(12) D. H. Williams and R. G. Cooks, *J. Chem. Soc., Chem. Commun.*, 663 (1968).
(13) A. S. Siegel, *Org. Mass Spectrom.*, **3**, 1417 (1970).
(14) C. W. Tsang and A. G. Harrison, *Org. Mass Spectrom.*, **5**, 877 (1971).

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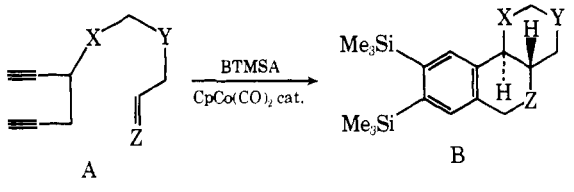
A Cobalt-Catalyzed Steroid Synthesis

Sir:

The steroid nucleus has been the target of numerous, often ingenious, synthetic schemes.[1] We recently reported the cobalt-catalyzed one-step synthesis of tricyclic ring systems B via cooligomerization of diynes A with bis(trimethylsilyl) acetylene (BTMSA) in the presence of $CpCo(CO)_2$[2] (Scheme I). In this reaction five new carbon-carbon bonds are formed with control of stereochemistry to result in what one might envisage to constitute the ABC-ring portion of the steroid moiety. We now wish to report the successful application of this scheme to the synthesis of steroidal structures.[3]

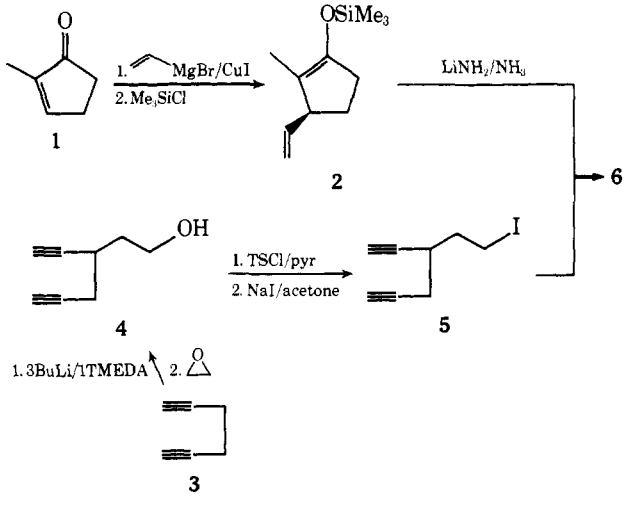
A convergent approach as outlined in Scheme II was adopted for the synthesis of the crucial 1,5-hexadiyne precursor **6**. 2-Methylcyclopent-2-enone (**1**),[4] when treated with vinylmagnesium bromide (CuI, THF; −60 to −40 °C; 45 min) followed by addition of trimethylsilylchloride (HMPA, Et_3N; −40 °C to room temperature; 30 min), gave the enol ether **2** in 89% yield.[5,6] In a parallel line of experiments diynol **4**[2] was quantitatively converted to the corresponding *p*-toluenesulfonate (TsCl, pyridine; 0 °C; 14 h),[5] which on exposure to Finkelstein conditions (45 °C; 30 h), gave iodide **5** in 96% yield.[5,6] The regiospecific enolate generated from **2** ($LiNH_2$, NH_3 (l), THF; 30 min)[7] was stereospecifically alkylated with 3 equiv of **5** to give after column chromatography (silica) 64% diynenone **6** as a mixture of diastereomers[5,6] in addition to 1.9 equiv recovered **5**. This reaction establishes the desired stereochemistry around what is to become the trans-CD-ring junction of the steroid nucleus. Although separable by chromatography, mixture **6** was reacted further as such since on

