anthracene recovered was 54%. No endoperoxide was obtained.

γ-Irradiation of 9,10-diphenylanthracene (V) in O_2-purged benzene (2.7 mg/mL) was carried out for 18 h. On column chromatography no oxidation products were obtained.[14] When 2 mg/mL of 9,10-diphenylanthracene endoperoxide in benzene was γ-irradiated, it was seen by UV that V was produced in 24% yield after 8 h.

9-Methylanthracene Dimer. On photolysis of 0.1 g/mL of II in benzene at 0–20 °C under N_2 for 6 h, the white precipitate amounted to 21%. Recrystallization from benzene gave white crystals (mp 250–252 °C, lit.[26] mp >250 °C) of low solubility in organic solvents. Anal. ($C_{30}H_{24}$) C, H.

γ-Irradiation of II in benzene (20 mg/mL) was carried out under N_2 for 20 h. No dimer could be isolated. When 2 mg of dimer and 7 mL of benzene were sealed under N_2 and γ-irradiated, UV showed production of II in 38% yield after 6 h.

Quenching Experiments with Bis(2-butene-2,3-dithiolato)nickel(II) (XII) and β-Carotene. Complex XII was prepared by using the literature procedure.[27] Solutions of I in benzene (7.1 mg/mL) containing varying amounts of XII were purged with O_2 while photolyzed at 25 °C for periods of 6 min. It was seen by NMR spectroscopy that 0.02 mg/mL of XII quenched 50% of the reaction. In γ experiments, no quenching was observed with 0.02 mg/mL or 0.06 mg/mL of XII. When 0.06 mg/mL of XII in oxygenated benzene was γ-irradiated for short time periods, the solution lost its blue-violet color; the visible spectrum showed complete disappearance of XII (λ_{max} 770 nm). To this γ-irradiated solution was added 7.1 mg/mL of I; photolysis of this mixture showed no quenching effect.

Benzene solutions (0.05 mg/mL) of IV containing varying amounts of β-carotene were photolyzed with O_2 purging, with naphthacene loss monitored spectroscopically (λ 475 nm). β-Carotene addition of 0.001 mg/mL effected 50% quenching. γ Experiments showed no quenching by 0.005 mg/mL of β-carotene. Spectroscopy (λ 459 nm) showed destruction of β-carotene on γ-irradiation for short times.

(26) R. Calas and R. Lalande, *Bull. Soc. Chim. Fr.*, 763 (1959).

(27) G. N. Schrauzer and V. P. Mayweg, *J. Am. Chem. Soc.*, **87**, 1483 (1965).

Cooligomerizations of 3-Substituted 1,5-Hexadiynes with Bis(trimethylsilyl)acetylene Catalyzed by Cobalt. A General Synthesis of Tricyclic Ring Systems from Acyclic Precursors[1]

Raymond L. Funk[2] and K. Peter C. Vollhardt*[3]

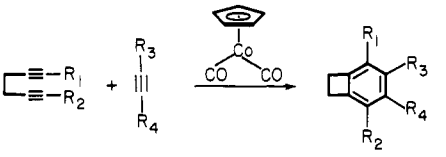
Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. *Received January 4, 1980*

Abstract: A one-step synthesis of polycycles is described which utilizes a $CpCo(CO)_2$-catalyzed cooligomerization of substituted 1,5-hexadiynes with bis(trimethylsilyl)acetylene solvent to produce intermediate benzocyclobutenes which may be subsequently or concomitantly ring opened to furnish intermediate *o*-xylylenes. The latter dienes react intermolecularly with solvent to yield ultimately 2,3,6,7-tetrakis(trimethylsilyl)naphthalene (**6**), substrate to a variety of electrophiles. Intramolecular trapping by appended dienophiles results in the formation of tricyclic systems containing ortho-bis-silylated benzenes and a variety of heteroatoms via exo transition states leading to trans ring fused compounds. Only in one case, **31**, was a significant proportion of the cis isomer observed. Protodesilylation may be achieved with acid to give the parent systems. In the case of **17** containing an aldehyde as a dienophile the cobalt-catalyzed cyclization results in ketal **22**. A general synthetic entry into 3-alkylated 1,5-hexadiynes was found via the in situ generation of 1,3,6-trilithio-1,5-hexadiyne.

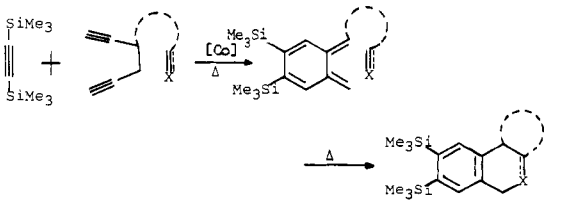
Benzocyclobutenes **1** have in the last decade been shown to be versatile building blocks in polycycle synthesis by virtue of their propensity to thermally open the four-membered ring to generate *o*-xylylenes **2**, reactive enophiles in the Diels–Alder reaction. When

the four-membered ring bears a dienophile carrying side chain, intramolecular cycloaddition furnishes a tricyclic system often with good regio- and stereoselectivity. This synthetic method, first discovered by Oppolzer,[4] has recently been exploited by several groups in the construction of natural products.[5] Despite advances in approaches aimed at improving the general availability of benzocyclobutenes the most serious drawback of the above methodology has been the relative difficulty of constructing variably substituted members of the series by simple and effective reactions. We had some time ago suggested[6] as a possible solution

Scheme I



Scheme II



(1) Taken in part from the Ph.D. Thesis of R. L. Funk, University of California, Berkeley, 1978.

(2) Regents' Intern Fellow, 1975–1978.

(3) Fellow of the Alfred P. Sloan Foundation, 1976–1980; Camille and Henry Dreyfus Teacher-Scholar, 1978–1983.

(4) W. Oppolzer, *J. Am. Chem. Soc.*, **93**, 3833, 3834 (1971); W. Oppolzer and K. Keller, *ibid.*, **93**, 3837 (1971).

(5) For reviews, see R. L. Funk and K. P. C. Vollhardt, *Chem. Soc. Rev.*, in press; K. P. C. Vollhardt, *Ann. N.Y. Acad. Sci.*, **333**, 241 (1980); W. Oppolzer, *Angew. Chem.*, **89**, 10 (1977); *Angew. Chem., Int. Ed. Engl.*, **16**, 10 (1977); *Synthesis*, 793 (1978); T. Kametani, *Pure Appl. Chem.*, **51**, 747 (1979); T. Kametani and K. Fukomoto, *Heterocycles*, **8**, 519 (1977); *Synthesis*, 319 (1976).

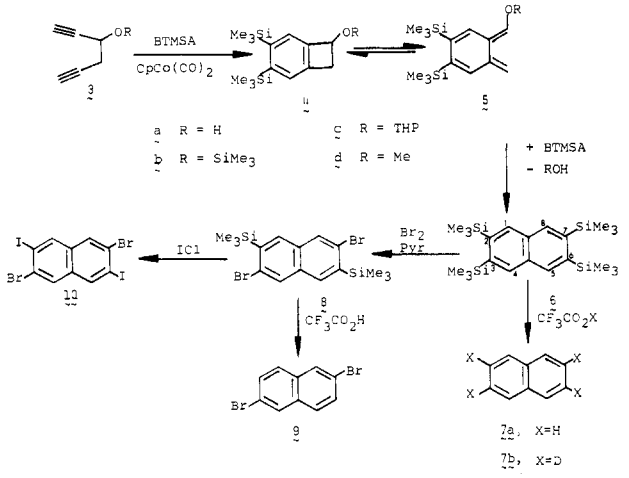
(6) R. L. Hillard III and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **99**, 4058 (1977).

0002-7863/80/1502-5245$01.00/0

to this problem the application of a transition metal catalyzed approach in which alkynes are cyclized to benzene derivatives.[7] Extension of this reaction to 1,5-hexadiynes was made possible by the finding that $(Cp)(Co)(CO)_2$ ($Cp = \eta^5$-C_5H_5) in contrast to other metals[8] acts as an excellent cooligomerization catalyst with terminal and substituted alkynes.[6] Best yields are realized when bis(trimethylsilyl)acetylene (BTMSA),[6] bis(trimethylsilyl)propyne,[9] or other alkyl trimethylsilylalkynes[9] are used as the cooligomerization partners, due to their (presumably sterically dictated) inability to autocyclize. When these monoynes are used as solvents, the diyne may be added slowly using syringe pump techniques under high-dilution conditions enabling good chemoselectivity. In this way, for example, 4,5-bis(trimethylsilyl)-benzocyclobutene is obtained in 68% yield.[6,10,11] The ready stepwise displacement of the trimethylsilyl groups in ortho-bis-substituted benzocycloalkenes[6,11] allows access to a large number of derivatives. Thus, with an efficient and simple synthetic entry into this class of compounds in hand, it appeared attractive to view 1,5-hexadiynes as precursors to *o*-xylylenes, trappable by dienophiles in situ inter- or intramolecularly to give more complex ring systems. This report deals with our successful attempts in this area which have led to the rapid chemo-, regio-, and stereospecific construction of polycycles from acyclic precursors.[12]

Results and Discussion

Intermolecular Trapping of in Situ Generated *o*-Xylylenes. Benzocyclobutenes with alkoxy substituents on the cyclobutene ring are subject to opening of the four-membered ring at temperatures above 100 °C.[13] Therefore, it was felt that 1,5-hexadiyn-3-ol (**3a**)[14a] would lead to *o*-xylylene **5a** during the acetylene



cooligomerization, the latter in turn trappable by the excess BTMSA employed. However, exposure of **3a** to the oligomerization conditions led only to an intractable polymeric mixture possibly resulting from thermal dehydration of **3a** to the unstable 1,5-hexadiyn-3-enes.[14b] Treatment of **3a** with trimethylsilyl chloride in pyridine afforded the trimethylsilyl ether **3b** in excellent yield (92%). Cooligomerization of diyne **3b** with BTMSA produced a single crystalline compound (30% yield) which displayed only two NMR absorptions at δ 7.96 and 0.46 in 1:9 ratio. The structure of the tetrakis(trimethylsilyl)naphthalene (**6**) is consistent with these, other spectral, and the analytical data.[15] This compound is presumably formed by trapping *o*-xylylene **5a** with BTMSA followed by aromatization either during the reaction or on chromatographic purification. The ethers **3c** and **3d** gave similar results.

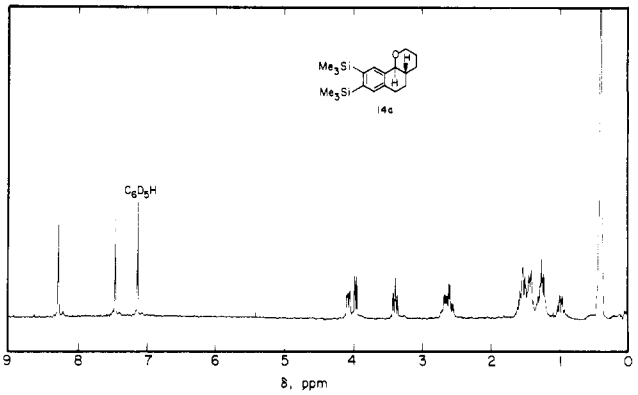


Figure 1. The 360-MHz NMR spectrum of **14a** in C_6D_6.

