New Phenanthrene Synthesis via Ortho Bis(aryne) Equivalents. Application to Permethylphenanthrene

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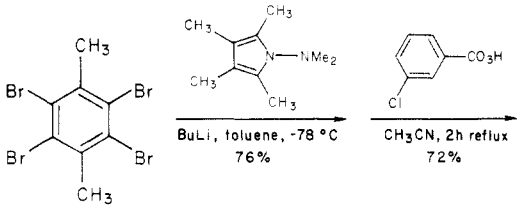
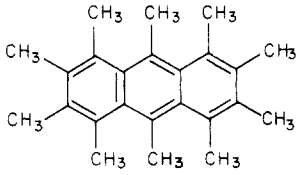
The ortho bis(aryne) equivalent 4,5-dibromo-3,6-diiodo-*o*-xylene (1) reacts with *n*-butyllithium in the presence of furans or N-substituted pyrroles to give diadducts. Removal of the oxygen or nitrogen bridges gives phenanthrenes. The method is applied to the synthesis of 9,10-dimethylphenanthrene (4), 1,4,5,8,9,10-hexamethylphenanthrene (7), and decamethylphenanthrene (11). The latter two compounds tautomerize in the central ring (to give 8 and 12, respectively) on mild treatment with acid.

In view of the large number and variety of known phenanthrene syntheses[1] one might well question the need for yet another. The new method we describe here is particularly advantageous for the synthesis from benzenes, in just two or three steps, of phenanthrenes containing substituents at the highly hindered 4,5-positions.[2,3]

In a recent communication[4] we described the use of tetrahaloarenes as bis(aryne) equivalents. With these reagents benzenes could be converted to anthracenes in just two steps. For example, decamethylanthracene was easily prepared in 54% overall yield by the two-step sequence shown in eq 1. We have now extended this methodology to phenanthrene synthesis.



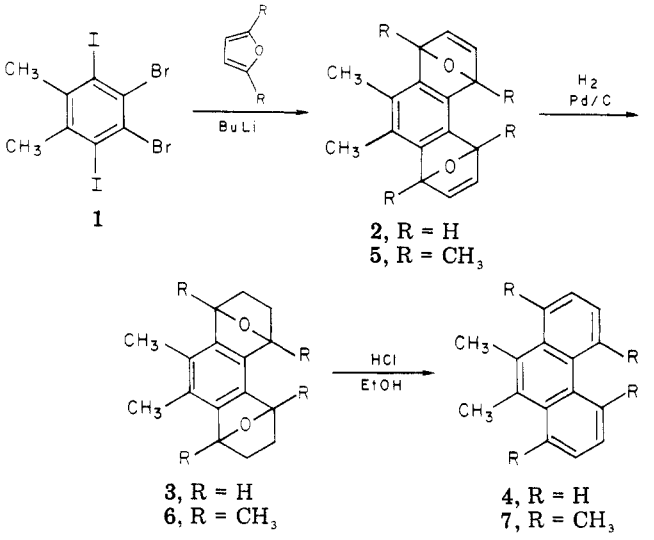


(1)

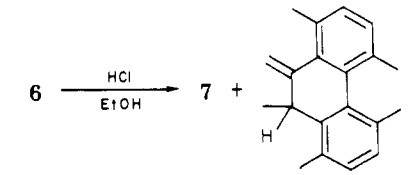
Results and Discussion

Treatment of a toluene solution of 4,5-dibromo-3,6-diiodo-*o*-xylene (**1**)[5] and excess furan at −78 °C with 2 equiv of *n*-butyllithium gave the diadduct **2** in 71% yield (Scheme I). The adduct melted fairly sharply at 260–262 °C, suggesting that it was mainly one isomer. The proton NMR spectrum had a singlet at δ 2.16 for the aromatic methyls and broad singlets at δ 5.60 and 6.80 for the bridgehead and vinyl protons, respectively. The structure of **2** was confirmed by hydrogenation to **3** and dehydration to the known 9,10-dimethylphenanthrene **4**.

Scheme I



When the sequence was repeated with 2,5-dimethylfuran, diadduct **5** was obtained in 34% yield as a 10:7 mixture of separable stereoisomers. Although the hydrogenation step proceeded smoothly and dehydration of the reduced adduct gave some of the desired **7**, the major product was **8** (eq 2). Separate treatment of **7** with HCl and ethanol also gave **8**.



