Facile Synthesis of Bicyclic and Tricyclic Skeletons by Cycloisomerizations of Hept-1-en-6-ynes and 4,9-Diheteradodeca-1,11-dien-6-ynes, Followed by [4 + 2] Cycloadditions

Lonneke J. van Boxtel,[a] Stefanie Körbe,[a] Mathias Noltemeyer,[b] and Armin de Meijere*[a]

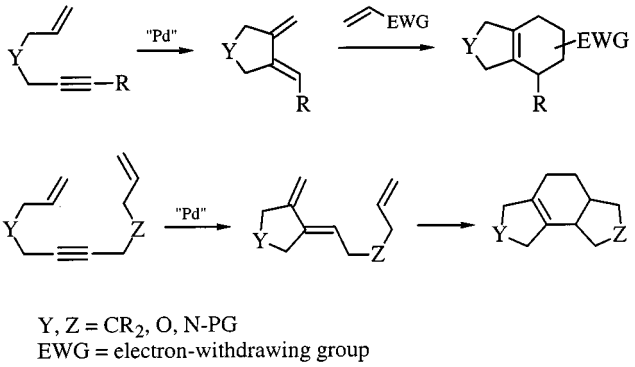
Dedicated to Professor Pierre Dixneuf on the occasion of his 60th birthday

Keywords: Catalysis / Cycloisomerization / Cyclizations / Diels−Alder reactions / Enynes / Palladium

Palladium-catalyzed intramolecular cross coupling of various 4-substituted hept-1-en-6-ynes, followed by intermolecular [4 + 2] cycloaddition with methyl acrylate and 2-chloro-2-cyclopropylideneacetate yielded both all-carbon and heteroanalogous bicyclic derivatives **8**, **9**, **18**, **19**, and **24** (24–71%). Cycloisomerization of the hydroxymethyl- and hydroxyethyl-substituted hept-1-en-6-ynes **5** and **15**, followed by Diels–Alder reaction with methyl acrylate, occurred with intramolecular transesterification to give the tricyclic lactones **11** (37%) and **16** (15%), respectively. Tricyclic systems containing up to three heteroatoms could be obtained from the corresponding dodeca-1,11-dien-6-ynes, by palladium-catalyzed cycloisomerization followed by intramolecular [4 + 2] cycloaddition. The scope and limitations of this single-operation tricyclization were evaluated. Symmetrically disubstituted dienynes with two nitrogen or two oxygen atoms reacted efficiently (41–90%) in this way, producing 5-6-5 ring-size combinations. Diastereoselectivities were poor in all cases (1:1 to 3.4:1). Unsymmetrically disubstituted dodeca-1,11-dien-6-ynes **44** and **48** underwent tricyclization with little or no regioselectivity to give **49/50** (7:3) and **51/52** (1:1).

Introduction

Among the various palladium-catalyzed C−C bond-forming reactions that have been steadily gaining increasing importance over the last decade, the enyne cycloisomerizations[1] are the only ones that match the atom economy of cycloadditions such as the Diels−Alder reaction. These cycloisomerizations, as well as the Heck reactions[2] that complement them,[3] have found numerous applications in the synthesis of biologically active and other interesting compounds of high molecular complexity.[1,3,4] Combinations of cycloisomerizations or Heck reactions with subsequent Diels−Alder reactions have also been used both in consecutive operation[1,5] and in sequential one-pot transformation modes.[6] Here we report a study dealing with the scope of the previously reported[6] intra−intermolecular cycloisomerization−Diels−Alder reaction sequence, which yields bicyclic systems, and also a new intra−intramolecular counterpart, affording tricyclic systems (Scheme 1).[7]



Scheme 1. Hept-1-en-6-yne cycloisomerization followed by an intermolecular or intramolecular [4 + 2] cycloaddition, producing bicyclic and tricyclic systems, respectively

Results

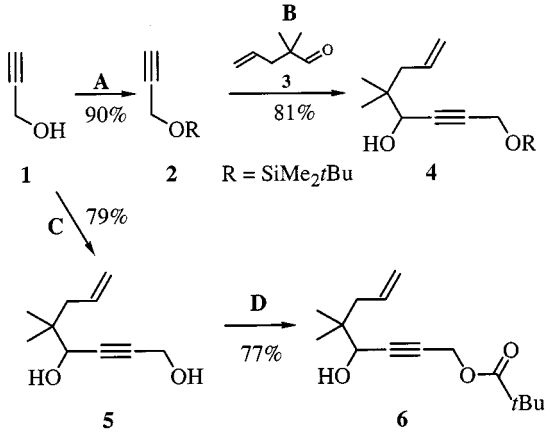
The Domino Reaction Consisting of Enyne Cycloisomerization and Intermolecular [4 + 2] Cycloaddition

With the skeleton of the illudin sesquiterpenes[8] in mind as potential targets, the 4,4-dimethyloct-1-en-6-yne-5,8-diol derivatives **4** and **6** were synthesized by standard procedures from propargyl alcohol (**1**) and 2-allylisobutyraldehyde (**3**). The aldehyde **3**, upon treatment with the lithiated silyl-protected propargyl alcohol **2**, gave the enyne **4** in 81% yield. Treatment of the aldehyde with the unprotected dilithiated

[a] Institut für Organische Chemie, Georg-August-Universität Göttingen,
Tammannstrasse 2, 37077 Göttingen, Germany
Fax: (internat.) + 49-551/399475
E-mail: Armin.deMeijere@chemie.uni-goettingen.de
[b] Institut für Anorganische Chemie, Georg-August-Universität Göttingen,
Tammannstrasse 4, 37077 Göttingen, Germany
Supporting information for this article is available on the WWW under http://www.eurjoc.com or from the author.

  1434−193X/01/0612−2283 $ 17.50+.50/0

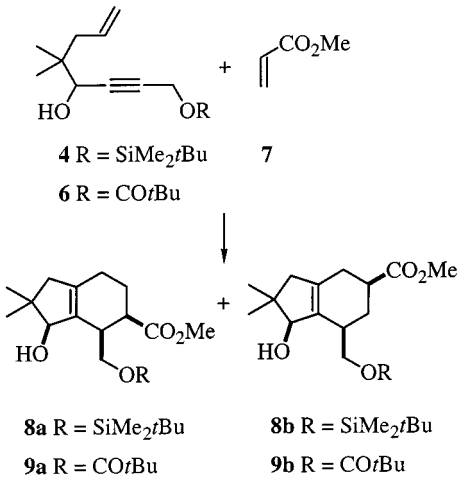
propargyl alcohol (**1**) produced the enyne **5**, which was subsequently acylated with pivaloyl chloride at the primary site to give the enyne **6** in 61% overall yield (Scheme 2).



Scheme 2. Preparation of enynes **4**, **5**, and **6**; **A**: *t*BuMe$_2$SiCl, imidazole, DMF, 20 °C, 19 h; **B**: 1) *n*BuLi, 2) aldehyde **3**, THF, −78 °C, 1 h; **C**: 1) 2 equiv. of *n*BuLi, 2) aldehyde **3**, THF, −78 °C, 15 h; **D**: pivaloyl chloride, CH_2Cl_2, pyridine, 0 °C, 14 h

The cycloisomerizations and subsequent Diels−Alder reactions were carried out on the model enynes **4** and **6** as domino-type reactions in one-pot operations, as these usually give higher yields than two-step procedures involving isolation of the intermediate dienes.[6] Hept-1-en-6-ynes of type **4** and **6**, with protected terminal hydroxymethyl groups, have previously been shown to cycloisomerize to 1,3-dienes rather than the 1,4-dienes that would result from a normal Alder−ene-type process.[1a,1b] The cycloisomerization−Diels−Alder sequences of **4** and **6** with methyl acrylate (**7**) were performed under a variety of conditions (see Table 1). Best yields of the cycloadducts **8** and **9** were obtained with 5 mol % of Pd(OAc)$_2$ and *N*,*N*′-bisbenzylideneethylenediamine (BBEDA)[9] in benzene at 70 °C in the presence of 3 equiv. of methyl acrylate (**7**). The formed bicyclic derivatives in each case were mixtures of two regioisomers, but both of these were pure all-*cis* diastereomers.[10] In the presence of 5 mol % of Pd(dba)$_2$, 10 mol % of SbPh$_3$,[11] or PPh$_3$ and acetic acid in benzene at 70 °C, no cycloisomerization of **4** occurred. The pivaloyl-protected alcohol **6**, however, in the presence of 5 mol % of Pd(dba)$_2$, 10 mol % of PPh$_3$, and acetic acid, gave cycloadduct **9**, but in lower yields than with Pd(OAc)$_2$/BBEDA (Scheme 3, Table 1).

In order to test whether the hydroxymethyl group in **5** would induce any regioselectivity in the Diels−Alder reaction after the cycloisomerization, the unprotected diol **5** was subjected to the same conditions as **4** and **6** in the presence of methyl acrylate (**7**). This resulted in the formation of the tricyclic lactone **11** in 37% isolated yield.[12] Apparently, the bicyclic methyl ester **10** was formed by [4 + 2] cycloaddition between **7** and the bis(exocyclic) diene resulting from cycloisomerization of **5**, but the quasi-*ortho* regioisomer immediately underwent intramolecular transesterification to yield the tricyclic lactone. Interestingly, neither the regioisomeric cycloadduct **12**, nor a lactone derived from it could be observed. Although the yield of **11** was only moderate, its formation may be taken as indication that the free hydroxymethyl group in **5** does indeed control the regiochemistry of the [4 + 2] cycloaddition. In order to improve the yield of the lactone **11**, treatment of **5** with methyl acrylate (**7**) under palladium catalysis conditions was carried out in the presence of 10 mol % of Ti(O*i*Pr)$_4$, which is known to catalyze transesterifications of esters with various alcohols under neutral conditions.[13] In this case, however, no lactone **11** was obtained, but only unidentified oligomeric and decomposition products. It may well be that, in the presence of Ti(O*i*Pr)$_4$, the dienyne **13** was initially formed by transesterification of methyl acrylate (**7**) with the diol **5**, but the intermediate diene formed by cycloisomerization of **13** may then have failed to undergo the intramolecular Diels−Alder reaction to the lactone, although there is no obvious reason for this failure,[14] except that **13** would have an unfavorable conformation in the ground state.[15] An attempted transformation of authentic **13**, prepared by treatment of the diol **5** with acryloyl chloride under the same conditions, also only produced a mixture of unidentified products. Cycliza-

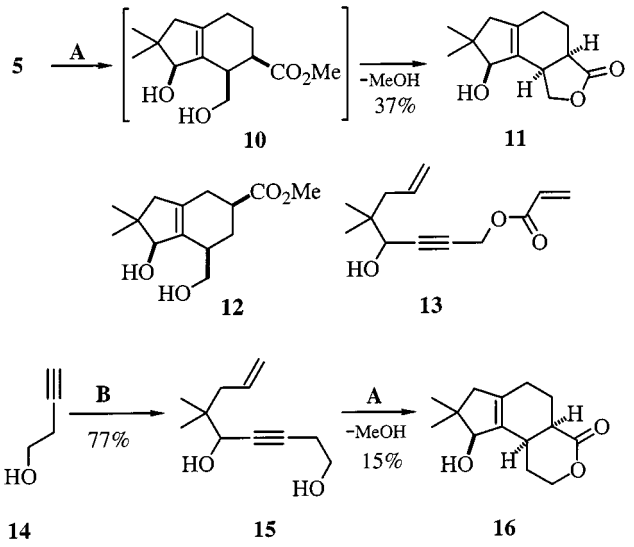


Scheme 3. Cycloisomerization of **4** and **6** followed by Diels−Alder reaction (for details see Table 1)

