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THE MONOMETHYL AND DIMETHYL DERIVATIVES OF BENZO[E]PYRENE

HONGMEE LEE, N. SHYAMASUNDAR, and RONALD G. HARVEY*
Ben May Laboratory, University of Chicago Chicago, IL 60637, U.S.A.

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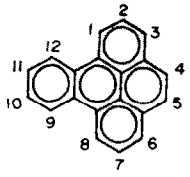
Abstract—Convenient syntheses of the previously unknown complete set of six isomeric monomethyl derivatives of benzo[e]pyrene, 1-, 2-, 3-, 4-, 9- and 10-methylbenzo[e]pyrene, are described. Syntheses of 1-, 2- and 3-methylbenzo[e]pyrene were accomplished through reaction of 7H-benzanthrene (or its 1-Me derivative as appropriate) with 1, 3-bis(dimethylamino)trimethinium perchlorate (or its 1-Me derivative) followed by thermal electrocyclic ring closure accompanied by elimination and aromatization. The earlier claim[16] that the analogous isomeric benzo[a]pyrene derivatives are principal products of reactions of this type is disproven. Synthesis of 3, 6- and 4, 5-dimethylbenzo[e]pyrene are also described. The structural assignments of all mono- and dimethyl benzo[e] pyrene products are supported by high resolution 270 MHz proton NMR spectra; the chemical shifts and coupling constants of all aromatic protons are fully assigned.

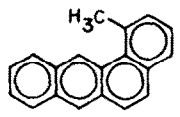
Surprisingly, the monoMe and diMe derivatives of the well known polycyclic aromatic hydrocarbon benzo[e]pyrene (BeP) are unknown.[1] Although the parent polyarene is a widespread environmental contaminant,[2] it is not established with certainty whether its Me derivatives are also products of incomplete combustion which are present in the atmosphere, automobile exhaust, cigaret smoke, etc.[3] However, this is reasonably likely, since Me derivatives of chrysene, pyrene, and other polyarenes have already been identified in these sources.[3-5]



BeP

Accurate characterization of the still unidentified methylated polyarenes present in pollution sources is of importance to carcinogenesis research, since Me substitution often profoundly enhances carcinogenic activity.[6-8] Conceivably the minor Me-substituted components may account for a substantial fraction of the total biological activity. More specifically, there is increasing evidence that introduction of Me groups into the bay positions of the benzo rings which are known to undergo enzymatic activation to reactive diol epoxide metabolites[7,9] blocks carcinogenic activity, while Me groups in the alternative bay region positions enhances activity. Thus 1-methylbenz[a]anthracene (**1**), 10-methylbenzo[a]pyrene (**2**) and 4-methylchrysene (**3**) are inactive or weakly active as carcinogens, while 12-methylbenz[a]anthracene (**4**), 11-methylbenzo[a]pyrene (**5**) and 5-methylchrysene (**6**) are all potent carcinogens.[7,8,10,11] Therefore, while BeP is weakly active as a carcinogen, it is conceivable that its Me derivatives, particularly 1-methylbenzo[e]pyrene, may exhibit a significantly enhanced level of biological activity.

We now report synthesis of the complete set of six isomeric monoMe derivatives of BeP (1-, 2-, 3-, 4-, 9-, and 10-BeP) as well as 3, 6- and 4, 5-dimethyl-BeP.



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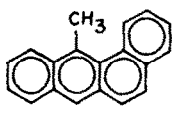

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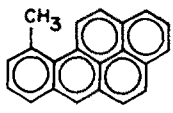

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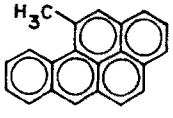

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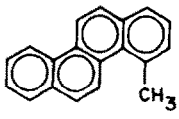

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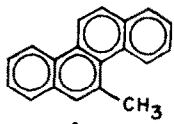

