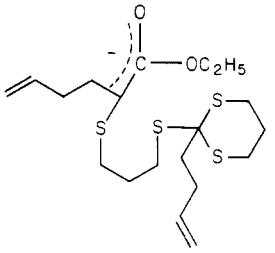
crude reaction mixture always indicated **5** as the major side product. However, when an inverse addition procedure was used, **4** was then obtained as the only product in excellent yield (85%).[6]

A plausible mechanism to account for the formation of **5** involves reaction at sulfur of dithiane **4** with the lithio anion **2** to generate the ester enolate **8**. In the presence



8

of ethyl chloroformate, **8** was trapped to yield dimer **5**. It was surprising that **2** served as a nucleophile toward sulfur and not the carbonyl group of **4**.[7]

Further experiments are required to determine the generality of this unusual dimerization reaction. We suspect, however, that formation of dimeric side products, such as **5**, can occur whenever 2-lithio-1,3-dithiane derivatives are alkylated with ethyl chloroformate. The inverse addition procedure allows the reaction to proceed in the normal manner. This technique insures a high yield of the desired product and avoids the use of excessive amounts of ethyl chloroformate.

Experimental Section

All ^1H NMR spectra were run in $CDCl_3$ solutions with tetramethylsilane as the internal standard, using either a Varian A-60A or a Varian XL-200 spectrometer operating in the FT mode. All ^{13}C NMR spectra were run on the same Varian XL-200 tuned to the carbon resonance frequency (50.3 MHz). The decoupler was gated on and off during various experiments to obtain noise-decoupled, off-resonance and coupled with NOE enhancement spectra. High-resolution mass spectra were recorded with a CEC 21-110B spectrometer at 70 eV.

Typical Procedure for the Addition of Ethyl Chloroformate to 2-(Buten-1-yl)-2-lithio-1,3-dithiane (2). To a magnetically stirred solution of 2-(buten-1-yl)-1,3-dithiane (11.30 g, 64.94 mmol) in 200 mL of tetrahydrofuran, cooled in a −35 °C bath, was added 41.40 mL of *n*-butyllithium (1.6 M in hexane, 66.24 mmol). Stirring was continued for 1.5 h while the cooling bath temperature was maintained between −25 and −20 °C. At the end of this period, the resulting rust-colored solution of **2** was cooled to −50 °C, and 9.82 g (90.92 mmol) of ethyl chloroformate was added over a 3–5-min period. After addition, the cooling bath was removed and the reaction allowed to warm to 0 °C. The solution was then poured into 150 mL of cold 1 N potassium hydrogen sulfate solution and thoroughly extracted with ether. The combined ether extracts were successively washed with 1 N sodium hydroxide solution, water, and saturated brine and dried through anhydrous sodium sulfate. Removal of the solvent in vacuo gave a residual yellow oil, which was chromatographed with 1 kg of silica gel. Elution with Skellysolve B-ethyl acetate (15:1, v/v) afforded 4.05 g of **4** and 5.20 g of dimer **5**, both as viscous colorless oils [TLC, Skellysolve-B–ethyl acetate (9:1)]: R_f 0.36 for **5** and 0.46 for **4**; mass spectrum, *m/e* calcd for **4** ($C_{11}H_{18}O_2S_2$, M^+) 246.0748, found 246.0735; mass spectrum, *m/e* for **5** calcd for $C_{14}H_{23}O_4S_2$ ($M^+ - \overline{SCH_2CH_2CH_2S(CH_2CH_2CH{=}CH_2)}CH$ 319.1038, found 319.1043.

Anal. Calcd for **4** ($C_{11}H_{18}O_2S_2$): C, 53.62; H, 7.36. Found: C, 53.87; H, 7.52. Calcd for **5** ($C_{22}H_{36}O_4S_4$): C, 53.62; H, 7.36. Found: C, 53.85; H, 7.42.

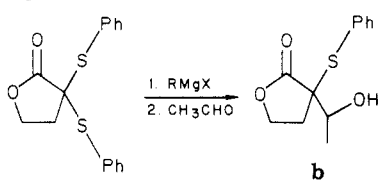
In other experiments, we have observed by TLC an increase in yield of **5** with respect to **4** when either the ethyl chloroformate addition was extended over a 15-min period or added to a −15 to −10 °C solution of **2**.

Inverse Addition Procedure. **2** was prepared as described above from 4.55 g (26.15 mmol) of 2-(buten-1-yl)-1,3-dithiane and 16.70 mL (26.70 mmol) of 1.6 M *n*-butyllithium in 100 mL of tetrahydrofuran. The solution of **2** was then added via a double needle canula, using nitrogen pressure over a 15-min period to a −78 °C solution of ethyl chloroformate (4.24 g, 39.22 mmol) in 30 mL of tetrahydrofuran. The resulting solution was allowed to warm to 0 °C and worked up in the same manner as previously described to yield 5.02 g (85%) of **4**.