Table 1. Palladium-catalyzed cycloisomerization of **4** and **6** under different conditions

Entry	Enyne	Conditions[a]	Product	Product ratio **a**/**b**	Yield (%)[b]
1	**4**	**A**	**8a**,**b**	1.4:1	44
2	**4**	**B**	**8a**,**b**	1.2:1	35
3	**4**	**C**	–	–	–[c]
4	**4**	**D**	–	–	–[c]
5	**6**	**A**	**9a**,**b**	2.9:1	71
6	**6**	**D**	**9a**,**b**	2.4:1	24

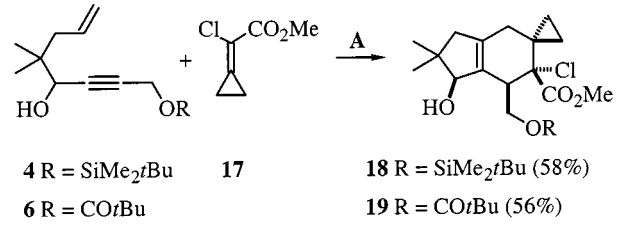
[a] **A**: Pd(OAc)$_2$ (5 mol %), BBEDA (10 mol %), **7** (3 equiv.), C_6H_6, 70 °C, 2 d; **B**: Pd(OAc)$_2$ (5 mol %), PPh$_3$ (10 mol %), **7** (3 equiv.), C_6H_6, 70 °C, 2 d; **C**: Pd(dba)$_2$ (5 mol %), SbPh$_3$ (10 mol %), AcOH (10 mol %), **7** (3 equiv.), C_6H_6, 70 °C, 2 d; **D**: Pd(dba)$_2$ (5 mol %), PPh$_3$ (10 mol %), AcOH (10 mol %), **7** (3 equiv.), C_6H_6, 70 °C, 2 d. − [b] Combined yields of **a** + **b**. − [c] Traces of starting material with unidentified compounds.



Scheme 4. Cyclization and further reactions of hydroxyalkyl-substituted hepta-1-en-6-ynes **5** and **15**; **A**: $Pd(OAc)_2$ (5 mol %), BBEDA (10 mol %), **7** (3 equiv.), C_6H_6, 70 °C, 18−24 h; **B**: 1) 2 equiv. of *n*BuLi, 2) aldehyde **3**, THF, −78 °C, 18 h

tion of the enynediol **15**, homologous with **5**, in the presence of methyl acrylate (**7**) gave the corresponding tricyclic δ-lactone **16**, but in an even lower yield of only 15% (Scheme 4).

The highly reactive dienophile methyl 2-chloro-2-cyclopropylideneacetate (**17**)[6,8] reacted under the optimized conditions [5 mol % $Pd(OAc)_2$, 10 mol % BBEDA] with both **4** and **6**, to give the spirocyclopropane-annulated hexahydroindenes **18** and **19**, respectively, as single regioisomers (Scheme 5), but those with the spirocyclopropane and α-chloro ester moieties in the wrong positions for further elaboration towards the illudins.[8] The relative configuration of **19** was proven by an X-ray crystal structure analysis (Figure 1).[16] In an attempt to use the sterically more demanding *tert*-butyl 2-chloro-2-cyclopropylideneacetate instead of the methyl ester **17** − in order to redirect the regioselectivity − no cycloadduct was observed. The *tert*-butyl ester was reisolated, while the intermediate diene underwent oligomerization and decomposition.



Scheme 5. Cycloisomerization of **4** and **6** and intermolecular Diels−Alder reactions with methyl 2-chloro-2-cyclopropylideneacetate (**17**); **A**: $Pd(OAc)_2$ (5 mol %), BBEDA (10−11 mol %), **17** (1.2−1.4 equiv.), C_6H_6, 70 °C, 2−4 d

Synthesis of Bicyclic Compounds Containing Heteroatoms

For many metal-catalyzed reactions, incorporation of heteroatoms such as nitrogen in the substrates can cause

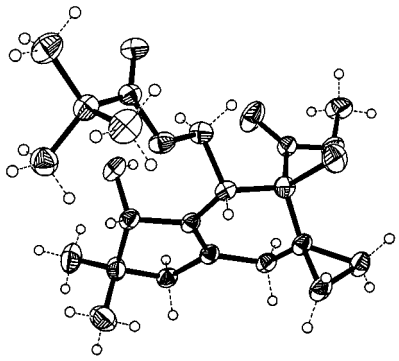
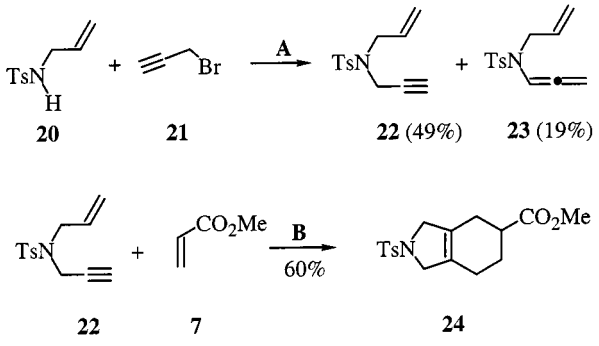


Figure 1. Structure of compound **19** in the crystal (see ref.[16])

problems, because they are able to coordinate to the transition metal and inhibit the reaction or change the reaction mode.[17] To test the influence of nitrogen atoms in the type of precursors under discussion, the enyne **22** was prepared in 49% yield, accompanied by 19% of the enallene **23**, by deprotonation of *N*-allyl-*p*-toluenesulfonamide with sodium hydride in tetrahydrofuran and alkylation with propargyl bromide (**21**). Treatment of the azaenyne **22** with 5 mol % of $Pd(dba)_2$ in the presence of 3 equiv. of methyl acrylate (**7**), 10 mol % of PPh_3, and acetic acid in benzene at 80 °C did indeed give the expected azabicycle **24** (60% yield); other catalyst systems gave lower yields (Scheme 6).

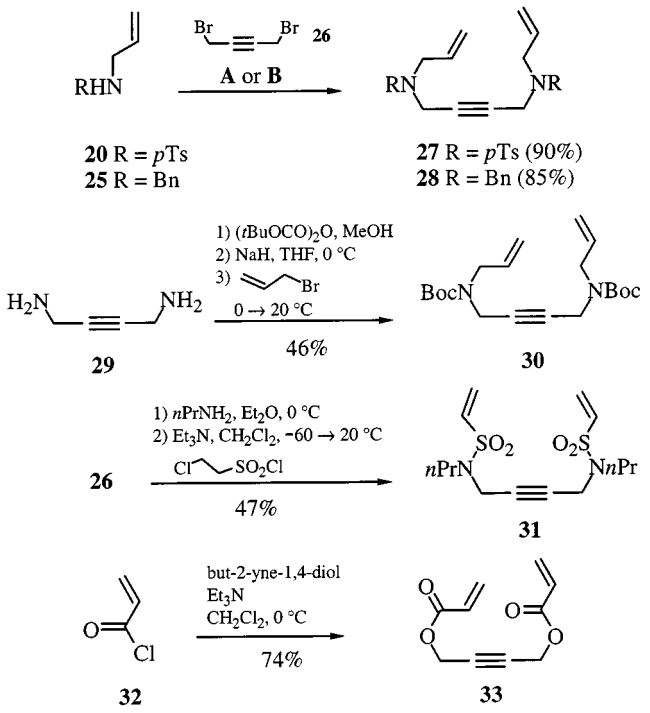


Scheme 6. Preparation and further reactions of *N*-tosyl-4-azahept-1-en-6-yne (**22**); **A**: NaH (1.1 equiv.), THF, 0 °C, 16 h (longer reaction times resulted in the formation of more enallene **23**); **B**: $Pd(dba)_2$ (5 mol %), PPh_3 (10 mol %), AcOH (10 mol %), **7** (3 equiv.), C_6H_6, 80 °C, 18 h

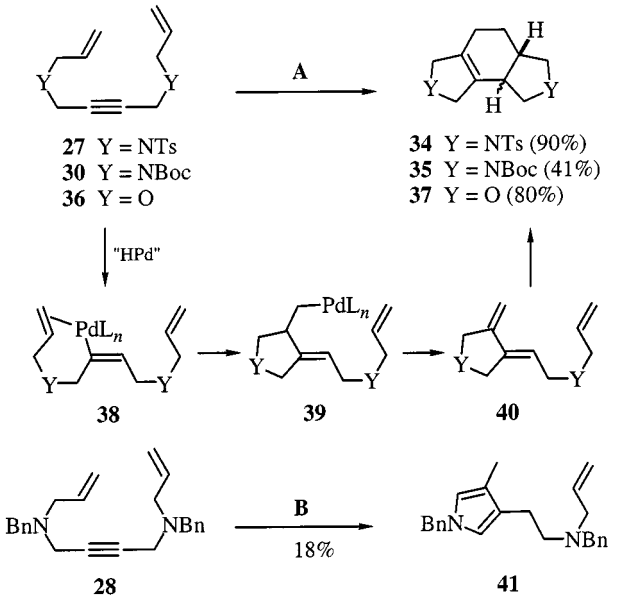
Enyne Cycloisomerization Followed by Intramolecular [4 + 2] Cycloaddition

Sequential enyne cycloisomerization and intermolecular [4 + 2] cycloaddition can be developed into an enyne cycloisomerization followed by an intramolecular [4 + 2] cycloaddition, giving tricyclic systems. A few examples of this domino reaction have previously been reported, but only unsymmetrical dienynes were used.[1f] It appeared to be of interest to cyclize symmetrical dienynes, some of which are particularly easily accessible.

For example, 1,4-dibromobut-2-yne (**26**) could be aminated twice with *N*-allyl-*N*-tosylamine (**20**) to give *N*,*N*′-diallyl-*N*,*N*′-ditosylbut-2-yne-1,4-diamine (**27**) in 90% yield



Scheme 7. Syntheses of nitrogen-containing dodeca-1,11-dien-6-ynes; **A**: NaH, THF, 0 °C; **B**: Et_2O, 0 °C



Scheme 8. Cyclizations of 4,9-diheteradodeca-1,11-dien-6-ynes, producing diheterotricyclic systems; **A**: $Pd(dba)_2$ (2.5−5 mol %), PPh_3 (9−10 mol %), AcOH (10−110 mol %), C_6H_6, 80 °C, 2−88 h; **B**: $Pd(OAc)_2$ (5 mol %), BBEDA (10 mol %), C_6H_6, 80 °C, 120 h

(Scheme 7). 1,4-Dibromobut-2-yne (**26**), upon double amination with *N*-allyl-*N*-benzylamine (**25**), gave *N*,*N*′-diallyl-*N*,*N*′-dibenzylbut-2-yne-1,4-diamine (**28**) (85%). A third nitrogen-containing dienyne was synthesized by protecting but-2-yne-1,4-diamine (**29**) with two *tert*-butoxycarbonyl groups and then alkylating twice with allyl bromide, to give di-*tert*-butyl *N*,*N*′-diallylbut-2-yne-1,4-dicarbamate (**30**) in 46% overall yield. Treatment of 1,4-dibromobut-2-yne (**26**) with *n*-propylamine and ethenesulfonyl chloride yielded the sulfonamide **31** (47%). The diacrylate **33** was obtained by esterification of but-2-yne-1,4-diol with acryloyl chloride (**32**) (Scheme 7).

