product. 3,4-Dimethylpent-3-en-2-one was prepared from 2-methyl-2-butene and acetylchloride according to House et al.[37] 3-Methyloct-3-en-2-one was prepared from methyl ethyl ketone and pentaldehyde according to Levy et al.[33] 3-Methylnon-3-en-2-one was prepared from methyl ethyl ketone and *n*-heptaldehyde according to Levy et al.[33]

All these products were recovered unchanged even after 5 days of incubation.

4-Methylhex-4-en-3-one was prepared from diethyl ketone and acetaldehyde according to Levy et al.[33] One product formed and was purified. (*R*)-(−)-4-Methylhexan-3-one: 95% yield; structure confirmed by NMR; $[\alpha]^{25}_{578}$ −29° (*c* 0.118, $CHCl_3$) (lit.[18] $[\alpha]$ −30°). The optical purity (>95%) was confirmed by comparison of NMR spectra of racemic and optically active product in the presence of tris[3-[(trifluoromethyl)hydroxymethylene]-*d*-camphorato]europium(III).

4-Methylhept-4-en-3-one was prepared from diethyl ketone and propionaldehyde according to Levy et al.[33] One product formed and was purified. (*R*)-(−)-4-Methylheptan-3-one: 95% yield; structure confirmed by NMR; $[\alpha]^{25}_{578}$ −23° (*c* 0.12, $CHCl_3$) (lit.[19] $[\alpha]^{27}_{D}$ −21.5° (*c* 1, hexane).

Experiments Using Culture Medium with Modified pH. Method a. Solid Ca CO_3 (6 g L^{-1}) was added to the standard medium described above. Under these conditions cyclohex-2-en-1-one in the usual concentration gave only cyclohexanone.

Method b. Ammonium sulfate was replaced by 10 g L^{-1} of peptone in the same standard culture medium. Under these conditions cyclohex-2-en-1-one in the usual concentrations gave cyclohexanone (90%) and cyclohexanol (10%).

Acknowledgment. We thank Dr. F. Huet (Orsay) for a sample of the 2-methylene ketal of cyclohexanone and Dr. G. Dauphin and J. C. Gramain (Clermont) for stimulating discussions bearing on this study.

Registry No. (*S*)-(+)-**1a**, 15466-88-3; (*R*)-(−)-**1b**, 54307-74-3; (*S*)-(−)-**2a**, 24965-87-5; (*R*)-(+)-**2b**, 13368-65-5; (±)-*cis*-**3**, 24965-90-0; (±)-*trans*-**3**, 23068-71-5; (±)-**4**, 67120-83-6; (*S*)-(+)-**5a**, 22554-27-4; (*R*)-(−)-**5b**, 22554-29-6; (−)-(1*R*-2*S*)-**6a**, 19043-02-8; (+)-(1*S*,2*R*)-**6b**, 15963-35-6; **7**, 42747-41-1; (*R*)-(+)-**8**, 79918-73-3; (1*S*,2*R*)-**9**, 79918-74-4; (−)-**10**, 6485-40-1; (+)-**11**, 5524-05-0; (+)-**12**, 20549-48-8; (+)-**13**, 619-02-3; (−)-**14**, 53796-79-5; (−)-**15**, 53796-80-8; **16** (R_1 = Bu; R_2 = Me), 79918-75-5; **16** (R_1 = Me; R_2 = Et), 1187-80-0; **16** (R_1 = Me; R_2 = Pr), 39899-08-6; **16** (R_1 = Me; R_2 = Bu), 60438-53-1; **16** (R_1 = Me; R_2 = Pent), 54615-56-4; (*R*)-**17** (R_1 = Bu; R_2 = Me), 69856-95-7; (*S*)-**17** (R_1 = Me; R_2 = Et), 79980-77-1; (*S*)-**17** (R_1 = Me; R_2 = Pr), 69856-94-6; **18** (R_1 = Me; R_2 = Et), 2313-65-7; **18** (R_1 = Me; R_2 = Pr), 31367-46-1; **19** (R = Me), 52883-78-0; **19** (R = Et), 22319-31-9; (*R*)-**20** (R = Me), 77858-08-3; (*R*)-**20** (R = Et), 51532-31-1; **21**, 3045-98-5; (±)-4-methylcyclohex-2-en-1-one, 79980-78-2; 4-methylcyclohexanone, 589-92-4; *cis*-4-methylcyclohexanol, 7731-28-4; *trans*-4-methylcyclohexanol, 7731-29-5; 3-methylenepentan-2-one, 4359-77-7; (*S*)-(−)-3-methylpentan-2-one, 2695-53-6; 3-methylpentan-2-ol, 365-60-6; 4-methylpent-3-en-2-one, 141-79-7; 3,4-dimethylpent-3-en-2-one, 684-94-6; (±)-5-methylcyclohex-2-en-1-one, 54352-35-1.

(37) H. O. House, Chia Yeh Chu, J. M. Wilkins, and M. J. Umen, *J. Org. Chem.*, **40**, 1460 (1975).

Synthesis of Large-Ring Analogues of Estrone by a Ring-Expansion Route

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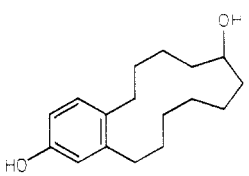
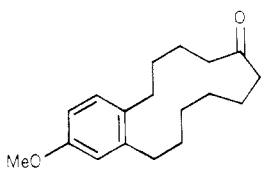
A synthetic methodology is described wherein a sequence of three ring expansions is used to convert cycloheptanone to 4′-methoxy-5,6-benzocyclodecenone, which was tested for estrogenic properties but showed no uterotrophic activity. Attempts to selectively expand the large ring by one more carbon to 8,9:13,14-diseco-18-norestrone were not successful.

We recently reported[1] the synthesis of 8,9:13,14-diseco-18-norestradiol, **1**, which is the first analogue of the human sex hormones wherein the B, C, and D rings are replaced by a single ring. The present paper describes an alternative synthetic route directed toward compound **2**, which is another member of this general class of large-ring hormone analogues. The preparation of these compounds is part of a program to determine to what extent these flexible analogues will mimic the biological properties of the corresponding steroidal hormones which are quite rigid.[2]



1

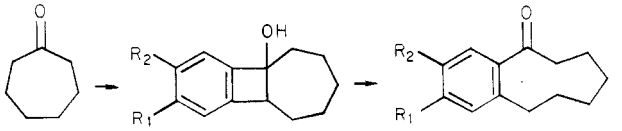


2

(1) Thies, R. W.; Yue, S. *J. Chem. Soc., Chem. Comm.* **1980**, 950.
(2) Biological activity has been observed in several mono seco cases; e.g., Voight, W.; Castro, A.; Covey, D. F.; Robinson, C. H. *Acta Endocrinol.* **1978**, *87* 668 and earlier papers in that series; Morrow, D. F.; Dallow, D. *Ann. Rep. Med. Chem.* **1971**, *7*, 182; Crossley, N. S., *J. Chem. Soc. C* **1971**, 2491.

