and 1.76 g (5 mmol) of **8b** were reacted exactly as described for **9a**. The isolation and purification were done in the same way too. **9b** (283 mg, 8.8%) could be obtained as slightly yellow crystals: mp 268–270 °C; ^{1}H NMR ($CDCl_3$) [aromatic region, see Table I and Figure 2] δ 4.3 (m br, 4, $ArCH_2Ar$, 2, CH_2CH_3), 3.6 (m br, 4, $ArCH_2Ar$), 2.15 (s, 3, CH_3), 1.36 (t, 3, CH_2CH_3), 1.25 (s, 9, $C(CH_3)_3$); MS, *m/e* 642 (M^+). Anal. Calcd for $C_{42}H_{42}O_6$: C, 78.48; H, 6.59; O, 14.93. Found: C, 76.50; H, 6.65; O, 14.20.

5-Methyl-11-*tert*-butyl-17-carbethoxy-23-phenyl-25,26,27,28-tetrahydroxycalix[4]arene (9c). **6c** (2.00 g, 4.4 mmol) and 1.59 g (4.4 mmol) of **8c** were reacted exactly as described for **9a**. The isolation and purification were done in the same way too. **9c** (210 mg, 7.4%) could be obtained as slightly yellow crystals: mp 185–188 °C; ^{1}H NMR ($CDCl_3$) [aromatic region, see Table I and Figure 2] δ 4.3 (m br, 4, $ArCH_2Ar$, 2, CH_2CH_3), 3.6 (m br, 4, $ArCH_2Ar$), 2.12 (s, 3, CH_3), 1.33 (t, 3, CH_2CH_3), 1.24 (s, 9, $C(CH_3)_3$); MS, *m/e* 642 (M^+). Anal. Calcd for $C_{42}H_{42}O_6$: C, 78.48; H, 6.59; O, 14.93. Found: C, 77.15; H, 6.52; O, 13.70.

5-Methyl-11-*tert*-butyl-17-cyclohexyl-23-octyl-25,26,27,28-tetrahydroxycalix[4]arene (9d). To a boiling mixture of 300 mL of dry dioxane and 3 mL (27 mmol) of $TiCl_4$ was added a solution of 1.67 g (3.6 mmol) of **6d** and 1.43 g (3.6 mmol) of **8a** in 150 mL of dioxane during 6 h. The homogeneous solution was refluxed for further 50 h, filtered, and evaporated. The residue was extracted by three 20-mL portions of methylene chloride and the solution separated by flash chromatography (CH_2Cl_2/silica gel). Further chromatographic purification with carbon tetrachloride (monitored by TLC) finally led to the isolation of two fractions—174 mg of a viscous oil, the structure of which is still unknown, and 345 mg (14%) of **9d** in form of white crystals: mp 192 °C; ^{1}H NMR ($CDCl_3$) δ 10.23 (s, 4, OH), 7.04 and 7.02 (d, 2, ArH(*tert*-butyl)), 6.86, 6.84, 6.82 (s br, 2, ArH-(cyclohexyl) 2, ArH(*n*-octyl), 2, ArH(methyl)), 4.25, 4.18 (m br, 4, $ArCH_2Ar$), 3.46 (m br, 4, $ArCH_2Ar$), 2.40 (t, 2, $ArCH_2C_7H_{15}$), 2.28 (m, 1, C_6H_{11}), 2.13 (s, 3, CH_3), 1.74 (m, 5, C_6H_{11}), 1.51 (m, 2, $ArCH_2CH_2C_6H_{13}$), 1.27 (m, 10, C_8H_{17}, 5, C_6H_{11}), 1.22 (s, 9, $C(CH_3)_3$), 0.87 (t, 3, $C_7H_{14}CH_3$); MS, *m/e* 689 (M^+). Anal. Calcd for $C_{47}H_{60}O_4$: C, 81.93; H, 8.78; O, 9.29. Found: C, 81.05; H, 8.74; O, 8.56.

5,11-Dimethyl-17-*tert*-octyl-23-cyclohexyl-25,26,27,28-tetrahydroxycalix[4]arene (9e). A solution of 2.23 g (5 mmol) of **6e** and 1.82 g (5 mmol) of 2,6-bis(bromomethyl)-4-cyclohexylphenol in 200 mL of dry dioxane was dropped slowly into a boiling mixture of 3.29 mL (30 mmol) of $TiCl_4$ in 400 mL of dioxane during 8 h. The whole mixture was refluxed under argon atmosphere for a further 24 h. Finally the dark red solution was evaporated, the residue was dissolved in $CHCl_3$ and after the addition of 50 g of silica gel evaporated to dryness again. The silica gel was extracted in a Soxhlet apparatus by boiling $CHCl_3$ for 16 h, and the extract was further purified by flash chromatography (silica gel/$CHCl_3$). From the first fractions, 750 mg of crude product was obtained, which on trituration with acetone gave 375 mg (12%) of pure **9e**: mp 238–239 °C; ^{1}H NMR ($CDCl_3$) δ 10.14 (s, 4, OH), 7.01 and 6.97 (d, 2, ArH(*tert*-octyl)), 6.86, 6.84, 6.82 (s/d br, 6 Ar H), 4.18 (m, br, 4, $ArCH_2Ar$), 3.44 (m br, 4, $ArCH_2Ar$), 2.24 (m, 1, C_6H_{11}), 2.16 (s, 3, CH_3), 2.13 (s, 3, CH_3), 1.74 (m, 5, C_6H_{11}), 1.29 (m, 5, C_6H_{11}), 1.61 (s, 2, $C(CH_3)_2CH_2C(CH_3)_3$), 1.25 (s, 6, $C(CH_3)_2$), 0.66 (s, 9, $C(CH_3)_3$); MS, *m/e* 646 (M^+), 575 ($M^+ - C_5H_{11}$). Anal. Calcd for $C_{44}H_{54}O_4$: C, 81.69; H, 8.41; O, 9.89. Found: C, 79.40; H, 8.70; O, 8.85.

5,11-Dimethyl-17-*tert*-octyl-23-chloro-25,26,27,28-tetrahydroxycalix[4]arene (9f). **6e** (2.23 g, 5 mmol), 1.58 g (5 mmol) of 2,6-bis(bromomethyl)-4-chlorophenol, and 2.75 mL (25 mmol) of $TiCl_4$ were reacted exactly as described for **9e**. After evaporation of the reaction mixture, the residue was directly purified by flash chromatography ($CHCl_3$/silica gel). A crude product (200 mg) was isolated from the first fractions, which on trituration with acetone gave 80 mg (3%) of pure **9f**: mp 287 °C; ^{1}H NMR ($CDCl_3$) δ 10.06 (s, 4, OH), 7.04 and 6.99 (d, 2, ArH(*tert*-octyl)), 6.98 (s, 2, ArH(Cl)), 6.87 and 6.84 (d br, 2, $ArH(CH_3)$), 6.81 (s, 2, $ArH-(CH_3)$), 4.16 (m br, 4, $ArCH_2Ar$), 3.42 (m br, 4, $ArCH_2Ar$), 2.17 (s, 3, CH_3), 2.11 (s, 3, CH_3), 1.62 (s, 2, $C(CH_3)_2CH_2C(CH_3)_3$), 1.27 (s, 6, $C(CH_3)_2$), 0.68 (s, 9, $C(CH_3)_3$); MS, *m/e* 598 (M^+), 527 ($M^+ - C_5H_{11}$). Anal. Calcd for $C_{38}H_{43}ClO_4$: 76.17; H, 7.23; Cl, 5.92; O, 10.68. Found: C, 73.67; H, 7.29; Cl, 6.33; O, 9.17.

Synthesis of New Cyclopenta-Fused PAH Isomers of Cata-Annelated Benzenoid Systems

R. Sangaiah* and Avram Gold

Department of Environmental Sciences and Engineering, School of Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina 27514

Received July 7, 1986

The syntheses of three new benz-annelated derivatives of aceanthrylene and acephenanthrylene are reported. These systems are of interest in studies on mechanisms of bioactivation and structure–activity correlations because of their predicted high level of biological activity. Of the three isomers, benz[*d*]aceanthrylene (**5**) has been synthesized by two routes involving Friedel–Crafts acylations of 1,2,3,4-tetrahydronaphthacene with chloroacetyl chloride or oxalyl chloride as the key step. The cyclic ketone product from each route has been successfully elaborated to **5**. Synthesis of benz[*k*]aceanthrylene (**9**) involves preparation of acenaphthene-3,4-dicarboxylic anhydride and its smooth conversion to **9**. A straightforward and high-yield synthesis of benz[*j*]acephenanthrylene (**27**) is described utilizing a Robinson annelation reaction of methyl vinyl ketone with a previously reported ketonic precursor of acephenanthrylene.