Upon treatment of **27** with 5 mol % of $Pd(dba)_2$, 10 mol % of PPh_3, and 20 mol % of acetic acid in benzene at 80 °C, it cyclized to give the diazatricycle **34** in 90% yield (Scheme 8). Other catalyst systems gave lower yields of **34** (Table 2). The *cis* and *trans* diastereomers of **34** were formed in a ratio of 1.8:1. This ratio did not change when the reaction was performed under different reaction conditions, such as in different solvents (benzene, acetonitrile, CH_2Cl_2), at different temperatures (45−80 °C), with other catalyst precursors, or with application of high pressure (10 kbar). Similar results have been reported for the reaction of 1,3,8-nonatriene, giving bicyclo[4.3.0]non-2-ene.[18] Only small changes in the *cis*/*trans* ratio were found over a wide range of temperatures, and no changes occurred under the influence of high pressure. The *cis* and *trans* isomers could be separated by crystallization.

It is particularly noteworthy that the intermediate triene formed from **27** in the initial cycloisomerization step undergoes the intramolecular Diels−Alder reaction under the conditions of the enyne cycloisomerization, i.e. at 80 °C. Previously reported transformations of this kind required higher temperatures or Lewis acid catalysis for the [4 + 2] cycloaddition to take place.[1e] The scope of this domino tricyclization process was tested with the other synthesized dienes, which were treated with palladium catalysts under various conditions. All efforts to tricyclize the benzyl-protected dienyne **28** to the tricyclic system were unsuccessful. Complete consumption of starting material was achieved after very long reaction times (at least 5 d), but inseparable mixtures of products were largely obtained. When 5 mol % of $Pd(OAc)_2$ and 10 mol % of BBEDA were used, one of the products was identified as the monocyclic pyrrole **41** (yield 18%, Scheme 8). The cyclization of the Boc-protected dienyne **30**, however, did give the diazatricycle **35**, albeit in moderate yield (41%). Under various other conditions, only inseparable mixtures or decomposition products were observed. Apparently, an electron-withdrawing group on the nitrogen atom is essential for a successful cyclization to take place (Scheme 8, Table 2).

Attempted tricyclization of the acyclic bis(ethenylsulfonamide) **31**, however, despite the electron-withdrawing groups attached to the nitrogen atoms, gave only intractable mixtures. Metz et al.[19] recently reported that intramolecular [4 + 2] cycloadditions of hexa-3,5-dien-1-yl ethenylsulfonamides, yielding bicyclic systems with six-membered sultam moieties, required high pressure (13 kbar) to proceed cleanly at ambient temperature, with side reactions occurring at reflux in toluene. High-pressure conditions were not examined in the case of **31**, in which the transition structure for the formation of the five-membered sultam must be more highly strained.

While the dienyl diether **36**, prepared as reported by Barbot et al.,[20] cyclized under the same catalytic system conditions as used with **27**, giving the corresponding dioxatricy-

Table 2. Palladium-catalyzed cycloisomerizations followed by intramolecular [4 + 2] cycloadditions of nitrogen- and oxygen-containing dodecadienynes under various conditions

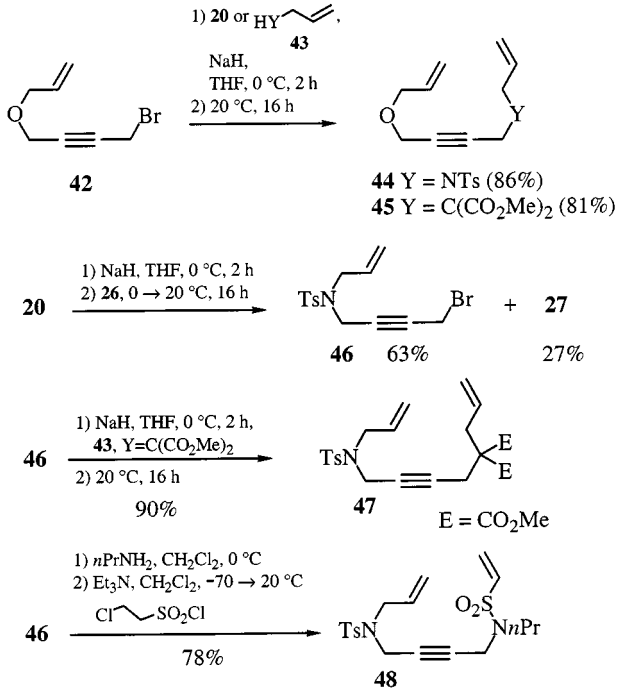
Entry	Dienyne	Conditions[a]	Reaction time [h]	Product	Yield (%)	Ratio[b] *cis*/*trans*
1	**27**	**A**	3	**34**	90	1.8:1
2	**27**	**B**	24	**34**[c]	–	–
3	**27**	**B**[d]	168	**34**	57	1.8:1
4	**27**	**C**	74	**34**	88	1.8:1
5	**27**	**D**	24	**34**[c]	–	–
6	**30**	**A**	88	**35**	41	1:1
7	**30**	**D**	24	–[e]	–	–
8	**36**	**A**	20	**37**	80	3.4:1
9	**36**	**D**	48	–[e]	–	–
10	**28**	**A**	72	–[e]	–	–
11	**28**	**D**	120	**41**	18	–
12	**28**	**E**	48	s.m.[f]	–	–

[a] **A**: $Pd(dba)_2$ (2.5–5 mol %), PPh_3 (9–10 mol %), AcOH (10–110 mol %), C_6H_6, 80 °C; **B**: $Pd(dba)_2$ (5 mol %), PPh_3 (10 mol %), AcOH (20 mol %), MeCN, 80 °C; **C**: $Pd(dba)_2$ (5 mol %), PPh_3 (10 mol %), AcOH (20 mol %), CH_2Cl_2, 40 °C, 10 kbar; **D**: $Pd(OAc)_2$ (5 mol %), BBEDA (10 mol %), C_6H_6, 80 °C; **E**: $Pd(OAc)_2$ (5 mol %), PPh_3 (10 mol %), AcOH (20 mol %), C_6H_6, 80 °C. – [b] *cis*/*trans* ratios were determined from the ^{13}C NMR spectra. – [c] The product was formed, but contained an inseparable by-product. – [d] 10 kbar, room temp. – [e] A mixture of unidentified compounds was formed. – [f] s. m. = starting material.

cle **37** in 80% yield, all attempts to tricyclize the acyclic diacrylate **33** yielded only oligomeric material. It is not certain whether the precursor diacrylate or the monocyclic intermediate underwent polymerization.

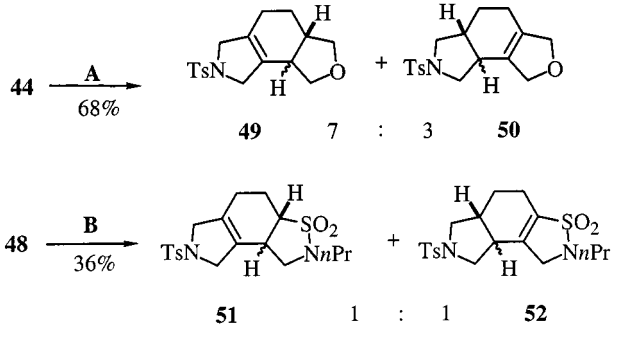
Tricyclization of Unsymmetrically Substituted 4,9-Diheteradodeca-1,11-dien-6-ynes

In view of the apparent differences in reactivities of the different symmetrically disubstituted 4,9-diheteradodecadienynes (reaction time of 3 h for dienyne **27** versus 20 h for dienyne **36**), the unsymmetrically disubstituted dienynes **44**, **45**, **47**, and **48** were prepared in order to examine the possibility of unidirectional tricyclization of such compounds. Alkylation of *N*-allyl-*N*-tosylamine (**20**) and dimethyl 2-allylmalonate (**43**) with propargyl bromide **42** gave the oxaazadienyne **44** and dioxadienyne **45** in 86 and 81% yield, respectively. Monoamination of 1,4-dibromobut-2-yne (**26**) with **20** and subsequent alkylation of **43** with the resulting monobromide **46** yielded the azadienyne **47** (57% overall). Successive treatment of **46** with *n*-propylamine and 2-chloroethanesulfonyl chloride in the presence of triethylamine gave the sulfonamide **48** (78%) (Scheme 9).



Scheme 9. Synthesis of unsymmetrically substituted dodeca-1,11-dien-6-ynes

The palladium-catalyzed tricyclization of the dienyne **44** gave oxaazatricycles **49** and **50**, with a slight selectivity for **49** (ratio 7:3, both as mixtures of two diastereomers, *cis*/*trans* ratio[21] 2.6:1, 4.4:1, respectively) in 68% yield (Scheme 10). Apparently, the addition of the palladium species to the triple bond occurs with a certain degree of regioselectivity in the sense that intramolecular carbopalladation incorporating the allylamine unit is slightly favored. The product ratio was not detectably influenced by using acetonitrile instead of benzene, and application of a different catalyst cocktail [$Pd(OAc)_2$, BBEDA] produced even poorer results in that a range of unidentified products was



Scheme 10. Tricyclizations of unsymmetrical 4,9-diheteradodecadienynes; **A**: $Pd(dba)_2$ (6 mol %), PPh_3 (13 mol %), MeCN, 80 °C, 16 h; **B**: $Pd(dba)_2$ (6 mol %), PPh_3 (13 mol %), AcOH (22 mol %), C_6H_6, 80 °C, 16 h

observed. The tricyclization of dienyne **48** also gave a mixture of two products, the thiadiazatricycles **51** and **52**, but in a ratio of 1:1 (less than 10% of the other diastereomer for both compounds). In this transformation, apparently, no regioselectivity of the initial hydropalladation occurred, so no differentiation between the two terminal double bonds could result. Attempts to carry out tricyclizations of dienynes **45** and **47** (under the conditions **A**−**E** as listed in Table 2) only gave inseparable mixtures.