Scheme I

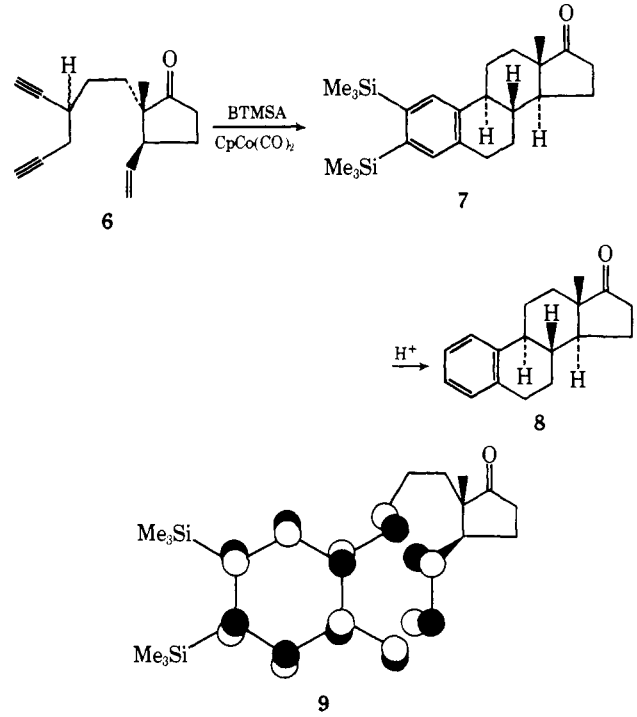


A B

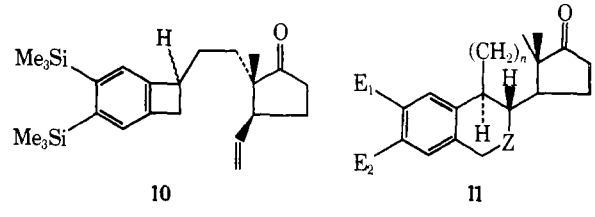
Scheme II



cyclization and conrotatory outward benzocyclobutene ring opening both diastereomers were expected to give the same *o*-xylylene intermediate (e.g., **9**). Indeed cooligomerization



of **6** with BTMSA (solvent) in the presence of catalytic (5 mol %) amounts of $CpCo(CO)_2$ under oxygen-free conditions using syringe pump techniques (35-h addition time)[2] followed by continued heating gave racemic 2,3-bis(trimethylsilyl)-estra-1,3,5(10)-trien-17-one (**7**) in 71% yield as colorless crystals.[5,6] Shorter reaction times allowed the isolation of the two diastereomeric benzocyclobutene intermediates **10**, separated by column chromatography on silica. Slow addition of **10** to refluxing decane under N_2 cleanly gave **7**. Chemical



structural proof for **7** was obtained by quantitative protodesilylation to estra-1,3,5(10)-trien-17-one (**8**) (CF_3COOH-CCl_4-ether, 10:10:1; room temperature; 20 h) identical[8] (TLC R_f, IR, ^1H NMR, ^{13}C NMR[9], *m/e*) with an authentic sample of *d*-estratrienone.

The stereospecificity observed in the **6** → **7** transformation is remarkable and parallels that observed in other intramolecular cycloadditions to *o*-xylylenes derived from benzocyclobutenes.[10] Based on our model studies,[2] an exo-transition state leading to a trans-BC-ring junction was anticipated. Molecular models[3] as well as recent work[10] indicate that a transition state of the type shown in structure **9** (drawn as an *o*-xylylene HOMO-ene LUMO interaction) seems to be preferred. Thus, the desired trans-anti-trans arrangement in **7** is obtained rather than the trans-syn-trans form. The reason for this preference may be found in steric considerations. Thus, the other possible exo-transition state suffers from a sterically interfering methyl group, and a pseudoboat (as opposed to a pseudochair in **9**) arrangement of the carbon chain linking diene and dienophile.

To our knowledge the described approach constitutes the shortest synthesis of the steroid nucleus from an acyclic pre-

cursor: 28% overall yield from commercially available 1,5-hexadiyne (**3**) and 40% from 2-methylcyclopent-2-enone (**1**). In addition, the reported scheme should allow for considerable variation of the structure of the final product. We have previously demonstrated the extensive electrophilic substitution chemistry of *o*-bis(trimethylsilyl)arenes[2,11] as well as the scope of the A → B transformation (Scheme I). Easy access to a variety of steroids of the type **11** can thus be envisaged, in particular the unknown 7-azaestratriene derivatives, incorporating the tetrahydroisoquinoline moiety into the steroid nucleus, the unknown C norsteroids, and the synthetically useful 11-hydroxy[12] and A-ring aza analogues.[13]