The versatility of the *o*-bis(trimethylsilyl) aromatic unit in organic transformations as applied to **6** serves to provide chemical proof for its structure as well as to demonstrate its usefulness as a precursor to other substituted naphthalenes. For example, treatment with an excess of CF_3CO_2H yields naphthalene (**7a**) quantitatively; CF_3CO_2D cleanly results in 2,3,6,7-tetradeuterionaphthalene (**7b**) in 95% yield. Bromination (2 equiv) can be clearly followed by NMR spectroscopy and proceeds via the monobromo derivative exclusively to the sterically and electronically dictated 2,6-dibromo isomer **8** in 89% yield. Protodesilylation of **8** gives 2,6-dibromonaphthalene (**9**) identical with authentic material.[17] Treatment of **8** with iodine monochloride (2 equiv) converts it into the dibromodiiodonaphthalene **10**. The remarkable selectivity in electrophilic substitutions of **6** indicates that by proper choice and application of electrophiles a large variety of complex substituted naphthalenes might become available.[18]

We next turned our attention to the intramolecular variant of the synthetic Scheme II. The 1,5-hexadiyn-3-ol **3a** was chosen as a starting point for the synthesis of several model compounds with attached carbon chains containing potential dienophiles introduced into the molecule by Williamson ether syntheses. The labile 1-alkoxy-substituted benzocyclobutenes[13] resulting from cooligomerization of the alkoxy-substituted diynes were expected to be prone to four-membered-ring opening followed by intramolecular Diels–Alder trapping of the intermediate *o*-xylylenes.

Alkylation of the sodium salt of **3a**, formed from NaH in THF, with 5-iodo-1-pentene gave 3-(4-pentenyloxy)-1,5-hexadiyne (**11a**) in good yield (70%). Slow addition of the diyne **11a** to refluxing BTMSA containing catalytic amounts of $CpCo(CO)_2$ followed by chromatographic purification afforded a single naphthopyran

(7) C. W. Bird, "Transition Metal Intermediates in Organic Synthesis", Academic Press, New York, 1967, Chapter 1; F. L. Bowden and A. B. P. Lever, *Organomet. Chem. Rev.*, **3**, 227 (1968); W. Hübel in "Organic Synthesis via Metal Carbonyls", Vol. I, I. Wender and P. Pino, Eds., Wiley, New York, 1968, Chapter 2; P. M. Maitlis, *Pure Appl. Chem.*, **30**, 427 (1972); L. P. Yur'eva, *Russ. Chem. Rev. (Engl. Transl.)*, **43**, 48 (1974); S. Otsuka and A. Nakamura, *Adv. Organomet. Chem.*, **14**, 245 (1976); R. S. Dickson and P. J. Fraser, *ibid.*, **12**, 323 (1974); E. Müller, *Synthesis*, 761 (1974); K. P. C. Vollhardt, *Acc. Chem. Res.*, **10**, 1 (1977).

(8) $(C_6H_5CN)_2PdCl_2$, $[(C_6H_5)_3P]_4Pt$, $[(C_6H_5)_3P]_2Ni(CO)_2$, $Co_2(CO)_8$, $[(C_6H_5)_3P]_3RhCl$, $TiCl_4$–R_3Al: K. P. C. Vollhardt, unpublished observations.

(9) E. R. F. Gesing, J. A. Sinclair, and K. P. C. Vollhardt, *J. Chem. Soc., Chem. Commun.*, 286 (1980).

(10) The yield of this compound may be improved to 68% from the value quoted in ref 6 by using more catalyst (ca. 30 mol %) and faster addition times of diyne (20 h). These conditions speed up cooligomerization and decrease the amount of subsequent cycloaddition of the *o*-xylylene to BTMSA.

(11) W. G. L. Aalbersberg, A. J. Barkovich, R. L. Funk, R. L. Hillard III, and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **97**, 5600 (1975).

(12) A preliminary description of parts of this work has appeared: R. L. Funk and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **98**, 6755 (1976); *J. Chem. Soc., Chem. Commun.*, 833 (1976).

(13) T. Kametani, M. Kajiwara, T. Takahashi, and K. Fukumoto, *Tetrahedron*, **31**, 949 (1975).

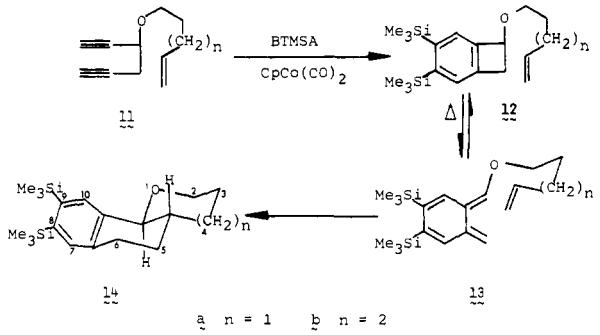
(14) (a) F. Sondheimer, Y. Amiel, and Y. Gaoni, *J. Am. Chem. Soc.*, **84**, 270 (1962); (b) W. H. Okamura and F. Sondheimer, *ibid.*, **89**, 5991 (1967).

(15) The spectral characteristics of **6** reflect the marked effect of substitution by four bulky trimethylsilyl groups: steric deshielding[16a] of the proton magnetic resonances and bathochromic shifts and increased extinction coefficients of the electronic absorptions.[16b]

(16) (a) W. Adcock, B. D. Gupta, T. C. Khor, D. Doddrell, and W. Kitching, *J. Org. Chem.*, **41**, 751 (1976); (b) D. Seyferth, D. R. Blank, and A. B. Evnin, *J. Am. Chem. Soc.*, **89**, 4793 (1967).

(17) J. Paviot and J. Hoarau, *J. Chim. Phys. Phys.-Chim. Biol.*, **64**, 1415 (1967).

(18) See, for example, L. A. Levy, presented at the 175th National Meeting of the American Chemical Society, Anaheim, Calif., March 13–17, 1978, Abstracts, No. ORGN 200.

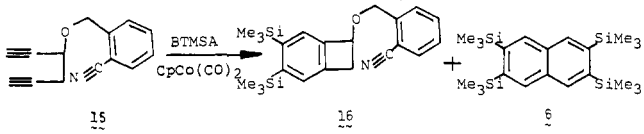


14a. The structure of **14a** is in accord with its spectral characteristics, in particular the 360-MHz NMR spectrum (Figure 1). Two sharp singlets of equal intensity in the aromatic region suggested that the compound was a single isomer. Furthermore, the C-10b proton exhibits a sharp doublet at δ 3.97 with a coupling constant of 9.5 Hz, consistent with the trans stereochemistry of the BC ring junction. The fact that this coupling is slightly lower than that observed in a typical trans-fused decalin (11–12 Hz) can be explained by the known tendency of electronegative atoms such as oxygen to reduce vicinal coupling constants.[19] The equatorial C-2 hydrogen at δ 4.07 (br d, J = 11 Hz) is deshielded relative to the axial C-2 hydrogen at δ 3.38 (ddd, J = 13, 11, 2 Hz), which is consistent with the known tendency of equatorial hydrogens to show, on the average, chemical shifts 0.6 ppm downfield from their axial counterparts.[19] The coupling patterns of these two protons are consistent with the expected two small couplings (J_{eq-eq}, J_{eq-ax}) and one large coupling (J_{gem}) for the equatorial C-2 hydrogen, and two large couplings (J_{ax-ax}, J_{gem}) and one small (J_{ax-eq}) for the axial C-2 hydrogen.

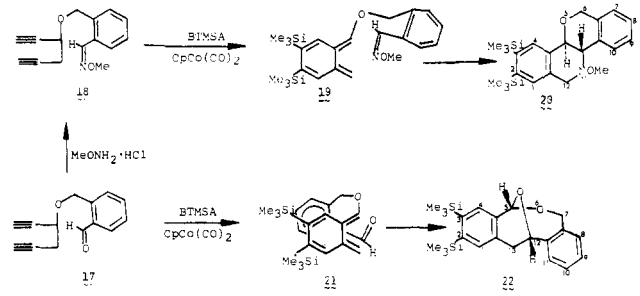
The stereospecific formation of the *trans*-naphthopyran **14a** implied that the reaction proceeded via the exo transition state **13a**. It is not entirely obvious why exo addition is favored, but it will be seen that the difference in activation energies for the exo and endo transition states is small.

The cocyclization of the homologous 3-(5-hexenyloxy)-1,5-hexadiyne (**11b**) was not nearly as selective. At least three different products were formed which indicated that not only had exo additions in *o*-xylylene **13b** taken place, but also endo and perhaps regioisomeric addition of the olefin. Moreover, a considerable amount (18%) of tetrakis(trimethylsilyl)naphthalene (**6**) was produced via competitive intermolecular trapping of *o*-xylylene **13b** by BTMSA followed by loss of hex-5-en-1-ol.

Our next concern was to determine whether the cobalt catalyst was compatible with dienophiles other than a carbon–carbon double bond. Alkylation of the sodium salt of **3a** with commercially available *o*-(bromomethyl)benzonitrile furnished **15** (96%). Exposure of **15** to the cobalt-catalyzed cyclization conditions gave benzocyclobutene **16** (28%) and naphthalene **6** (18%)



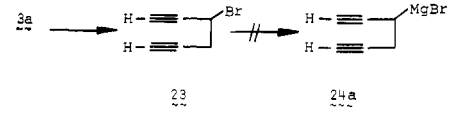
but none of the desired cycloadduct. This contrasts with Oppolzer's finding that nitriles add to *o*-xylylenes intramolecularly.[20] Apparently, intermolecular cycloaddition of the *o*-xylylene resulting from **16** with solvent BTMSA is more favored than the intramolecular cycloaddition with the nitrile group. This may be due to a combination of two factors: the nitrile group is known to be a very poor dienophile[21] and models indicate that the proper orientation required for cycloaddition is quite strained. Therefore, we decided to convert the nitrile group into a more reactive dienophile, an oxime ether. Oppolzer[20] and Kametani[5,22] had previously shown that imines and oxime ethers reacted efficiently with *o*-xylylenes. Reduction of the nitrile **15** with diisobutylaluminum hydride gave the aldehyde **17** (74%), which was treated with methoxyammonium chloride to produce the oxime ether **18** (81%). Cyclization of **18** led to the isolation of the crystalline



tetrahydroisoquinoline **20** (45%) and the naphthalene **6** (18%). The trans stereochemistry of the cycloadduct **20** was firmly established in both the 60- and 360-MHz NMR spectra. The C-4b proton resonance appears as a doublet at δ 5.41 (J = 10 Hz) and the C-10b proton resonance as a doublet at δ 4.18 (J = 10 Hz). A decoupling experiment verified the mutual coupling between these two protons. The trans stereochemistry again implicates exo transition state **19** in the cycloaddition.

In contrast to the straightforward cyclization of oxime ether **18**, the aldehyde **17** cyclized in a completely different manner. Along with naphthalene **6** (14%) we isolated a new crystalline compound to which we assign the structure **22** (49%) based on spectral data, particularly the NMR absorptions. The distinguishing feature of this spectrum was the sharp singlet at δ 5.90 which is not consistent with the 11-oxo compound analogous to **20**. Rather the low-field resonance and absence of coupling are consistent with the C-5 proton in **22**. Further supporting resonances at δ 5.07 (a triplet, the C-12 hydrogen), 5.11 and 4.70 (each a doublet, the diastereotopic C-7 hydrogens), and 3.04 (a doublet, the accidentally isochronous C-13 hydrogens) confirmed the assigned structure. Assuming that the C-5 and C-12 hydrogens are cis to one another as in **22** (the isomeric trans structure is highly strained), one is led to conclude that the regioisomeric endo addition of the aldehyde to the *o*-xylylene as in **21** has taken place to give a bridged rather than an annelated product. A favorable dipolar interaction between the alkoxy-substituted diene and the polarized carbonyl function may be responsible for the outcome of this cycloaddition.

The viability of the synthetic approach outlined in Scheme II appeared demonstrated by the above examples. However, generality was lacking since only 3-alkoxy-1,5-hexadiynes had been employed as *o*-xylylene precursors. Functionalization of 1,5-hexadiynes at the 3 position, in particular alkylation at that position, required further investigation. To this end, 3-bromo-1,5-hexadiyne (**23**) was prepared in fair yield by treating the tosylate of 1,5-hexadiyn-3-ol with LiBr in Me_2SO (54% from **3a**). Attempts to form the Grignard reagent **24a** from **23**, were, however, unsuccessful, even when employing "highly reactive" magnesium metal,[23] prepared by reducing $MgCl_2$ with potassium, and bromide **23** was recovered unchanged.