Experimental Section

General: ^{1}H NMR spectra were recorded with a Bruker AM 250 spectrometer (250 MHz) at ambient temperature in $CDCl_3$, using $CHCl_3$ (δ = 7.26) or tetramethylsilane (δ = 0.00) as internal standard. Chemical shifts (δ) are quoted in ppm and coupling constants (*J*) are given in absolute values in Hz to the nearest 0.1 Hz. The following abbreviations are used for the signal multiplicities: s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), and br (broad). − ^{13}C NMR spectra were recorded with a Bruker AM 250 (62.9 MHz) at ambient temperature in $CDCl_3$, with δ($CDCl_3$) = 77.0 as internal standard. Multiplicities were determined by the DEPT pulse sequence and are given as follows: + = CH or CH_3, − = CH_2, and C_{quat} = C. If signals could not be assigned unambiguously, the corresponding atoms concerned are marked with an asterisk (*). − Infrared spectra were recorded with a Bruker FT-IR spectrometer IFS 66. − Mass spectra were recorded with a Varian MAT CH 7, MAT 731 using electron impact ionization at 70 eV or direct chemical ionization with NH_3 as reactant gas. High-resolution mass spectra (HRMS) were obtained with a Varian MAT 311, INCOS 50 with Varian 34000 (GC-MS) using preselected ion peak matching at R ≈ 10000 to be within ±2 ppm. − Elemental analyses were performed by the Mikroanalytisches Labor des Instituts für Organische Chemie der Universität Göttingen, Germany. − All solvents were distilled before use. − Chromatography: for standard chromatography Merck silica gel 60 (230−400 mesh, 0.063−0.200 mm) was used, and for flash chromatography Macherey−Nagel silica gel 60 (70−230 mesh, 0.040−0.063 mm). TLC plates: Macherey−Nagel foils: Alugram Sil G/UV, detection under UV light at 254 or 366 nm. If the substances were not UV-active, the plates were developed with potassium permanganate or anisaldehyde solution. − Unless specified otherwise, solutions of NH_4Cl, $NaHCO_3$, and NaCl were saturated aqueous solutions. Anhydrous solvents were prepared according to standard laboratory techniques. All reactions with organometallic substances were performed under nitrogen and with exclusion of water. In these cases the glassware used was heated in vacuo to remove all of the moisture. − Reactions under high pressure were performed in sealed Teflon tubes in a high-pressure apparatus from Fa. Andreas Hofer GmbH, Mülheim. − All chemicals were used as commercially available, unless otherwise noted. The substances 3-*tert*-butyldimethylsilyloxy-1-propyne (**2**),[22] 2,2-dimethylpent-4-enal (**3**),[23] *N*-allyl-*p*-toluenesulfonamide (**20**),[24] *N*-allyl-*N*-benzylamine (**25**),[25] 1,4-dibromobut-2-yne (**26**),[26] but-2-yne-1,4-diamine (**29**),[27] 1-(allyloxy)-4-bromobut-2-yne (**42**)[28] and 1,4-bis(allyloxy)but-2-yne (**36**)[20] were prepared according to literature procedures.

General Procedure for One-Pot Enyne Cycloisomerization Followed by Diels−Alder Reaction (GP 1): Palladium acetate (5 mol %) and the ligand (10 mol %) were added to a solution of the respective enyne (1 mmol) and the dienophile (3 mmol) in anhydrous benzene (10 mL) in a screw-cap Pyrex bottle. Nitrogen was bubbled through the reaction mixture for 5 min; the bottle was then closed and heated to 70 °C for the given time. The reaction mixture was filtered through a bed of Celite and charcoal and washed with Et_2O. The crude product was purified by chromatography on silica gel, with pentane/Et_2O mixtures.

Methyl 4-*tert*-Butyldimethylsilyloxymethyl-2,3,4,5,6,7-hexahydro-3-hydroxy-2,2-dimethyl-1*H*-indene-5-carboxylate (8a) and Methyl 4-*tert*-Butyldimethylsilyloxymethyl-2,3,4,5,6,7-hexahydro-3-hydroxy-2,2-dimethyl-1*H*-indene-6-carboxylate (8b). − Method A: As described in GP 1, enyne **4** (283 mg, 1.00 mmol) and methyl acrylate (**7**) (258 mg, 3.00 mmol) in anhydrous benzene (10 mL) were treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol %) and *N*,*N*′-bis(benzylidene)ethylenediamine (24 mg, 0.10 mmol, 10 mol %) at 70 °C for 2 d. Column chromatography on silica gel (18 g, column 2.0 × 15 cm, pentane/Et_2O, 4:1) yielded Fraction I: 94 mg (26%) of **8a**, R_f (pentane/Et_2O, 4:1) = 0.35, as a colorless oil. − IR (film): $\tilde{\nu}$ = 3447 cm^{-1} (OH), 2857, 1740 (C=O), 1472, 1363, 1259 ($SiCH_3$), 1163, 1080, 1006, 834, 785. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.07 [s, 3 H, $Si(CH_3)_2$], 0.09 [s, 3 H, $Si(CH_3)_2$], 0.89 [s, 9 H, $SiC(CH_3)_3$], 0.99 (s, 3 H, 2-CH_3), 1.09 (s, 3 H, 2-CH_3), 1.75 (m_c, 1 H, 6-H), 1.86 (AB, $^2J_{AB}$ = 16.1 Hz, 1 H, 1-H), 1.91−2.02 (m, 2 H, 6-H, 7-H), 2.10−2.15 (m, 1 H, 7-H), 2.25 (AB, $^2J_{AB}$ = 16.1 Hz, 1 H, 1-H), 2.62 (ddd, ^3J = 3.0, ^3J = 5.2, ^3J = 13.3 Hz, 1 H, 5-H), 2.71−2.75 (m, 1 H, 4-H), 3.57−3.64 (m, 2 H, CH_2OSi), 3.70 (s, 3 H, CO_2CH_3), 3.89 (br s, 1 H, 3-H), 4.12 (d, ^3J = 2.7 Hz, 1 H, OH). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = −5.52 (+, $SiCH_3$), −5.49 (+, $SiCH_3$), 18.4 [C_{quat}, Si*C*$(CH_3)_3$], 20.6 (−, C-7*), 22.6 (+, 2-CH_3), 25.7 (−, C-6*), 25.8 [+, $SiC(CH_3)_3$], 28.6 (+, 2-CH_3), 39.7 (+, C-4), 41.5 (C_{quat}, C-2), 42.8 (+, C-5), 48.3 (−, C-1), 51.5 (+, CO_2CH_3), 65.4 (−, CH_2OSi), 85.6 (+, C-3), 137.6 (C_{quat}, C-3a*), 140.0 (C_{quat}, C-7a*), 174.8 (C_{quat}, CO_2CH_3). − MS (EI, 70 eV), *m*/*z* (%) = 368 (2) [M$^+$], 311 (33) [M$^+$ − C_4H_9], 293 (16) [M$^+$ − C_4H_9 − H_2O], 279 (19) [M$^+$ − C_4H_8 − H_2O − CH_3], 219 (65) [M$^+$ − $OSi(CH_3)_2C(CH_3)_3$ − H_2O], 206 (14) [M$^+$ − $CH_2OSi(CH_3)_2C(CH_3)_3$ − OH], 191 (13) [M$^+$ − $CH_2OSi(CH_3)_2C(CH_3)_3$ − OH − CH_3], 159 (100) [M$^+$ − $CH_2OSi(CH_3)_2C(CH_3)_3$ − H_2O − CH_3 − OMe], 147 (18) [M$^+$ − $CH_2OSi(CH_3)_2C(CH_3)_3$ − OH − CO_2Me], 89 (17), 81 (17), 75 (27). − $C_{20}H_{36}O_4Si$ (368.6): calcd. C 65.17, H 9.84; found C 64.91, H 9.67. − Fraction II: 65 mg (18%) of **8b**, R_f (pentane/Et_2O, 4:1) = 0.29, as a colorless oil. − IR (film): $\tilde{\nu}$ = 3471 cm^{-1} (OH), 2857, 1740 (C=O), 1472, 1362, 1258 ($SiCH_3$), 1170, 1086, 1040, 1005, 840. − ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.08 [s, 6 H, $Si(CH_3)_2$], 0.89 [s, 9 H, $SiC(CH_3)_3$], 0.98 (s, 3 H, 2-CH_3), 1.09 (s, 3 H, 2-CH_3), 1.50 (m_c, 1 H, 5-H), 1.81 (m_c, 1 H, 1-H), 1.97 (m_c, 1 H, 5-H), 2.17−2.26 (m, 2 H, 7-H), 2.35−2.40 (m, 1 H, 1-H), 2.37−2.42 (m, 1 H, 4-H), 2.59 (dddd, ^3J = 2.9, ^3J = 6.5, ^3J = 13.0, ^3J = 16.2 Hz, 1 H, 6-H), 3.58 (dd, ^2J = 10.3, ^3J = 6.0 Hz, 1 H, CH_2OSi), 3.68 (d, ^3J = 3.4 Hz, 1 H, OH), 3.69 (s, 3 H, CO_2CH_3), 3.87 (dd, ^2J = 10.3, ^3J = 4.1 Hz, 1 H, CH_2OSi), 4.02 (br s, 1 H, 3-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = −5.5 [+, $Si(CH_3)_2$], −5.3 [+, $Si(CH_3)_2$], 18.2 [C_{quat}, Si*C*$(CH_3)_3$], 22.8 (+, 2-CH_3), 25.8 [+, $SiC(CH_3)_3$], 29.08 (+, 2-CH_3), 29.09 (−, C-7), 29.6 (−, C-5), 39.2 (+, C-4), 39.9 (+, C-6), 41.2 (C_{quat}, C-2), 49.0 (−, C-1), 51.7 (+, CO_2CH_3), 66.0 (−, CH_2OSi), 84.4 (+, C-3), 136.1 (C_{quat}, C-3a*), 139.7 (C_{quat}, C-7a*), 176.0 (C_{quat}, CO_2CH_3). − MS (EI, 70 eV), *m*/*z* (%) = 368 (1) [M$^+$], 337 (2) [M$^+$ − OMe], 311 (7) [M$^+$ − C_4H_9], 293 (2) [M$^+$ − C_4H_9 − H_2O], 223 (3) [M$^+$ − $CH_2OSi(CH_3)_2C(CH_3)_3$], 219 (16) [M$^+$ − $OSi(CH_3)_2C(CH_3)_3$ − H_2O], 163 (29) [M$^+$ − $OSi(CH_3)_2C(CH_3)_3$ − CO_2Me − CH_3], 161 (31) [M$^+$ − $OSi(CH_3)_2C(CH_3)_3$ − CO_2Me − OH], 159 (30) [M$^+$ − $CH_2OSi(CH_3)_2C(CH_3)_3$ − H_2O − CH_3 − OMe], 139 (17), 98 (14), 81 (100),

57 (44) [$C_4H_9^+$], 43 (48). − $C_{20}H_{36}O_4Si$ (368.6): calcd. C 65.17, H 9.84; found C 65.25, H 9.97.

Method B: When PPh_3 (10 mol %, 26 mg, 0.10 mmol) was used instead of *N*,*N*′-bis(benzylidene)ethylenediamine under conditions otherwise identical with those of Method A, 69 mg (19%) of **8a** and 58 mg (16%)of **8b** were isolated.

Method C: When enyne **4** (283 mg, 1.00 mmol) and methyl acrylate (**7**) (258 mg, 3.00 mmol) were treated with $Pd(dba)_2$ (29 mg, 0.050 mmol), $SbPh_3$ (35 mg, 0.10 mmol), and acetic acid (6.0 mg, 0.10 mmol) in anhydrous benzene (10 mL) at 70 °C for 2 d, the ^{1}H NMR spectrum of the crude product showed traces of starting material and unidentified compounds.

Method D: When PPh_3 was used as a ligand under conditions otherwise identical with those in Method C, 178 mg (63% recovery) of **4** and an unidentified compound were obtained.

