234c** (142 mg, 18%, colorless solid) as a mixture of two diastereomers (ratio 1.6:1 according to NMR). R_f = 0.51 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 2952, 2854, 1736, 1605, 1573, 1515, 1437, 1375, 1248, 1199, 1174, 1131, 1081, 1023, 863, 803, 768 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.15 (d, *J* = 6.9 Hz, 3 H, CH_3), 1.16 (d, *J* = 6.6 Hz, 3 H, CH_3), 2.15–2.41 (m, 2 H, 1-H or 4-H), 2.52–2.61 (m, 3 H, 1-H

or 4-H), 2.71–3.08 [m, 7 H, 2 × (2-H + 3-H), 1-H or 4-H], 3.67 (s, 3 H, OCH_3), 3.68 (s, 6 H, 2 × OCH_3), 3.69 (s, 3 H, OCH_3), 3.73–3.82 (m, 2 H, 2 × 5-H), 3.84 (s, 6 H, 2 × OCH_3), 3.85 (s, 3 H, OCH_3), 3.86 (s, 3 H, OCH_3), 4.09–4.22 (m, 4 H, 2 × 7-H), 6.73 (s, 1 H, Ar), 6.78 (s, 2 H, Ar), 6.80 (s, 1 H, Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 16.52 (+, CH_3), 17.46 (+, CH_3), 26.91 (–, C-1 or C-4), 28.01 (–, C-1 or C-4), 30.45 (–, C-1 or C-4), 31.31 (–, C-1 or C-4), 40.91 (+, C-2 or C-3), 40.96 (+, C-2 or C-3), 41.55 (+, C-2 or C-3), 41.82 (+, C-2 or C-3), 52.00 (+, 4 × OCH_3), 55.78 (+, 2 × OCH_3), 55.84 (+, 2 × OCH_3), 67.31 (–, C-7), 67.40 (–, C-7), 69.39 (+, C-5), 69.95 (+, C-5), 108.07 (+, Ar), 108.48 (+, Ar), 111.65 (+, Ar), 111.99 (+, Ar), 128.84 (C_{quat}), 129.32 (C_{quat}), 131.56 (C_{quat}), 132.08 (C_{quat}), 133.19 (C_{quat}), 133.61 (C_{quat}), 134.21 (C_{quat}), 134.49 (C_{quat}), 148.07 (C_{quat}), 148.30 (C_{quat}), 148.72 (2 × C_{quat}), 174.47 (C_{quat}, C=O), 174.59 (C_{quat}, C=O), 174.77 (C_{quat}, C=O), 175.11 (C_{quat}, C=O); MS (70 eV, EI), m/z (%): 390 (100) [M^+], 375 (47) [$M^+ - CH_3$], 359 (22), 312 (16), 287 (55), 253 (9), 227 (12), 59 (10); elemental analysis calcd (%) for $C_{21}H_{26}O_7$ (390.4): C 64.60, H 6.71; found: C 64.35, H 6.41. Proton and carbon chemical shifts are given in one series for both diastereomers together because ^{1}H NMR and ^{13}C NMR spectra were not appropriate to classify all of the peaks for each diastereomers. IR, EI mass and elemental analysis were carried out for the mixture of diastereomers.

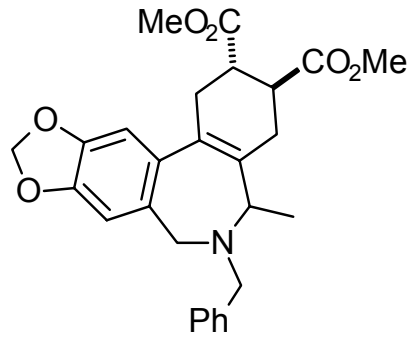
2,3-Dimethyl 5-methyl-2,3,5,7-tetrahydro-1H,4H-6,9,11-trioxa-benzo[3,4]cyclohepta[1,2-f]indene-dicarboxylate (234d) :



According to GP, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), (6-iodo-benzo[1,3]dioxol-5-yl)-methanol (**231d**, 556 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **234d** (155 mg, 21%, colorless solid) as a mixture of two diastereomers (ratio 1.6:1 according to NMR). R_f = 0.24 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 2977, 2953, 2907, 2857, 1724, 1504, 1484, 1436, 1381, 1324, 1267, 1242, 1195, 1155, 1077, 1039, 1014, 976, 934, 871, 820, 793, 739 cm^{-1}; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.17 (d, J = 6.6 Hz, 3 H, CH_3), 1.18 (d, J = 7.0 Hz, 3 H, CH_3), 2.17–2.41 (m, 2 H,

1-H or 4-H), 2.52–2.64 (m, 3 H, 1-H or 4-H), 2.74–2.89 (m, 2 H, 1-H or 4-H), 2.91–3.05 [m, 3 H, 2 × (2-H or 3-H), 1-H or 4-H], 2.08–3.13 [m, 2 H, 2 × (2-H or 3-H)], 3.72 (s, 9 H, 3 × OCH_3), 3.74 (s, 3 H, OCH_3), 3.77–3.90 (m, 2 H, 2 × 5-H), 4.10 (t, J = 10.5 Hz, 2 H, 7-H), 4.27 (d, J = 3.0 Hz, 1 H, 7-H), 4.32 (d, J = 3.3 Hz, 1 H, 7-H), 5.96 (s, 2 H, 10-H), 5.97 (s, 2 H, 10-H), 6.76 (s, 1 H, Ar), 6.78 (s, 1 H, Ar), 6.80 (s, 1 H, Ar), 6.81 (s, 1 H, Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 16.47 (+, CH_3), 17.34 (+, CH_3), 26.73 (–, C-1 or C-4), 27.96 (–, C-1 or C-4), 30.33 (–, C-1 or C-4), 31.30 (–, C-1 or C-4), 40.84 [+, 2 × C-2 or C-3)], 41.51 (+, C-2 or C-3), 41.74 (+, C-2 or C-3), 52.04 (+, 4 × OCH_3), 67.24 (–, C-7), 67.36 (–, C-7), 69.28 (+, C-5), 69.74 (+, C-5), 101.16 (–, C-10), 101.23 (–, C-10), 105.48 (+, Ar), 105.87 (+, Ar), 109.09 (+, Ar), 109.45 (+, Ar), 130.03 (C_{quat}), 130.57 (C_{quat}), 131.67 (C_{quat}), 132.23 (C_{quat}), 133.60 (C_{quat}), 134.17 (C_{quat}), 134.77 (C_{quat}), 136.02 (C_{quat}), 146.71 (C_{quat}), 146.97 (C_{quat}), 147.64 (C_{quat}), 147.73 (C_{quat}), 174.42 (C_{quat}, C=O), 174.50 (C_{quat}, C=O), 174.75 (C_{quat}, C=O), 175.10 (C_{quat}, C=O); MS (70 eV, EI), m/z (%): 374 (64) [M^+], 359 (34) [$M^+ - CH_3$], 343 (16), 314 (21), 296 (34), 271 (100), 239 (20), 237 (28), 211 (35), 181 (64), 153 (27), 128 (12), 115 (11), 57 (26), 43 (73); elemental analysis calcd (%) for $C_{20}H_{22}O_7$ (374.4): C 64.16, H 5.92; found: C 64.39, H 5.80. Proton and carbon chemical shifts are given in one series for both diastereomers together because ^{1}H NMR and ^{13}C NMR spectra were not appropriate to classify all of the peaks for each diastereomers. IR, EI mass and elemental analysis were carried out for the mixture of diastereomers.

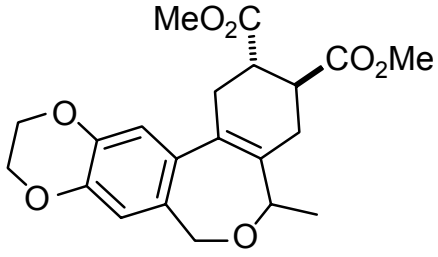
2,3-Dimethyl 6-benzyl-5-methyl-2,3,4,5,6,7-hexahydro-1H-9,11-dioxa-6-aza-benzo[3,4] cyclohepta[1,2-f]indene-dicarboxylate (234e) :



According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol) benzyl-(6-iodo-benzo[1,3]dioxol-5-ylmethyl)amine (**231e**, 734 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 1:1) to yield **234e** (185 mg, 20%, colorless solid) as a mixture of two diastereomers (ratio 1.5:1 according to NMR). R_f = 0.52 (light petroleum/ethyl acetate 1:1); *IR (KBr): $\tilde{\nu}$ = 2948, 2891, 2789, 1732,

1502, 1483, 1457, 1437, 1369, 1325, 1261, 1239, 1177, 1129, 1035, 930, 884, 826, 749, 730, 703 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.01 (d, *J* = 6.8 Hz, 3 H, CH_3), 1.13 (d, *J* = 6.8 Hz, 3 H, CH_3), 2.27–2.73 [m, 8 H, 2 × (1-H + 4-H)], 2.79–3.00 (m, 3 H, 2-H, 3-H, 5-H), 3.06–3.23 [m, 7 H, (2-H + 3-H), (Bn or 7-H), 5-H], 2.48–3.62 (m, 3 H, Bn or 7-H), 3.70 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 3.72 (s, 3 H, OCH_3), 3.74 (s, 3 H, OCH_3), 3.70–3.74 (m, 1 H, Bn or 7-H)*, 5.91–5.94 (m, 4 H, 2 × 10-H), 6.64 (s, 1 H, Ar), 6.65 (s, 1 H, Ar), 6.73 (s, 1 H, Ar), 6.78 (s, 1 H, Ar), 7.24–7.29 (m, 10 H, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 16.12 (+, CH_3), 17.62 (+, CH_3), 30.50 (–, C-1 or C-4), 30.61 (–, C-1 or C-4), 30.79 (–, C-1 or C-4), 31.82 (–, C-1 or C-4), 41.18 (+, C-2 or C-3), 41.21 (+, C-2 or C-3), 41.80 (+, C-2 or C-3), 41.86 (+, C-2 or C-3), 52.03 (+, 4 × OCH_3), 54.31 (–, Bn or C-7), 55.38 (–, Bn or C-7), 55.46 (–, Bn or C-7), 56.88 (+, C-5), 57.23 (+, C-5), 57.23 (–, Bn or C-7), 100.94 (–, C-10), 100.99 (–, C-10), 105.55 (+, Ar), 105.97 (+, Ar), 109.66 (+, Ar), 109.90 (+, Ar), 126.85 (+, 2 × Ph), 128.27 (+, 2 × Ph), 128.33 (+, 2 × Ph), 128.79 (+, 2 × Ph), 128.87 (+, 2 × Ph), 129.39 (C_{quat}), 129.79 (C_{quat}), 131.23 (C_{quat}), 132.06 (C_{quat}), 132.58 (C_{quat}), 133.21(C_{quat}), 134.65 (C_{quat}), 135.65 (C_{quat}), 139.83 (C_{quat}), 139.95 (C_{quat}), 146.24 (C_{quat}), 146.34(C_{quat}), 146.95 (C_{quat}), 146.97 (C_{quat}), 174.68 (C_{quat}, C=O), 174.78 (C_{quat}, C=O), 174.95 (C_{quat}, C=O), 175.35 (C_{quat}, C=O); MS (70 eV, EI), m/z (%): 448 (100) [M^+], 432 (4) [$M^+ - CH_3$], 91 (72); elemental analysis calcd (%) for $C_{27}H_{29}NO_6$ (463.5): C 69.96, H 6.31; found: C 70.22, H 6.11. Proton and carbon chemical shifts are given in one series for both diastereomers together because ^1H NMR and ^{13}C NMR spectra were not appropriate to classify all of the peaks for each diastereomers. IR, EI mass and elemental analysis were carried out for the mixture of diastereomers. * This multiplet sits under singlets of methoxy groups.

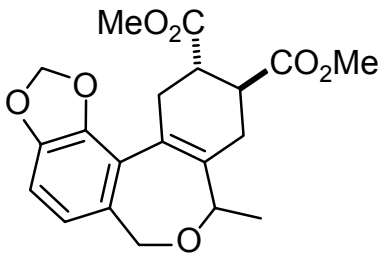
2,3-Dimethyl 5-methyl-2,3,5,7,10,11-hexahydro-1H,4H-6,9,12-trioxa-benzo[3,4] cyclohepta[1,2-b]naphthalene-dicarboxylate (234f) :



According to GP, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), (7-iodo-2,3-dihydro-benzo[1,4]dioxin-6-yl)-methanol (**231f**, 584 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue

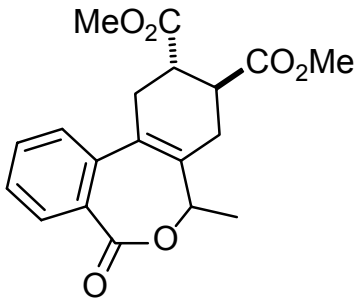
was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **234f** (178 mg, 23%, colorless solid) as a mixture of two diastereomers (ratio 1.1:1 according to NMR). R_f = 0.55 (light petroleum/ethyl acetate 3:1); IR (KBr): $\tilde{\nu}$ = 2952, 2849, 1728, 1573, 1500, 1437, 1370, 1309, 1248, 1197, 1177, 1156, 1067, 1041, 1002, 978, 948, 926, 901, 887, 847, 783, 749 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.20 (d, *J* = 6.6 Hz, 3 H, CH_3), 1.21 (d, *J* = 6.6 Hz, 3 H, CH_3), 2.18–2.42 (m, 2 H, 1-H or 4-H), 2.54–2.56 (m, 2 H, 1-H or 4-H), 2.63–2.65 (m, 1 H, 1-H or 4-H), 2.74–2.87 (m, 2 H, 1-H or 4-H), 2.91–3.05 [m, 3 H, 2 × (2-H or 3-H), 1-H or 4-H], 3.08–3.13 [m, 2 H, 2 × (2-H or 3-H)], 3.73 (s, 9 H, 3 × OCH_3), 3.75 (s, 3 H, OCH_3), 3.83–3.98 (m, 2 H, 2 × 5-H), 4.11–4.34 (m, 4 H, 2 × 7-H), 4.26 [s, 8 H, 2 × (10-H + 11-H)], 6.80 (s, 1 H, Ar), 6.82 (s, 1 H, Ar), 6.84 (s, 2 H, Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 16.59 (+, CH_3), 17.58 (+, CH_3), 26.93 (–, C-1 or C-4), 28.04 (–, C-1 or C-4), 30.38 (–, C-1 or C-4), 31.33 (–, C-1 or C-4), 40.82 [+, 2 × C-2 or C-3)], 41.53 (+, C-2 or C-3), 41.76 (+, C-2 or C-3), 51.95 (+, OCH_3), 51.99 (+, 3 × OCH_3), 64.28 [–, 2 × (C-10 + C-11)], 67.07 (–, 2 × C-7), 69.45 (+, C-5), 70.31 (+, C-5), 114.09 (+, Ar), 114.46 (+, Ar), 117.45 (+, Ar), 117.77 (+, Ar), 129.86 (C_{quat}), 130.13 (C_{quat}), 131.51 (C_{quat}), 131.83 (C_{quat}), 133.04 (C_{quat}), 133.85 (C_{quat}), 134.08 (C_{quat}), 135.23 (C_{quat}), 142.61 (C_{quat}), 142.88 (C_{quat}), 143.29 (C_{quat}), 143.36 (C_{quat}), 174.46 (C_{quat}, C=O), 174.55 (C_{quat}, C=O), 174.80 (C_{quat}, C=O), 175.16 (C_{quat}, C=O); MS (70 eV, EI), m/z (%): 388 (54) [M^+], 373 (22) [M^+ – CH_3], 357 (14), 328 (22), 310 (44), 285 (100), 251 (32), 225 (45), 59 (32), 49 (45), 43 (51); elemental analysis calcd (%) for $C_{21}H_{24}O_7$ (388.4): C 64.94, H 6.23; found: C 64.64, H 6.03. Proton and carbon chemical shifts are given in one series for both diastereomers together because ^1H NMR and ^{13}C NMR spectra were not appropriate to classify all of the peaks for each diastereomers. IR, EI mass and elemental analysis were carried out for the mixture of diastereomers.

10,11-Dimethyl 8-methyl-6,8,9,10,11,12-hexahydro-1,3,7-trioxa-benzo[6,7]cyclohepta [1,2-e]indene-dicarboxylate (234g) :



According to GP, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), (5-iodo-benzo[1,3]dioxol-4-yl)-methanol (**231g**, 556 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 1:1) to yield **234g** (219 mg, 29%, colorless solid) as a mixture of two diastereomers (ratio 1.1:1 according to NMR). R_f = 0.56 (light petroleum/ethyl acetate 1:1); IR (KBr): $\tilde{\nu}$ = 2972, 2953, 2686, 1725, 1503, 1480, 1457, 1437, 1379, 1275, 1247, 1197, 1176, 1102, 1082, 1070, 1041, 1014, 977, 933, 887, 859, 797, 744 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.17 (d, *J* = 6.1 Hz, 3 H, CH_3), 1.18 (d, *J* = 6.9 Hz, 3 H, CH_3), 2.17–2.41 (m, 2 H, 9-H or 12-H), 2.46–2.58 (m, 3 H, 9-H or 12-H), 2.71–3.10 [(m, 7 H, , 2 × (10-H + 11-H), 9-H or 12-H)], 3.69 (s, 9 H, 3 × OCH_3), 3.71 (s, 3 H, OCH_3), 3.86–3.97 (m, 2 H, 2 × 8-H), 3.97 (d, *J* = 11.3 Hz, 1 H, 6-H), 4.04 (d, *J* = 11.1 Hz, 1 H, 6-H), 4.68 (t, *J* = 11.0 Hz, 2 H, 6-H), 5.95 (d, *J* = 4.5 Hz, 4 H, 2 × 2-H), 6.75 (d, *J* = 1.9 Hz, 2 H, Ar), 6.78 (s, 2 H, Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 16.53 (+, CH_3), 17.43 (+, CH_3), 26.65 (–, C-9 or C-12), 28.03 (–, C-9 or C-12), 30.54 (–, C-9 or C-12), 31.61 (–, C-9 or C-12), 40.78 (+, C-10 or C-11), 40.84 (+, C-10 or C-11), 41.55 (+, C-10 or C-11), 41.86 (+, C-10 or C-11), 52.00 (+, 2 × OCH_3), 52.05 (+, 2 × OCH_3), 59.84 (–, 2 × C-6), 69.83 (+, C-8), 70.41 (+, C-8), 101.11 (–, C-2), 101.20 (–, C-2), 107.81 (+, Ar), 107.85 (+, Ar), 117.48 (C_{quat}), 117.73 (C_{quat}), 118.61 (+, Ar), 119.07 (+, Ar), 131.18 (C_{quat}), 131.61 (C_{quat}), 133.45 (C_{quat}), 134.04 (C_{quat}), 135.19 (C_{quat}), 136.51 (C_{quat}), 145.31 (C_{quat}), 145.64 (C_{quat}), 146.46 (C_{quat}), 146.75 (C_{quat}), 174.46 (C_{quat}, C=O), 174.51 (C_{quat}, C=O), 174.81 (C_{quat}, C=O), 175.17 (C_{quat}, C=O); MS (70 eV, EI), m/z (%): 374 (74) [M^+], 359 (13) [$M^+ - CH_3$], 343 (17), 314 (26), 296 (83), 271 (100), 255 (30), 237 (40), 211 (46), 207 (24), 181 (66), 153 (28), 128 (15), 43 (22); elemental analysis calcd (%) for $C_{20}H_{22}O_7$ (374.4): C 64.16, H 5.92; found: C 64.12, H 5.74. Proton and carbon chemical shifts are given in one series for both diastereomers together because ^1H NMR and ^{13}C NMR spectra were not appropriate to classify all of the peaks for each diastereomers. IR, EI mass and elemental analysis were carried out for the mixture of diastereomers.

2,3-Dimethyl 5-methyl-7-oxo-1,2,3,4,5,7-hexahydro-dibenzo[c,e]oxepine-dicarboxylate (241) :



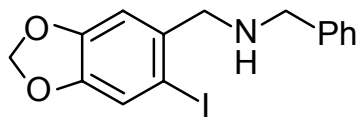
According to GP, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), 2-iodobenzoic acid (**240**, 468 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **241** (55 mg, 8%, yellowish oil) as a mixture of two diastereomers (ratio 1.8:1 according to NMR). R_f = 0.30 (light petroleum/ethyl acetate 3:1); IR (film): $\tilde{\nu}$ = 3064, 2978, 2951, 2847, 1734, 1601, 1437, 1382, 1327, 1285, 1259, 1198, 1175, 1125, 1093, 1058, 1025, 1010, 936, 917, 769, 714 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ = 1.42 (d, J = 7.4 Hz, 3 H, CH_3), 1.45 (d, J = 7.1 Hz, 3 H, CH_3), 2.26–2.39 (m, 2 H, 1-H or 4-H), 2.56–2.63 (m, 3 H, 1-H or 4-H), 2.80–3.14 [m, 7 H, 2 × (2-H + 3-H), 1-H or 4-H], 3.67 (s, 3 H, OCH_3), 3.68 (s, 3 H, OCH_3), 3.70 (s, 3 H, OCH_3), 3.71 (s, 3 H, OCH_3), 4.71–4.79 (m, 2 H, 2 × 5-H), 7.30–7.41 (m, 4 H, Ar), 7.48–7.55 (m, 2 H, Ar), 7.82–7.86 (m, 2 H, Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 15.82 (+, CH_3), 16.48 (+, CH_3), 26.79 (–, C-1 or C-4), 27.47 (–, C-1 or C-4), 30.25 (–, C-1 or C-4), 31.11 (–, C-1 or C-4), 40.75 (+, C-2 or C-3), 40.86 (+, C-2 or C-3), 41.05 (+, C-2 or C-3), 41.28 (+, C-2 or C-3), 52.15 (+, 4 × OCH_3), 72.80 (+, 2 × C-5), 125.37 (+, Ar), 125.97 (+, Ar), 128.08 (+, Ar), 128.30 (+, Ar), 130.73 (+, Ar), 130.85 (C_{quat}), 131.03 (+, Ar), 131.82 (C_{quat}), 132.02 (+, Ar), 133.81 (C_{quat}), 134.08 (C_{quat}), 134.37 (C_{quat}), 134.49 (C_{quat}), 136.76 (C_{quat}), 137.95 (C_{quat}), 169.95 (C_{quat}, C=O), 170.07 (C_{quat}, C=O), 173.92 (C_{quat}, C=O), 174.06 (C_{quat}, C=O), 174.45 (C_{quat}, C=O), 174.60 (C_{quat}, C=O); MS (70 eV, EI), m/z (%): 344 (10) [M^+], 312 (29), 284 (30), 267 (37), 253 (86), 239 (28), 207 (41), 181 (100), 165 (49), 152 (26), 115 (13), 59 (16); HRMS-ESI for $C_{19}H_{20}O_6$ (344.37): $[M + H]^+$ 345.13314, calcd. 345.13326, $[M + NH_4]^+$ 362.15974, calcd. 362.15981. Proton and carbon chemical shifts are given in one series for both diastereomers together because ^1H NMR and ^{13}C NMR spectra were not appropriate to classify all of the peaks for each diastereomers. IR, EI mass and elemental analysis were carried out for the mixture of diastereomers.

*2.9.2.2. Attempts for the synthesis of heterocycles **237** and **239***

8,9-Dimethyl 6-methyl-5,6,7,8,9,10-hexahydro-phenanthridine-dicarboxylate (237):
According to GP, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), 2-iodo-aniline (**236**, 438 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1). Separated fractions could not be identified and desired product **237** could not be observed.

2,3-Dimethyl 5-methyl-1,3,4,5,7,8-hexahydro-2H-6-oxa-dibenzo[a,c]cyclooctene -dicarboxylate (239):
According to GP-A, $Pd(OAc)_2$ (22.4 mg, 100 µmol), tri-2-furylphosphine (46.4 mg, 200 µmol), Et_3N (202 mg, 2.00 mmol), 2-(2-iodo-phenyl)-ethanol (**238**, 496 mg, 2.00 mmol) and methylenespiropentane (**81**, 320 mg, 4.00 mmol) were stirred in anhydrous DMF (1 mL) at 80 °C for 3 h. After cooling the mixture to room temperature, dimethyl fumarate (**68d**, 576 mg, 4.00 mmol) was added, and the mixture stirred at 80 °C for 48 h. After work-up and drying ($MgSO_4$), the solvent was removed in a rotatory evaporator. The residue was subjected to column chromatography on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1). Separated fractions could not be identified and desired product **239** could not be observed.

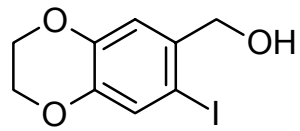
*2.9.3. Preparation of functionalized aryliodides **231e** and **231f***



Benzyl-(6-iodo-benzo[1,3]dioxol-5-ylmethyl)amine (231e):
A solution of 5-chloromethyl-6-iodo-benzo[1,3]dioxole (**245d**, 0.785 g, 2.65 mmol), benzylamine (1.16 mL, 10.6 mmol) and K_2CO_3 (1.82 g, 13.2 mmol) in DME (15 mL) was refluxed. The reaction was checked with TLC during reflux process, when the starting dioxole disappeared (4 h), it was stopped and cooled to room temperature. The reaction mixture was filtrated and concontrated in a rotatory evaporator. The residue was subjected to on silica gel (100 g, 3 × 30 cm, light petroleum/ethyl acetate 3:1) to yield **234e** (0.812 g, 84%, yellowish oil). IR (film): $\tilde{\nu}$ = 3315, 3084, 3061, 3025, 2893, 2829, 1500, 1476, 1453, 1406, 1385, 1363,

1230, 1113, 1039, 933, 864, 829, 738, 698 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.78 (bs, 1 H, NH), 3.75 (s, CH_2), 3.80 (s, CH_2), 5.96 (s, OCH_2O), 6.95 (s, 1 H, Ar), 7.24–7.36 (m, 6 H, Ar, Ph); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 52.93 (–, CH_2), 57.36 (–, CH_2), 87.09 (C_{quat}), 101.51 (–, OCH_2O), 109.86 (+, Ar), 118.52 (+, Ar), 126. 95 (+, Ph), 128. 14 (+, 2 × Ph), 128. 34 (+, 2 × Ph), 135.62 (C_{quat}), 139.99 (C_{quat}), 147.37 (C_{quat}), 148.33 (C_{quat}); MS (70 eV, EI), m/z (%): 367 (26) [M^+], 276 (14), 261 (42), 240 (41), 135 (74), 106 (18), 91 (100), 76 (14). elemental analysis calcd (%) for $C_{15}H_{14}INO_2$ (330.4): C 49.07, H 3.84; found: C 48.95, H 3.83.

(7-iodo-2,3-dihydro-benzo[1,4]dioxin-6-yl)methanol (231f):



To a solution of (2,3-dihydro-benzo[1,4]dioxin-6-yl)methanol (**244f**, 2.15 g, 12.93 mmol) in dry $CHCl_3$ (30 mL) at – 5 °C were successively added silver trifluoroacetate (3.14 g, 14.2 mmol) and iodine (3.61 g, 14.2 mmol). After stirring for 5 min, the resulting heterogeneous mixtire was filtered through a celite pad. The filtrate was than washed with saturated aqueous $Na_2S_2O_3$ (10 mL), dried with $MgSO_4$, filtered and concentrated in vacuo to give pale yellow solid. Recrystallization from $CHCl_3$ afforded **231f** (3.5 g, 92%, white solid). IR (KBr): $\tilde{\nu}$ = 3283, 2977, 2922, 1734, 1576, 1483, 1456, 1401, 1299, 1273, 1260, 1180, 1147, 1070, 1051, 1042, 986, 962, 917, 892, 874, 852, 705, 664 cm^{-1}; ^1H NMR (250 MHz, $CDCl_3$): δ = 1.90 (bs, 1 H, OH), 4.24 [s, $O(CH_2)_2O$], 4.56 (s, 2 H, Bn), 6.97 (s, 1 H, Ar), 7.31 (s, 1 H, Ar); ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 64.13 [–, $O(CH_2)_2O$], 68.34 (–, Bn), 85.44 (C_{quat}), 117.17 (+, Ar), 127.00 (+, Ar), 135.56 (C_{quat}), 143.42 (C_{quat}), 143.71 (C_{quat}), 155.37 (C_{quat}); MS (70 eV, EI), m/z (%): 392 (100) [M^+], 137 (40), 93 (9), 65 (14), 53 (18), 50 (15). elemental analysis calcd (%) for $C_9H_9IO_3$ (292.1): C 37.01, H 3.11; found: C 36.81, H 2.85.

D. Conclusion and Outlook

The first part of this study focused on new developments in the domino Heck-Diels-Alder reaction with bicyclopropylidene (**66**) as an extension of this already powerful methodology. Although, in previous studies[29b], mono-substituted bicyclopropylidenes such as methyl bicyclopropylidene carboxylate (**66E**), and n-pentylbicyclopropylidene were utilized as coupling partners of iodobenzene (**67**), this new version of the domino reaction was limited only one successful example. To establish this concept as another dimension of the domino reaction involving all scope and limitations, four differently substituted bicyclopropylidenes (**66B**–**E**) were coupled with aryl iodides in the presence of a dienophile. Among them, the most impressive result was achieved by methyl bicycopropylidenecarboxylate (**66E**). The reaction yielded regiodiastereomeric mixture of spiro[2.5]octenes (*cis*/*trans*, *trans*-**104E** and *cis*/*trans*, *cis*-**105E**) stemming from the opening of the only unsubstituted cyclopropane ring. The result was supported with X-ray crystal structure analyses of major diastereomers (*cis*/*trans*, *trans*-**104E**). Another interesting result was obtained by employing the boronate substituted bicylopropylidene (**66B**). In this case, the reaction mainly produced the spiro[2.5]octene (**109a**) lacking the boronate substituent together with the mixture of diastereomers *cis*/*trans*, *trans*-**104B**. The formation of **109a** was attributed to opening of the substituted cyclopropyl ring and following deboropalladation process. Moreover, the reaction of methyl bicyclopropylidenecarboxylate (**66E**) with sterically encumbered aryl iodide, 2-iodo-1,3-dimethyl benzene, without a dienophile produced regioisomeric mixtures of allylidenecyclopropane derivatives *trans*-**119E**, *cis*-**120E** and **121E**. The minor component **121E** was only allylidenecyclopropane arising from opening of the substituted cyclopropane ring. In the light of these results, it has been concluded that the domino Heck-Diels-Alder reaction with mono-substituted bicyclopropylidenes was quite selective with respect to the identity of substituents. Reactions performed with methyl bicyclopropylidenecarboxylate (**66E**) produced a mixture of spirooctenes occuring by opening of unsubstituted cyclopropane moiety. This must be caused by complexation of palladium species with heteroatoms of the ester in carbopalladation step. Correspondingly, reactions with bicyclopropylidenes having no available heteroatoms in their substituents such as the reaction of 2-(tributylstannyl)bicylopropylidene (**66C**) furnished mainly the spiro[2.5]octene **109b** occurring by the opening of the substituted cyclopropane ring. Therefore, by this study, not only combinatorial potential of domino Heck-Diels-Alder reaction with bicyclopropylidene (**66**) was enriched but also valuable perspectives for this domino reaction was gained.

Another avenue was opened up by employing series of transformations to the spiro[2.5]octene derivative **127** prepared by the domino Heck-Diels-Alder reaction involving bicyclopropylidene (**66**), iodobenzene (**67**) and itaconic dimethyl ester (**126**). The diester functionality in this spirooctene was converted to *N*-phenylimide by three simple operations to achieve dispiroheterocyclic structure **130**. Thus, this work demonstrated that the domino process of bicyclopropylidene by appropriate selection of adducts can serve various precursors that allow further valuable synthetic manipulations.