Therefore an alternative approach to 3-substituted 1,5-hexadiynes was sought. Scheinmann and co-workers[24] had reported

(19) L. M. Jackman and S. Sternhell, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed., Pergamon Press, Elmsford, N.Y., 1969.

(20) W. Oppolzer, *Angew. Chem.*, **84**, 1108 (1972); *Angew. Chem., Int. Ed. Engl.*, **11**, 1031 (1972).

(21) S. B. Needleman and M. C. Chang Kuo, *Chem. Rev.*, **62**, 405 (1962); Yu. A. Arbuzov, *Russ. Chem. Rev.* (*Engl. Transl.*), **33**, 407 (1964); Yu. A. Titov, *ibid.*, **31**, 267 (1962).

(22) T. Kametani, J. Kajiwara, T. Takahashi, and K. Fukumoto, *J. Chem. Soc., Perkin Trans. 1*, 737 (1975).

(23) R. D. Rieke, *Top. Curr. Chem.*, **59**, 1 (1975).

(24) S. Bhanu and F. Scheinmann, *J. Chem. Soc., Perkin Trans. 1*, 1218 (1979).

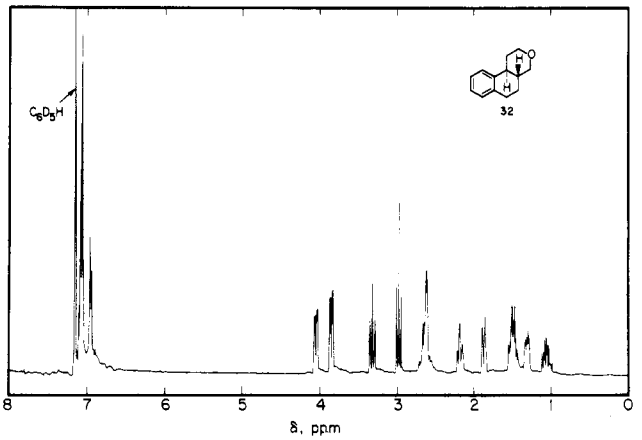


Figure 2. The 360-MHz NMR spectrum of **32** in C_6D_6.

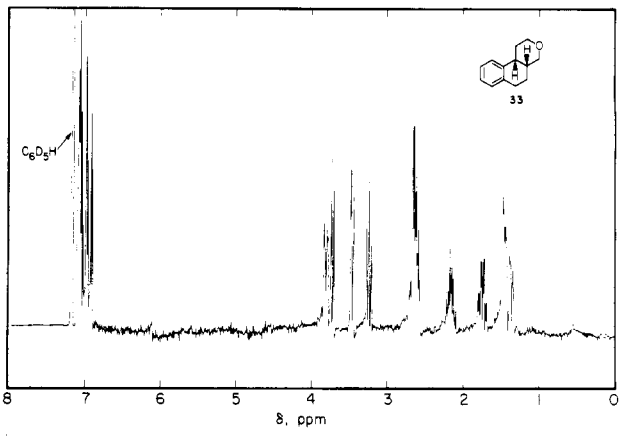
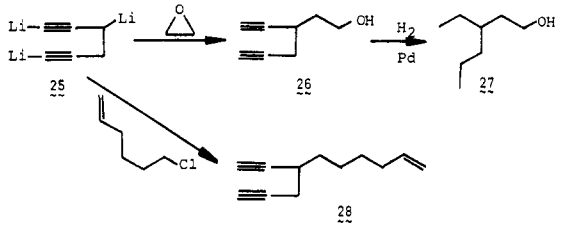


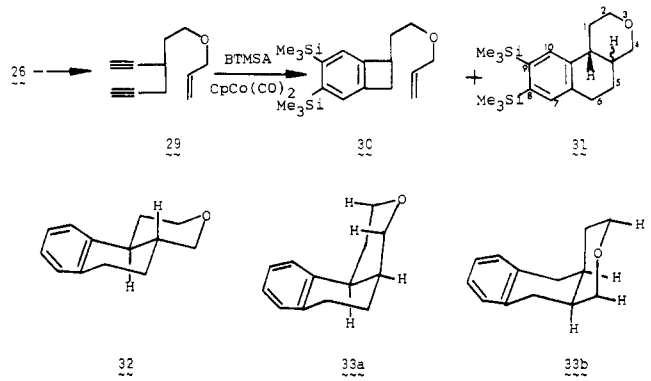
Figure 3. The 360-MHz NMR spectrum of **33** in C_6D_6.

that 1,3-dilithioacetylides may be obtained by treating a terminal alkylacetylene with butyllithium (2 equiv) and that these dianions could be regiospecifically alkylated at the 3 position with an alkyl halide (1 equiv). Indeed, treatment of 1,5-hexadiyne with butyllithium (3 equiv) and TMEDA (1 equiv) generated the trilithio compound **25**, which was regiospecifically monoalkylated at the 3 position using ethylene oxide to give after protonation the hexynol **26** in good yield (65%). Hydrogenation of **26** afforded the branched octanol **27**, which was a single compound by gas chromatography. More importantly, no 1-octanol was observed which would have formed if **25** had been alkylated at the terminal position and the resulting alcohol hydrogenated. Treatment of **25** with 6-iodohex-1-ene gave mostly 1,11-dodecadiene. Evidently, transmetalation to give 6-lithiohex-1-ene took place, which is alkylated by 6-iodohex-1-ene. Alkylation with 6-chlorohex-1-ene, however, proceeded to the functionalized 1,5-hexadiyne **28** in good yield (84%).



25 26 27 28

Having solved the problem of synthesizing 3-alkyl-substituted 1,5-hexadiynes we turned our attention to their use in polycycle synthesis. Alkylation of the sodium salt of alcohol **26** with allyl bromide gave the ether **29** in high yield (86%). Cooligomerization of **29** with BTMSA catalyzed by $CpCo(CO)_2$ afforded the benzocyclobutene **30** (52%) and the naphthopyrans **31** (41%). The

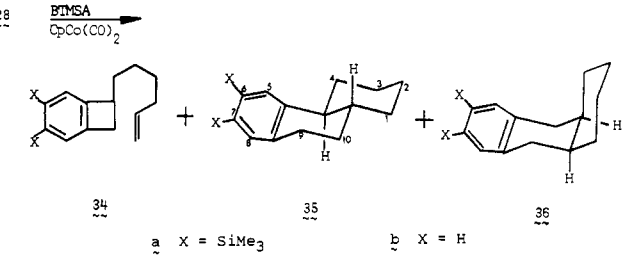


29 30 31

32 33a 33b

benzocyclobutene **30** could be converted to its cyclized isomer **31** in excellent yield (93%) by refluxing in decane. Unlike the previous examples, it appeared from the NMR signals in the aromatic region that the naphthopyran **31** was a mixture of cis and trans isomers. Protodesilylation of **31** gave an oil which by gas chromatography revealed a separable mixture (1:4) of the two isomers. The major isomer was assigned the trans stereochemistry on the basis of the 360-MHz ^1H NMR spectrum (Figure 2). The C-10b proton resonance at δ 2.18 is a broad doublet of doublets with two large (J = 12, 12 Hz) couplings and one small coupling (broadening) as would be expected for this proton (two J_{ax-ax}, one J_{ax-eq}). Therefore, the J_{10b-4a} coupling constant is 12 Hz and the major isomer must be the *trans*-naphthopyran **32**. The other resonances in the spectrum are in complete agreement with this assignment. One would expect the C-2 and C-4 protons (α to the oxygen) to be the most deshielded of the nonaromatic protons and in turn of these four the two equatorial ones should be the most deshielded.[19] The C-2 equatorial proton resonates at δ 4.05 and its splitting pattern (br dd, J = 11, 4 Hz) is consistent with the expected one large (J_{gem}) and two small (J_{eq-ax}, J_{eq-eq}) couplings. The C-4 equatorial proton resonates at δ 3.85 and its coupling pattern (dd, J = 12, 4 Hz) is consistent with one large (J_{gem}) and one small (J_{eq-ax}) coupling. The axial C-2 proton at δ 3.32 has the expected coupling pattern (ddd, J = 13, 11, 2 Hz) that would arise from two large (J_{gem}, J_{ax-ax}) and small (J_{ax-eq}) couplings. Finally, the C-4 axial proton at δ 2.97 is split (dd, J = 12, 11 Hz) as expected with two large (J_{ax-ax}, J_{gem}) couplings. The benzylic C-6 protons are an unresolved multiplet at δ 2.62.

The minor isomer is assigned the *cis*-naphthopyran structure **33** in analogy to our findings in the cyclization of **28** leading to the isomeric octahydrophenanthrene isomers (vide infra). Unfortunately, the usually diagnostic C-10b proton is masked in the 360-MHz NMR spectrum (Figure 3) by the two benzylic C-6 protons (complex multiplet at δ 2.65). However, this appears to be typical, since one encounters the same situation in the 360-MHz NMR spectrum of authentic *cis*-octahydrophenanthrene **36b**



34 35 36

a X = $SiMe_3$ b X = H

(three-proton multiplet at δ 2.70; see Experimental Section). The ethereal C-2 and C-4 proton resonances and splitting patterns are not only consistent with structure **33** but also indicate the presence of **33b** as the preferred conformer. The higher field absorptions (δ 3.46, 3.25) are again assigned to the two axial protons (vide supra), and the lower field signals (δ 3.81, 3.73) to the equatorial protons. If **33a** were to be the preferred conformer, then the axial C-2 proton should have two large (J_{gem}, J_{ax-ax}) and one small (J_{ax-eq}) couplings and the axial C-4 proton would be expected to exhibit two large couplings (J_{gem}, J_{ax-ax}). In **33b**, on the other hand, the axial C-2 proton should have a coupling pattern similar to that of **33a**, but the axial C-4 proton should have only one large (J_{gem}) and one small (J_{ax-eq}) coupling. It is the latter situation

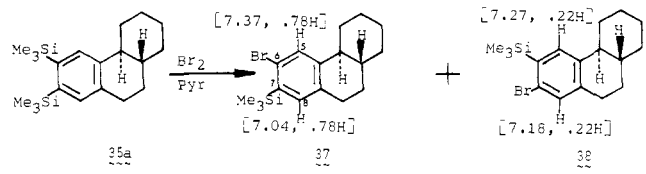
which is observed in the axial C-4 proton at δ 3.46 (br dd, J = 12, 3 Hz) and the axial C-2 proton at δ 3.25 (ddd, J = 12, 12, 3 Hz).