Methyl 2,3,4,5,6,7-Hexahydro-3-hydroxy-2,2-dimethyl-4-pivaloxymethyl-1*H*-indene-5-carboxylate (9a) and Methyl 2,3,4,5,6,7-Hexahydro-3-hydroxy-2,2-dimethyl-4-pivaloxymethyl-1*H*-indene-6-carboxylate (9b): As described in GP 1, enyne **6** (252 mg, 1.00 mmol) and methyl acrylate (**7**) (258 mg, 3.00 mmol) in anhydrous benzene (10 mL) were treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol %) and *N*,*N*′-bis(benzylidene)ethylenediamine (24 mg, 0.10 mmol, 10 mol %) at 70 °C for 2 d. The crude product was purified by chromatography on silica gel (18 g, column 2.0 × 15 cm, pentane/Et_2O, 3:1) yielding Fraction I: 179 mg (53%) of **9a**, R_f (pentane/Et_2O, 3:1) = 0.16, as a colorless oil. − IR (film): $\tilde{\nu}$ = 3498 cm^{-1} (OH), 2956, 2905, 2838, 1729 (C=O), 1481, 1464, 1436, 1399, 1364, 1285, 1229, 1161, 1035, 994. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.97 (s, 3 H, 2-CH_3), 1.06 (s, 3 H, 2-CH_3), 1.16 [s, 9 H, $C(CH_3)_3$], 1.90−2.14 (m, 7 H, 1,6,7-H, OH), 2.62−2.69 (m, 1 H, 5-H), 2.75−2.83 (m, 1 H, 4-H), 3.72 (s, 3 H, CO_2CH_3), 4.09 (dd, ^3J = 2.8, ^2J = 11.8 Hz, 1 H, 4-CH_2), 4.12 (br s, 1 H, 3-H), 4.53 (dd, ^3J = 5.5, ^2J = 11.8 Hz, 1 H, 4-CH_2). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 21.4 (−, C-7*), 22.9 (+, 2-CH_3), 25.3 (−, C-6*), 27.1 [+, C(CH_3)$_3$], 28.4 (+, 2-CH_3), 37.5 (+, C-4), 38.7 [C_{quat}, $C(CH_3)_3$], 41.2 (C_{quat}, C-2), 43.3 (+, C-5), 48.6 (−, C-1), 51.7 (+, CO_2CH_3), 64.5 (−, 4-CH_2), 87.1 (+, C-3), 133.0 (C_{quat}, C-3a**), 140.6 (C_{quat}, C-7a**), 174.5 (C_{quat}, CO_2CH_3), 179.0 [C_{quat}, $OCOC(CH_3)$]. − MS (DCI, NH_3), *m*/*z* (%) = 694 (17) [2 M + NH_4^+], 676 (29) [2 M + NH_4^+ − H_2O], 356 (21) [M + NH_4^+], 338 (100) [M + NH_4^+ − H_2O]. − $C_{19}H_{30}O_5$ (338.4): calcd. C 67.43, H 8.93; found C 67.51, H 9.07. − Fraction II: 61 mg (18%) of **9b**, R_f (pentane/Et_2O, 1:1) = 0.35, as a colorless oil. − IR (film): $\tilde{\nu}$ = 3501 cm^{-1} (OH), 2956, 2869, 2842, 1729 (C=O), 1481, 1463, 1437, 1398, 1366, 1286, 1231, 1166, 1075, 1035, 994, 888, 772. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.97 (s, 3 H, 2-CH_3), 1.04 (s, 3 H, 2-CH_3), 1.18 [s, 9 H, $C(CH_3)_3$], 1.50 (m_c, 1 H, 5-H), 1.77−2.64 (m, 9 H, 1,4,5,6,7-H, OH), 3.67 (s, 3 H, CO_2CH_3), 4.01 (br s, 1 H, 3-H), 4.10 (dd, ^3J = 7.1, ^2J = 11.1 Hz, 1 H, 4-CH_2), 4.37 (dd, ^3J = 4.7, ^2J = 11.1 Hz, 1 H, 4-CH_2). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 22.5 (+, 2-CH_3), 27.2 [+, C(CH_3)$_3$], 28.6 (+, 2-CH_3), 30.0 (−, C-7), 30.2 (−, C-5), 36.6 (+, C-4), 38.8 [C_{quat}, $C(CH_3)_3$], 39.7 (C_{quat}, C-2), 41.3 (+, C-6), 48.4 (−, C-1), 51.8 (+, CO_2CH_3), 66.8 (−, 4-CH_2), 85.2 (+, C-3), 134.5 (C_{quat}, C-3a*), 140.5 (C_{quat}, C-7a*), 175.7 (C_{quat}, CO_2CH_3), 178.3 [C_{quat}, $OCOC(CH_3)_3$]. − MS (DCI, NH_3), *m*/*z* (%) = 694 (27) [2 M + NH_4^+], 676 (22) [2 M + NH_4^+ − H_2O], 356 (48) [M + NH_4^+], 338 (100) [M + NH_4^+ − H_2O]. − $C_{19}H_{30}O_5$ (338.4): calcd. C 67.43, H 8.93; found C 67.58, H 9.04.

Method B: Upon treatment of enyne **6** (252 mg, 1.00 mmol) and methyl acrylate (**7**) (258 mg, 3.00 mmol) with $Pd(dba)_2$ (29 mg, 0.050 mmol), PPh_3 (26 mg, 0.10 mmol), and acetic acid (6.0 mg, 0.10 mmol) in anhydrous benzene (10 mL) at 70 °C for 2 d, 58 mg (17%) of **9a** and 24 mg (7%) of **9b** were obtained.

1,3a,4,5,6,7,8,8b-Octahydro-8-hydroxy-7,7-dimethyl-3*H*-indeno[4,5-*c*]furan-3-one (11): As described in GP 1, a mixture of enyne **5** (168 mg, 1.00 mmol) and methyl acrylate (**7**) (258 mg, 3.00 mmol) in anhydrous benzene (10 mL) was treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol %) and *N*,*N*′-bis(benzylidene)ethylenediamine (24 mg, 0.10 mmol, 10 mol %) at 70 °C for 1 d. Column chromatography on silica gel (18 g, column 2.0 × 15 cm, pentane/Et_2O, 1:2) yielded 83 mg (37%) of **11** as colorless crystals, m.p. 87−88 °C, R_f (pentane/Et_2O, 1:2) = 0.25. − IR (KBr): $\tilde{\nu}$ = 3492 cm^{-1} (OH), 2944, 2928, 2841, 1757 (O−C=O), 1482, 1365, 1218, 1163, 1001. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.01 (s, 3 H, CH_3), 1.03 (s, 3 H, CH_3), 1.62 (br s, 1 H, OH), 1.79−2.26 (m, 6 H, 4,5,6-H), 2.73−2.80 (m, 1 H, 8b-H), 3.12 (br s, 1 H, 3a-H), 4.07 (br s, 1 H, 8-H), 4.37 (dd, ^2J = 8.9, ^3J = 6.8 Hz, 1 H, 1-H), 4.54 (dd, ^2J = 8.9, ^3J = 6.8 Hz, 1 H, 1-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 20.7 (−, C-4*), 22.5 (+, CH_3), 23.1 (−, C-5*), 28.4 (+, CH_3), 36.3 (+, C-8b**), 38.9 (+, C-3a**), 41.1 (C_{quat}, C-7), 48.9 (−, C-6*), 71.4 (−, C-1), 86.8 (+, C-8), 131.9 (C_{quat}, C-8a***), 142.0 (C_{quat}, C-5a***), 179.2 (C_{quat}, C-3). − MS (EI, 70 eV), *m*/*z* (%) = 222 (38) [M^+], 207 (51) [M^+ − CH_3], 204 (28) [M^+ − H_2O], 153 (65), 149 (34), 110 (41), 107 (48), 91 (51), 43 (100). − $C_{13}H_{18}O_3$ (222.3): calcd. C 70.25, H 8.16; found C 69.95, H 8.20.

1,4a,5,6,7,8,9,9b-Octahydro-9-hydroxy-8,8-dimethylcyclopenta[*f*]-isochromene-4(2*H*)-one (16): As described in GP 1, enyne **15** (182 mg, 1.00 mmol) was heated with methyl acrylate (**7**) (258 mg, 3.00 mmol), $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol %), and *N*,*N*′-bis(benzylidene)ethylenediamine (24 mg, 0.10 mmol, 10 mol %) in anhydrous benzene (10 mL) at 70 °C for 18 h. Chromatography on silica gel (18 g, column 2.0 × 15 cm, pentane/Et_2O, 1:1) gave 36 mg (15%) of **16** as colorless crystals, m.p. 128−129 °C, R_f (pentane/Et_2O, 1:1) = 0.23. − IR (KBr): $\tilde{\nu}$ = 3513 (OH), 2974, 2956, 2886, 2834, 1707 (O−C=O), 1475, 1361, 1257, 1161, 1057, 1039. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.03 (s, 3 H, CH_3), 1.05 (s, 3 H, CH_3), 1.27 (d, ^3J = 7.4 Hz, 1 H, OH), 1.92−2.28 (m, 8 H, 1,5,6,7-H), 2.64−2.79 (m, 2 H, 4a,9b-H), 4.06 (d, ^3J = 7.4 Hz, 1 H, 9-H), 4.23−4.33 (m, 1 H, 2-H), 4.38−4.46 (m, 1 H, 2-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 22.6 (+, CH_3), 24.3 (−, C-1*), 25.0 (−, C-5*), 26.9 (−, C-6*), 28.4 (+, CH_3), 33.4 (+, C-9b**), 40.6 (+, C-4a**), 41.3 (C_{quat}, C-8), 48.4 (−, C-7*), 69.1 (−, C-2), 87.4 (+, C-9), 134.8 (C_{quat}, C-9a***), 141.3 (C_{quat}, C-6a***), 174.2 (C_{quat}, C-4). − MS (EI, 70 eV), *m*/*z* (%) = 236 (9) [M^+], 218 (45), 203 (100), 175 (19), 145 (33), 131 (28), 91 (36). − $C_{14}H_{20}O_3$ (236.3): calcd. C 71.16, H 8.53; found C 71.07, H 8.37.

