Cascade Radical Cyclizations via Biradicals Generated from (*Z*)-1,2,4-Heptatrien-6-ynes

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Abstract: On heating in refluxing benzene, acyclic enyne−allene **4** underwent intramolecular transformations in a sequence with an initial Myers cycloaromatization to form α,3-didehydrotoluene biradical **5** followed by a 5-*exo* cyclization of the benzenoid radical center in **5** to produce **6**. Biradical **6** then decayed through a 1,5-hydrogen shift to furnish *o*-quinodimethane **7**, which in turn was captured in an intramolecular Diels−Alder reaction to afford **8** having the tetracyclic steroidal skeleton in a single step from **4** in 50% isolated yield. Similarly, acyclic enyne−allene **16** having one of the tethers shortened by one carbon atom furnished **18** having the fused 5,6,6,5-ring system. Tetracycle **19** substituted with an angular methyl group was obtained from **17**. In the cases of **24** and **34**, a predominant 1,5-hydrogen shift of an allylic hydrogen to the benzenoid radical center of biradicals **26** and **35** followed by a homolytic coupling produced spiro derivatives **31** and **40**, respectively. On the other hand, a preferential 7-*endo* ring closure of biradicals **41** and **49**, derived from **25** and **48**, gave predominantly the tricyclic derivatives **46** and **54**, respectively. Similarly, cascade radical cyclizations via biradicals generated from enyne−allenes **67**−**70** produced the bicyclic spiro compounds **77**−**80** having a four-membered ring.

Introduction

Free radical reactions have many unique features, and their synthetic applications are rapidly expanding.[1] It is intriguing to imagine the various possibilities of having two radical centers in the same molecule simultaneously to induce synergistic and cooperative effects between them and thereby create new chemical transformations. Of the few reported methods for generating biradicals suitable for subsequent synthetic elaborations,[2−6] the Myers cycloaromatization reaction of (*Z*)-1,2,4-heptatrien-6-ynes (enyne−allenes) to α,3-didehydrotoluene biradicals is particularly attractive because the reaction occurs under mild thermal conditions[2] and various synthetic routes to enyne−allenes with diverse chemical structures are becoming available.[2,7]

We recently reported a new method for synthesis of enyne−allene **4** having two additional carbon−carbon double bonds attached to the enyne−allene system by the synthetic sequence outlined in Scheme 1.[7b] Lithiation of 5-(trimethylsilyl)-1,5,6-octatriene with *tert*-butyllithium followed by *B*-methoxy-9-borabicyclo[3.3.1]nonane (*B*-MeO-9-BBN) and $^4/_3$ BF_3·OEt_2 produced γ-(trimethylsilyl)allenylborane **1**. Condensation of **1** generated in situ with the conjugated allenic aldehyde **2** proceeded smoothly and furnished, after treatment with 2-aminoethanol, the condensation adduct **3**. The subsequent H_2SO_4-induced Peterson elimination produced **4** having predominantly the *Z* geometry (*Z*:*E* = 96:4). On heating in refluxing benzene, acyclic enyne−allene **4** underwent intramolecular transformations in a sequence with an initial Myers cycloaromatization to form α,3-didehydrotoluene biradical **5** followed by a 5-*exo* cyclization of the benzenoid radical center in **5** to produce **6**.

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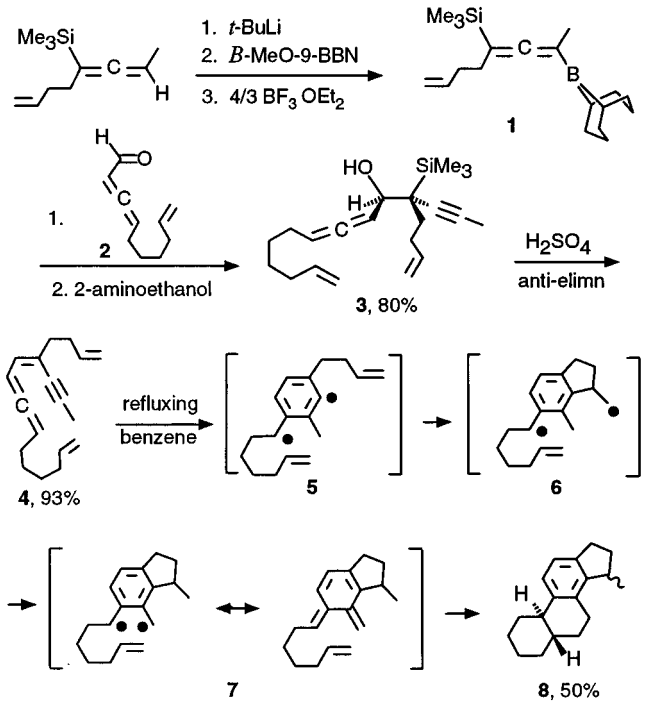
Scheme 1

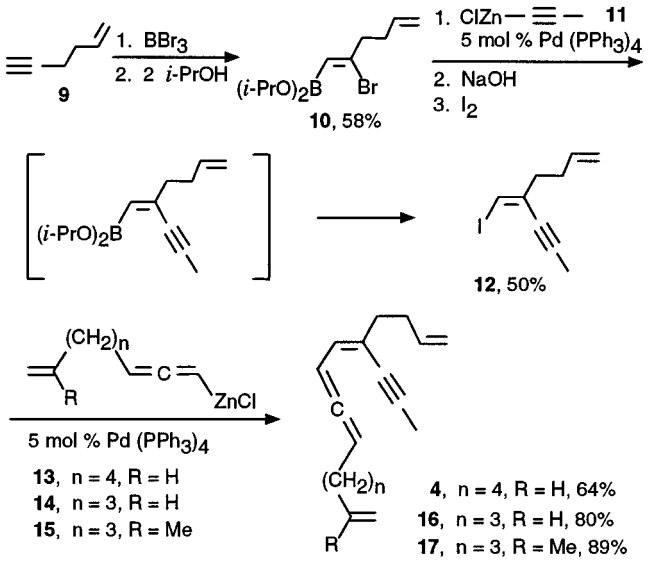


Biradical **6** then decayed through a 1,5-hydrogen shift to furnish *o*-quinodimethane **7**, which in turn was captured in an intramolecular Diels−Alder reaction to afford **8** having the tetracyclic steroidal skeleton in a single step from **4** in 50% isolated yield.[7b] We now have extended this synthetic pathway to other carbocyclic structures by varying the length of the tethers connecting the two additional carbon−carbon double bonds to the enyne−allene system. The use of simple alkyl side chains attached to the enyne−allene system for cascade radical cyclizations was also investigated.

Results and Discussion

In addition to the method described in Scheme 1 for synthesis of acyclic enyne−allenes, we also reported an alternative procedure involving bromoboration of a terminal alkyne with BBr_3 followed by two consecutive $Pd(PPh_3)_4$-catalyzed cross-coupling reactions with organozinc chlorides derived from terminal alkynes and allenes.[7c] We elected to use this highly convergent synthetic method at the outset to prepare acyclic enyne−allenes **4**, **16**, and **17** for the cascade radical cyclizations (Scheme 2). Enyne−allene **4** was again synthesized by this new procedure in order to determine whether this synthetic method will tolerate the presence of additional carbon−carbon double bonds. Treatment of 1-hexen-5-yne (**9**)[8] with BBr_3[9] followed by esterification with isopropyl alcohol[10] furnished the corresponding (*Z*)-alkenylboronic ester **10** in 58% isolated yield. The presence of a terminal carbon−carbon double bond in **9** did not appear to interfere with bromoboration. Conversion of **10** to enynyl iodide **12** was achieved by using the $Pd(PPh_3)_4$-catalyzed cross-coupling reaction with alkynylzinc chloride **11**,[9,11] derived from 1-lithio-1-propyne and anhydrous zinc chloride, followed by treatment with NaOH and iodine.[10,12] A second $Pd(PPh_3)_4$-catalyzed cross-coupling reaction between **12** and allenylzinc chloride **13**,[13] derived from treating 1,2,8-nonatriene with *n*-butyllithium followed by anhydrous zinc chloride, proceeded smoothly to furnish enyne−allene **4** having predominantly the *Z* geometry (*Z*:*E* = 97:3). Similarly, enyne−allene **16** having one of the tethers shortened by one carbon atom and **17** having a methyl substituent at the internal position of one of the additional double bonds as well as a shorter tether were synthesized by cross coupling with allenylzinc chlorides **14** and **15**, derived from 1,2,7-octatriene and 7-methyl-1,2,7-octatriene, respectively.