Registry No. **4**, 82951-41-5; **5**, 82963-09-5; 2-(3-buten-1-yl)-1,3-dithiane, 16885-20-4; ethyl chloroformate, 541-41-3.

(6) D. Seebach and E. J. Corey, *J. Org. Chem.*, **40**, 231 (1975). These authors obtained by inverse addition a 60% yield of **3** (R = CH_3) when 10 mmol of **1** (R = CH_3) was added to a −73 °C tetrahydrofuran solution of 200 mmol of ethyl chloroformate.

(7) B. M. Trost and M. T. K. Mao, *Tetrahedron Lett.*, 3523 (1980). A similar reaction was observed where a Grignard reagent reacted with lactone a exclusively at sulfur and the resulting enolate trapped with acetaldehyde to give alcohol b.



a b

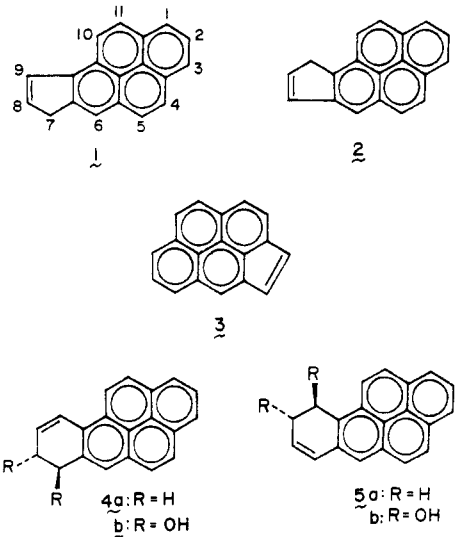
Synthesis of 7*H*- and 9*H*-Cyclopenta[*a*]pyrene

Hongmee Lee and Ronald G. Harvey*

Ben May Laboratory, University of Chicago, Chicago, Illinois 60637

Received March 23, 1982

The polycyclic hydrocarbons 7*H*- and 9*H*-cyclopenta[*a*]pyrene (**1** and **2**), unknown prior to these studies, are

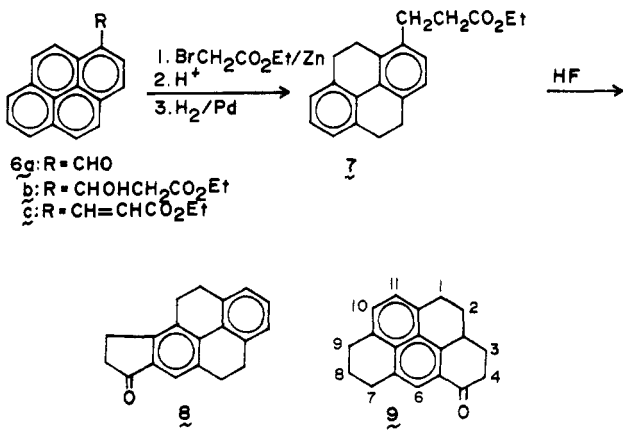


of interest as potential mutagens and carcinogens to test theories of carcinogenesis. The 7*H* isomer, **1**, is structurally related to cyclopenta[*cd*]pyrene (**3**), 7,8-dihydrobenzo[*a*]pyrene (**4a**), and *trans*-7,8-dihydroxy-7,8-dihydrobenzo[*a*]pyrene (**4b**) in that these molecules all contain an olefinic bond linked to the 1-position of pyrene. The latter three compounds exhibit mutagenic[1-4] and carcinogenic[3-5]

(1) Eisenstadt, E.; Gold, A. *Proc. Natl. Acad. Sci. U.S.A.* **1978**, *75*, 1667.