Methyl 4′-*tert*-Butyldimethylsilyloxymethyl-5′-chloro-2′,3′,4′,5′,6′,7′hexahydro-3′-hydroxy-2′,2′-dimethylspiro[cyclopropane-1,6′-[1*H*]indene]-5′-carboxylate (18): As described in GP 1, a mixture of enyne **4** (266 mg, 0.942 mmol) and methyl 2-chloro-2-cyclopropylideneacetate (**17**) (161 mg, 1.10 mmol) in anhydrous benzene (10 mL) was treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol %) and *N*,*N*′-bis(benzylidene)ethylenediamine (24 mg, 0.10 mmol, 11 mol %) at 70 °C for 4 d. Column chromatography on silica gel (18 g, column 2.0 × 15 cm, pentane/Et_2O, 4:1) yielded 233 mg (58%) of **18**, R_f (pentane/Et_2O, 4:1) = 0.38, as a colorless oil. − IR (film): $\tilde{\nu}$ = 3467 cm^{-1} (OH), 2953, 2858, 1747 (C=O), 1472, 1363, 1255 ($SiCH_3$), 1094, 1005, 938, 842, 783. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.10 [s, 3 H, $Si(CH_3)_2$], 0.11 [s, 3 H, $Si(CH_3)_2$], 0.23−0.31 (m, 1 H, *c*Pr-H), 0.51−0.59 (m, 1 H, *c*Pr-H), 0.90 [s, 9 H, $SiC(CH_3)_3$], 1.08 (s, 6 H, 2′-CH_3), 1.14−1.21 (m, 1 H, *c*Pr-H), 1.32−1.38 (m, 1 H, *c*Pr-H), 1.84−1.96 (m, 2 H, 7′-H*),

2.14−2.25 (m, 2 H, 1′-H*), 2.96−3.00 (m, 1 H, 4′-H), 3.74 (s, 3 H, CO_2CH_3), 3.85 (dd, ^3J = 3.1, ^2J = 9.8 Hz, 1 H, CH_2OSi), 3.98−4.04 (m, 1 H, CH_2OSi), 4.08 (br s, 1 H, 3′-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = −5.4 [+, $Si(CH_3)_2$], −5.3 [+, $Si(CH_3)_2$], 10.3 (−, *c*Pr-C), 14.2 (−, *c*Pr-C), 18.2 [C_{quat}, $SiC(CH_3)_3$], 22.4 (C_{quat}, C-6′), 22.8 (+, 2′-CH_3), 25.8 [+, $SiC(CH_3)_3$], 28.3 (+, 2′-CH_3), 37.8 (−, C-7′), 42.1 (C_{quat}, C-2′), 47.8 (−, C-1′), 51.7 (+, C-4′), 52.6 (+, CO_2CH_3), 64.6 (−, CH_2OSi), 73.4 (C_{quat}, C-5′), 85.3 (+, C-3′), 135.8 (C_{quat}, C-3a′*), 137.8 (C_{quat}, C-7a′*), 168.9 (C_{quat}, CO_2CH_3). − MS (EI, 70 eV), *m*/*z* (%) = 430/428 (2/4) [M^+], 373/371 (5/13) [$M^+ - C_4H_9$], 335 (13) [$M^+ - C_4H_9 - HCl$], 281/279 (9/24) [$M^+ - H_2O - OSi(CH_3)_2C(CH_3)_3$], 249/247 (7/24) [$M^+ - H_2O - OSi(CH_3)_2C(CH_3)_3 - MeOH$], 243 (35) [$M^+ - H_2O - OSi(CH_3)_2C(CH_3)_3 - HCl$], 231 (100), 199 (22), 183 (17), 143 (14), 105 (22), 81 (29), 75 (56), 73 (65), 41 (25). − $C_{22}H_{37}ClO_4Si$ (429.1): calcd. C 61.58, H 8.69; found C 61.42, H 8.46.

Methyl 5′-Chloro-2′,3′,4′,5′,6′,7′-hexahydro-3′-hydroxy-2′,2′-dimethyl-4′-pivaloxymethylspiro[cyclopropane-1,6′-[1*H*]indene]-5′-carboxylate (19): As described in GP 1, a mixture of enyne **6** (252 mg, 1.00 mmol) and methyl 2-chloro-2-cyclopropylideneacetate (**17**) (200 mg, 1.40 mmol) in anhydrous benzene (10 mL) was treated with $Pd(OAc)_2$ (11 mg, 0.050 mmol, 5 mol %) and *N*,*N*′-bis(benzylidene)ethylenediamine (24 mg, 0.10 mmol, 10 mol %) at 70 °C for 2 d. Column chromatography on silica gel (18 g, column 2.0 × 15 cm, pentane/Et_2O, 1:1) yielded 222 mg (56%) of **19** as colorless crystals, m.p. 100−102 °C, R_f (pentane/Et_2O, 1:1) = 0.27. − IR (KBr): $\tilde{\nu}$ = 3494 cm^{-1} (OH), 2978, 2957, 2916, 1742 (C=O), 1720, 1483, 1462, 1415, 1399, 1364, 1296, 1248, 1173, 1093, 1062, 1036. − ^1H NMR (250 MHz, $CDCl_3$): δ = 0.29−0.37 (m, 1 H, *c*Pr-H), 0.48−0.56 (m, 1 H, *c*Pr-H), 0.99 (s, 3 H, 2′-CH_3), 1.01−1.08 (m, 1 H, *c*Pr-H), 1.09 (s, 3 H, 2′-CH_3), 1.21 [s, 9 H, $C(CH_3)_3$], 1.28−1.36 (m, 1 H, *c*Pr-H), 1.67−1.81 (m, 3 H, 7′-H*, OH), 2.20−2.40 (m, 2 H, 1′-H*), 3.04 (br s, 1 H, 4′-H), 3.75 (s, 3 H, CO_2CH_3), 4.10 (br s, 1 H, 3′-H), 4.63−4.78 (m, 2 H, 4′-CH_2). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.2 (−, *c*Pr-C), 11.4 (−, *c*Pr-C), 22.5 (+, 2′-CH_3), 23.6 (C_{quat}, C-6′), 27.2 [+, $C(CH_3)_3$], 28.5 (+, 2′-CH_3), 36.9 (−, C-7′), 38.6 [C_{quat}, $C(CH_3)_3$], 41.8 (C_{quat}, C-2′), 47.3 (−, C-1′), 48.2 (+, C-4′), 53.0 (+, CO_2CH_3), 64.0 (−, 4′-CH_2), 73.6 (C_{quat}, C-5′), 85.2 (+, C-3′), 135.0 (C_{quat}, C-3a′*), 140.2 (C_{quat}, C-7a′*), 169.7 (C_{quat}, CO_2CH_3), 178.2 [C_{quat}, O*C*-$OC(CH_3)_3$]. − MS (EI, 70 eV), *m*/*z* (%) = 345 (4) [$M^+ - Cl - H_2O$], 278 (6) [$M^+ - COC_4H_9 - Cl$], 261 (100) [$M^+ - COC_4H_9 - Cl - OH$], 243 (34), 227 (14), 183 (6), 91 (6), 57 (23) [$C_4H_9^+$], 41 (7). − MS (DCI, NH_3), *m*/*z* (%) = 818/816/814 (2/9/13) [2 M + NH_4^+], 800/798/796 (2/10/13) [2 M + $NH_4^+ - H_2O$], 418/416 (13/34) [M + NH_4^+], 400/398 (35/100) [M + $NH_4^+ - H_2O$]. − $C_{21}H_{31}ClO_5$ (398.9): calcd. C 63.23, H 7.83; found C 63.33, H 7.94.

Methyl 2,3,4,5,6,7-Hexahydro-2-tosyl-1*H*-isoindole-5-carboxylate (24): As described in GP 1, enyne **22** (249 mg, 1.00 mmol) was heated with methyl acrylate (**7**) (258 mg, 3.00 mmol), $Pd(dba)_2$ (29 mg, 0.050 mmol, 5 mol %), PPh_3 (26 mg, 0.10 mmol, 10 mol %), and acetic acid (6.0 mg, 0.10 mmol, 10 mol %) in anhydrous benzene (10 mL) at 80 °C for 1 d. Chromatography on silica gel (18 g, column 2.0 × 15 cm, CH_2Cl_2) gave 202 mg (60%) of **24** as colorless crystals, m.p. 86−88 °C, R_f (CH_2Cl_2) = 0.18. − IR (KBr): $\tilde{\nu}$ = 2951 cm^{-1}, 2845, 1731 (C=O), 1598, 1493, 1438, 1343, 1165, 1102, 816, 720, 664, 594. − ^1H NMR (250 MHz, $CDCl_3$): δ = 1.61−1.73 (m, 2 H, 7-H), 2.02−2.06 (m, 3 H, 5,6-H), 2.15 (d, ^3J = 7.7 Hz, 2 H, 4-H), 2.42 (s, 3 H, CH_3), 3.66 (s, 3 H, CO_2CH_3), 3.98 (m_c, 4 H, 1,3-H), 7.33 (d, ^3J = 8.4 Hz, 2 H, Ph-H), 7.71 (d, ^3J = 8.4 Hz, 2 H, Ph-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 21.5 (+, CH_3), 22.1 (−, C-7*), 24.8 (−, C-6*), 25.2 (−, C-4*), 39.0 (+, C-5), 51.8 (+, CO_2CH_3), 56.8 (−, C-1,3), 127.4 (+, Ph-C), 128.4 (C_{quat}, C-3a**), 129.6 (C_{quat}, C-7a**), 129.7 (+, Ph-C), 134.3 (C_{quat}, Ph-C), 143.3 (C_{quat}, Ph-C), 175.3 (C_{quat}, CO_2CH_3). − MS (EI, 70 eV), *m*/*z* (%) = 335 (33) [M^+], 274 (10), 249 (48), 180 (51) [M^+ − tosyl], 155 (34) [tosyl$^+$], 120 (90), 94 (81), 91 (100) [$C_7H_7^+$], 65 (18). − $C_{17}H_{21}NO_4S$ (335.4): calcd. C 60.87, H 6.31, N 4.18; found C 60.56, H 6.29, N 4.04.

1,2,3,3a,4,5,6,7,8,8b-Decahydro-2,7-ditosylpyrrolo[3,4-*e*]isoindole (34): A round-bottomed flask with reflux condenser was charged with *N*,*N*′-diallyl-*N*,*N*′-ditosylbut-2-yne-1,4-diamine (**27**) (0.473 g, 1.00 mmol), [bis(benzylidene)acetone]palladium (0.026 g, 0.045 mmol), PPh_3 (0.026 g, 0.099 mmol), and benzene (4 mL). After the mixture had been degassed and put under nitrogen, acetic acid (0.012 g, 0.2 mmol) was added. The mixture was heated under reflux for 2 h and then concentrated in vacuo to 1 mL. This residue was purified by column chromatography (1.5 × 13 cm, 15 g of silica gel, CH_2Cl_2, R_f = 0.12), yielding 0.426 g (90%) of **34** as a colorless solid, decomp. 180 °C. − IR (KBr): $\tilde{\nu}$ = 2940 cm^{-1} (CH_2), 2845, 1596 (C=C), 1476, 1335, 1159, 1101, 1049, 817, 667, 600, 549. − ^1H NMR (250 MHz, $CDCl_3$): δ = 1.22−1.37, 1.52−1.61, 1.69−1.82, 1.95−2.02 and 2.22−2.34 (5 m, 5 H, CH_2 and CH), 2.43 (br s, 7 H, 2 CH_3 and CH), 2.72−3.05 (m, 2 H, 1-H*), 3.33−3.60 (m, 2 H, 3-H*), 3.80−3.91 (m, 4 H, 6-H, 8-H), 7.33 (d, ^3J = 8.1 Hz, 4 H, Ph-H), 7.65−7.68 (2 d, ^3J = 8.1 Hz, 4 H, Ph-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 20.7 (−, CH_2), 21.5 (+, CH_3), 23.1, 23.5 and 23.6 (−, CH_2), 36.3, 36.4, 41.0 and 42.8 (+, CH), 49.9, 50.5, 51.2 and 51.6 (−, NCH_2), 54.7, 55.6, 56.4 and 56.7 (−, NCH_2), 127.2, 127.25, 127.29 and 127.4 (+, Ph-C), 128.4 and 128.6 (C_{quat}, C=C), 129.7, 129.75 and 129.79 (+, Ph-C), 131.9 and 132.1 (C_{quat}, C=C), 133.4, 134.5, 143.5 and 143.7 (C_{quat}, Ph-C). Because of the presence of two isomers (*cis* and *trans*) most of the signals appear twice. − MS (EI, 70 eV), *m*/*z* (%) = 472 (4) [M^+], 317 (100) [M^+ − tosyl], 155 (19) [tosyl$^+$], 146 (39), 91 (38) [$C_7H_7^+$]. − $C_{24}H_{28}N_2O_4S_2$ (472.6): calcd. C 61.00, H 5.98, N 5.93; found C 60.72, H 6.01, N 6.14. − The crystallization of **34** to separate the *cis* and *trans* isomers was induced by dissolving the solid in CH_2Cl_2, adding pentane and cooling to −20 °C in a freezer. The *cis*/*trans* ratio was checked by NMR measurements. The *cis*/*trans* ratio in the obtained mixture was 1.8 to 1.