Scheme 2



The thermally-induced cascade cyclization of **4**, synthesized by the procedure outlined in Scheme 2, gave essentially identical results as observed previously (Scheme 1).[7b] The carbon tetracycle **8** having predominantly the trans ring junction (trans:cis = 92:8) was obtained in 51% isolated yield (0.233 g, 0.971 mmol) by dropwise addition of a solution of **4** (0.460 g, 1.92 mmol) in 250 mL of benzene into 600 mL of refluxing benzene over a period of 10 h followed by an additional 4 h of reflux. The assignment of the trans ring junction to the major isomers was based on the chemical shift correlation of the ^{13}C NMR signals with those of other closely related structures.[14] Because the stereogenic center on the five-membered ring did not exert a significant influence on the facial selectivity of the Diels−

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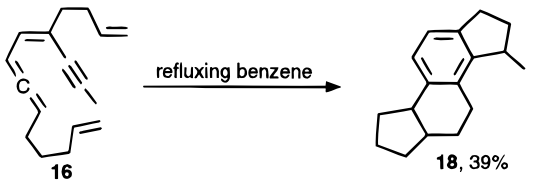
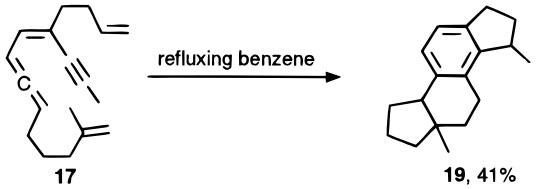
Alder reaction, a 1:1 mixture of the two diastereomers of the trans isomers of **8** was produced.[7b]

Thermolysis of enyne−allene **16** with a shorter tether was likewise conducted in refluxing benzene to furnish **18** having the fused 5,6,6,5-ring system in 39% yield (eq 1). The tetracyclic compound **18** was found to be a 3:3:2:2 mixture of all four possible diastereomers presumably because of a lack of facial selectivity as well as little preference for either the *exo* or the *endo* attack during the intramolecular Diels−Alder reaction to capture the corresponding *o*-quinodimethane at the last step of the cascade sequence.[14] Placing a methyl substituent at the internal position of one of the additional carbon−carbon double bonds in **17** was intended to produce an angular methyl group in the final tetracyclic structure. Indeed, **19** having the 5,6,6,5-ring system with an angular methyl group was obtained as a 1:1:7:9 mixture of four diastereomers in 41% yield (eq 2). The improved stereoselectivity is presumably due to a preference for either an *exo* or an *endo* attack during the intramolecular Diels−Alder reaction, producing either the cis or the trans ring junction (not determined) predominantly.



(1)

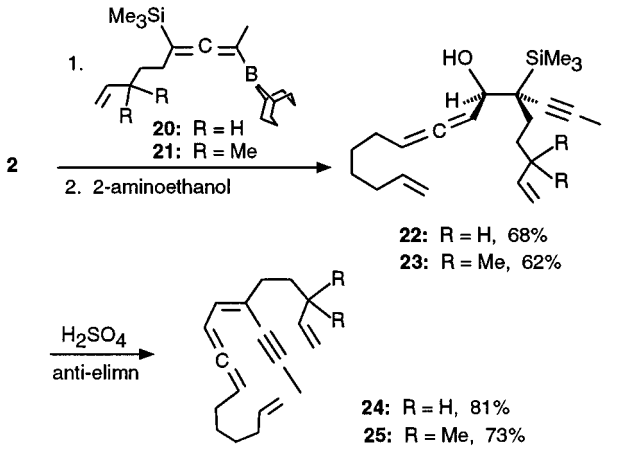


(2)

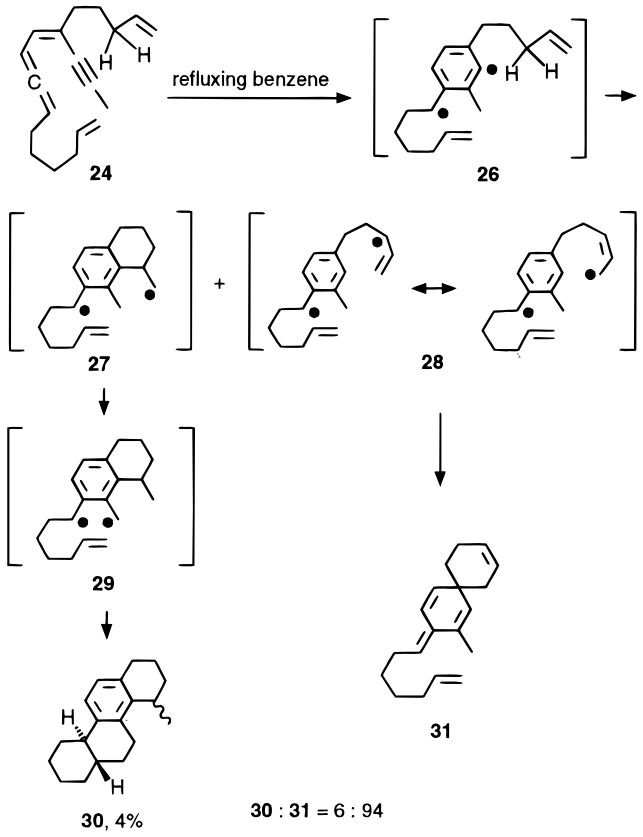
The possibility of constructing the fused 6,6,6,6-ring system by using enyne−allene **24** having one of the tethers elongated by one carbon atom compared to **4** for the cascade radical cyclization was also investigated. Attempts to synthesize **24** by the reaction sequence outlined in Scheme 2 were unsuccessful. Bromoboration of 1-hepten-6-yne with BBr_3 followed by treatment with isopropyl alcohol produced the desired alkenylboronic ester only in very low isolated yield. The reaction produced mostly an intractable tar. Fortunately, it was possible to synthesize acyclic enyne−allene **24** (*Z*:*E* = 97:3) by reverting back to the reaction sequence outlined in Scheme 1 with an initial condensation between the conjugated allenic aldehyde **2** and γ-(trimethylsilyl)allenylborane **20** to afford **22** followed by an H_2SO_4-induced Peterson elimination (Scheme 3).

Thermolysis of **24** produced, in addition to a small amount of the anticipated tetracyclic compound **30** (ca. 4% isolated yield, 1:1 mixture of two diastereomers) having the fused 6,6,6,6-ring system, the bicyclic spiro derivative **31** as the major product (**30**:**31** = 6:94) (Scheme 4). Apparently, instead of trapping the benzenoid radical in **26** by one of the intramolecular carbon−carbon double bonds in a 6-*exo* fashion to afford biradical **27** leading to **30**, the majority of the reaction proceeded through a 1,5-hydrogen shift to furnish **28** containing an allylic radical. The preference for the benzenoid radical center in **26** to undergo a 1,5-hydrogen shift instead of the desired 6-*exo* radical cyclization had also been observed in other closely related systems.[15] The subsequent attack on the *ipso* carbon of the benzene ring by the terminus of the allylic radical led to homolytic coupling that produced **31**.

Scheme 3



Scheme 4



It was difficult to separate **31** from **30** by column chromatography and HPLC. However, the ^1H and ^{13}C NMR spectra of the crude reaction mixture obtained by simple removal of benzene appeared to indicate a clean transformation of **24** to **30** and **31** (ca. 80−90%) with minor contamination from other unidentified products. The assignment of the bicyclic spiro structure to **31** was further supported by additional one- and two-dimensional NMR measurements (COSY, HETCOR, and DEPT). The exocyclic double bond in **31** was assigned the *E* geometry on the basis of the measurement of the nuclear Overhauser effect. We were able to isolate **30** only by treating the crude reaction mixture with an excess of $BH_3{\cdot}SMe_2$ followed by an oxidative treatment with alkaline H_2O_2 to convert **31** to