(2)

8

The structure **8** is assigned from its proton NMR spectrum, which showed a doublet at δ 0.88 for the aliphatic methyl coupled to a one-proton quartet at δ 3.43 (J = 8 Hz), as well as peaks for the vinyl protons, aromatic protons, and aromatic methyls. The one-proton quartet was further split into doublets (J = 2 Hz) through coupling with one of the vinyl protons. This additional coupling

(1) For recent reviews, see: Floyd, A. J.; Dyke, S. F.; Ward, S. E. *Chem. Rev.* **1976**, *76*, 509. Sainsbury, M. In Rodd, E. H. "Chemistry of Carbon Compounds"; Elsevier: Amsterdam, 1979; Vol. III, part H, pp 104–114.

(2) By use of the original syntheses of 4,5-dimethylphenanthrene (Newman, M. S.; Whitehouse, H. S. *J. Am. Chem. Soc.* **1979**, *71*, 3664; Badger, G. M.; Campbell, J. E.; Cook, J. W.; Raphael, R. A.; Scott, A. I. *J. Chem. Soc.* **1950**, 2326), both of which involved the multistepped degradation of pyrene, a number of new methods appeared because of high interest in helical chirality (leading, ultimately, to helicene chemistry). Key papers include those by: Wittig, G.; Zimmermann, H. *Chem. Ber.* **1953**, *86*, 629. Bergman, E. D.; Pelchowicz, Z. *J. Am. Chem. Soc.* **1953**, *75*, 2663. Mosby, W. L. *J. Org. Chem.* **1954**, *19*, 294. Newman, M. S.; Wise, Richard M. *J. Am. Chem. Soc.* **1956**, *78*, 450. Mislow, K.; Joshua, H. *Ibid.* **1965**, *87*, 666. Bestmann, H. J.; Häberlein, H.; Eisele, W. *Chem. Ber.* **1966**, *99*, 28. Hausigk, D. *Tetrahedron Lett.* **1969**, 5263. Newman, M. S.; Lilje, K. C. *J. Org. Chem.* **1979**, *44*, 4944.

(3) For papers dealing with the strain in 4,5-dimethylphenanthrenes, see: Frisch, M. A.; Barker, C.; Margrave, J. L.; Newman, M. S. *J. Am. Chem. Soc.* **1963**, *85*, 2356. Karnes, H. A.; Kybett, B. D.; Wilson, M. H.; Margrave, J. L.; Newman, M. S. *Ibid.* **1965**, *87*, 5554. Dougherty, R. C.; Bertorello, H. E.; de Bertorello, M. M. *Org. Mass Spectrom.* **1971**, *5*, 1321. Allinger, N. L.; Kao, J. *J. Am. Chem. Soc.* **1977**, *99*, 975. Bushmelev, V. A.; Shakirov, M. M.; Derendyaev, B. G.; Koptyug, V. A. *Zh. Org. Khim.* **1979**, *15*, 1934; *J. Org. Chem. USSR (Engl. Transl.)* **1979**, *15*, 1747.

(4) Hart, H.; Lai, C.-Y.; Nwokogu, G.; Shamoulian, S.; Teuerstein, A.; Zlotogorski, C. *J. Am. Chem. Soc.* **1980**, *102*, 6649.

(5) Hart, H.; Shamoulian, S.; Takehira, Y. *J. Org. Chem.*, in press.

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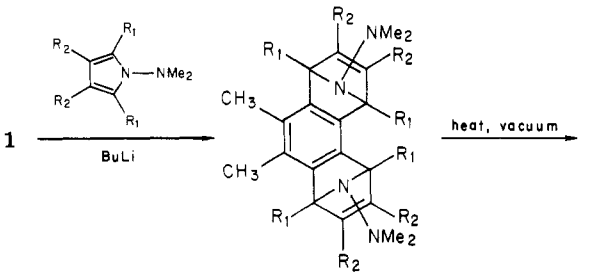
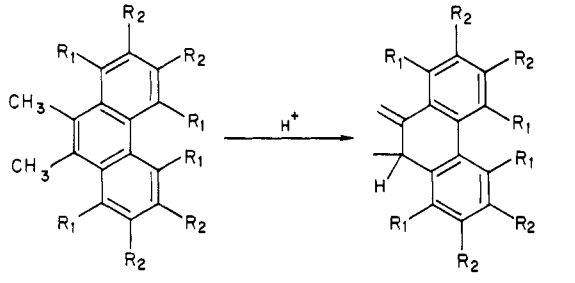
Scheme II