0022-3263/82/1947-4364$01.25/0

Scheme I

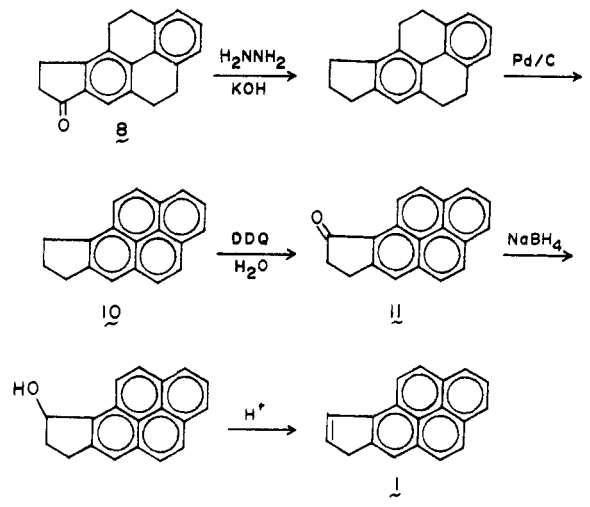


activity, and **4b** has been implicated as the proximate carcinogenic metabolite of the potent carcinogen benzo[*a*]pyrene.[4] Recent research indicates that **3** and **4** are oxidized enzymatically to epoxide derivatives, which are the biologically active forms.[4] On the other hand, 9*H*-cyclopenta[*a*]pyrene (**2**) is a homologue of 9,10-dihydrobenzo[*a*]pyrene (**5a**) in which the olefinic bond is conjugated with the 2-position of pyrene. Both **5a** and its diol derivative **5b** are essentially inactive biologically.[3,4] On the basis of these analogies, it is predicted that **1** should exhibit significant mutagenic and carcinogenic activities, while **2** should be inactive.

Results and Discussion

Synthesis of **1** and **2** was accomplished from pyrene-1-carboxaldehyde (**6a**) via the key intermediate 4,5,8,9,10,11-hexahydro-7-oxo-7*H*-cyclopenta[*a*]pyrene (**8**). The latter was efficiently synthesized (Scheme I) by Reformatski reaction of **6a**, followed by acid-catalyzed dehydration to afford ethyl *trans*-3-(1-pyrenyl)acrylate (**6c**). Hydrogenation of the latter over the K-region specific catalyst 10% palladium/charcoal[7] took place with addition of 3 molar equiv of hydrogen to yield ethyl 3-(4,5,9,10-tetrahydro-1-pyrenyl)propionate (**7**). Hydrogenation of the 4,5,9,10-positions was necessary in order to direct subsequent cyclization to the 2-position in preference to the electronically favored 10-position.[8] Compound **7** on treatment with liquid HF underwent smooth cyclization to **8**. When this reaction was carried out on larger scale, there was obtained a minor product identified as 5-oxo-1,2,2a,3,4,7,8,9-octahydro-5*H*-benzo[*cd*]pyrene (**9**). The structure of **9** was confirmed by conversion to the known hydrocarbon 6*H*-benzo[*cd*]pyrene by reduction with $NaBH_4$, acid-catalyzed dehydration of the resulting alcohol, and dehydrogenation with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). Compound **9** is believed to arise from cyclization of ethyl 3-(1,2,3,6,7,8-hexahydro-1-pyrenyl)propionate formed as a minor byproduct in the hydrogenation of **6c**.

Scheme II



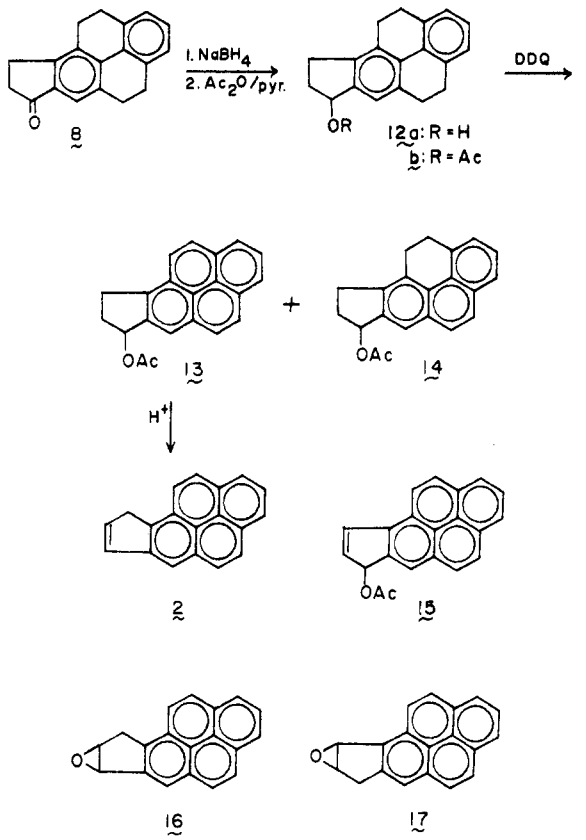
Conversion of the ketone **8** to 7*H*-cyclopenta[*a*]pyrene was achieved through the sequence in Scheme II. Wolff–Kishner reduction of the carbonyl function, followed by catalytic rearomatization, gave 8,9-dihydro-7*H*-cyclopenta[*a*]pyrene (**10**). Oxidation of the latter directly to the corresponding ketone 7,8-dihydro-9-oxo-9*H*-cyclopenta[*a*]pyrene (**11**) was accomplished with DDQ in aqueous dioxane. This relatively novel reaction has precedent in two examples of oxidation of alkyl aromatic compounds with DDQ in methanol reported earlier from this laboratory.[9,10] This oxidation is believed to involve initial hydride abstraction by DDQ regiospecifically in the 9-position in accord with theoretical prediction of carbonium ion stability,[9,11,12] followed by reaction of the resulting carbonium ion intermediate with water to yield the corresponding alcohol, further oxidation of which with DDQ gives **11**. The 500-MHz high-resolution NMR spectrum of **11** was clearly consistent with its assignment as the 9-oxo rather than the 7-oxo isomer. Particularly diagnostic was the large downfield shift of the adjacent H proton to δ 9.49. This assignment was further confirmed by a nuclear Overhauser effect experiment in which irradiation of the H_7 signal was observed to result in significant enhancement of the adjacent H_6 singlet peak.