The finding that cyclization of **29** results in the formation of cis and trans isomers **32** and **33** has a close analogy in the literature. Thus, a nitrogen analogue to **30** was reported by Oppolzer to give a 12:87 cis:trans mixture of intramolecular cycloadducts.[25]

To elucidate the stereochemical outcome of the cyclization reaction in an all-carbocyclic case and provide chemical correlation of the products with known octahydrophenanthrenes, **28** was subjected to the cooligomerization conditions. Benzocyclobutene **34a** (60%) and *trans*-octahydrophenanthrene **35a** (22%) were formed, shown later to be contaminated with a trace amount (<5%) of the cis isomer **36a**. Refluxing pure **34a** in decane gave the cycloadduct **35a** containing the same amount of cis isomer **36a** in excellent yield (97%). The stereochemistry was initially assigned on the basis of the 360-MHz ^{1}H NMR spectrum. The aromatic singlets at δ 7.80 and 7.52 are of nearly equal intensity, indicating that within the sensitivity of ^{1}H NMR a single isomer had been formed. The diagnostic C-4a proton resonance at δ 2.25 has the expected splitting pattern (br dd, J = 12, 12 Hz) resulting from two large couplings (two J_{ax-ax}) and one small coupling (J_{ax-eq}). One of the large splittings (12 Hz) is due to coupling of the protons on C-4a–10a, thus proving the assigned stereochemistry. The coupling pattern and chemical shift of the C-4a proton resonance in **35a** are very similar to the corresponding proton resonance in naphthopyran **32**. Interestingly, the equatorial C-4 proton resonates at lower field (δ 2.57, br dd, J = 12.5, 3 Hz) than the tertiary benzylic C-4a proton. The assignment of this absorption to this proton was confirmed by an irradiation experiment which removed the small coupling (J_{ax-eq}) in the C-4a proton resonance. Models indicate that the equatorial C-4 proton is nearly in the plane of the benzene ring where it would benefit the most from the deshielding effect of the diamagnetic anisotropy of the aromatic ring. Additionally, a sterically deshielding interaction with the C-5 proton (vide infra) is present.[29]

Protodesilylation of **35a** with trifluoroacetic acid gave the *trans*-octahydrophenanthrene **35b** in nearly quantitative yield (97%). Although **35b** appeared pure by gas chromatography (one peak), the ^{13}C NMR spectrum indicated otherwise. In addition to the 13 resonances (the C-6 and C-7 carbons are isochronous) observed for the *trans*-octahydrophenanthrene **35b**, nine trace (<5%) signals were observed which pointed to the presence of cis isomer **36b**.[26]

Having established the stereoselective formation of the trans isomer **35a**, we investigated briefly substitution of the trimethylsilyl groups by electrophiles other than proton. The bromination of **35a** in CCl_4 was monitored by NMR spectroscopy and the reaction stopped after 1 equiv of bromine had been consumed. Two unequal pairs (78:22; see **37** and **38**) of aromatic singlets indicated that two isomers had been formed with some regioselectivity. The

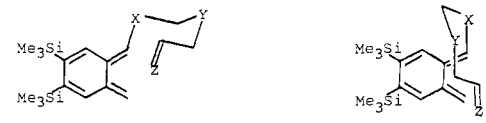


35a **37** **38**

major isomer was tentatively assigned to be 6-bromo-7-trimethylsilyloctahydrophenanthrene (**37**).[29]

The most downfield aromatic proton of the two isomers should be the C-5 proton which is ortho to a bromine atom and exposed to the "bay region" effect as in **37**. Conversely, the most upfield proton should be the C-8 proton next to a trimethylsilyl group as in **37**.[30] The NMR spectrum shows the predominance of these two signals; therefore, **37** should be the major isomer.[31]

Several comments are in order with respect to the products described in this paper. First, the stereochemistry of the new ring junction is almost always exclusively trans.[32] A cobalt-"catalyzed" cis–trans isomerization was ruled out by exposure of *cis*-octahydrophenanthrene **36b** to simulated reaction conditions (1,5-hexadiyne, $CpCo(CO)_2$, in refluxing BTMSA) and its quantitative recovery. This observation suggests that, when there are no other constraints on the system, the exo transition state **39** representing a structure formed by conrotatory outward opening of the four-membered ring in the intermediate benzocyclobutene is more favored than its endo counterpart **40**.



39 **40**

Second, regioisomers of the cycloadducts observed occur when added flexibility in the transition state to *o*-xylylene cycloaddition is available (cf. **11b** → **14b**) or when electronic effects operate (cf. **17** → **22**).

Third, intermediate benzocyclobutenes may be isolated only in the cases of the kinetically more stable, alkylated derivatives **30** and **34a**. Protodesilylation of **34a** with CF_3CO_2H followed by thermolysis in boiling decane results in **35b** and **36b** with no apparent change in the trans–cis isomer ratio, ruling out any unusual contribution of the trimethylsilyl groups and the cobalt catalyst to the relative stabilities of **39** and **40**.

It is clear from this work that 1,5-hexadiynes can be regarded as synthetic precursors to *o*-xylylenes. This new methodology provides a striking simplification of currently available routes to natural products via benzocyclobutenes. The attractive features include high yields, high stereoselectivity, and apparent control of aromatic ring substitution.

Experimental Section

NMR spectra were recorded on a Varian T-60, Hitachi Perkin-Elmer R-24B (60 MHz), a home-built 180-MHz instrument, and the 360-MHz instrument at the Stanford Magnetic Resonance Laboratory. Data are reported as follows: chemical shift, in parts per million downfield of internal tetramethylsilane (Me_4Si) (multiplicity, coupling constant(s),

(25) W. Oppolzer, *Tetrahedron Lett.*, 1001 (1974).

(26) H. Christol, A. Gaven, Y. Pietrasanta, and J. L. Vernet, *Bull. Soc. Chim. Fr.*, 4510 (1971). The ^{13}C NMR spectrum of **36b** showed 13 distinct resonances, the chemical shifts of nine of which coincided with the observed trace signals in the ^{13}C NMR spectrum of **36a**. It is interesting to note that the C-4a ^{13}C-carbon resonance in *cis*-**36b** is upfield 4 ppm compared with the C-4a carbon resonance in *trans*-**35b**, in complete agreement with the trend found for the corresponding carbons in *cis*- and *trans*-decalin.[27] Presumably, the extra γ-gauche interactions are responsible for the greater shieldings in the cis isomers.[28] The *cis*-octahydrophenanthrene **36b** was equilibrated with the trans isomer by treatment with palladium on charcoal at 230 °C. The ^{13}C NMR spectrum revealed a 60:40 mixture of trans:cis isomers, a single peak by gas chromatography.

(27) E. Lippmaa and T. Pehk, *Eest; NSV Tead. Akad. Toim., Keem., Geol.*, **17**, 287 (1968).

(28) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, 1972.

(29) The C-5 protons in octahydrophenanthrenes are known to be deshielded by ca. 0.5 ppm relative to the C-8 protons because of the steric ("bay region") effect of the equatorial C-4 proton: W. Nagata, T. Terasawa, and K. Tori, *J. Am. Chem. Soc.*, **86**, 3746 (1964). In addition, protons ortho to bromine on an aromatic ring are shielded by 0.22 ppm (relative to benzene), whereas the meta protons are shielded by 0.13 ppm. Protons ortho and meta to trimethylsilyl groups are essentially unchanged relative to benzene.[30]

(30) (a) The spectrum of trimethylsilylbenzene shows a multiplet (δ 7.45–7.13) centered at δ 7.26 (CCl_4). (b) V. Bazant, M. Horak, and V. Chvalousky, "Organosilicon Compounds 3, Advances in Organosilicon Chemistry", Institute of Chemical Process Fundamentals, Czechoslovak Academy of Sciences, Prague, 1973.

(31) This regioselectivity is difficult to account for, but is in qualitative agreement with the finding that *p*-trimethylsilylethylbenzene brominates faster (by a factor of 1.4) than *p*-trimethylsilylisopropylbenzene in acetic acid: L. M. Stock and H. C. Brown, *Adv. Phys. Org. Chem.*, **1**, 35–154, 70–71 (1963).

(32) An alternative mechanism in which the benzocyclobutene opens by a conrotatory inward process to give an *o*-xylylene which undergoes cycloaddition via the endo mode could also account for the favored trans products. However, this mechanism seems unlikely in light of the fact that *o*-xylylenes with alkyl groups in the "inward" position undergo [1,5] sigmatropic hydrogen migrations in preference to cycloadditions: T. Kametani, M. Tsubuki, Y. Shiratori, Y. Kato, H. Nemoto, M. Ihara, K. Fukumoto, F. Satoh, and H. Inoue, *J. Org. Chem.*, **42**, 2672 (1977).

number of protons). The 360-MHz spectra were referenced to the C_6D_5H peak 7.18 ppm downfield from Me_4Si. The ^{13}C NMR spectra were obtained on a Nicolet TT-23 (25.14 MHz) instrument and chemical shifts are reported in parts per million downfield from Me_4Si referenced to the central peak of the deuteriochloroform triplet (77.0 ppm downfield from Me_4Si) or the central peak of the benzene triplet (128.0 ppm downfield from Me_4Si). Infrared absorption spectra were obtained on one of Perkin-Elmer Models 710A, 137, or 421, and were referenced to polystyrene (1601 cm^{-1}). Electronic spectra were recorded on a Cary 118 UV spectrometer in 95% ethanol. Mass spectra and elemental analyses were provided by the Mass Spectral Service and the Microanalytical Laboratory, respectively, of the University of California, Berkeley. Melting points were determined in open Pyrex capillary tubes on a Thomas-Hoover Unimelt apparatus. Melting points and boiling points are uncorrected. Gas chromatography was performed on a Varian Aerograph Model 920 with a 10 ft × $^1/_4$ in. glass 20% UCW98 on Chromosorb DMCS-AW 60/80 (conditioned at 210 °C) column. All chromatography was carried out on E. M. Reagents silica gel (70–230 mesh ASTM), and all preparative TLC on commercial silica gel plates (Merck) or on plates prepared with E. M. Reagents silica gel PF-254 containing $CaSO_4$ and fluorescent indicator. Solvents were dried by distillation over an appropriate drying agent under a nitrogen atmosphere and stored under nitrogen and over Linde molecular sieves (4A). All reactions involving organometallic or moisture-sensitive reagents were performed under dry nitrogen. Vacuum-line operations were carried out on a high-vacuum (mercury diffusion) multiple-line apparatus. Solvents and reagents to be used in the presence of $CpCo(CO)_2$ were degassed on the vacuum line and purged with dried, air-free (MnO tower) nitrogen. Benzocyclobutenes were dissolved in decane and degassed by this method before thermolysis. Evaporation of solvents was performed first at aspirator pressure on a Büchi rotary evaporator and then at ca. 0.05 Torr at room temperature until a constant weight was obtained.

3-Trimethylsilyloxy-1,5-hexadiyne (3b). 1,5-Hexadiyn-3-ol (**3a**,[14a] 0.94 g, 10 mmol) and trimethylsilyl chloride (1.77 mL, 14.2 mmol) were added to pyridine (9.4 mL) and stirred for 2 h at room temperature. The mixture was diluted with ether (125 mL), washed with ice-cold 3 M H_2SO_4 (18.8 mL), saturated $NaHCO_3$, and brine, and dried ($MgSO_4$). Evaporation of the solvent followed by distillation afforded a colorless liquid (1.52 g, 92%): bp 55–56 °C (9 mm); IR (neat) 3300, 2950, 2130, 1420, 1255, 1100, and 930 cm^{-1}; NMR (CCl_4) δ 4.38 (dt, J = 2.0, 6.8 Hz, 1 H), 2.49 (dd, J = 6.8, 2.5 Hz, 2 H), 2.33 (t, J = 2.5 Hz, 1 H), 0.17 (s, 9 H).

Anal. Calcd for $C_9H_{14}OSi$: C, 65.00; H, 8.49. Found: C, 64.99; H, 8.61.

2,3,6,7-Tetrakis(trimethylsilyl)naphthalene (6). 3-Trimethylsilyloxy-1,5-hexadiyne (**3b**, 1590 mg, 9.58 mmol) and $CpCo(CO)_2$ (30 μL, 0.24 mmol) were dissolved in BTMSA (6 g, 35 mmol) and added to refluxing BTMSA (4 g, 24 mmol) over a period of 93 h. The mixture was then refluxed for another 24 h and cooled, and all the volatiles were vacuum transferred off to give recovered BTMSA usable as such in further cyclizations. Chromatography of the orange residue on silica gel (150 g, petroleum ether as eluent) gave a white, crystalline solid (1195 mg, 30%): R_f 0.50 (petroleum ether as eluent); mp 232–233 °C; IR (CCl_4) 2990, 1410, 1260, 1110, and 800 cm^{-1}; m/e (rel intensity) 416 (M^+, 19.84), 401 (17.07), 385 (16.77), 313 (15.38), 73 (100); NMR (CCl_4) δ 7.96 (s, 4 H), 0.46 (s, 36 H); λ_{max} (95% EtOH) 244 nm (log ϵ 5.15), 256 sh (4.14), 273 (4.84), 284 sh (3.75), 292 sh (3.54), 311 sh (2.79), 320 (2.91), 326 (2.92), and 334 (3.16).