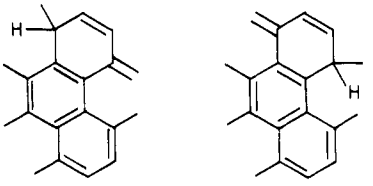
9, $R_1 = CH_3$; $R_2 = H$
10, $R_1 = R_2 = CH_3$



7, $R_1 = CH_3$; $R_2 = H$
11, $R_1 = R_2 = CH_3$

8, $R_1 = CH_3$; $R_2 = H$
12, $R_1 = R_2 = CH_3$

tends to rule out alternative structures **8a** and **8b** (the two other alternatives in which the aromaticity of only one ring in **7** is disrupted through tautomerization).



8a **8b**

Our target shifted at this point to the search for a better route to **7** [and to permethylphenanthrene (**11**)], a route which would avoid acid in the bridge removal step. Schultz[6] has used *N*-aminopyrroles in arene synthesis, and we have applied his method to a variety of highly hindered polynuclear arenes.[7] Consequently, we replaced the 2,5-dimethylfuran with *N*-(dimethylamino)-2,5-dimethylpyrrole[8] and obtained diadduct **9** (Scheme II) in 46% yield as a mixture of syn and anti isomers. On pyrolysis at 150 °C and 0.1 torr for 1 h **9** gave a nearly quantitative yield of 1,4,5,8,9,10-hexamethylphenanthrene (**7**). In a similar manner, adduct **10** was prepared (44% yield) from *N*-(dimethylamino)-2,3,4,5-tetramethylpyrrole[7] and converted (97% yield) to decamethylphenanthrene (**11**).

The structures of **7** and **11** are based on their method of synthesis and spectra. Thus **7** showed three six-proton singlets for the aromatic methyls (δ 2.449, 2.631, and 2.817) and an AB quartet centered at δ 7.171 for the four aromatic protons. In the case of **11**, only aromatic methyls were observed. The ^{13}C spectrum for **7** showed the expected ten signals (three in the aliphatic methyl region and seven in the aromatic region). With **11**, the ^{13}C spectrum showed one fewer aliphatic methyl signal and one fewer aromatic carbon signal due to accidental overlapping. The ultraviolet spectra of **7** and **11** were very similar, each having a long-wavelength maximum at about 325 nm. The structure of **11** was further evident from its rapid and quantitative isomerization at room temperature with trifluoroacetic acid (TFA) to its tautomer **12**.

In summary, we have demonstrated that the ortho bis(aryne) equivalent **1** can be converted to phenanthrenes in two (or three) steps and that the method can be used to synthesize hindered phenanthrenes such as decamethylphenanthrene.

Experimental Section

General Procedures. ^1H NMR spectra were measured at 60 MHz (Varian T-60) or at 180 MHz (Bruker) in $CDCl_3$ with $(CH_3)_4Si$ as an internal standard. Chemical shifts are reported in parts per million (δ). ^{13}C NMR spectra were measured in $CDCl_3$ on a Varian CFT-20 spectrometer. IR spectra were determined on a Perkin-Elmer 167 spectrometer. UV spectra were obtained with a Cary 219 spectrometer. Mass spectra were measured at 70 eV by using a Finnigan 4000 with the INCOS data system, operated by Mr. Ernest Oliver. The high-resolution mass spectrum was obtained with a Varian CH5 spectrometer. Melting points (Fisher Scientific electrothermal melting point apparatus) are uncorrected. Microanalyses were performed by Spang Microanalytical Laboratory. The silica gel for chromatography was 230–400 mesh; the alumina was neutral grade Brockmann activity I.

9,10-Dimethyl-1,4,5,8-tetrahydrophenanthrene 1,4:5,8-Diendoxide (2). To a stirred suspension of 4,5-dibromo-3,6-diiodo-*o*-xylene (1;[5] 2.16 g, 5 mmol) and furan (2 g, 29 mmol) in dry toluene (100 mL) under argon at −78 °C was added dropwise over 4 h 12 mmol of *n*-butyllithium in 100 mL of hexane. After the mixture gradually warmed to room temperature, 1 mL of methanol was added, and the solution was washed with water and dried ($MgSO_4$). Concentration on a rotary evaporator gave a solid residue which was chromatographed on alumina with 1:1 hexane/chloroform as eluant to give 0.854 g (71%) of **2**: mp 260–262 °C; ^1H NMR δ 2.13 (s, 6 H), 5.60 (br s, 4 H), 6.80 (br s, 4 H); mass spectrum, *m/e* (relative intensity) 238 (27), 181 (46), 167 (100), 165 (85), 152 (41), 115 (46).