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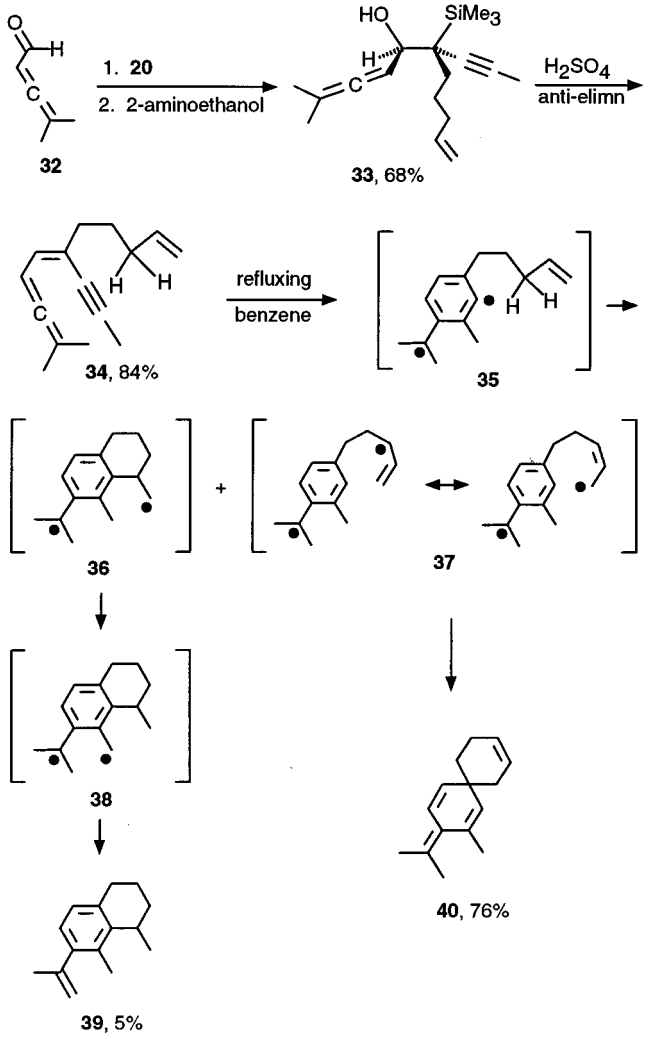
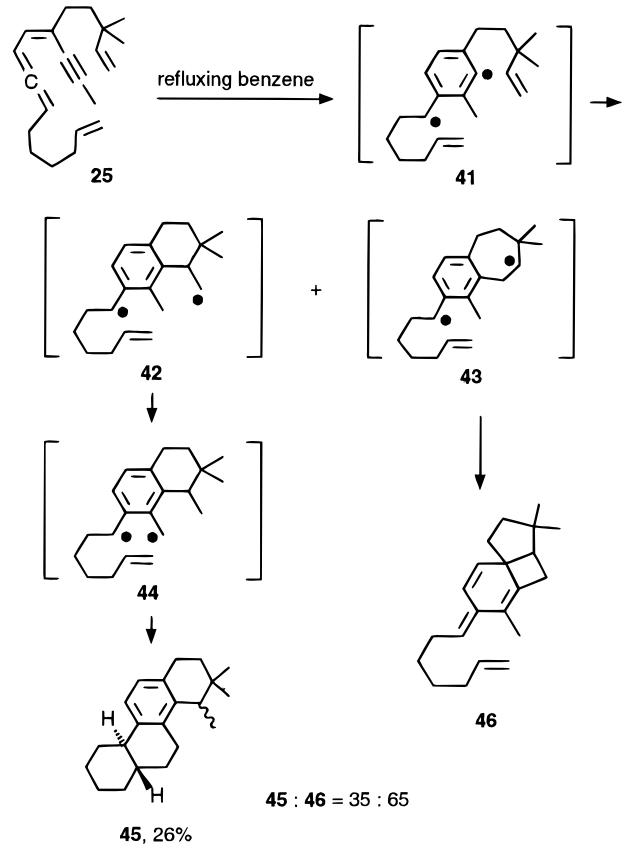
Scheme 5



Scheme 6



a more polar adduct, allowing isolation of **30** by column chromatography.

Since one of the carbon−carbon double bonds in **24** did not participate in the cascade radical cyclization to furnish the bicyclic derivative **31**, we therefore synthesized acyclic enyne−allene **34** having only one additional double bond attached to the enyne−allene system through a three-carbon tether by using the conjugated allenic aldehyde **32** for condensation with **20** as described previously (Scheme 5).[7a] Thermolysis of **34** indeed produced the expected bicyclic spiro derivative **40** having a simplified structure, thus facilitating structural elucidation. A minor set of the ^{1}H NMR signals attributable to the presence of the tetrahydronaphthalene derivative **39** (**39**:**40** = 6:94) was also observed. Apparently, *o*-quinodimethane **38** derived from the 6-*exo* radical cyclization decayed through a 1,5-hydrogen shift to produce **39** as observed previously.[7a] Again, the ^{1}H NMR spectrum of the crude reaction mixture indicated a relatively clean transformation of **34** to **39** (ca. 5%) and **40** (76%). The yields of **39** and **40** were determined by adding a carefully determined amount of 1,4-dimethoxybenzene as an internal standard to the crude reaction mixture for the ^{1}H NMR integration.

An attempt was made to try to eliminate the possibility of the 1,5-hydrogen shift from **26** to **28** so as to direct the cascade radical cyclization toward the 6-*exo* pathway leading to the fused 6,6,6,6-ring system. Enyne−allene **25** having two methyl groups in place of the two allylic hydrogens in **24** was thus synthesized for this purpose as outlined in Scheme 3. After **25** was heated at reflux in benzene, the ^{1}H NMR spectrum of the crude reaction mixture indicated the presence of the anticipated tetracyclic adduct **45**, which was later isolated (26% yield) and identified as a 1:1 mixture of two diastereomers having the trans ring junction. However, **45** remained as the minor adduct, and a more predominant set of ^{1}H NMR signals attributable to the presence of the tricyclic derivative **46** (**45**:**46** = 35:65) were observed (Scheme 6). Undoubtedly, the tricyclic derivative **46** arises from a 7-*endo* ring closure of **41** to furnish **43**,[16] leading to **46** by attack on the benzene ring by the homobenzylic radical center in **43** to accomplish homolytic coupling.

Again, it was only possible to separate **45** from **46** by treating the crude reaction mixture with an excess of BH_3·SMe_2 followed by an oxidative treatment with alkaline H_2O_2 to convert **46** to a more polar adduct, allowing isolation of **45** by column chromatography. As in the case of **8**, the tetracycle **45** appeared to have predominantly the trans ring junction and exist as a 1:1 mixture of two diastereomers.

Acyclic enyne−allene **48** was also synthesized as a simplified analogue of **25** (Scheme 7). On heating in refluxing benzene, **48** was converted to the bicyclic adduct **53** and the tricyclic derivative **54** as expected (**53**:**54** = 35:65) (Scheme 7). The ^{1}H NMR spectrum of the crude reaction products also indicated a clean conversion of **48** to **53** and **54** (ca. 80−90%). It was possible to partially separate **53** from **54** by HPLC, allowing a complete elucidation of the highly unusual structure of **54** by a wide range of NMR experiments, including COSY, HETCOR, NOESY, and DEPT.

While tricyles **46** and **54** contain a strained four-membered ring and do not possess aromaticity as in **45** and **53**, the transformations from **25** to **46** and from **48** to **54** can still be expected to be highly exothermic. In each case, the overall

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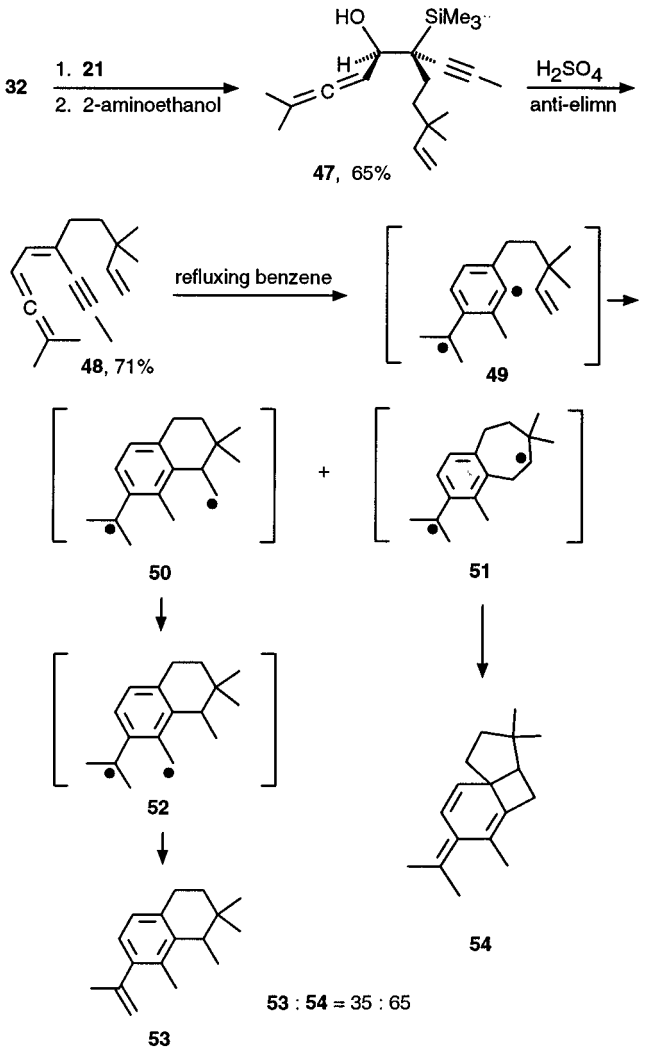
Scheme 7

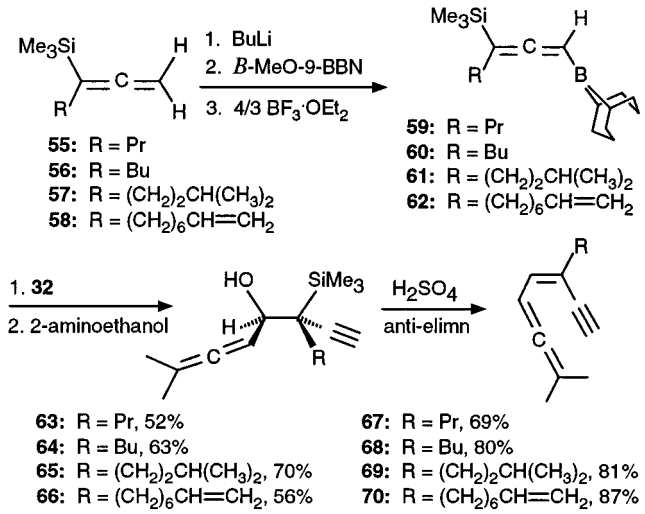


transformation involves trading three π bonds for three σ bonds, a driving force of ca. 60 kcal/mol. Nevertheless, the attack on the *ipso* carbon of the benzene ring by the homobenzylic radical in **43** and **51** is remarkable and must overcome the formation of a strained four-membered ring along with the loss of aromaticity. Evidently, the gain in forming a σ bond by the intramolecular radical−radical combination is enough to override these unfavorable factors. However, this σ bond must be significantly weakened with lower bond energy, making **46** and **54** reactive and prone to decomposition.