Results and Discussion

Synthesis of compound **2** requires that a substituted benzo unit be fused to a large ring in a particular position relative to the carbonyl group. Relatively few methods have been reported for attaching benzo moieties to medium or large rings and still fewer for substituted benzo cases.[3] This synthesis utilizes a variation of a reaction developed by Caubere,[4] which simultaneously expands a ring ketone and attaches the benzo unit; e.g., cycloheptanone had been converted to the cyclobutanol **3a** which can then be rearranged to the benzocyclononanone **4a**. In the present



3a, R_1 = H; R_2 = H
b, R_1 = OMe; R_2 = H
c, R_1 = H; R_2 = OMe

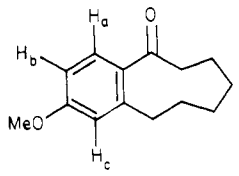
4a-c

case, cycloheptanone was treated with sodium amide and

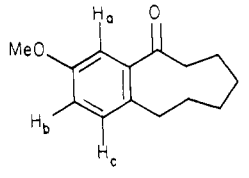
(3) Thies, R. W.; Seitz, E. P. *J. Org. Chem.* **1978**, *43*, 1050.
(4) Caubere, P. *Acc. Chem. Res.* **1974**, *7*, 301 and references therein.

0022-3263/82/1947-0798$01.25/0

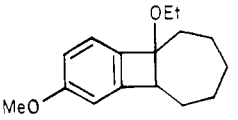
p-bromoanisole, which gave a 44:26:30 mixture of **3b**, **3c**, and 2-arylcycloheptanone. The latter product could be removed with Girard's T reagent; however, some care was needed since the alcohol group of **3b** is partially converted to the corresponding ether **5b** during the Girard's T reaction in refluxing ethanol. If refluxing is allowed to proceed for too long a period, all of **3b** is converted to **5b**. The *p*-methoxy substituent apparently favors a solvolysis reaction; no such reaction was observed with **3a** or **3c**. The ethyl ether could be converted back to **3b** by refluxing in aqueous acetone with a catalytic amount of acid. Treatment of the **3b–3c** mixture with potassium hydride in hexamethylphosphoric triamide (HMPT) gave a mixture of **4b** and **4c** along with a small amount of the ethyl ether which was not affected by these conditions. No 2-aryl ketone product was observed in this case although we have observed that type of product if tetrahydrofuran (THF) is used with similar compounds. Fortunately, the product mixture was readily separated by flash chromatography, which gave pure samples of **4b** and **4c**, which were assigned the structures indicated by comparing the NMR spectra for the aromatic protons which were spread apart with shift reagents. The desired isomer **4b** exhibited an ABX aromatic pattern which was especially distinguishable by a doublet at δ 7.41 (J = 8 Hz), which is assigned to the proton closest to the carbonyl (H_a). Addition of shift



4b



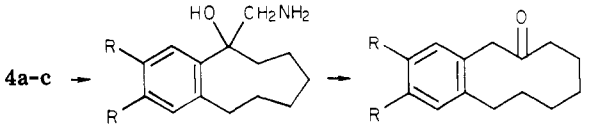
4c



5b

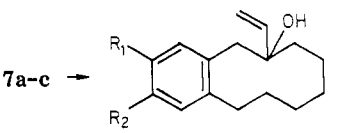
reagent spreads the chemical shifts so that H_b (dd, J = 8, 2 Hz) and H_c (d, J = 2 Hz) are clearly identifiable from their coupling patterns. As shift reagent is added, the chemical shifts move downfield in the order $H_a \gg H_c > H_b$ (8:2:1), which is the order predicted by the formula[5] $\Delta\delta = k(3\cos^2\theta - 1)/r^3$ if the dihedral angle between the carbonyl group and the benzene ring is any value up to 90°. In a similar way for compound **4c**, the aromatic protons H_a (d, J = 2 Hz), H_b (dd, J = 8, 2 Hz) and H_c (d, J = 8 Hz) of **4c** are readily discerned once shift reagent is added although they are a complex ABC pattern before addition. The change in chemical shift with added shift reagent follows the order $H_a \gg H_c > H_b$ (18:4:3), which is again the expected order for all carbonyl-aromatic dihedral angles up to 90°. In both cases, the H_a resonance moves much faster than the other two and is readily identified by its coupling pattern, which by itself clearly distinguishes the isomers.

After **4b** was obtained in pure form, attention was turned to a ring expansion sequence that would ultimately provide the desired disecosteroid system. The first stage required a one carbon expansion of **4b** which would place the carbonyl β to the aromatic ring. Our past experience[1,6] with medium and large rings suggested that a Tiffeneau–Demjanov rearrangement method with use of trimethylsilyl cyanide (Me_3SiCN) offered the best chance of success. Treatment of **4b** with Me_3SiCN, using potassium cyanide/crown ether complex as a catalyst,[7] smoothly afforded the trimethylsilyl cyanohydrin, which was reduced directly to the corresponding amino alcohol (**6b**). After purification by an acidic extraction procedure, treatment of **6b** with nitrous acid gave a smooth conversion to the ring expanded ketone **7b** with no observable formation of the isomeric ketone in which the carbonyl is α to the aromatic ring. In other systems we have studied, formation of some α isomer or competitive enolate formation can seriously limit the yield.[1] The expansion of **4b** to **7b** is relatively favorable in those regards and gave an 86% overall conversion. The same ring-expansion sequence was applied to the related ketones **4a** and **4c** with comparable results.

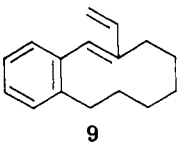


6a-c **7a-c**

The next step of the sequence involves the addition of vinylmagnesium bromide to ketone **7b**, a reaction which turned out to be less straightforward than expected. Under the usual conditions[8] wherein the reagent is generated and reacted in THF, the conversion of **7b** to **8b** was only 20%, which was somewhat surprising since *cis*-cyclodec-3-en-1-one had been reacted previously[9] in 54% yield. Tests on **7a** indicated that removing the THF from the Grignard reagent and replacing it with a less polar solvent gave better conversions presumably because that favors addition to the carbonyl relative to enolate formation. Conversions of 70–80% were obtained with refluxing ether or toluene at 50 °C. In both cases, the Grignard reagent was not totally soluble and increased temperature was required to give a reasonable reaction time. At even higher temperatures for toluene, a minor amount of dehydration product **9** also formed. Ether was somewhat more convenient and was used for the reactions of **7b** and **7c**, which both gave a 41% yield of product (**8b** and **8c**); a distinct improvement over the THF conditions (20%) but still substantially less than the unsubstituted case **7a**.