Cyclopenta-fused polycyclic aromatic hydrocarbons (PAH) are a unique class of PAH present in the environment. Initial biochemical studies have suggested that epoxidation of the cyclopenta ring is a major pathway of enzymatic transformation.[1–4] Resonance stabilization energy[5,6] ($\Delta E_{deloc}/\beta$), which has been shown to correlate with biological activity,[6] is in general larger for benzylic carbonium ions derived from ring-opened cyclopenta epoxides[7,8] than those derived from other peripheral arene

(1) Gold, A.; Nesnow, S.; Moore, M.; Garland, H.; Curtis, J.; Howard, B.; Graham, D.; Eisenstadt, E. *Cancer Res.* **1980**, *40*, 4482.

(2) Sangaiah, R.; Gold, A.; Ball, L. M.; Kohan, M.; Bryant, B. J.; Rudo, K.; Claxton, L.; Nesnow, S. In *Polynuclear Aromatic Hydrocarbons: Chemistry and* Carcinogenesis; Cooke, M., Dennis, A. J. Ed.; Battelle: Columbus, OH, 1985; p 795.

(3) Kohan, M. J.; Sangaiah, R.; Ball, L. M.; Gold, A. *Mutat. Res.* **1985**, *155*, 95.

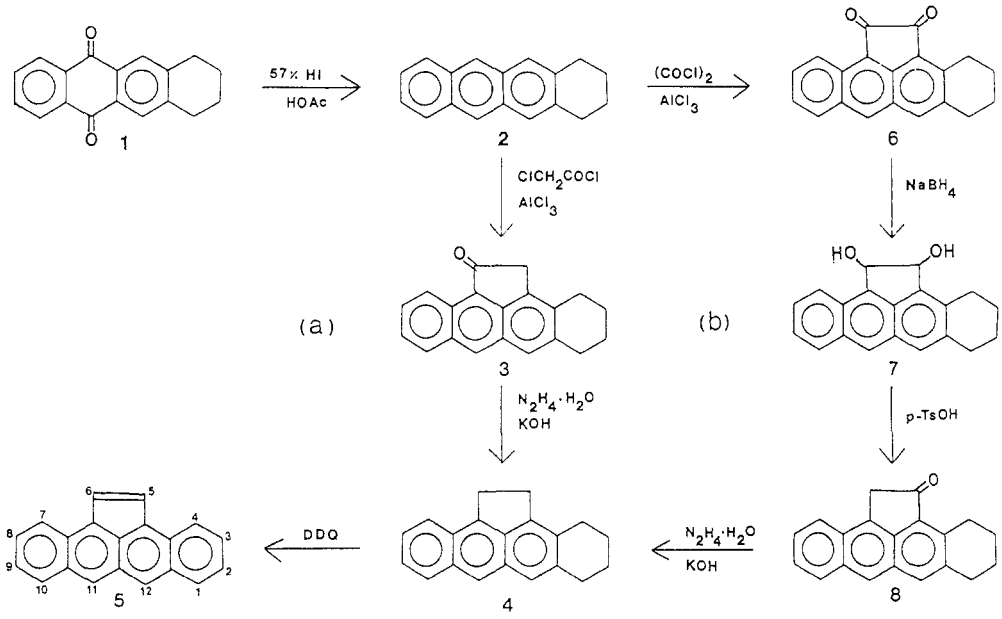
(4) Nesnow, S.; Leavitt, S.; Easterling, R.; Watts, S. H.; Toney, S. H.; Claxton, L.; Sangaiah, R.; Toney, G. E.; Wiley, J.; Fraher, P.; Gold, A. *Cancer Res.* **1984**, *44*, 4993.

(5) Dewar, M. J. S.; Dougherty, R. C. *The PMO Theory of Organic Chemistry*; Plenum: New York, 1975; Chapter 4, pp 131–196.

(6) Jerina, D. M.; Lehr, R. E.; Yagi, H.; Hernandez, O.; Dansette, P. M.; Wislocki, P. G.; Wood, A. W.; Chang, R. L.; Levin, W.; Conney, A. H. In *In Vitro Metabolic Activation in Mutagenesis Testing*; DeSerres, F. J., Fouts, J. R., Bend, J. R., Philpot, R. M., Ed.; Elsevier North Holland Biomedical: Amsterdam, 1976; pp 159–177.

0022-3263/87/1952-3205$01.50/0

Scheme I



oxides or bay region diol epoxides. The expected high level of activity for many cyclopenta PAH prompted us to investigate their metabolism to elucidate mechanisms of bioactivation and structure–activity relationships for active metabolites.

We have to date synthesized and studied the biological activity of aceanthrylene,[2,3,9] acephenanthrylene,[2,3] and a number of their benzannelated derivatives[4,10,11] and have concluded that oxidation of the cyclopenta ring is a primary pathway for metabolic activation of most of the mutagenic and carcinogenic compounds identified. In continuing studies on cyclopenta-fused PAH, we have undertaken synthesis of benz[*d*]aceanthrylene (**5**) and benz[*k*]aceanthrylene (**9**), because cyclopenta epoxide derived carbonium ions of these two isomers have the largest $\Delta E_{deloc}/\beta$ values (1.0887) theoretically possible for isomeric five-ring PAH.[7] We have also synthesized and characterized benz[*j*]acephenanthrylene (**27**), a cyclopenta-fused chrysene isomer, in order to investigate the effect of cyclopenta ring fusion on the bay region metabolism of the chrysene nucleus.

We report herein efficient and straightforward syntheses for compounds **5**, **9**, and **27**. The synthetic strategies are completely different from those reported for the cyclopenta-fused isomers based on the benz[*a*]anthracene skeleton,[10] which involved cyclodehydration of the appropriate benzanthrylacetic acids as the key step. Cyclodehydration of an arylacetic acid is not favorable for the naphthacene-derived systems, because the high stability of benzylic carbonium ions fused at peri positions[5] results primarily in decarbonylation of naphthacenylacetic acids rather than the desired cyclodehydration. Cyclodehydration of an arylacetic acid is not favorable for the chrysene nucleus because the most readily accessible derivative, 6-chrysenylacetic acid, requires intramolecular acylation of the unreactive C_7 position (reactivity number[12] N_t = 1.80).

Results and Discussion

Benz[*d*]aceanthrylene (5). The synthesis of benz[*d*]aceanthrylene was initially attempted by Friedel–Crafts acylation directly on naphthacene itself with chloroacetyl chloride and oxalyl chloride. No identifiable product was obtained from the chloroacetyl chloride reaction, and naphthacene-5-carboxylic acid was recovered as the only major product from the oxalyl chloride condensation. Since both chloroacetyl chloride and oxalyl chloride condense across the meso and peri positions of anthracene to yield cyclopenta-fused derivatives,[13,14] 1,2,3,4-tetrahydronaphthacene (**2**) was selected as starting material for condensation. Compound **2** was obtained in excellent yield by reduction of 1,2,3,4-tetrahydronaphthacene-6,11-quinone[15,16] with hydriodic acid in acetic acid.[17] Friedel–Crafts acylation of **2** with chloroacetyl chloride and $AlCl_3$ in dry methylene chloride gave cyclic ketone **3** in 22% yield. The structure of **3** was confirmed by ^1H NMR. The presence of two one-proton aromatic singlets requires the C_5–C_6 ring fusion (C_6–C_7 fusion would result in three aromatic singlets). Because meso proton resonances are shifted downfield, the singlet at δ 8.28 has been assigned to the meso proton at C_{11} and the higher field singlet to the peri proton at C_{12}. The orientation of the addition has been established by the presence of the low-field aromatic doublet (δ 9.13), which must result from the peri proton at C_7 in the pseudo bay region adjacent to the carbonyl group at C_6. The remaining doublet (δ 9.06) must arise from the proton at C_{10}.

Wolff–Kishner reduction of **3** followed by dehydrogenation of the resulting hexahydro derivative **4** with 3 mol equiv of 2,3-dichloro-5,6-dicyanoquinone (DDQ) afforded benz[*d*]aceanthrylene (**5**) in 10% overall yield (Scheme Ia).