Reduction of **11** with $NaBH_4$, followed by *p*-toluenesulfonic acid catalyzed dehydration of the resulting alcohol, furnished 7*H*-cyclopenta[*a*]pyrene. Under the mild acidic conditions employed, equilibration of **1** with the 9*H* isomer was not a significant problem. In contrast, attempted synthesis of **1** through reaction of the *p*-toluenesulfonylhydrazine of **11** with methyllithium gave a 1:1 mixture of **1** and **2**.

9*H*-Cyclopenta[*a*]pyrene was synthesized from **8** by the method in Scheme III. Reduction of **8** with $NaBH_4$ and acetylation gave 7-acetoxy-4,5,8,9,10,11-hexahydro-7*H*-cyclopenta[*a*]pyrene (**12b**). Dehydrogenation of **12b** with DDQ yielded a mixture of 7-acetoxy-8,9-dihydro-7*H*-cyclopenta[*a*]pyrene (**13**) (66%) and its 10,11-dihydro

(2) Gold, A.; Nesnow, S.; Moore, M.; Garland, H.; Gaynelle, C.; Howard, B.; Graham, D.; Eisenstadt, E. *Cancer Res.* **1980**, *40*, 4482.
(3) Sims, P.; Grover, P. L. *Adv. Cancer Res.* **1974**, *20*, 166.
(4) Harvey, R. G. *Acc. Chem. Res.* **1981**, *14*, 214.
(5) Neal, J.; Trieff, N. M. *Health Lab. Sci.* **1972**, *9*, 32.
(6) Wood, A. W.; Levin, W.; Chang, R. L.; Huang, M. T.; Ryan, D. E.; Thomas, P. E.; Lehr, R. E.; Kumar, S.; Koreeda, M.; Akagi, H.; Ittah, Y.; Dansette, P.; Yagi, H.; Jerina, D. M.; Conney, A. H. *Cancer Res.* **1980**, *40*, 642.
(7) Fu, P. P.; Lee, H. M.; Harvey, R. G. *J. Org. Chem.* **1980**, *45*, 2797.
(8) Cyclization of β-1-pyrenylpropionic acid in liquid HF yields 4,5-dihydro-5-oxo-3*H*-benzo[*c,d*]pyrene: Reid, D. H.; Bonthrone, W. *J. Chem. Soc.* **1965**, 5920.
(9) Fu, P. P.; Harvey, R. G. *Chem. Rev.* **1978**, *78*, 317.
(10) Fu, P. P.; Cortez, C.; Sukumaran, K. B.; Harvey, R. G. *J. Org. Chem.* **1979**, *44*, 4265.
(11) Formation of a carbonium ion intermediate by initial hydride abstraction is favored in the bay region position by the theoretically calculated greater delocalization energy ($\Delta E_{deloc}/\beta$) in this region.[12] This is shown experimentally by the reaction of 7,8,9,10-tetrahydrobenzo[*a*]pyrene with DDQ to yield, 7,8-dihydrobenzo[*a*]pyrene rather than 9,10-dihydrobenzo[*a*]pyrene.[13]
(12) Fu, P. P.; Harvey, R. G.; Beland, F. A. *Tetrahedron* **1978**, *34*, 857.
(13) Fu, P. P.; Lee, H. M.; Harvey, R. G. *Tetrahedron Lett.* **1978**, 551.

Scheme III



derivative **14** (7%). Attempts to drive this reaction further to completion or all the way to 7-acetoxy-7*H*-cyclopenta[*a*]pyrene (**15**) with a larger excess of DDQ or longer reaction time resulted in diminished yields and formation of tarry products. Treatment of **13** with *p*-toluenesulfonic acid in refluxing benzene afforded dirrectly 9*H*-cyclopenta[*a*]pyrene.

The high-resolution 500-MHz proton NMR spectra of **1** and **2** clearly distinguished these isomers, confirming their structural assignments. The most diagnostic features of the spectrum of **1** were the vinylic H_9 (δ 7.70) and the aromatic H_{10} (δ 8.40) protons, which exhibited significant downfield shifts relative to the corresponding protons of **2** (δ 7.30 and 8.11, respectively), confirming the presence of the former in the sterically crowded bay region.