In the second part of this study, a new one-pot, two-step, four-component queuing cascade was introduced. The cascade produced in the first step allylidenecyclopropane derivatives (**174a**–**e**) generated by nucleophilic trapping of respective π-allylpalladium intermediates. In the second step, these allylidenecyclopropanes (**174a**–**e**) were allowed to undergo immediate Diels-Alder reactions upon addition of various dienophiles. Palladium-catalyzed cross-coupling of bicyclopropylidene (**66**) with iodoethene (**173**) in the presence of a secondary amine **78** and addition of dienophiles **68a**–**e** in the second step, 8-(1'-aminoethyl)-substituted spiro[2.5]oct-7-ene derivatives (**175aa**–**ad** and **175bb**–**eb**) were obtained in 29–66% yield. The same one-pot, two-step queuing cascade could be carried out with other iodoalkenes including cyclic ones (**191**–**196**) and with cyclic dienophiles such as *N*-phenylmaleimide **189** and *N*-phenyltriazolinedione **122** to furnish highly substituted spirooctenes and spirocyclopropanated oligoheterocycles (**176**–**179ab** and **180**–**188a**). Furthermore, spirocyclopropanated heterobicycles such as **207**, **209** (25 and 38% yield, respectively) were also obtained by an inter-intra-intermolecular version of this queuing cascade involving 1-hydroxyethyl and 1-aminoethyl substituted iodoethenes **206**, **208**. In conclusion, another dimension of diversity has been added to an already powerful combinatorial approach to libraries of spiro[2.5]octene derivatives[29b]. The new one-pot, two-step four-component queuing cascade led to a particularly rich pattern of substituents by variation of the iodoalkenes, the nucleophiles and the dienophiles, exceeding those of the previously described spirocyclopropanated carbo- and heterocyclic skeletons[29b]. This sequential transformation may also open up new approaches to natural products containing spiro[2.5]octene substructures.[31]

In the last chapter, another one-pot, two-step yet three-component queuing cascade involving methylenespiropentane (**81**), functionalized aryliodides **231a**–**g** and dimethyl fumarate **68d** was presented as a general methodology for the construction of benzoxepine and benzoazepine derivatives **234a**–**g**. Palladium-catalyzed cross-coupling of methylenespiropentane (**81**) with o-

iodo benzylic alcohols or amines **231a**–**g**, firstly generated seven-membered heteroexocyclic dienes **232a**–**g** via series of rearrangements and intramolecularly trapping of respective π-allylpalladium intermediates. These dienes (**232a**–**g**), in the second step, upon addition of dimethyl fumarate **68d** underwent Diels-Alder reactions to furnish benzoxepine and benzoazepine derivatives **234a**–**g** in 18-29% yield. Numerous attempts to increase the yield of this cascade reaction were unsuccessful. Despite having low yields, the new three-component, two-step cascade provided valuable fused heterocyclic ring systems **234a**–**g** commonly found in the structure of biologically active natural and synthetic compounds[73]. Moreover, this approach might be pioneering study for the next generation of palladium-catalyzed reactions with methylenespiropentane (**81**).

E. References and Notes

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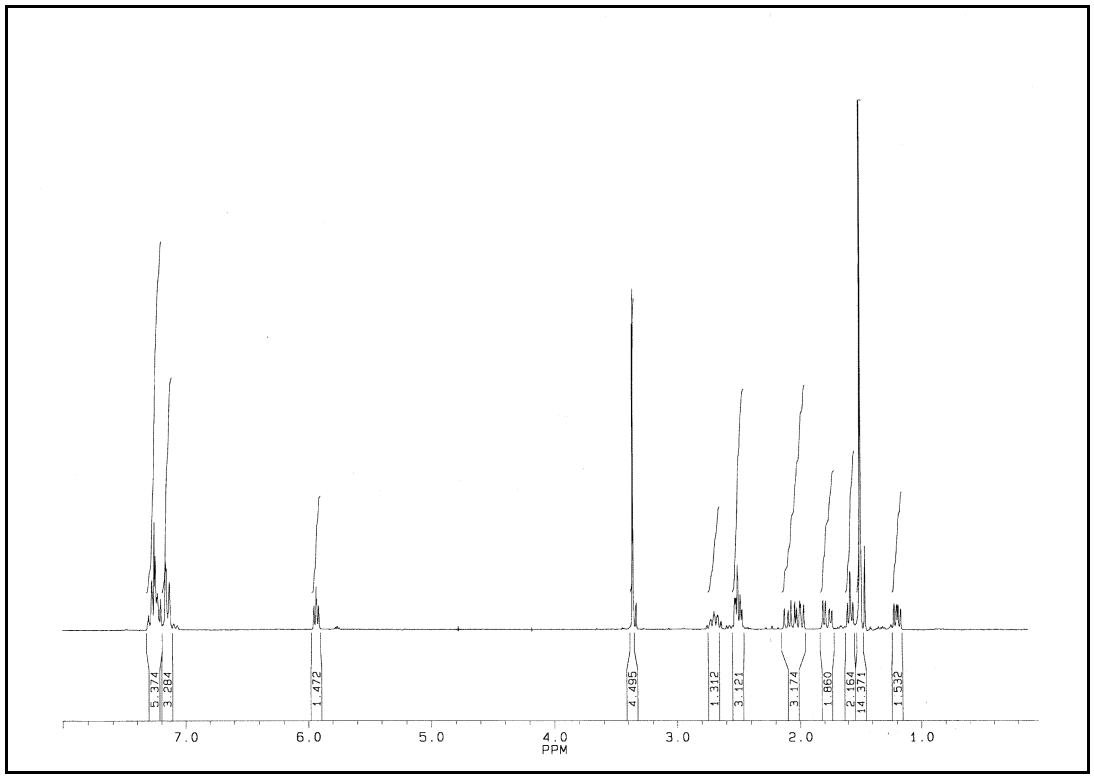
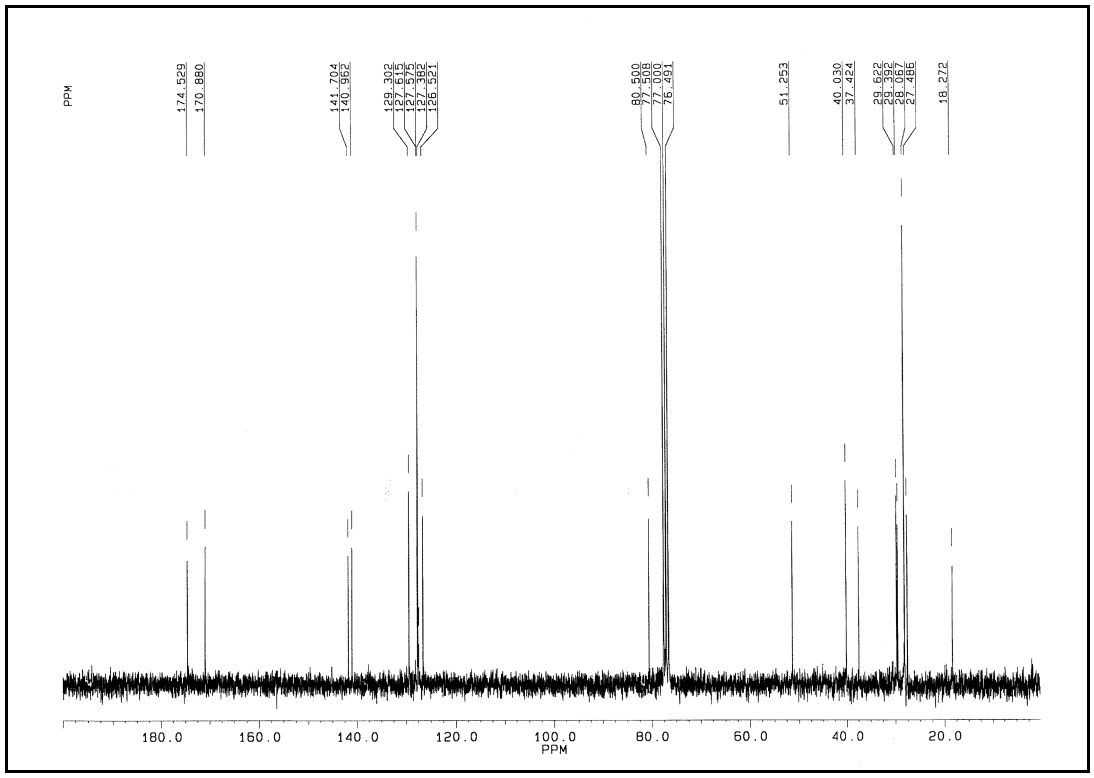
F. Spectra

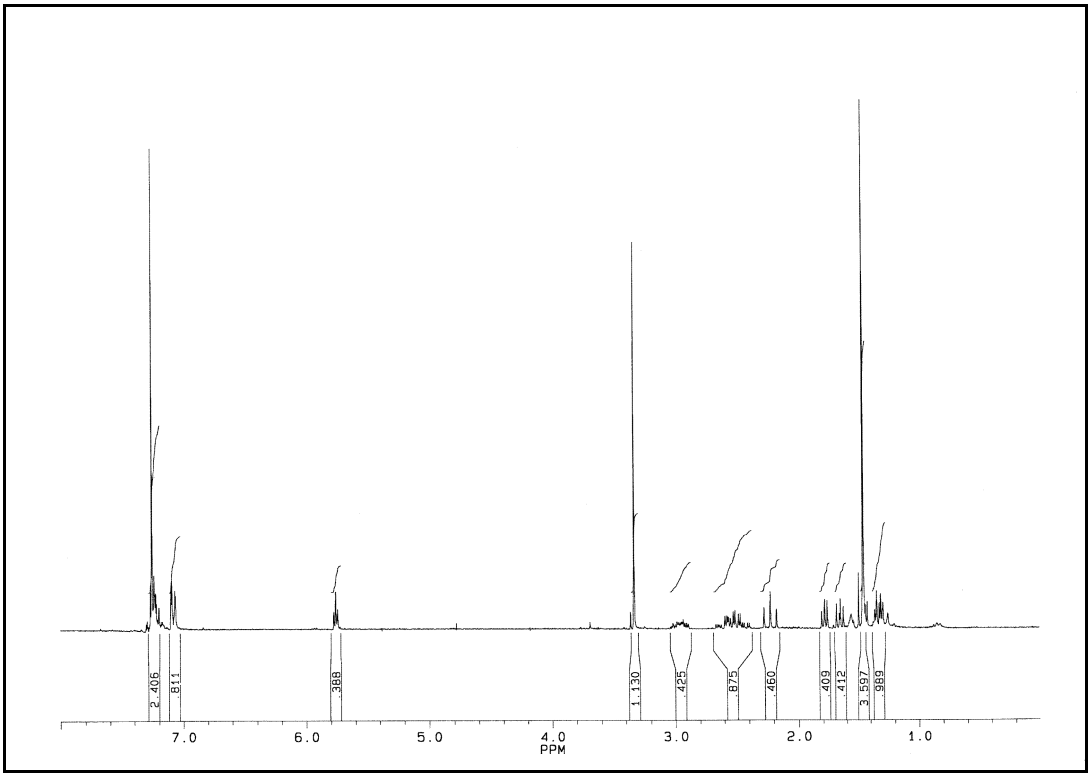
1. ^{1}H-NMR Spectra

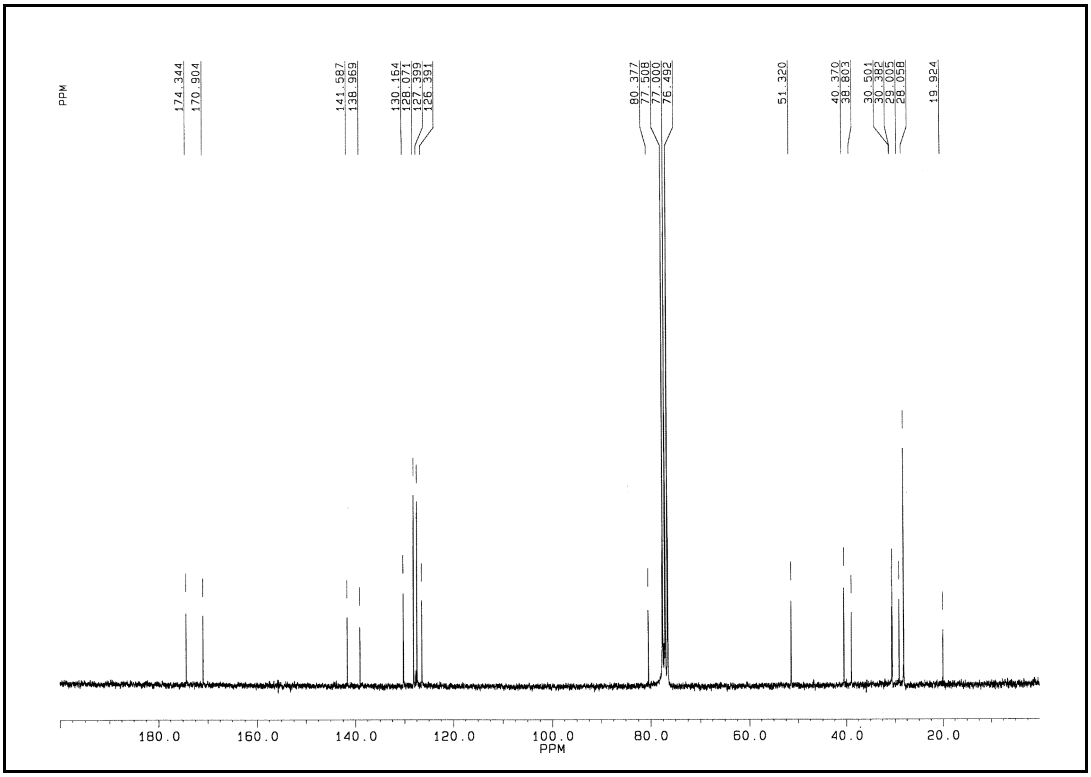
2. ^{13}C-NMR Spectra



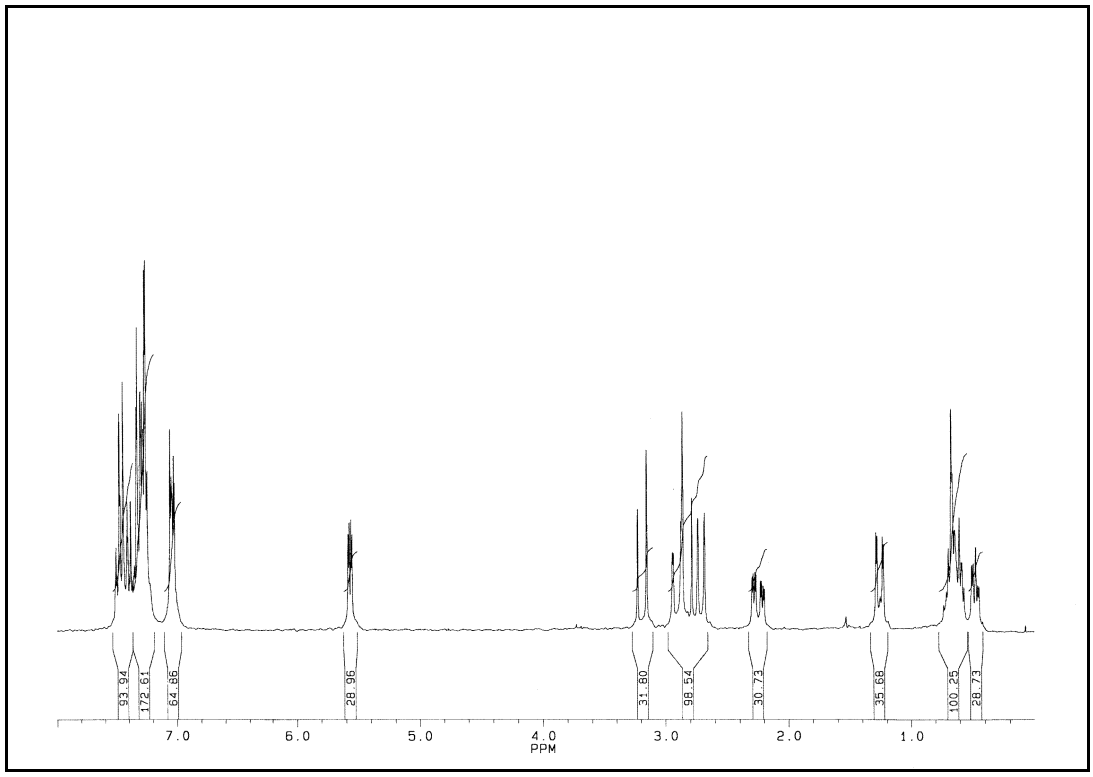


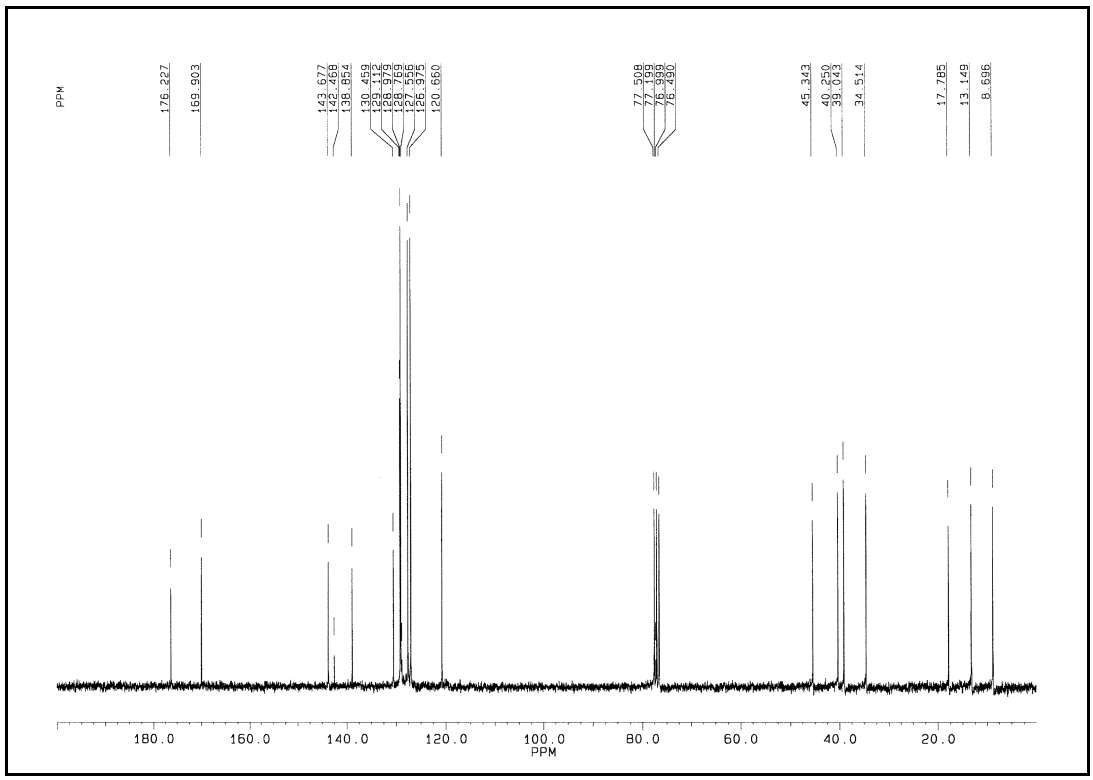
5-*tert*-Butyl-1-methyl 8-phenylspiro[2.5]oct-7-ene-1,5-dicarboxylate (*cis*, *trans*-**104E**)



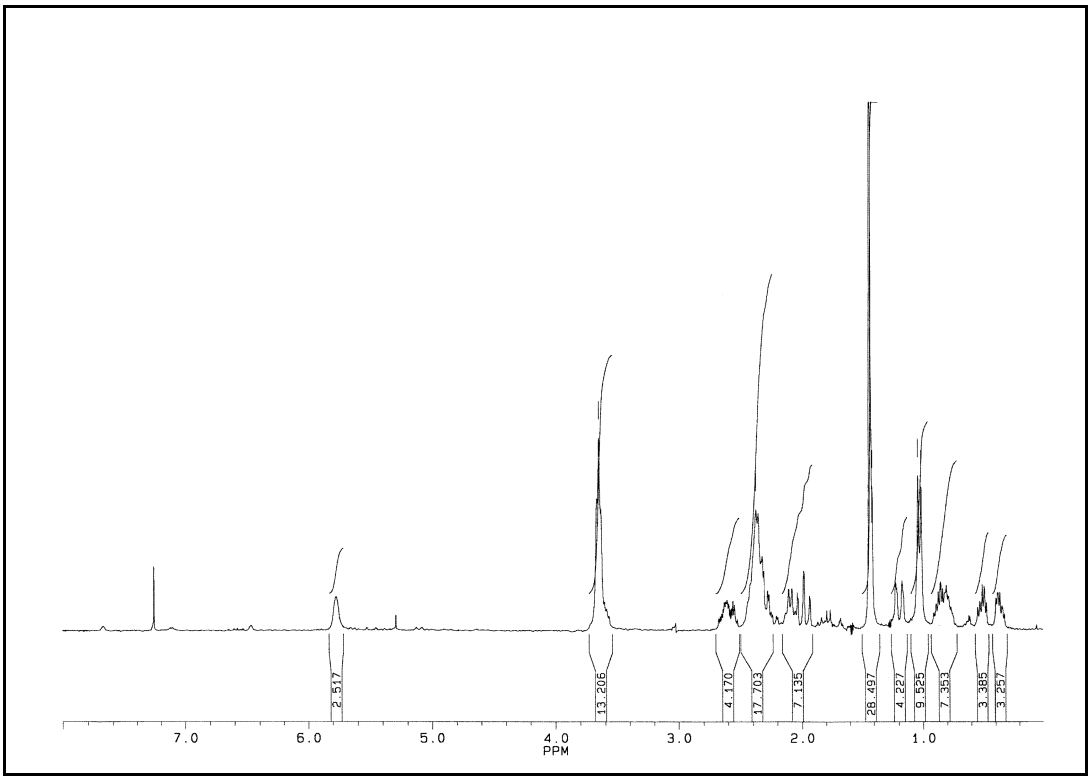


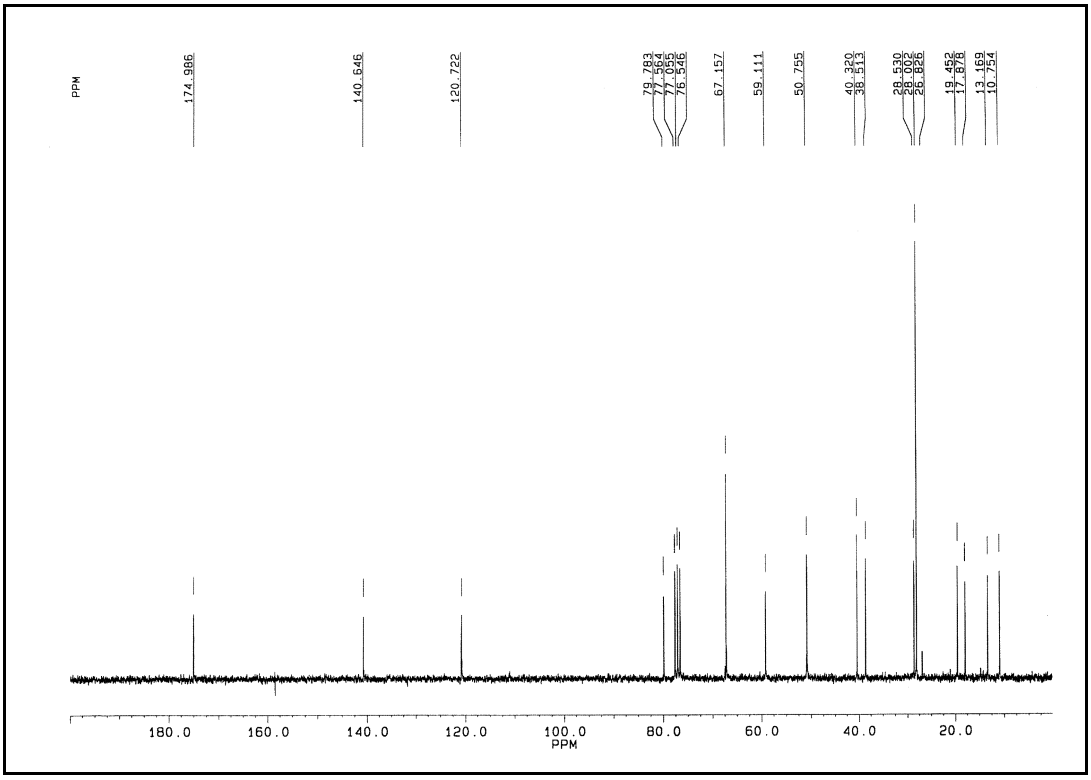
5-*tert*-Butyl-1-methyl 8-phenylspiro[2.5]oct-7-ene-1,5-dicarboxylate (*trans*, *trans*-**104E**)





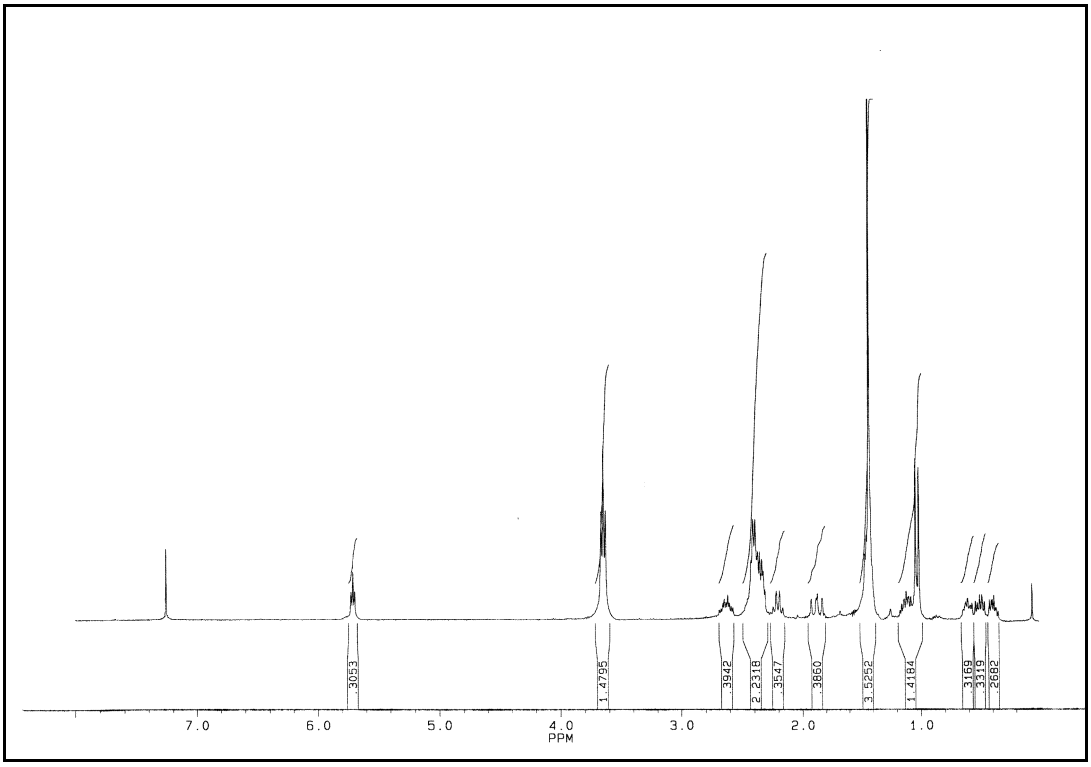
7,12-Diphenyl-7-azadispiro[2.1.4.3]dodec-11-ene-6,8-dione (**130**)

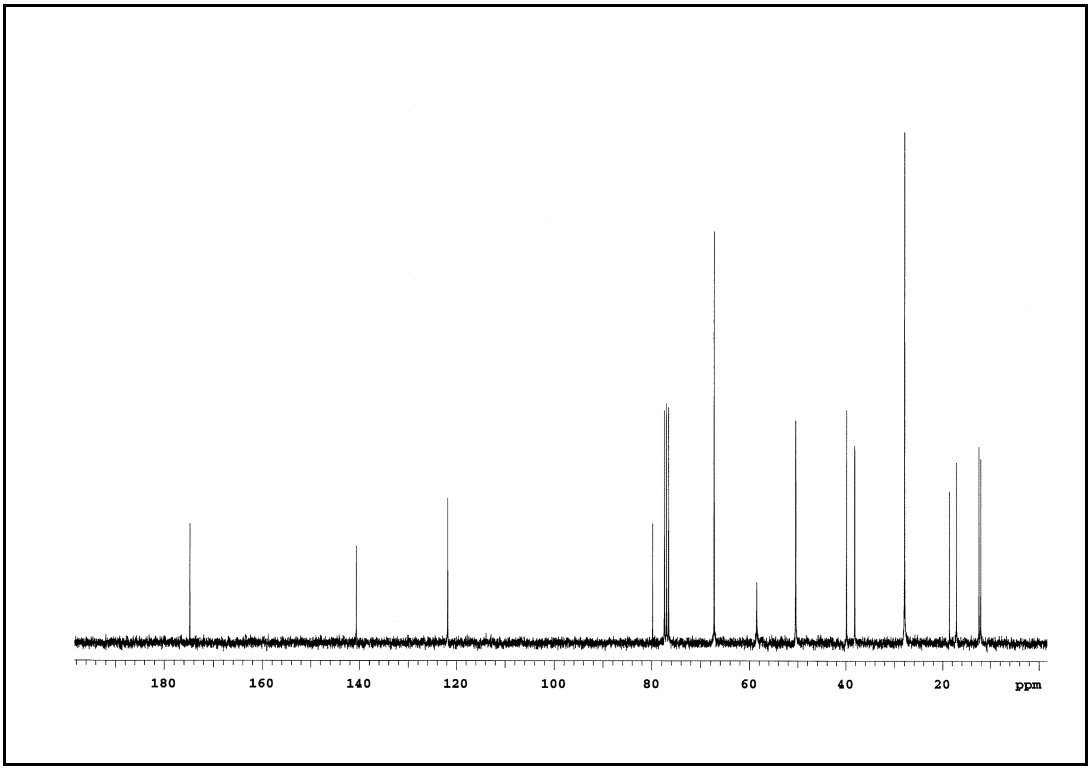




tert-Butyl 8-(1-morpholin-4-ylethyl)spiro[2.5]oct-7-ene-5-carboxylate (**175ab**)