The overall yield of **5** could be improved by Friedel–Crafts acylation of compound **2** with oxalyl chloride and $AlCl_3$ in carbon disulfide, which gave cyclic diketone **6** in 82% yield (Scheme Ib). The structural assignment **6** was

(7) Fu, P. P.; Beland, F. A.; Yang, S. D. *Carcinogenesis (London)* **1980**, *1*, 725.
(8) Silverman, B. D.; Lowe, J. P. *Cancer Biochem. Biophys.* **1984**, *7*, 203.
(9) Sangaiah, R.; Gold, A. *Org. Prep. Proced. Int.* **1985**, *17*, 53.
(10) Sangaiah, R.; Gold, A.; Toney, G. E. *J. Org. Chem.* **1983**, *48*, 1632.
(11) Nesnow, S.; Gold, A.; Sangaiah, R.; Triplett, L. L.; Slaga, T. J. *Cancer Lett. (Shannon, Irel.)* **1984**, *22*, 263.
(12) Calculated by the method described in ref 5.
(13) Plummer, B. F.; Al-Saigh, Z. Y.; Arfan, M. *J. Org. Chem.* **1984**, *49*, 2069.
(14) Becker, H. D.; Hansen, L.; Anderson, K. *J. Org. Chem.* **1985**, *50*, 277.
(15) Fieser, L. F. *J. Am. Chem. Soc.* **1931**, *53*, 2329.
(16) Stepan, V.; Vodehnal, J. *Collect. Czech. Chem. Commun.* **1971**, *36*, 3964.
(17) Konieczny, M.; Harvey, R. G. *J. Org. Chem.* **1979**, *44*, 4813.

Table I. ^{1}H NMR Data for the Title Compounds[a]

compd	chemical shifts (δ)
5[b]	7.35 (dt, 2 H, J = 6.5 Hz, $H_{2,9}$), 7.52 (dt, 2 H, J = 6.7, 1.1 Hz, $H_{3,8}$), 7.63 (s, 2 H, etheno $H_{5,6}$), 8.10 (d, 2 H, J = 8.49 Hz, peri $H_{1,10}$), 8.30 (dd, 2 H, J = 8.76, 0.80 Hz, peri $H_{4,7}$), 8.75 (s, 2 H, meso $H_{11,12}$)
9[b]	7.18 (d, 1 H, J = 5.1 Hz, etheno H_2), 7.47 (dt, 2 H, J = 6.6 Hz, $H_{9,10}$), 7.62 (dd, 1 H, J = 6.6 Hz, H_4), 7.90 (d, 1 H, J = 5.1 Hz, etheno H_1), 7.91 (br d, 1 H, J = 6.3 Hz, H_3), 8.10 (br t, 3 H, J = 6.6 Hz, peri $H_{5,8,11}$), 8.91 (s, 1 H, meso H_{6or7}), 8.94 (s, 1 H, meso H_{7or6}), 9.07 (s, 1 H, meso H_{12})
27[c]	7.22 (s, 2 H, etheno $H_{4,5}$), 7.60–7.75 (m, 4 H, $H_{2,3,8,9}$), 8.00 (dd, 1 H, J = 7.88, 1.45 Hz, peri H_{10}), 8.02 (d, 1 H, J = 8.86 Hz, H_{11}), 8.48 (dd, 1 H, J = 7.51, 1.30 Hz, bay region H_7), 8.66 (d, 1 H, J = 8.89 Hz, bay region H_{12}), 8.82 (br d, 1 H, 8.32 Hz, bay region H_1), 8.97 (s, 1 H, bay region H_6)

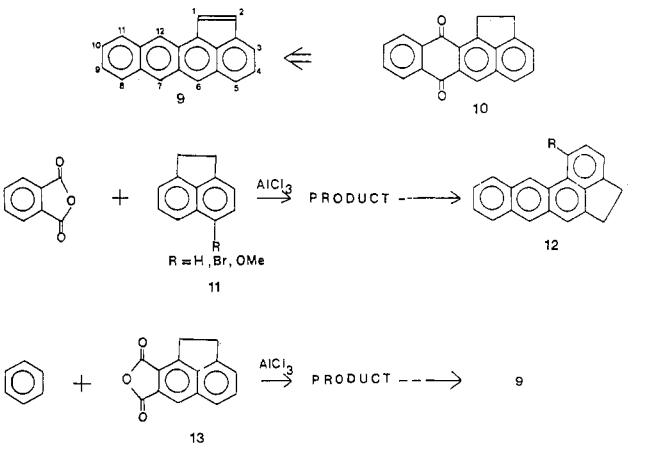
[a] Spectra were measured at 250 MHz on a Bruker Wm250 spectrometer. [b] Acetone-d_6 was used as solvent. [c] $CDCl_3$ was used as solvent.

confirmed by the appearance of two aromatic singlets at δ 8.55 (meso H_{11}) and δ 7.90 (peri H_{12}) and a downfield aromatic doublet at δ 8.92, consistent with the location of H_7 in the pseudo bay region adjacent to a carbonyl functionality on the five-membered ring. On reduction with sodium borohydride in ethanol–water medium, **6** afforded diol **7**, which was dehydrated smoothly by refluxing with a catalytic amount of *p*-toluenesulfonic acid in dry benzene to monoketone **8**. Treatment of **8** by the reduction–dehydrogenation sequence described for ketone **3** gave compound **5** in 22% overall yield.

The physicochemical characteristics of **5** are consistent with the benz[*d*]aceanthrylene structure. The mass spectrum is typical of PAH,[18] consisting of a molecular ion as base peak and a prominent peak at half the molecular weight, corresponding to the doubly charged molecular ion. The elemental composition $C_{20}H_{12}$ was confirmed by high-resolution mass measurement of the molecular ion and elemental analysis. The C_2 symmetry of **5** is evident in the ^{1}H NMR in which the etheno protons (H_5, H_6) and the meso protons (H_{11}, H_{12}) appear as two-proton singlets (Table I).

Benz[*k*]aceanthrylene (9). In the synthesis of benz[*k*]aceanthrylene, use of an acenaphthene derivative as synthon was chosen as a means of avoiding a potentially unfavorable cyclodehydration for formation of the five-membered ring. Scheme II illustrates the two strategies devised for synthesis of the key intermediate 1,2-dihydrobenz[*k*]aceanthrylene-7,12-quinone (**10**). Since condensation of phthalic anhydride with acenaphthene or C_5-substituted **11** yielded exclusively the benz[*k*]acephenanthrylene skeleton, the alternative condensation of acenaphthene-3,4-dicarboxylic anhydride (**13**) with benzene was attempted. Anhydride **13** was obtained by Scheme III. 1-Bromoindane from bromination of 1-indanol with phosphorus tribromide[19] was condensed with triethyl 1,1,2-ethanetricarboxylate[20] to give indane triester **14**. Decarbethoxylation[21] of **14** in refluxing dimethyl sulfoxide in the presence of NaCl and water produced the indane succinic ester **15** cleanly in high yield. Treatment of **15** with sodium ethoxide and ethyl formate and cyclodehydration of the resulting enolic derivative **16** with a mixture of phosphoric and sulfuric acids gave dihydroacenaphthenedicarboxylic ester **17**. Dehydrogenation of **17** by 1 mol equiv of DDQ yielded acenaphthene diester **18** which, on hydrolysis with methanolic KOH, afforded acenaphthene-3,4-dicarboxylic acid (**19**). Dehydration of **19** in refluxing acetic anhydride gave a quantitative yield of cyclic anhydride **13**. Friedel–Crafts acylation of **13** in benzene with $AlCl_3$ as catalyst afforded a mixture of keto