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References and Notes

(1) A. A. Akhrem and Y. A. Titov, "Total Steroid Synthesis", Plenum Press, New York, N.Y., 1970; K. Nakanishi in K. Nakanishi, T. Goto, S. Itô, S. Natori, and S. Nozoe, Ed., "Natural Products Chemistry", Vol. 1, Academic Press, New York, N.Y., 1974, Chapter 6.
(2) R. L. Funk and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **98**, 6755 (1976); see also W. G. L. Aalbersberg, A. J. Barkovich, R. L. Funk, R. L. Hillard III, and K. P. C. Vollhardt, *ibid.*, **97**, 5600 (1975); R. L. Hillard III and K. P. C. Vollhardt, *Angew. Chem.*, **87**, 744 (1975); *Angew. Chem., Int. Ed. Engl.*, **14**, 712 (1975); R. L. Funk and K. P. C. Vollhardt, *J. Chem. Soc., Chem. Commun.*, 833 (1976); R. L. Hillard III and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, **99**, 4058 (1977); K. P. C. Vollhardt, *Acc. Chem. Res.*, **10**, 1 (1977).
(3) This conceptual scheme was first conceived in 1973 and publicly outlined at the 30th Annual Northwest Regional Meeting of the American Chemical Society, Honolulu, Hawaii, June 12–13, 1975.
(4) I. J. Rinkes, *Recl. Trav. Chim. Pays-Bas*, **57**, 176 (1938); A. M. Gaddis and L. W. Butz, *J. Am. Chem. Soc.*, **69**, 1203 (1947). **1** can also be prepared from 2-methylcyclopentane-1,3-dione via 3-ethoxy-2-methyl-2-cyclopentenone followed by reduction with diisobutylaluminum hydride and acidic workup, in a procedure adapted from W. F. Gannon and H. O. House, "Organic Syntheses", Collect. Vol. V, Wiley, New York, N.Y., 1973, p 294.
(5) All new compounds reported exhibited satisfactory spectral and/or analytical characteristics.
(6) **2**: colorless liquid; bp 48 °C (2.6 mm); *m/e* (rel intensity) 196 (M^+, 22), 73 (Me_3Si, 100); NMR (60 MHz) (CCl_4) δ 0.22 (s, 9 H) 1.47 (br s, 3 H), 1.4–2.5 (m, 4 H), 3.00 (m, 1 H), 4.93 (dd, J = 9, 2.5 Hz, 1 H), 5.00 (dd, J = 17.5, 2.5 Hz, 1 H), 5.70 (overlapping (5 lines) ddd, J = 17.5, 10, 9 Hz, 1 H). **5**: colorless liquid; bp 92 °C (6 mm); *m/e* (rel intensity) 232 (M^+, 0.3), 77 (100); NMR (60 MHz) (CCl_4) δ 1.9–3.1 (m, 5 H), 2.33 (t, J = 2.5 Hz, 1 H), 2.43 (d, J = 2.5 Hz, 1 H), 3.28 (dt, J = 6, 1 Hz, 2 H); IR (neat) $\nu_{C\equiv CH}$ 3310, 2145 cm^{-1}. **6**: colorless oil; *m/e* (rel intensity) 228 (M^+, 0.2), 124 (100); NMR (60 MHz) (CCl_4) δ 0.85, 1.03 (2s, 3 H), 1.2–2.8 (m, 14 H), 5.13 (dd, J = 16, 2.5 Hz, 1 H), 5.14 (dd, J = 10, 2.5 Hz, 1 H), 5.90 (m, 1 H); IR (neat) $\nu_{C\equiv CH}$ 3330, 2150 cm^{-1}, $\nu_{C=O}$ 1740 cm^{-1}. **7**: colorless crystals; mp 155–157 °C; *m/e* (rel intensity) 398 (M^+, 25), 383 (44), 73 (100); NMR (60 MHz) (CCl_4) δ 0.37 (s, 18 H), 0.93 (s, 3 H), 1.0–3.0 (m, 15 H), 7.27 (br s, 1 H), 7.52 (br s, 1 H); IR (neat) $\nu_{C=O}$ 1743 cm^{-1}.
(7) E. S. Binkley and C. H. Heathcock, *J. Org. Chem.*, **40**, 2156 (1975).
(8) The melting point of racemic **8** (107–109 °C) is somewhat lower than that of optically pure material (138–141 °C). We thank Dr. F. Li, Syntex Research, for a sample of authentic *d*-estra-1,3,5(10)-trien-17-one.
(9) See also T. A. Wittstruck and K. I. H. Williams, *J. Org. Chem.*, **38**, 1542 (1973).
(10) T. Kametani, H. Nemoto, H. Ishikawa, K. Shiroyama, H. Matsumoto, and K. Fukumoto, *J. Am. Chem. Soc.*, **99**, 3461 (1977); T. Kametani, Y. Hirai, F. Satoh, and K. Fukumoto, *J. Chem. Soc., Chem. Commun.*, 16 (1977); W. Oppolzer, *Angew. Chem.*, **89**, 10 (1977); *Angew. Chem., Int. Ed. Engl.*, **16**, 10 (1977).
(11) Oxygenated derivatives of the estrone type should be available via oxidative cleavage of the arylsilicon bond, as demonstrated for simple arylsilanes: J. R. Kalman, J. T. Pinhey, and S. Sternhell, *Tetrahedron Lett.*, 5369 (1972).
(12) See, for example, R. W. Freerksen, W. E. Pabst, M. L. Raggio, S. A. Sherman, R. R. Wrobie, and D. S. Watt, *J. Am. Chem. Soc.*, **99**, 1536 (1977).
(13) S. Danishefsky and P. Cain, *J. Am. Chem. Soc.*, **98**, 4975 (1976); for a cobalt catalyzed route to annelated pyridines, see A. Naiman and K. P. C. Vollhardt, unpublished work.
(14) (a) Regents' Intern Fellow, 1975–1978; (b) Fellow of the Alfred P. Sloan Foundation, 1976–1978.