In comparison with **46** and **54**, the transformations from **24** to **31** and from **34** to **40** involve converting only two π bonds to two σ bonds. But unlike **46** and **54**, the structures of **31** and **40** do not contain a strained four-membered ring. The possibility of attacking the *ipso* carbon of the benzene ring by the terminus of the allylic radical in **28** and **37** alleviates the constraint of forming a four-membered ring via the intramolecular radical−radical combination. This option will not be available if the 4-pentenyl substituent of the enyne−allene system in **24** and **34** is replaced with a propyl group which then could lead to the formation of a bicyclic spiro structure having a four-membered ring. Enyne−allenes **67**−**70** (Scheme 8) were synthesized to test the feasibility of producing such a bicyclic spiro structure via cascade biradical cyclizations.

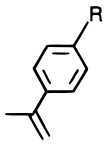
Treatment of terminal allenes **55**−**58** with *n*-butyllithium followed by *B*-MeO-9-BBN and $^4/_3$ BF_3·OEt_2 produced γ-(trimethylsilyl)allenylboranes **59**−**62**. Condensation of **59**−**62** generated *in situ* with the allenic aldehyde **32** followed by

Scheme 8



treatment with 2-aminoethanol afforded **63**−**66** with high diastereoselectivity (de ≥92%). The subsequent H_2SO_4-induced Peterson elimination of **63**−**66** at −20 °C then produced enyne−allenes **67**−**70** (*Z*:*E* ≥ 96:4) along with ca. 2−6% of the cycloaromatized adducts **71**−**74**.

It was observed previously that the Myers cyclization of (*Z*)-7-methyl-3,5,6-octatrien-1-yne having only a small hydrogen atom at the acetylenic terminus occurred at 37 °C with a half-life of ca. 70 min. Similarly, cyclizations of enyne−allenes **67**−**70** also occurred readily at room temperature, and the reactions were found to be complete within 18 h, significantly faster than those of enyne−allenes **34** and **48** having a methyl substituent at the acetylenic terminus. The faster rates of cyclizations of **67**−**70** are responsible for the formation of small amounts of the cycloaromatized adducts **71**−**74** (2−6%) even though the Peterson elimination of **63**−**66** was carried out at −20 °C to try to prevent their formation.

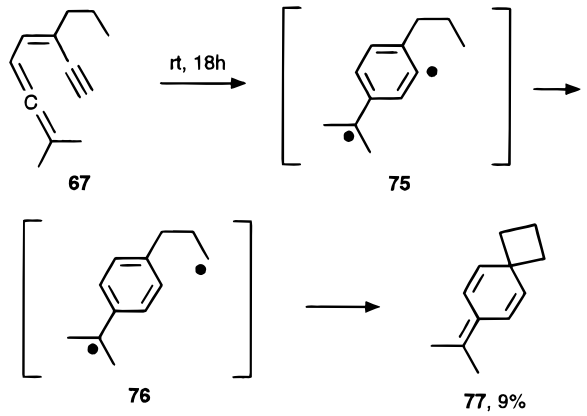


71: R = Pr
72: R = Bu
73: R = $(CH_2)_2CH(CH_3)_2$
74: R = $(CH_2)_6CH{=}CH_2$

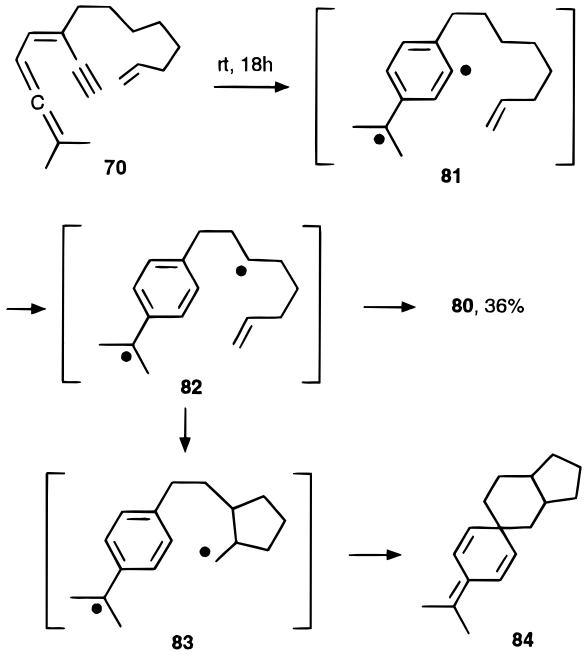
The cascade radical cyclization of **67** was conducted at high dilution (ca. 3×10^{-4} M) in benzene, and the mixture was stirred at room temperature for 18 h. Benzene was then removed *in vacuo*, and 1 mL of C_6D_6 was added along with a carefully determined amount of 1,4-dimethoxybenzene as an internal standard for the ^{1}H NMR integration to determine the yields of the reaction products. It was gratifying to observe that the ^{1}H NMR spectrum of the concentrated reaction mixture indicated the presence of the bicyclic spiro compound **77** in 9% yield (Scheme 9). The amount of the cycloaromatized adduct **71** (9%) did not appear to be significantly more than what was originally present (6%) in the starting enyne−allene **67**. It was possible to separate out a small amount of **77** by HPLC for structural elucidation by the ^{1}H NMR and MS.

Apparently **77** arises from a reaction pathway involving an initial formation of the α,3-didehydrotoluene biradical **75** followed by an intramolecular 1,5-hydrogen shift to form **76**,

Scheme 9



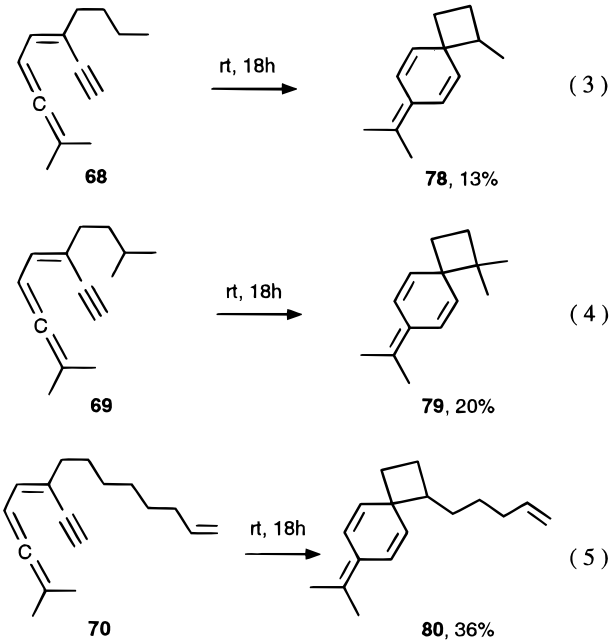
Scheme 10



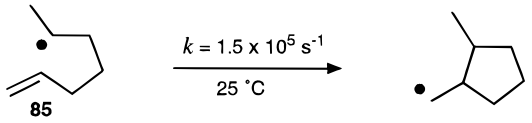
which then undergoes an intramolecular radical−radical combination by attacking the *ipso* carbon of the benzene ring to furnish **77**. In comparison with the transformation from **37** to **40**, the homolytic coupling of **76** to form **77** suffers from the formation of a strained four-membered ring. However, the primary alkyl radical in **76** is more reactive than the allylic radical in **37**.