Scheme II

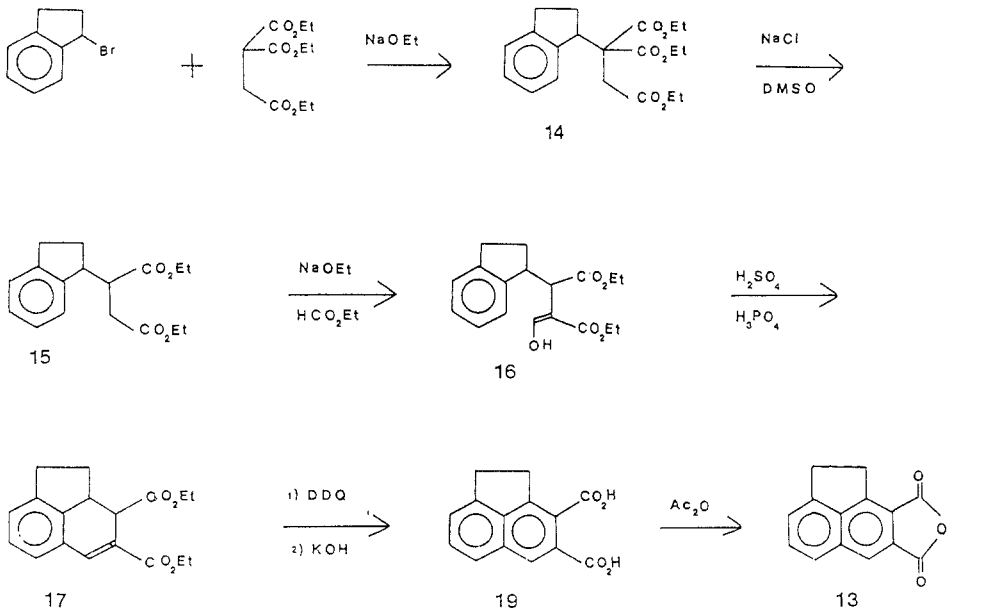


acids **20**. (Separation of the mixture **20** was not attempted since both keto acids were expected to yield quinone **10** on cyclization.) The mixture **20** smoothly cyclized to quinone **10** in an $AlCl_3$/NaCl melt at 130–140 °C. Scheme IV shows the reduction of quinone **10** with zinc and NaOH[15] to furnish the tetrahydro derivative **21**, which was dehydrogenated to benz[*k*]aceanthrylene (**9**) by 2 mol equiv of DDQ. Mass spectrometry and elemental analysis of **9** confirmed the composition of $C_{20}H_{12}$. Three singlets in the ^{1}H NMR spectrum corresponding to the three meso protons (H_6, H_7, H_{12}) and the appearance of the etheno protons as an AX quartet confirm the asymmetric fusion of the five-membered ring. The lack of a true bay region, reflected in the absence of any resonances below δ 9 (Table I), confirms the assigned structure and rules out a benz[*k*]acephenanthrylene carbon framework.

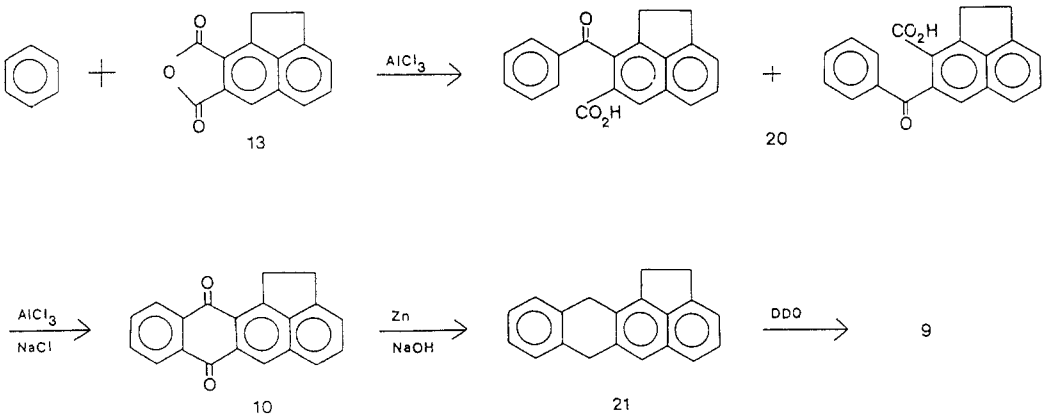
Benz[*j*]acephenanthrylene (27). Although synthesis of the 4,5-dihydro derivative of benz[*j*]acephenanthrylene has been reported,[22] the overall yield was low, and the completely unsaturated PAH (**27**) has not been described. A new route to the target compound was devised, shown in Scheme V, based on a synthon (**22**) already containing the fused cyclopenta ring, as in the case of benz[*k*]aceanthrylene. Starting ketone **22** was easily prepared by a published[23] method and converted to keto ester **23** by heating with sodium hydride and diethyl carbonate. The keto ester was subjected to Robinson annelation with methyl vinyl ketone by a published procedure[24] to give diketo ester **24** in high yield. Diketo ester **24** smoothly underwent ring closure in boiling aqueous KOH to afford enone **25** with the desired carbon framework. Wolff–Kishner reduction of **25** to octahydro derivative **26** followed by dehydrogenation with 4 mol equiv of DDQ in refluxing benzene produced benz[*j*]acephenanthrylene in 37%

(18) Benyon, J. H. *The Mass Spectra of Organic Molecules*; Elsevier: New York, 1968; p 1.
(19) Smith, L. H. *Organic Syntheses*; Wiley: New York, 1955; Collect. Vol. III, p 793.
(20) Adler, K.; Pascher, F.; Vagt, H. *Ber. Dtsch. Chem. Ges. B* **1942**, *75*, 1501.
(21) Krapcho, A. P.; Lovey, A. J. *Tetrahedron Lett.* **1973**, 957.
(22) Lewis, C. I.; Chang, J. Y.; Spears, A. W. *J. Org. Chem.* **1969**, *34*, 1176.
(23) Scott, L. T.; Reinhardt, G.; Roelofs, N. H. *J. Org. Chem.* **1985**, *50*, 5886.
(24) Wilds, A. L.; Werth, R. J. *J. Org. Chem.* **1952**, *17*, 1149.

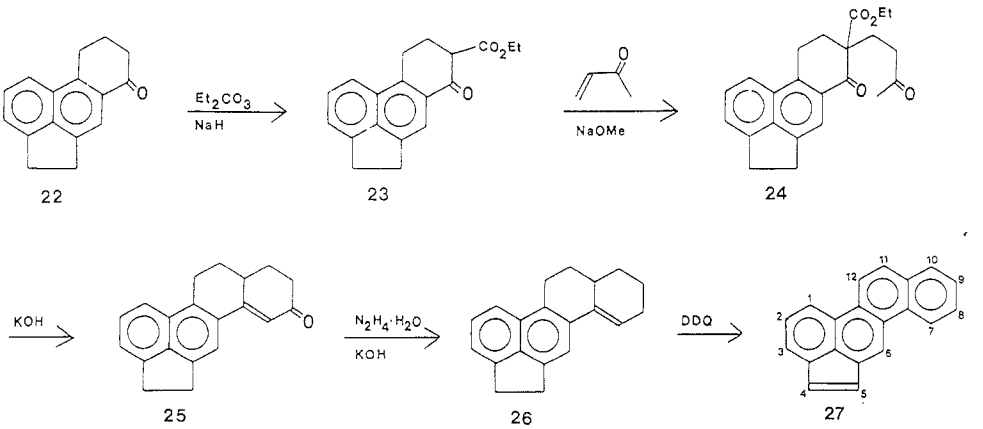
Scheme III



Scheme IV



Scheme V



overall yield. Accurate mass measurement of the molecular ion and elemental analysis confirmed the $C_{20}H_{12}$ isomeric composition of **27**. Unlike the case of the parent acephenanthrylene[25] ring system and the benz-annelated isomer benz[*k*]acephenanthrylene,[10] the proton resonances of the etheno bridge (H_4, H_5) appear as a singlet because both protons are accidentally isochronous. Of the four bay region proton signals, the low-field singlet can be unequivocally assigned to H_6 and the doublet at δ 8.72 to H_{12}. By virtue of the observed long-range intra-ring coupling, the remaining two doublets must be associated with H_1 and H_7 but cannot be more specifically assigned (Table I). Like other cyclopenta PAH,[10,26,27] compounds **5**, **9**, and **27** do not fluoresce under long-wavelength UV light (360 nm) and

(25) Krishnan, S.; Hites, R. A. *Anal. Chem.* **1981**, *53*, 342.

(26) Gold, A.; Eisenstadt, E.; Schultz, J. *Tetrahedron Lett.* **1978**, 4491.
(27) Eisenstadt, E.; Shpizner, B.; Gold, A. *Biochem. Biophys. Res. Commun.* **1981**, *100*, 965.

are highly colored: **5** and **9** are violet and **27** is orange-yellow. Aerobic solutions of **5** and **9** decompose within 24 h, possibly via *endo*-peroxide formation.[28]

Experimental Section

^1H NMR spectra were obtained at ambient temperature either at 250 MHz on a Bruker WM250 or at 200 MHz on a Bruker AC200 spectrometer. Mass spectra were obtained on a VG 7070F micromass mass spectrometer with an electron impact source at 70 eV. UV–visible spectra were recorded on a Perkin-Elmer 124 double-beam spectrophotometer. Infrared (IR) spectra were taken on a Beckman 4250 spectrophotometer. HPLC was performed with a Varian 5000 LC, Perkin-Elmer LC-85B spectrophotometric detector, and Spectra-Physics SP-4270 integrator on a Dupont-Zorbax C-8 9.4 mm × 2.5 cm column with methanol/water (85:15) linear-gradient mixtures over 6 min. Melting points were determined on a Fisher Johns melting point apparatus and are uncorrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, TN.