2,7-Di-*tert*-butyl 1,2,3,3a,4,5,6,7,8,8b-Decahydropyrrolo[3,4-*e*]isoindole-2,7-dicarbamate (35): A round-bottomed flask with reflux condenser was charged with **30** (0.364 g, 1.00 mmol), PPh_3 (0.026 g, 0.099 mmol), $Pd_2(dba)_3{\cdot}CHCl_3$ (0.026 g, 0.025 mmol), acetic acid (0.066 g, 1.1 mmol), and 5 mL of benzene under N_2, and the mixture was heated at 80 °C for 88 h. CH_2Cl_2 (15 mL) was added, and the mixture was extracted with 10 mL of $NaHCO_3$ solution and dried with $MgSO_4$, and the solvents were evaporated in vacuo. The remaining solid was purified by column chromatography [1.5 × 13 cm, 15 g of flash silica gel, pentane/CH_2Cl_2/Et_2O, 1:3:0 to 0:1:1, R_f = 0.03 (CH_2Cl_2)], yielding 0.150 g (41%) of **35** as a colorless oil. − IR (film): $\tilde{\nu}$ = 2975 cm^{-1}, 2931 (CH_2), 2879, 1700 (C=O), 1478, 1456, 1404, 1366, 1255, 1170, 1123, 882, 772, 736. − ^1H NMR [300 MHz, $C_2D_2Cl_4$, 100 °C, δ($C_2H_2Cl_4$) = 5.98]: δ = 1.25−1.87 (m, 20 H, CH_2 and CH_3), 2.00−2.45 (m, 3.5 H, CH and CH_2), 2.64−2.71 (m, 0.5 H, CH*), 2.88−3.25 (m, 2 H, NCH_2), 3.43−3.62 (m, 2 H, NCH_2), 3.90−4.17 (m, 4 H, NCH_2). − ^{13}C NMR [75.5 MHz, $C_2D_2Cl_4$ (δ = 73.6), 100 °C, APT]: δ = 20.8, 23.5, 23.7 and 23.8 (−, CH_2), 28.2 (+, CH_3), 36.1, 36.2, 41.1 and 42.7 (+, CH), 48.0, 48.8, 49.4, 49.8, 52.9, 54.1, 54.8 and 55.2 (−, NCH_2), 78.59, 78.61, 78.69 and 78.72 [−, $C(CH_3)_3$], 129.5, 129.7, 131.3 and 131.5 (−, C=C), 153.7, 154.1 and 154.2 (−, C=O). Because two isomers (*cis* and *trans*) were present, most of the signals

appear twice. The *cis*/*trans* ratio was 1:1. − MS (EI, 70 eV), *m*/*z* (%) = 364 (4) [M^+], 307 (41) [$M^+ - C_4H_9$], 251 (56) [$M^+ - C_4H_9 - C_4H_8$], 207 (50) [M+ − BOC − C_4H_8], 57 (100) [$C_4H_9^+$]. − $C_{20}H_{32}N_2O_4$ (364.5), calcd. C 65.91, H 8.85, N 7.69; found C 66.16, H 8.86, N 7.81.

3,3a,4,5,6,8,8b-Octahydro-1*H*-furo[3,4-*d*]isobenzofuran (37): A round-bottomed flask with reflux condenser was charged with 1,4-bis(allyloxy)but-2-yne (**36**) (0.170 g, 1.02 mmol), $Pd(dba)_2$ (0.024 g, 0.042 mmol), PPh_3 (0.024 g, 0.09 mmol), acetic acid (0.006 g, 0.1 mmol), and 3 mL of benzene under nitrogen, and the mixture was heated for 20 h at 80 °C. The mixture was concentrated to 0.5 mL and the residue purified by column chromatography (1.5 × 13 cm, 15 g of silica gel, CH_2Cl_2, R_f = 0.06), yielding 0.136 g (80%) of **37** as a colorless oil. − IR (film): $\tilde{\nu}$ = 2928 cm^{-1} (CH_2), 2855, 1755, 1479, 1437, 1360, 1304, 1086 (C−O), 1044, 905, 885, 805, 738. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.60−1.93 (m, 2 H, CH_2), 2.01−2.11 (m, 2 H, CH_2), 2.45−2.61 (m, 1 H, CH), 2.68−2.74 (m, 1 H, CH), 3.35−3.69 (m, 2 H, 1-H*), 3.89−4.15 (m, 2 H, 3-H*), 4.54 (br s, 4 H, 6-H and 8-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.5, 22.8, 23.0 and 23.7 (−, CH_2), 36.6, 37.3, 42.0 and 44.6 (+, CH), 69.1, 70.7, 70.9, 71.8, 75.4, 76.6, 76.9 and 77.4 (−, OCH_2), 130.0 and 132.3 (C_{quat}, C=C). − MS (EI, 70 eV), *m*/*z* (%) = 166 (88) [M^+], 164 (58), 119 (42), 107 (62), 105 (54), 91 (100), 79 (56). − $C_{10}H_{14}O_2$ (166.2): calcd. 166.0993; found 166.0993. − The *cis*/*trans* ratio of the isolated mixture was 3.4:1, as determined by NMR measurements.

***N*-Allyl-*N*-benzyl-*N*-[2-(1-benzyl-4-methyl-1*H*-pyrrol-3-yl)ethyl]-amine (41):** *N*,*N*′-Diallyl-*N*,*N*′-dibenzylbut-2-yne-1,4-diamine (**26**) (0.298 g, 0.865 mmol), $Pd(OAc)_2$ (0.010 g, 0.045 mmol), BBEDA (0.022 g, 0.093 mmol), and 4 mL of benzene were heated under N_2 in a Pyrex flask at 80 °C for 120 h. Alumina was added to the reaction mixture and the solvent was evaporated. This mixture was put on top of a column and purified (20 g of alumina grade II, pentane/CH_2Cl_2, 1:2, R_f = 0.25), yielding 0.053 g (18%) of **41** as a colorless oil. − IR (film): $\tilde{\nu}$ = 3027 cm^{-1}, 2921 (CH_2), 2797, 1532 (C=C), 1495, 1453, 1397, 1370, 1154, 1028, 918, 773, 736, 699. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 2.04 (s, 3 H, CH_3), 2.63−2.77 (m, 4 H, CH_2), 3.23 (d, ^3J = 5.3 Hz, 2 H, CH_2), 3.72 (s, 2 H, CH_2), 4.97 (s, 2 H, CH_2), 5.18−5.32 (m, 2 H, CH=CH_2), 5.91−6.07 (m, 1 H, C*H*=CH_2), 6.45 (s, 2 H, 2-H and 5-H), 7.16−7.44 (m, 10 H, Ph-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 10.1 (+, CH_3), 23.0 (−, CH_2), 53.0 (−, NCH_2), 54.4 (−, NCH_2), 56.8 (−, NCH_2), 58.0 (−, NCH_2), 117.1 (−, CH=*C*H_2), 117.8 (C_{quat}, C-3*), 118.7 (+, C-2**), 118.9 (+, C-5**), 121.1 (C_{quat}, C-4*), 126.7 (+, Ph-C), 127.0 (+, Ph-C), 127.4 (+, Ph-C), 128.1 (+, Ph-C), 128.6 (+, Ph-C), 128.8 (+, Ph-C), 136.1 (+, *C*H=CH_2), 138.4 (C_{quat}, Ph-C), 139.7 (C_{quat}, Ph-C). − MS (EI, 70 eV), *m*/*z* (%) = 344 (7) [M^+], 253 (13) [M^+ − benzyl], 160 (100), 91 (75) [$C_7H_7^+$]. − $C_{24}H_{28}N_2$ (344.5): calcd. 344.2252; found 344.2252.

3,3a,4,5,6,5,6,7,8,8b-Octahydro-7-tosyl-1*H*-furo[3,4-*e*]isoindole (49) and 3,4,5,5a,6,7,8,8a-Octahydro-7-tosyl-1*H*-furo[3,4-*e*]isoindole (50): A round-bottomed flask with reflux condenser was charged with *N*-allyl-4-(allyloxy)-*N*-tosylbut-2-yne-1-ylamine (**44**) (0.190 g, 0.595 mmol), $Pd(dba)_2$ (0.019 g, 0.034 mmol), PPh_3 (0.020 mg, 0.076 mmol), and 3 mL of MeCN, and the mixture was heated at 80 °C for 16 h. The solvent was evaporated, and the remaining solid was purified by column chromatography [1.5 × 13 cm, 15 g of silica gel, pentane/CH_2Cl_2, 4:1 to 0:1, R_f = 0.06 (CH_2Cl_2)], yielding 0.130 g (68%) of a colorless solid, a mixture of the two products **49** and **50** in a ratio of 7:3. The *cis*/*trans* ratio of **49** was 2.6:1, the *cis*/*trans* ratio of **50** was 4.4:1. − Analysis of the mixture: ^{1}H NMR (250 MHz, $CDCl_3$): δ = 1.15−1.69 (m, 2 H, CH_2), 1.85−2.11 (m, 2.6 H, CH and CH_2), 2.37 (br s, 3.7 H, CH_3 and CH), 2.54−2.60 (m, 0.7 H, CH), 2.76−3.07 (m, 1.3 H, CH_2), 3.29−3.61 (m, 2.0 H, CH_2), 3.78−3.94 (m, 2.3 H, CH_2), 4.29−4.46 (m, 2.4 H, CH_2), 7.36 (d, ^3J = 8.2 Hz, 2 H, Ph-H), 7.63−7.68 (m, 2 H, Ph-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 19.3 and 21.3 (−, CH_2), 21.3 (+, CH_3), 22.2, 23.3 and 23.6 (−, CH_2), 35.4, 36.5, 36.8, 37.4, 40.4, 42.3, 43.1 and 44.1 (+, CH), 50.1, 50.6, 51.1, 51.5, 53.4, 54.9, 56.0, 56.3, 56.8, 68.7, 70.5, 71.8, 74.9, 76.0, 76.8 and 77.1 (−, CH_2), 127.0, 127.2, 128.4 and 128.6 (+, Ph-C), 129.0, 129.3, 131.2, 132.7, 133.1, 133.3, 133.7, 133.9 (C_{quat}, C=C), 134.0, 134.4, 143.25, 143.31 (C_{quat}, Ph-C). − MS (EI, 70 eV), *m*/*z* (%) = 319 (11) [M^+], 164 (100) [M^+ − tosyl], 155 (13) [tosyl$^+$], 91 (60) [$C_7H_7^+$]. − $C_{17}H_{21}NO_3S$ (319.4): calcd. 319.1242; found 319.1242.