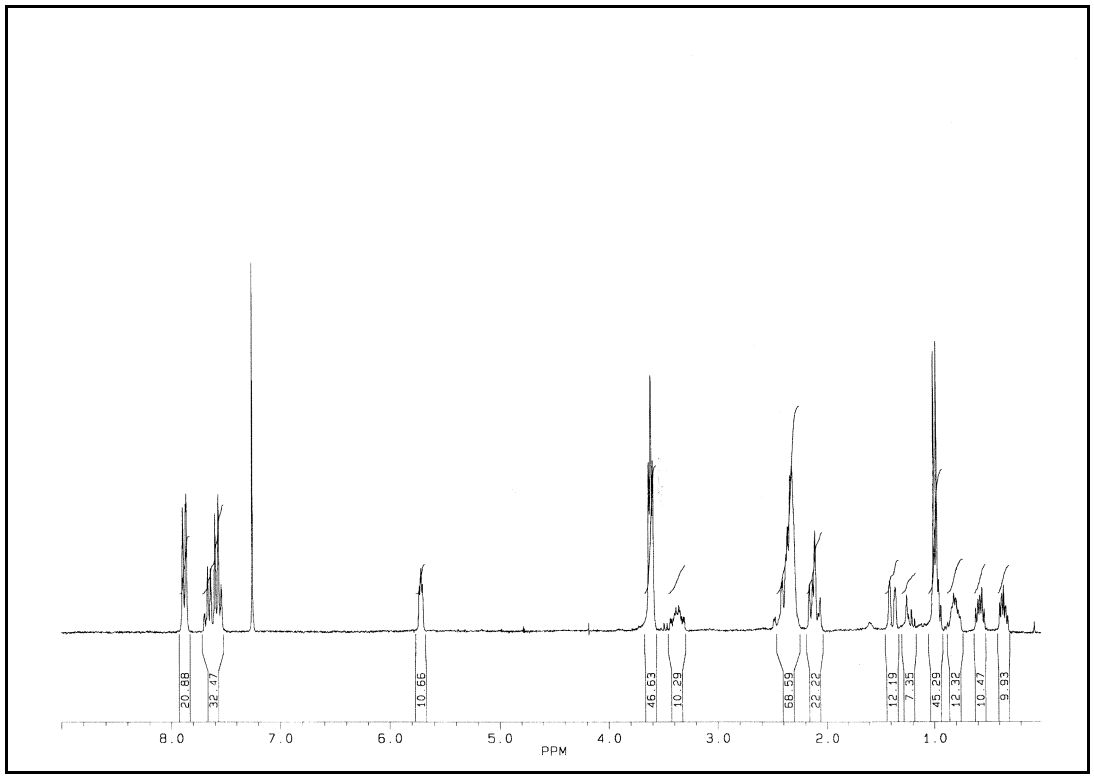
Major diastereomer

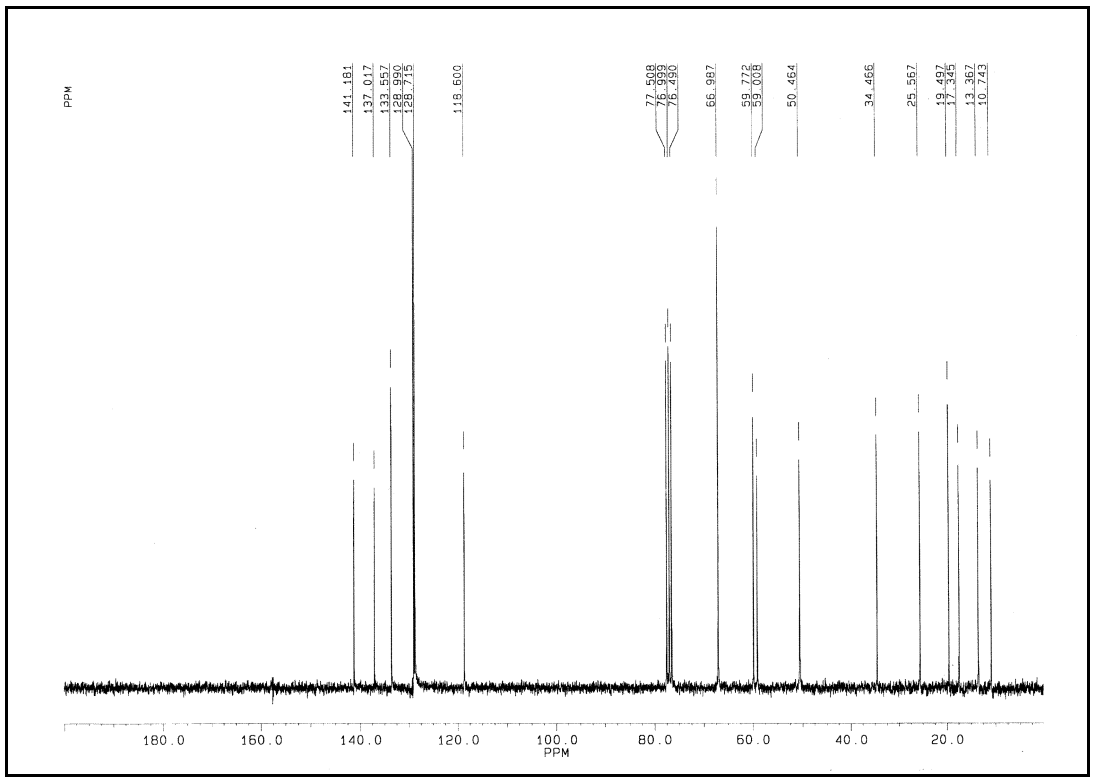




tert-Butyl 8-(1-morpholin-4-ylethyl)spiro[2.5]oct-7-ene-5-carboxylate (**175ab**)

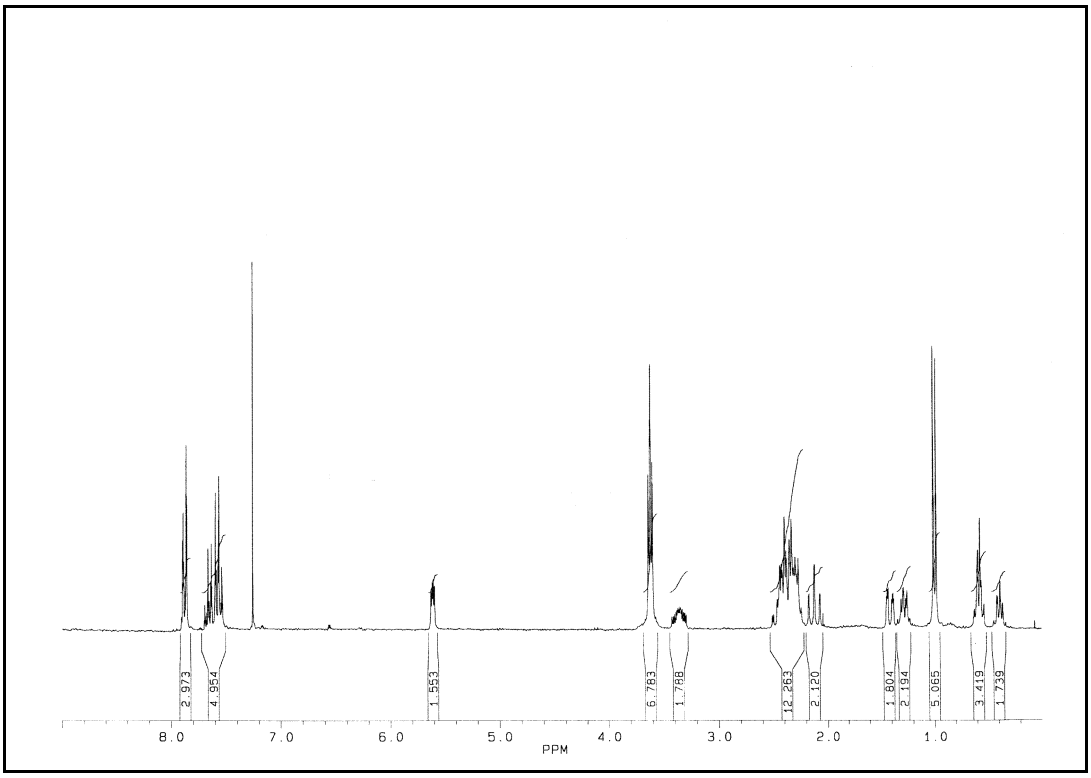
Minor diastereomer

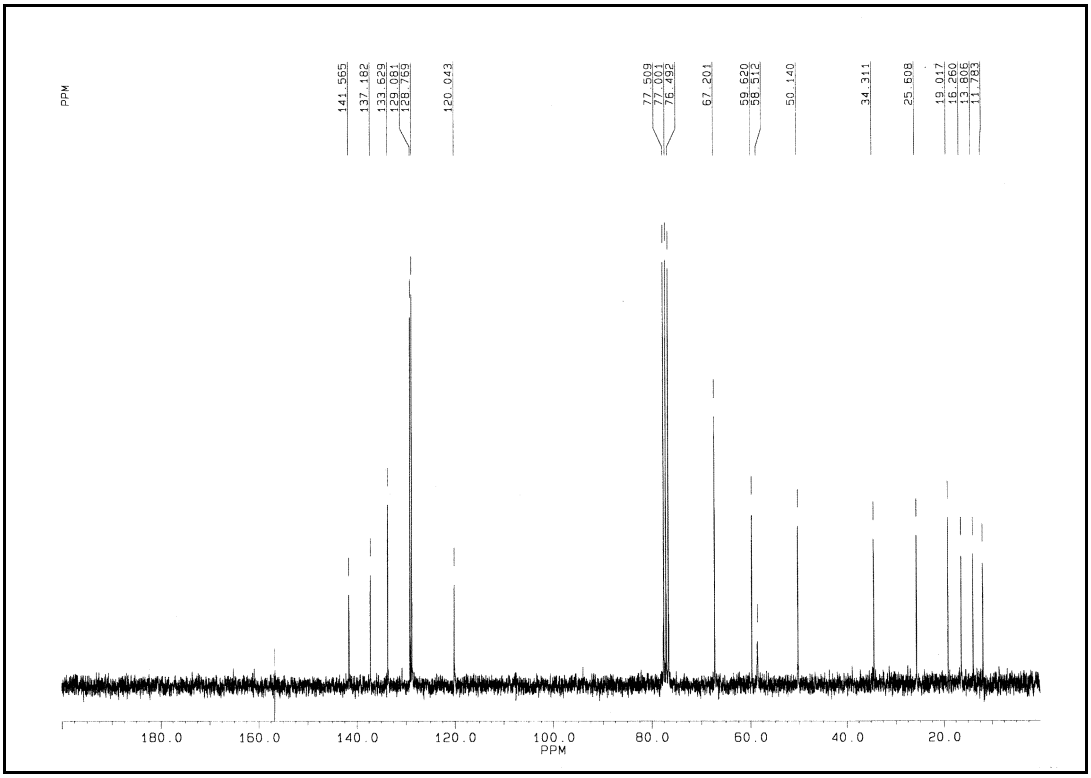




4-[1-(7-Benzenesulfonylspiro[2.5]oct-4-ene-4-yl)-ethyl]-morpholine (**175ac**)

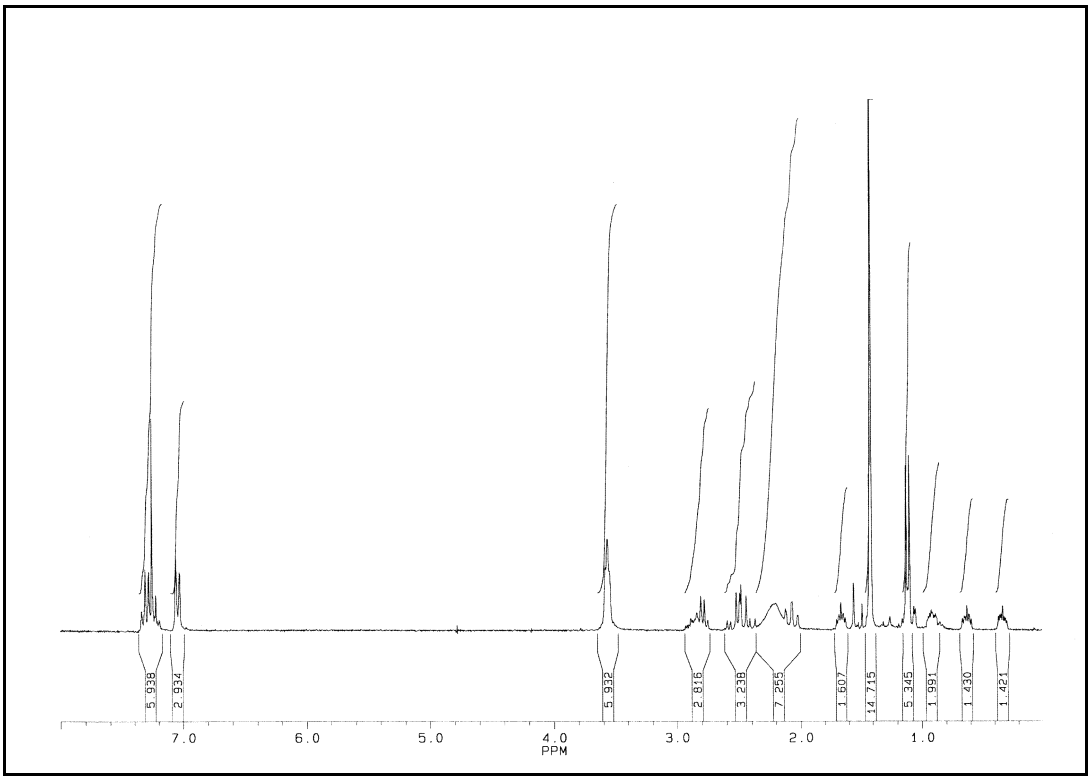
Major diastereomer

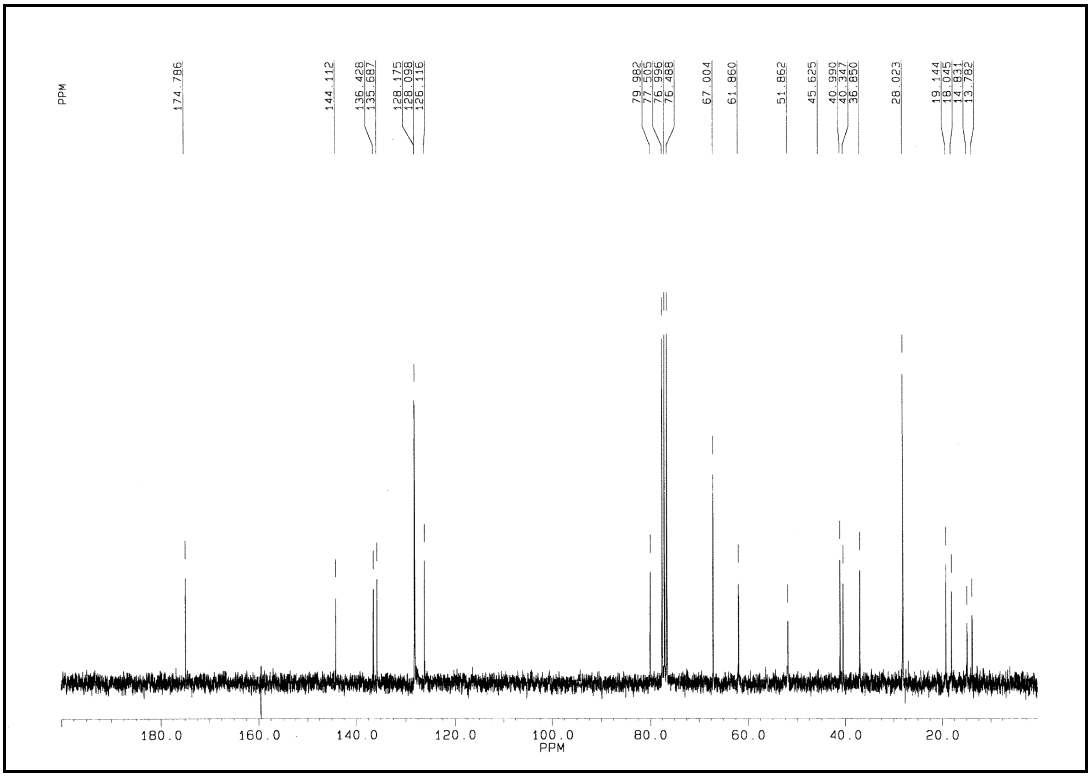




4-[1-(7-Benzenesulfonylspiro[2.5]oct-4-ene-4-yl)-ethyl]-morpholine (**175ac**)

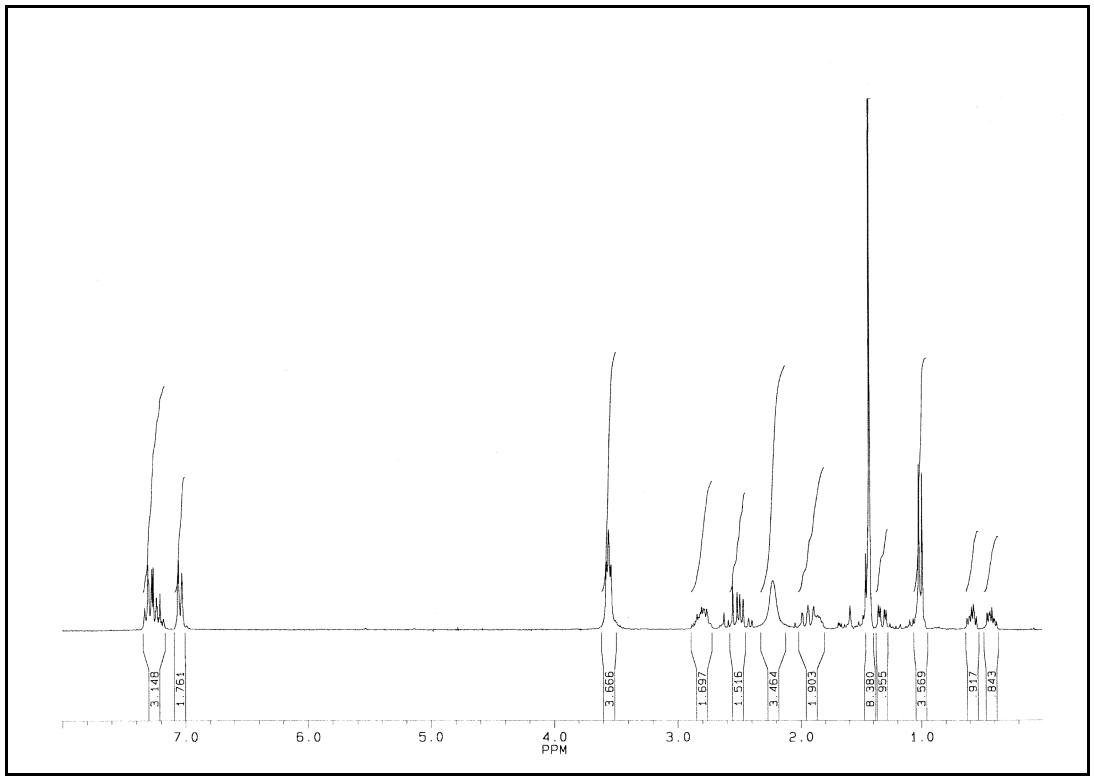
Minor diastereomer

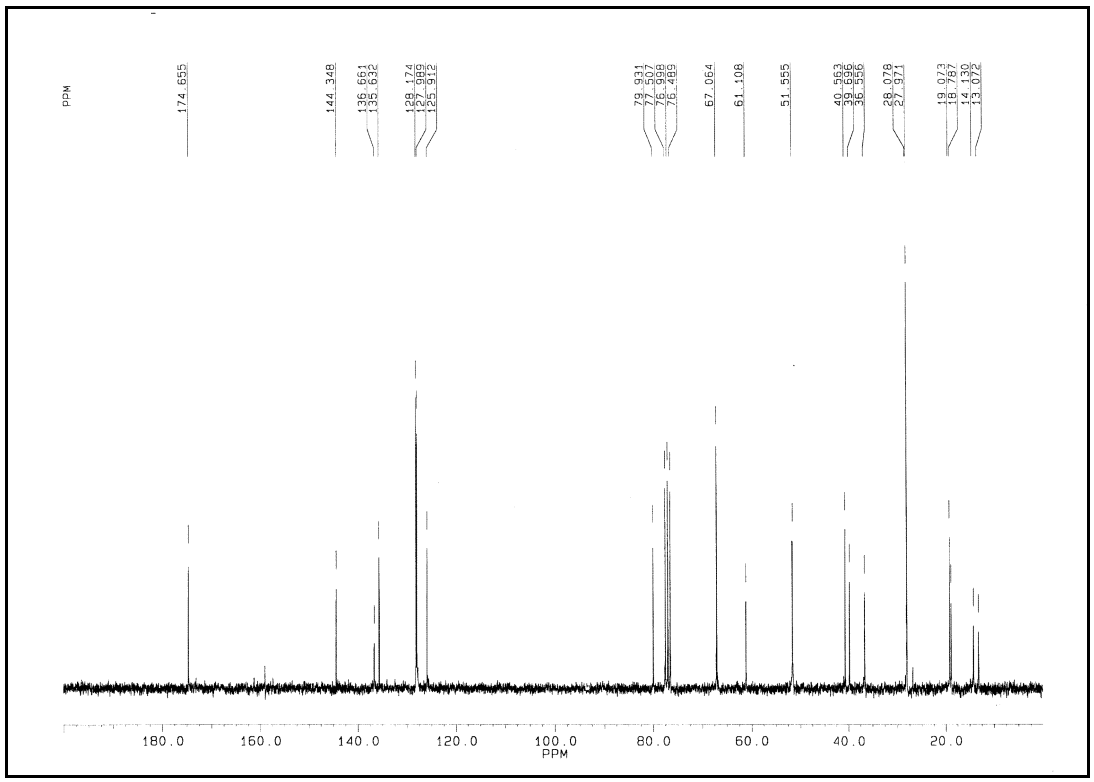




tert-Butyl 8-(1-morpholin-4-ylethyl)-7-phenylspiro[2.5]oct-7-ene-5-carboxylate (**176ab**)

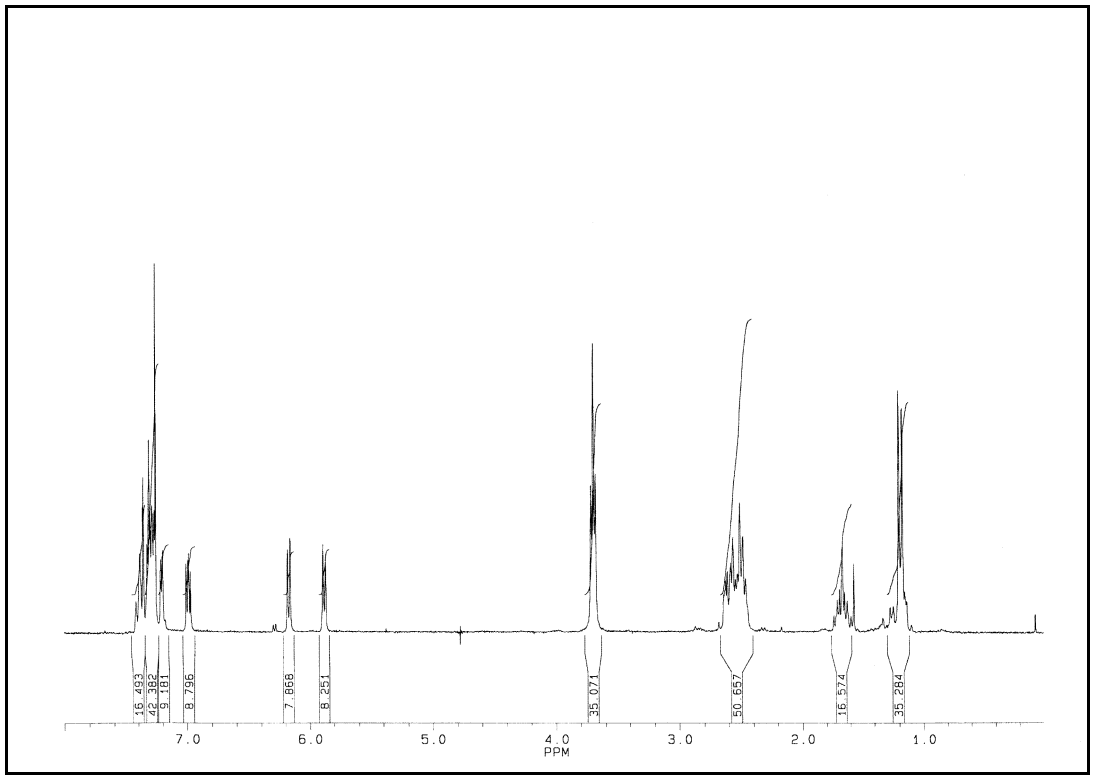
Major diastereomer

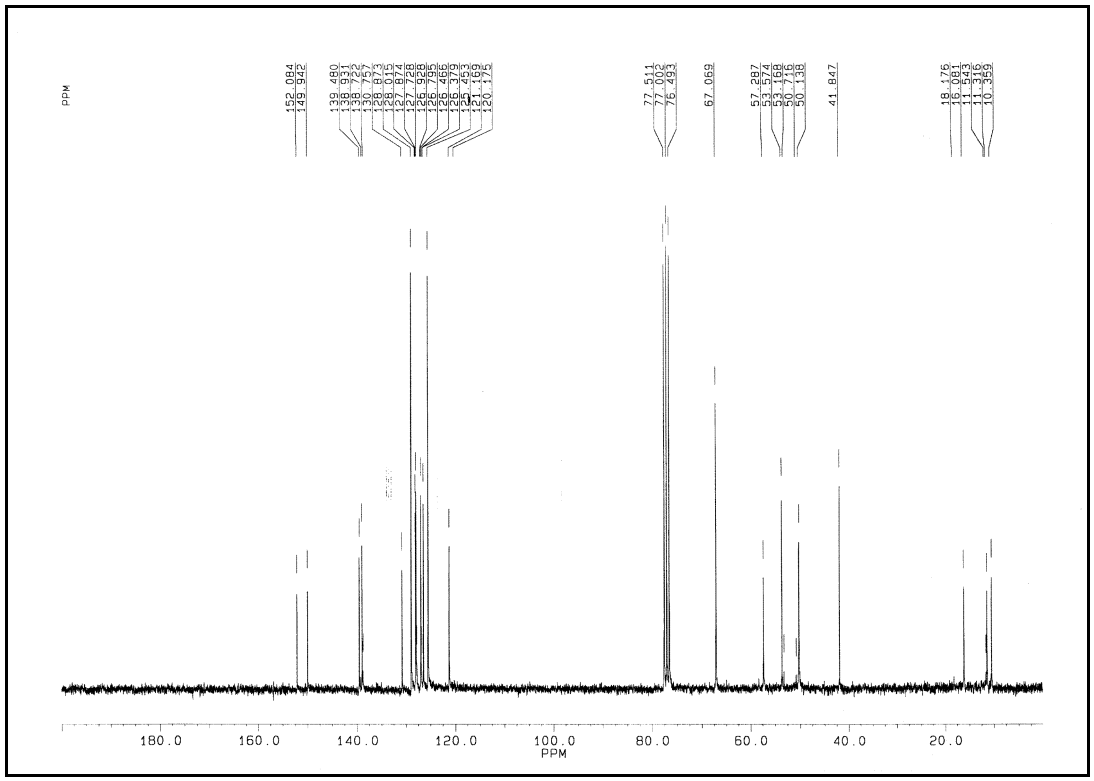




tert-Butyl 8-(1-morpholin-4-ylethyl)-7-phenylspiro[2.5]oct-7-ene-5-carboxylate (**176ab**)

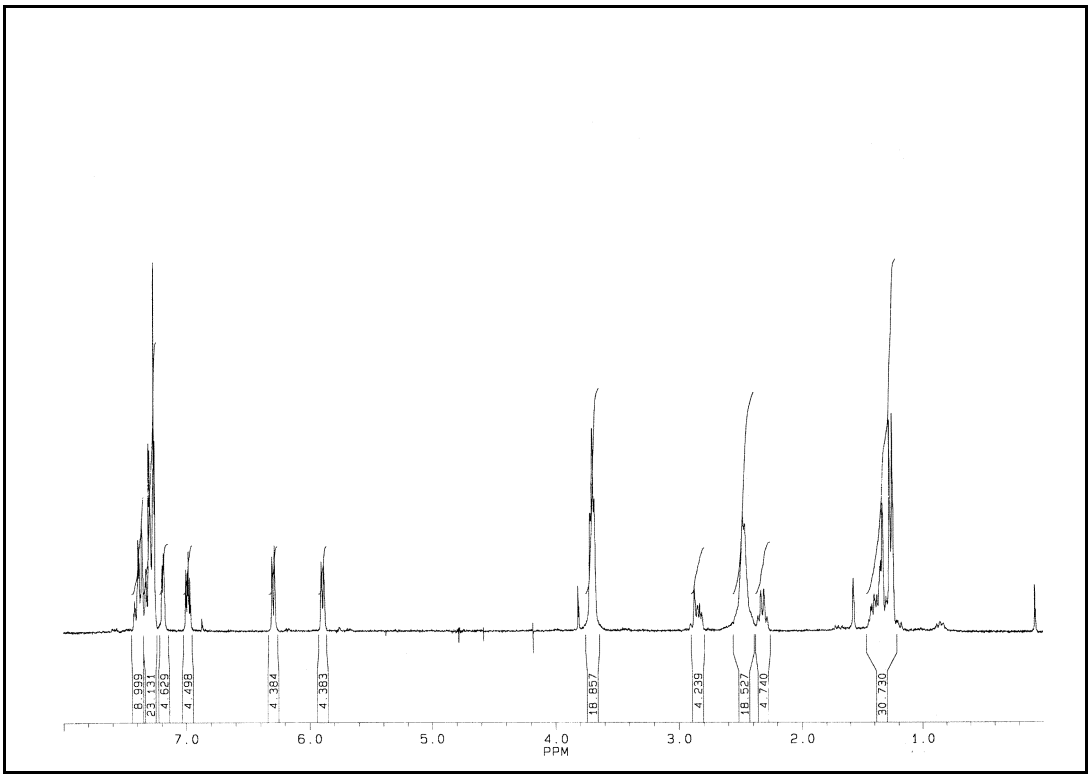
Minor diastereomer

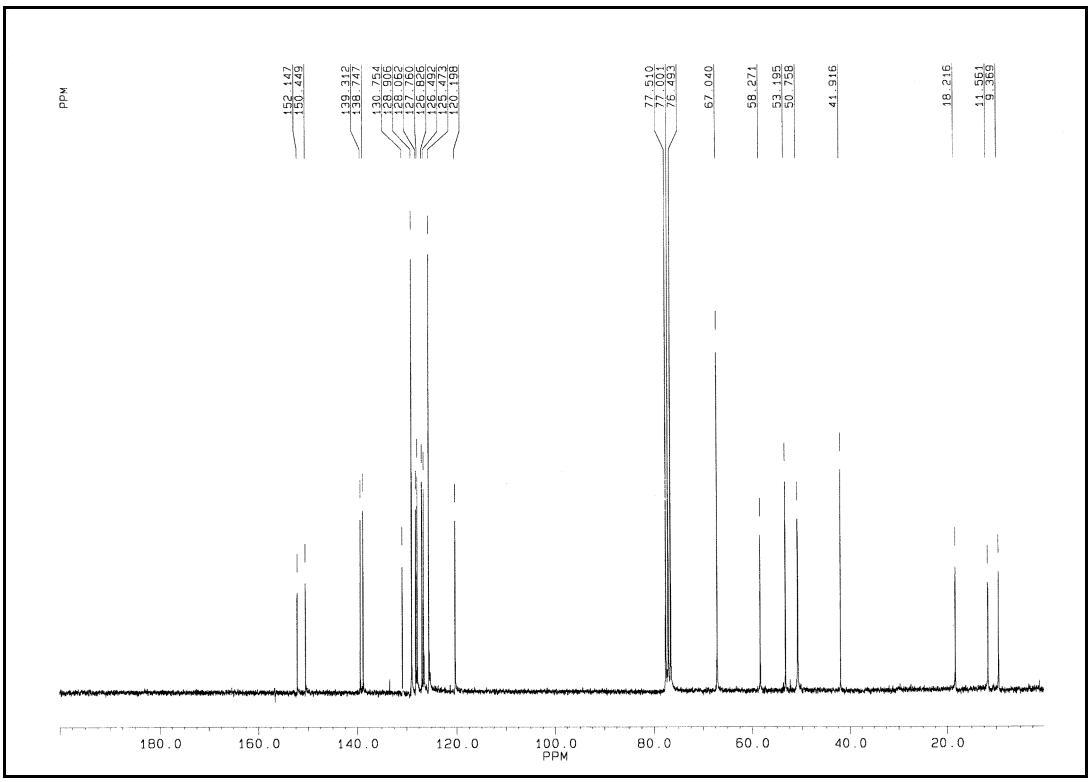




6'-(1-Morpholin-4-ylethyl)-2'-phenyl-8'-(thiophen-2-yl)spiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo[1,2-a]pyridazine]-1',3'-dione (**182a**)