Anal. Calcd for $C_{22}H_{40}Si_4$: C, 63.38; H, 9.67. Found: C, 63.54; H, 9.57.

Naphthalene (7a). Tetrakis(trimethylsilyl)naphthalene (**6**, 42 mg, 0.10 mmol) was dissolved in CCl_4 (0.5 mL) and CF_3CO_2H (0.5 mL) and stirred at room temperature for 12 h. The mixture was diluted with ether, poured onto saturated $NaHCO_3$, washed with $NaHCO_3$ and brine, and dried. Evaporation gave a white solid (13 mg, 100%) which had identical spectral properties when compared to authentic naphthalene: mp 81–82 °C; IR (CCl_4) 2950, 1570, 1510, 1125, 1005, and 780 cm^{-1}; NMR (CCl_4) δ 7.77 (m, 4 H), 7.43 (m, 4 H).

2,3,6,7-Tetradeuterionaphthalene (7b). The tetrasilylnaphthalene **6** (37 mg, 0.089 mmol) was dissolved in CCl_4 (0.5 mL) and CF_3CO_2D (0.5 mL) and stirred at room temperature for 12 h. The mixture was worked up in the same manner as in the above reaction with CF_3CO_2H to give a white solid (11.1 mg, 95%): mp 80–82 °C; m/e (rel intensity) 132 (M^+, 100), 105 (12.02), 66 (12.88); IR (CCl_4) 2945, 1570, 1510, and 780 cm^{-1}; NMR (CCl_4) δ 7.80 (s, 4 H).

2,6-Dibromo-3,7-bis(trimethylsilyl)naphthalene (8). The tetrasilylnaphthalene **6** (104 mg, 0.25 mmol) and pyridine (40.6 μL, 0.50 mmol) were dissolved in CCl_4 (0.75 mL). The mixture was cooled in an ice bath, bromine (52 μL, 1 mmol) was added, and the solution was stirred for 3 h at room temperature. The mixture was diluted with ether, washed with saturated $Na_2S_2O_3$, saturated $NaHCO_3$, and brine, and dried ($MgSO_4$). Evaporation gave a white solid which crystallized from ether as long, white needles (95 mg, 89%): R_f 0.55 (petroleum ether as eluent); mp 213–215 °C; m/e (rel intensity) 432 (M^+ + 2, 12.57), 430 (M^+, 25.11), 428 (M^+ – 2, 11.48), 416 (100), 73 (94); IR (CCl_4) 2995, 1550, 1250, 1105, 830 cm^{-1}; NMR (CCl_4) δ 7.93 (br s, 2 H), 7.60 (br s, 2 H), 0.50 (s, 18 H).

Exact Mass. Calcd for $C_{16}H_{22}Si_2{}^{79}Br^{79}Br$: 427.9628. $C_{16}H_{22}Si_2{}^{79}Br^{81}Br$: 429.9608. Found: 427.9627; 429.9590.

2,6-Dibromonaphthalene (9). Bis(trimethylsilyl)dibromonaphthalene (**8**, 25.0 mg, 0.058 mmol) was desilylated as described for **7a** to give a white solid (15.8 mg, 95%): mp 156–160 °C (lit. 159–160 °C[17]); m/e (rel intensity) 288 (M^+ + 2, 4.61), 286 (M^+, 9.69), 284 (M^+ – 2, 5.00), 126 (10.21), 57 (13.52), 18 (100); IR (CCl_4) 2990, 1250, 1110, 1055, 885, and 850 cm^{-1}; NMR (CCl_4) δ 7.94 (m, 2 H), 7.57 (m, 4 H).

Exact Mass. Calcd for $C_{10}H_6{}^{79}Br^{79}Br$: 283.8837. $C_{10}H_6{}^{79}Br^{81}Br$: 285.8822. Found: 283.8833; 285.8805.

2,6-Dibromo-3,7-diiodonaphthalene (10). To a solution of dibromobis(trimethylsilyl)naphthalene **8** (75 mg, 0.17 mmol) in $CHCl_3$ (1 mL) was added ICl (36 μL, 0.70 mmol). The mixture was stirred for 20 h and then diluted with CH_2Cl_2, washed with saturated $Na_2S_2O_3$, saturated $NaHCO_3$, and brine, dried ($MgSO_4$), and evaporated to give a white solid (83 mg, 88%) which crystallized from CS_2: mp >210 °C dec; m/e (rel intensity) 540 (M^+ + 2, 2.66), 538 (M^+, 5.72), 536 (M^+ – 2, 3.19), 263 (24.89), 183 (17.34), 149 (87.65), 43 (100); IR (CS_2) 2900, 1450, 1250, 1110, 935, 845, and 760 cm^{-1}; NMR (CS_2) δ 8.17 (s, 2 H), 7.90 (s, 2 H).

Anal. Calcd for $C_{10}H_4Br_2I_2$: C, 22.33; H, 0.75. Found: C, 22.46; H, 1.24.

3-(4-Pentenyloxy)-1,5-hexadiyne (11a). Sodium hydride (72 mg, 1.2 mmol, 50% oil dispersion) was weighed into a three-necked flask and washed with dry petroleum ether (5 mL). THF (1 mL) was added followed by 1,5-hexadiyn-3-ol (**3a**, 100 mg, 1.06 mmol) in THF (1 mL). After the evolution of hydrogen had ceased, 5-iodo-1-pentene (215 mg, 1.1 mmol) was added in THF (1 mL) and stirred at 45 °C for 15 h. The mixture was then partitioned between ether and water. The organic layer was washed with water and brine, dried ($MgSO_4$), and evaporated to give a yellow oil. The oil was then chromatographed on a preparative thin layer plate (ether–petroleum ether (5:95) as eluent) to give a colorless oil (120 mg, 70%): R_f 0.43 (ether–petroleum ether (5:95) as eluent); m/e (rel intensity) 162 (M^+, 0.32), 105 (6.42), 95 (14.46), 65 (100), 55 (96.33); IR (neat) 3290, 2950, 2140, 1645, 1330, and 1050 cm^{-1}; NMR (C_7D_8) δ 5.77 (m, 1 H), 5.00 (m, 2 H), 3.97 (dt, J = 2.0, 6.5 Hz, 1 H), 3.8–3.0 (m, 2 H), 2.43 (dd, J = 6.5, 2.5 Hz, 2 H), 2.27–1.2 (m, 6 H).

3-(5-Hexenyloxy)-1,5-hexadiyne (11b). The alkoxide generated from **3a** (376 mg, 4 mmol) was alkylated with 6-iodo-1-hexene (1144 mg, 5.44 mmol) in the same manner as for **11a**. Evaporation of the solvent and chromatography gave a colorless oil (613 mg, 87%): R_f 0.46 (ether–petroleum ether (5:95) as eluent); m/e (rel intensity) 176 (M^+, 0.10), 95 (4.22), 91 (6.38), 83 (68.02), 67 (21.15), 55 (100); IR (neat) 3300, 2940, 2120, 1640, 1420, 1330, 1100, and 910 cm^{-1}; NMR (C_6D_6) δ 5.70 (m, 1 H), 4.93 (m, 2 H), 3.97 (dt, J = 2.0, 6.5 Hz, 1 H), 3.8–3.0 (m, 2 H), 2.45 (dd, J = 6.5, 2.5 Hz, 2 H), 2.27–1.2 (m, 8 H).

***trans*-8,9-Bis(trimethylsilyl)-3,4,4a,5,6,10b-hexahydro-2*H*-naphtho[1,2-*b*]pyran (14a).** The pentenyloxyhexadiyne **11a** (120 mg, 0.74 mmol) in degassed octane (7 mL) was cyclized with BTMSA (2.1 g, 12.3 mmol) in refluxing octane (7 mL) as in the synthesis of **6**. The brown residue was chromatographed on two preparative TLC plates (two developments with ether–petroleum ether (1:99) as eluent) to give an oil (147 mg, 60%): m/e (rel intensity) 332 (M^+, 25.19), 317 (100), 259 (21.61), 147 (5.33), 73 (29.37); IR (neat) 2970, 1580, 1255, 1100, and 830 cm^{-1}; NMR (360 MHz, C_6D_6) δ 8.29 (br s, 1 H), 7.47 (br s, 1 H), 4.07 (br d, J = 11 Hz, 1 H), 3.97 (d, J = 9.5 Hz, 1 H), 3.38 (ddd, J = 13, 11, 2 Hz, 1 H), 2.67 (ddd, J = 17, 11.5, 6 Hz, 1 H), 2.57 (ddd, J = 17, 6, 1.5 Hz, 1 H), 1.64–1.00 (m, 7 H), 0.49 (s, 18 H).

Exact Mass. Calcd for $C_{19}H_{32}OSi_2$: 332.1992. Found: 332.1972.

Cooligomerization of Diyne 11b with BTMSA. The diyne **11b** (570 mg, 3.24 mmol) was cyclized as described in the synthesis of **6**. The reddish brown residue was chromatographed on silica (100 g, ether–petroleum ether (1:99) as eluent) to give tetrakis(trimethylsilyl)naphthalene (**6**, 240 mg, 18%) and a mixture of three compounds (A–C) which were further purified by preparative TLC. Compound A: NMR (CCl_4) δ 7.63 (br s, 1 H), 7.30 (br s, 1 H), 5.30 (m, 2 H), 4.53 (br s, 1 H), 3.5–1.0 (m, 11 H), 0.30 (s, 18 H); m/e (rel intensity) 346 (M^+, 1.98), 331 (3.91), 147 (14.40), 97 (11.42), 73 (100). Compound B: NMR (CCl_4) δ 7.17 (br s, 1 H), 6.97 (br s, 1 H), 5.40 (m, 2 H), 4.50 (m, 1 H), 3.5–1.0 (m, 11 H), 0.27 (s, 18 H); m/e (rel intensity) 346 (M^+, 1.34), 279 (6.80), 263 (16.73), 205 (17.40), 91 (14.75), 82 (27.78), 73 (100). Compound C: NMR (CCl_4) δ 7.70 (br s, 1 H), 7.27 (br s, 1 H), 5.37 (m, 1 H), 4.00 (m, 2 H), 3.5–1.0 (m, 11 H), 0.27 (s, 18 H); m/e (rel intensity) 346 (M^+,

7.23), 331 (25.36), 315 (23.27), 147 (10.79), 83 (10.33), 73 (100).

2-[[(1-Ethynyl-3-butynyl)oxy]methyl]benzonitrile (15). Sodium hydride (336 mg, 7 mmol, 50% oil dispersion) was weighed into a flask and washed with dry petroleum ether (5 mL). THF (10 mL) was added followed by 1,5-hexadiyn-3-ol (**3a**, 470 mg, 5 mmol) in THF (5 mL). After the evolution of hydrogen had ceased, 2-(bromomethyl)benzonitrile (1176 mg, 6.0 mmol) in THF (5 mL) was added and the mixture was stirred at 45 °C for 12 h. Ether–water workup gave an orange oil. Chromatography on silica gel (50 g, ether–petroleum ether (18:82) as eluent) gave recovered 2-(bromomethyl)benzonitrile (140 mg, 0.71 mmol) and a colorless oil (1000 mg, 96%): R_f 0.19 (ether–petroleum ether (1:4) as eluent); *m/e* (rel intensity) 209 (M^+, 0.53), 170 (37.29), 130 (12.47), 116 (100), 89 (43.07); IR (neat) 3300, 2900, 2240, 2100, 1455, and 1090 cm^{-1}; NMR (C_6D_6) δ 7.06 (m, 4 H), 4.85 (d, J = 13 Hz, 1 H), 4.48 (d, J = 13 Hz, 1 H), 4.05 (dt, J = 2.0, 7.0 Hz, 1 H), 2.50 (dd, J = 7.0, 2.5 Hz, 2 H), 2.20 (d, J = 2.0 Hz, 1 H), 1.87 (t, J = 2.5 Hz, 1 H).