In view of the potential biological importance of the epoxide derivatives of **1** and **2**, their synthesis was also investigated. Epoxidation of **2** with *m*-chloroperbenzoic acid took place smoothly to afford 7,8-dihydro-7,8-epoxy-9*H*-cyclopenta[*a*]pyrene (**16**). However, attempted analogous preparation of the epoxide derivative of **1** (**17**) failed to provide the desired product. Alternative synthetic approaches to **17** through cyclization of the bromohydrin or *trans*-dihydrodiol derivatives of **1** were also unsuccessful. It appears that **17** may be considerably less stable than **16**. This is not unexpected, since the epoxide derived from **4a** (also a bay region epoxide) is considerably less stable than the analogous epoxide derivative of **5**. This is also consistent with theory, since the energy required for ring opening of an epoxide to form a zwitterion is generally less for a bay region than for a non bay region epoxide.[4,12,14]

Experimental Section

Materials and Methods. The NMR spectra were obtained on a Varian EM 360 or the University of Chicago 500-MHz NMR spectrometer in $CDCl_3$ with tetramethylsilane as internal standard unless specified otherwise. Melting points are uncorrected. All new compounds that were isolated and characterized gave satisfactory microanalysis for C and H within ±0.3%.

Ethyl 3-(1-Pyrenyl)-3-hydroxypropionate (6b). Zinc powder (3.26 g, 50 mmol) (activated by washing successively with dilute HCl, H_2O, acetone, and ether) and a few crystals of I_2 were charged into a dry flask equipped with a reflux condenser. A solution of pyrene-1-carboxaldehyde (11.55 g, 50 mmol) and ethyl bromoacetate (8.35 g, 50 mmol) in benzene was added in portions over 0.5 h and refluxed for 3 h under N_2. Dilute hydrochloric acid was added, and the product was worked up conventionally to afford **6b** (15.62 g, 98%) as a white solid: mp 94–96 °C (EtOAc–hexane); NMR δ 1.30 (t, 3, CH_3), 3.0 (d, 2, CH_2CO_2), 4.30 (q, 2, CH_2CH_3), 6.30 (t, 1, CHOH), 8.0–8.5 (m, 9, aromatic).

Ethyl *trans*-3-(1-Pyrenyl)propenoate (6c). A solution of **6b** (15.62 g, 49 mmol) and *p*-toluenesulfonic acid (2.5 g) in benzene (30 mL) was heated at reflux for 2 h. The usual workup gave **6c** (14.29 g, 94%): mp 102–103 °C (EtOAc); NMR δ 1.48 (t, 3, CH_3), 4.50 (q, 2, CH_2), 6.80 (d, 1, H_2, $J_{2,3}$ = 16 Hz), 8.0–8.5 (m, 8, aromatic), 8.6 (d, 1, H_{10}), 8.95 (d, 1, H_3, $J_{2,3}$ = 16 Hz). The relatively large coupling between the vinylic protons ($J_{2,3}$ = 16 Hz) supports the trans stereochemical assignment.

Ethyl 3-(4,5,9,10-Tetrahydro-1-pyrenyl)propionate (7). Hydrogenation of **6c** (9 g, 29 mmol) in EtOAc (20 mL) was conducted over a 10% Pd/C catalyst[7] (7 g) at ambient temperature at 50 psig for 5 days. Following removal of the catalyst by filtration, evaporation gave **7** (8.68 g, 94%) as an oil: NMR δ 1.30 (t, 3, CH_3), 2.3–3.3 (m, 4, $CH_2CH_2CO_2$), 2.9 (s, 8, $H_{4,5,9,10}$), 4.15 (q, 2, CH_2CH_3), 7.05–7.25 (m, 5, aromatic). A small broad multiplet was also present at δ 1.35–1.95, indicative of the presence of what was assumed to be a small amount of ethyl 3-(1,2,3,6,7,8-hexahydro-1-pyrenyl)propionate. The percentage of this minor byproduct varied from 5 to 10% (by NMR), depending upon reaction time, scale, and other experimental variables. Since this minor component could not be readily removed, the product was employed directly in the next step. Hydrogenation of **6b** under the same conditions as **6c** afforded **7** directly, but in lower overall yield (~50%).

4,5,8,9,10,11-Hexahydro-7-oxo-7*H*-cyclopenta[*a*]pyrene (8). A solution of **7** (4.87 g, 15.4 mmol) in liquid HF was stirred overnight. The HF was removed by evaporation, and the solid residue was dissolved in THF, adsorbed on silica gel, and evaporated to dryness in vacuo. The solid adsorbed on silica gel was placed on top of a column of silica gel. Elution with benzene afforded **8** (3.6 g, 89%) as a white solid: mp 152–154 °C (EtOAc); NMR δ 2.6–3.2 (m, 4, $H_{8,9}$), 2.8 (s, 8, $H_{4,5,10,11}$), 7.1 (m, 3, $H_{1,2,3}$), 7.5 (s, 1, H_6).