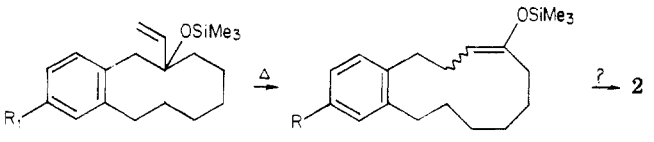
8a, R_1 = H; R_2 = H
b, R_1 = H; R_2 = OMe
c, R_1 = OMe; R_2 = H



9

The synthetic plan now called for a [1,3] sigmatropic shift which would expand the ring size of **8b** to a 12-membered ring, preferably with the enol generated in a specific position. Thus conversion of **8b** to the trimethylsiloxy derivative (**10b**) followed by pyrolysis should give the trimethylsilyl enol ether (**11b**) by analogy with earlier work.[3,10] Compound **11b** would then be specifically expanded to **2** by the method described earlier,[11] which involves a carbenoid addition to the double bond followed by a ferric chloride catalyzed rearrangement. Unfortunately, test pyrolyses of **10a** at about 300 °C gave only low yields of a product (presumably **11a**), which hydrolyzed

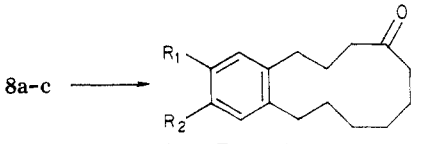
(5) Cramer, R. E.; Dubois, R.; Seff, K. *J. Am. Chem. Soc.* **1974**, *96*, 4125.
(6) Thies, R. W.; Meshgini, M.; Chiarello, R. H.; Seitz, E. P. *J. Org. Chem.* **1980**, *45*, 185.
(7) Evans, D. A.; Carroll, G. L.; Truesdale, L. K. *J. Org. Chem.* **1974**, *39*, 914. Evans, D. A.; Truesdale, L. K. *Tetrahedron Lett.* **1973**, 4929.
(8) Thies, R. W. *J. Am. Chem. Soc.* **1972**, *94*, 7074.
(9) Thies, R. W.; Billigmeier, J. E. *J. Am. Chem. Soc.* **1974**, *96*, 200.
(10) Thies, R. W.; Shih, H. J. *J. Org. Chem.* **1977**, *42*, 280.
(11) Ito, Y.; Fujii, S.; Saegusa, T. *J. Org. Chem.* **1976**, *41*, 2073.



10a, R = H
b, R = OMe

11a,b

to the ring-expanded ketone **12a**. Different conditions might help; however, several variations were tried and did not offer much encouragement. The earlier work on [3,3] and [1,3] oxy-Cope[3,12] reactions had demonstrated that dramtic rate enhancements and, in some cases, improved yields can be achieved by generating the potassium alkoxide in a highly dissociating media. This proved to be quite effective for **8b**, which rearranged in high yield when treated with potassium hydride in HMPA at room temperature. The related systems **8a** and **8c** rearrange in a like manner except that they rearranged approximately 20 and 32 times faster, respectively. This qualitatively agrees with the earlier substituent effects[6] for such [1,3] shifts, which had suggested that the migrating center must bear substantial negative charge during the rearrangement.

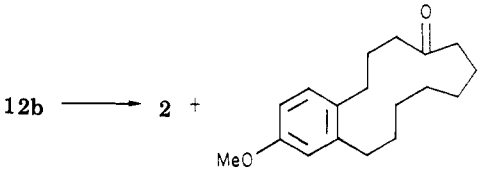


12a, R_1 = H; R_2 = H
b, R_1 = H; R_2 = OMe
c, R_1 = OMe; R_2 = H
d, R_1 = H; R_2 = OH

With **12b** in hand, it seemed worthwhile to determine whether removal of the methyl group would present a problem for such large ring ketones. Treatment of **12b** with aluminum chloride/ethanethiol[1,13] gave no useful product and boron tribromide in methylene chloride[14] only gave a low yield of impure **12d**; however, hydrobromic acid/acetic acid[15] produced **12d** cleanly in 71% yield.

What is still lacking is a selective means of expanding **12b** to **2**. One possibility would be to trap the enolate anion that results from the [1,3] anionic rearrangement, e.g., adding trimethylsilyl chloride (Me_3SiCl) would in principle lead to **11b**. Testing of this approach on **8a**, adding Me_3SiCl directly to the HMPT solution or adding it to a solution diluted with dioxane,[16] did not give a significant amount of **11a**. *tert*-Butyldimethylsilyl chloride also failed and acetic anhydride gave only low yields of the enol acetate. Attempts to trap the enolate of a model system, cyclododecanone, generated with potassium hydride and HMPT suggested that methyl tosylate was probably the best trapping agent for these conditions, but even at best only about 60% was trapped as the enol ether. The conditions necessary for the [1,3] shift seem to work against effective trapping. This approach was not carried further, partly because of the low conversions to the enolate, which was not easy to purify, and also because it seemed quite possible[12] that during the relatively long reaction times, the enolates could equilibrate prior to being captured.

One final experiment was carried out to determine if a Me_3SiCN ring expansion might give an unexpectedly selective formation of **2** or at least a reasonably separable mixture. The only surprise was that the yield was quite low (<15%). GC analysis of the volatile product showed small amounts of starting ketone and an unknown compound along with a single peak which showed the correct mass for the addition of one methylene group. The infrared spectrum confirmed that it contained saturated ketone, but the ^1H NMR showed two equal-sized methoxy peaks separated by 1 Hz as would be expected for a 50:50 mixture of **2** and the other predicted expansion product **13**. Further, GC, LC, and crystallization separations were not successful, which further confirmed that this approach to **2** is not an attractive one.



13

In summary, the route herein described is a novel and effective approach to compound **12b**, but a selective conversion to **2** was not found. Since **12b** is just one methylene unit short of **2**, it could conceivably show estrogenic behavior; however, molecular models indicate that the missing methylene would not allow the oxygens to be the correct distance. Not surprisingly **12b** showed no significant uterotropic properties. Other analogues could be made by this method; however, our other route[1] to such compounds has proved more advantageous in that regard.