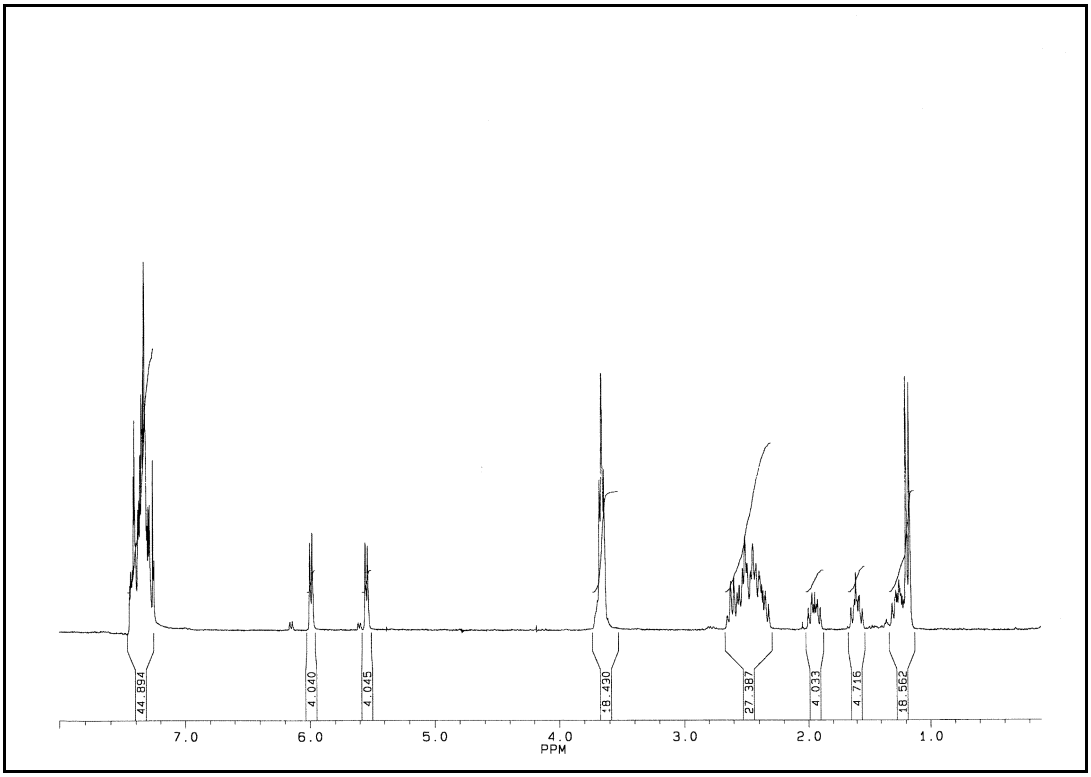
1. diastereomer

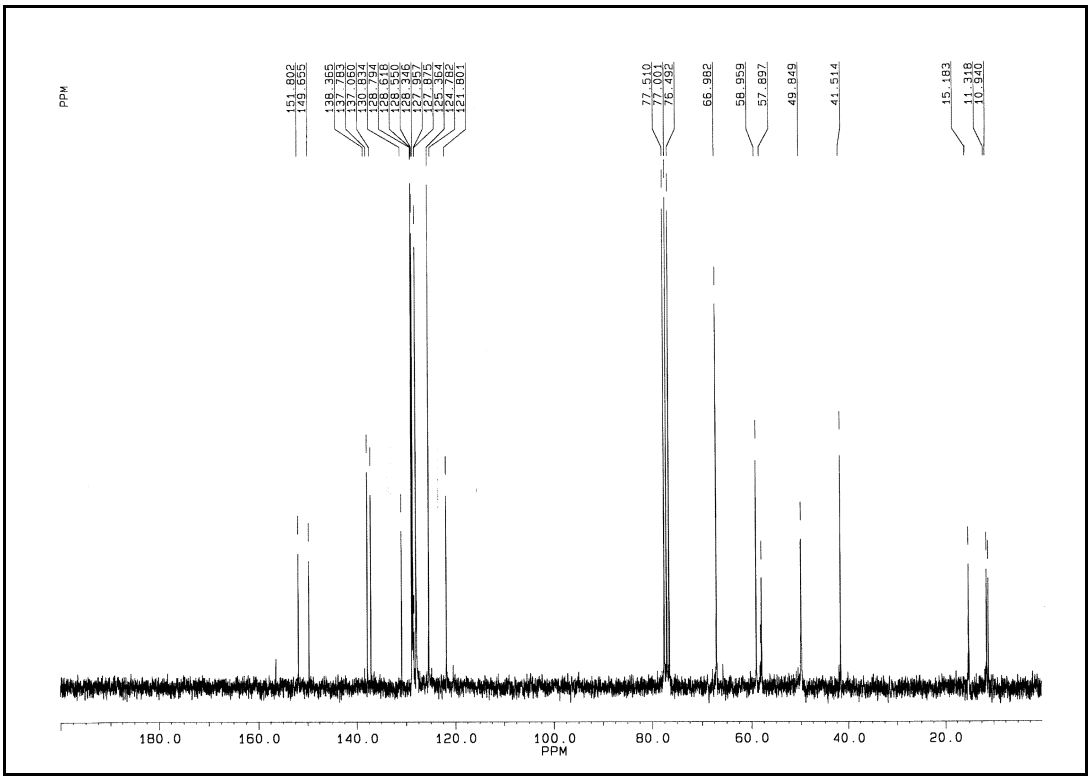




6'-(1-Morpholin-4-ylethyl)-2'-phenyl-8'-(thiophen-2-yl)spiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo[1,2-a]pyridazine]-1',3'-dione (**182a**)

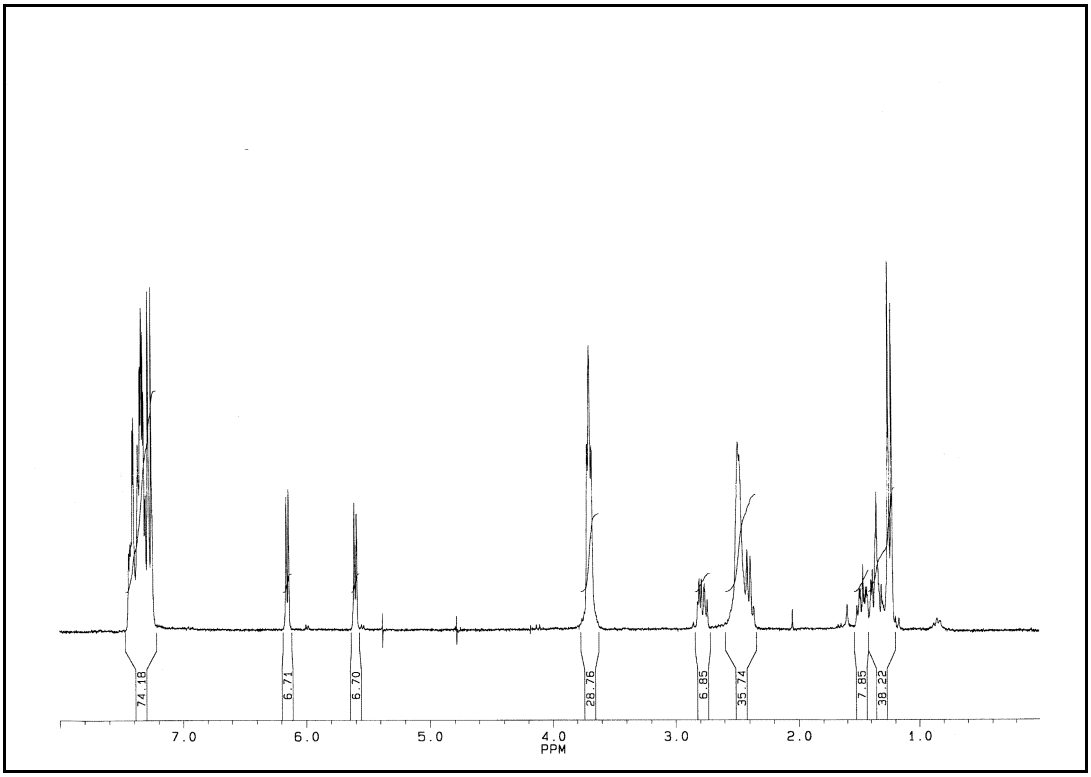
2. diastereomer

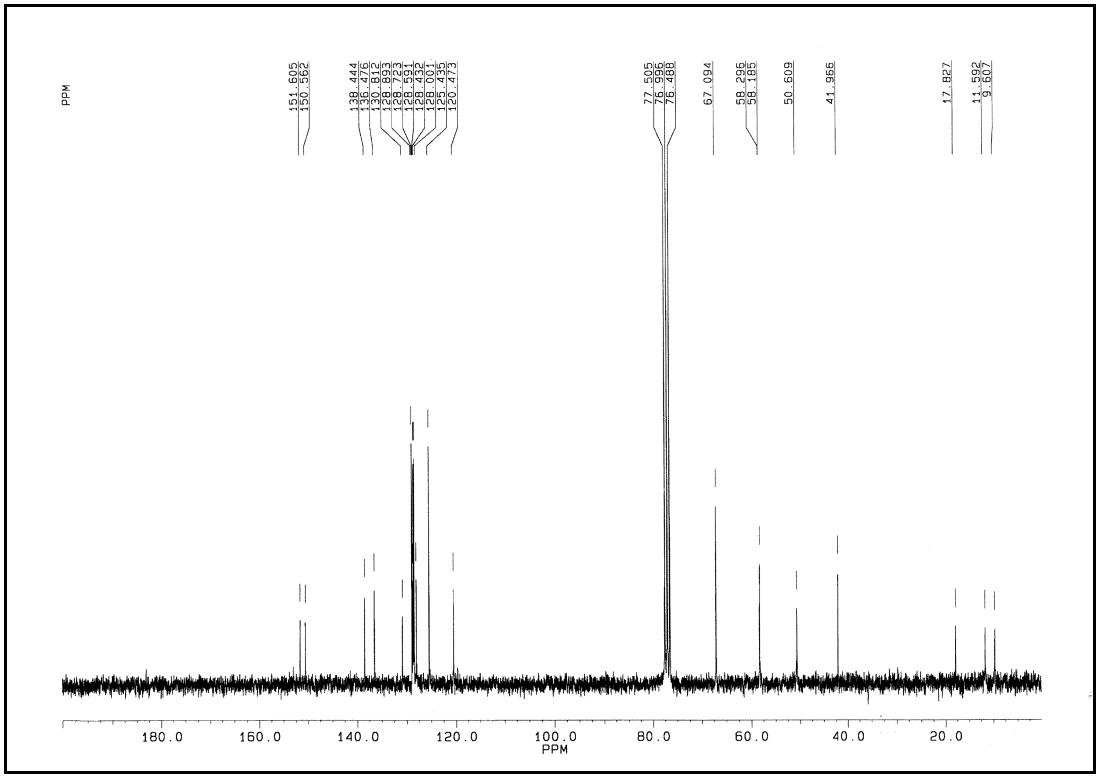




6'-(1-Morpholin-4-ylethyl)-2',8'-diphenylspiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo-[1,2-a]pyridazine]-1',3'-dione (**183a**)

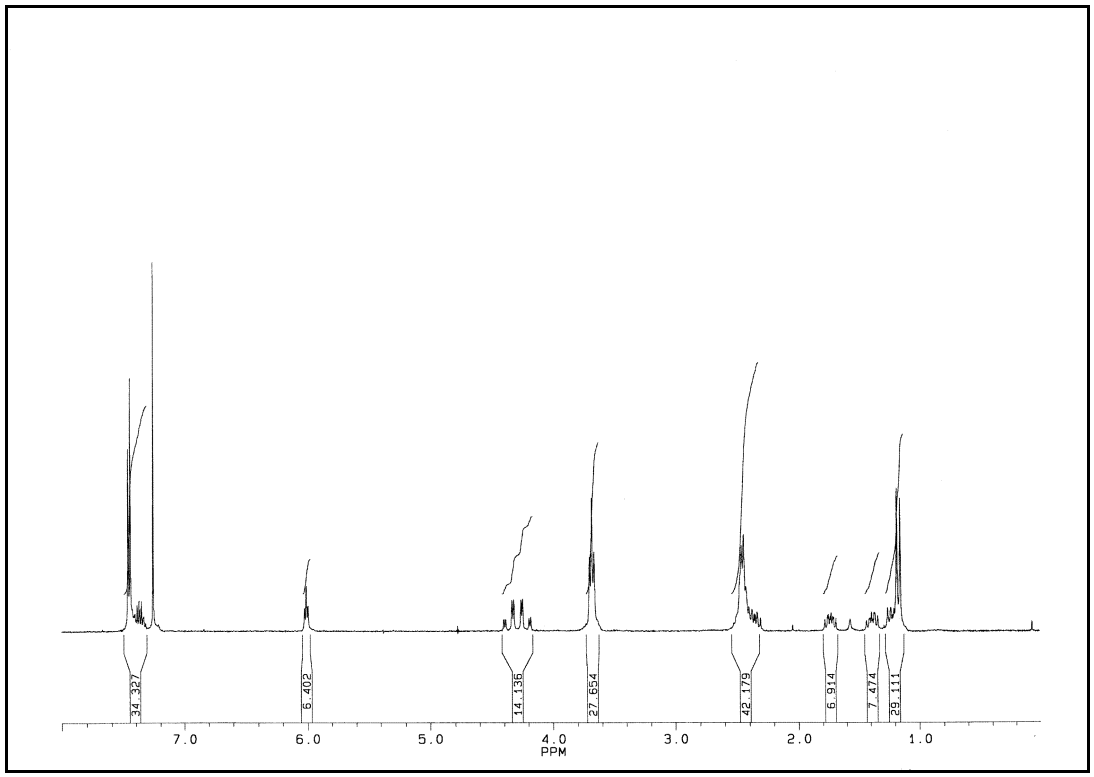
Major diastereomer

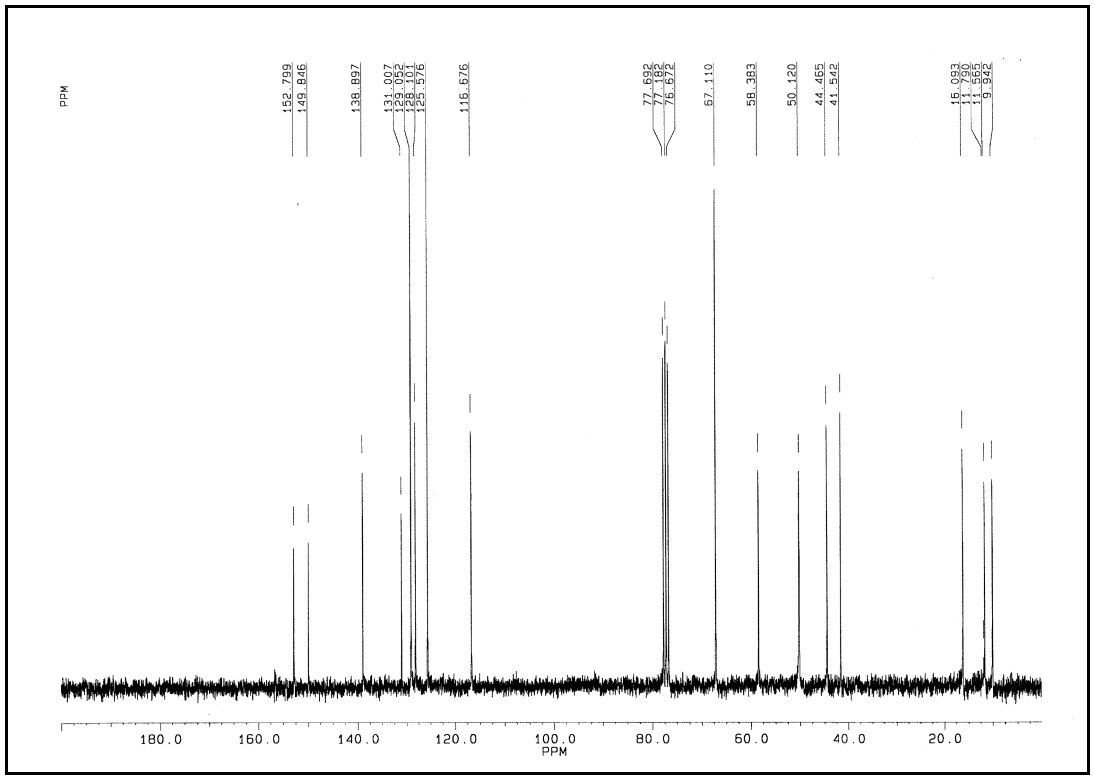




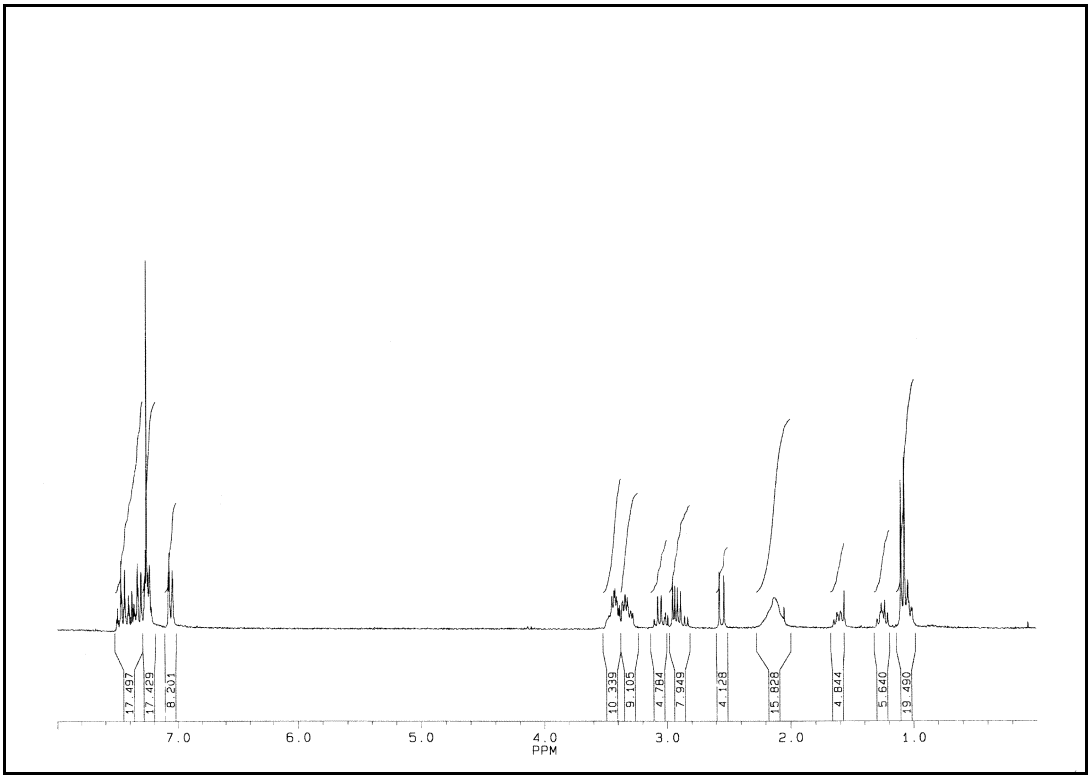
6'-(1-Morpholin-4-ylethyl)-2',8'-diphenylspiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo-[1,2-a]pyridazine]-1',3'-dione (**183a**)

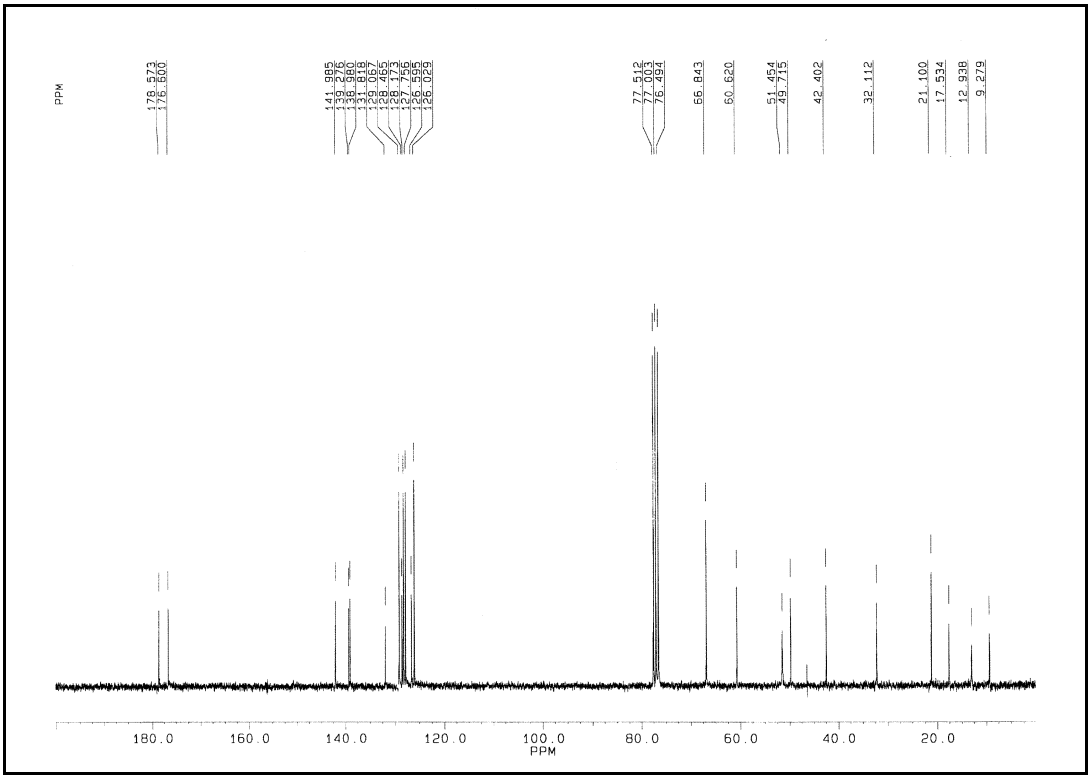
Minor diastereomer





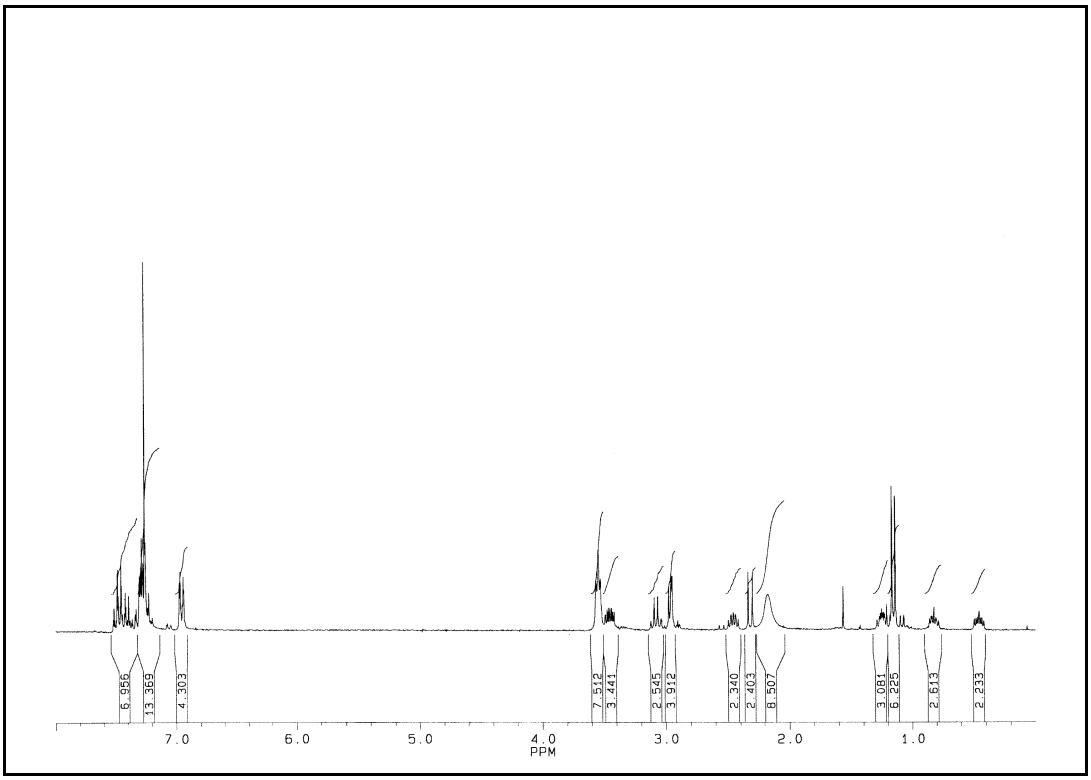
6'-(1-Morpholin-4-ylethyl)-2'-phenylspiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo[1,2-a] pyridazine]-1',3'-dione (**184a**)

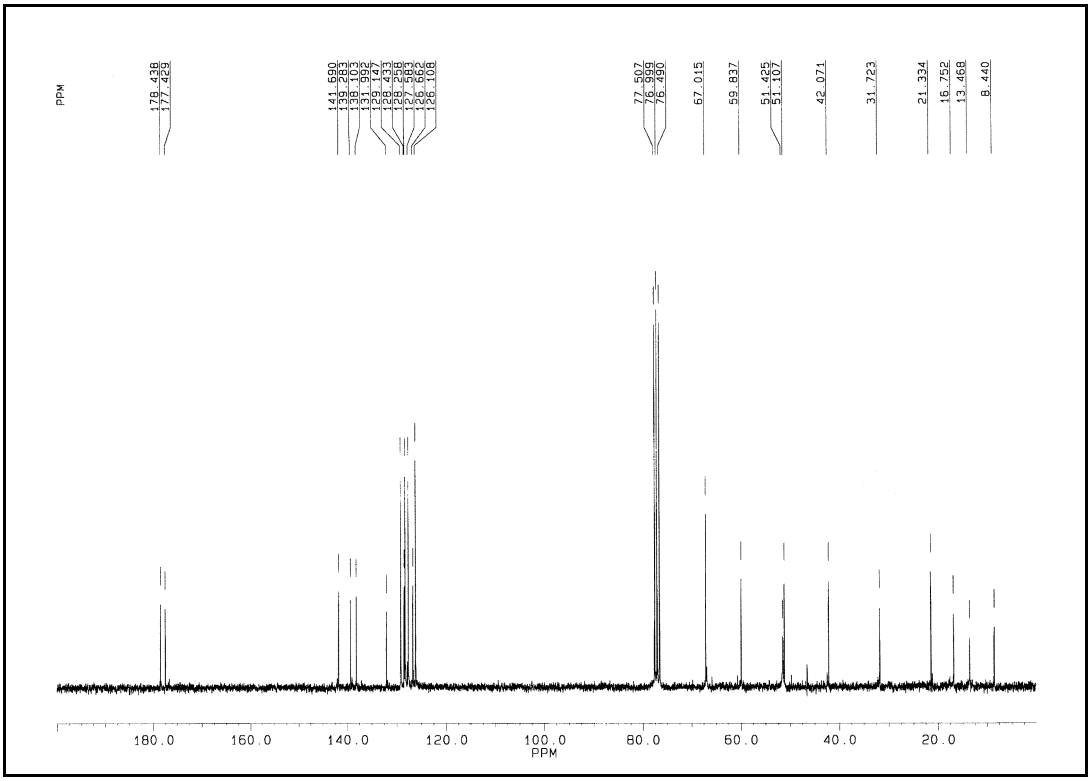




5-(1'-(Morpholin-4"-yl)ethyl)-2,6-diphenylspiro[cyclopropane-1',4-(3a,4,7,7a-tetrahydroisoindole)]-1,3-dione (**187a**)

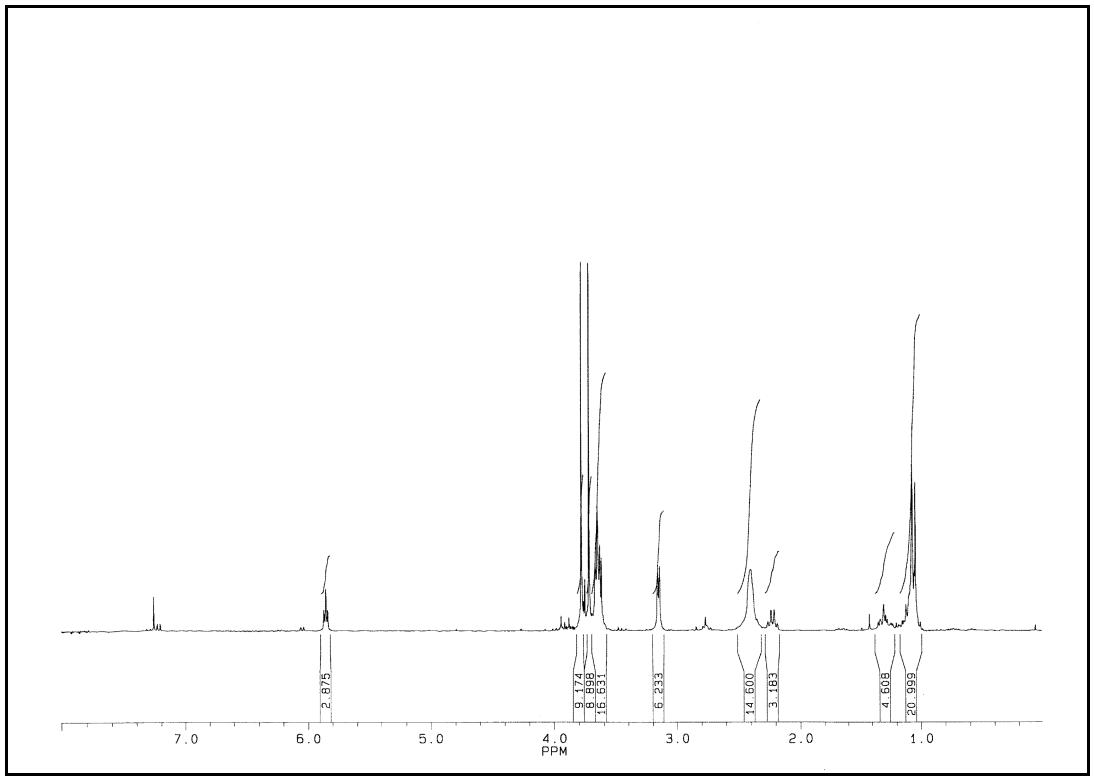
Major diastereomer

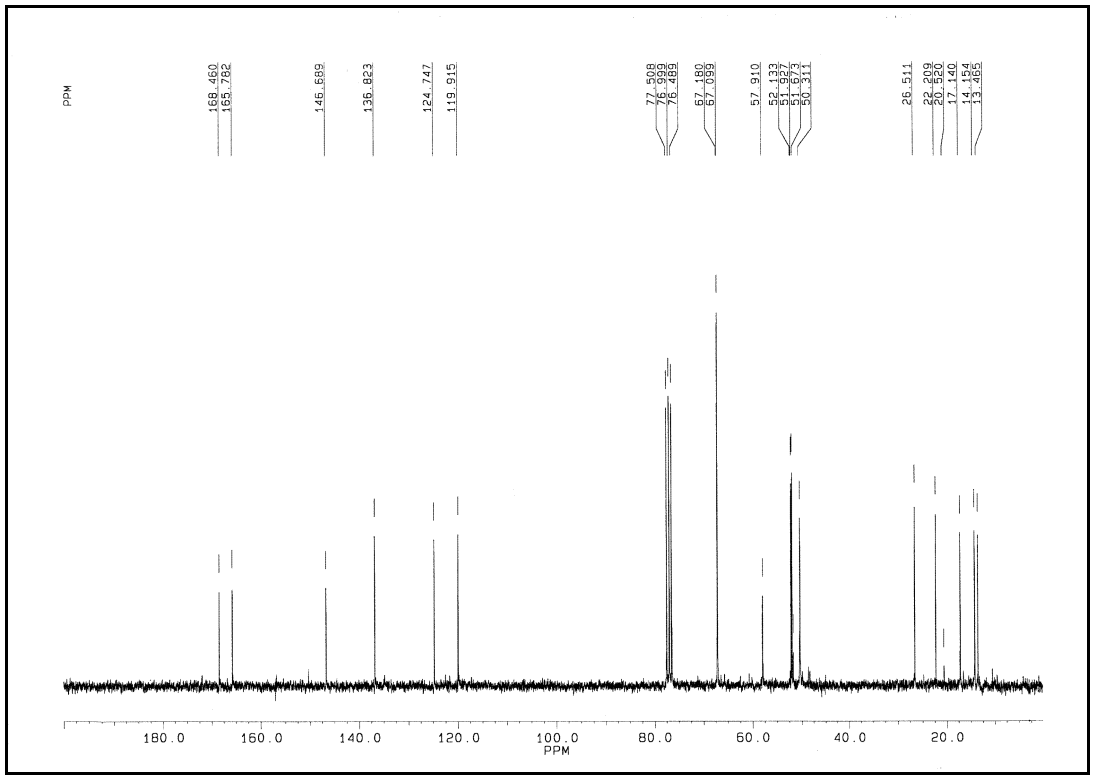




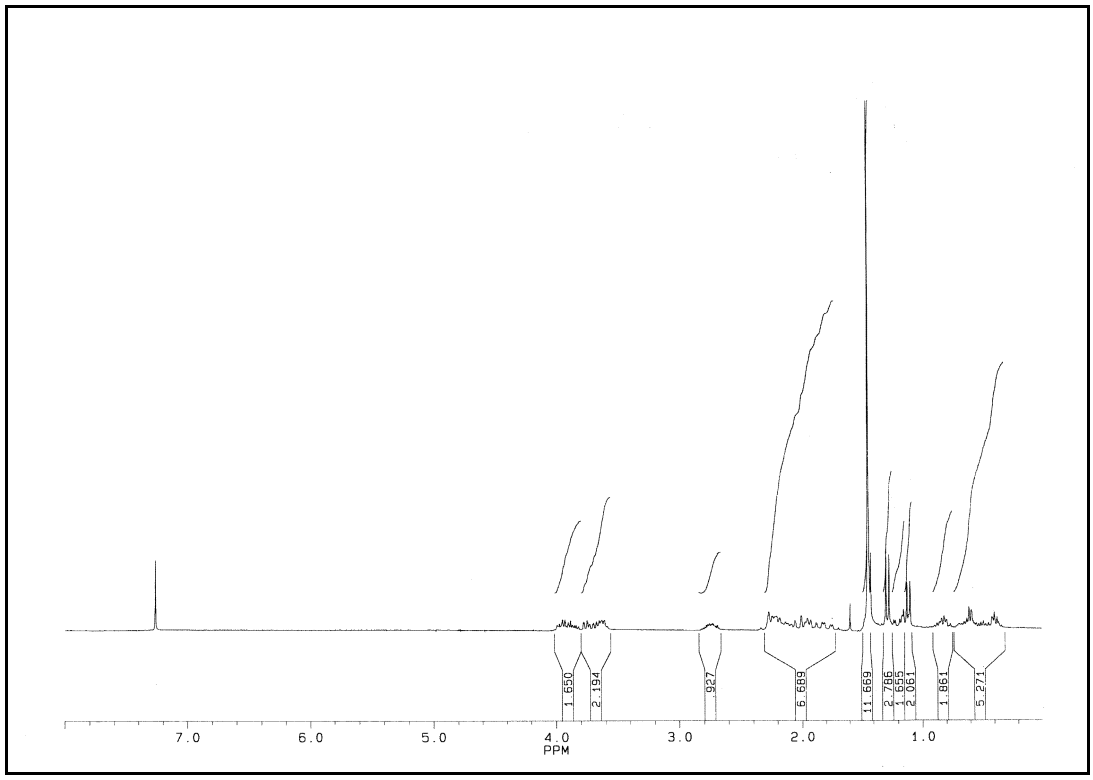
5-(1'-(Morpholin-4"-yl)ethyl)-2,6-diphenylspiro[cyclopropane-1',4-(3a,4,7,7a-tetrahydroisoindole)]-1,3-dione (**187a**)