When this reaction was carried out on larger scale (28 g of **7**) there was obtained in addition to **8** a second product (2.3 g, 10%) identified as 5-oxo-1,2,2a,3,4,7,8,9-octahydro-5*H*-benzo[*cd*]pyrene (**9**): mp 158–159 °C (EtOAc–hexane); NMR δ 1.6–2.5 (m, 6, $H_{2,3,8}$), 2.5–3.3 (m, 9, $H_{1,2a,4,7,9}$), 7.25 (s, 2, $H_{10,11}$), 7.8 (s, 1, H_6).

The structure of **9** was confirmed by conversion to 6*H*-benzo[*cd*]pyrene. Reduction of **9** (200 mg) with $NaBH_4$ (150 mg) in MeOH (50 mL) at room temperature for 2.5 h gave 5-hydroxy-1,2,2a,3,4,5,7,8,9-octahydrobenzo[*cd*]pyrene (200 mg): mp 171–172 °C (EtOAc); NMR δ 1.4–2.3 (m, 9, $H_{2,2a,3,4,8}$), 2.6–3.25 (m, 7, $H_{1,7,9}$, OH), 4.85 (m, 1, H_5), 7.1 (s, 2, $H_{10,11}$), 7.4 (s, 1, H_6). Dehydration of the alcohol (107 mg) with *p*-toluenesulfonic acid (15 mg) was carried out in refluxing benzene (50 mL) for 2 h. Following the usual workup, chromatography on Florisil gave 1,2,2a,3,7,8,9-hexahydrobenzo[*cd*]pyrene (95 mg): mp 61–62 °C (hexane); NMR δ 1.5–2.4 (m, 5, $H_{2,2a,8}$), 2.8–3.2 (m, 8, $H_{1,3,7,9}$), 6.1 (m, 1, H_4), 6.5 (d, 1, H_5, $J_{4,5}$ = 10 Hz), 6.9–7.15 (m, 3, aromatic). The olefin (94 mg) and DDQ (260 mg) were heated in refluxing benzene (20 mL) for 2 h under N_2. The reaction mixture was poured on a column of neutral alumina (activity I), eluted with benzene, and further purified by chromatography on Florisil. Elution with hexane gave 6*H*-benzo[*cd*]pyrene (55 mg, 60%): mp

(14) Jerina, D. M.; Lehr, R. E.; Yagi, H.; Hernandez, O.; Dansette, P. M.; Wislocki, P. G.; Wood, A. W.; Chang, P. L.; Levin, W.; Conney, A. H. In "In Vitro Metabolic Activation in Mutagenesis Testing"; de Serres, F. J., et al., Eds., Elsevier: Amsterdam, 1976, p 159.
(15) Johnson, A. W. *J. Org. Chem.* **1958**, *24*, 833.
(16) Jütz, C.; Kirchlecher, R.; Seidel, H. J. *Chem. Ber.* **1969**, *102*, 2301.

124–125 °C (cyclohexane) (lit.[15,16] 123–124, 134–135 °C); NMR (500 MHz) δ 4.98 (s, 2, H_6), 7.45 (dd, 2, $H_{5,7}$), 7.50 (t, 2, $H_{4,8}$), 7.72 (dd, 2, $H_{3,9}$), 7.76 (d, 2, $H_{1,11}$ or $H_{2,10}$), 7.80 (d, 2, $H_{1,11}$ or $H_{2,10}$); $J_{1,2} = J_{10,11} = 8.6$, $J_{3,4} = J_{4,5} = J_{7,8}$, $J_{8,9} = 7.1$, $J_{3,5} = J_{7,9} = 1.2$ Hz.

4,5,8,9,10,11-Hexahydro-7*H*-cyclopenta[*a*]pyrene. A solution of **8** (1 g, 3.8 mmol), hydrazine hydrate (1 g), and KOH (1 g) in diethylene glycol (100 mL) was heated at reflux overnight under N_2. The usual workup, followed by chromatography on silica gel, gave on elution with hexane 4,5,8,9,10,11-hexahydro-7*H*-cyclopenta[*a*]pyrene (863 mg, 92%): mp 82–83 °C (ethanol); NMR δ 2.1 (m, 2, H_8), 2.7–3.1 (m, 4, $H_{7,9}$), 2.8 (s, 8, $H_{4,5,10,11}$), 7.1 (m, 4, $H_{1,2,3,6}$).