1,4,5,8,9,10-Hexamethyl-1,4,5,8-tetrahydrophenanthrene 1,4:5,8-Diendoxide (5). The procedure was the same as for **2** except that 2,5-dimethylfuran was used in place of furan. The first chromatographic fraction gave 0.30 g (20%) of the major isomer of **5**: mp 167–168 °C; ^1H NMR δ 1.86 (s, 6 H), 1.90 (s, 6 H), 2.13 (s, 6 H), 6.50 (s, 4 H); ^{13}C NMR δ 14.30, 19.15, 20.27, 88.51, 89.31, 125.94, 140.95, 146.27, 146.53, 147.01; mass spectrum, *m/e* (relative intensity) 294 (4), 268 (14), 251 (86), 242 (25), 225 (43), 208 (100), 193 (23), 178 (21). Further elution gave 0.204 g (14%) of the minor isomer of **5**: mp 166–168 °C; ^1H NMR δ 1.96 (s, 6 H), 2.00 (s, 6 H), 2.13 (s, 6 H), 6.43 (dd, J = 12, 4 Hz, 4 H); ^{13}C NMR δ 14.48, 19.04, 19.19, 89.35, 89.94, 126.12, 141.02, 145.18, 145.49, 146.18; mass spectrum, *m/e* (relative intensity) 294 (3), 268 (6), 251 (45), 242 (16), 225 (26), 209 (100), 193 (21), 178 (15).

Hydrogenation of 2. A solution of **2** (1.19 g, 5 mmol) in 100 mL of ethyl acetate was hydrogenated for 1 h over 0.5 g of 10% Pd/C at room temperature and 45 psi of hydrogen. The catalyst was filtered, the solution was concentrated (rotary evaporator), and the remaining oil was crystallized from hexane to give 1.075 g (89%) of **3**: mp 162–164 °C; ^1H NMR δ 1.16–1.43 (m, 8 H), 2.13 (br s, 6 H), 5.33 (m, 4 H); mass spectrum, *m/e* (relative intensity) 242 (6), 214 (27), 185 (100), 128 (7); with chemical ionization, *m/e* 243 [$(M + 1)^+$].

Hydrogenation of 5. The minor isomer of **5** (100 mg) in 100 mL of ethyl acetate was hydrogenated for 0.5 h over 100 mg of 10% Pd/C as for **2**. The product was crystallized from methanol to give 90 mg (89%) of **6**: mp 134–135 °C; ^1H NMR δ 1.20–1.73 (m, 8 H), 1.86 (s, 6 H), 1.90 (s, 6 H), 2.23 (s, 6 H); mass spectrum, *m/e* (relative intensity) 298 (1.4), 270 (19), 242 (100); with chemical ionization, *m/e* 299 [$(M + 1)^+$].

Dehydration of 3. A solution of **3** (1.07 g, 4.4 mmol) in 100 mL of absolute ethanol was saturated with hydrogen chloride by bubbling gas through the solution for 10 min. The resulting solution was heated at reflux (2 h), cooled, and evaporated (rotary evaporator). The residue was taken up in chloroform (100 mL), washed with 10% aqueous Na_2CO_3 and water, and dried ($MgSO_4$).

(6) Schultz, A. G.; Shen, M. *Tetrahedron Lett.* **1979**, 2969. Schultz, A. G.; Shen, M.; Ravichamdran, R. *Ibid.* **1981**, 1767.
(7) Lai, C.-Y. Ph.D. Dissertation, Michigan State University, 1981.
(8) Broadbent, H. S.; Burnham, W. S.; Olsen, R. K.; Sheeley, R. M. *J. Heterocycl. Chem.* **1968**, *5*, 755.