Interestingly when enyne−allene **67** was dissolved in C_6D_6 at a higher concentration (ca. 0.4 M) in order to allow the progress of the reaction to be monitored by the ^{1}H NMR, the presence of the bicyclic spiro compound **77** was not detected after 18 h at room temperature. Instead, the cycloaromatized adduct **71** was produced in 34% yield. Presumably, at higher concentration the intermolecular disproportionation of biradicals **75** or **76** became more favorable in producing **71** predominantly. A similar concentration effect in directing the course of the reaction of the biradical intermediates derived from the Moore cyclization of enyne−ketenes was also observed previously.[4e]

Similarly, keeping enyne−allenes **68**, **69**, and **70** in benzene at high dilution furnished the bicyclic spiro adducts **78** (13%), **79** (20%), and **80** (36%), respectively (eqs 3−5), along with ca. 1−3% of the cycloaromatized adducts **72**−**74** which were originally present in the starting enyne−allenes. The strained spiro compounds **77**−**80** appeared to be labile and showed propensity for decomposition in large portions during removal of benzene *in vacuo* to produce more concentrated samples in order to allow determination of the yields by the ^{1}H NMR integration using 1,4-dimethoxybenzene as the internal standard.



Enyne−allene **70** having an additional carbon−carbon double bond attached to the enyne−allene system with a six-carbon tether was synthesized in order to study the possibility of capturing the secondary alkyl radical center in **82** by the terminal double bond intramolecularly in a typical 5-*exo* fashion to give a new biradical **83** (Scheme 10). It was hoped that perhaps **83** could undergo an intramolecular radical−radical combination by attacking the *ipso* carbon of the benzene ring to furnish **84**. Furthermore, since the rate constant for the 5-*exo* radical cyclization of **85** (k_{5-exo} = 1.5 × 10^5 s^{-1} at 25 °C) having a secondary alkyl radical center had been reported (eq 6),[16]



determination of the relative yield between **80** and the adducts derived from biradical **83** would allow an estimation of the rate constant of the transformation from **82** to **80**. While there was no evidence that **84** was produced, the formation of **80** in 36% yield indicates that the direct attack of the secondary alkyl radical in **82** on the *ipso* carbon of the benzene ring to furnish **80** is very facile and at least competitive with the 5-*exo* radical cyclization of **82** to form **83**.

Conclusions

The cascade radical cyclizations via biradicals generated from acyclic enyne−allenes provide new pathways to the fused tetracyclic structures in a single step. The presence of two radicals in the same molecule simultaneously also creates opportunities to allow new interactions between these reactive centers, making it possible to form highly unusual and reactive chemical structures not easily accessible by other synthetic methods.

Experimental Section

General procedures for manipulation of organoboranes and other organometallic reagents were described previously.[17] All reactions were conducted in oven-dried (120 °C) glassware under a nitrogen atmosphere. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were distilled from sodium benzophenone ketyl prior to use. The following reagents were purchased from Aldrich Chemical Co., Inc., and were used without further purification: BBr_3, $BH_3{\cdot}SMe_2$, 9-borabicyclo[3.3.1]nonane (9-BBN-H), $Pd(PPh_3)_4$, $ZnCl_2$, LiBr, 2-aminoethanol, 1,7-octadiene, 3-methyl-1,2-butadiene, 5-bromo-1-pentene, 8-bromo-1-octene, methyl propargyl ether, methyl 3,3-dimethyl-4-pentenoate, propargyl chloride, 3-butyn-2-ol, chlorotrimethylsilane, methylmagnesium chloride (3.0 M in THF), allylmagnesium bromide (1.0 M in Et_2O), *tert*-butyllithium (1.7 M in pentane), and *n*-butyllithium (2.5 M in hexanes). Hexamethylphosphoric triamide (HMPA) was also purchased from Aldrich and was distilled from CaH_2 prior to use. 2,3,9-Decatrienal (**2**),[7b] 1-hexen-5-yne (**9**),[8] 1,2,8-nonatriene,[18] 4-methyl-2,3-pentadienal (**32**),[19] 5-bromo-2-methyl-1-pentene,[20] *B*-methoxy-9-borabicyclo[3.3.1]nonane (*B*-MeO-9-BBN),[21] 3-(trimethylsilyl)-1,2-hexadiene (**55**),[22] 3-(trimethylsilyl)-1,2-heptadiene (**56**),[22] and 6-methyl-3-(trimethylsilyl)-1,2-heptadiene (**57**)[22] were prepared according to the reported procedures. 6-(Trimethylsilyl)-1,6,7-nonatriene was obtained in 78% isolated yield by sequential treatment of a dispersion of CuBr and LiBr in THF with 4-pentenylmagnesium bromide in THF and the methanesulfonate of 4-(trimethylsilyl)-3-butyn-2-ol as described previously.[22] Similarly, 3,3-dimethyl-6-(trimethylsilyl)-1,6,7-nonatriene (70% yield) and 3-(trimethylsilyl)-1,2,10-undecatriene (**58**, 84% yield) were prepared from 3,3-dimethyl-4-pentenylmagnesium bromide and 7-octenylmagnesium bromide, respectively. 5-Bromo-3,3-dimethyl-1-pentene[23] was prepared by reducing methyl 3,3-dimethyl-4-pentenoate with $LiAlH_4$ (86%) followed by treating the methanesulfonate of the resulting alcohol with LiBr in refluxing acetone for 6 h (64%). Silica gel (70−230 mesh) for column chromatography was also obtained from Aldrich. Cuprous bromide was purchased from Fluka, and 1-propyne was obtained from Farchan. ^1H (270 MHz) and ^{13}C (67.9 MHz) NMR spectra were recorded in $CDCl_3$ or C_6D_6 using Me_4Si, $CHCl_3$ (^1H δ 7.26), $CDCl_3$ (^{13}C δ 77.02), C_6D_5H (^1H δ 7.15), or C_6D_6 (^{13}C δ 128.00) as internal standard. Nuclear Overhauser effect, DEPT, and two-dimensional NMR (DQCOSY, HETCOR, NOESY) spectra were obtained at 300 MHz at 25 °C. Standard pulse sequences were used. T_1 analysis was performed to ensure a sufficient delay period was used between NOE irradiation pulses. Mass spectra were obtained at 70 eV.

(*Z*)-(2-Bromo-1,5-hexadienyl)diisopropoxyborane (10). To a solution of 6.58 g of 1-hexen-5-yne (**9**)[8] (82.3 mmol) in 30 mL of dry pentane under a nitrogen atmosphere at −78 °C was added with a syringe 7.6 mL of BBr_3 (20.1 g, 80 mmol). After 1 h at −78 °C, the mixture was allowed to warm to room temperature and stirred overnight. The solution was then cooled to −20 °C and transferred via cannula into a second flask containing a mixture of 50 mL of 2-propanol and 50 mL of pentane at −20 °C. After 30 min, the top layer was separated, and the bottom layer was extracted with cold pentane (3 × 20 mL). The top layer and the pentane extracts were combined and concentrated. The residue was then distilled at reduced pressure (64−66 °C/0.06 Torr) to furnish 13.3 g (46.1 mmol, 58%) of **10** as a colorless liquid: IR (neat) 1641, 989, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ 5.97 (1 H, s), 5.76 (1 H, ddt, J = 17.1, 10.2, and 6.6 Hz), 5.05 (1 H, dm, J = 17 and 2 Hz), 4.98 (1 H, dm, J = 10 and 2 Hz), 4.40 (2 H, septet, J = 6.1 Hz), 2.56 (2 H, t, J = 7.3 Hz), 2.32 (2 H, q, J = 7 Hz), 1.17 (6 H, d, J = 6.0 Hz); ^{13}C NMR ($CDCl_3$) δ 137.43, 136.57, 124 (br), 115.59, 66.50, 43.41, 32.20, 24.44; MS *m*/*e* 275 and 273 ($M^+ - 15$), 209.

(*Z*)-1-Iodo-2-(1-propynyl)-1,5-hexadiene (12). To a 100 mL flask were added 5.78 g of **10** (20.0 mmol), 1.15 g of $Pd(PPh_3)_4$ (1.0 mmol), and 20 mL of dry THF. The mixture was degassed by three cycles of freeze−thaw and kept under a nitrogen atmosphere at room temperature for 1 h. In a second flask, 1-propynylzinc chloride was prepared by treating a degassed solution of 1-propyne (25 mmol) in 40 mL of THF with 10 mL of a 2.5 M solution of *n*-butyllithium (25 mmol) in hexanes for 10 min followed by the addition of a degassed solution of 3.4 g of anhydrous zinc chloride (25.0 mmol) in 5 mL of THF. The solution of 1-propynylzinc chloride was then transferred via cannula into the first flask at room temperature. After 5 min, the reaction mixture was heated at reflux for 3 h before being cooled to 0 °C and was treated sequentially with 32 mL of a 6 N NaOH and 12.7 g of iodine (50 mmol) in 20 mL of Et_2O. After 1 h of stirring at room temperature, an excess of saturated $Na_2S_2O_3$ solution was introduced to reduce I_2. An additional 30 mL of Et_2O was added, and the organic layer was separated. The aqueous layer was extracted with Et_2O (3 × 20 mL). The combined organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (silica gel/hexanes) to furnish 2.46 g (10.0 mmol, 50%) of **12** as a light yellow liquid: IR (neat) 2227, 1640, 994, 915 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.31 (1 H, s), 5.77 (1 H, ddt, J = 17.1, 10.2, and 6.3 Hz), 5.03 (1 H, dm, J = 17 and 2 Hz), 4.98 (1 H, dm, J = 10 and 1 Hz), 2.30 (4 H, br), 2.03 (3 H, s); ^{13}C NMR ($CDCl_3$) δ 137.05, 136.71, 115.37, 93.13, 82.30, 80.63, 38.67, 32.34, 4.65; MS *m*/*e* 246 (M^+), 205, 119.