6-Oxo-1,2,3,4,5,6-hexahydrobenz[*d*]aceanthrylene (2). 1,2,3,4-Tetrahydronaphthacene-6,11-quinone (1; 4.0 g, 15.3 mmol), prepared by published procedures,[15,16] was heated at reflux with HI (57%, 15 mL) and glacial HOAc (185 mL) for 6 h. The reaction mixture was poured into $Na_2S_2O_5$ solution (1%, 800 mL), and the precipitate collected by filtration was purified by recrystallization from benzene to give tetrahydronaphthacene (**2**): 3.37 g, 95%; colorless needles; mp 236 °C (lit.[21] mp 237 °C); ^1H NMR (60 MHz, CD_2Cl_2) δ 2.30 (m, 4 H, $H_{2,3}$), 3.45 (m, 4 H, benzylic $H_{1,4}$), 7.82 (dd, 2 H, J = 8 Hz, $H_{8,9}$), 8.18 (s, 2 H, $H_{5,12}$), 8.42 (dd, 2 H, peri $H_{7,10}$), 8.76 (s, 2 H, meso $H_{6,11}$).

6-Oxo-1,2,3,4,5,6-hexahydrobenz[*d*]aceanthrylene (3). To a solution of **2** (510 mg, 2.2 mmol) and chloroacetyl chloride (0.18 mL, 2.25 mmol) in dry CH_2Cl_2 (20 mL) was added $AlCl_3$ (600 mg, 4.48 mmol) in portions with stirring at −5 to 0 °C. The reaction mixture was stirred at room temperature for 4 h and then poured into ice–hydrochloric acid. The organic layer was separated, the aqueous layer was extracted with additional CH_2Cl_2 (100 mL), and the combined organic phases were washed with sodium bicarbonate solution (5%, 100 mL) and water (100 mL) and dried (Na_2SO_4). Evaporation of the solvent yielded crude ketone **3**, which was purified by chromatography on silica with benzene/CH_2Cl_2 (1:1) eluant. Collection of the fluorescent yellow band afforded compound **3**: 131 mg, 22%; mp 225–226 °C dec; ^1H NMR (200 MHz, CD_2Cl_2) δ 1.92 (m 4 H, $H_{2,3}$), 2.94 (m, 4 H, benzylic $H_{1,4}$), 3.77 (s, 2 H, CH_2CO), 7.22 (s, 1 H, peri H_{12}), 7.58 (dt, 1 H, J = 8.33 Hz, H_9), 7.71 (dt, 1 H, J = 8.33 Hz, H_8), 8.06 (d, 1 H, J = 8.33 Hz, peri H_{10}), 8.28 (s, 1 H, meso H_{11}), 9.13 (d, 1 H, J = 8.33 Hz, peri H_7); mass spectrum, m/e (relative intensity) 272 (100, M^+), 270 (32, M − H_2), 268 (23, M − 2 H_2), 241 (60, M − (H_2 + HCO)), 239 (63, M − (2 H_2 + HCO)); IR (KBr) 1680 cm^{-1} (C=O); UV (methanol) [λ_{max}, nm (ε × 10^4)] 427 (0.37), 406 (0.44), 377 (0.51), 366 (0.34), 269 (4.90), 238 (2.11). Anal. Calcd for $C_{20}H_{16}O$: C, 88.24; H, 5.88. Found: C, 87.77; H, 5.98.

1,2,3,4,5,6-Hexahydrobenz[*d*]aceanthrylene (4). A mixture of ketone **3** (120 mg, 0.44 mmol), diethylene glycol (10 mL), hydrazine monohydrate (0.5 mL), and KOH (0.5 g) was refluxed for 6 h, cooled to room temperature, and poured into excess water. The product was extracted with CH_2Cl_2 (2 × 50 mL) and the organic extract washed with water (100 mL) and dried (Na_2SO_4). The crude product, obtained after evaporation of solvent, was purified by chromatography on silica gel with chloroform/benzene (3:1) eluant to give **4**: 86 mg, 76%; mp 142–143 °C; ^1H NMR (200 MHz, CD_2Cl_2) δ 1.90 (m 4 H, $H_{2,3}$), 2.90 (br t, 2 H, J = 6.1 Hz, benzylic H_1), 3.05 (br t, 2 H, J = 6.1 Hz, benzylic H_4), 3.40 (t, 2 H, J = 5.4 Hz, benzylic H_5), 3.75 (t, 2 H, J = 5.3 Hz, benzylic H_6), 7.39 (dd, 2 H, J = 6.5, 6.6 Hz, $H_{8,9}$), 7.45 (s, 1 H, H_{12}), 7.94 (dd, 1 H, J = 6.7, 3.5 Hz, H_{10}), 7.97 (dd, 1 H, J = 6.4, 3.1 Hz, H_7), 8.02 (s, 1 H, H_{11}); mass spectrum, m/e (relative intensity) 258 (100, M^+), 256 (38, M − H_2), 252 (20, M − 3 H_2), 230 (14, M − C_2H_4), 202 (13, M − 2 C_2H_4).

5,6-Dioxo-1,2,3,4,5,6-hexahydrobenz[*d*]aceanthrylene (6). A mixture of **2** (1.3 g, 5.6 mmol), oxalyl chloride (2.5 g, 20 mmol), CS_2 (8 mL), and $AlCl_3$ (0.8 g, 6 mmol) was stirred at 0 °C for 2 h. Further addition of $AlCl_3$ (0.7 g, 5.2 mmol) and CS_2 (8 mL) was followed by stirring for 4 h at 0 °C and overnight at room temperature. The reaction mixture was poured into ice–water, heated to distill the CS_2, cooled, and extracted with $CHCl_3$ (2 × 100 mL). Evaporation of solvent followed by chromatography on silica gel with $CHCl_3$ eluant gave diketone **6**: 1.31 g, 82%; red needles; mp 248–250 °C dec (benzene); ^1H NMR (200 MHz, CD_2Cl_2) δ 1.56 (m 2 H, H_2), 1.93 (m, 2 H, H_3), 3.08 (m, 2 H, benzylic H_1), 3.42 (m, 2 H, benzylic H_4), 7.61 (t, 1 H, J = 9 Hz, H_9), 7.75 (t, 1 H, J = 9 Hz, H_8), 7.90 (s, 1 H, peri H_{12}), 8.08 (d, 1 H, J = 9 Hz, peri H_{10}), 8.55 (s, 1 H, meso H_{11}), 8.93 (d, 1 H, J = 9 Hz, peri H_7); mass spectrum, m/e (relative intensity) 286 (68, M^+), 258 (100, M − CO), 229 (21, M − (CO + HCO)), 202 (22, M − 2(CO + C_2H_4)); IR (KBr) 1700 cm^{-1} (C=O); UV (methanol) [λ_{max}, nm (ε × 10^4)] 405 (0.72), 372 (1.26), 362 (1.08), 261 (13.96). Anal. Calcd for $C_{20}H_{14}O_2$: C, 83.92; H, 4.90. Found: C, 84.21; H, 4.76.

5,6-Dihydroxy-1,2,3,4,5,6-hexahydrobenz[*d*]aceanthrylene (7). To a mixture of diketone **6** (1.20 g, 4.21 mmol), ethanol (260 mL), and water (40 mL) was added sodium borohydride (3.80 g, 0.1 mol) in portions with stirring. The reaction mixture was stirred for 20 h at room temperature and decomposed with ice–water (400 mL) and solid NH_4Cl (10 g). The precipitated diol **7** (1.20 g, 100%) was filtered, dried, and used directly in the next step.