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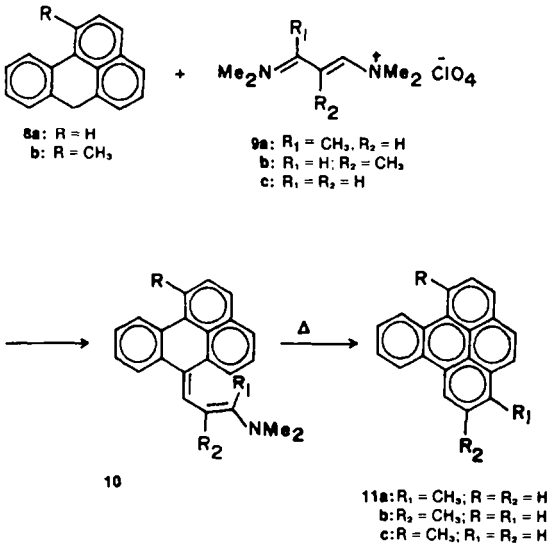
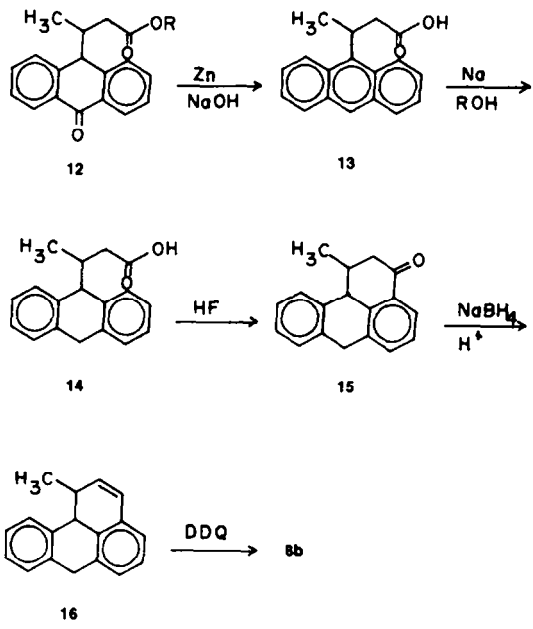
RESULTS AND DISCUSSION

Very little is known concerning the patterns of electrophilic substitution of BeP other than the report by Lang and Zander[12] that reaction of BeP with excess bromine affords 3, 6-dibromobenzo[e]pyrene. This finding was confirmed recently in this laboratory and bromination of BeP with one molar equivalent of bromine shown to afford 3-bromobenzo[e]pyrene (**7**).[13] Treatment of BeP with *o*-chloranil and HBr by the method of Wilk and Hoppe[14] was also shown to afford **7**.[13] Thus, **7** provides a convenient starting compound for the synthesis of 3-methylbenzo[e]pyrene (**11a**). This was readily accomplished via metal exchange of **7** with *n*-butyllithium followed by alkylation of 3-lithiobenzo[e]pyrene with methyl iodide.

An alternative synthetic approach to 3-methylbenzo[e]pyrene utilizing the relatively cheaper and more easily available starting compound benzanthrene (**8a**) was also developed (Scheme I). Initial base-catalyzed condensation between **8a** and the "vinamidinium salt" **9a**[15] followed by thermal electrocyclic ring closure with concurrent elimination of dimethylamine by the method of Jutz[16] furnished **11a** identical in its high resolution



Scheme 1.



Scheme 2.

270 MHz NMR spectrum with **11a** from the previous synthesis. Neither the 1-methyl isomer of BeP nor 1- or 3-methylbenzo[a]pyrene could be detected by NMR or tlc[17] as products of this reaction. While nonformation of 1-methylbenzo[e]pyrene is understandable on steric grounds, exclusive formation of **11a** was unexpected, since analogous reaction of **8a** with the unsubstituted salt **9c** is reported by Jutz *et al.*[16] to furnish BeP and benzo[a]pyrene in 2:1 ratio. However, careful reinvestigation of the latter reaction afforded only BeP with no detectable trace of the isomeric benzo[a]pyrene by NMR, tlc, or UV.[17,18]

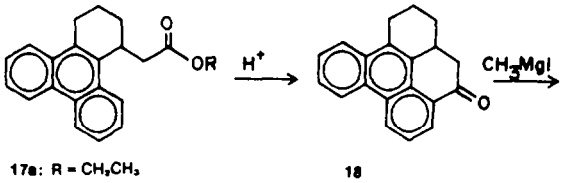
Analogous reaction of **8a** with 1,3-bis(dimethylamino)-2-methyltrimethinium perchlorate (**9b**) also took place smoothly and regiospecificially to furnish 2-methylbenzo[e]pyrene (**11b**). This finding is contrary to the prior claim by Jutz *et al.*[16] that 2-methylbenzo[a]pyrene is the principal product of this reaction. The high resolution NMR spectrum of **11b** was consistent only with the assigned 2-methylbenzo[e]pyrene structure. In particular, the four bay region protons $H_{1,8,9,12}$ appear at characteristic low field. $H_{9,12}$ which are furthest from the site of substitution are only slightly displaced (δ 8.82) from the analogous protons of BeP (δ 8.78), while H_1 appears as a singlet shifted to higher field ($\Delta\delta = +0.14$) consistent with its location adjacent to the methyl group. H_8 is also only slightly displaced ($\delta = 8.86$) and is coupled to H_7 ($J_{7,8} = 7.8$ Hz). The H_3 proton also appears as a singlet shifted to higher field ($\Delta\delta = +0.10$) in agreement with expectation. Other diagnostic features are the absence of a signal for the H_2 proton of BeP and the presence of a methyl singlet at δ 2.82. The chemical shifts and splitting patterns of the remaining protons were similar to those of BeP. The compound previously identified as 2-methylbenzo[a]pyrene[16] is, therefore, now reassigned as 2-Me-BeP. No trace of the 2-methylbenzo[a]pyrene isomer was detectable in the crude or purified product by NMR or tlc analysis.[17]