Experimental Section

General Procedures. Spectral measurements utilized Perkin-Elmer 727B infrared, Varian EM 360, HA 100 and FT-80 NMR, Atlas CH7 and CDC 110B mass spectrometer instruments. GC analyses were carried out on a Varian 1200 (FID) chromatograph, using column A (4 ft × 0.125 in., 7.4% OV-101 on 80/100 Chromosorb G) unless specified as column B (4 ft × 0.125 in., 3% AN600 on 60/80 Chromosorb G). Preparative GC used a Varian 920 chromatograph with a 2 ft × 0.25 in. 4.9% OV-101 on 80/100 Chromosorb G column.

Flash chromatography was carried out with EM silica gel 60 (0.040–0.063 mm) following the published procedure.[18]

Tetrahydrofuran (THF) and diethyl ether were distilled from the sodium benzophenone dianion under nitrogen. Hexamethylphosphoric triamide (HMPT) was dried by storing over 13X molecular sieves (predried under nitrogen at 350 °C for 4 h). Other solvents were dried according to standard published procedures.[19,20]

8,9-(5-Methoxybenzo)bicyclo[5.2.0]non-8-en-1-ol (3b) and 8,9-(4-Methoxybenzo)bicyclo[5.2.0]non-8-en-1-ol (3c). One fresh 20 g bottle of Fischer $NaNH_2$ was added under nitrogen to 250 mL of dry THF and then 28.8 g (0.256 mol) of cycloheptanone in 30 mL of THF was added dropwise with Hershberg stirring over 1 h. Stirring was continued for 2 h and then 24.0 g (0.128 mol) of *p*-bromoanisole was added over 1 h followed by stirring overnight. The reaction mixture was poured into ice/HCl and then extracted into ether solution, which was washed with saturated $NaHCO_3$ and dried ($MgSO_4$). Removal of solvent gave 40.9 g of dark brown oil. Kugelrohr distillation at 1 mm afforded 9.0 g of cycloheptanone (bath temperature, ≤95 °C) and then 24.2 g of a dark yellow semisolid (bath temperature, 95–156 °C), which

(12) Evans, D. A.; Nelson, J. V. *J. Am. Chem. Soc.* **1980**, *102*, 774.
(13) Node, M.; Nishida, K.; Ichikawa, K.; Fuji, K.; Fujita, E. *Chem. Lett.* **1979**, 97. Node, M.; Hori, H.; Fujita, E. *J. Chem. Soc. Perkin Trans 1* **1976**, 2237.
(14) McOmie, J. F. W.; Watts, M. L.; West, D. E. *Tetrahedron* **1968**, *24*, 2289.
(15) Long, L., Jr.; Berger, A. *J. Org. Chem.* **1941**, *6*, 852.
(16) Dioxane had been used previously as a solvent for trapping the enolate.
(17) Hudrlik, P. F.; Takacs, J. M. *J. Org. Chem.* **1978**, *43*, 3861.
(18) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(19) Wilberg, K. B. "Laboratory Technique in Organic Chemistry"; McGraw-Hill: New York, 1960.
(20) Fieser, L. F.; Fieser, M. "Reagents for Organic Chemistry"; Wiley: New York, 1967; Vol. 1.

GC analysis (column B) indicated was a 44:26:30 mixture of **3b**, **3c**, and the 2-arylcycloheptanones. The semisolid corresponds to a 87% yield from *p*-bromoanisole.

The ketone byproducts were removed by refluxing for 1 h a mixture of 19.33 g of the above semisolid, 10 g of Girard's Reagent T, 100 mL of absolute ethanol, and 4 mL of acetic acid and then allowing the mixture to cool until a precipitate formed (ca. 2.5 h). The precipitate was removed by filtration and washed with ethanol. The combined ethanol washings were then poured into ice–$NaHCO_3$ and extracted into ether at 0 °C as described earlier,[10] which gave 10.53 g of oily crystals. Analysis by GC showed 88% was **3b** and **3c**, 11% was the ethyl ether **5b**, and 1.5% was 2-arylcycloheptanones. In other runs with longer reflux times, the amount of side-product **5b** increased substantially.

2-Methoxy- and 3-Methoxy-7,8,9,10,11-pentahydro-5(6*H*)-benzocyclononenones (4b and 4c). A 31.9 g (0.197 mol) portion of 24.7% potassium hydride in oil was washed with hexane[3] and combined with 100 mL of HMPT at 0 °C. Two batches (19.5 g) of the above mixture containing **3b** and **3c** were taken up in 75 mL of HMPT and added to the potassium hydride dropwise. The ice bath was removed, and the mixture was allowed to stir overnight. The reaction was then cooled to 0 °C and quenched cautiously with water. The aqueous layer was extracted 4 times with 150-mL portions of water, 1 time with 150 mL of saturated $NaHCO_3$, and 1 time with brine and dried over magnesium sulfate. Filtering and rotary evaporating yielded 18.4 g of dark brown mobile oil. GC analysis (column B) indicated a 3:2 ratio of **4b** to **4c**. Flash chromatography of 10.0 g of this material with 10% ethyl acetate/pentate afforded 1.12 g of **5b**, 2.37 g of **4c**, a 2.31-g overlap fraction of **4b** and **4c**, and 3.51 g of **4b**. **5b**: NMR (CCl_4) δ 6.94 (dd, J = 2, 8 Hz, 1 H), 6.70–6.50 (m, 2 H), 3.70 (s, 3 H), 3.43 (q, J = 7 Hz, 2 H), 3.55–3.30 (m, 1 H), 2.20–1.20 m, 10 H), 1.12 (t, J = 7 Hz, 3 H); IR (neat) 3060, 2980, 2930, 2850, 2755, 1605, 1590, 1475, 1440, 1390, 1350, 1325, 1270, 1240, 1215, 1190, 1125, 1090, 1065, 1020, 995, 970, 950, 930, 810, 780, 730 cm^{-1}; mass spectrum, m/e (relative %) 246 (26.1), 203 (81.1), 201 (100), 200 (31.9), 175 (47.6); high-resolution mass spectrum, m/e 246.161 (calcd for $C_{16}H_{22}O_2$, 246.162). **4c**: NMR (CCl_4) δ 6.92 (m, 3 H), 3.82 (s, 3 H), 2.83 (m, 4 H), 2.04–1.29 (m, 8 H); IR (neat) 3060, 2990, 2910, 2840, 1680, 1650, 1595, 1560, 1480, 1450, 1400, 1310, 1270, 1250, 1225, 1175, 1020, 985, 920, 855, 810, 690 (cm^{-1}; mass spectrum, m/e (relative %) 218 (51.8), 175 (100), 162 (28.4), 161 (30.8); high-resolution mass spectrum, m/e 218.130 (calcd for $C_{14}H_{18}O_2$, 218.131). **4b**: NMR (CCl_4) δ 7.41 (d, J = 8 Hz, 1 H), 6.66 (dd, J = 8, 2 Hz, 1 H), 6.59 (d, J = 2 Hz, 1 H), 3.80 (s, 3 H), 2.96 (br t, 2 H), 2.74 (br t, 2 H), 2.02–1.25 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 208.77, 161.76, 142.85, 134.53, 130.30, 116.31, 111.44, 55.24, 41.75, 32.30, 31.38, 27.20, 26.20, 23.84; IR (neat) 3060, 3000, 2920, 2850, 1695, 1660, 1600, 1580, 1495, 1465, 1440, 1410, 1350, 1320, 1240, 1160, 1105, 1080, 1030, 1000, 990, 915, 810 (cm^{-1}; mass spectrum, m/e (relative %) 218 (45.8), 175 (46.0), 162 (56.2), 161 (100); high-resolution mass spectrum, m/e 218.131 (calcd for $C_{14}H_{18}O_2$, 218.131).