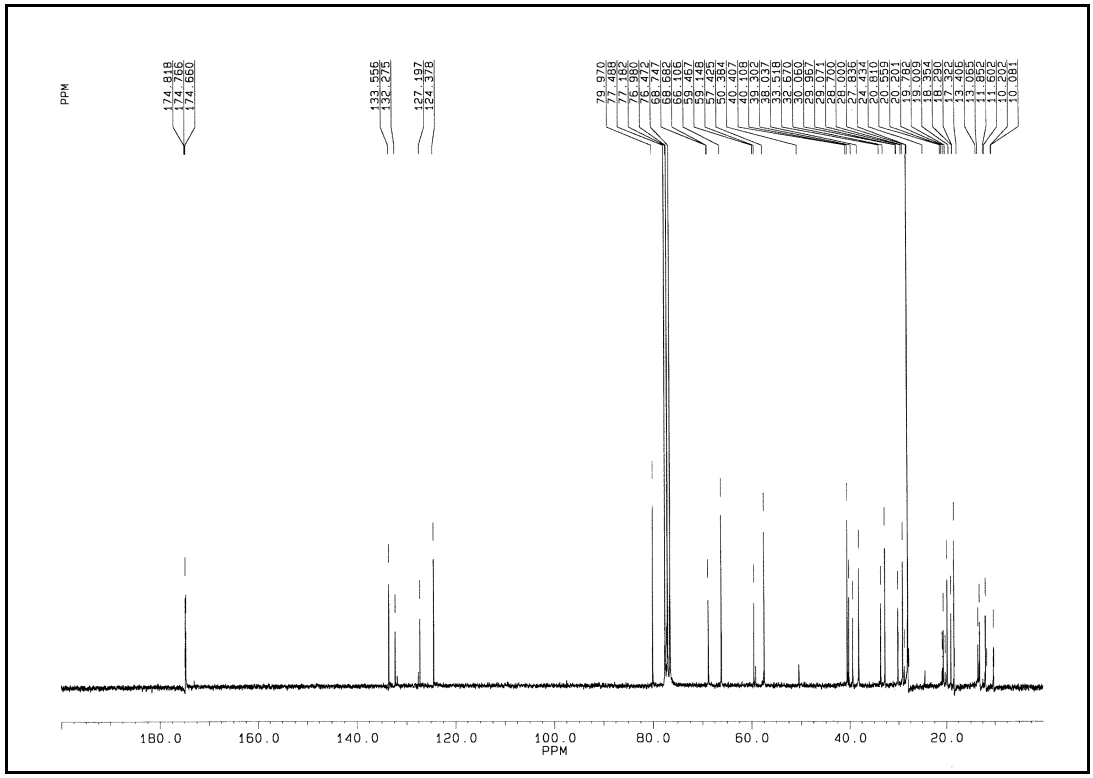
Minor diastereomer



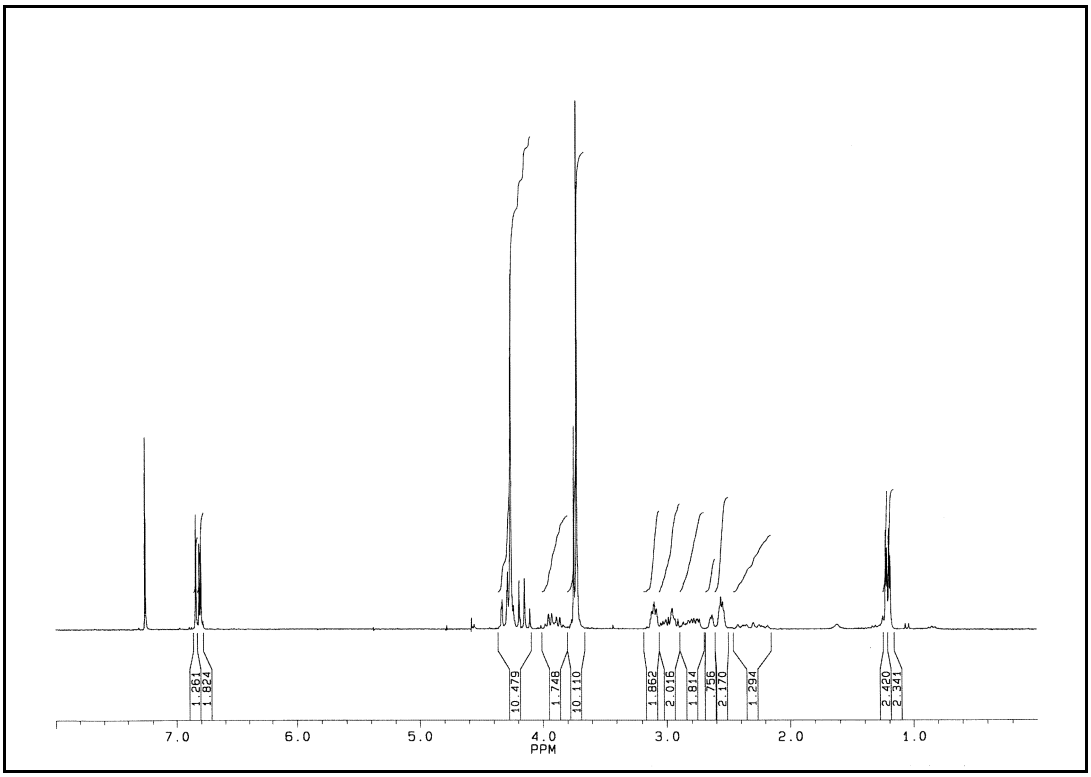


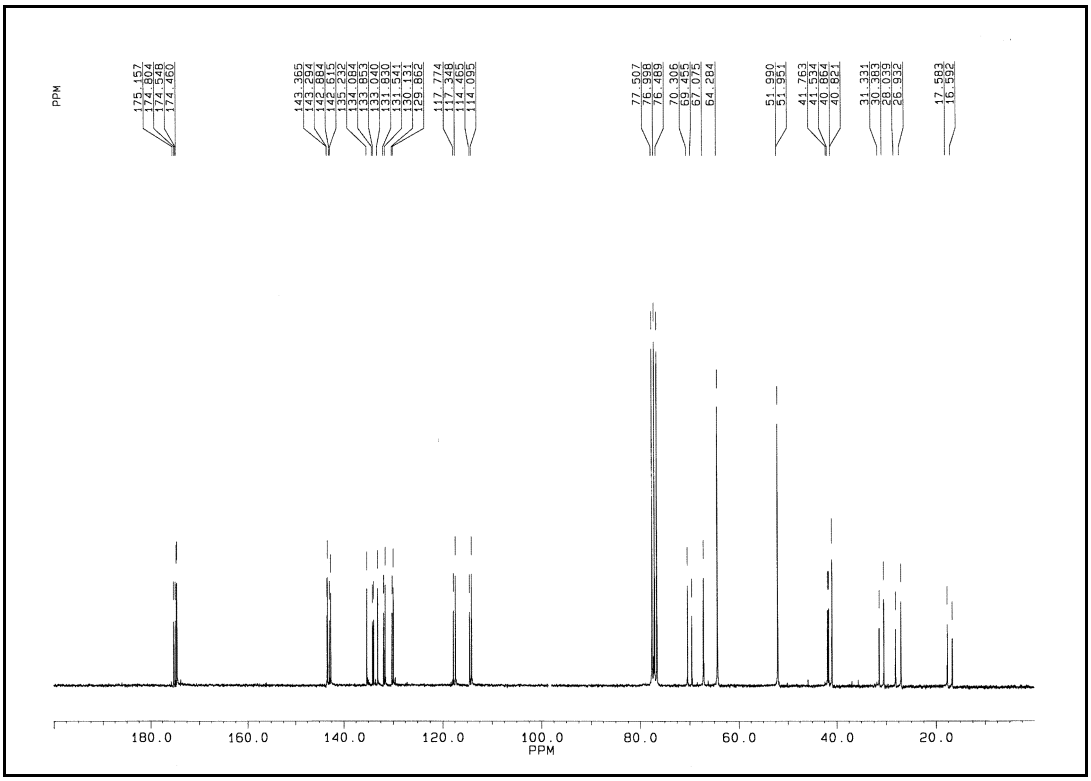
Dimethyl 8-(1-morpholin-4-ylethyl)spiro[2.5]octa-4,7-diene-4,5-dicarboxylate (**188a**)



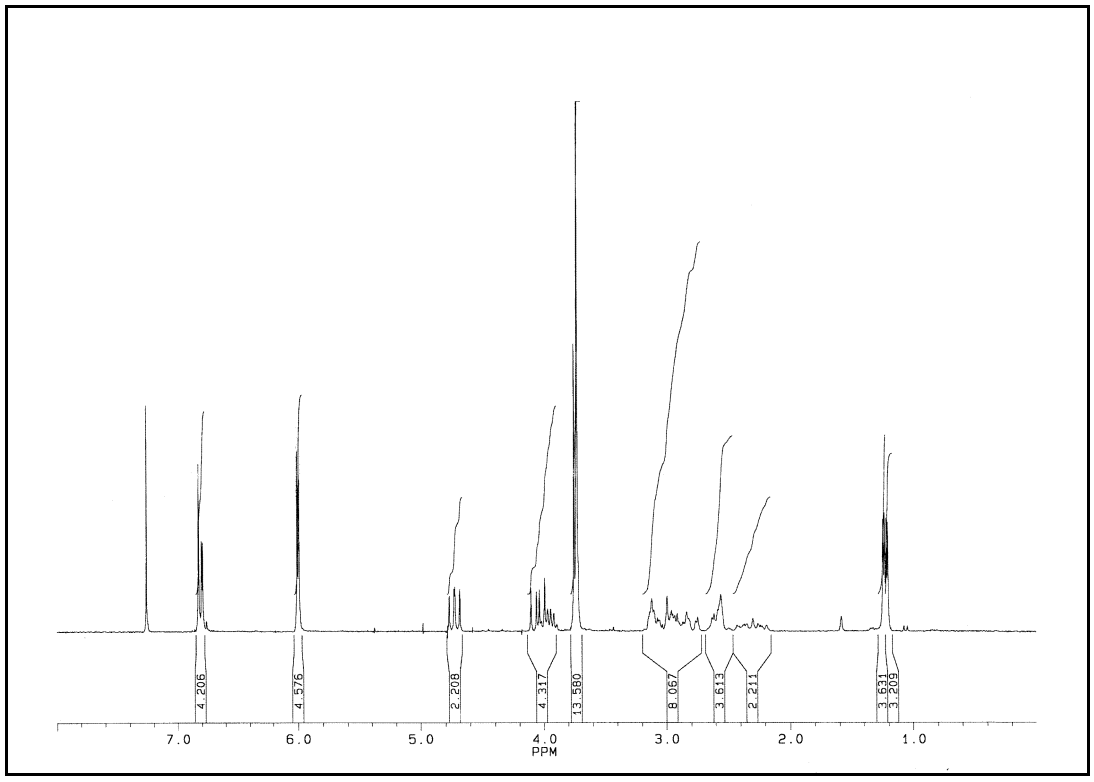


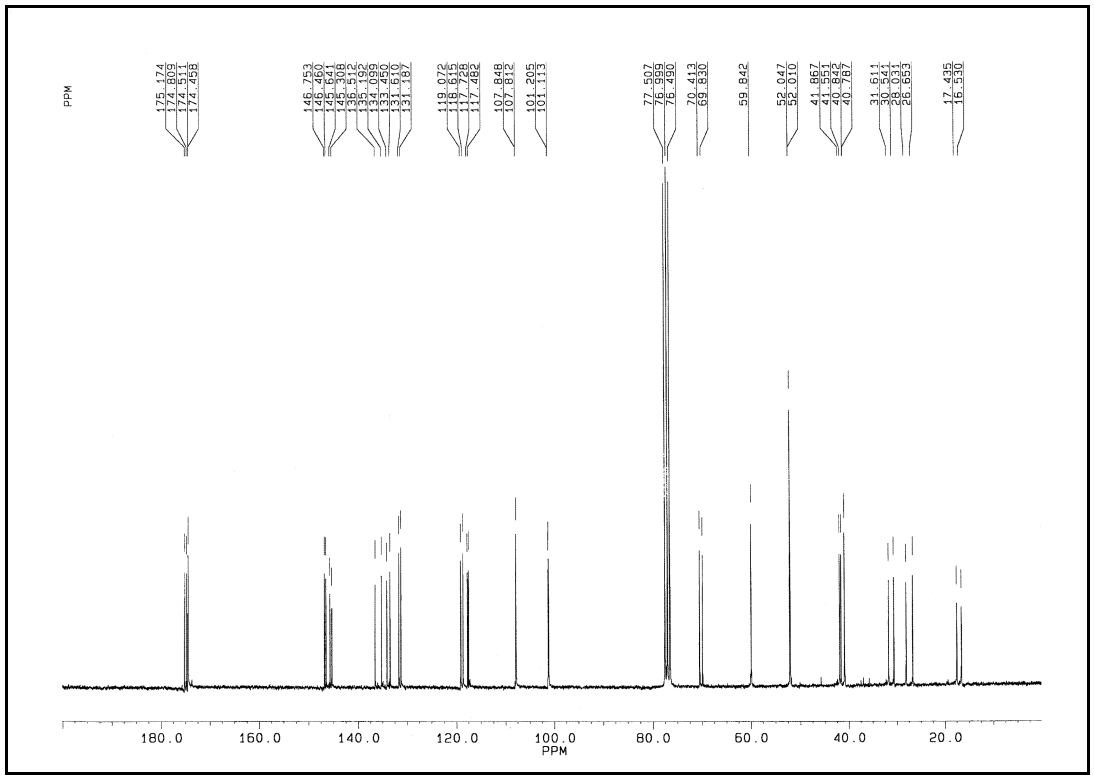
2-Methyl-8-*tert*-butoxycarbonylspiro[cyclopropane-1',10-(3-oxabicyclo[4.4.0] dec-1(6)-ene)] (**207**)





2,3-Dimethyl 5-methyl-2,3,5,7,10,11-hexahydro-1H,4H-6,9,12-trioxa-benzo[3,4] cyclohepta [1,2-b]naphthalene-dicarboxylate (234f**)**





10,11-Dimethyl 8-methyl-6,8,9,10,11,12-hexahydro-1,3,7-trioxa-benzo[6,7]cyclohepta
[1,2-e]indene-dicarboxylate (**234g**)

G. Crystal Data

1. 5-tert-Butyl-1-methyl 8-phenylspiro[2.5]oct-7-ene-1,5-dicarboxylate (*cis*, *trans*-**104E**)
2. 5-tert-Butyl-1-methyl 8-phenylspiro[2.5]oct-7-ene-1,5-dicarboxylate (*trans*, *trans*-**104E**)
3. Methyl 8-phenyl-1-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)spiro[2.5]oct-7-ene-5-carboxylate (*cis*, *trans*-**104B**)
4. 6'-[1-Morpholin-4-ylethyl]-2'-phenylspiro[cyclopropane-1,5'(10a'*H*)-5',7',8',9',10',10a'-hexahydro-[1,2,4]triazolo[1,2-a]cinnoline]-1,3-dione (**180a**)
5. 6'-(1-Morpholin-4-ylethyl)-2'-phenylspiro[cyclopropane-1,5'(8'*H*)-[1,2,4]triazolo[1,2-a]pyridazine]-1',3'-dione (**184a**)
6. 2-Methyl-3-(toluene-4-sulfonyl)-8-*tert*-butoxycarbonylspiro[cyclopropane-1',10-(3-aza-bicyclo[4.4.0]dec-1(6)-ene)] (**209**)
7. 2,3-Dimethyl 9,10-dimethoxy-5-methyl-1,2,3,4,5,7-hexahydro-dibenzo[c,e]oxepine-dicarboxylate (**234c**)

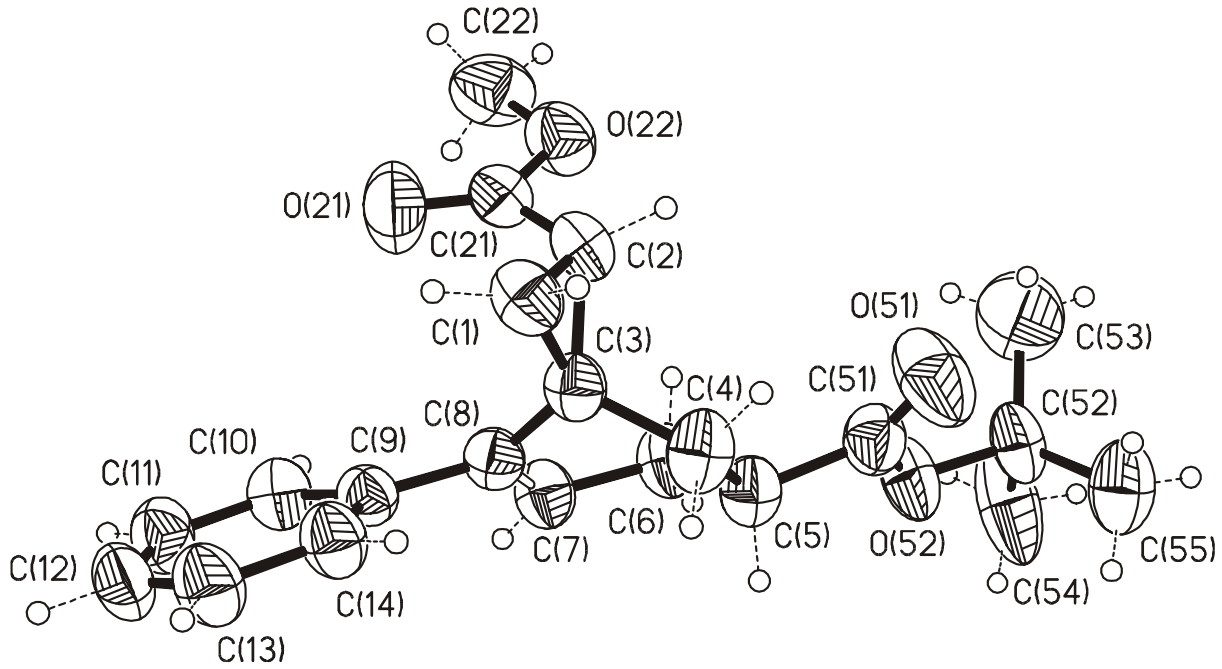


Table 1. Crystal data and structure refinement for *cis*, *trans*-**104E**

Identification code	adm173	
Empirical formula	$C_{21}H_{26}O_4$	
Formula weight	342.42	
Temperature	200(2) K	
Wavelength	71.073 pm	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 1718.9(3) pm	α = 90°.
	b = 637.12(13) pm	β = 94.58(3)°.
	c = 1748.3(4) pm	γ = 90°.
Volume	1.9085(7) nm^3	
Z	4	
Density (calculated)	1.192 Mg/m^3	
Absorption coefficient	0.081 mm^{-1}	
F(000)	736	
Crystal size	0.50 x 0.50 x 0.50 mm^3	
Theta range for data collection	3.58 to 24.97°.	
Index ranges	-20<=h<=20, -7<=k<=7, -20<=l<=20	
Reflections collected	6956	
Independent reflections	3342 [R(int) = 0.0781]	
Completeness to theta = 24.97°	99.6 %	
Max. and min. transmission	0.9605 and 0.9605	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	3342 / 0 / 231
Goodness-of-fit on F^2	1.043
Final R indices [I>2sigma(I)]	R1 = 0.0548, wR2 = 0.1398
R indices (all data)	R1 = 0.0765, wR2 = 0.1560
Extinction coefficient	0.0078(10)
Largest diff. peak and hole	0.350 and -0.169 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (pm^2x 10^{-1}) for *cis*, *trans*-**104E**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	4538(1)	-1703(4)	6873(1)	59(1)
C(2)	4619(1)	-203(4)	6223(1)	56(1)
C(3)	3878(1)	-265(3)	6664(1)	49(1)
C(4)	3153(1)	-1102(4)	6208(2)	62(1)
C(5)	2680(1)	661(4)	5780(1)	59(1)
C(6)	3040(2)	2824(4)	5925(1)	60(1)
C(7)	3270(1)	3080(4)	6763(1)	54(1)
C(8)	3695(1)	1598(3)	7133(1)	47(1)
C(9)	3909(1)	1692(3)	7970(1)	47(1)
C(10)	4161(1)	3563(4)	8321(1)	58(1)
C(11)	4313(1)	3675(4)	9106(1)	67(1)
C(12)	4219(2)	1952(5)	9556(1)	69(1)
C(13)	3978(2)	87(5)	9219(1)	68(1)
C(14)	3827(1)	-39(4)	8434(1)	58(1)
C(21)	5144(1)	1594(4)	6347(1)	59(1)
O(21)	5420(1)	2221(4)	6953(1)	94(1)
O(22)	5278(1)	2530(3)	5688(1)	71(1)
C(22)	5798(2)	4312(5)	5747(2)	86(1)
O(51)	2776(1)	-1319(4)	4611(1)	107(1)
C(51)	2558(1)	205(4)	4921(1)	61(1)
O(52)	2124(1)	1699(3)	4578(1)	71(1)
C(52)	1922(2)	1760(4)	3738(1)	66(1)
C(53)	2654(2)	1786(8)	3322(2)	129(2)
C(54)	1457(3)	3763(5)	3654(2)	120(2)
C(55)	1411(2)	-63(5)	3506(2)	86(1)

Table 3. Bond lengths [pm] and angles [deg] for *cis*, *trans*-**104E**.

C(1)-C(3)	148.1(3)	C(8)-C(3)-C(2)	118.32(18)
C(1)-C(2)	150.1(3)	C(4)-C(3)-C(2)	114.89(19)
C(2)-C(21)	146.3(3)	C(3)-C(4)-C(5)	112.10(19)
C(2)-C(3)	154.2(3)	C(6)-C(5)-C(51)	110.9(2)
C(3)-C(8)	149.0(3)	C(6)-C(5)-C(4)	112.78(18)
C(3)-C(4)	152.2(3)	C(51)-C(5)-C(4)	111.3(2)
C(4)-C(5)	154.4(3)	C(7)-C(6)-C(5)	109.4(2)
C(5)-C(6)	152.3(4)	C(8)-C(7)-C(6)	119.5(2)
C(5)-C(51)	152.8(3)	C(7)-C(8)-C(9)	122.4(2)
C(6)-C(7)	149.6(3)	C(7)-C(8)-C(3)	115.40(19)
C(7)-C(8)	133.0(3)	C(9)-C(8)-C(3)	121.94(18)
C(8)-C(9)	148.1(3)	C(14)-C(9)-C(10)	117.9(2)
C(9)-C(14)	138.3(3)	C(14)-C(9)-C(8)	121.2(2)
C(9)-C(10)	139.3(3)	C(10)-C(9)-C(8)	120.87(19)
C(10)-C(11)	137.9(3)	C(11)-C(10)-C(9)	120.6(2)
C(11)-C(12)	136.7(4)	C(12)-C(11)-C(10)	120.6(2)
C(12)-C(13)	137.5(4)	C(11)-C(12)-C(13)	119.6(2)
C(13)-C(14)	137.9(3)	C(12)-C(13)-C(14)	120.2(2)
C(21)-O(21)	119.5(3)	C(13)-C(14)-C(9)	121.1(2)
C(21)-O(22)	133.3(3)	O(21)-C(21)-O(22)	122.2(2)
O(22)-C(22)	144.4(3)	O(21)-C(21)-C(2)	126.1(2)
O(51)-C(51)	118.7(3)	O(22)-C(21)-C(2)	111.6(2)
C(51)-O(52)	132.4(3)	C(21)-O(22)-C(22)	116.0(2)
O(52)-C(52)	148.1(3)	O(51)-C(51)-O(52)	124.6(2)
C(52)-C(55)	149.3(4)	O(51)-C(51)-C(5)	125.5(2)
C(52)-C(54)	150.7(4)	O(52)-C(51)-C(5)	109.7(2)
C(52)-C(53)	150.3(4)	C(51)-O(52)-C(52)	123.2(2)
C(3)-C(1)-C(2)	62.27(15)	O(52)-C(52)-C(55)	109.6(2)
C(21)-C(2)-C(1)	118.7(2)	O(52)-C(52)-C(54)	101.5(2)
C(21)-C(2)-C(3)	118.03(19)	C(55)-C(52)-C(54)	109.6(2)
C(1)-C(2)-C(3)	58.25(14)	O(52)-C(52)-C(53)	110.0(2)
C(1)-C(3)-C(8)	123.24(18)	C(55)-C(52)-C(53)	112.0(3)
C(1)-C(3)-C(4)	119.4(2)	C(54)-C(52)-C(53)	113.7(3)
C(8)-C(3)-C(4)	111.58(18)		
C(1)-C(3)-C(2)	59.48(14)		

Table 4. Anisotropic displacement parameters ($pm^2 x\ 10^{-1}$) for *cis*, *trans*-**104E**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	73(2)	54(1)	50(1)	5(1)	6(1)	10(1)
C(2)	68(1)	60(1)	42(1)	-3(1)	9(1)	1(1)
C(3)	56(1)	47(1)	43(1)	8(1)	0(1)	-1(1)
C(4)	75(2)	47(1)	63(2)	6(1)	-8(1)	-8(1)
C(5)	63(1)	61(2)	52(1)	-1(1)	-2(1)	-3(1)
C(6)	74(2)	53(1)	50(1)	6(1)	-5(1)	5(1)
C(7)	64(1)	49(1)	49(1)	1(1)	-1(1)	4(1)
C(8)	50(1)	45(1)	44(1)	5(1)	4(1)	-3(1)
C(9)	49(1)	50(1)	43(1)	3(1)	5(1)	2(1)
C(10)	66(1)	52(1)	55(1)	1(1)	1(1)	1(1)
C(11)	74(2)	67(2)	58(2)	-15(1)	-2(1)	0(1)
C(12)	77(2)	88(2)	40(1)	-2(1)	1(1)	8(2)
C(13)	85(2)	70(2)	48(1)	13(1)	5(1)	-3(1)
C(14)	71(1)	54(1)	48(1)	5(1)	3(1)	-6(1)
C(21)	56(1)	73(2)	47(1)	-1(1)	9(1)	1(1)
O(21)	98(1)	127(2)	56(1)	-7(1)	-4(1)	-42(1)
O(22)	84(1)	75(1)	57(1)	4(1)	15(1)	-13(1)
C(22)	87(2)	77(2)	98(2)	1(2)	31(2)	-15(2)
O(51)	131(2)	113(2)	74(1)	-23(1)	-10(1)	63(2)
C(51)	62(1)	62(2)	56(1)	-3(1)	-5(1)	4(1)
O(52)	103(1)	63(1)	44(1)	-5(1)	-10(1)	14(1)
C(52)	98(2)	60(2)	39(1)	-3(1)	-5(1)	-5(1)
C(53)	130(3)	182(4)	78(2)	18(3)	25(2)	-48(3)
C(54)	220(4)	71(2)	60(2)	0(2)	-44(2)	33(2)
C(55)	107(2)	77(2)	69(2)	5(2)	-19(2)	-10(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (pm^2x 10^{-1}) for *cis*, *trans*-**104E**.