Anal. Calcd for $C_{14}H_{11}NO$: C, 80.36; H, 5.29. Found: C, 79.86; H, 5.43.

2-[[(4,5-Bis(trimethylsilyl)benzocyclobutenyl)oxy]methyl]benzonitrile (16). The benzonitrile **15** (600 mg, 2.87 mmol) in degassed octane (8 mL) was reacted as in the preparation of **6**. Silica gel chromatography (50 g, ether–petroleum ether (6:94) as eluent) gave **6** (210 mg, 18%) and **16** as a white solid (310 mg, 28%): mp 90–92 °C; R_f 0.14 (ether–petroleum ether (5:95) as eluent); *m/e* (rel intensity) 379 (M^+, 8.00), 167 (21.17), 149 (63.17), 105 (70.67), 73 (40.17); IR (CCl_4) 2950, 2225, 1400, 1250, and 860 cm^{-1}; NMR (CCl_4) δ 7.77 (br s, 1 H), 7.43 (m, 5 H), 5.00 (br s, 1 H), 4.63 (br s, 2 H), 3.0 (m, 2 H), 0.43 (s, 9 H), 0.38 (s, 9 H).

Anal. Calcd for $C_{22}H_{29}Si_2ON$: C, 68.17; H, 7.54; N, 3.61. Found: C, 68.82; H, 7.57; N, 3.58.

2-[[(1-Ethynyl-3-butynyl)oxy]methyl]benzaldehyde (17). Diisobutylaluminum hydride (2.74 g, 20% in hexane, 3.86 mmol) in toluene (2 mL) was added to a −78 °C solution of the benzonitrile **15** (745 mg, 3.56 mmol) in toluene (7 mL) over a period of 30 min. The mixture was stirred for 1 h at −78 °C and partitioned between ether and 1 M HCl and the aqueous layer was extracted with ether. The combined ether extracts were washed with 1 M HCl, $NaHCO_3$, and brine and dried ($MgSO_4$). Evaporation of the ether gave a white solid which crystallized from ether–petroleum ether (560 mg, 74%): R_f 0.29 (ether–petroleum ether (1:4) as eluent); mp 48.5–49 °C; *m/e* (rel intensity) 212 (M^+, 0.01), 135 (100), 118 (39.59), 105 (18.00), 91 (52.97), 77 (33.36); IR (CCl_4) 3300, 2990, 1690, 1600, 1200, and 1090 cm^{-1}; NMR (C_6D_6) δ 10.06 (s, 1 H), 7.56 (m, 2 H), 7.19 (m, 2 H), 5.19 (d, J = 14 Hz, 1 H), 4.78 (d, J = 14 Hz, 1 H), 4.13 (dt, J = 2, 6.5 Hz, 1 H), 2.53 (dd, J = 6.5, 2.5 Hz, 2 H), 2.27 (d, J = 2 Hz, 1 H), 1.96 (t, J = 2.5 Hz, 1 H).

2-[[(1-Ethynyl-3-butynyl)oxy]methyl]benzaldehyde *O*-Methyloxime (18). To benzaldehyde **17** (300 mg, 1.41 mmol) in pyridine (7 mL) was added molecular sieves (0.5 g, 4A) followed by methoxyamine hydrochloride (133.6 mg, 1.60 mmol). The mixture was stirred for 90 min at room temperature and then the pyridine was vacuum transferred. The residue was dissolved in ether, washed with water, 3 M HCl, $NaHCO_3$, and brine, and dried (Na_2SO_4). Evaporation of the ether gave a colorless oil (275 mg, 81%): R_f 0.45 (ether–petroleum ether (1:4) as eluent); *m/e* (rel intensity) 241 (M^+, 1.20), 210 (7.73), 164 (100), 148 (24.59), 132 (53.67), 116 (60.59), 77 (47.01); IR (neat) 3300, 2940, 2120, 1600, 1080, and 1050 cm^{-1}; NMR (C_6D_6) δ 8.47 (s, 1 H), 7.80 (dd, J = 5, 3 Hz, 1 H), 7.20 (m, 3 H), 4.87 (d, J = 12 Hz, 1 H), 4.47 (d, J = 12 Hz, 1 H), 4.12 (dt, J = 2, 6.5 Hz, 1 H), 3.90 (s, 3 H), 2.51 (dd, J = 6.5, 2.5 Hz, 2 H), 2.38 (d, J = 2 Hz, 1 H), 2.02 (t, J = 2.5 Hz, 1 H).

2,3-Bis(trimethylsilyl)-11-methoxy-4b,10b,11,12-tetrahydro-6*H*-[2]benzopyrano[4,3-*c*]isoquinoline (20). The *O*-methyloxime **18** (241 mg, 1.12 mmol) was cyclized as in the synthesis of **6**. Silica gel chromatography (80 g, ether–petroleum ether (5:95) as eluent) gave **6** (85 mg, 18%) and a white solid which crystallized from petroleum ether to give **20** (207 mg, 45%): R_f 0.32 (ether–petroleum ether (5:95) as eluent); mp 170–171 °C; *m/e* (rel intensity) 411 (M^+, 13.66), 380 (41.20), 262 (19.02), 205 (13.01), 111 (20.22), 83 (42.19), 73 (100); IR (KBr) 2950, 1360, 1260, 1090, and 840 cm^{-1}; NMR (C_6D_6, 360 MHz) δ 8.37 (s, 1 H), 8.0 (d, J = 7.5 Hz, 1 H), 7.45 (s, 1 H), 7.20 (dd, J = 7.5, 7.5 Hz, 1 H), 7.06 (dd, J = 7.5, 7.5 Hz, 1 H), 6.66 (d, J = 7.5 Hz, 1 H), 5.41 (d, J = 10 Hz, 1 H), 4.94 (d, J = 18.5 Hz, 1 H), 4.88 (d, J = 18.5 Hz, 1 H), 4.32 (d, J = 18 Hz, 1 H), 4.18 (d, J = 10 Hz, 1 H), 4.13 (d, J = 18 Hz, 1 H), 3.37 (s, 3 H), 0.44 (s, 9 H), 0.43 (s, 9 H).

Anal. Calcd for $C_{23}H_{33}NO_2Si_2$: C, 67.10; H, 8.08; N, 3.40. Found: C, 66.88; H, 8.12; N, 3.59.

2,3-Bis(trimethylsilyl)-5,7,12,13-tetrahydro-5,12-epoxydibenzo[*c*,*g*]oxonin (22). The benzaldehyde **17** (250 mg, 1.18 mmol) with toluene (3 mL) as cosolvent was reacted as in the preparation of **6**. Chromatography on silica gel (100 g, ether–petroleum ether (5:95) as eluent) gave **6** (69 mg, 14%) and a yellow solid (187 mg, 49%) which crystallized from ether–methanol as colorless crystals of **22**: R_f 0.29 (ether–petroleum ether (5:95) as eluent); mp 115–116 °C; *m/e* (rel intensity) 382 (M^+, 38.50), 367 (23.46), 263 (35.85), 119 (100); IR ($CHCl_3$) 2950, 1250, 1100, 1035, and 835 cm^{-1}; NMR (C_6D_6, 360 MHz) δ 7.66 (s, 1 H), 7.47 (s, 1 H), 7.07 (dd, J = 8, 7 Hz, 1 H), 7.01 (dd, J = 8, 7 Hz, 1 H), 6.87 (br dd, J = 9, 7 Hz, 2 H), 5.90 (s, 1 H), 5.11 (d, J = 14 Hz, 1 H), 5.07 (t, J = 9 Hz, 1 H), 4.70 (d, J = 14 Hz, 1 H), 3.04 (d, J = 9 Hz, 2 H), 0.42 (s, 9 H), 0.38 (s, 9 H).

Anal. Calcd for $C_{22}H_{30}O_2Si_2$: C, 69.06; H, 7.90. Found: C, 69.22; H, 7.93.

3-Bromo-1,5-hexadiyne (23). To a solution of 1,5-hexadiyn-3-ol (**3a**, 824 mg, 8.8 mmol) in pyridine (20 mL) was added *p*-toluenesulfonyl chloride (3040 mg, 16 mmol) at 0 °C. The solution was kept at 0 °C overnight in a refrigerator and then lactic acid (1.34 mL) added. The solution was placed in the refrigerator for another 5 h and then partitioned between cold ether (50 mL) and cold 3 M HCl (90 mL). The aqueous layer was extracted with two more portions of ether and the combined ether extracts were washed with 3 M HCl, $NaHCO_3$, and brine and dried ($MgSO_4$). Evaporation of the ether left the crude tosylate, which was dissolved in Me_2SO (15 mL). Lithium bromide (1144 mg, 13.2 mmol) was added and the reaction temperature was increased to 70 °C over a period of 90 min. Aqueous ethereal workup and evaporation of the ether left a yellow oil which was distilled to give a colorless oil (754 mg, 54%): bp 50 °C (10 mm); *m/e* (rel intensity) 158 (M^+ + 1, 7.15), 156 (M^+ − 1, 7.48), 93 (10.35), 77 (100), 74 (13.37), 55 (35.96); IR (neat) 3290, 2975, 2140, 1410, 1235, 1160, 905, and 650 cm^{-1}; NMR (CCl_4) δ 4.50 (dt, J = 7, 2.5 Hz, 1 H), 2.91 (dd, J = 7, 2.5 Hz, 2 H), 2.58 (d, J = 2.5 Hz, 1 H), 2.06 (t, J = 2.5 Hz, 1 H).

Attempted Formation of Grignard Reagent 24a. To $MgCl_2$ (291 mg, 3.05 mmol) and KI (332 mg, 2 mmol) in dry THF (10 mL) was added potassium (23 mg, 6 mmol, weighed under mineral oil and washed with dry THF). The mixture was refluxed for 2.5 h, producing a dark gray, viscous solution, and then cooled to −65 °C. 3-Bromo-1,5-hexadiyne (**23**, 314 mg, 2 mmol) was added in THF (2 mL) and the solution temperature was allowed to rise to −10 °C. Injection of a sample onto the gas chromatograph showed no disappearance of bromide **23**. Ethylene oxide (0.396 mL, 8 mmol) was added and the mixture was allowed to stir at room temperature overnight. The mixture was poured onto saturated NH_4Cl; the ether layer was separated, washed with water and brine, and dried ($MgSO_4$). Evaporation of the ether left the bromide **23** (300 mg).

3-Ethynyl-5-hexyn-1-ol (26). To a cold (−30 °C) solution of butyllithium (184 mL, 460 mmol, 2.48 M in hexane) in THF (100 mL) in a three-necked flask equipped with an overhead stirrer and a cold-finger condenser was added tetramethylethylenediamine (23.1 mL, 150 mmol) followed by the syringe pump addition of 1,5-hexadiyne (11.9 g, 150 mmol) in THF (50 mL) over a period of 3 h. A white precipitate immediately formed which slowly disappeared to give a turquoise-green solution. After the addition was complete, stirring was continued at −20 °C until the white precipitate had completely disappeared (3–4 h). The solution was cooled to −65 °C and ethylene oxide (10 g, 230 mmol) was added via a cannula. The solution was allowed to warm to −10 °C, where it immediately turned to a bright yellow slush. THF (200 mL) was added, and the mixture was stirred for 3 h at −10 °C and then partitioned between ether and saturated NH_4Cl. Standard aqueous workup and distillation gave a colorless liquid (12.1 g, 65%): bp 105 °C (14 mm); *m/e* (rel intensity) 122 (M^+, 2.06), 104 (3.80), 103 (18.16), 94 (30.31), 91 (52.68), 77 (37.36), 53 (100); IR (neat) 3400, 3300, 2120, 1435, and 1050 cm^{-1}; NMR (CCl_4) δ 3.76 (br t, J = 7 Hz, 2 H), 3.33 (br s, 1 H), 2.70 (m, 1 H), 2.50 (d, J = 2 Hz, 1 H), 2.37 (t, J = 2 Hz, 1 H), 2.06 (dd, J = 6, 2 Hz, 2 H), 1.87 (m, 2 H).