Preparation of 8,9-(5-Methoxybenzo)bicyclo[5.2.0]non-8-en-1-ol (3b) from 1-Ethoxy-8,9-(5-methoxybenzo)bicyclo[5.2.0]non-8-ene (5b). A 0.700-g (2.85 mmol) portion of **5b** was dissolved in 20 mL of 80% aqueous acetone and 4 drops of H_2SO_4 was added. After the mixture was stirred for 5.5 h, GC analysis indicated only about 20% reaction, so an additional 0.5 mL of H_2SO_4 was added, and the mixture was allowed to stir overnight. An aliquot taken then showed about 80% reaction, and an additional 0.5 mL of H_2SO_4 was added. After an additional 6 h of stirring, no significant change was observed in the reaction miixture. The reaction mixture was then neutralized with saturated $NaHCO_3$ and extracted 3 times with 20-mL portions of ether. The combined ether layers were washed 1 time with saturated $NaHCO_3$ and 1 time with brine and then dried ($MgSO_4$). Filtration and concentration gave 0.509 g of yellowish crystals. Flash chromatography with 10% ethyl acetate/pentane afforded 0.397 g of alcohol **4b** as off white crystals, mp 94–95 °C, and 0.083 g of starting material **5b**, for an adjusted yield of 72.6%: NMR (CCl_4) δ 6.94 (d, J = 8 Hz, 1 H), 6.70–6.50 (m, 2 H), 3.72 (s, 3 H), 3.40–3.16 (m, 1 H), 2.32–1.12 (m, 11 H); IR (neat) 3600–3150, 3080, 3025, 2940, 2870, 1905, 1600, 1485, 1455, 1370, 1340, 1280, 1255, 1190, 1135, 1055, 1035, 980, 960, 865, 830 cm^{-1}; mass spectrum, m/e (relative %) 218 (15.7), 175 (100), 162 (21.7), 161 (19.1); high-resolution mass spectrum, m/e 218.131 (calcd for $C_{14}H_{18}O_2$, 218.131).

2-Methoxy-7,8,9,10,11,12-hexahydro-6(5*H*)-benzocyclodecenone (7b). A mixture of 3.038 g (13.9 mmol) of **4b** and 0.108 g of 18-crown-6/potassium cyanide catalyst,[7] was stirred for 35 min, during which time it went from yellow to bright orange. Next, 2.50 mL (20.9 mmol) of trimethylsilyl cyanide (Me_3SiCN) was added, and the mixture was allowed to stir overnight. An anhydrous ether suspension of $LiAlH_4$ (1.225 g, 30.6 mmol) was added cautiously, and the mixture was allowed to stir for 2 h, during which time it took on a gray-green color. The reaction mixture was quenched cautiously with 1.2 mL of water, followed by 1.2 mL of 15% NaOH and finally 3.6 mL of water. The light brown precipitate which formed was extracted 4 times with 30-mL portions of refluxing ether. The combined ether extracts were extracted with 10% H_2SO_4 until the ether layer turned clear (6 times, 60-mL portions). The ether layer was washed 2 times with 100-mL portions of saturated $NaHCO_3$ and 1 time with 100 mL of brine and then dried ($MgSO_4$). Filtration and concentration gave 0.088 g of light brown oil. Analysis by GC (column B) of this oil indicated that this oil consisted mainly of starting material **4b**.

The acidic extract was cooled in an ice bath and made basic with 15% NaOH, which caused copious amounts of white crystals to form. The basic extract and crystals were extracted 3 times with 100-mL portions of ether, and the combined ether layers were washed 1 time with 100 mL of $NaHCO_3$ and 1 time with 100 mL of brine. After drying ($MgSO_4$), the ether was removed by rotary evaporation, leaving 4.272 g of white crystals of **6b**.

The crystals were dissolved in 60 mL of 10% v/v HOAc and the solution cooled to 0 °C, and 40 mL of 1.25 M $NaNO_2$ was added in 10-mL portions. The mixture was allowed to stir overnight. The contents of the reaction were made basic with 15% NaOH and extracted 3 times with 100-mL portions of ether. The combined ether layers were washed 1 time with 100 mL of $NaHCO_3$ and 1 time with 100 mL of brine, dried over magnesium sulfate, filtered, and concentrated by rotary evaporation, yielding 2.784 g of yellow crystals (86%). Analysis by GC (column B) indicated 94.6% product **7b** and 5.6% starting material **4b**. An analytical sample was recrystallized from hexane, affording white crystals: mp 71–72 °C; NMR (CCl_4) δ 7.02 (d, J = 9 Hz, 1 H), 6.74–6.60 (m, 2 H), 3.76 (s, 3 H), 3.56 (s, 2 H), 2.59 (br t, 2 H), 2.28 (br t, 2 H), 1.80–1.24 (m, 6 H), 1.10–0.88 (m, 2 H); IR (neat) 3060, 2940, 2860, 1710, 1610, 1575, 1505, 1475, 1425, 1350, 1320, 1295, 1260, 1215, 1205, 1190, 1180, 1090, 985, 880, 810 cm^{-1}; high-resolution mass spectrum, m/e 232.145 (calcd for $C_{15}H_{20}O_2$, 232.146).

3-Methoxy-7,8,9,10,11,12-hexahydro-6(5*H*)-benzocyclodecenone (7c) was prepared from **4c** by the above procedure, which gave an 84% yield of product which was 94% **7c** by GC (column B). Recrystallization from hexane gave **7c**: mp 72–73 °C; NMR (CCl_4) δ 7.10 (d, J = 8 Hz, 1 H), 6.92–6.74 (m, 2 H), 3.83 (s, 3 H), 3.63 (s, 2 H), 2.56 (br t, 2 H), 2.32 (br t, 2 H), 1.87–1.30 (m, 6 H), 1.26–1.05 (m, 2 H); IR (CCl_4) 3010, 2945, 2870, 2845, 2765, 1715, 1620, 1555, 1505, 1475, 1450, 1325, 1300, 1255, 1215, 1160, 1110, 1050, 1010, 980, 875 cm^{-1}; 232.147 (calcd for $C_{15}H_{20}O_2$, 232.146).