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strati-Bisporphyrins. A Novel Cyclophane System

Sir:

The primary electron donor in bacterial photosynthesis is a dimer of bacteriochlorophyll molecules. The evidence for this assertion comes from ESR and ENDOR measurements on the cation resulting from the initial photoact.[1] Similar electron delocalization is known to occur in the radical-ion species of cyclophanes, triptycenes, and other intimate ring systems.[2] This delocalization is strongly dependent on the geometry of these multiring compounds. Linear and loosely stacked dimers of porphyrins have been synthesized,[3,4] but the ring–ring interactions appear to be minimal. In the cases of chlorophyll dimers held together by hydrogen-bonding nucleophiles and urea-linked binary prophyrins, substantial spectral alterations have been observed.[5,6] To evaluate the influence of distance and orientation parameters on the electron-transfer phenomena, we have begun the synthesis of well-defined dimeric systems in which transannular interactions can be observed. Recently, we reported the first member of a new class of macrocyclic cyclophanes, tetra-*meso*-[*p,p'*-(2-phenoxyethoxycarbonylphenyl)]-*strati*-bisporphyrin, III.[7,8] Now we present the proof of structure and some interesting spectral properties of this compound.

strati-Bisporphyrin III was synthesized by application of the tetraaldehyde modification[9] of the Adler–Longo porphyrin condensation procedure.[10] A suitable porphyrin tetraaldehyde, II, was derived from a porphyrin tetrahydroxide, I, by acylation with *p*-chlorocarbonylbenzaldehyde (Figure 1).

Tetra-*meso*-[*p*-(2-hydroxyethoxy)phenyl] porphyrin, I, was made by the reaction of pyrrole with *p*-2-hydroxyethoxybenzaldehyde[11] in refluxing acidified xylene (8 mM in trifluoroacetic acid).[12] The xylene precipitate was recrystallized from dimethylformamide yielding 14% I: mp >330 °C; ν_{max} (KBr) 1240, 1605 cm^{-1}; λ_{max} (pyridine) 426 nm (ε 471 000, 14-nm half-width), 521 (16 500), 558 (13 000), 595 (5090), 653 (7500).[13] Anal. Calcd for $C_{52}H_{46}N_4O_8$ (mol wt 854.9): C, 73.05; H, 5.42; N, 6.55; Found: C, 72.80; H, 5.36; N, 6.54. I was reacted with the thionyl chloride generated acid chloride of *p*-carboxybenzaldehyde in methylene chloride–pyridine–diisopropylethylamine (DIEA) (50:25:2). At completion, the solution was neutralized with aqueous base and the products were extracted into chloroform, concentrated, and precipitated with methanol. The precipitate was chromatographed with chloroform on deactivated alumina[14] and the first band was collected. Crystallization from $CHCl_3$–MeOH resulted in 40% yield of tetraaldehyde II: mp 225–228 °C; ν_{max} (KBr) 1240, 1275, 1605, 1705, 1725 cm^{-1}; λ_{max} (pyridine) 425 nm (ε 464 000, 14-nm half-width), 519 (17 400), 556 (12 700), 593 (5330), 651 (7170);[13] FT NMR (220 MHz, 1 mM in $CDCl_3$)[15] δ NH at −2.77 (2 H, s), CH_2O at 4.61 (8 H, t, J = 4 Hz), CO_2CH_2 at 4.89 (8 H, t, J = 4 Hz), C_6H_4O at 7.31 (8 H, d, J = 8 Hz), 8.12 (8 H, d, J = 8 Hz), $C_6H_4CO_2$ at 7.99 (8 H, d, J = 8 Hz), 8.32 (8 H, d, J = 8 Hz), β-pyrrole H at 8.83 (8 H, s), CHO at 10.11 ppm (4 H, s). Anal. Calcd for $C_{84}H_{62}N_4O_{16}$ (mol wt 1383.4): C, 72.93; H, 4.52; N, 4.05. Found: C, 71.72; H, 4.36; N, 4.05.[16a]

strati-Bisporphyrin III was made by the addition of II and pyrrole (4 equiv) to refluxing propionic acid–ethylbenzene (1:1) (0.4 mM in II). After 1.5 h, the solvent was removed by evaporation and the pyridine-soluble products were collected and fractionated on a Bio-Beads S-X1 exclusion gel.[17] After a long, diminishing band of polymeric porphyrins (R 0.5–1.0), III eluted as a narrow, isolated purple band (R 0.45) followed by a faint yellow band of pyrrole by-products.[18] This elution pattern is consistent with III being a compact, stacked dimer. On this same column the more extended and solvated porphyrins I and II migrated with Rs of 0.61 and 0.67, respectively, while unsubstituted tetraphenylporphyrin eluted at R