Anal. Calcd for $C_8H_{10}O$: C, 78.65; H, 8.25. Found: C, 78.42; H, 8.20.

3-Ethylhexan-1-ol (27). The ethynylhexynol **26** (51 mg, 0.42 mmol) was dissolved in 95% ethanol (20 mL), palladium on charcoal (5 mg) was added, and the mixture was stirred underneath an atmosphere of hydrogen. After the uptake of H_2 had ceased (40 mL, 1.78 mmol), the mixture was filtered, diluted with ether, washed with water and brine, and dried ($MgSO_4$). Evaporation of the ether left a colorless liquid (48 mg, 88%). Gas chromatography (column temperature 155 °C) indicated a single compound with a lower retention time (7.6 min) than 1-octanol (9 min): *m/e* (rel intensity) 130 (M^+, 1.36), 112 (9.58), 84 (75.55), 83 (57.35), 55 (100); NMR (CCl_4) δ 3.49 (br t, J = 7 Hz, 2 H), 2.80 (br s, 1 H), 1.8–0.6 (m, 15 H).

4-Ethynyl-9-decen-1-yne (28). To a cold (−30 °C) solution of butyllithium (27 mL, 67.5 mmol, 2.5 M in hexane) in THF (20 mL) was added tetramethylethylenediamine (3.4 mL, 22.5 mmol) followed by the syringe pump addition of 1,5-hexadiyne (1755 mg, 22.5 mmol) in THF (5 mL) over a period of 3 h. After the addition was complete, the solution was stirred until the white precipitate had completely disap-

peared (3 h) to give a deep blue solution. The solution was cooled to −50 °C. 6-Chloro-1-hexene was added in THF (5 mL) in one portion, and the solution was allowed to warm to room temperature. After 1 h at room temperature the solution (now green with precipitate) was quenched with NH_4Cl and extracted with petroleum ether. The combined petroleum ether extracts were washed with water, NH_4Cl, $NaHCO_3$, and brine and dried (Na_2SO_4). Evaporation of the solvent left an oil which was distilled to give a colorless liquid (3030 mg, 84%): bp 80 °C (5 mm); *m/e* (rel intensity) 159 (1.82), 117 (38.24), 92 (96.13), 78 (100), 67 (32.14); IR (neat) 3300, 3100, 2950, 2125, 1640, 1000, and 910 cm^{-1}; NMR (CCl_4) δ 5.73 (m, 1 H), 5.00 (m, 2 H), 2.95–1.17 (m, 13 H).

Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 89.66; H, 10.26.

3-[2-(2-Propenyloxy)ethyl]-1,5-hexadiyne (29). Sodium hydride (102 mg, 2.1 mmol, 50% oil dispersion) was weighed into a flask and washed with dry petroleum ether (5 mL). THF (2 mL) was added followed by ethynylhexynol **26** (153 mg, 1.5 mmol) in THF (2 mL). After the evolution of hydrogen had ceased, allyl bromide (0.25 mL, 2.8 mmol) was added and the mixture was heated at 50 °C for 12 h. Standard workup with ether–water, evaporation of the solvent, and filtration through silica gel (15 g, ether–petroleum ether (5:95) as eluent) gave a colorless liquid (210 mg, 86%): IR (neat) 3295, 2950, 2140, 1645, and 1050 cm^{-1}; NMR (C_6D_6) δ 5.90 (m, 1 H), 5.17–4.83 (m, 2 H), 3.80 (m, 2 H), 3.47 (t, *J* = 7 Hz, 2 H), 2.67 (m, 1 H), 2.30 (d, *J* = 2 Hz, 1 H), 2.20 (t, *J* = 2 Hz, 1 H), 2.0–1.5 (m, 4 H).

***cis*- and *trans*-8,9-Bis(trimethylsilyl)-2,4,4a,5,6,10b-hexahydro-1*H*-naphtho[2,1-*c*]pyran (31).** The substituted 1,5-hexadiyne **29** (200 mg, 1.2 mmol) was reacted as in the synthesis of **6**. Chromatography on silica gel (75 g, ether–petroleum ether (1:99) as eluent) gave two major components: benzocyclobutene **30** (214 mg, 52%) as a colorless oil [*m/e* (rel intensity) 332 (M^+, 8.24), 317 (7.90), 286 (9.11), 230 (14.09), 147 (6.45), 73 (100); IR (neat) 2950, 1640, 1250, and 1100 cm^{-1}; NMR (C_6D_6, 360 MHz) δ 7.60 (s, 1 H), 7.53 (s, 1 H), 5.88 (m, 1 H), 5.28 (br d, *J* = 17 Hz, 1 H), 5.10 (br d, *J* = 10 Hz, 1 H), 3.87 (m, 2 H), 3.65 (m, 1 H), 3.47 (t, *J* = 6 Hz, 2 H), 3.30 (dd, *J* = 13, 10 Hz, 1 H), 2.78 (br d, *J* = 13 Hz, 1 H), 1.95 (m, 2 H), 0.43 (s, 9 H), 0.42 (s, 9 H)] and the *cis*- and *trans*-naphthopyrans **31** as a colorless oil (169 mg, 41%) [*m/e* (rel intensity) 332 (M^+, 25.10), 317 (59.69), 302 (47.88), 287 (100), 117 (30.92), 73 (37.61); IR (neat) 2975, 1260, 1110, and 840 cm^{-1}; NMR (CCl_4) δ 7.38 (br s, 0.80 H), 7.23 (v br s, 1.20 H), 4.2–3.0 (m, 4 H), 2.9–1.0 (m, 8 H), 0.36 (s, 18 H)].

Exact Mass. Calcd for $C_{19}H_{32}OSi_2$: 332.1974. Found: 332.1972.

The benzocyclobutene **30** (214 mg) was dissolved in degassed decane (50 mL) and refluxed for 30 h. Vacuum transfer of the decane left a yellow oil which was filtered through silica to give another portion of the naphthopyrans **31** (200 mg, 93%; 369 mg total, 90%).

***cis*- (33) and *trans*-2,4,4a,5,6,10a-Hexahydro-1*H*-naphtho[2,1-*c*]pyran (32).** The mixture of naphthopyrans **31** (150 mg, 0.45 mmol) was desilylated as shown in the preparation of **7a** to give a yellow oil (80 mg, 94%). Gas chromatography indicated two components (column temperature 202 °C, retention times of 31.2 and 33.8 min) in a ratio of 1:4. The mixture was separated by preparative GLC to give the minor, faster moving *cis*-naphthopyran **33**: *m/e* (rel intensity) 188 (M^+, 58.34), 157 (11.89), 143 (41.85), 129 (100), 115 (43.44), 58 (29.64); IR (neat) 2990, 1450, 1270, 1100, and 970 cm^{-1}; NMR (360 MHz, C_6D_6) δ 7.00 (m, 4 H), 3.81 (br dd, *J* = 12, 4 Hz, 1 H), 3.73 (d, *J* = 12 Hz, 1 H), 3.46 (dd, *J* = 12, 3 Hz, 1 H), 3.25 (ddd, *J* = 12, 12, 3 Hz, 1 H), 2.69 (m, 3 H), 2.17 (m, 1 H), 1.75 (m, 1 H), 1.40 (m, 3 H).

Exact Mass. Calcd for $C_{13}H_{16}O$: 188.1201. Found: 188.1198.

The second product was the major, slower moving *trans*-naphthopyran **32**: *m/e* (rel intensity) 188 (M^+, 83.94), 157 (53.87), 143 (88.71), 129 (100), 115 (62.53), 59 (49.49); IR (neat) 2995, 1450, 1275, 1100, 970, 880, and 765 cm^{-1}; NMR (360 MHz, C_6D_6) δ 7.02 (m, 4 H), 4.05 (br dd, *J* = 11, 4 Hz, 1 H), 3.85 (dd, *J* = 12, 4 Hz, 1 H), 3.32 (ddd, *J* = 13, 11, 2 Hz, 1 H), 2.97 (dd, *J* = 12, 11 Hz, 1 H), 2.62 (m, 2 H), 2.18 (br dd, *J* = 12, 12 Hz, 1 H), 1.87 (br d, *J* = 13 Hz, 1 H), 1.48 (m, 2 H), 1.32 (m, 1 H), 1.05 (m, 1 H).

Exact Mass. Calcd for $C_{13}H_{16}O$: 188.1201. Found: 188.1200.

***cis*- (36a) and *trans*-6,7-Bis(trimethylsilyl)-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (35a).** The ethynyldecenyne **28** (715 mg, 4.47 mmol) was cyclized as described for the synthesis of **6**. Chromatography on silica gel (250 g, petroleum ether as eluent) gave two major components: first *trans*-octahydrophenanthrene **35a** with <5% *cis*-octahydrophenanthrene **36a** (329 mg, 22%) as a colorless oil: R_f 0.44 (petroleum ether as eluent); *m/e* (rel intensity) 330 (M^+, 45.19), 315 (77.56), 299 (29.36), 149 (13.23), 131 (10.82), 111 (14.73), 97 (24.95), 73 (100); IR (neat) 2950, 1450, 1250, 1140, and 840 cm^{-1}; NMR (360 MHz, C_6D_6) δ 7.80 (s, 1 H), 7.52 (s, 1 H), 2.77 (m, 2 H), 2.57 (br dd, *J* = 12.5, 3 Hz, 1 H), 2.25 (br dd, *J* = 12, 12 Hz, 1 H), 1.98–0.94 (m, 10 H), 0.47 (s, 9 H), 0.46 (s, 9 H).

Anal. Calcd for $C_{20}H_{34}Si_2$: C, 72.65; H, 10.36. Found: C, 72.21; H, 10.32.

Second, the benzocyclobutene **34a** was obtained as a colorless oil (880 mg, 60%): R_f 0.41; *m/e* (rel intensity) 330 (M^+, 12.49), 315 (23.59), 299 (20.94), 227 (13.20), 131 (11.00), 73 (100); IR (neat) 3090, 2930, 1640, 1460, 1250, 1090, and 840 cm^{-1}; NMR (360 MHz, C_6D_6) δ 7.57 (s, 1 H), 7.52 (s, 1 H), 5.78 (m, 1 H), 5.00 (m, 2 H), 3.40 (ddd, *J* = 14, 10, 3 Hz, 1 H), 3.26 (dd, *J* = 14, 10 Hz, 1 H), 2.70 (dd, *J* = 14, 3 Hz, 1 H), 1.99 (m, 2 H), 1.88–1.05 (m, 6 H), 0.42 (s, 9 H), 0.40 (s, 9 H).

The benzocyclobutene **34a** (880 mg) was dissolved in degassed decane (70 mL) and refluxed for 30 h. Vacuum transfer of the solvent and filtration through silica gave another portion of the octahydrophenanthrenes **35a** and **36a** (856 mg, 97% conversion; 1186 mg total, 80%).