7,8,9,10,11,12-Hexahydro-6(5*H*)-benzocyclodecenone (7a) was prepared from **4a** by the above procedure, which gave a 60% yield of **7a** which was recrystallized from pentane: mp 41.5–42.5 °C; NMR (CCl_4) δ 7.13 (m, 4 H), 3.63 (s, 2 H), 2.64 (br t, 2 H), 2.31 (br t, 2 H), 1.84–1.24 (m, 6 H), 1.22–0.86 (m, 2 H); IR (CCl_4) 3080, 3040, 2940, 2870, 1705, 1610, 1500, 1475, 1455, 1355, 1225, 1175, 990, 930, 885 cm^{-1}; high-resolution mass spectrum, m/e 202.136 (calcd for $C_{14}H_{18}O$, 202.136).

2-Methoxy-6-vinyl-7,8,9,10,11,12-hexahydro-6(5*H*)-benzocyclodecenol (8b). A 56.2-mmol portion of vinylmagnesium bromide was prepared in THF[8] and then the THF was removed under vacuum and replaced by 75 mL of ether. Next, 2.502 g (10.8 mmol) of ketone **7b** in 50 mL of anhydrous ether was added slowly to the Grignard solution over 5 h.[21] The reaction was followed by GC; the 1:3 product to starting material ratio observed at 4.5

(21) The later results strongly suggest that adding the ketone to a refluxing ether solution of vinyl Grignard reagent would give a better conversion.

h did not change upon stirring overnight at room temperature or upon reflux for 4.5 h. The mixture was cooled and quenched with saturated NH_4Cl and extracted twice with 50-mL portions of ether. The ether extract was washed with saturated NH_4Cl, saturated $NaHCO_3$, and saturated NaCl and dried over $MgSO_4$, which gave 2.821 g of yellow oil. This mixture was taken up in 50 mL of ether and added over 1.75 h to 49.2 mmol of vinyl Grignard in 75 mL of refluxing ether. After 7 h of reflux and 13 h at room temperature, the reaction was worked up as above. Kugelrohr distillation afforded 1.877 g of viscous yellow oil (5:1 product to starting material by GC analysis).

Flash chromatography of the above mixture with 10% EtOAc/pentane afforded 0.156 g of **7b**, 0.073 of **7b** and **8b**, and 1.089 g of 97% pure **8b** (40% yield). Recrystallization from hexane gave pure **8b**: mp 54–55 °C; NMR (CCl_4) δ 7.22 (br d, 1 H), 6.63 (m, 2 H), 6.01 (dd, J = 18, 10 Hz, 1 H), 5.33 (br d, J = 18 Hz, 1 H), 5.05 (dd, J = 10, 2 Hz, 1 H), 3.75 (s, 3 H), 3.28–1.06 (m, 15 H); IR (neat) 3650–3150, 3095, 3000, 2910, 2850, 2795, 2695, 1640, 1605 1570, 1495, 1475, 1450, 1415, 1335, 1280, 1245, 1200, 1165, 1150, 1120, 1030, 985, 953, 910, 855, 840, 810, 790, 750, 715 cm^{-1}; mass spectrum, m/e (relative %), 216 (10.0), 260 (91.1), 242 (25.1), 136 (100.0), 135 (88.5); high-resolution mass spectrum, m/e 260.177 (calcd for $C_{17}H_{24}O_2$, 260.178).

3-Methoxy-6-vinyl-7,8,9,10,11,12-hexahydro-6(5*H*)-benzocyclodecenol (8c) was prepared and purified in the same manner as **8b** to give a 42% yield of an oil (94% **8c** by GC): NMR (CCl_4) δ 7.06–6.50 (m, 3 H), 5.98 (dd, J = 18, 10 Hz, 1 H), 5.31 (br d, J = 18 Hz, 1 H), 5.02 (d, J = 10 Hz, 1 H), 3.70 (s, 3 H), 3.16–2.22 (m, 5 H), 2.09–1.02 (m, 10 H); IR (neat) 3650–3150, 3095, 3000, 2910, 2850, 2755, 2695, 1640, 1605, 1570, 1495, 1475, 1450, 1415, 1345, 1315, 1250, 1190, 1155, 1110, 1040, 990, 960, 915, 865, 815, 725 cm^{-1}; mass spectrum, m/e (relative %), 261 (3.1) 260 (27.1), 242 (9.4), 136 (49.0), 135 (100.0); high-resolution mass spectrum, m/e 260.178 (calcd for $C_{17}H_{24}O_2$, 260.178).

6-Vinyl-7,8,9,10,11,12-hexahydro-6(5*H*)-benzocyclodecenol (8a) was prepared and purified as above except that the ketone was added directly to the refluxing ether solution of Grignard reagent and refluxed for 7 h and was not reacted again. After the same workup and purification as above, 4.03 g of **7a** gave back 1.11 g of recovered **7a** and 2.39 g of **8a**: mp 58.0–60.5 °C; NMR (CCl_4) δ 7.50–6.90 (m, 4 H), 6.03 (br dd, J = 17, 11 Hz, 1 H), 5.34 (br d, J = 17 Hz, 1 H), 5.06 (dd, J = 11, 2 Hz, 1 H), 3.48–2.30 (m, 5 H), 2.26–0.92 (m, 10 H); IR (CCl_4) 3700–3200, 3580, 3090, 3040 2950, 2890, 2740, 1970, 1940, 1860, 1660, 1620, 1595, 1510, 1495, 1465, 1435, 1365, 1310, 1290, 1280, 1180, 1150, 1130, 1075, 1015, 985, 940, 920, 885, 815, 805, 765, 740 cm^{-1}; high-resolution mass spectrum, m/e 230.167 (calcd for $C_{16}H_{22}O$; 230.167).

When the same reaction was carried out with toluene, rather then diethyl ether, increased temperature was required to obtain a reasonable rate of conversion (11 h at 55–58 °C, 5 h at 78 °C, overnight at 93 °C, and then briefly to reflux). Flash chromatography eventually gave yielded 5% of **7a**, 16% of **8a**, and 14% of dehydration product **9**: NMR (CCl_4) δ 7.36–6.72 (m, 4 H) 6.55 (s, 1 H), 6.35 (dd, J = 17, 11 Hz, 1 H) 5.23 (dd, J = 17, 1 Hz, 1 H), 5.03 (dd, J = 11, 1 Hz, 1 H), 2.94–1.96 (m, 4 H), 1.92–0.92 (m, 8 H); IR (CCl_4) 3130, 3090, 3060, 2960, 2890, 1650, 1620, 1500, 1470, 1450, 1425, 1380, 1360, 1310, 1285, 1120, 1050, 1000, 910, 865, 790, 750, 705 cm^{-1}; mass spectrum, m/e (relative %) 213 (13.7), 212 (77.7), 155 (54.0), 142 (84.0), 141 (100).