1,3,3a,4,5,6,8,8b-Octahydro-2-propyl-7-tosyl-2*H*,7*H*-isoindoyl-[4,5-*d*]isothiazole 3,3-Dioxide (51) and 1,3,4,5,5a,6,8,8a-Octahydro-2-propyl-7-tosyl-2*H*,7*H*-isoindoyl[4,5-*d*]isothiazole 3,3-Dioxide (52): A mixture of *N*-allyl-*N*′-propyl-*N*-tosyl-*N*′-(vinylsulfonyl)but-2-yne-1,4-diamine (**48**) (0.365 g, 0.889 mmol), $Pd(dba)_2$ (0.029 g, 0.053 mmol), PPh_3 (0.031 g, 0.12 mmol), acetic acid (0.012 g, 0.20 mmol), and 5 mL of benzene was heated at 80 °C for 100 h in a Pyrex flask. The mixture was concentrated to a volume of approx. 0.5 mL. The residue was purified by column chromatography [1.5 × 13 cm, 15 g of flash silica gel, pentane/CH_2Cl_2/Et_2O, 1:2:0 to 0:10:1, R_f = 0.12 (CH_2Cl_2)], yielding 0.130 g (ca. 36%) of a colorless oil. This contained the two products **51** and **52** in ratio 1:1, but also 10% of an unknown product. − Analysis of the mixture: IR (film): $\tilde{\nu}$ = 2964 cm^{-1}, 2933 (CH_2), 2874, 1598 (C=C), 1457, 1343, 1290, 1164, 1092, 1040, 817, 736, 667, 592, 549. − ^{1}H NMR (250 MHz, $CDCl_3$): δ = 0.83−0.96 (m, 6 H, CH_3), 1.15−1.33 (m, 1 H, CH_2), 1.39−2.01 (m, 7 H, CH_2), 2.08−2.23 (m, 2 H, CH_2), 2.30−2.47 (m, 8 H, CH_3, CH_2, CH), 2.72−3.16 (m, 10 H, NCH_2, CH), 3.22−3.33 (m, 2 H, NCH_2, CH), 3.41−3.83 (m, 4 H, NCH_2), 3.93−4.14 (m, 4 H, NCH_2), 7.30 (d, ^3J = 8.3 Hz, 4 H, Ph-H), 7.69 (d, ^3J = 8.3 Hz, 4 H, Ph-H). − ^{13}C NMR (62.9 MHz, $CDCl_3$, DEPT): δ = 11.1 and 11.2 (+, CH_3), 17.3, 20.5, 20.7, 21.0, 21.3 (−, CH_2), 21.38, 21.46 (+, CH_3), 22.9 (−, CH_2), 30.4, 35.8, 37.6 (+, CH), 45.9, 46.2, 49.3, 49.8, 51.6 and 52.6 (−, NCH_2), 54.8 (+, CH), 54.9, 56.7 (−, NCH_2), 127.1, 127.4 (C_{quat}, C=C), 127.3, 129.7, 129.8, 129.9 (+, Ph-C), 132.4, 133.4 (C_{quat}, C=C), 138.7, 139.0, 143.7, 143.9 (C_{quat}, Ph-C). − MS (EI, 70 eV), *m*/*z* (%) = 410 (4) [M^+], 381 (18) [$M^+ - C_2H_5$], 346 (30) [$M^+ - SO_2$], 255 (90) [M^+ − tosyl], 191 (100) [M^+ − tosyl − SO_2], 91 (47) [$C_7H_7^+$]. − $C_{19}H_{26}N_2O_4S_2$ (410.6): calcd. 410.1334; found 410.1334.

Acknowledgments

This work was supported by the TMR Marie Curie Research Training Grants Program of the European Union, the Graduiertenkolleg "Kinetik und Selektivität chemischer Prozesse in verdichteter fluider Phase" and the Fonds der Chemischen Industrie. We are indebted to the companies BASF AG, Bayer AG, Chemetall GmbH, and Degussa-Hüls AG for generous gifts of chemicals, to Professor Dr. Peter Metz, Dresden, for helpful discussions, and to Dr. Burkhard Knieriem for his careful proofreading of the final manuscript.

[1] [1a] B. M. Trost, *Acc. Chem. Res.* **1990**, *23*, 34−42. − [1b] B. M. Trost, M. J. Krische, *Synlett* **1998**, 1−16. − [1c] B. M. Trost, Y. Li, *J. Am. Chem. Soc.* **1996**, *118*, 6625−6633. − [1d] B. M. Trost, *Angew. Chem.* **1995**, *107*, 285−307; *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 259−281. − [1e] B. M. Trost, D. L. Romero, F. Rise, *J. Am. Chem. Soc.* **1994**, *116*, 4268−4278. − [1f] B. M. Trost, G. J. Tanoury, M. Lautens, C. Chan, D. T. MacPherson,

J. Am. Chem. Soc. **1994**, *116*, 4255−4267. − [1g] B. M. Trost, Y. Shi, *J. Am. Chem. Soc.* **1991**, *113*, 701−703. − [1h] B. M. Trost, Y. Shi, *J. Am. Chem. Soc.* **1993**, *115*, 9421−9438. − [1i] B. M. Trost, *Acc. Chem. Res.* **1990**, *23*, 34−42. − [1j] B. M. Trost, P. A. Hipskind, J. Y. L. Chung, C. Chan, *Angew. Chem.* **1989**, *101*, 1559−1561; *Angew. Chem. Int. Ed. Engl.* **1989**, *28*, 1502−1504. − [1k] B. M. Trost, S.-F. Chen, *J. Am. Chem. Soc.* **1986**, *108*, 6053−6054. − [1l] B. M. Trost, M. Lautens, *J. Am. Chem. Soc.* **1985**, *107*, 1781−1783.

[2] S. Bräse, A. de Meijere, in: *Metal-catalyzed Cross-coupling Reactions* (Eds.: F. Diederich, P. J. Stang), Wiley-VCH, Weinheim, **1998**, pp. 99−166.

[3] [3a] A. de Meijere, F. E. Meyer, *Angew. Chem.* **1994**, *106*, 2473−2506; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 2379−2411. − [3b] A. de Meijere, S. Bräse, *J. Organomet. Chem.* **1999**, *576*, 88−110.

[4] [4a] B. M. Trost, F. J. Fleitz, W. J. Watkins, *J. Am. Chem. Soc.* **1996**, *118*, 5146−5147. − [4b] M. J. Krische, B. M. Trost, *Tetrahedron* **1998**, *54*, 3693−3704. − [4c] B. M. Trost, M. J. Krische, *J. Am. Chem. Soc.* **1999**, *121*, 6131−6141.

[5] F. E. Meyer, H. Henniges, A. de Meijere, *Tetrahedron Lett.* **1992**, *33*, 8039−8042.

[6] K. H. Ang, S. Bräse, A. G. Steinig, F. E. Meyer, A. Llebaria, K. Voigt, A. de Meijere, *Tetrahedron* **1996**, *52*, 11503−11528.

[7] Bis(exocyclic) 1,3-dienes can also be formed by cyclization of acetylenic vinyllithium compounds, generated from the corresponding acetylenic vinyl bromides by lithium−bromine exchange; cf.: W. F. Bailey, N. M. Wachter-Jurcsak, M. R. Pineau, T. V. Ovaska, R. R. Warren, C. E. Lewis, *J. Org. Chem.* **1996**, *61*, 8216−8228.

[8] [8a] H. Primke, G. S. Sarin, S. Kohlstruk, G. Adiwidjaja, A. de Meijere, *Chem. Ber.* **1994**, *127*, 1051−1064. − [8b] For a review see: A. de Meijere, S. I. Kozhushkov, L. P. Hadjiarapoglou, *Top. Curr. Chem.* **1999**, *207*, 149−227.

[9] BBEDA is known to be an efficient ligand for the cycloisomerization of enynes substituted at the acetylenic terminus; cf. ref.[1j]

[10] The ^{13}C NMR spectra of both regioisomers each showed only one set of peaks, the relative configuration was proven by COSY-NMR measurements.

[11] According to ref.[1h], $SbPh_3$ gave better yields than PPh_3 or $P(o\text{Tol})_3$ when terminally substituted enynes were cycloisomerized.

[12] NOESY-NMR measurements revealed a *cis*-lactone ring juncture.

[13] R. Imwinkelried, M. Schiess, D. Seebach, *Org. Synth.* **1987**, *65*, 230−232.

[14] Cf. W. R. Roush, in: *Comprehensive Organic Synthesis* (Eds.: B. M. Trost, I. Fleming), vol. 5, Pergamon Press, Oxford, **1991**, pp. 513−550.

[15] In spite of such a conformation being preferred (cf.: P. Deslongchamps, *Stereoelectronic Effects in Organic Chemistry*, Pergamon Press, Oxford, **1983**, p. 54), such systems have been shown to undergo intramolecular Diels−Alder reactions readily; cf.: M. E. Jung, J. Gervay, *J. Am. Chem. Soc.* **1991**, *113*, 224−232.

[16] Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-151406. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

[17] D. Solé, Y. Cancho, A. Llebaria, J. M. Moretó, A. Delgado, *J. Org. Chem.* **1996**, *61*, 5895−5904.

[18] [18a] Y.-T. Lin, K. N. Houk, *Tetrahedron Lett.* **1985**, *26*, 2269−2272. − [18b] M. K. Diedrich, D. Hochstrate, F.-G. Klärner, B. Zimny, *Angew. Chem.* **1994**, *106*, 1135−1137; *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1079−1081.

[19] B. Plietker, D. Seng, R. Fröhlich, P. Metz, *Tetrahedron* **2000**, *56*, 873−879.

[20] F. Barbot, B. Dauphin, P. Miginiac, *Synthesis* **1985**, 768−770.

[21] *cis*/*trans* ratios according to relative ^{13}C NMR signal intensities.

[22] M. W. Logue, K. Teng, *J. Org. Chem.* **1982**, *47*, 2549−2553.

[23] T. Cuvigny, H. Normant, *Bull. Soc. Chim. Fr.* **1970**, 3976−3980.

[24] A. J. Hubert, A. Feron, G. Goebbels, R. Warin, P. Teyssié, *J. Chem. Soc., Perkin Trans. 2* **1977**, 11−14.

[25] R. A. Mitsch, N. H. Cromwell, *J. Org. Chem.* **1960**, *25*, 1719−1722.

[26] L. Brandsma, *Preparative Acetylenic Chemistry*, 2nd ed., Elsevier, Amsterdam, **1988**, pp. 275−276.

[27] M. M. Fraser, R. A. Raphael, *J. Chem. Soc.* **1952**, 226−228.

[28] A. G. M. Barrett, S. P. D. Baugh, D. C. Braddock, K. Flack, V. C. Gibson, M. R. Giles, E. L. Marshall, P. A. Procopiou, A. J. P. White, D. J. Williams, *J. Org. Chem.* **1998**, *63*, 7893−7907.

Received November 23, 2000
[O00602]