Synthesis of 1-methylbenzo[e]pyrene (**11c**) by an analogous route required 1-methylbenzanthrene (**8b**) as the starting compound. The latter was synthesized from anthrone via the sequence in Scheme II. Conversion of anthrone to 1-methyl-3-keto-1, 2, 3, 11b-tetrahydro-7H-benzanthrene (**15**) was accomplished by a modification of the method of Patton and Daub.[19] Michael condensation of anthrone with ethyl crotonate followed by hydrolysis and reduction with zinc and alkali and further reduction with sodium and amyl alcohol gave β-(9,10-dihydro-9-anthryl)butyric acid (**14**). Cyclization of the latter in liquid HF gave **15** in good overall yield. Reduction of **15** with $NaBH_4$ and acid-catalyzed dehydration afforded 1,11b-dihydro-7H-benzanthrene (**16**) which underwent dehydrogenation with DDQ to **8b**. The NMR spectrum of **8b** exhibited Me, benzylic, and aryl peaks in the ratio 3:2:9 expected for the 7H-benzanthrene structure, ruling out the 1H- and 3-H-benzanthrene isomers. Apparently the severe steric crowding in the bay region of **8b** is insufficient to shift the tautomeric equilibrium in favor of the latter isomers.

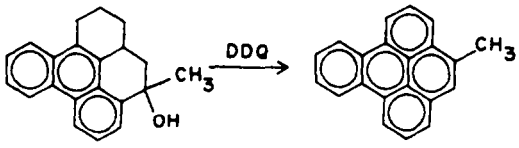
Condensation of 1-methyl-7H-benzanthrene with 1,3-bis(dimethylamino)trimethinium perchlorate (**9c**) followed by cyclization in refluxing quinoline afforded 1-methylbenzo[e]pyrene (**11c**) in 64% yield.

Synthesis of 4-methylbenzo[e]pyrene (**19**) was based on ethyl 1 - (1,2,3,4 - tetrahydrotriphenylenyl)acetate (**17a**), an intermediate in the recently reported synthesis of 4-hydroxybenzo[e]pyrene.[13] Alkaline hydrolysis of **17a** gave the free acid **17b** cyclization of which in liquid HF afforded 5 - oxo - 1,2,3,3a,4,5 - hexahydrobenzo[e]pyrene (**18**) (Scheme 3). Reaction of **18** with methylmagnesium iodide and dehydrogenation with DDQ provided **19** in good overall yield.

The syntheses of 9- and 10-methylbenzo[e]pyrene are based on 9-oxo-9, 10, 11, 12-tetrahydrobenzo[e]pyrene (**20**) and *trans*-9, 10-dibenzoyloxy-1, 2, 3, 6, 7, 8, 9, 10, 11, 12-decahydrobenzo[e]pyrene (**21a**), respectively, intermediates in the previously described synthesis of the 9, 10-dihydrodiol of BeP.[20] Synthesis of 9-methylbenzo[e]pyrene (**22**) was conveniently achieved through reaction of **20** with methylmagnesium iodide followed by simultaneous dehydration and dehydrogenation with DDQ. The high resolution NMR spectrum of **22** confirmed this structural assignment (*cf.* Experimental). Analogous synthesis of 10-methylbenzo[e]pyrene (**24**) was accomplished from the unconjugated ketone **23** which was



17a: R = CH_2CH_3 18



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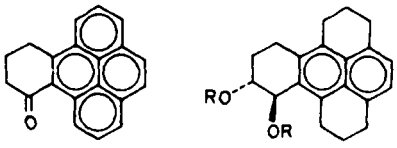
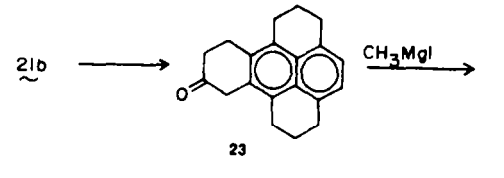
Scheme 3.



20 21a: R = Bz
b: R = H

obtained from **21a** via basic methanolysis to the free diol (**21b**) followed by acid-catalyzed dehydration (Scheme 4). Reaction of **23** with methylmagnesium iodide followed by dehydration-dehydrogenation with DDQ furnished **24**.