(*Z*)-5-(1-Propynyl)-1,5,7,8,14-pentadecapentaene (4).[7b] To a degassed solution of 0.49 g of 1,2,8-nonatriene[18] (4.0 mmol) in 10 mL of THF at −70 °C was added 1.6 mL of a 2.5 M solution of *n*-butyllithium (4.0 mmol) in hexanes. After 2 h at −70 °C, a degassed solution of 0.545 g of anhydrous zinc chloride (4.0 mmol) in 10 mL of THF was introduced via cannula followed by a degassed mixture of 0.984 g of **12** (4.0 mmol) and 0.231 g of $Pd(PPh_3)_4$ (0.20 mmol) in 10 mL of THF. The reaction mixture was then charged with 5 mL of HMPA and was allowed to warm to room temperature. After 2 h, 30 mL of a saturated NH_4Cl solution and 30 mL of pentane were added, and the organic layer was separated. The aqueous layer was extracted with pentane (3 × 20 mL), and the combined organic layers were dried over $MgSO_4$ and concentrated. The residue was purified by column chromatography (silica gel/hexanes) to furnish 0.617 g (2.57 mmol, 64%) of **4** (*Z*:*E* = 97:3) as a light yellow liquid: IR (neat) 2232, 1940, 1641, 993, 911 cm^{-1}; ^1H NMR (C_6D_6) δ 6.76 (1 H, ddt, J = 10.8, 6.4, and 3 Hz), 6.16 (1 H, d, J = 10.8 Hz), 5.75 (1 H, ddt, J = 17, 10, and 6 Hz), 5.73 (1 H, ddt, J = 17, 10, and 6 Hz), 5.26 (1 H, q, J = 6.8 Hz), 5.05−4.90 (4 H, m), 2.30 (2 H, q), 2.21 (2 H, t), 1.90 (4 H, m), 1.61 (3 H, s), 1.30 (4 H, m); ^{13}C NMR (C_6D_6) δ 208.63, 138.95, 138.03, 130.94, 123.32, 115.08, 114.59, 93.50, 92.87, 92.31, 78.46, 37.43, 33.85, 33.16, 28.92, 28.81, 28.59, 4.15; MS *m*/*e* 240 (M^+), 225, 197.

(5α)-(±)-15-Methylgona-8,11,13-triene (8).[7b] A solution of 0.460 g (1.92 mmol) of **4** in 250 mL of degassed dry benzene was introduced dropwise to 600 mL of refluxing benzene (degassed) under a nitrogen atmosphere over a period of 10 h followed by an additional 4 h of reflux. Benzene was then removed by simple distillation. In order to facilitate separation and purification, the residue was treated with an excess of a 0.5 M solution of 9-BBN-H in THF at room temperature for 2 h followed by oxidation with an excess of alkaline H_2O_2 (30%). Pentane (25 mL) was added, and the organic layer was separated, washed with water, and concentrated. Purification by column chromatography (silica gel/hexanes) furnished 0.233 g (0.971 mmol, 51%) of **8** (trans:cis = 92:8) as a colorless liquid: IR (neat) 1475, 1446, 811 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.225 (d, J = 7.9 Hz) and 7.213 (d, J = 7.7 Hz) (1 H, the aromatic hydrogens of the two diastereomers), 7.11 (1 H, d, J = 7.7 Hz), 3.32 (1 H, septet, J = 7.3 Hz), 3.15−3.0 (1 H, m), 2.9−2.7 (3 H, m), 2.52 (1 H, d, J = 12.6 Hz), 2.4−2.2 (2 H, m), 2.0−1.8 (5 H, m), 1.6−1.2 (6 H, m), 1.247 and 1.228 (3 H, d, J = 7 Hz); ^{13}C NMR ($CDCl_3$) δ 147.28, 147.12, 140.33, 140.23, 138.61, 138.42, 132.92, 132.66, 124.00, 123.69, 121.66, 44.15, 43.69, 40.62, 40.20, 38.25, 37.81, 34.47, 34.40, 34.17, 33.97, 31.58, 31.29, 30.70, 30.59,

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30.52, 30.19, 27.20, 27.10, 26.96, 26.32, 26.25, 26.23, 18.90, 18.86; MS *m*/*e* 240 (M^+), 225, 212, 197; HRMS calcd for $C_{18}H_{24}$ 240.1878, found 240.1883. Due to the presence of a stereogenic center on the five-membered ring, the isolated material contains two diastereomers in essentially 1:1 ratio. A minor set of doublets (8%) at ca. δ 7.09 and 7.01 (J = 7.9 Hz) in the ^{1}H NMR spectrum is attributed to the signals of the aromatic hydrogens of the isomers having the cis ring junction.

(6*R*,7*R*)-6-(1-Propynyl)-6-(trimethylsilyl)-1,8,9,15-hexadecatetraen-7-ol (22). To a solution of 1.164 g of 6-(trimethylsilyl)-1,6,7-nonatriene (6.00 mmol) in 20 mL of THF at −78 °C was introduced with a syringe 3.5 mL of a 1.7 M solution of *tert*-butyllithium (6.0 mmol) in pentane. After 0.5 h of stirring at −78 °C and then 1 h at −40 °C, 1.0 mL of *B*-MeO-9-BBN (0.91 g, 6.0 mmol) was added, and the reaction mixture was allowed to warm to 0 °C. After 40 min, 1.0 mL of BF_3·OEt_2 (1.13 g, 8.0 mmol) was introduced. The reaction mixture was kept at 0 °C for 15 min and then was allowed to warm to room temperature. After 15 min, the solution was cooled to 0 °C, and 0.90 g (6.0 mmol) of **2** was introduced. The reaction mixture was allowed to warm to room temperature. After 2 h, THF and pentane were removed at reduced pressure under a stream of dry N_2, and the pressure was then restored with N_2. Pentane (30 mL) was added followed by 1.0 mL of 2-aminoethanol, and a white precipitate formed almost immediately. After 15 min, the precipitate was removed by filtration (inert nitrogen atmosphere no longer needed), and the filtrate was washed with water, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (silica gel/hexanes and then 2.5% of ethyl acetate in hexanes) to furnish 1.399 g (4.07 mmol, 68%) of **22** as a yellow liquid: IR (neat) 3560, 2167, 1962, 1641, 1247, 992, 911, 842 cm^{-1}; ^{1}H NMR (C_6D_6) δ 5.9−5.65 (3 H, m), 5.19 (1 H, m), 5.08−4.94 (4 H, m), 4.49 (1 H, m), 2.05 (2 H, m), 1.95−1.85 (4 H, m), 1.85−1.7 (4 H, m), 1.54 and 1.53 (3 H, s), 1.30 (4 H, m), 0.315 and 0.312 (9 H, s); ^{13}C NMR (C_6D_6) δ 202.14, 201.80, 138.98, 138.86, 114.69, 95.57, 95.35, 95.09, 94.98, 81.62, 81.54, 80.00, 73.61, 73.15, 35.12, 35.07, 34.38, 33.98, 33.87, 33.84, 30.69, 30.48, 29.02, 28.90, 28.68, 26.59, 3.59, −1.24, −1.27; MS *m*/*e* 344 (M^+), 326, 73. Because of an essentially random selection of the allenic chiral axis during condensation which was of no chemical consequence in producing **24**, the isolated material was a 1:1 mixture of two diastereomers.

(*Z*)-6-(1-Propynyl)-1,6,8,9,15-hexadecapentaene (24). To 10 mL of a 1:1 mixture of pentane and Et_2O containing 70 mg of concentrated H_2SO_4 at 0 °C was added 1.39 g (4.04 mmol) of **22** in 10 mL of a 1:1 mixture of pentane and Et_2O. After 1 h of vigorous stirring at 0 °C, 20 mL of water and 20 mL of pentane were added. The organic layer was then separated, dried over $MgSO_4$, and concentrated. The residue was purified by column chromatography (silica gel/pentane) to furnish 0.839 g (3.30 mmol, 81%) of **24** (*Z*:*E* = 97:3) as a colorless liquid: IR (neat) 2224, 1940, 1640, 992, 911 cm^{-1}; ^{1}H NMR (C_6D_6) δ 6.75 (1 H, ddt, J = 10.6, 6.4, and 3.1 Hz), 6.17 (1 H, d, J = 10.4 Hz), 5.71 (2 H, ddt, J = 17.0, 10.3, and 6.6 Hz), 5.27 (1 H, q, J = 6.8 Hz), 5.03−4.90 (4 H, m), 2.13 (2 H, t, J = 7.5 Hz), 2.0−1.85 (6 H, m), 1.64 (2 H, quintet, J = 7.5 Hz), 1.62 (3 H, s), 1.30 (4 H, m); ^{13}C NMR (C_6D_6) δ 208.59, 138.95, 138.70, 130.81, 123.84, 114.84, 114.60, 93.55, 92.65, 92.31, 78.59, 37.25, 33.86, 33.34, 28.95, 28.83, 28.61, 28.12, 4.19; MS *m*/*e* 254 (M^+), 239, 211.