2-Methoxy-5,6,9,10,11,12,13,14-octahydro-8(7*H*)-benzocyclododecenone (12b). A 2.60-g portion of 24.7% KH in oil (16.0 mmol) was washed 5 times with hexane[3] under nitrogen and then combined with 50 mL of HMPT. Then, 0.642 g (2.46 mmol) of **8b** in 30 mL of HMPT was added slowly to the KH/HMPT. The reaction mixture took on a dark brown color. After the mixture was stirred for 8 h at 25%, an aliquot showed no starting material by GC analysis. The mixture was quenched cautiously with water, and the aqueous layer was extracted 5 times with 60-mL portions of ether. The combined ether extracts were washed 5 times with 80-mL portions of water, 1 time with 80 mL of saturated $NaHCO_3$, and 1 time with 80 mL of brine. After drying over magnesium sulfate and filtering, rotary evaporation gave 0.604 g (94.0% material yield) of an orangish solid. GC analysis of this solid indicated it was 96% pure **12b**. Preparative GC gave a white solid: mp 67–68 °C; ^1H NMR (CCl_4) δ 6.99 (d, J = 9 Hz, 1 H)), 6.68–6.49 (m, 2 H), 3.71 (s, 3 H), 2.68–2.18 (m, 8 H), 2.16–1.04 (m, 10 H); ^{13}C NMR ($CDCl_3$) δ 212.50, 157.57, 142.26, 131.57, 128.98, 114.86, 111.67, 55.10, 41.70, 38.97, 30.65, 29.53, 27.79, 25.29, 25.19, (double intensity) 23.01; IR (CCl_4) 2940, 2860, 1715, 1610, 1580, 1505, 1470, 1445, 1365, 1330, 1290, 1250, 1205, 1160, 1100, 1040, 995, 985, 855 cm^{-1}; high-resolution mass spectrum, m/e 260.179 (calcd for $C_{17}H_{24}O_2$, 260.178).

3-Methoxy-5,6,9,10,11,12,13,14-octahydro-8(7*H*)-benzocyclododecanone (12c) was prepared in the same way as **12b** using 0.12 g of 24.7% KH, 4.2 mL of dry HMPT and 43 mg of **8c** at 25 °C for 2 h. The product (32.3 mg) was purified by preparative GC. Analysis by GC with an internal standard indicated a 54% yield of **12c**: NMR (CCl_4) δ 6.91 (d, J = 9 Hz, 1 H), 6.7–6.5 (m, 2 H), 3.72 (s, 3 H), 2.8–2.35 (m, 8 H), 2.35–2.0 (m, 2 H), 1.1–2.0 (m, 8 H); IR (CCl_4) 2930, 2860, 1710, 1610, 1580, 1500, 1465, 1445, 1365, 1290, 1250, 1205, 1160, 1100, 1040, 880, 870, 850 cm^{-1}; high-resolution mass spectrum, m/e 260.177 (calcd for $C_{17}H_{24}O_2$, 260.178).

5,6,9,10,11,12,13,14-Octahydro-8(7*H*)-benzocyclodecenone (12a) was prepared in a similar way by adding dropwise 0.284 g (1.23 mmol) of **8a** in 5 mL of HMPT to 4.88 mmol of KH in 20 mL of HMPT with ice cooling under nitrogen. After 7 h at 25 °C the reaction mixture was cooled and cautiously quenched with 2 mL of water and 1 mL of 10% H_2SO_4. After a workup similar to that used for **12c**, Kugelrohr distillation (130 °C, 1 mm) yielded 0.198 g (70%) of **12a**: NMR (CCl_4) δ 7.02 (s, 4 H), 3.04–1.88 (m, 10 H), 1.84–0.96 (m, 8 H); IR (CCl_4) 3070, 3025, 2940, 2870, 1715, 1605, 1495, 1465, 1450, 1365, 1255, 1220, 1050, 825 cm^{-1}; high-resolution mass spectrum, m/e 230.165 (calcd for $C_{16}H_{22}O$, 230.167).

Pyrolyses of 6-[(trimethylsilyl)oxy]-6(5*H*)-vinyl-7,8,9,10,11,12-hexahydrobenzocyclodecene (11a) and the subsequent product analysis used procedures described earlier.[8] The trimethylsilyl derivative was prepared by a modification of the earlier procedure wherein 0.4 mmol of **10a** was stirred for 23 h with a 1:2:10 mixture of trimethylsilyl chloride, hexamethyldisilazane, and pyridine with workup as described earlier.[8] Pyrolysis for 3 h at ca. 300 °C gave at least seven products. The trimethylsilyl enol ether was not strongly evident in the NMR; hydrolysis of the mixture did give **10a** but only in 6% yield.

Rearrangement of the Potassium Salt of 6-Vinyl-7,8,9,10,11,12-hexahydro-6(5*H*)-benzocyclodecenol (8a) in HMPT, Followed by Attempted Trapping of the Enolate with Trimethylsilyl Chloride. A 50-mL flask under nitrogen was charged with 0.373 g (2.30 mmol) of 24.7% KH (Ventron) and the KH was washed as usual[3] with hexane. HMPT (15 mL) was added, and the mixture was cooled in an ice bath. Next, 0.240 g (1.04 mmol) of the alcohol **8a** was dissolved in 10 mL of HMPT and added slowly to the KH/HMPT mixture via syringe, which gave a bright orange solution. The mixture was stirred for 10 h, and then cooled in an ice bath, and 0.5 mL (3.8 mmol) of trimethylsilyl chloride (Me_3SiCl) was added in 0.1-mL aliquots. The solution went from orange-brown to pale yellow. The mixture was poured into a separatory funnel and washed 3 times with 40-mL portions of cold hexane. The combined hexane layers were washed 8 times with 20-mL portions of cold 5% $NaHCO_3$ dried over magnesium sulfate, filtered, and rotary evaporated, yielding 0.141 g of light yellow oil which contained no vinyl or trimethylsilyl protons in the NMR. All spectral and analytical data were identical with the corresponding data for **12a**. Other attempts to trap the enolates prepared similarly to that above were also unsuccessful. Adding dioxane[17] to the mixture before quenching with Me_3SiCl failed to trap any enolate. Varying the workup procedure failed to alter the results. Attempted trapping with *tert*-butyldimethylsilyl chloride also failed. Trapping of the enolate with freshly distilled acetic anhydride appeared to be partially successful (ca. 50% trapping by GC analysis as evidenced by a carbonyl band at 1760 cm^{-1} in the IR and a singlet at δ 2.31 in the NMR. The vinylic proton of the enol acetate was not clearly established, however.