***cis*- (36b) and *trans*-1,2,3,4,4a,9,10,10a-Octahydrophenanthrene (35b).** The mixture of octahydrophenanthrenes **35a** and **36a** (220 mg, 0.67 mmol) was protodesilylated as shown in the preparation of **7a** to give a colorless oil (120 mg, 97%). Gas chromatography showed only one peak (column temperature, 215 °C; retention time, 22 min): *m/e* (rel intensity) 186 (M^+, 100), 158 (22.40), 143 (56.98), 129 (66.86), 117 (32.48), 104 (31.51), 91 (26.68); IR (neat) 2950, 2850, 1490, 1450, 1240, and 850 cm^{-1}; NMR (360 MHz, C_6D_6) δ 7.25 (d, *J* = 7.5 Hz, 1 H), 7.08 (m, 2 H), 7.00 (d, *J* = 6.5 Hz, 1 H), 2.70 (m, 2 H), 2.32 (br dd, *J* = 12.5, 3 Hz, 1 H), 2.13 (ddd, *J* = 12, 12, 3 Hz, 1 H), 1.83–0.92 (m, 10 H); ^{13}C NMR (C_6D_6) δ 140.65, 137.04, 129.32, 125.85, 125.77, 44.10, 40.92, 34.67, 31.32, 31.06, 30.25, 27.25, 26.65, plus trace signals (<5%) from the cis isomer **36b** at 142.22, 136.14, 40.54, 34.28, 32.14, 31.59, 29.83, 24.27, 21.94.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.73. Found: C, 90.25; H, 9.73.

Preparation and Thermolysis of 1-(5-Hexenyl)benzocyclobutene (34b). The benzocyclobutene **34a** (150 mg, 0.45 mmol) was desilylated as above to give a colorless oil (81 mg, 97%): NMR (CCl_4) δ 7.02 (m, 4 H), 5.67 (m, 1 H), 5.00 (m, 2 H), 3.6–3.4 (m, 3 H), 2.33–1.17 (m, 8 H). Refluxing in decane for 20 h gave an oil which by ^{13}C NMR spectral comparison was identical with the material described in the preceding experiment.

***cis*-1,2,3,4,4a,9,10,10a-Octahydrophenanthrene (36b).** The *cis*-octahydrophenanthrene **36b** was prepared according to the method of Christol et al.[26] and purified by preparative gas chromatography (column temperature, 215 °C; retention time, 22 min): NMR (360 MHz, C_6D_6) δ 7.07 (m, 4 H), 2.70 (m, 3 H), 1.90 (m, 2 H), 1.63 (m, 5 H), 1.38 (m, 4 H); ^{13}C NMR (C_6D_6) δ 142.22, 136.14, 128.95, 125.88, 125.82, 40.54, 34.28, 32.14, 31.59, 29.83, 26.45, 24.27, 21.94.

Isomerization of *cis*-Octahydrophenanthrene 36b. The *cis*-octahydrophenanthrene **36b** (0.6 mL) and 10% palladium on charcoal (300 mg) were heated in a sealed tube at 230 °C for 12 h. The components of the gas chromatographic peak with the same retention time as starting material were collected. The ^{13}C NMR of this material showed a 60:40 ratio of the *trans*-:*cis*-octahydrophenanthrene carbons (assuming equal relaxation times for analogous carbons).

***trans*-6-Bromo-7-trimethylsilyl- (37) and *trans*-7-Bromo-6-trimethylsilyl-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (38).** The (>95% pure) *trans*-bis(trimethylsilyl)octahydrophenanthrene (**35a**, 57 mg, 0.172 mmol) was dissolved in CCl_4 (0.6 mL) and added to an NMR tube. Pyridine (13.9 μL, 0.172 mmol) was added followed by bromine (17.8 μL, 0.34 mmol) and the reaction mixture was quickly placed in the NMR probe. The reaction was monitored by following the disappearance of the starting material's trimethylsilyl peak (δ 0.33) in the NMR spectrum and the appearance of the product's trimethylsilyl peak (δ 0.37) as well as the appearance of trimethylsilyl bromide (δ 0.59). After 80 min the reaction was complete (δ 0.36 and 0.59 peaks of equal height, complete disappearance of δ 0.33 peak). The reaction mixture was poured onto a saturated sodium thiosulfate solution and extracted with petroleum ether and the combined petroleum ether extracts were washed with thiosulfate, water, and brine and dried ($MgSO_4$). Evaporation of the petroleum ether left a yellow oil which was filtered through silica gel (10 g, petroleum ether as eluent) to give a colorless oil (54 mg, 93%): R_f 0.50 (petroleum ether as eluent); *m/e* (rel intensity) 338 (M^+, 30.07), 336 (M^+, 31.91), 323 (100), 321 (98.73), 243 (41.44), 241 (40.98), 129 (25.98), 73 (88.30); IR (neat) 2950, 1580, 1450, 1250, 1120, and 845 cm^{-1}; NMR (CCl_4) δ 7.37 (br s, 0.78 H), 7.27 (br s, 0.22 H), 7.18 (br s, 0.22 H), 7.04 (br s, 0.78 H), 2.90–1.10 (m, 14 H).

Exact Mass. Calcd for $C_{17}H_{25}Si^{79}Br$: 336.0909. $C_{17}H_{25}Si^{81}Br$: 338.0889. Found: 336.0902; 338.0877.

Acknowledgments. We wish to thank W. G. L. Aalbersberg, J. R. Fritch, A. Naiman, R. Nunlist, and E. S. Sternberg for assisting in the acquisition of high-field ^1H and ^{13}C NMR data. Stimulating discussions with Professors C. H. Heathcock, T.

Kametani, D. S. Noyce, and W. Oppolzer are also gratefully noted. Financial and material support was received from the National Science Foundation (CHE 7601783), the National Institutes of Health (GM22479), Cancer Research Funds of the University of California, Committee on Research, Chevron Research Co., Pressure Chemicals Co., and Silar Laboratories. The Stanford Magnetic Resonance Laboratory is supported by Grants NSF-GR 23633 and NIH-RR 00711.

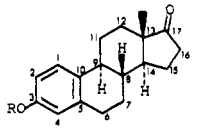
Transition-Metal-Catalyzed Alkyne Cyclizations. A Cobalt-Mediated Total Synthesis of *dl*-Estrone[1]

Raymond L. Funk[2] and K. Peter C. Vollhardt*[3]

Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. *Received January 4, 1980*

Abstract: A cobalt-catalyzed total synthesis of racemic steroids (including estrone **1**) is described based on the cooligomerization of substituted 1,5-hexadiyne **3** with monoalkynes. An unsuccessful strategy for the synthesis of starting material **3** via chloroethyl derivative **18** was abandoned in favor of a convergent synthesis via 3-(2-iodoethyl)-1,5-hexadiyne (**19**) on one hand and enol ether **20** on the other. Compound **3** reacted with BTMSA in the presence of $CpCo(CO)_2$ to give racemic 2,3-bis(trimethylsilyl)estratrienone (**24a**) via benzocyclobutenes **23**. Similarly, **3** cyclized with trimethylsilyl(methoxy)ethyne to furnish in low yield (via benzocyclobutene intermediates) steroids **24c,d**, the former providing *dl*-estrone methyl ether on protodesilylation. Estrone could be obtained with poor regiochemical control from ketal **33** by bromination, followed by conversion of the bromine moiety to a hydroxyl group. However, selective protodesilylation of **24a** at low temperatures to 3-trimethylsilylestratrienone (**24g**) followed by oxidative cleavage of the phenyl–silicon bond with $Pb(OOCCF_3)_4$ gave **1**: five steps from 2-methylcyclopentenone (21.5%) and six steps from 1,5-hexadiyne (15.1%). A slight improvement of yields is realized via cyclization of the ethylene ketal **29** (23.1 and 16.2%, respectively).

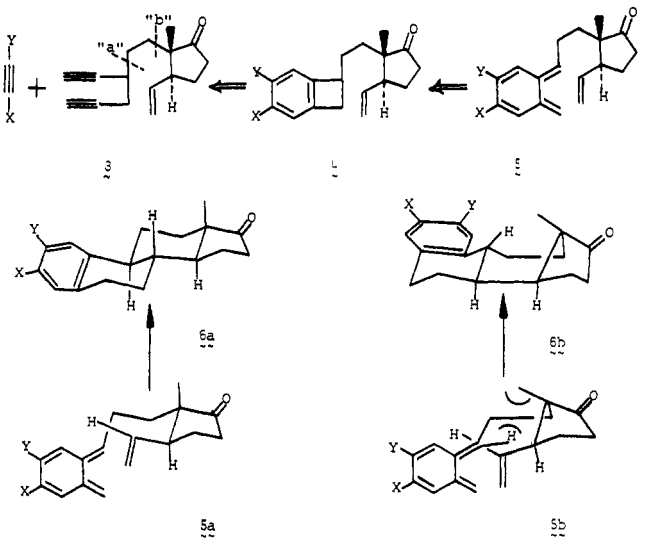
Estrone (**1**) constitutes a challenging synthetic target on which to measure the utility of novel methodology[4-6] and as a relay point en route to contraceptive drugs.[7,8] Of the many successful



1 R = H
2 R = Me

strategies the AD → ABCD[6] possibility has been exploited relatively infrequently. Rare examples are the Smith–Hughes synthesis employing a double condensation[6] and the Johnson–Bartlett approach utilizing a cationic olefin cyclization.[9] A retrosynthetic analysis of the estrone nucleus suggests another alternative in which the two central rings are constructed by an intramolecular Diels–Alder reaction of an intermediate *o*-xylylene **5** (Scheme I). Concurrent with and preceding our efforts in this field[10] several groups devised similar strategies to a variety of

Scheme I



steroids relying on the various ways available to construct precursors to *o*-xylylenes of type **5**.[11] Our approach to the steroid nucleus and ultimately **1** attempted to exploit a previously deveoped cobalt-catalyzed stereospecific one-step construction of tricyclic ring systems from acyclic precursors.[10,12]

Results and Discussion

Synthesis of Steroid Precursor Diyne 3. The highly stereoselective cobalt-catalyzed formation of trans-annelated polycycles,[12] particularly *trans*-1,2,3,4,4a,9,10,10a-octahydrophenanthrene, suggested the possibility of employing an intramolecular cycloaddition to an appropriate *o*-xylylene to construct what one might

(1) Taken in part from the Ph.D. Thesis of R. L. Funk, University of California, Berkeley, 1978.
(2) Regents' Intern Fellow, 1975–1978.
(3) Fellow of the Alfred P. Sloan Foundation, 1976–1980; Camille and Henry Dreyfus Teacher-Scholar, 1978–1983.
(4) L. F. Fieser and M. Fieser, "Steroids", Reinhold, New York, 1959.
(5) R. Wiechert, *Angew. Chem.*, **82**, 331 (1970); *Angew. Chem., Int. Ed. Engl.*, **9**, 321 (1970).
(6) A. A. Akhrem and Y. A. Titov, "Total Steroid Synthesis", Plenum Press, New York, 1970; R. T. Blickenstaff, A. C. Ghosh, and G. C. Wolf, "Total Synthesis of Steroids", Academic Press, New York, 1974.
(7) R. Wiechert, *Angew. Chem.*, **89**, 513 (1977); *Angew. Chem., Int. Ed. Engl.*, **16**, 506 (1977).
(8) D. Lednicer, Ed., "Contraception: The Chemical Control of Fertility", Marcel Dekker, New York, 1969; D. Lednicer and L. A. Mitscher, "Organic Chemistry of Drug Synthesis", Wiley-Interscience, New York, 1977.
(9) P. A. Bartlett and W. S. Johnson, *J. Am. Chem. Soc.*, **95**, 7501 (1973).
(10) Preliminary reports of this work have appeared: R. L. Funk and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **99**, 5483 (1977); **101**, 215 (1979). The conceptual scheme of a steroid synthesis via cobalt catalysis was conceived by us in 1973 and first publicly outlined at the 30th Annual Northwest Regional Meeting of the American Chemical Society, Honolulu, Hawaii, June 12–13, 1975.
(11) For recent reviews, see R. L. Funk and K. P. C. Vollhardt, *Chem. Soc. Rev.*, in press; W. Oppolzer, *Synthesis*, 793 (1978); T. Kametani, *Pure Appl. Chem.*, **51**, 747 (1979).
(12) R. L. Funk and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **98**, 6755 (1976); preceding paper in this issue.

0002-7863/80/1502-5253$01.00/0