Atom	x	y	z	U(eq)
H(1A)	4465	-3207	6745	71
H(1B)	4856	-1430	7361	71
H(2A)	4574	-818	5695	68
H(4A)	2818	-1822	6561	75
H(4B)	3311	-2147	5831	75
H(5A)	2153	684	5984	70
H(6A)	3505	2980	5629	72
H(6B)	2658	3922	5752	72
H(7A)	3114	4291	7028	65
H(10A)	4229	4773	8016	70
H(11A)	4484	4962	9337	80
H(12A)	4319	2043	10097	82
H(13A)	3916	-1118	9528	81
H(14A)	3664	-1338	8207	69
H(22A)	5847	4901	5235	129
H(22B)	6312	3863	5970	129
H(22C)	5587	5381	6077	129
H(53A)	2926	441	3397	194
H(53B)	2995	2924	3524	194
H(53C)	2518	2010	2773	194
H(54A)	1035	3727	4000	180
H(54B)	1233	3901	3123	180
H(54C)	1799	4962	3785	180
H(55A)	986	-157	3847	128
H(55B)	1719	-1358	3543	128
H(55C)	1192	130	2976	128

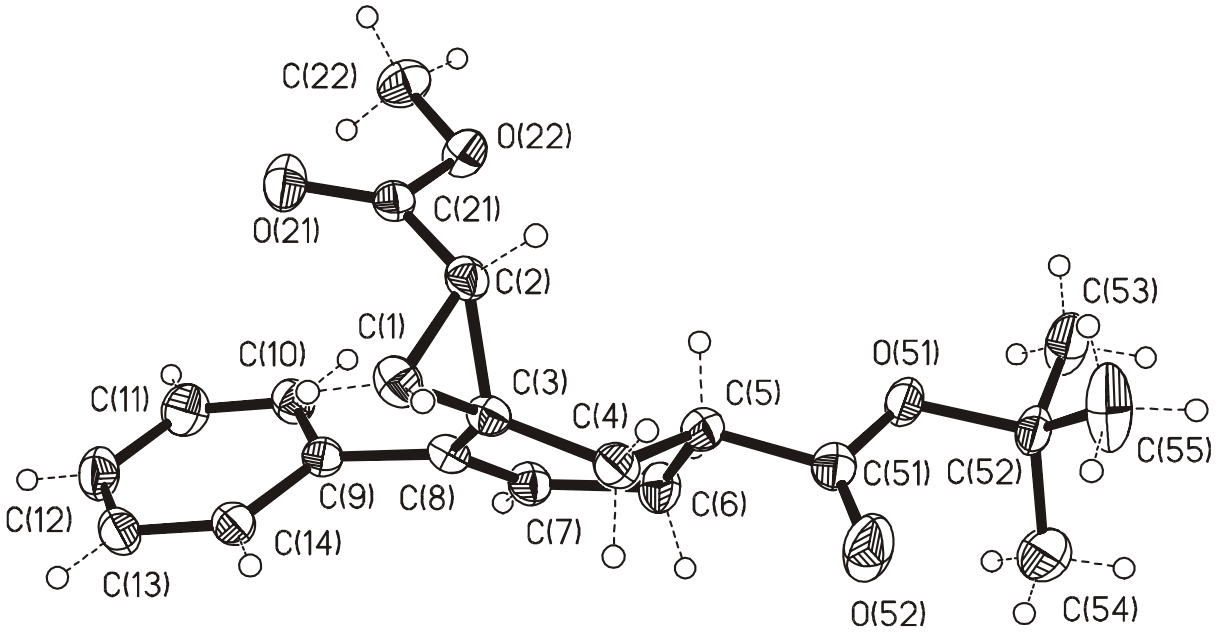


Table 1. Crystal data and structure refinement for *trans*, *trans*-**104E**.

Identification code	adm175	
Empirical formula	$C_{21}H_{26}O_4$	
Formula weight	342.42	
Temperature	140(2) K	
Wavelength	71.073 pm	
Crystal system	Monoclinic	
Space group	Cc	
Unit cell dimensions	a = 628.33(13) pm	α = 90°.
	b = 2413.4(5) pm	β = 99.42(3)°.
	c = 1274.9(3) pm	γ = 90°.
Volume	1.9073(7) nm^3	
Z	4	
Density (calculated)	1.192 Mg/m^3	
Absorption coefficient	0.081 mm^{-1}	
F(000)	736	
Crystal size	0.70 x 0.20 x 0.20 mm^3	
Theta range for data collection	1.69 to 24.77°.	
Index ranges	-7<=h<=7, -28<=k<=28, -14<=l<=15	
Reflections collected	5426	
Independent reflections	3037 [R(int) = 0.0498]	
Completeness to theta = 24.77°	98.7 %	
Max. and min. transmission	0.9839 and 0.9453	
Refinement method	Full-matrix least-squares on F^2	

Data / restraints / parameters	3037 / 2 / 230
Goodness-of-fit on F^2	1.057
Final R indices [I>2sigma(I)]	R1 = 0.0375, wR2 = 0.1052
R indices (all data)	R1 = 0.0383, wR2 = 0.1062
Absolute structure parameter	-1.0(9)
Largest diff. peak and hole	0.156 and -0.131 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (pm^2x 10^{-1}) for *trans*, *trans*-**104E**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	9712(3)	2486(1)	2021(2)	28(1)
C(2)	8199(3)	2559(1)	2804(1)	24(1)
C(3)	7725(3)	2837(1)	1705(1)	23(1)
C(4)	7997(3)	3459(1)	1733(2)	26(1)
C(5)	5927(3)	3727(1)	1961(2)	26(1)
C(6)	4072(3)	3593(1)	1048(2)	30(1)
C(7)	4144(3)	3002(1)	674(2)	26(1)
C(8)	5786(3)	2648(1)	947(1)	23(1)
C(9)	5599(3)	2077(1)	485(1)	23(1)
C(10)	3778(3)	1761(1)	551(2)	28(1)
C(11)	3463(4)	1246(1)	61(2)	35(1)
C(12)	4999(4)	1039(1)	-502(2)	35(1)
C(13)	6833(3)	1344(1)	-565(2)	30(1)
C(14)	7139(3)	1861(1)	-73(1)	25(1)
O(21)	7375(3)	1594(1)	2917(1)	41(1)
C(21)	6916(3)	2070(1)	3035(1)	25(1)
O(22)	5137(2)	2225(1)	3416(1)	29(1)
C(22)	3783(4)	1771(1)	3658(2)	36(1)
O(51)	4641(2)	4544(1)	2621(1)	29(1)
C(51)	6154(3)	4349(1)	2090(2)	29(1)
O(52)	7465(3)	4623(1)	1743(2)	52(1)
C(52)	4303(3)	5149(1)	2732(2)	29(1)
C(53)	2420(4)	5169(1)	3331(2)	42(1)
C(54)	3691(6)	5404(1)	1640(2)	61(1)
C(55)	6251(4)	5407(1)	3393(3)	55(1)

Table 3. Bond lengths [pm] and angles [deg] for *trans*, *trans*-**104E**.

C(1)-C(2)	149.7(3)	C(8)-C(3)-C(2)	118.06(15)
C(1)-C(3)	150.8(3)	C(1)-C(3)-C(2)	58.85(12)
C(2)-C(21)	148.5(3)	C(4)-C(3)-C(2)	114.10(15)
C(2)-C(3)	153.8(2)	C(3)-C(4)-C(5)	109.20(15)
C(3)-C(8)	149.7(3)	C(51)-C(5)-C(4)	111.89(15)
C(3)-C(4)	151.1(2)	C(51)-C(5)-C(6)	109.63(15)
C(4)-C(5)	152.2(3)	C(4)-C(5)-C(6)	109.31(15)
C(5)-C(51)	151.4(3)	C(7)-C(6)-C(5)	112.28(15)
C(5)-C(6)	154.1(3)	C(8)-C(7)-C(6)	125.64(17)
C(6)-C(7)	150.7(3)	C(7)-C(8)-C(9)	118.50(16)
C(7)-C(8)	134.1(3)	C(7)-C(8)-C(3)	118.93(16)
C(8)-C(9)	149.6(2)	C(9)-C(8)-C(3)	122.57(16)
C(9)-C(10)	138.9(3)	C(10)-C(9)-C(14)	118.23(17)
C(9)-C(14)	139.4(3)	C(10)-C(9)-C(8)	119.70(17)
C(10)-C(11)	139.0(3)	C(14)-C(9)-C(8)	121.94(17)
C(11)-C(12)	138.7(3)	C(11)-C(10)-C(9)	121.48(18)
C(12)-C(13)	138.1(3)	C(12)-C(11)-C(10)	119.65(19)
C(13)-C(14)	139.5(3)	C(13)-C(12)-C(11)	119.75(18)
O(21)-C(21)	120.1(2)	C(12)-C(13)-C(14)	120.36(18)
C(21)-O(22)	134.3(2)	C(9)-C(14)-C(13)	120.52(18)
O(22)-C(22)	145.0(2)	O(21)-C(21)-O(22)	122.89(17)
O(51)-C(51)	133.9(2)	O(21)-C(21)-C(2)	125.91(17)
O(51)-C(52)	148.6(2)	O(22)-C(21)-C(2)	111.19(15)
C(51)-O(52)	119.7(3)	C(21)-O(22)-C(22)	114.78(15)
C(52)-C(55)	150.3(4)	C(51)-O(51)-C(52)	121.19(15)
C(52)-C(53)	151.0(3)	O(52)-C(51)-O(51)	125.53(18)
C(52)-C(54)	151.2(3)	O(52)-C(51)-C(5)	124.50(18)
C(2)-C(1)-C(3)	61.60(12)	O(51)-C(51)-C(5)	109.94(15)
C(21)-C(2)-C(1)	117.64(15)	O(51)-C(52)-C(55)	110.15(18)
C(21)-C(2)-C(3)	119.81(16)	O(51)-C(52)-C(53)	102.46(15)
C(1)-C(2)-C(3)	59.55(12)	C(55)-C(52)-C(53)	109.6(2)
C(8)-C(3)-C(1)	123.52(16)	O(51)-C(52)-C(54)	109.30(17)
C(8)-C(3)-C(4)	113.28(15)	C(55)-C(52)-C(54)	114.2(2)
C(1)-C(3)-C(4)	117.78(16)	C(53)-C(52)-C(54)	110.5(2)

Table 4. Anisotropic displacement parameters ($pm^2 x\ 10^{-1}$) for *trans*, *trans*-**104E**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	25(1)	31(1)	26(1)	-4(1)	3(1)	2(1)
C(2)	26(1)	25(1)	19(1)	-3(1)	0(1)	3(1)
C(3)	23(1)	26(1)	20(1)	0(1)	6(1)	1(1)
C(4)	26(1)	27(1)	24(1)	-2(1)	5(1)	-2(1)
C(5)	29(1)	23(1)	27(1)	1(1)	8(1)	-1(1)
C(6)	29(1)	26(1)	34(1)	-1(1)	3(1)	6(1)
C(7)	26(1)	27(1)	23(1)	-1(1)	0(1)	2(1)
C(8)	24(1)	26(1)	19(1)	-1(1)	5(1)	0(1)
C(9)	28(1)	23(1)	18(1)	0(1)	0(1)	2(1)
C(10)	25(1)	30(1)	29(1)	-1(1)	6(1)	3(1)
C(11)	34(1)	31(1)	40(1)	-2(1)	4(1)	-4(1)
C(12)	43(1)	25(1)	34(1)	-6(1)	1(1)	4(1)
C(13)	34(1)	31(1)	24(1)	-4(1)	4(1)	8(1)
C(14)	24(1)	28(1)	22(1)	1(1)	2(1)	5(1)
O(21)	56(1)	24(1)	47(1)	-1(1)	20(1)	5(1)
C(21)	30(1)	24(1)	18(1)	0(1)	1(1)	5(1)
O(22)	28(1)	24(1)	34(1)	3(1)	6(1)	1(1)
C(22)	37(1)	34(1)	37(1)	6(1)	8(1)	-5(1)
O(51)	33(1)	18(1)	36(1)	0(1)	11(1)	0(1)
C(51)	33(1)	25(1)	31(1)	0(1)	10(1)	0(1)
O(52)	60(1)	29(1)	79(1)	-4(1)	43(1)	-7(1)
C(52)	38(1)	16(1)	36(1)	-1(1)	11(1)	1(1)
C(53)	42(1)	24(1)	62(2)	-4(1)	21(1)	-1(1)
C(54)	106(2)	35(1)	45(1)	12(1)	22(2)	26(1)
C(55)	42(1)	36(1)	89(2)	-26(1)	11(1)	-4(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (pm^2x 10^{-1}) for *trans*, *trans*-**104E**.

Atom	x	y	z	U(eq)
H(1A)	9751	2119	1678	33
H(1B)	11121	2679	2170	33
H(2A)	8703	2810	3418	29
H(4A)	8320	3592	1041	31
H(4B)	9217	3563	2292	31
H(5A)	5570	3567	2635	31
H(6A)	2677	3660	1291	36
H(6B)	4158	3845	444	36
H(7A)	2920	2869	205	31
H(10A)	2724	1899	939	33
H(11A)	2203	1037	113	42
H(12A)	4790	688	-842	42
H(13A)	7892	1201	-945	36
H(14A)	8408	2067	-120	30
H(22A)	2505	1920	3909	53
H(22B)	4596	1538	4213	53
H(22C)	3333	1549	3017	53
H(53A)	2840	5001	4034	63
H(53B)	1202	4964	2934	63
H(53D)	1998	5555	3413	63
H(54A)	4936	5394	1268	91
H(54D)	3240	5789	1712	91
H(54B)	2499	5193	1234	91
H(55D)	6678	5187	4040	83
H(55A)	5903	5785	3588	83
H(55B)	7441	5417	2984	83

Table 6. Torsion angles [deg] for *trans*, *trans*-**104E**.

C(3)-C(1)-C(2)-C(21)	110.07(18)	C(7)-C(8)-C(9)-C(14)	124.53(19)
C(2)-C(1)-C(3)-C(8)	-105.01(18)	C(3)-C(8)-C(9)-C(14)	-55.9(2)
C(2)-C(1)-C(3)-C(4)	102.76(17)	C(14)-C(9)-C(10)-C(11)	-1.0(3)
C(21)-C(2)-C(3)-C(8)	7.7(2)	C(8)-C(9)-C(10)-C(11)	174.97(18)
C(1)-C(2)-C(3)-C(8)	114.14(18)	C(9)-C(10)-C(11)-C(12)	0.3(3)
C(21)-C(2)-C(3)-C(1)	-106.46(18)	C(10)-C(11)-C(12)-C(13)	0.5(3)
C(21)-C(2)-C(3)-C(4)	144.49(17)	C(11)-C(12)-C(13)-C(14)	-0.6(3)
C(1)-C(2)-C(3)-C(4)	-109.04(17)	C(10)-C(9)-C(14)-C(13)	0.9(3)
C(8)-C(3)-C(4)-C(5)	54.18(19)	C(8)-C(9)-C(14)-C(13)	-174.98(17)
C(1)-C(3)-C(4)-C(5)	-150.83(16)	C(12)-C(13)-C(14)-C(9)	-0.1(3)
C(2)-C(3)-C(4)-C(5)	-84.71(19)	C(1)-C(2)-C(21)-O(21)	23.3(3)
C(3)-C(4)-C(5)-C(51)	175.29(14)	C(3)-C(2)-C(21)-O(21)	92.2(2)
C(3)-C(4)-C(5)-C(6)	-63.08(19)	C(1)-C(2)-C(21)-O(22)	-157.52(16)
C(51)-C(5)-C(6)-C(7)	164.08(16)	C(3)-C(2)-C(21)-O(22)	-88.58(19)
C(4)-C(5)-C(6)-C(7)	41.1(2)	O(21)-C(21)-O(22)-C(22)	-1.0(3)
C(5)-C(6)-C(7)-C(8)	-11.0(3)	C(2)-C(21)-O(22)-C(22)	179.73(16)
C(6)-C(7)-C(8)-C(9)	-179.01(17)	C(52)-O(51)-C(51)-O(52)	6.6(3)
C(6)-C(7)-C(8)-C(3)	1.4(3)	C(52)-O(51)-C(51)-C(5)	-171.64(16)
C(1)-C(3)-C(8)-C(7)	-176.59(17)	C(4)-C(5)-C(51)-O(52)	22.0(3)
C(4)-C(3)-C(8)-C(7)	-23.3(2)	C(6)-C(5)-C(51)-O(52)	-99.4(3)
C(2)-C(3)-C(8)-C(7)	113.90(19)	C(4)-C(5)-C(51)-O(51)	-159.69(16)
C(1)-C(3)-C(8)-C(9)	3.8(3)	C(6)-C(5)-C(51)-O(51)	78.87(19)
C(4)-C(3)-C(8)-C(9)	157.18(16)	C(51)-O(51)-C(52)-C(55)	-65.8(2)
C(2)-C(3)-C(8)-C(9)	-65.7(2)	C(51)-O(51)-C(52)-C(53)	177.63(18)
C(7)-C(8)-C(9)-C(10)	-51.3(2)	C(51)-O(51)-C(52)-C(54)	60.4(3)
C(3)-C(8)-C(9)-C(10)	128.27(19)		

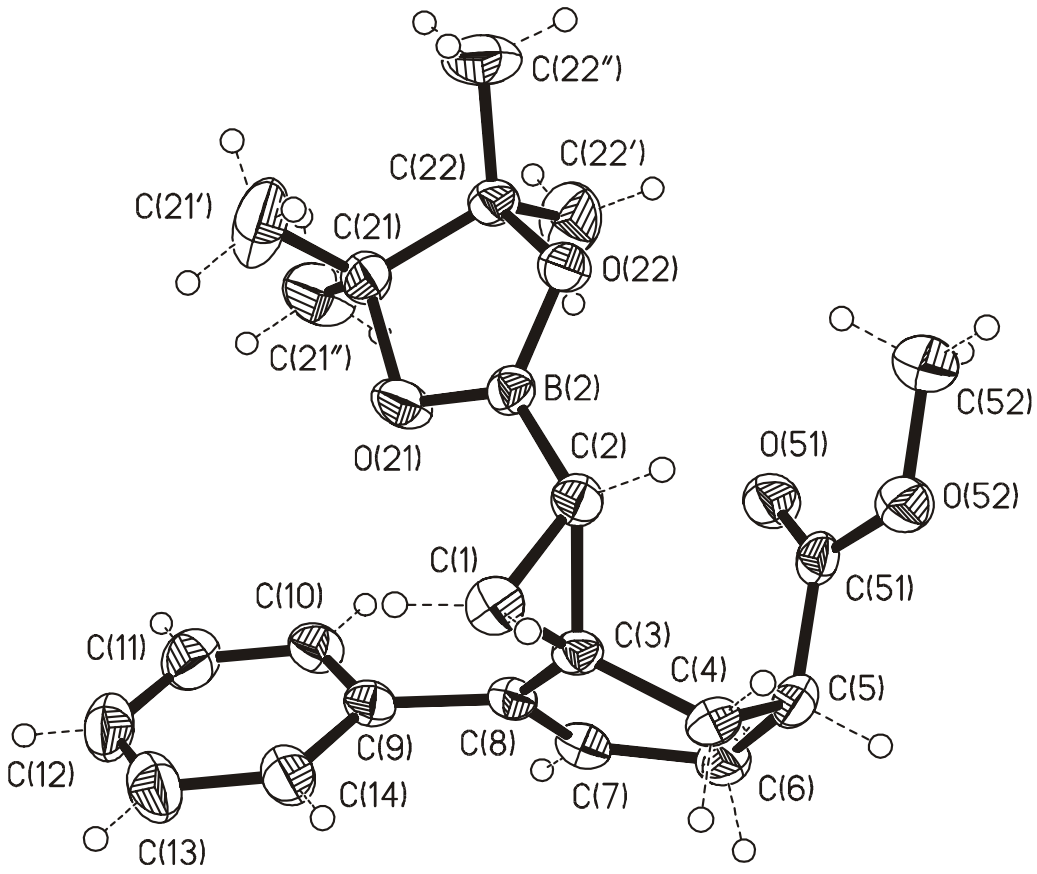


Table 1. Crystal data and structure refinement for *cis, trans*-**104B**.

Identification code	adm174	
Empirical formula	$C_{22}H_{29}BO_4$	
Formula weight	368.26	
Temperature	200(2) K	
Wavelength	71.073 pm	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 623.87(7) pm	α = 90°.
	b = 1643.88(13) pm	β = 97.141(10)°.
	c = 1005.23(8) pm	γ = 90°.
Volume	1.02293(16) nm^3	
Z	2	
Density (calculated)	1.196 Mg/m^3	
Absorption coefficient	0.080 mm^{-1}	
F(000)	396	
Crystal size	1.00 x 0.60 x 0.40 mm^3	
Theta range for data collection	3.52 to 24.91°.	
Index ranges	-7<=h<=7, -3<=k<=19, -11<=l<=11	
Reflections collected	2344	

Independent reflections	2209 [R(int) = 0.0541]
Completeness to theta = 24.91°	99.7 %
Max. and min. transmission	0.9688 and 0.9245
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2209 / 1 / 249
Goodness-of-fit on F^2	1.064
Final R indices [I>2sigma(I)]	R1 = 0.0373, wR2 = 0.0975
R indices (all data)	R1 = 0.0387, wR2 = 0.0991
Absolute structure parameter	0.0(12)
Largest diff. peak and hole	0.160 and -0.210 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (pm^2x 10^{-1}) for *cis, trans*-**104B**.´U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	7336(3)	6014(2)	3355(2)	30(1)
C(2)	5436(4)	6147(1)	2268(2)	28(1)
B(2)	4018(4)	6917(2)	2187(2)	26(1)
C(3)	5435(3)	5457(2)	3325(2)	25(1)
C(4)	5568(4)	4614(2)	2730(2)	30(1)
C(5)	3263(4)	4301(2)	2235(2)	32(1)
C(6)	1956(4)	4245(2)	3418(2)	35(1)
C(7)	2410(3)	4921(2)	4414(2)	31(1)
C(8)	3955(3)	5480(2)	4407(2)	26(1)
C(9)	4342(4)	6057(2)	5556(2)	28(1)
C(10)	2697(4)	6554(2)	5908(2)	35(1)
C(11)	3013(5)	7051(2)	7029(3)	46(1)
C(12)	4990(5)	7055(2)	7829(3)	47(1)
C(13)	6628(5)	6568(2)	7501(3)	47(1)
C(14)	6327(4)	6073(2)	6370(2)	37(1)
O(21)	3380(3)	7329(1)	3237(2)	42(1)
C(21)	2436(4)	8096(2)	2733(2)	35(1)
C(21')	4210(6)	8733(2)	2961(4)	65(1)
C(21")	560(6)	8301(2)	3494(3)	59(1)
O(22)	3316(3)	7264(1)	979(1)	33(1)
C(22)	1804(4)	7903(2)	1213(2)	29(1)
C(22")	2094(6)	8599(2)	266(3)	53(1)
C(22')	-453(5)	7546(2)	903(3)	55(1)

O(51)	646(3)	5283(1)	1239(2)	39(1)
C(51)	2173(3)	4851(2)	1148(2)	28(1)
O(52)	3110(3)	4785(1)	18(2)	38(1)
C(52)	2298(5)	5335(2)	-1056(3)	47(1)

Table 3. Bond lengths [pm] and angles [deg] for *cis, trans*-**104B**.

C(1)-C(3)	149.5(3)	C(3)-C(1)-C(2)	61.94(14)
C(1)-C(2)	152.4(3)	C(1)-C(2)-B(2)	123.1(2)
C(2)-B(2)	154.1(4)	C(1)-C(2)-C(3)	58.11(15)
C(2)-C(3)	155.4(3)	B(2)-C(2)-C(3)	125.96(19)
B(2)-O(21)	135.4(3)	O(21)-B(2)-O(22)	113.1(2)
B(2)-O(22)	136.3(3)	O(21)-B(2)-C(2)	126.2(2)
C(3)-C(8)	151.2(3)	O(22)-B(2)-C(2)	120.6(2)
C(3)-C(4)	151.6(3)	C(1)-C(3)-C(8)	121.6(2)
C(4)-C(5)	155.0(3)	C(1)-C(3)-C(4)	119.00(18)
C(5)-C(51)	151.3(3)	C(8)-C(3)-C(4)	112.04(19)
C(5)-C(6)	152.6(3)	C(1)-C(3)-C(2)	59.95(15)
C(6)-C(7)	149.8(4)	C(8)-C(3)-C(2)	121.70(19)
C(7)-C(8)	133.3(3)	C(4)-C(3)-C(2)	113.16(17)
C(8)-C(9)	149.0(3)	C(3)-C(4)-C(5)	109.62(18)
C(9)-C(10)	139.2(3)	C(51)-C(5)-C(6)	111.29(19)
C(9)-C(14)	139.7(3)	C(51)-C(5)-C(4)	110.4(2)
C(10)-C(11)	138.6(4)	C(6)-C(5)-C(4)	109.47(19)
C(11)-C(12)	138.6(4)	C(7)-C(6)-C(5)	113.7(2)
C(12)-C(13)	137.0(4)	C(8)-C(7)-C(6)	125.8(2)
C(13)-C(14)	139.1(4)	C(7)-C(8)-C(9)	118.9(2)
O(21)-C(21)	145.7(3)	C(7)-C(8)-C(3)	119.5(2)
C(21)-C(21'')	151.4(4)	C(9)-C(8)-C(3)	121.26(19)
C(21)-C(21')	151.9(4)	C(10)-C(9)-C(14)	117.9(2)
C(21)-C(22)	156.2(3)	C(10)-C(9)-C(8)	121.1(2)
O(22)-C(22)	145.1(3)	C(14)-C(9)-C(8)	120.8(2)
C(22)-C(22'')	151.3(4)	C(11)-C(10)-C(9)	121.2(2)
C(22)-C(22')	152.2(4)	C(10)-C(11)-C(12)	120.0(3)
O(51)-C(51)	120.1(3)	C(13)-C(12)-C(11)	119.6(2)
C(51)-O(52)	134.4(3)	C(12)-C(13)-C(14)	120.6(2)
O(52)-C(52)	145.0(3)	C(13)-C(14)-C(9)	120.7(3)

B(2)-O(21)-C(21)	107.87(18)	O(22)-C(22)-C(22')	106.9(2)
O(21)-C(21)-C(21")	108.7(2)	C(22")-C(22)-C(22')	110.0(2)
O(21)-C(21)-C(21')	106.8(2)	O(22)-C(22)-C(21)	102.46(17)
C(21")-C(21)-C(21')	111.4(3)	C(22")-C(22)-C(21)	115.3(2)
O(21)-C(21)-C(22)	101.89(19)	C(22')-C(22)-C(21)	113.2(2)
C(21")-C(21)-C(22)	115.0(2)	O(51)-C(51)-O(52)	123.0(2)
C(21')-C(21)-C(22)	112.2(2)	O(51)-C(51)-C(5)	126.0(2)
B(2)-O(22)-C(22)	107.54(16)	O(52)-C(51)-C(5)	111.0(2)
O(22)-C(22)-C(22")	108.32(19)	C(51)-O(52)-C(52)	115.5(2)

Table 4. Anisotropic displacement parameters ($pm^2 x\ 10^{-1}$) for *cis, trans*-**104B**.

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

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	25(1)	32(1)	34(1)	1(1)	4(1)	-1(1)
C(2)	31(1)	28(1)	26(1)	0(1)	6(1)	-2(1)
B(2)	28(1)	24(1)	27(1)	0(1)	5(1)	-3(1)
C(3)	25(1)	24(1)	26(1)	3(1)	1(1)	5(1)
C(4)	32(1)	24(1)	33(1)	1(1)	2(1)	6(1)
C(5)	38(1)	22(1)	36(1)	-4(1)	2(1)	0(1)
C(6)	40(1)	28(1)	35(1)	5(1)	1(1)	-7(1)
C(7)	31(1)	36(1)	26(1)	6(1)	3(1)	1(1)
C(8)	26(1)	26(1)	23(1)	4(1)	-1(1)	3(1)
C(9)	33(1)	30(1)	22(1)	4(1)	6(1)	-2(1)
C(10)	37(1)	38(2)	29(1)	4(1)	5(1)	3(1)
C(11)	63(2)	39(2)	39(1)	-3(1)	20(1)	1(1)
C(12)	68(2)	41(2)	33(1)	-9(1)	12(1)	-17(2)
C(13)	49(2)	54(2)	36(1)	-4(1)	-2(1)	-17(2)
C(14)	39(1)	40(2)	30(1)	-2(1)	2(1)	-4(1)
O(21)	59(1)	42(1)	24(1)	3(1)	4(1)	23(1)
C(21)	42(1)	29(1)	33(1)	-4(1)	-2(1)	9(1)
C(21')	58(2)	43(2)	88(2)	-27(2)	-18(2)	6(2)
C(21")	74(2)	64(2)	41(2)	1(2)	18(1)	35(2)
O(22)	44(1)	29(1)	26(1)	1(1)	7(1)	10(1)
C(22)	33(1)	26(1)	29(1)	2(1)	3(1)	8(1)
C(22")	68(2)	43(2)	51(2)	19(1)	15(1)	17(2)

C(22')	40(1)	57(2)	64(2)	-8(2)	-11(1)	-4(1)
O(51)	39(1)	40(1)	36(1)	1(1)	3(1)	9(1)
C(51)	29(1)	24(1)	31(1)	-6(1)	0(1)	-3(1)
O(52)	45(1)	36(1)	34(1)	2(1)	8(1)	4(1)
C(52)	60(2)	44(2)	37(1)	7(1)	8(1)	1(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (pm^2x 10^{-1}) for *cis, trans*-**104B**.

Atom	x	y	z	U(eq)
H(1A)	8681	5787	3076	36
H(1B)	7559	6417	4090	36
H(2A)	5720	5945	1369	33
H(4A)	6286	4238	3416	36
H(4B)	6437	4633	1971	36
H(5A)	3382	3743	1852	39
H(6A)	399	4251	3074	42
H(6B)	2276	3720	3881	42
H(7A)	1518	4953	5112	37
H(10A)	1333	6553	5370	41
H(11A)	1874	7389	7250	55
H(12A)	5209	7393	8600	56
H(13A)	7982	6568	8051	56
H(14A)	7482	5743	6150	44
H(21A)	4761	8754	3917	98
H(21B)	3625	9266	2669	98
H(21C)	5387	8589	2445	98
H(21D)	1093	8384	4443	88
H(21E)	-482	7853	3406	88
H(21F)	-144	8799	3125	88
H(22A)	1553	8436	-653	80
H(22B)	3630	8736	318	80
H(22C)	1286	9074	519	80
H(22D)	-633	7319	-5	83
H(22E)	-1529	7974	966	83
H(22F)	-651	7115	1550	83
H(52A)	3156	5274	-1803	70

H(52B)	2405	5897	-727	70
H(52C)	783	5206	-1363	70

Table 6. Torsion angles [°] for *cis, trans*-**104B**.