5-Oxo-1,2,3,4,5,6-hexahydrobenz[*d*]aceanthrylene (8). A mixture of the diol **7** (1.20 g, 4.14 mmol) and *p*-toluenesulfonic acid (120 mg) in dry benzene (150 mL) was heated under reflux for 2 h. The benzene solution was washed with brine (2 × 100 mL), dried (Na_2SO_4), and evaporated. The crude product was purified by chromatography on alumina with benzene eluant to yield monoketone **8**: 0.80 g, 71%; yellow crystals; mp 189–190 °C dec (hexane); ^1H NMR (200 MHz, CD_2Cl_2) δ 1.56 (m 2 H, H_2), 1.90 (m, 2 H, H_3), 3.10 (m, 2 H, benzylic H_1), 3.46 (m, 2 H, benzylic H_4), 4.06 (s, 2 H, CH_2CO), 7.46 (m, 2 H, $H_{8,9}$), 7.89 (s, 1 H, peri H_{12}), 7.90 (d, 1 H, J = 8 Hz, peri H_{10}), 8.02 (d, 1 J, J = 8 Hz, peri H_7), 8.25 (s, 1 H, meso H_{11}); mass spectrum, m/e (relative intensity) 272 (100, M^+), 270 (30, M − H_2), 268 (25, M − 2 H_2), 241 (63, M − (H_2 + HCO)), 239 (65, M − (2 H_2 + HCO)); IR (KBr) 1710 cm^{-1} (C=O); UV (methanol) [λ_{max}, nm (ε × 10^4)] 427 (0.51), 407 (0.58), 377 (0.71), 358 (0.54), 270 (4.97), 250 (8.30). Anal. Calcd for $C_{20}H_{16}O$: C, 88.24; H, 5.88. Found: C, 88.36; H, 6.19.

1,2,3,4,5,6-Hexahydrobenz[*d*]aceanthrylene (4). From ketone 8. Wolff–Kishner reduction of ketone **8** (636 mg, 2.47 mmol) carried out as described above for ketone **3** gave pure **4**, 420 mg, 70%.

Benz[*d*]aceanthrylene (5). A solution of **4** (182 mg, 0.70 mmol) and DDQ (480 mg, 2.1 mmol) in dry benzene (100 mL) was refluxed under nitrogen for 2.5 h. The cooled solution was filtered and the filtrate passed through a column of alumina. The dark purple residue, obtained after evaporation of solvent, was chromatographed on alumina with hexane/benzene (9:1) eluant. Compound **5** was collected as a violet nonfluorescent band: 103 mg, 58%; mp >300 °C; ^1H NMR (250 MHz, acetone-d_6) see Table I; UV (heptane) [λ_{max}, nm (ε × 10^4) 405 (0.79), 396 (0.29), 381 (0.35), 301 (sh, 0.79), 282 (1.98), 258 (1.43); accurate mass molecular ion 252.0933, calcd for $C_{20}H_{12}$ 252.0937; mass spectrum, m/e (relative intensity) 252 (100, M^+), 250 (21, M − H_2), 126 (26, M^{2+}), 125 (16, $(M - H_2)^{2+}$); HPLC retention time 3.57 min; IR (KBr) 3020, 1620, 1490, 1410, 1305, 1210, 1160, 1090, 920, 850, 800, 770 cm^{-1}. Anal. Calcd for $C_{20}H_{12}$: C, 95.24; H, 4.76. Found: C, 95.45; H, 4.77.

Diethyl 2-(1-Indanyl)succinate (15). The triester **14** (27 g, 74.6 mmol), prepared by condensation of 1-bromoindane with triethyl 1,1,2-ethanetricarboxylate as described by Alder et al.,[20] was refluxed with NaCl (8.2 g, 0.14 mmol), water (4 g, 0.22 mol), and dimethyl sulfoxide (160 mL) at 178–183 °C for 6 h. The reaction mixture was cooled at room temperature, poured into excess water, and extracted with ether (3 × 200 mL). The ether extract was washed with water (2 × 100 mL) and dried (Na_2SO_4). Evaporation of solvent furnished crude product, which was purified by chromatography on alumina with benzene eluant to give diester **15** as an oily substance, 18.4 g, 85%.

Diethyl 2a,3-Dihydroacenaphthene-3,4-dicarboxylate (17). To a suspension of powdered sodium (1.37 g, 0.06 mol) in dry ether (25 mL) was added a solution of absolute ethanol (3.46 mL, 0.06

(28) DuFraisse, C.; Horclois, R. *Bull. Soc. Chim. Fr., Mem.* **1936**, *3*, 1880.

(29) Vodehnal, J.; Stepan, V. *Collect. Czech. Chem. Commun.* **1971**, *36*, 3980.

mol) in dry ether (15 mL) and the mixture refluxed for 10 h. The reaction mixture was cooled to −10 to −15 °C and a solution of the diester **15** (8 g, 0.028 mol) and ethyl formate (4.3 g, 0.058 mol) in dry ether (20 mL) added with vigorous stirring. The mixture was stirred for 4 h at −10 °C and 72 h at room temperature. The reaction mixture was then added to ice–water (200 mL) and the aqueous layer extracted with ether (2 × 100 mL) to remove the unreacted diester **15** (the combined ether extract afforded 3.3 g of unreacted **15**). After acidification with dilute H_2SO_4, the aqueous layer was extracted with ether (3 × 200 mL). Evaporation of the ether gave formyl derivative **16** (4.814 g, 55%) as an oily substance, which was used directly in the next step.

A mixture of H_3PO_4 (90%, 17.3 mL) and H_2SO_4 (98%, 3.7 mL) cooled to −10 °C was added to **16** (4.814 g, 0.015 mol) precooled to −10 °C. The reaction mixture was allowed to warm to 0 °C with stirring, which was continued for 2 h at 0–10 °C. The reaction mixture was then poured into ice–water (100 mL) and partially neutralized with NaOH (40%, 52 mL; with cooling), and the product was extracted into ether (3 × 100 mL). The ether extract was washed with water (100 mL), dried, and evaporated to give dihydroacenaphthenedicarboxylic acid ester **17**. The crude product was flash chromatographed on alumina with benzene as eluant to furnish **17** as oily semisolid: IR (neat) 1730 (C=O), 1705 cm^{-1} (C=C—C=O); UV (methanol) [λ_{max}, nm ($\epsilon \times 10^4$)] 292 (0.90), 233 (1.28), 227 (1.25).

Diethyl Acenaphthene-3,4-dicarboxylate (18). A solution of diester **17** (4.30 g, 0.014 mol) in dry benzene (100 mL) was heated at reflux with DDQ (3.25 g, 0.014 mol) for 2 h. After filtration, the reaction mixture was chromatographed on alumina with benzene eluant to yield pure diethyl acenaphthacene-3,4-dicarboxylatae (**18**): 3.76 g, 88%; yellow crystals (methanol); mp 94–95 °C; ^1H NMR (300 MHz, CD_2Cl_2) δ 1.40 (two t, 6 H, J = 6 Hz, ester CH_3), 3.42 (br t, 2 H, J = 6 Hz, benzylic H_1), 3.55 (br t, 2 H, J = 6 Hz, benzylic H_2), 4.31–4.40 (two q, 4 H, J = 6 Hz, ester CH_2), 7.45 (br d, 1 H, J = 6 Hz, H_8), 7.59 (t, 1 H, J = 6, 9 Hz, H_7), 7.69 (br d, 1 H, J = 9 Hz, H_6), 8.01 (s, 1 H, H_5)); mass spectrum, m/e (relative intensity) 298 (17, M^+), 252 (40, M − EtOH), 224 (100, M − EtOEt); IR (KBr) 1730 cm^{-1} (C=O); UV (methanol) [λ_{max}, nm ($\epsilon \times 10^4$)] 340 (0.54), 327 (0.54), 287 (sh, 1.20), 272 (sh, 1.30), 243 (5.65), 232 (sh, 5.27). Anal. Calcd for $C_{18}H_{18}O_4$: C, 72.48; H, 6.04. Found: C, 72.65; H, 6.11.

Acenaphthene-3,4-dicarboxylic Acid (19). Diester **18** (3.60 g, 0.012 mol) was heated with a mixture of aqueous KOH (45%, 40 mL) and methanol (160 mL) for 2 h on a steam bath. The methanol was boiled off, and the residue, dissolved in water (150 mL), was acidified with concentrated HCl to give diacid **19**: 2.8 g, 96%; mp 244–246 °C, remelts and decomposes at 255–256 °C; mass spectrum, m/e (relative intensity) 224 (80, M − H_2O), 180 (36, M − (H_2O + CO_2)), 152 (100, M − (H_2O + CO_2 + CO)); IR (KBr) 1690 cm^{-1} (C=O). Anal. Calcd for $C_{14}H_{10}O_4$: C, 69.42; H, 4.13. Found: C, 69.10; H, 4.23.