8,9-Dihydro-7*H*-cyclopenta[*a*]pyrene (10). A mixture of the product of the foregoing reaction (310 mg, 1.26 mmol) and 10% Pd/C (30 mg) was heated at 220 °C under N_2 for 2 h.[9] The usual workup, followed by chromatography on silica gel, gave, on elution with hexane–benzene (8:2), **10** (300 mg, hexane): NMR δ 2.25 (t, 2, H_8), 3.35 (q, 4, $H_{7,9}$), 7.9–8.25 (m, 8, aromatic).

7,8-Dihydro-9-oxo-9*H*-cyclopenta[*a*]pyrene (11). A solution of **10** (104 mg, 0.43 mmol) and DDQ (279 mg, 1.23 mmol) in 10% aqueous dioxane (50 mL) was heated at reflux overnight. The solution was cooled and chromatographed through a column of neutral alumina eluted with dioxane. Evaporation of the solvent afforded **11** (81 mg, 74%): mp 206–208 °C (EtOAc); NMR (500 MHz) δ 2.94 (t, 2, H_8), 3.48 (t, 2, H_7), 8.02 (d, 1, H_4 or H_5), 8.05 (d, 1, H_2), 8.11 (s, 1, H_6), 8.16 (d, 1, H_4 or H_5), 8.25 (d, 1, H_3), 8.29 (d, 1 H_1), 8.31 (d, 1, H_{11}), 9.49 (d, 1 H_{10}), $J_{1,2} = J_{2,3} = 7.6$, $J_{4,5} = 8.9$, $J_{10,11} = 9.1$ Hz.

7*H*-Cyclopenta[*a*]pyrene (1). A mixture of **11** (644 mg, 2.5 mmol) and $NaBH_4$ (380 mg, 10 mmol) was taken up in THF (70 mL) and MeOH (80 mL) and stirred at room temperature for 2.5 h. After the usual workup, evaporation of the solvent afforded the alcohol (60 mg, 93%): mp 148–149 °C (EtOAc); NMR δ 2.2–3.7 (m, 4 $H_{7,8}$), 6.1 (m, 1, H_9), 8.0–8.6 (m, 8, aromatic). A solution of the alcohol (90 mg, 0.35 mmol) and *p*-toluenesulfonic acid (10 mg) was heated in refluxing benzene for 30 min. The usual workup, followed by chromatography on 2% 2,4,7-trinitrofluorenone on silica gel,[17] furnished, on elution with hexane, **1** (49 mg, 58%); mp 125–127 °C; NMR (500 MHz) δ 3.78 (s, 2, H_7), 6.9 (m, 1, H_8), 7.7 (m, 1, H_9), 7.97 (t, 1, H_2), 8.0 (d, 1, H_4 or H_5), 8.1 (d, 1 H_4 or H_5), 8.1 (d, 1, H_{11}), 8.2 (d, 1, $H_{1,3}$), 8.3 (s, 1, H_6), 8.4 (d, 1, H_{10}), $J_{1,2} = J_{2,3} = 7.7$, $J_{4,5} = 8.9$, $J_{8,9} = 5.7$, $J_{10,11} = 9.0$ Hz; UV λ_{max} (EtOH) 222 nm (ε 24 440), 244 (36 000), 250 (42 200), 275 (20 800), 285 (30 000), 325 shoulder (11 800), 342 (28 300), 360 (40 300).

7-Acetoxy-4,5,8,9,10,11-hexahydro-7*H*-cyclopenta[*a*]pyrene (12b). A mixture of **8** (1.3 g, 5 mmol) and $NaBH_4$ was taken up in THF (20 mL) and methanol (20 mL) and stirred at ambient temperature for 2.5 h. After the usual workup, evaporation afforded the alcohol **12a** (1.1 g, 85%): NMR δ 2.6–3.1 (m, 4, $H_{8,9}$), 2.9 (s, 8, $H_{4,5,10,11}$), 5.27 (t, 1, H_7), 6.15 (m, 4, $H_{1,2,3,6}$).

To a solution of acetic anhydride (15 mL) and pyridine (6 mL) was added **12a** (747 mg, 2.8 mmol), and the resulting solution was stirred at room temperature overnight. The usual workup, followed by chromatography on silica gel, gave, on elution with benzene, **12b** (860 mg, 99%): mp 85–87 °C (EtOAc–hexane); NMR δ 2.05 (s, 3, CH_3), 2.6–3.1 (m, 4, $H_{8,9}$), 2.85 (s, 8, $H_{4,5,10,11}$), 6.2 (m, 1, H_7) 7.1 (m, 4, aromatic).