Trapping of the Enolate of Cyclododecanone by Methyl *p*-Toluenesulfonate. A solution of 8 mL of cyclododecanone enolate prepared as above from 1.04 g of 24.7% KH and 1.00 g of cyclododecanone in 10 mL of HMPT was cooled to 0 °C in an ice bath. Next, 0.72 mL (ca. 1.25 excess based on KH) of freshly distilled (134–135 °C, 3.5 mm) methyl *p*-toluenesulfonate (MeOTs) was added. This mixture was allowed to stir for 27 h, and then

poured into a separatory funnel containing cold saturated $NaHCO_3$. The aqueous layer was extracted with four 60-mL portions of cold ether, and the combined ether layers were washed 4 times with 60-mL portions of cold water, 1 time with saturated $NaHCO_3$, and 1 time with brine. Drying over magnesium sulfate, filtering, and rotary evaporation yielded 0.659 g of oil which contained a fair amount of MeOTs. The mixture was taken up in ether and washed 2 times with Et_3N. After workup of the ether layer, 0.278 g of a dark yellow oil was isolated, which appeared to be ca. 60% methyl enol ether and 40% cyclododecanone by GC analysis and as evidenced by the methyl singlet at δ 3.41 and a broad triplet at δ 4.27 (vinyl proton).

2-Hydroxy-5,6,9,10,11,12,13,14-octahydro-8(7*H*)-Benzocyclododecenone (12d). A solution of 0.0296 g of **13** in 1 mL of 48% HBr and 1 mL of acetic acid was stirred at reflux for 5 h. The cooled reaction was worked up by neutralizing with saturated $NaHCO_3$, extracting with ether, and washing with ether layer 2 times with saturated $NaHCO_3$ and 1 time with brine. After drying ($MgSO_4$), rotary evaporation gave 0.0199 g (71% yield) of **12d** as light yellow crystals: NMR ($CDCl_3$) δ 7.06 (d, J = 9 Hz, 1 H), 6.72–6.59 (m, 2 H), 5.25 (br s, 1 H), 2.80–2.27 (m, 8 H), 2.04–1.05 (m, 10 H); IR (neat) 3700–3100, 3040, 2950, 2875, 2705, 1705, 1620, 1595, 1510, 1475, 1455, 1375, 1355, 1290, 1250, 1170, 1135, 1115, 1035, 970, 920, 880, 830, 740 cm^{-1}; mass spectrum, m/e (relative %) 246 (100.0), 213 (24.6), 173 (26.4), 159 (51.7).

One-Carbon Expansion of 12b. The Me_3SiCN ring expansion procedure that was used earlier to prepare **7b** was applied to **12b** but only gave a low yield (<15%) of product. Analysis by GLC showed relative amounts of starting material (ca. 9%), an uncharacterized component of longer retention time (ca. 18%), and the major component, which corresponded to product, with the longest retention time (ca. 73%). The NMR spectrum of this mixture looked very similar to that of starting material, except there were two peaks of approximately equal height separated by about 1 Hz, corresponding to the methoxy hydrogens. The IR also was similar (carbonyl at 1710 cm^{-1}). A GC sample of the major component was collected for high-resolution mass spectrum, m/e 274.193 (calcd for $C_{18}H_{26}O_2$, 274.193).

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Registry No. 2, 80262-93-7; **3b**, 80262-94-8; **3c**, 80262-95-9; **4a**, 830-77-3; **4b**, 80262-96-0; **4c**, 80262-97-1; **5b**, 80262-98-2; **6b**, 80262-99-3; **7a**, 80263-00-9; **7b**, 80263-01-0; **7c**, 80263-02-1; **8a**, 80263-03-2; **8a**-K, 80263-04-3; **8b**, 80263-05-4; **8c**, 80263-06-5; **9**, 80263-07-6; **10a**, 80263-08-7; **11a**, 80263-09-8; **12a**, 80263-10-1; **12b**, 80263-11-2; **12c**, 80263-12-3; **12d**, 80263-13-4; **13**, 80263-14-5; cycloheptanone, 502-42-1; *p*-bromoanisole, 104-92-7; cyclododecanone, 830-13-7.

New Dimeric Indole Alkaloids from *Stenosolen heterophyllus*: Structure Determinations and Synthetic Approach[1]

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Structures of eight new dimeric indole alkaloids of the ervafoline 1–4 and ervafolidine series 5–8, isolated from *Stenosolen heterophyllus* (Vahl) Mgf (Apocynaceae), were investigated by use of mass spectrometry, ^1H and ^{13}C nuclear magnetic resonance, and X-ray crystallography. A biogenetic pathway was proposed to take into account the formation of these unusual alkaloids, and, finally, a synthetic approach based on this proposal has been developed.

Introduction

Examination of the leaves of *Stenosolen heterophyllus* (Vahl) Mgf (Apocynaceae),[3,4] a shrub from French Guyana, has resulted in the isolation of several monomeric[1c,5] and two classes of four dimeric indole alkaloids.

Preliminary communications from our laboratories described the structural determination of the four dimeric alkaloids 1–4 of the ervafoline family.[1a-1c] In this paper we report the structural investigation of the second ervafolidine family of alkaloids 5–8 as well as X-ray studies concerning both series. Finally, in support of our efforts directed toward the synthesis of the new type of dimer, we present a synthetic approach inspired from our pro-

(1) Part of this work was published as preliminary communications: (a) Henriques, A.; Kan, C.; Ahond A.; Riche, C.; Husson, H.-P. *Tetrahedron Lett.* **1978**, 3707–3710. (b) Henriques, A.; Kan, S.-K.; Lounasmaa, M. *Acta Chem. Scand.*, **1979**, **B 33**, 775-776; (c) Henriques, A.; Kan, C.; Husson, H.-P.; Lounasmaa, M. *Acta Chem. Scand., Ser. B* **1980**, *34*, 509–512. (d) Henriques, A.; Husson, H.-P. *Tetrahedron Lett.* **1981**, *22*, 567–570.

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(3) (a) Vahl, M. *Ecol. Am.* **1798**, *2*, 22. (b) Vahl, M. *Icones Pl. Am.* **1799**, *2*, Table 14.

(4) Markgraf, F. *Notizbl. Botan. Gart. Berlin 16* **1938**, 122.

(5) Henriques, A.; Kan, C.; Jasor, Y.; Moretti, Y.; Husson, H.-P., unpublished results.

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