(6aα,10aβ)-1,2,3,4,5,6,6a,7,8,9,10,10a-Dodecahydro-4-methylchrysene (30) and (*E*)-3-(6-Heptenylidene)-2-methylspiro[5.5]undeca-1,4,8-triene (31). The same procedure was repeated as described for **8** except that **24** (0.360 g, 1.42 mmol) was used. Benzene was removed by simple distillation, and the ^{1}H NMR spectrum of the residue indicated a clean transformation of **24** to **30** and **31** (ca. 80−90%) (**30**:**31** = 6:94). The presence of **31** in the residue can be clearly identified. The spiro derivative **31** exhibited the following spectral data: IR (neat) 1640, 992, 909 cm^{-1}; ^{1}H NMR (C_6D_6) δ 6.54 (1 H, d, J = 10.1 Hz), 5.85 (1 H, dt, J = 10.1 and 1.8 Hz), 5.72 (1 H, ddt, J = 17, 10, and 7 Hz), 5.67 (1 H, m), 5.61 (1 H, s), 5.59 (1 H, m), 5.40 (1 H, t, J = 7.5 Hz), 4.98 (1 H, dm, J = 17 and 2 Hz), 4.94 (1 H, dm, J = 10 and 1 Hz), 2.15 (2 H, q, J = 7 Hz), 2.00 (2 H, m), 1.96 (4 H, m), 1.82 (3 H, d, J = 1.1 Hz), 1.51 (2 H, t, J = 6.3 Hz), 1.31 (4 H, m); ^{13}C NMR (C_6D_6) δ 138.97, 135.70, 133.03, 132.39, 130.58, 126.42, 125.00, 124.23, 121.76, 114.65, 37.81, 37.17, 34.49, 34.07, 29.84, 29.02, 27.52, 22.44, 19.95; MS *m*/*e* 254 (M^+), 200, 118. The assignment of the bicyclic spiro structure to **31** was further supported by additional NMR measurements, including COSY, HETCOR, and DEPT. Because **31** is prone to decomposition, its elemental composition was not further analyzed.

The fused tetracycle **30** was separated from **31** by treating the residue in THF with an excess of BH_3·SMe_2 followed by an oxidative treatment with alkaline H_2O_2 (30%) to convert **31** to a more polar adduct, allowing isolation of 0.0164 g (0.065 mmol, ca. 4%) of **30** (1:1 mixture of two diastereomers) by column chromatography (silica gel/hexanes) as a liquid: ^{1}H NMR (C_6D_6) δ 7.19 (1 H, d, J = 8 Hz), 6.96 (1 H, d, J = 7.9 Hz), 2.95 (1 H, m), 2.8−2.6 (4 H, m), 2.37 (1 H, m), 2.21 (1 H, t), 1.9−1.5 (8 H, m), 1.4−1.1 (6 H, m), 1.14 and 1.10 (3 H, d, J = 7.0 Hz); MS *m*/*e* 254 (M^+), 239, 211; HRMS calcd for $C_{19}H_{26}$ 254.2035, found 254.2055.

(*Z*)-10-Methyl-6-(1-propynyl)-1,6,8,9-undecatetraene (34). The same procedure was repeated as described for **24** except that **33** (0.50 g, 1.72 mmol) was used to furnish 0.290 g (1.45 mmol, 84%) of **34** (*Z*:*E* = 96:4) as a colorless liquid: IR (neat) 2224, 1946, 1640, 992, 911 cm^{-1}; ^{1}H NMR (C_6D_6) δ 6.69 (1 H, d of septet, J = 10.8 and 2.8 Hz), 6.17 (1 H, dm, J = 10.8 and 0.5 Hz), 5.71 (2 H, ddt, J = 17.1, 10.2, and 6.7 Hz), 4.98 (1 H, dm, J = 17 and 1.5 Hz), 4.93 (1 H, dm, J = 11 and 1 Hz), 2.15 (2 H, td, J = 7.7 and 1 Hz), 1.96 (2 H, q, J = 7.1 Hz), 1.66 (2 H, quintet, J = 7.3 Hz), 1.63 (3 H, s), 1.59 (6 H, d, J = 2.9 Hz); ^{13}C NMR (C_6D_6) δ 206.36, 138.74, 131.63, 123.32, 114.77, 96.20, 92.35, 91.75, 78.72, 37.27, 33.37, 28.16, 20.43, 4.16; MS *m*/*e* 200 (M^+), 185, 146; HRMS calcd for $C_{15}H_{20}$ 200.1565, found 200.1569.

8-(1-Methylethenyl)-1,2,3,4-tetrahydro-1,2,2-trimethylnaphthalene (53) and 1,2,3,3a,4,6-Hexahydro-3,3,5-trimethyl-6-(1-methylethylidene)cyclopenta[1,4]cyclobuta[1,2]benzene (54). The same procedure was repeated as described for **8** except that **48** (0.256 g, 1.12 mmol) was used. Benzene was removed by simple distillation, and the ^{1}H NMR spectrum of the residue indicated a clean transformation of **48** to **53** and **54** (ca. 80−90%) (**53**:**54** = 35:65). Compounds **53** and **54** were partially separated by preparative HPLC to allow structural elucidations. **53**: ^{1}H NMR (C_6D_6) δ 7.03 (1 H, d, J = 7.8 Hz), 6.91 (1 H, d, J = 7.8 Hz), 5.16 (1 H, m, J = 0.9 Hz), 4.93 (1 H, m, J = 0.9 Hz), 2.72 (2 H, dd, J = 10 and 7 Hz), 2.60 (1 H, q, J = 6.6 Hz), 2.25 (3 H, s), 1.96 (3 H, m), 1.77 (1 H, ddd, J = 13, 11, and 8 Hz), 1.17 (1 H, dd, J = 13 and 6 Hz), 1.01 (3 H, d, J = 6.6 Hz), 0.96 (3 H, s), 0.84 (3 H, s); ^{13}C NMR (C_6D_6) δ 147.72, 142.62, 141.60, 133.10, 132.13, 126.89, 125.63, 114.52, 41.16, 32.30, 29.58, 29.01, 26.94 (2 carbons), 25.04, 18.08, 15.42; MS *m*/*e* 228 (M^+), 213, 199. **54**: ^{1}H NMR (C_6D_6) δ 6.62 (1 H, d, J = 9.2 Hz), 5.84 (1 H, d, J = 9.2 Hz), 2.51 (1 H, dd, J = 15 and 8 Hz), 2.41 (1 H, dd, J = 15 and 6 Hz), 2.10 (1 H, t, J = 6.5 Hz), 1.91 (3 H, s), 1.82 (3 H, s), 1.81 (2 H, m), 1.72 (3 H, s), 1.38 (2 H, m), 0.90 (3 H, s), 0.87 (3 H, s); ^{13}C NMR (C_6D_6) δ 142.20, 132.98, 131.09, 127.41, 127.35, 123.93, 60.65, 55.86, 42.05, 38.58, 36.54, 30.40, 27.26, 23.63, 23.26, 21.29, 17.80; MS *m*/*e* 228 (M^+), 213, 199. The structures of **53** and **54** were further supported by additional one- and two-dimensional NMR measurements (COSY, HETCOR, NOESY, and DEPT). Because **54** is prone to decomposition, its elemental composition was not further analyzed.