The residue after removal of the chloroform was chromatographed over silica gel (hexane eluant) to give 0.854 g (95%) of 9,10-dimethylphenanthrene: mp 140 °C (from methanol) (lit.[9] mp 140.5 °C); ^{1}H NMR δ 2.66 (s, 6 H), 7.50 (m, 4 H), 8.00 (m, 2 H), 8.53 (m, 2 H); ^{13}C NMR δ 15.86, 122.75, 124.54, 125.38, 126.51, 129.24, 129.43, 132.21; mass spectrum, *m/e* (relative intensity) 206 (100), 191 (82), 178 (12), 165 (32).

Dehydration of 6. A solution of **6** (100 mg) in 50 mL of absolute ethanol was saturated with hydrogen chloride and dehydrated as with **3**. The workup gave 65 mg of viscous oil which was resolved by gas–liquid chromatography (10% SE-30 on Chromosorb W at 200 °C) into two fractions. The first (25%) was 1,4,5,8,9,10-hexamethylphenanthrene (vide infra), and the second (75%) was its tautomer **8**: ^{1}H NMR δ 0.88 (d, *J* = 8 Hz, 3 H), 2.23 (s, 6 H), 2.33 (s, 3 H), 2.40 (s, 3 H), 3.43 (dq, *J* = 8, 2 Hz, 1 H), 4.93 (d, *J* = 2 Hz, 1 H), 5.20 (d, *J* = 2 Hz, 1 H), 6.86 (s, 2 H), 7.00 (s, 2 H); mass spectrum, *m/e* (relative intensity) 262 (trace), 220 (35), 205 (100), 145 (10); with chemical ionization, *m/e* 263 [(M + 1)$^+$].

Anal. Calcd for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.56; H, 8.49.

***N,N*-Bis(dimethylamino)-1,4,5,8,9,10-hexamethyl-1,4,5,8-tetrahydrophenanthrene-1,4:5,8-diimine (9).** The procedure and scale was the same as for the preparation of **2** except that *N*-(dimethylamino)-2,5-dimethylpyrrole[8] (1.38 g, 10 mmol) was used in place of furan. The crude product was triturated with hexane (20 mL) to give 0.45 g (24%) of a single isomer of **9**: mp 147–149 °C; ^{1}H NMR δ 1.80 (s, 6 H), 1.83 (s, 6 H), 2.16 (s, 6 H), 2.28 (br s, 12 H), 6.43 (br s, 4 H); ^{13}C NMR δ 14.93, 18.72, 19.43, 45.69, 74.71, 76.15, 126.44, 145.75, 146.00, 146.52, 146.75; mass spectrum, *m/e* (relative intensity) 321 (54), 276 (92), 262 (100), 116 (32); with chemical ionization, *m/e* 379 [(M + 1)$^+$].

The oily residue obtained from concentrating the hexane solution was chromatographed on alumina. Hexane eluted unreacted pyrrole. Further elution with chloroform gave 0.432 g (22%) of additional **9** as a mixture of anti and syn isomers.

***N,N*-Bis(dimethylamino)-1,2,3,4,5,6,7,8,9,10-decamethyl-1,4,5,8-tetrahydrophenanthrene-1,4:5,8-diimine (10).** The procedure and scale was the same as for **9** except that *N*-(dimethylamino)-2,3,4,5-tetramethylpyrrole[7] was used as the diene. A workup as with **9** gave 0.35 g (16%) of a single isomer of **10**: mp 174–175 °C; ^{1}H NMR δ 1.56 (s, 6 H), 1.60 (s, 6 H), 1.76 (s, 6 H), 1.80 (s, 6 H), 2.16 (s, 6 H), 2.43 (s, 12 H); ^{13}C NMR δ 10.50, 11.38, 14.77, 17.63, 18.69, 45.83, 76.12, 76.30, 125.68, 141.50, 145.16, 145.95, 148.31; mass spectrum, *m/e* (relative intensity) 318 (100), 304 (9), 288 (13); with chemical ionization, *m/e* 435 [(M + 1)$^+$]. Further workup of the hexane extract as with **9** gave an additional 0.614 g (28%) of **10** as a mixture of anti and syn isomers.