C(3)-C(1)-C(2)-B(2)	114.8(2)	C(8)-C(9)-C(10)-C(11)	175.6(2)
C(1)-C(2)-B(2)-O(21)	-38.1(4)	C(9)-C(10)-C(11)-C(12)	-0.4(4)
C(3)-C(2)-B(2)-O(21)	34.1(4)	C(10)-C(11)-C(12)-C(13)	0.2(4)
C(1)-C(2)-B(2)-O(22)	140.3(2)	C(11)-C(12)-C(13)-C(14)	0.3(4)
C(3)-C(2)-B(2)-O(22)	-147.5(2)	C(12)-C(13)-C(14)-C(9)	-0.7(4)
C(2)-C(1)-C(3)-C(8)	-110.9(2)	C(10)-C(9)-C(14)-C(13)	0.5(4)
C(2)-C(1)-C(3)-C(4)	101.5(2)	C(8)-C(9)-C(14)-C(13)	-175.1(2)
B(2)-C(2)-C(3)-C(1)	-110.1(3)	O(22)-B(2)-O(21)-C(21)	-9.5(3)
C(1)-C(2)-C(3)-C(8)	110.7(2)	C(2)-B(2)-O(21)-C(21)	169.0(2)
B(2)-C(2)-C(3)-C(8)	0.6(3)	B(2)-O(21)-C(21)-C(21")	143.8(2)
C(1)-C(2)-C(3)-C(4)	-111.2(2)	B(2)-O(21)-C(21)-C(21')	-95.9(3)
B(2)-C(2)-C(3)-C(4)	138.7(2)	B(2)-O(21)-C(21)-C(22)	22.0(2)
C(1)-C(3)-C(4)-C(5)	-155.34(19)	O(21)-B(2)-O(22)-C(22)	-8.8(3)
C(8)-C(3)-C(4)-C(5)	54.1(2)	C(2)-B(2)-O(22)-C(22)	172.6(2)
C(2)-C(3)-C(4)-C(5)	-88.0(2)	B(2)-O(22)-C(22)-C(22")	143.9(2)
C(3)-C(4)-C(5)-C(51)	61.5(2)	B(2)-O(22)-C(22)-C(22')	-97.6(2)
C(3)-C(4)-C(5)-C(6)	-61.3(2)	B(2)-O(22)-C(22)-C(21)	21.7(2)
C(51)-C(5)-C(6)-C(7)	-84.9(2)	O(21)-C(21)-C(22)-O(22)	-26.1(2)
C(4)-C(5)-C(6)-C(7)	37.5(3)	C(21")-C(21)-C(22)-O(22)	-143.5(2)
C(5)-C(6)-C(7)-C(8)	-7.4(3)	C(21')-C(21)-C(22)-O(22)	87.8(2)
C(6)-C(7)-C(8)-C(9)	-173.4(2)	O(21)-C(21)-C(22)-C(22")	-143.5(2)
C(6)-C(7)-C(8)-C(3)	-0.3(3)	C(21")-C(21)-C(22)-C(22")	99.1(3)
C(1)-C(3)-C(8)-C(7)	-173.4(2)	C(21')-C(21)-C(22)-C(22")	-29.6(3)
C(4)-C(3)-C(8)-C(7)	-23.7(3)	O(21)-C(21)-C(22)-C(22')	88.7(3)
C(2)-C(3)-C(8)-C(7)	114.8(2)	C(21")-C(21)-C(22)-C(22')	-28.7(3)
C(1)-C(3)-C(8)-C(9)	-0.4(3)	C(21')-C(21)-C(22)-C(22')	-157.4(3)
C(4)-C(3)-C(8)-C(9)	149.2(2)	C(6)-C(5)-C(51)-O(51)	9.6(3)
C(2)-C(3)-C(8)-C(9)	-72.3(3)	C(4)-C(5)-C(51)-O(51)	-112.2(3)
C(7)-C(8)-C(9)-C(10)	-57.6(3)	C(6)-C(5)-C(51)-O(52)	-169.01(19)
C(3)-C(8)-C(9)-C(10)	129.4(2)	C(4)-C(5)-C(51)-O(52)	69.2(2)
C(7)-C(8)-C(9)-C(14)	117.9(3)	O(51)-C(51)-O(52)-C(52)	6.0(3)
C(3)-C(8)-C(9)-C(14)	-55.1(3)	C(5)-C(51)-O(52)-C(52)	-175.3(2)
C(14)-C(9)-C(10)-C(11)	0.1(4)		

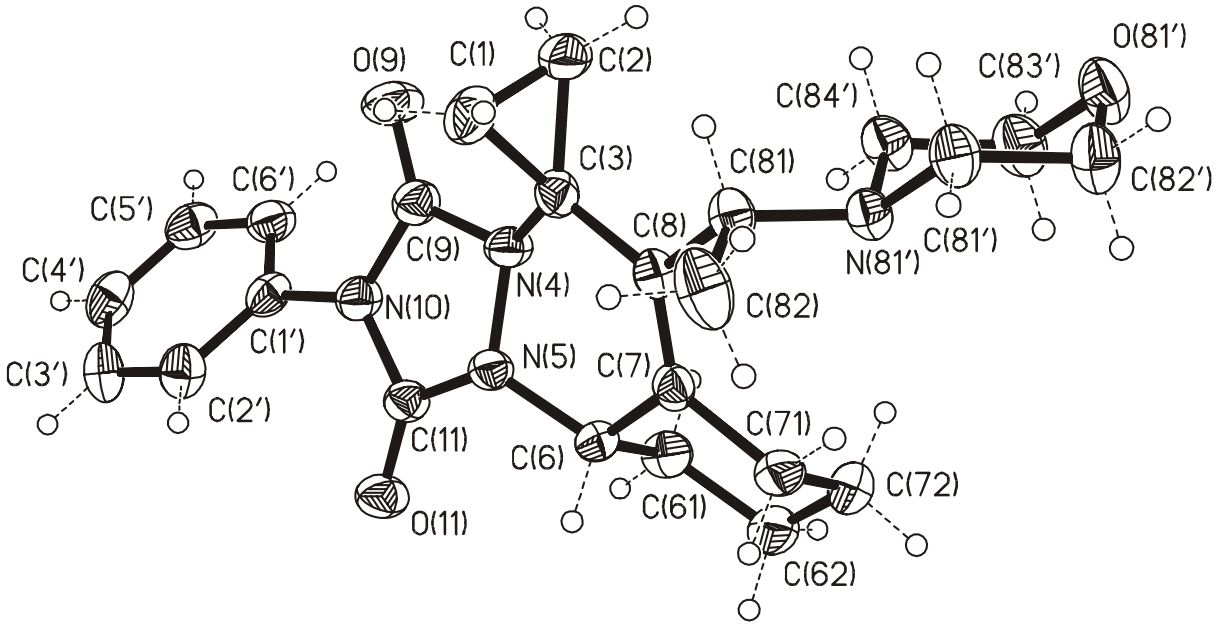


Table 1. Crystal data and structure refinement for **180a** (Major diastereomer).

Identification code	adm168	
Empirical formula	$C_{24}H_{30}N_4O_3$	
Formula weight	422.52	
Temperature	200(2) K	
Wavelength	71.073 pm	
Crystal system	Orthorhombic	
Space group	P2(1)2(1)2(1)	
Unit cell dimensions	a = 919.67(18) pm	α = 90°.
	b = 1352.8(3) pm	β = 90°.
	c = 1733.3(4) pm	γ = 90°.
Volume	2.1565(7) nm^3	
Z	4	
Density (calculated)	1.301 Mg/m^3	
Absorption coefficient	0.087 mm^{-1}	
F(000)	904	
Crystal size	0.50 x 0.50 x 0.50 mm^3	
Theta range for data collection	3.56 to 24.96°.	
Index ranges	-2<=h<=10, -16<=k<=16, -20<=l<=20	
Reflections collected	2892	
Independent reflections	2575 [R(int) = 0.0374]	

Completeness to theta = 24.96°	99.4 %
Max. and min. transmission	0.9577 and 0.9577
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2575 / 0 / 281
Goodness-of-fit on F^2	1.037
Final R indices [I>2sigma(I)]	R1 = 0.0374, wR2 = 0.0912
R indices (all data)	R1 = 0.0400, wR2 = 0.0943
Absolute structure parameter	0.00
Largest diff. peak and hole	0.144 and -0.227 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (pm^2x 10^{-1}) for **180a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1')	-4279(3)	7583(2)	12542(1)	30(1)
C(1)	-117(3)	4983(2)	12108(1)	40(1)
C(2)	919(3)	5759(2)	11825(1)	38(1)
C(2')	-5656(3)	7249(2)	12727(1)	36(1)
C(3)	-447(3)	5557(2)	11374(1)	28(1)
C(3')	-6543(3)	7823(2)	13190(1)	40(1)
N(4)	-1553(2)	6334(1)	11405(1)	29(1)
C(6')	-3766(3)	8469(2)	12833(1)	36(1)
C(4')	-6051(3)	8712(2)	13484(1)	41(1)
N(5)	-2864(2)	6061(1)	11042(1)	27(1)
C(5')	-4658(3)	9021(2)	13306(1)	38(1)
C(6)	-2765(3)	5842(2)	10215(1)	26(1)
C(7)	-1464(3)	5200(2)	10074(1)	26(1)
C(8)	-427(3)	5048(2)	10601(1)	27(1)
O(9)	-1131(2)	7138(1)	12577(1)	47(1)
C(9)	-1921(3)	6861(2)	12067(1)	31(1)
N(10)	-3422(2)	7019(1)	12014(1)	31(1)
O(11)	-5231(2)	6597(1)	11122(1)	37(1)
C(11)	-3996(3)	6558(2)	11359(1)	27(1)
C(61)	-2717(3)	6768(2)	9706(1)	33(1)
C(62)	-2635(3)	6462(2)	8857(1)	39(1)
C(71)	-1470(3)	4838(2)	9249(1)	33(1)
C(72)	-1409(3)	5741(2)	8709(1)	40(1)
N(81')	1688(2)	4578(1)	9786(1)	27(1)

O(81')	4300(2)	5161(1)	9013(1)	43(1)
C(81')	2888(3)	3891(2)	9652(1)	33(1)
C(81)	826(3)	4317(2)	10475(1)	30(1)
C(82)	239(3)	3256(2)	10436(2)	46(1)
C(82')	3714(3)	4192(2)	8938(2)	40(1)
C(83')	3145(3)	5841(2)	9146(2)	41(1)
C(84')	2305(3)	5576(2)	9862(1)	33(1)

Table 3. Bond lengths [pm] and angles [deg] for **180a**.

C(1')-C(6')	138.2(3)	C(71)-C(72)	154.0(3)
C(1')-C(2')	138.3(3)	N(81')-C(81')	146.2(3)
C(1')-N(10)	142.8(3)	N(81')-C(84')	147.1(3)
C(1)-C(2)	149.9(4)	N(81')-C(81)	147.5(3)
C(1)-C(3)	152.1(3)	O(81')-C(82')	142.2(3)
C(2)-C(3)	150.4(3)	O(81')-C(83')	142.5(3)
C(2')-C(3')	138.4(3)	C(81')-C(82')	150.8(3)
C(3)-N(4)	146.4(3)	C(81)-C(82)	153.5(3)
C(3)-C(8)	150.6(3)	C(83')-C(84')	150.5(3)
C(3')-C(4')	138.2(4)		
N(4)-C(9)	139.2(3)	C(6')-C(1')-C(2')	120.8(2)
N(4)-N(5)	140.9(3)	C(6')-C(1')-N(10)	120.6(2)
C(6')-C(5')	137.9(3)	C(2')-C(1')-N(10)	118.6(2)
C(4')-C(5')	138.4(4)	C(2)-C(1)-C(3)	59.75(16)
N(5)-C(11)	135.6(3)	C(1)-C(2)-C(3)	60.83(16)
N(5)-C(6)	146.6(3)	C(1')-C(2')-C(3')	119.4(2)
C(6)-C(7)	149.9(3)	N(4)-C(3)-C(2)	115.49(19)
C(6)-C(61)	153.3(3)	N(4)-C(3)-C(8)	111.63(18)
C(7)-C(8)	133.5(3)	C(2)-C(3)-C(8)	122.4(2)
C(7)-C(71)	151.3(3)	N(4)-C(3)-C(1)	118.28(19)
C(8)-C(81)	153.5(3)	C(2)-C(3)-C(1)	59.42(17)
O(9)-C(9)	120.5(3)	C(8)-C(3)-C(1)	120.63(19)
C(9)-N(10)	140.0(3)	C(4')-C(3')-C(2')	120.7(3)
N(10)-C(11)	139.9(3)	C(9)-N(4)-N(5)	107.11(18)
O(11)-C(11)	120.9(3)	C(9)-N(4)-C(3)	124.53(18)
C(61)-C(62)	153.1(3)	N(5)-N(4)-C(3)	112.98(17)
C(62)-C(72)	151.3(4)	C(5')-C(6')-C(1')	118.9(2)

C(3')-C(4')-C(5')	118.9(2)	C(9)-N(10)-C(1')	125.75(19)
C(11)-N(5)-N(4)	110.26(16)	O(11)-C(11)-N(5)	127.2(2)
C(11)-N(5)-C(6)	123.00(19)	O(11)-C(11)-N(10)	127.8(2)
N(4)-N(5)-C(6)	115.89(18)	N(5)-C(11)-N(10)	105.08(19)
C(6')-C(5')-C(4')	121.3(2)	C(62)-C(61)-C(6)	109.56(19)
N(5)-C(6)-C(7)	109.05(18)	C(72)-C(62)-C(61)	111.9(2)
N(5)-C(6)-C(61)	113.49(18)	C(7)-C(71)-C(72)	108.56(19)
C(7)-C(6)-C(61)	110.87(19)	C(62)-C(72)-C(71)	112.4(2)
C(8)-C(7)-C(6)	123.19(19)	C(81')-N(81')-C(84')	107.86(19)
C(8)-C(7)-C(71)	126.9(2)	C(81')-N(81')-C(81)	112.49(17)
C(6)-C(7)-C(71)	109.79(19)	C(84')-N(81')-C(81)	110.77(17)
C(7)-C(8)-C(3)	122.0(2)	C(82')-O(81')-C(83')	109.1(2)
C(7)-C(8)-C(81)	122.50(19)	N(81')-C(81')-C(82')	109.83(19)
C(3)-C(8)-C(81)	115.47(19)	N(81')-C(81)-C(8)	111.38(17)
O(9)-C(9)-N(4)	128.2(2)	N(81')-C(81)-C(82)	112.16(19)
O(9)-C(9)-N(10)	126.5(2)	C(8)-C(81)-C(82)	110.2(2)
N(4)-C(9)-N(10)	105.3(2)	O(81')-C(82')-C(81')	111.41(19)
C(11)-N(10)-C(9)	110.90(19)	O(81')-C(83')-C(84')	111.3(2)
C(11)-N(10)-C(1')	123.3(2)	N(81')-C(84')-C(83')	110.05(18)

Table 4. Anisotropic displacement parameters ($pm^2 x\ 10^{-1}$) for **180a**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1')	34(1)	31(1)	24(1)	-4(1)	-2(1)	7(1)
C(1)	43(2)	48(1)	28(1)	5(1)	-1(1)	12(1)
C(2)	29(1)	54(1)	32(1)	-8(1)	-4(1)	7(1)
C(2')	44(2)	29(1)	35(1)	-3(1)	7(1)	0(1)
C(3)	25(1)	32(1)	27(1)	2(1)	2(1)	6(1)
C(3')	42(2)	41(1)	38(1)	2(1)	15(1)	2(1)
N(4)	24(1)	34(1)	29(1)	-6(1)	-4(1)	3(1)
C(6')	35(1)	39(1)	33(1)	-5(1)	-5(1)	1(1)
C(4')	50(2)	41(1)	31(1)	-6(1)	6(1)	14(1)
N(5)	23(1)	32(1)	27(1)	-6(1)	-2(1)	1(1)
C(5')	45(2)	36(1)	33(1)	-11(1)	-4(1)	6(1)
C(6)	26(1)	28(1)	23(1)	-3(1)	-2(1)	-2(1)
C(7)	26(1)	26(1)	27(1)	-1(1)	4(1)	-5(1)

C(8)	26(1)	26(1)	28(1)	1(1)	5(1)	-1(1)
O(9)	36(1)	63(1)	42(1)	-24(1)	-10(1)	9(1)
C(9)	31(1)	34(1)	29(1)	-5(1)	-1(1)	2(1)
N(10)	29(1)	34(1)	30(1)	-7(1)	-1(1)	4(1)
O(11)	27(1)	43(1)	40(1)	-12(1)	-4(1)	5(1)
C(11)	27(1)	26(1)	29(1)	-5(1)	-1(1)	-1(1)
C(61)	35(1)	30(1)	34(1)	3(1)	-4(1)	-3(1)
C(62)	40(1)	46(1)	30(1)	8(1)	-3(1)	-9(1)
C(71)	30(1)	38(1)	32(1)	-9(1)	-1(1)	-3(1)
C(72)	39(2)	56(2)	26(1)	1(1)	2(1)	-6(1)
N(81')	26(1)	23(1)	31(1)	-3(1)	5(1)	-2(1)
O(81')	36(1)	42(1)	51(1)	-8(1)	16(1)	-8(1)
C(81')	34(1)	29(1)	37(1)	-2(1)	7(1)	5(1)
C(81)	28(1)	28(1)	32(1)	2(1)	6(1)	4(1)
C(82)	47(2)	30(1)	61(2)	7(1)	20(2)	0(1)
C(82')	43(2)	33(1)	43(1)	-6(1)	16(1)	-4(1)
C(83')	39(2)	33(1)	49(1)	1(1)	9(1)	-6(1)
C(84')	31(1)	27(1)	42(1)	-8(1)	6(1)	-5(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (pm^2x 10^{-1}) for 1**80a**.

Atom	x	y	z	U(eq)
H(1A)	-703	5135	12573	48
H(1B)	177	4283	12056	48
H(2A)	1852	5534	11602	46
H(2B)	973	6386	12118	46
H(2'A)	-5990	6630	12537	43
H(3'A)	-7500	7605	13306	48
H(6'A)	-2816	8693	12709	43
H(4'A)	-6660	9103	13805	49
H(5'A)	-4308	9626	13513	46
H(6A)	-3649	5455	10068	31
H(61A)	-3598	7172	9795	40
H(61B)	-1856	7172	9842	40
H(62A)	-3568	6154	8703	46

H(62B)	-2490	7058	8534	46
H(71A)	-2364	4452	9147	40
H(71B)	-619	4406	9156	40
H(72A)	-468	6085	8781	48
H(72B)	-1458	5513	8167	48
H(81A)	2502	3213	9586	40
H(81B)	3549	3892	10102	40
H(81C)	1484	4361	10933	35
H(82A)	1052	2788	10464	69
H(82B)	-285	3161	9950	69
H(82C)	-423	3141	10870	69
H(82D)	4514	3717	8845	47
H(82E)	3054	4171	8487	47
H(83A)	2480	5841	8697	49
H(83C)	3549	6516	9202	49
H(84C)	2958	5601	10316	40
H(84A)	1513	6061	9943	40

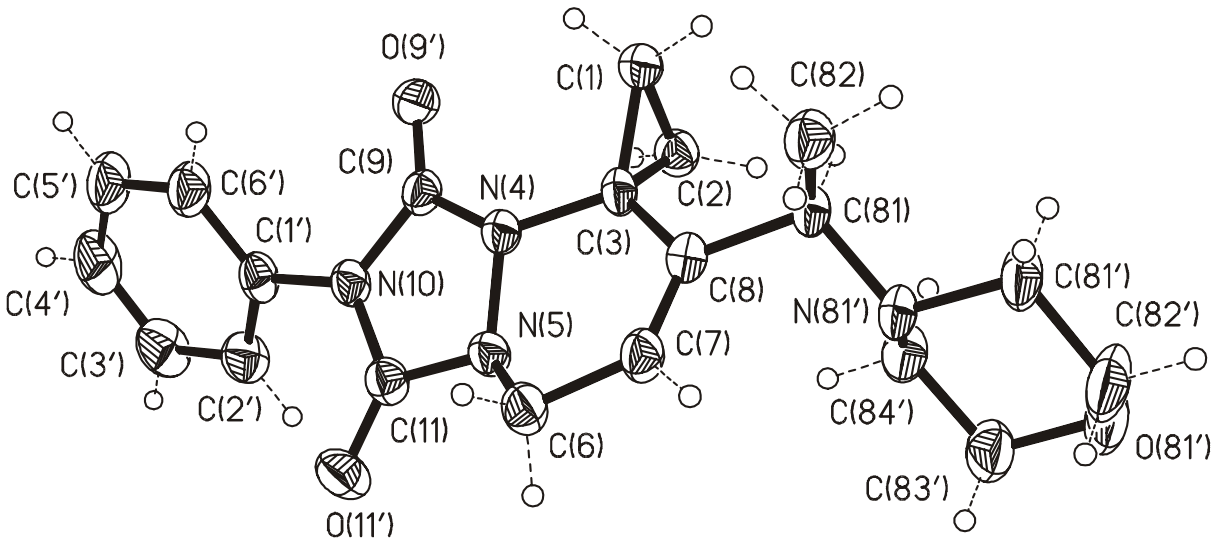


Table 1. Crystal data and structure refinement for **184a**

Identification code	adm165x	
Empirical formula	$C_{20}H_{24}N_4O_3$	
Formula weight	368.43	
Temperature	200(2) K	
Wavelength	71.073 pm	
Crystal system	Orthorhombic	
Space group	Pbca	
Unit cell dimensions	a = 1465.6(2) pm	α = 90°.
	b = 836.46(14) pm	β = 90°.
	c = 2988.6(4) pm	γ = 90°.
Volume	3.6638(10) nm^3	
Z	8	
Density (calculated)	1.336 Mg/m^3	
Absorption coefficient	0.092 mm^{-1}	
F(000)	1568	
Crystal size	0.80 x 0.80 x 0.80 mm^3	
Theta range for data collection	3.70 to 25.04°.	
Index ranges	-2<=h<=17, 0<=k<=9, -35<=l<=35	
Reflections collected	3239	
Independent reflections	3204 [R(int) = 0.1306]	
Completeness to theta = 25.04°	99.2 %	
Max. and min. transmission	0.9301 and 0.9301	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3204 / 0 / 246	
Goodness-of-fit on F^2	1.072	
Final R indices [I>2sigma(I)]	R1 = 0.0602, wR2 = 0.1657	

R indices (all data)	R1 = 0.0667, wR2 = 0.1757
Extinction coefficient	0.0071(12)
Largest diff. peak and hole	0.351 and -0.293 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (pm^2x 10^{-1}) for **184a**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	5212(1)	2449(3)	7866(1)	32(1)
C(1')	3618(1)	261(3)	6294(1)	32(1)
C(2)	5220(1)	665(3)	7905(1)	32(1)
C(2')	3394(2)	-1236(3)	6130(1)	40(1)
C(3)	4328(1)	1542(2)	7863(1)	27(1)
C(3')	3506(2)	-1536(3)	5675(1)	50(1)
N(4)	3823(1)	1472(2)	7443(1)	29(1)
C(4')	3852(2)	-375(4)	5396(1)	53(1)
N(5)	3038(1)	466(2)	7458(1)	30(1)
C(5')	4072(2)	1105(4)	5564(1)	51(1)
C(6)	2340(1)	1002(3)	7773(1)	35(1)
C(6')	3938(2)	1441(3)	6014(1)	41(1)
C(7)	2794(2)	1435(3)	8203(1)	33(1)
C(8)	3690(1)	1642(2)	8250(1)	29(1)
O(9')	4925(1)	1843(2)	6893(1)	37(1)
C(9)	4189(1)	1378(2)	7021(1)	28(1)
N(10)	3532(1)	579(2)	6763(1)	29(1)
O(11')	2121(1)	-612(2)	6906(1)	43(1)
C(11)	2808(1)	70(3)	7024(1)	31(1)
N(81')	3702(1)	938(2)	9048(1)	32(1)
O(81')	3939(2)	-1408(2)	9740(1)	56(1)
C(81)	4089(1)	2038(2)	8709(1)	30(1)
C(81')	3971(2)	1373(3)	9504(1)	43(1)
C(82)	3924(2)	3793(3)	8816(1)	39(1)
C(82')	3613(2)	148(4)	9830(1)	59(1)
C(83')	3674(2)	-1851(3)	9299(1)	49(1)
C(84')	4029(2)	-680(3)	8960(1)	39(1)

Table 3. Bond lengths [pm] and angles [deg] for **184a**.

C(1)-C(2)	149.7(3)	N(4)-C(3)-C(8)	110.66(16)
C(1)-C(3)	150.2(3)	N(4)-C(3)-C(1)	117.63(16)
C(1')-C(6')	137.6(3)	C(8)-C(3)-C(1)	120.53(17)
C(1')-C(2')	138.4(3)	N(4)-C(3)-C(2)	119.59(16)
C(1')-N(10)	143.3(2)	C(8)-C(3)-C(2)	120.45(16)
C(2)-C(3)	150.4(3)	C(1)-C(3)-C(2)	59.73(14)
C(2')-C(3')	139.3(3)	C(4')-C(3')-C(2')	120.5(2)
C(3)-N(4)	145.7(2)	C(9)-N(4)-N(5)	108.16(15)
C(3)-C(8)	149.1(3)	C(9)-N(4)-C(3)	126.46(17)
C(3')-C(4')	137.7(4)	N(5)-N(4)-C(3)	113.91(15)
N(4)-C(9)	137.2(3)	C(5')-C(4')-C(3')	120.0(2)
N(4)-N(5)	142.6(2)	C(11)-N(5)-N(4)	107.95(15)
C(4')-C(5')	137.5(4)	C(11)-N(5)-C(6)	120.49(16)
N(5)-C(11)	138.1(3)	N(4)-N(5)-C(6)	113.90(16)
N(5)-C(6)	146.0(3)	C(4')-C(5')-C(6')	120.3(2)
C(5')-C(6')	138.9(3)	N(5)-C(6)-C(7)	108.44(17)
C(6)-C(7)	149.1(3)	C(1')-C(6')-C(5')	119.4(2)
C(7)-C(8)	133.1(3)	C(8)-C(7)-C(6)	124.29(19)
C(8)-C(81)	152.7(3)	C(7)-C(8)-C(3)	121.88(18)
O(9')-C(9)	120.9(2)	C(7)-C(8)-C(81)	120.09(18)
C(9)-N(10)	140.4(3)	C(3)-C(8)-C(81)	118.01(17)
N(10)-C(11)	138.4(3)	O(9')-C(9)-N(4)	128.45(19)
O(11')-C(11)	121.0(2)	O(9')-C(9)-N(10)	126.23(18)
N(81')-C(84')	145.9(3)	N(4)-C(9)-N(10)	105.30(16)
N(81')-C(81')	146.5(3)	C(11)-N(10)-C(9)	111.21(16)
N(81')-C(81)	148.1(3)	C(11)-N(10)-C(1')	124.25(17)
O(81')-C(82')	141.2(4)	C(9)-N(10)-C(1')	124.47(17)
O(81')-C(83')	142.2(3)	O(11')-C(11)-N(5)	126.28(19)
C(81)-C(82)	152.2(3)	O(11')-C(11)-N(10)	128.08(19)
C(81')-C(82')	150.8(4)	N(5)-C(11)-N(10)	105.62(16)
C(83')-C(84')	150.4(3)	C(84')-N(81')-C(81')	108.02(17)
C(2)-C(1)-C(3)	60.23(13)	C(84')-N(81')-C(81)	109.11(17)
C(6')-C(1')-C(2')	121.0(2)	C(81')-N(81')-C(81)	112.22(17)
C(6')-C(1')-N(10)	119.37(19)	C(82')-O(81')-C(83')	108.9(2)
C(2')-C(1')-N(10)	119.58(19)	N(81')-C(81)-C(82)	113.26(17)
C(1)-C(2)-C(3)	60.04(13)	N(81')-C(81)-C(8)	109.38(16)
C(1')-C(2')-C(3')	118.8(2)	C(82)-C(81)-C(8)	109.70(17)

N(81')-C(81')-C(82')	109.8(2)	O(81')-C(83')-C(84')	111.1(2)
O(81')-C(82')-C(81')	112.7(2)	N(81')-C(84')-C(83')	111.6(2)

Table 4. Anisotropic displacement parameters ($pm^2 x\ 10^{-1}$) for **184a**. The anisotropic displacement factor exponent takes the form: $-2\ \pi^2\ [\ h^2\ a^{*2} U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	33(1)	37(1)	26(1)	0(1)	0(1)	-6(1)
C(1')	34(1)	42(1)	20(1)	-5(1)	-2(1)	3(1)
C(2)	29(1)	38(1)	31(1)	1(1)	-1(1)	1(1)
C(2')	44(1)	47(1)	29(1)	-8(1)	0(1)	-3(1)
C(3)	32(1)	32(1)	18(1)	0(1)	-4(1)	0(1)
C(3')	55(2)	61(2)	34(1)	-21(1)	-2(1)	-2(1)
N(4)	29(1)	37(1)	20(1)	1(1)	-1(1)	-4(1)
C(4')	57(2)	79(2)	23(1)	-11(1)	-3(1)	4(1)
N(5)	26(1)	41(1)	23(1)	-1(1)	0(1)	-4(1)
C(5')	58(2)	70(2)	25(1)	7(1)	-1(1)	0(1)
C(6)	27(1)	52(1)	25(1)	-1(1)	1(1)	1(1)
C(6')	52(1)	45(1)	25(1)	1(1)	-4(1)	-1(1)
C(7)	33(1)	45(1)	22(1)	0(1)	2(1)	1(1)
C(8)	32(1)	31(1)	23(1)	2(1)	-1(1)	2(1)
O(9')	39(1)	48(1)	25(1)	-2(1)	4(1)	-12(1)
C(9)	34(1)	31(1)	21(1)	1(1)	1(1)	-1(1)
N(10)	33(1)	35(1)	20(1)	-3(1)	-1(1)	-1(1)
O(11')	33(1)	64(1)	34(1)	-11(1)	0(1)	-10(1)
C(11)	28(1)	37(1)	27(1)	-2(1)	-1(1)	2(1)
N(81')	40(1)	37(1)	18(1)	2(1)	-1(1)	2(1)
O(81')	85(1)	51(1)	31(1)	13(1)	-12(1)	-2(1)
C(81)	35(1)	37(1)	18(1)	1(1)	-1(1)	-1(1)
C(81')	64(2)	45(1)	21(1)	0(1)	-4(1)	0(1)
C(82)	52(1)	37(1)	28(1)	-1(1)	-1(1)	-2(1)
C(82')	93(2)	62(2)	21(1)	5(1)	2(1)	-3(2)
C(83')	67(2)	43(1)	37(1)	9(1)	-11(1)	-4(1)
C(84')	52(1)	38(1)	29(1)	2(1)	-2(1)	2(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (pm^2x 10^{-1}) for **184a.**

Atom	x	y	z	U(eq)
H(1A)	5422	2925	7580	39
H(1B)	5362	3080	8136	39
H(2A)	5374	197	8200	39
H(2B)	5434	42	7644	39
H(2'A)	3169	-2044	6324	48
H(3'A)	3341	-2549	5556	60
H(4'A)	3940	-597	5087	64
H(5'A)	4317	1901	5372	61
H(6A)	1890	139	7824	41
H(6B)	2015	1942	7650	41
H(6'A)	4067	2477	6128	49
H(7A)	2420	1571	8460	40
H(81A)	4763	1858	8696	36
H(81B)	3722	2440	9579	52
H(81C)	4644	1427	9524	52
H(82A)	4261	4084	9087	59
H(82B)	3270	3972	8864	59
H(82C)	4134	4454	8566	59
H(82D)	3796	459	10137	71
H(82E)	2938	143	9818	71
H(83A)	3000	-1893	9281	59
H(83B)	3913	-2931	9231	59
H(84A)	4705	-686	8966	47
H(84B)	3831	-1015	8657	47

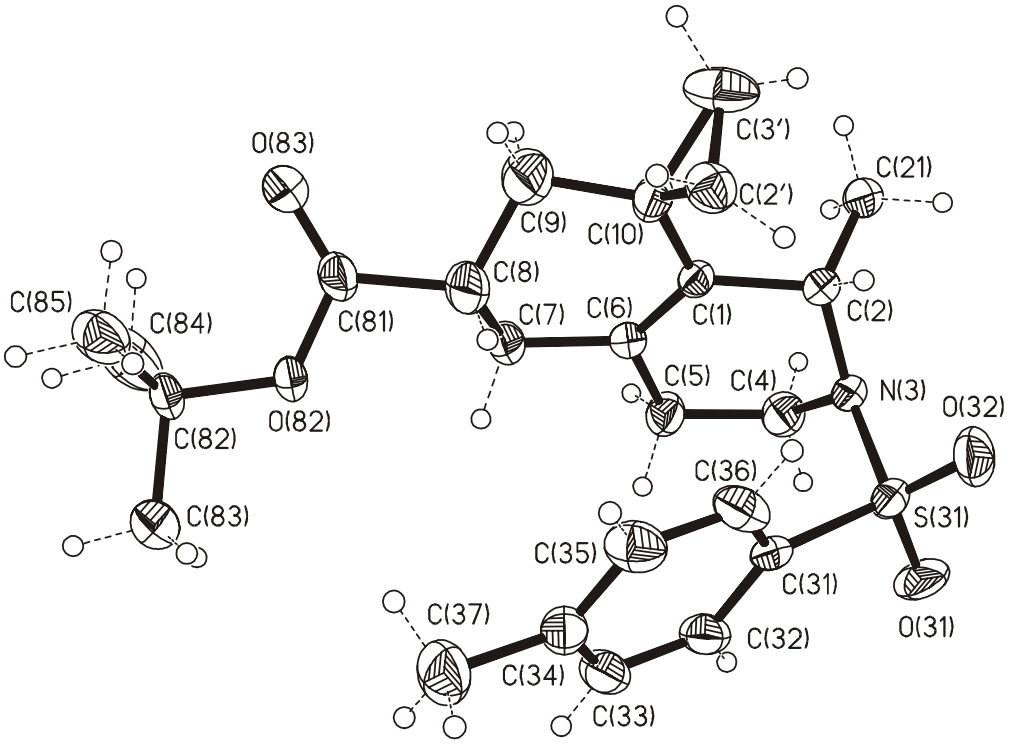


Table 1. Crystal data and structure refinement for **209**.