Acenaphthene-3,4-dicarboxylic Anhydride (13). The 3,4-diacid **19** (2.76 g, 11.4 mmol) was refluxed with acetic anhydride (20 mL) for 2 h. Evaporation of the acetic anhydride under vacuum yielded the anhydride **13**: 2.56 g, 100%; mp 256–257 °C dec; ^1H NMR (200 MHz, acetone-d_6) δ 3.63 (br t, 2 H, J = 4.8, 6.6 Hz, benzylic H_1), 3.72 (br t, 2 H, J = 7.2, 4.2 Hz, benzylic H_2), 7.73 (br d, 1 H, J = 7.2 Hz, H_8), 7.86 (t, 1 H, J = 8.1, 7.2 Hz, H_7), 8.06 (br d, 1 H, J = 8.1 Hz, H_6), 8.42 (s, 1 H, H_5); mass spectrum, m/e (relative intensity) 224 (90, M^+), 180 (40, M − CO_2), 152 (100, M − (CO_2 + CO)); IR (KBr) 1825, 1780 cm^{-1} (C=O); UV (methanol) [λ_{max}, nm ($\epsilon \times 10^4$)] 336 (0.37), 300 (0.56), 284 (0.75), 272 (0.81), 241 (5.31). Anal. Calcd for $C_{14}H_8O_3$: C, 75.00; H, 3.57. Found: C, 74.77; H, 3.62.

1,2-Dihydrobenz[*k*]aceanthrylene-7,12-quinone (10). A mixture of anhydride **13** (2.54 g, 11.3 mmol) and anhydrous $AlCl_3$ (3.14 g, 11.3 mmol) in dry benzene (10 mL) was heated at 100 °C for 8 h. The reaction mixture was cooled and decomposed with cold, dilute HCl. The benzene was removed by steam distillation and the precipitated acid mixture **20** filtered from the aqueous layer after cooling on ice. The acid mixture (2.91 g, 85%) was dried under vacuum and used directly in the next step.

Keto acid mixture **20** (2 g, 6.62 mmol), anhydrous $AlCl_3$ (20 g, 0.15 mol), and NaCl (4 g, 0.07 mol) were heated, and the resulting melt was stirred vigorously at 130–140 °C for 1 h. The reaction mixture, cooled to room temperature, was treated carefully with ice–water (200 mL) and extracted with $CHCl_3$ (3 × 100 mL). Evaporation of the solvent followed by purification of the crude product by chromatography on alumina with $CHCl_3$ eluant afforded pure quinone **10**: 1.03 g, 55%; yellow crystals; mp 225–226 °C dec (methanol); ^1H NMR (200 MHz, CD_2Cl_2) δ 3.53 (t, 2 H, J = 5.7 Hz, benzylic H_2), 3.93 (t, 2 H, J = 5.7 Hz, benzylic H_1), 7.56 (dd, 1 H, J = 6.98, 0.9 Hz, H_3), 7.69 (t, 1 H, J = 6.96 Hz, H_4), 7.81 (m, 2 H, $H_{9,10}$), 7.86 (dd, 1 H, J = 7.0, 0.8 Hz, peri H_5), 8.32 (dd, 1 H, J = 4.4, 1.8 Hz, H_{11}), 8.34 (dd, 1 H, J = 4.4, 1.8 Hz, H_8), 8.68 (s, 1 H, H_6); mass spectrum, m/e (relative intensity) 284 (100, M^+), 255 (19, M − HCO), 226 (39, M − 2 HCO), 113 (22, (M − 2 HCO)$^{2+}$); IR (KBr) 1660 cm^{-1} (C=O); UV (methanol) [λ_{max}, nm ($\epsilon \times 10^4$)] 422 (sh, 1.25), 412 (1.29), 295 (4.86), 283 (5.14), 277 (5.00), 250 (10.57). Anal. Calcd for $C_{20}H_{12}O_2$; C, 84.51; H, 4.23. Found: C, 84.32; H, 4.15.

1,2,7,12-Tetrahydrobenz[*k*]aceanthrylene (21). Quinone **10** (1.0 g, 3.52 mmol) in ethanol (100 mL) was stirred with NaOH (20%, 10 mL) and zinc dust (5 g, 76 mmol) under reflux for 6 h. The reaction mixture was cooled to room temperature and filtered and, after distillation of the ethanol, the filtrate was extracted with benzene (2 × 100 mL). The benzene extract was washed with water (100 mL), dried, and evaporated to give **21** (0.77 g, 85%), which was used directly in the next step (the color of **21** darkens from yellow to brown when kept at room temperature).

Benz[*k*]aceanthrylene (9). A solution of compound **21** (174 mg, 0.68 mmol) and DDQ (308 mg, 1.36 mmol) in dry benzene (100 mL) was refluxed under nitrogen for 2 h. The reaction mixture was cooled and subjected to flash chromatography on alumina with benzene. The solution was evaporated to dryness, and the purple solid obtained was rechromatographed on alumina with heptane/benzene (8:2). The violet, nonfluorescent fraction afforded benz[*k*]aceanthrylene **9**: 0.108 g, 63%; violet needles (methanol); mp >300 °C; ^1H NMR (250 MHz, acetone-d_6) see Table I; UV (heptane) [λ_{max}, nm ($\epsilon \times 10^4$)] 492 (0.15), 462 (0.17), 434 (0.15), 395 (0.36), 293 (7.07), 283 (6.02), 261 (5.33), 227 (4.73), 216 (5.13); accurate mass of molecular ion 252.0932, calcd for $C_{20}H_{12}$ 252.0937; mass spectrum, m/e (relative intensity) 252 (100, M^+), 226 (5, M − C_2H_2), 126 (50, M^{2+}), 113 (21, (M − C_2H_2)$^{2+}$); HPLC retention time 3.50 min; IR (KBr) 3040, 1610, 1460, 1370, 1330, 1270, 1230, 940, 880, 850, 750, 730 cm^{-1}. Anal. Calcd for $C_{20}H_{12}$: C, 95.24; H, 4.76. Found: C, 95.29; H, 4.77.

8-Carbethoxy-7-oxo-4,5,7,8,9,10-hexahydroacephenanthrylene (23). To a mixture of sodium hydride (0.612 g, 25.5 mmol) and diethyl carbonate (2.14 g, 18.1 mmol) in dry benzene (20 mL) was added dropwise a solution of ketone **22** (2.0 g, 9 mmol; prepared from acenaphthene by published methods[23]) in dry benzene (30 mL) with refluxing and vigorous stirring. After completion of the addition (1 h), the reaction mixture was refluxed for 1 h and cooled to room temperature and glacial HOAc (2 mL) added dropwise. Cold water (50 mL) was added to dissolve solids, the benzene layer was separated, and the acidic aqueous layer was extracted with benzene (3 × 50 mL). The combined benzene layers were washed with cold water (100 mL), dried (Na_2SO_4), and evaporated to give keto ester **23**: 2.49 g, 94%; mp 84–85 °C (methanol).

8-Oxo-4,5,8,9,10,10a,11,12-octahydrobenz[*j*]acephenanthrylene (25). A solution of anhydrous methyl vinyl ketone (1.14 g, 16.3 mmol) in dry methanol (5 mL) and dry benzene (15 mL) was added dropwise over 10 min at room temperature to a stirred solution of keto ester **23** (2.4 g, 8.16 mmol) and sodium methoxide (10 mg) in dry methanol (10 mL) and dry benzene (15 mL). After being stirred for 20 h at room temperature, the reaction mixture was treated with water (100 mL) and the product extracted thoroughly with benzene (3 × 80 mL). The benzene extract was washed with dilute HCl (5%, 100 mL) and water (100 mL) and dried over Na_2SO_4. Evaporation of solvent afforded crude diketo ester **24** (2.58 g, 87%) as an oil, which was used directly for cyclization in the next step.

To a refluxing suspension of diketo ester **24** (2.58 g, 7.09 mmol) in water (150 mL) was added a solution of KOH (2.0 g, 37.8 mol) in water (50 mL) over 10 min under nitrogen. After refluxing for 2 h, the reaction mixture was treated again with aqueous KOH (5.5 g, 98 mmol/50 mL H_2O), heated for an additional 6 h, cooled under nitrogen to room temperature, and extracted with benzene (2 × 100 mL). The benzene extract was dried (Na_2SO_4) and evaporated to give crude product, which was purified by chro-

matography on alumina using benzene as eluant to give olefinic ketone **25**: 1.72 g, 89%; mp 125–127 °C (methanol); ^{1}H NMR (200 MHz, CD_2Cl_2) δ 1.05–2.3 (four m, 4 H, $H_{10,11}$), 2.50 (m, 2 H, benzylic H_{12}), 2.70 (m, 1 H, H_9), 3.05 (m, 1 H, H_9), 3.37 (br s, 4 H, benzylic $H_{4,5}$), 4.06 (m, 1 H, methynyl H_{10a}), 6.68 (d, 1 H, J = 2.4 Hz, olefinic H_7), 7.36 (br s, 1 H, J = 6.6 Hz, H_3), 7.50 (dd, 1 H, J = 6.6, 8.4 Hz, H_2), 7.66 (s, 1 H, H_6), 7.73 (d, 1 H, J = 8.4 Hz, H_1); mass spectrum, m/e (relative intensity) 274 (100, M^+), 246 (49, $M - C_2H_4$), 217 (29, $M - (C_2H_4 + HCO)^+$); IR (KBr) 1720 cm^{-1} (C=O); UV (methanol) [λ_{max}, nm ($\epsilon \times 10^4$)] 368 (sh, 0.29), 321 (0.90), 288 (1.42), 225 (1.54). Anal. Calcd for $C_{20}H_{18}O$: C, 87.59; H, 6.57. Found: C, 87.41; H, 6.34.