1,4,5,8,9,10-Hexamethylphenanthrene (7). Diadduct **9** (50 mg) was sealed under vacuum (0.1 torr) in a small glass tube and heated at 150 °C for 1 h. The product was chromatographed on alumina with hexane to give 31 mg (90%) of **7** which was recrystallized from methanol: mp 85–86 °C; ^{1}H NMR δ 2.449 (s, 6 H), 2.631 (s, 6 H), 2.817 (s, 6 H), 7.171 (AB q, *J* = 7.8 Hz, 4 H); ^{13}C NMR δ 20.79, 22.02, 25.47, 126.08, 129.69, 130.11, 130.59, 131.58, 132.93, 134.64; mass spectrum, *m/e* (relative intensity) 262 (100), 247 (13), 232 (23), 217 (10); IR (KBr) 2850, 2900, 1450, 1360, 800, 790 cm^{-1}; UV (heptane) λ_{max} 324 nm (log ε 4.43), 266 (4.90), 241 (4.64).

Anal. Calcd for $C_{20}H_{22}$: C, 91.55; H, 8.45. Found: C, 91.65; H, 8.46.

Decamethylphenanthrene (11). The procedure, with 100 mg of **10**, was the same as for **7**, except that the tube was heated at 170–180 °C for 2 h. The resulting **11** (64 mg, 97%) was recrystallized from methanol–chloroform: mp 165–167 °C; ^{1}H NMR δ 2.33 (br s, 18 H), 2.46 (s, 6 H), 2.53 (s, 6 H); in C_6D_6 δ 2.227 (s, 12 H), 2.356 (s, 6 H), 2.368 (s, 6 H), 2.491 (s, 6 H); ^{13}C NMR δ 16.57, 20.88, 21.08, 21.96, 128.15, 128.98, 130.06, 131.73, 133.73, 134.38; mass spectrum, *m/e* (relative intensity) 318 (100), 303 (7), 288 (17), 273 (14); UV (heptane) λ_{max} 325 nm (log ε 4.14), 277 (4.73).

Anal. Calcd for $C_{24}H_{30}$: C, 90.50; H, 9.50. Found: C, 90.69; H, 9.50.

Isomerization of 7 to 8. A solution of **7** (100 mg) in ethanol (50 mL) saturated with hydrogen chloride was treated as described for the dehydration of **6**. GLC analysis of the crude reaction product showed it to contain 24% of recovered **7** and 76% of **8**.

Isomerization of 11 to 12. To a solution of **11** (30 mg) in 5 mL of chloroform was added 10 drops of trifluoroacetic acid. The resulting blue solution was stirred at room temperature for 10 min, and then 5 mL of water was added. The organic layer was dried ($MgSO_4$) and concentrated to give a quantitative yield of **12** which was recrystallized from ethanol: mp 208–209 °C; ^{1}H NMR δ 0.93 (d, *J* = 7 Hz, 3 H), 2.06 (s, 6 H), 2.30 (br s, 12 H), 2.40 (s, 6 H), 3.56 (q, *J* = 7 Hz, 1 H), 4.80 (d, *J* = 2 Hz, 1 H), 5.26 (d, *J* = 2 Hz, 1 H); mass spectrum, *m/e* (relative intensity) 318 (94), 303 (100), 288 (8), 273 (26), 258 (11).

Acknowledgment. We are indebted to the National Science Foundation (Grant No. CHE 80-17746) and the National Institutes of Health (Grant No. GM 15997) for financial support of this research.

(9) De Ridder, R.; Martin, R. H. *Bull. Soc. Chim. Belg.* **1960**, *69*, 534.

Electrochemical Oxidation of Morphinandienones[1]

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The (±)-morphinandienones, *O*-methylflavinantine, *O*-benzyllaudanine, and *O*-methylflavinine, were synthesized by electrochemical oxidation of laudanosine, *O*-benzylpallidine, and norlaudanosine. With use of acetonitrile containing fluoroboric acid as solvent, the yields exceeded 70%. Upon further, separate oxidation in acidic acetonitrile, *O*-methylflavinantine produced *trans*-10-hydroxy-*O*-methylflavinantine stereospecifically in 38% yield, together with an oxohomomorphinan containing an acetal function in 41% isolated yield. The structure of the latter was determined by X-ray crystallography. Similarly, anodic oxidation of *O*-benzylpallidine produced *trans*-10-hydroxy-*O*-benzylpallidine (41%) and the corresponding oxohomomorphinan (37%). *trans*-10-Hydroxy-*O*-methylflavinine was isolated in 13% yield from the oxidation of *O*-methylflavinine.

The facile formation of morphinandienones through anodic coupling of benzyltetrahydroisoquinolines is now well established.[2] With use of acetonitrile containing fluoroboric acid as solvent-supporting electrolyte system,

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