Identification code	adm185	
Empirical formula	$C_{24}H_{33}NO_4S$	
Formula weight	431.57	
Temperature	133(2) K	
Wavelength	71.073 pm	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 1135.4(2) pm	α = 90°.
	b = 1289.1(3) pm	β = 108.00(3)°.
	c = 1632.3(3) pm	γ = 90°.
Volume	2.2723(8) nm^3	
Z	4	
Density (calculated)	1.262 Mg/m^3	
Absorption coefficient	0.172 mm^{-1}	
F(000)	928	
Crystal size	0.30 x 0.20 x 0.20 mm^3	
Theta range for data collection	1.89 to 24.82°.	
Index ranges	-13<=h<=13, -15<=k<=15, -19<=l<=18	
Reflections collected	33280	
Independent reflections	3897 [R(int) = 0.0774]	
Completeness to theta = 24.82°	99.1 %	
Max. and min. transmission	0.9664 and 0.9502	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3897 / 0 / 276
Goodness-of-fit on F^2	1.021
Final R indices [I>2sigma(I)]	R1 = 0.0536, wR2 = 0.1333
R indices (all data)	R1 = 0.0873, wR2 = 0.1439
Largest diff. peak and hole	0.974 and -0.403 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (pm^2x 10^{-1}) for **209**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	7263(3)	724(2)	2483(2)	23(1)
C(2)	7513(3)	1890(2)	2486(2)	28(1)
C(2')	9425(3)	244(2)	3559(2)	33(1)
C(3')	8666(3)	548(3)	4105(2)	50(1)
N(3)	7100(2)	2319(2)	1599(1)	26(1)
C(4)	5812(3)	2054(2)	1121(2)	35(1)
C(5)	5591(3)	884(2)	1071(2)	32(1)
C(6)	6396(3)	285(2)	1829(2)	24(1)
C(7)	6167(3)	-869(2)	1755(2)	33(1)
C(8)	7266(4)	-1474(2)	2403(2)	51(1)
C(9)	7578(4)	-984(3)	3267(2)	47(1)
C(10)	8046(3)	86(2)	3220(2)	30(1)
C(21)	6872(4)	2513(2)	3032(2)	44(1)
S(31)	8104(1)	2403(1)	1067(1)	35(1)
O(31)	7492(3)	2951(2)	290(2)	54(1)
C(31)	8448(3)	1139(2)	778(2)	28(1)
C(32)	7765(3)	708(2)	-2(2)	35(1)
O(32)	9215(2)	2812(2)	1659(2)	50(1)
C(33)	7997(3)	-306(3)	-185(2)	36(1)
C(34)	8894(3)	-900(2)	395(2)	33(1)
C(35)	9585(3)	-436(3)	1162(2)	39(1)
C(36)	9369(3)	576(3)	1350(2)	36(1)
C(37)	9116(4)	-2015(3)	196(3)	51(1)
C(81)	6873(3)	-2616(2)	2391(2)	40(1)
O(82)	6880(2)	-3048(2)	1650(1)	45(1)
C(82)	6590(3)	-4147(2)	1455(2)	28(1)

O(83)	6627(2)	-3074(2)	2970(1)	40(1)
C(83)	6751(4)	-4264(3)	573(2)	46(1)
C(84)	5287(3)	-4386(3)	1431(3)	61(1)
C(85)	7532(3)	-4814(3)	2094(2)	45(1)

Table 3. Bond lengths [pm] and angles [deg] for **209**.

C(1)-C(6)	133.4(4)	C(82)-C(84)	150.0(4)
C(1)-C(10)	150.2(4)	C(82)-C(85)	151.0(4)
C(1)-C(2)	152.9(4)	C(82)-C(83)	151.4(4)
C(2)-N(3)	148.5(4)	C(6)-C(1)-C(10)	121.1(3)
C(2)-C(21)	153.9(4)	C(6)-C(1)-C(2)	120.7(3)
C(2')-C(3')	147.1(5)	C(10)-C(1)-C(2)	118.1(2)
C(2')-C(10)	150.4(4)	N(3)-C(2)-C(1)	111.1(2)
C(3')-C(10)	151.9(5)	N(3)-C(2)-C(21)	107.9(2)
N(3)-C(4)	146.9(4)	C(1)-C(2)-C(21)	113.2(2)
N(3)-S(31)	163.6(2)	C(3')-C(2')-C(10)	61.4(2)
C(4)-C(5)	152.8(4)	C(2')-C(3')-C(10)	60.4(2)
C(5)-C(6)	150.4(4)	C(4)-N(3)-C(2)	113.2(2)
C(6)-C(7)	150.9(4)	C(4)-N(3)-S(31)	118.5(2)
C(7)-C(8)	157.1(5)	C(2)-N(3)-S(31)	118.7(2)
C(8)-C(9)	148.5(5)	N(3)-C(4)-C(5)	112.2(2)
C(8)-C(81)	153.8(5)	C(6)-C(5)-C(4)	114.5(3)
C(9)-C(10)	149.0(4)	C(1)-C(6)-C(5)	123.4(3)
S(31)-O(32)	143.1(3)	C(1)-C(6)-C(7)	123.3(3)
S(31)-O(31)	143.1(3)	C(5)-C(6)-C(7)	113.2(2)
S(31)-C(31)	177.3(3)	C(6)-C(7)-C(8)	110.7(3)
C(31)-C(36)	137.4(4)	C(9)-C(8)-C(81)	113.7(3)
C(31)-C(32)	138.7(4)	C(9)-C(8)-C(7)	109.6(3)
C(32)-C(33)	138.5(4)	C(81)-C(8)-C(7)	107.4(3)
C(33)-C(34)	138.6(5)	C(8)-C(9)-C(10)	109.2(3)
C(34)-C(35)	139.1(5)	C(9)-C(10)-C(1)	114.6(3)
C(34)-C(37)	151.1(4)	C(9)-C(10)-C(2')	117.0(3)
C(35)-C(36)	137.9(5)	C(1)-C(10)-C(2')	120.8(2)
C(81)-O(83)	121.8(4)	C(9)-C(10)-C(3')	112.5(3)
C(81)-O(82)	133.4(4)	C(1)-C(10)-C(3')	122.2(3)
O(82)-C(82)	146.7(3)	C(2')-C(10)-C(3')	58.2(2)

O(32)-S(31)-O(31)	120.07(16)	C(35)-C(34)-C(37)	121.2(3)
O(32)-S(31)-N(3)	106.28(13)	C(36)-C(35)-C(34)	121.2(3)
O(31)-S(31)-N(3)	106.01(14)	C(31)-C(36)-C(35)	119.9(3)
O(32)-S(31)-C(31)	107.30(15)	O(83)-C(81)-O(82)	124.7(3)
O(31)-S(31)-C(31)	107.73(14)	O(83)-C(81)-C(8)	126.2(3)
N(3)-S(31)-C(31)	109.10(12)	O(82)-C(81)-C(8)	109.1(3)
C(36)-C(31)-C(32)	120.3(3)	C(81)-O(82)-C(82)	122.4(2)
C(36)-C(31)-S(31)	119.2(2)	O(82)-C(82)-C(84)	110.9(3)
C(32)-C(31)-S(31)	120.4(2)	O(82)-C(82)-C(85)	109.7(3)
C(33)-C(32)-C(31)	119.1(3)	C(84)-C(82)-C(85)	112.6(3)
C(32)-C(33)-C(34)	121.6(3)	O(82)-C(82)-C(83)	102.5(2)
C(33)-C(34)-C(35)	117.9(3)	C(84)-C(82)-C(83)	111.2(3)
C(33)-C(34)-C(37)	121.0(3)	C(85)-C(82)-C(83)	109.4(3)

Table 4. Anisotropic displacement parameters ($pm^2 x\ 10^{-1}$)for adm185. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	27(2)	20(1)	24(2)	1(1)	12(1)	-2(1)
C(2)	39(2)	24(2)	22(2)	0(1)	11(1)	-7(1)
C(2')	32(2)	34(2)	31(2)	-1(1)	5(1)	0(1)
C(3')	51(2)	69(3)	26(2)	4(2)	7(2)	20(2)
N(3)	40(1)	19(1)	23(1)	1(1)	14(1)	-3(1)
C(4)	43(2)	29(2)	31(2)	4(1)	7(2)	2(1)
C(5)	37(2)	27(2)	29(2)	4(1)	5(1)	-4(1)
C(6)	28(2)	23(2)	21(2)	0(1)	8(1)	-2(1)
C(7)	47(2)	24(2)	26(2)	-2(1)	5(2)	-7(1)
C(8)	92(3)	21(2)	39(2)	3(2)	19(2)	9(2)
C(9)	59(2)	35(2)	41(2)	5(2)	6(2)	3(2)
C(10)	32(2)	26(2)	30(2)	5(1)	5(1)	-6(1)
C(21)	84(3)	23(2)	33(2)	-3(1)	31(2)	-7(2)
S(31)	58(1)	22(1)	36(1)	-2(1)	30(1)	-7(1)
O(31)	104(2)	29(1)	43(2)	15(1)	44(2)	11(1)
C(31)	40(2)	26(2)	24(2)	1(1)	19(1)	-3(1)
C(32)	46(2)	35(2)	25(2)	1(1)	13(2)	4(2)
O(32)	57(2)	39(1)	67(2)	-22(1)	40(1)	-25(1)
C(33)	39(2)	41(2)	31(2)	-10(2)	14(2)	-6(2)

C(34)	37(2)	30(2)	41(2)	-4(1)	22(2)	-2(1)
C(35)	39(2)	45(2)	36(2)	0(2)	14(2)	10(2)
C(36)	34(2)	46(2)	29(2)	-12(2)	10(1)	-3(2)
C(37)	59(2)	34(2)	67(3)	-7(2)	31(2)	3(2)
C(81)	66(2)	20(2)	29(2)	-1(1)	5(2)	5(2)
O(82)	89(2)	18(1)	28(1)	-4(1)	17(1)	-10(1)
C(82)	35(2)	18(1)	30(2)	-6(1)	8(1)	-2(1)
O(83)	58(2)	30(1)	33(1)	-3(1)	15(1)	0(1)
C(83)	68(2)	36(2)	34(2)	-6(2)	15(2)	-6(2)
C(84)	39(2)	76(3)	71(3)	-38(2)	20(2)	-16(2)
C(85)	55(2)	42(2)	38(2)	-4(2)	13(2)	17(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (pm^2x 10^{-1}) for **209**.

Atoms	x	y	z	U(eq)
H(2A)	8427	2002	2731	34
H(2'A)	9952	-380	3729	40
H(2'B)	9787	805	3299	40
H(3'A)	8551	1298	4184	60
H(3'B)	8716	112	4614	60
H(4A)	5606	2339	530	42
H(4B)	5253	2383	1406	42
H(5A)	4712	752	1022	39
H(5B)	5733	618	541	39
H(7A)	6077	-1097	1159	40
H(7B)	5387	-1031	1878	40
H(8A)	8007	-1430	2195	61
H(9A)	8218	-1399	3689	56
H(9B)	6832	-959	3459	56
H(21A)	7132	3240	3057	66
H(21B)	7105	2226	3617	66
H(21C)	5972	2469	2771	66
H(32A)	7146	1104	-407	42
H(33A)	7531	-603	-719	44
H(35A)	10216	-823	1564	47

H(36A)	9857	883	1875	43
H(37A)	9087	-2458	677	76
H(37B)	9930	-2075	111	76
H(37C)	8473	-2234	-329	76
H(83A)	7596	-4067	601	69
H(83B)	6159	-3813	162	69
H(83C)	6602	-4987	384	69
H(84A)	5212	-4313	2010	92
H(84B)	5079	-5098	1227	92
H(84C)	4717	-3902	1038	92
H(85A)	8368	-4601	2111	68
H(85B)	7402	-5543	1919	68
H(85C)	7438	-4730	2667	68

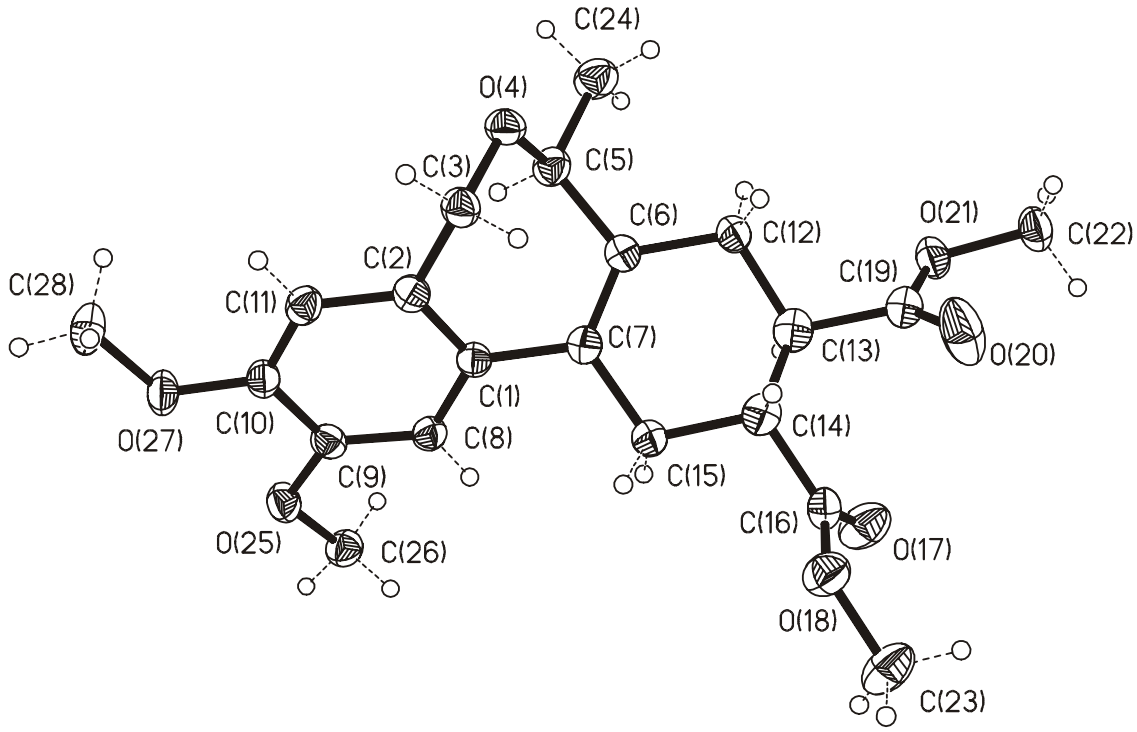


Table 1. Crystal data and structure refinement for **231c** (Major diastereomer).

Identification code	adm183	
Empirical formula	$C_{21}H_{26}O_7$	
Formula weight	390.42	
Temperature	133(2) K	
Wavelength	71.073 pm	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 727.68(7) pm	α = 109.904(7)°.
	b = 1188.90(12) pm	β = 93.316(8)°.
	c = 1290.95(12) pm	γ = 106.331(8)°.
Volume	0.99306(17) nm^3	
Z	2	
Density (calculated)	1.306 Mg/m^3	
Absorption coefficient	0.098 mm^{-1}	
F(000)	416	
Crystal size	0.30 x 0.30 x 0.30 mm^3	
Theta range for data collection	1.70 to 24.79°.	
Index ranges	-8<=h<=7, -13<=k<=13, -15<=l<=15	
Reflections collected	11159	
Independent reflections	3356 [R(int) = 0.0370]	
Completeness to theta = 24.79°	98.3 %	

Max. and min. transmission	0.9713 and 0.9713
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3356 / 0 / 253
Goodness-of-fit on F^2	1.115
Final R indices [I>2sigma(I)]	R1 = 0.0505, wR2 = 0.1480
R indices (all data)	R1 = 0.0672, wR2 = 0.1562
Largest diff. peak and hole	0.839 and -0.314 e.Å^{-3}

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters (pm^2x 10^{-1}) for **231c**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

Atom	x	y	z	U(eq)
C(1)	3714(3)	3313(2)	10699(2)	23(1)
C(2)	5087(3)	3080(2)	10011(2)	24(1)
C(3)	7168(3)	3920(2)	10403(2)	26(1)
O(4)	8176(2)	3736(2)	11302(1)	28(1)
C(5)	6992(4)	3502(2)	12112(2)	28(1)
C(6)	5908(3)	4454(2)	12499(2)	24(1)
C(7)	4328(3)	4327(2)	11825(2)	23(1)
C(8)	1762(3)	2531(2)	10328(2)	24(1)
C(9)	1218(3)	1517(2)	9325(2)	24(1)
C(10)	2601(4)	1289(2)	8623(2)	25(1)
C(11)	4499(4)	2078(2)	8970(2)	26(1)
C(12)	6627(4)	5490(2)	13643(2)	27(1)
C(13)	5095(4)	6121(2)	14064(2)	38(1)
C(14)	4123(4)	6394(2)	13166(2)	37(1)
C(15)	3095(4)	5181(2)	12159(2)	26(1)
C(16)	2673(4)	7065(2)	13599(2)	31(1)
O(17)	1841(3)	7012(2)	14373(2)	46(1)
O(18)	2390(3)	7720(2)	12988(1)	37(1)
C(19)	6090(4)	7328(2)	15069(2)	35(1)
O(20)	6497(4)	8390(2)	15086(2)	57(1)
O(21)	6469(3)	7059(2)	15952(1)	35(1)
C(22)	7465(4)	8130(2)	16955(2)	33(1)
C(23)	1079(5)	8441(3)	13326(2)	45(1)
C(24)	8331(4)	3437(3)	13023(2)	36(1)
O(25)	-611(2)	649(2)	8945(1)	30(1)

C(26)	-1946(4)	722(2)	9716(2)	30(1)
O(27)	1909(3)	254(2)	7650(1)	32(1)
C(28)	3244(4)	-19(2)	6909(2)	37(1)

Table 3. Bond lengths [pm] and angles [deg] for **231c**.

C(1)-C(2)	139.9(3)	C(2)-C(1)-C(8)	119.0(2)
C(1)-C(8)	140.9(3)	C(2)-C(1)-C(7)	120.2(2)
C(1)-C(7)	148.1(3)	C(8)-C(1)-C(7)	120.7(2)
C(2)-C(11)	140.1(3)	C(11)-C(2)-C(1)	119.5(2)
C(2)-C(3)	150.4(3)	C(11)-C(2)-C(3)	121.4(2)
C(3)-O(4)	144.8(3)	C(1)-C(2)-C(3)	119.1(2)
O(4)-C(5)	144.2(3)	O(4)-C(3)-C(2)	114.09(17)
C(5)-C(6)	152.1(3)	C(3)-O(4)-C(5)	113.93(17)
C(5)-C(24)	152.0(3)	O(4)-C(5)-C(6)	111.89(17)
C(6)-C(7)	134.2(3)	O(4)-C(5)-C(24)	106.10(19)
C(6)-C(12)	151.0(3)	C(6)-C(5)-C(24)	115.86(19)
C(7)-C(15)	151.0(3)	C(7)-C(6)-C(12)	122.4(2)
C(8)-C(9)	137.7(3)	C(7)-C(6)-C(5)	119.0(2)
C(9)-O(25)	137.3(3)	C(12)-C(6)-C(5)	118.6(2)
C(9)-C(10)	141.5(3)	C(6)-C(7)-C(1)	120.2(2)
C(10)-O(27)	136.7(3)	C(6)-C(7)-C(15)	122.9(2)
C(10)-C(11)	137.9(3)	C(1)-C(7)-C(15)	116.87(19)
C(12)-C(13)	153.7(3)	C(9)-C(8)-C(1)	120.9(2)
C(13)-C(19)	151.9(4)	O(25)-C(9)-C(8)	124.6(2)
C(13)-C(14)	149.7(4)	O(25)-C(9)-C(10)	115.30(19)
C(14)-C(16)	151.7(3)	C(8)-C(9)-C(10)	120.1(2)
C(14)-C(15)	152.8(3)	O(27)-C(10)-C(11)	125.7(2)
C(16)-O(17)	120.9(3)	O(27)-C(10)-C(9)	115.3(2)
C(16)-O(18)	132.6(3)	C(11)-C(10)-C(9)	119.0(2)
O(18)-C(23)	144.5(3)	C(10)-C(11)-C(2)	121.4(2)
C(19)-O(20)	120.5(3)	C(6)-C(12)-C(13)	112.6(2)
C(19)-O(21)	131.9(3)	C(19)-C(13)-C(14)	110.7(2)
O(21)-C(22)	143.9(3)	C(19)-C(13)-C(12)	108.4(2)
O(25)-C(26)	142.9(3)	C(14)-C(13)-C(12)	111.3(2)
O(27)-C(28)	142.8(3)	C(13)-C(14)-C(16)	111.1(2)
		C(13)-C(14)-C(15)	111.0(2)

C(16)-C(14)-C(15)	109.6(2)	O(20)-C(19)-O(21)	123.5(2)
C(7)-C(15)-C(14)	112.7(2)	O(20)-C(19)-C(13)	126.4(2)
O(17)-C(16)-O(18)	123.4(2)	O(21)-C(19)-C(13)	110.1(2)
O(17)-C(16)-C(14)	126.3(2)	C(19)-O(21)-C(22)	115.39(19)
O(18)-C(16)-C(14)	110.3(2)	C(9)-O(25)-C(26)	116.58(17)
C(16)-O(18)-C(23)	116.47(19)	C(10)-O(27)-C(28)	117.62(19)

Table 4. Anisotropic displacement parameters ($pm^2 x\ 10^{-1}$) for **231c**. The anisotropic displacement factor exponent takes the form: $-2\pi^2 [h^2 a^{*2} U^{11} + ... + 2 h k a^* b^* U^{12}]$

Atom	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(1)	26(1)	23(1)	22(1)	8(1)	2(1)	10(1)
C(2)	27(1)	25(1)	22(1)	11(1)	4(1)	10(1)
C(3)	26(1)	29(1)	23(1)	10(1)	4(1)	9(1)
O(4)	23(1)	36(1)	25(1)	11(1)	5(1)	11(1)
C(5)	30(1)	31(1)	25(1)	10(1)	7(1)	12(1)
C(6)	24(1)	24(1)	23(1)	9(1)	4(1)	6(1)
C(7)	26(1)	23(1)	22(1)	9(1)	6(1)	7(1)
C(8)	26(1)	25(1)	23(1)	9(1)	4(1)	11(1)
C(9)	25(1)	24(1)	24(1)	9(1)	1(1)	7(1)
C(10)	30(1)	23(1)	20(1)	6(1)	3(1)	10(1)
C(11)	31(1)	28(1)	22(1)	10(1)	7(1)	13(1)
C(12)	28(1)	26(1)	24(1)	6(1)	0(1)	9(1)
C(13)	40(2)	35(1)	35(1)	6(1)	2(1)	15(1)
C(14)	39(2)	37(1)	31(1)	5(1)	3(1)	18(1)
C(15)	28(1)	26(1)	24(1)	7(1)	2(1)	10(1)
C(16)	32(2)	27(1)	26(1)	1(1)	2(1)	10(1)
O(17)	58(1)	47(1)	49(1)	26(1)	16(1)	30(1)
O(18)	38(1)	41(1)	36(1)	15(1)	11(1)	19(1)
C(19)	36(2)	30(1)	33(1)	3(1)	0(1)	14(1)
O(20)	84(2)	38(1)	35(1)	12(1)	-14(1)	5(1)
O(21)	36(1)	25(1)	33(1)	3(1)	-6(1)	7(1)
C(22)	38(2)	30(1)	24(1)	3(1)	-1(1)	7(1)
C(23)	63(2)	40(2)	50(2)	24(1)	20(2)	31(2)
C(24)	40(2)	40(1)	35(1)	16(1)	7(1)	21(1)
O(25)	26(1)	28(1)	26(1)	3(1)	2(1)	4(1)
C(26)	26(1)	29(1)	33(1)	8(1)	6(1)	8(1)

O(27)	35(1)	28(1)	23(1)	0(1)	4(1)	8(1)
C(28)	45(2)	33(1)	26(1)	3(1)	12(1)	12(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters (pm^2x 10^{-1}) for **231c**.

Atom	x	y	z	U(eq)
H(3A)	7874	3764	9763	32
H(3B)	7201	4811	10658	32
H(5A)	6000	2647	11739	34
H(8A)	810	2705	10776	29
H(11A)	5427	1939	8494	31
H(12A)	7802	6139	13613	32
H(12B)	7000	5132	14180	32
H(13A)	4089	5538	14304	45
H(14A)	5142	6959	12915	44
H(15A)	1875	4719	12339	31
H(15B)	2746	5402	11518	31
H(22A)	7684	7838	17562	50
H(22B)	6672	8690	17164	50
H(22C)	8717	8590	16823	50
H(23A)	988	8889	12823	68
H(23B)	1570	9053	14093	68
H(23C)	-211	7869	13290	68
H(24A)	8947	2795	12690	54
H(24B)	7575	3215	13570	54
H(24C)	9335	4261	13398	54
H(26A)	-3196	62	9357	45
H(26B)	-2130	1553	9947	45
H(26C)	-1426	602	10374	45
H(28A)	2570	-778	6249	55
H(28B)	4309	-161	7292	55
H(28C)	3769	695	6677	55

Table 6. Torsion angles [deg] for **231c**.

C(8)-C(1)-C(2)-C(11)	-0.1(3)	C(19)-C(13)-C(14)-C(16)	-57.0(3)
C(7)-C(1)-C(2)-C(11)	176.88(18)	C(12)-C(13)-C(14)-C(16)	-177.6(2)
C(8)-C(1)-C(2)-C(3)	179.65(18)	C(19)-C(13)-C(14)-C(15)	-179.2(2)
C(7)-C(1)-C(2)-C(3)	-3.4(3)	C(12)-C(13)-C(14)-C(15)	60.2(3)
C(11)-C(2)-C(3)-O(4)	-108.6(2)	C(6)-C(7)-C(15)-C(14)	16.4(3)
C(1)-C(2)-C(3)-O(4)	71.7(2)	C(1)-C(7)-C(15)-C(14)	-163.86(19)
C(2)-C(3)-O(4)-C(5)	-38.1(2)	C(13)-C(14)-C(15)-C(7)	-45.2(3)
C(3)-O(4)-C(5)-C(6)	-48.5(3)	C(16)-C(14)-C(15)-C(7)	-168.21(19)
C(3)-O(4)-C(5)-C(24)	-175.72(18)	C(13)-C(14)-C(16)-O(17)	-25.4(4)
O(4)-C(5)-C(6)-C(7)	76.9(3)	C(15)-C(14)-C(16)-O(17)	97.6(3)
C(24)-C(5)-C(6)-C(7)	-161.3(2)	C(13)-C(14)-C(16)-O(18)	156.0(2)
O(4)-C(5)-C(6)-C(12)	-104.5(2)	C(15)-C(14)-C(16)-O(18)	-81.0(3)
C(24)-C(5)-C(6)-C(12)	17.3(3)	O(17)-C(16)-O(18)-C(23)	3.0(4)
C(12)-C(6)-C(7)-C(1)	178.41(19)	C(14)-C(16)-O(18)-C(23)	-178.3(2)
C(5)-C(6)-C(7)-C(1)	-3.0(3)	C(14)-C(13)-C(19)-O(20)	-17.3(4)
C(12)-C(6)-C(7)-C(15)	-1.8(3)	C(12)-C(13)-C(19)-O(20)	105.0(3)
C(5)-C(6)-C(7)-C(15)	176.71(19)	C(14)-C(13)-C(19)-O(21)	162.8(2)
C(2)-C(1)-C(7)-C(6)	-44.9(3)	C(12)-C(13)-C(19)-O(21)	-74.8(3)
C(8)-C(1)-C(7)-C(6)	132.0(2)	O(20)-C(19)-O(21)-C(22)	-1.5(4)
C(2)-C(1)-C(7)-C(15)	135.3(2)	C(13)-C(19)-O(21)-C(22)	178.3(2)
C(8)-C(1)-C(7)-C(15)	-47.8(3)	C(8)-C(9)-O(25)-C(26)	-8.6(3)
C(2)-C(1)-C(8)-C(9)	2.8(3)	C(10)-C(9)-O(25)-C(26)	169.35(18)
C(7)-C(1)-C(8)-C(9)	-174.13(19)	C(11)-C(10)-O(27)-C(28)	-2.0(3)
C(1)-C(8)-C(9)-O(25)	174.38(19)	C(9)-C(10)-O(27)-C(28)	179.92(19)
C(1)-C(8)-C(9)-C(10)	-3.5(3)		
O(25)-C(9)-C(10)-O(27)	1.6(3)		
C(8)-C(9)-C(10)-O(27)	179.68(18)		
O(25)-C(9)-C(10)-C(11)	-176.64(18)		
C(8)-C(9)-C(10)-C(11)	1.4(3)		
O(27)-C(10)-C(11)-C(2)	-176.73(19)		
C(9)-C(10)-C(11)-C(2)	1.3(3)		
C(1)-C(2)-C(11)-C(10)	-2.0(3)		
C(3)-C(2)-C(11)-C(10)	178.31(19)		
C(7)-C(6)-C(12)-C(13)	15.8(3)		
C(5)-C(6)-C(12)-C(13)	-162.7(2)		
C(6)-C(12)-C(13)-C(19)	-166.78(19)		
C(6)-C(12)-C(13)-C(14)	-44.8(3)		

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Publications

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"Palladium-catalyzed Cross-coupling Reactions and Electrocyclizations – Efficient Combinations for New Cascade Reactions" A. de Meijere, M. Schelper, M. Knoke, **B**. **Yucel,** H. W. Sünnemann, R. P. Scheurich, L. Arve, *J. Organomet. Chem.* **2003**, *687*, 249–255.

"A Two-Step Four-Component Queuing Cascade Involving a Heck Coupling, π-Allylpalladium Trapping and Diels-Alder Reaction" **B**. **Yucel,** L. Arve, A. de Meijere, *Tetrahedron* **2005***, 61,* 11355–11373.

Lebenslauf

Ich wurde am 20.09.1976 als Sohn von Ülkü und Orhan Yücel, beide Lehrer, in Ankara geboren; ich bin türkischer Staatsangehöriger. Nach meinem Abschluss an dem Yildirim Beyazit Berufsgymnasium für die Technische Industrie (1993), nahm ich im September 1994 mein Studium der Chemie an der Middle East Technical University (METU) in Ankara auf. Während meines Studiums absolvierte ich u.a. ein Praktikum bei der Weber & Broutin Markem Bau-Chemikalien AG in Izmir (1998). Im Anschluss an meinen ersten Studienabschluss, Bachelor of Science (B.S.), im September 1999, folgte im Januar 2002 mein Abschluss als Master of Science (M.S.); Thema der Masterarbeit: „The Reaction of Ferrocenyl Chromium Carbene Complex with Cyclobutenediones“. Von März 2002 bis November 2005 war ich Doktorand am Institut für Organische und Biomolekulare Chemie an der Georg-August-Universität Göttingen. Unter Leitung von Prof. Dr. Armin de Meijere fertigte ich meine Dissertation mit dem Titel „One-pot, Two-step Queuing Cascades Involving π-Allylpalladium Trapping and Diels-Alder Reaction“ an und war währenddessen als wissenschaftlicher Assistent für die Betreuung verschiedener Praktika und Tutorien zuständig.