7-Acetoxy-8,9-dihydro-7*H*-cyclopenta[a]pyrene (13). A solution of **12b** (804 mg, 2.6 mmol) and DDQ (1.31 g, 5.8 mmol) in anhydrous benzene (80 mL) was refluxed for 2 h under N_2. The solution was chromatographed on a silica gel column eluted with benzene. Evaporation of the solvent afforded 578 mg (73%) of a product consisting of **13** and **14** (or its 4,5-dihydro isomer) (10% by NMR). Recrystallization from ether–hexane gave the analytical sample of **13**: mp 100–102 °C; NMR δ 2.1 (s, 3, CH_3), 2.3–3.8 (m, 4, $H_{8,9}$), 6.6 (m, 1, H_7), 7.9–8.3 (m, 8, aromatic).

9*H*-Cyclopenta[*a*]pyrene (2). A solution of **13** (42 mg, 0.14 mmol) and *p*-toluenesulfonic acid (4 mg) was heated in refluxing benzene (20 mL) for 1 h under N_2. The usual workup, followed by chromatography on silica gel, yielded **2** (31 mg, 93%) as a white solid: mp 133–135 °C; NMR (500 MHz) δ 3.90 (s, 2, H_9), 6.89 (m, 1, H_8), 7.30 (m, 1, H_7), 8.02 (t, 1, H_2), 8.11 (d, 1, H_{10}), 8.16 (d, 1, H_{11}), 8.17 (d, 1, H_4), 8.22 (d, 1, H_1 or H_3), 8.23 (d, 1, H_1 or H_3), 8.26 (d, 1, H_5), 8.29 (s, 1, H_6); $J_{1,2} = J_{2,3} = 7.5$, $J_{4,5} = 9.0$, $J_{7,8} = 5.5$, $J_{10,11} = 8.9$ Hz; UV λ_{max} (EtOH) 263 nm shoulder (ε 55 960), 275 (68 600), 281 shoulder (33 200), 296 (25 270), 326 (20 940), 342 (36 800).

Conversion of **13** to **2** was also accomplished via methanolysis and dehydration. A suspension of **13** (65 mg, 0.22 mmol) in 30 mL of 5% KOH in MeOH was heated at reflux for 40 min. Conventional workup, followed by chromatography on a column of Florisil, gave the corresponding alcohol (46 mg, 82%): NMR δ 2.0–3.7 (m, 5, $H_{8,9}$, OH), 5.7 (t, 1, H_7), 7.2–8.3 (m, 8, aromatic). Dehydration of the alcohol was effected with *p*-toluenesulfonic acid (4 mg) in refluxing benzene (10 mL) for 20 min. The usual workup, followed by chromatography on a column of silica gel impregnated with 2% 2,4,7-trinitrofluorenone,[17] yielded **2** (30 mg, 58%) as a white solid identical by NMR with the sample obtained via the alternative route.

7,8-Dihydro-7,8-epoxy-9*H*-cyclopenta[*a*]pyrene (16). To a heterogeneous solution of CH_2Cl_2 (10 mL) and 0.5 M $NaHCO_3$ (10 mL) were added **2** (39 mg, 0.16 mmol) and *m*-chloroperbenzoic acid (41 mg, 0.24 mmol). The mixture was stirred at ambient temperature for 5 h and then worked up conventionally. Trituration of the product with ether–hexane gave **16** (21 mg, 53%) as a white solid: mp 158–160 °C; NMR (500 MHz) δ 3.51 (dd, 1, $H_{9\alpha}$ or $H_{9\beta}$), 3.84 (d, 1, $H_{9\alpha}$ or $H_{9\beta}$), 4.44 (t, 1, H_8), 4.66 (m, 1, H_7), 7.96 (t, 1, H_2), 8.0 (d, 1, H_{10}), 8.06 (m, 3, $H_{4,5,11}$), 8.16 (d, 1, H_1 or H_3), 8.18 (d, 1, H_1 or H_3), 8.31 (s, 1, H_6); $J_{1,2} = J_{2,3} = 7.3$, $J_{7,8} = J_{8,9} = 1.0$, $J_{10,11} = 7.5$, $J_{9\alpha,\beta} = 18$ Hz.

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Synthesis of Psicofuranine Cyclic 4′,6′-Monophosphate

Priscilla A. Sturm and Elmer J. Reist*

Bio-Organic Chemistry Laboratory, Life Sciences Division, SRI International, Menlo Park, California 94025

Jon P. Miller

Biomedical Research Laboratory, Life Sciences Division, SRI International, Menlo Park, California 94025

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Adenosine cyclic 3′,5′-monophosphate (cAMP) plays a key role in the regulation of a broad range of physiological processes.[1] The only known mechanism by which cAMP exerts its effects in eukaryotic cells is via the activation of cAMP-dependent protein kinases.[2] As part of our continuing studies on the ability of cAMP analogues to activate these enzymes,[3] we have synthesized the cyclic

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