4,5,8,9,10,10a,11,12-Octahydrobenz[*j*]acephenanthrylene (26). A mixture of enone **25** (1.50 g, 5.5 mmol) in benzene (20 mL), hydrazine monohydrate (9.3 mL), diethylene glycol (60 mL), and KOH (7.0 g) was heated at 100–105 °C for 1 h under nitrogen. The volatile components were distilled at 190–200 °C, and the concentrated reaction mixture was then heated at the same temperature for 6 h. Workup as described for **4** followed by flash chromatography on alumina with benzene/hexane (1:1) as eluant afforded **26**: 1.28 g, 90%; mp 125–126 °C (hexane); ^{1}H NMR (200 MHz, CD_2Cl_2) δ 1.26–1.66 (m, 4 H, $H_{9,10}$), 1.80–2.20 (m, 2 H, H_{11}), 2.28 (m, 2 H, H_{12}), 2.96 (m, 2 H, H_8), 3.34 (br s, 5 H, $H_{4,5}$, H_{10a}), 6.44 (br s, 1 H, olefinic H_7), 7.24 (d, 1 H, J = 6.8 Hz, H_3), 7.42 (dd, 1 H, J = 6.8, 7.55 Hz, H_2), 7.55 (s, 1 H, H_6), 7.62 (d, 1 H, J = 7.55 Hz, H_1); mass spectrum, m/e (relative intensity) 260 (100, M^+), 232 (16, $M - C_2H_4$), 217 (24, $M - (C_3H_6 + H)^+$); UV (heptane) [λ_{max}, nm ($\epsilon \times 10^5$)] 343 (sh, 0.28), 327 (sh, 0.38), 295 (sh, 1.02), 256 (2.55), 230 (3.66). Anal. Calcd for $C_{20}H_{20}$: C, 92.31; H, 7.69. Found: C, 92.33; H, 8.02.

Benz[*j*]acephenanthrylene (27). A solution of **26** (1.17 g, 4.5 mmol) and DDQ (4.50 g, 19.8 mmol) in dry benzene (100 mL) was refluxed for 5 h. The cooled solution was filtered and the filtrate chromatographed on alumina. Elution with benzene/hexane (1:9) and collection of the orange-yellow, nonfluorescent band furnished pure benz[*j*]acephenanthrylene (**27**): 0.930 g, 82%; mp 170–171 °C (hexane); ^{1}H NMR (250 MHz, $CDCl_3$) see Table I; UV (heptane) [λ_{max}, nm ($\epsilon \times 10^4$)] 376 (1.26), 358 (1.19), 342 (0.85), 314 (2.02), 301 (1.24), 272 (sh, 4.14), 258 (5.52); accurate mass of molecular ion 252.0933, calcd for $C_{20}H_{12}$ 252.0937; mass spectrum, m/e (relative intensity) 252 (100, M^+), 250 (24, $M - H_2$), 226 (14, $M - C_2H_2$), 126 (23, M^{2+}), 113 (17, $(M - C_2H_2)^{2+}$); HPLC retention time 3.47 min; IR (KBr) 3040, 1610, 1460, 1430, 1390, 1340, 1250, 1180, 1160, 880, 795, 755, 710 cm^{-1}. Anal. Calcd for $C_{20}H_{12}$: C, 95.24; H, 4.76. Found: C, 94.72; H, 4.94.

Acknowledgment. This work was supported in part by USPHS Grant ES 03343-04A and USEPA Grant 811817.

Registry No. **1**, 5349-90-6; **2**, 1148-84-1; **3**, 108665-19-6; **4**, 108665-20-9; **5**, 19770-52-6; **6**, 108665-21-0; **7**, 108665-22-1; **8**, 108665-23-2; **9**, 16683-64-0; **10**, 108665-24-3; **13**, 108665-25-4; **14**, 108665-26-5; **15**, 108665-27-6; **16**, 108665-28-7; **17**, 108674-99-3; **18**, 108665-29-8; **19**, 13055-36-2; **20** (isomer 1), 108665-30-1; **20** (isomer 2), 108665-35-6; **21**, 108665-31-2; **22**, 7467-80-3; **23**, 108675-00-9; **24**, 108665-32-3; **25**, 108665-33-4; **26**, 108665-34-5; **27**, 216-48-8; chloroacetyl chloride, 79-04-9; oxalyl chloride, 79-37-8; ethyl formate, 109-94-4; diethyl carbonate, 105-58-8; methyl vinyl ketone, 78-94-4.

A Microbially Based Approach for the Preparation of Chiral Molecules Possessing the Trifluoromethyl Group

Jenq Tain Lin, Takashi Yamazaki, and Tomoya Kitazume*

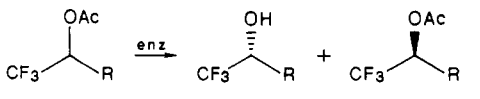
Department of Bioengineering, Tokyo Institute of Technology, Ookayama, Meguro-ku, Tokyo 152, Japan

Received December 1, 1986

The synthetic approach to both enantiomers and diastereomers with the trifluoromethyl group, involving the stereoselective hydrolysis of the ester group and acyclic stereoselection, is described. The absolute configuration of these trifluoromethylated molecules is determined. Especially, (*R*)-(+)- or (*S*)-(−)-hydroxy ketones possessing the trifluoromethyl group at asymmetrical carbon have been transformed to four diastereomeric 1,3-amino alcohols and 1,3-diols of the syn and anti configuration.

One objective of research in fluorine chemistry, required to support applications in F analogues of bioactive materials synthesis,[1-6] is the development of methodology[7-11] and/or reagents[12-15] suitable for synthesis of each enantiomeric and diastereomeric relationship with unusual selectivity and control. However, in fluorine chemistry, the absolute configuration of chiral materials and/or the synthetic methods giving both enantiomers or diastereomers with enantiomeric syn and anti configuration, have not been studied in detail.

Scheme I



(1) Tsushima, T. *Kagaku to Seibutsu* **1982**, *20*, 770.
(2) Souda, K.; Tanizawa, K.; Esaki, N. *Kagaku (Kyoto)* **1980**, *35*, 97 and references cited therein.
(3) Johnson, M.; Marcotte, P.; Donovan, J.; Walsh, C. *Biochemistry* **1977**, *18*, 1729.
(4) Walsh, C. *Tetrahedron* **1982**, *38*, 871.
(5) Filler, R.; Kobayashi, Y. *Biomedicinal Aspects of Fluorine Chemistry*; Kodansha and Elsevier Biomedical: Amsterdam, 1983.
(6) Smith, F. A. *Handbook of Experimental Pharmacology*; Springer-Verlag: Berlin, 1970; Vol. XX, Part 2, p 166.
(7) Quistad, G. B.; Cerf, D. C.; Schooley, D. A.; Staal, G. B. *Nature (London)* **1981**, *289*, 176.
(8) Aranda, G.; Jullien, J.; Martin, J. A. *Bull. Soc. Chim. Fr.* **1966**, 2850.
(9) Kollonitsch, J.; Marburg, S.; Perkins, L. M. *J. Org. Chem.* **1979**, *44*, 771.
(10) Groth, U.; Schallkope, U. *Synthesis* **1983**, 673.
(11) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *107*, 5186.
(12) Bucciarelli, M.; Forni, A.; Moretti, I.; Torre, G. *J. Chem. Soc., Chem. Commun.* **1978**, 456.
(13) Bucciarelli, M.; Forni, A.; Moretti, I.; Torre, G. *Synthesis* **1983**, 897.
(14) Kitazume, T.; Sato, T.; Kobayashi, T.; Lin, J. T. *J. Org. Chem.* **1986**, *51*, 1003.
(15) Kitazume, T.; Nakayama, Y. *J. Org. Chem.* **1986**, *51*, 2795.

0022-3263/87/1952-3211$01.50/0