(3*R*,4*R*)-3-Butyl-7-methyl-3-(trimethylsilyl)-5,6-octadien-1-yn-4-ol (64). To 0.99 g (5.90 mmol) of 3-(trimethylsilyl)-1,2-heptadiene (**56**) in 20 mL of THF at −78 °C was added with a syringe 2.1 mL of a 2.5 M solution of *n*-butyllithium (5.3 mmol) in hexanes. After 0.5 h at −78 °C, 0.92 mL of *B*-MeO-9-BBN (0.83 g, 5.3 mmol) was added, and the reaction mixture was allowed to warm to 0 °C. After 40 min, 0.87 mL of BF_3·OEt_2 (0.98 g, 6.9 mmol) was introduced, and the reaction mixture was stirred at 0 °C for 15 min and then at room temperature for 15 min. The solution was cooled to 0 °C, and 0.52 g (5.3 mmol) of the conjugated allenic aldehyde **32** in 5 mL of THF was added. After 0.5 h of stirring at room temperature, the mixture was concentrated with a water aspirator under a slow stream of nitrogen to half its original volume, and the pressure was restored with nitrogen. Hexanes (29 mL) was added followed by 0.70 mL of 2-aminoethanol, and a white precipitate appeared almost immediately. After 15 min, the precipitate was removed by filtration (inert nitrogen atmosphere no longer needed), and the filtrate was washed with water, dried over Na_2SO_4, and concentrated. The residue was purified by column chromatography (silica gel/hexanes and then 2% diethyl ether in hexanes) to furnish 0.889 g (3.36 mmol, 63%) of **64** (*RR*/*SS*:*RS*/*SR* =

96:4) as a yellow liquid: IR (neat) 3553, 3310, 2093, 1968, 1247, 841 cm^{-1}; ^1H NMR (C_6D_6) δ 5.59 (1 H, d of septet, J = 5 and 3 Hz), 4.50 (1 H, t, J = 5 Hz), 1.96 (1 H, s), 1.81−1.64 (5 H, m), 1.54 (3 H, d, J = 2.8 Hz), 1.52 (3 H, d, J = 3.0 Hz), 1.31 (2 H, sextet, J = 7.1 Hz), 0.91 (3 H, t, J = 7.3 Hz), 0.33 (9 H, s); ^{13}C NMR (C_6D_6) δ 199.65, 99.95, 92.85, 87.30, 73.33, 72.70, 34.04, 30.19, 29.28, 24.03, 20.58, 20.39, 14.24, −1.45; MS *m*/*e* 264 (M^+), 249, 221, 73. Anal. Calcd for $C_{16}H_{28}OSi$: C, 72.66; H, 10.67. Found: C, 72.64; H, 10.78.

(9*R*,10*R*)-9-Ethynyl-13-methyl-9-(trimethylsilyl)-1,11,12-tetradecatrien-10-ol (66). The same procedure was repeated as described for **64** except that 3-(trimethylsilyl)-1,2,10-undecatriene (**58**, 1.03 g, 4.60 mmol) was used to prepare **62** for condensation with the conjugated allenic aldehyde **32** (0.40 g, 4.2 mmol) to afford 0.743 g (2.33 mmol, 56%) of **66** (*RR*/*SS*:*RS*/*SR* > 97:3) as a yellow liquid: IR (neat) 3553, 3310, 2092, 1968, 1640, 1247, 996, 910, 842 cm^{-1}; ^1H NMR (C_6D_6) δ 5.76 (1 H, ddt, J = 17.0, 10.1, and 6.7 Hz), 5.60 (1 H, d of septet, J = 4.9 and 3.0 Hz), 5.02 (1 H, dm, J = 17 and 1 Hz), 4.97 (1 H, dm, J = 10 and 1 Hz), 4.50 (1 H, t, J = 4.9 Hz), 1.96 (1 H, s), 1.96 (2 H, q, J = 6.7 Hz), 1.82−1.75 (3 H, m), 1.73 (OH, d, J = 4.9 Hz), 1.58 (1 H, m), 1.56 (3 H, d, J = 3.0 Hz), 1.53 (3 H, d, J = 3.0 Hz), 1.35−1.22 (6 H, br), 0.34 (9 H, s); ^{13}C NMR (C_6D_6) δ 199.64, 139.14, 114.47, 99.93, 92.85, 87.28, 73.30, 72.70, 34.12, 34.09, 30.84, 30.46, 29.38, 29.33, 27.08, 20.62, 20.40, −1.45; MS *m*/*e* 318 (M^+), 275, 73; HRMS calcd for $C_{20}H_{34}OSi - CH_3$ 303.2144, found 303.2132 ($M^+ - CH_3$).

(*Z*)-9-Ethynyl-13-methyl-1,9,11,12-tetradecatetraene (70). To a 250-mL round-bottomed flask containing 3.0 mL of a 1:1 mixture of pentane and Et_2O and 0.07 g of concentrated H_2SO_4 at −20 °C was added via cannula 0.10 g (0.31 mmol) of **66** in 3.0 mL of a 1:1 mixture of pentane and Et_2O at −20 °C. The reaction mixture was stirred vigorously at −20 °C to spread the concentrated H_2SO_4 over a large surface area on the bottom of the flask, and the progress of the reaction was monitored with TLC (Et_2O:hexanes = 1:5). After 30 min, the Peterson elimination was complete, and 10 mL of pentane at 0 °C was added. The reaction mixture was poured into a separatory funnel containing 10 mL of cold water. The aqueous layer was separated, and the organic layer was washed with cold water (3 × 10 mL). The combined aqueous layers were extracted with cold pentane (3 × 10 mL). The combined organic layers were then quickly filtered through a short column packed with silica gel and $MgSO_4$ by applying pressure at the top of the column with nitrogen, and the column was finally eluded with 10 mL of cold pentane. The filtrate was collected at −20 °C to keep cycloaromatization of **70** to a minimum. Pentane was then evaporated *in vacuo* to furnish 0.062 g (0.27 mmol, 87%) of **70** (*Z*:*E* = 97:3) as a colorless liquid: IR (neat) 3304, 2082, 1939, 1639, 989, 910 cm^{-1}; ^1H NMR (C_6D_6) δ 6.63 (1 H, d of septet, J = 10.9 and 2.9 Hz), 6.24 (1 H, dq, J = 10.9 and 1 Hz), 5.75 (1 H, ddt, J = 17.0, 10.3, and 6.6 Hz), 5.01 (1 H, dm, J = 17 and 2 Hz), 4.97 (1 H, dm, J = 11 and 1 Hz), 2.94 (1 H, s), 2.10 (2 H, t, J = 7.1 Hz), 1.92 (2 H, q, J = 7 Hz), 1.56 (6 H, d, J = 2.8 Hz), 1.52 (2 H, m), 1.3−1.1 (6 H, m). The isolated material contained ca. 2% of the cycloaromatized adduct **74**. Because cycloaromatization of **70** occurs relatively rapidly at room temperature, the isolated material was used immediately without additional measurements of the spectral data and the elemental composition.

7-(1-Methylethylidene)-1-(4-pentenyl)spiro[3.5]nona-5,8-diene (80). A solution of 0.062 g (0.27 mmol) of enyne−allene **70** in 880 mL of benzene was stirred at room temperature under a nitrogen atmosphere for 18 h. The reaction mixture was then divided into two portions of equal volume. The first portion was placed in a 1000-mL flask and then was concentrated *in vacuo* with a water aspirator to ca. 1 mL, and the concentrated solution was transferred into a 25-mL flask. The 1000-mL flask was rinsed with 10 mL of hexanes, and the hexanes solution was transferred to the 25-mL flask. The combined solutions were concentrated *in vacuo* with a water aspirator to ca. 1 mL and then briefly at 0.5 Torr. The residue was dissolved in 1 mL of C_6D_6 along with 0.031 g (0.22 mmol) of 1,4-dimethoxybenzene as an internal standard for the ^1H NMR integration. The yield of **80** (36%) was determined by comparing the integrations of the signal of the aromatic hydrogens of 1,4-dimethoxybenzene at δ 6.74 with that of the olefinic hydrogen of **80** at δ 6.64. In addition, the reaction mixture was found to contain 3% of the cycloaromatized adduct **74**. The second portion was likewise concentrated, and a small amount of **80** was isolated by HPLC (silica/hexanes): ^1H NMR (C_6D_6) δ 6.64 (1 H, dd, J = 10.3 and 2.2 Hz), 6.47 (1 H, dd, J = 10.0 and 2.1 Hz), 5.99 (1 H, dd, J = 10.3 and 1.8 Hz), 5.72 (1 H, ddt, J = 17.0, 10.3, and 6.9 Hz), 5.67 (1 H, dd, J = 10 and 2 Hz), 4.98 (1 H, dm, J = 17 and 2 Hz), 4.94 (1 H, dm, J = 10 and 1 Hz), 2.12 (1 H, quintet, J = 8 Hz), 1.95−1.75 (5 H, m), 1.66 (3 H, s), 1.64 (3 H, s), 1.61 (1 H, m), 1.5−1.2 (4 H, m); ^{13}C NMR (C_6D_6) δ 139.16, 135.29, 129.93, 126.23, 123.99, 122.58, 114.45, 48.13, 45.70, 34.17, 33.96, 31.85, 26.62, 23.33, 20.03, 19.97; MS *m*/*e* 228 (M^+), 213, 185; HRMS calcd for $C_{17}H_{24}$ 228.1878, found 228.1888.

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Supporting Information Available: Synthetic procedures for **16**−**19**, **23**, **25**, **33**, **39**, **40**, **45**−**48**, **63**, **65**, **67**−**69**, **71**, and **77**−**79** and ^1H and/or ^{13}C NMR spectra of **4**, **8**, **10**, **12**, **16**−**19**, **22**−**25**, **31**, **33**, **34**, **40**, **45**, **47**, **48**, **53**, **54**, **63**−**71**, and **77**−**80** (74 pages). See any current masthead page for ordering and Internet access instructions.

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