The 3,6- and 4,5-dimethylbenzo[e]pyrenes (**25**, **26**) were synthesized from 3, 6-dibromobenzo[e]pyrene[12,13] and benzo[e]pyrene-4,5-dione,[21] respectively. Transmetallation of 3, 6-dibromobenzo[e]pyrene with n-BuLi



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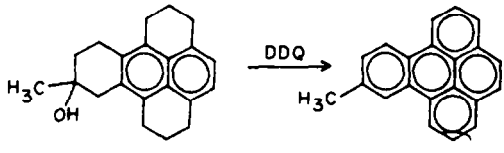

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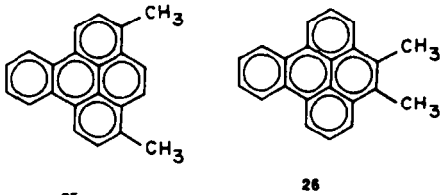
Scheme 4.



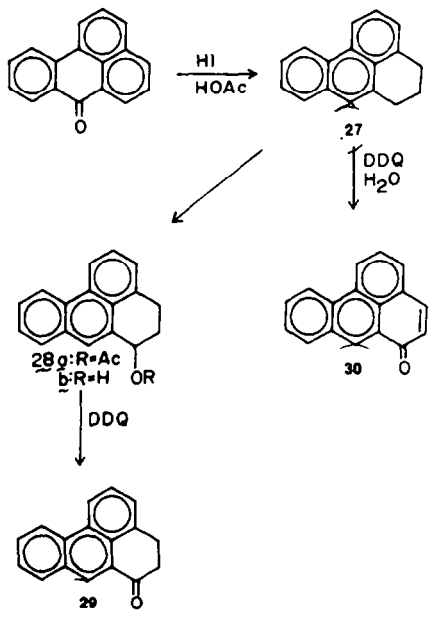
25 26

followed by alkylation with methyl iodide furnished **25** as a white solid, m.p. 178–180° in 90% yield. Reaction of BeP-4, 5-dione with MeLi provided the dimethyl diol essentially quantitatively. Reduction of the latter with hydriodic acid in acetic acid by the method of Konieczny and Harvey[22] afforded pure **26**.

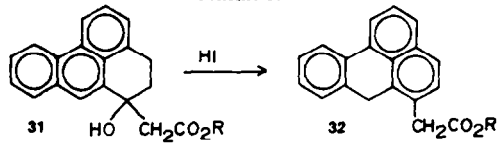
Prior to development of the successful synthetic route to 1- and 2-methyl-benzo[e]pyrene in Scheme 1, alternative methods for the construction of the substituted BeP ring system utilizing 4, 5-dihydro-6H-benzanthra-6-one (**29**) were explored (Scheme 5). The ketone **29** was prepared most conveniently from benzanthrone through reduction with HI and red phosphorus to 1, 10-trimethylenephenanthrene (**27**),[23] oxidation of the latter with lead tetraacetate to the 6-acetoxy derivative **28a**, methanolysis with KOH in methanol to **28b**, and oxidation with DDQ in dioxane. Oxidation of **27** with DDQ in aqueous dioxane furnished the previously unknown isomeric benzanthrone **30**.

Attempted Stobbe condensation of **29** with diethyl succinate as a means of introduction of the required three carbon structural unit proved unsuccessful. Reformatski reaction of **29** with zinc and ethyl bromoacetate took place smoothly to furnish the β-hydroxy ester **31**. Acid catalyzed dehydration of the latter afforded cleanly the more stable rearranged 7H-benzanthrene product **32**. Attempted reduction of **31** with HI in acetic acid also afforded **32** accompanied by unidentified side products. These synthetic approaches to the substituted BeP ring system were abandoned following attainment of the goal by the method in Scheme 1, since the alternative routes via **29** and **32** were more complex and offered no advantage.

The carcinogenic activities of all the mono- and dimethylbenzo[e]pyrenes are currently under investigation and will be reported separately.



Scheme 5.



EXPERIMENTAL

General. 3-Bromobenzo[e]pyrene,[13,14] 3,6-dibromobenzo-[e]pyrene[12,13] vinamidinium salts **9a–c**,[15] benzo[e]pyrene,[13] ethyl 1-(1,2,3,4-tetrahydrotriphenylenyl)-acetate,[13] compounds **20**,[18] **21a**,[18] and **27**[23] were synthesized as previously described. Benzo[e]pyrene-4,5-dione (m.p. > 320°, lit[20] > 320°) was synthesized from *cis*-4,5-dihydroxy-4,5-dihydrobenzo[e]pyrene[13] by oxidation with pyridine-SO_3 in dimethyl sulfoxide by the method of Harvey *et al.*[24] N-bromosuccinimide (NBS) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) were purchased from the Arapahoe Chemical Co.; NBS was recrystallized from water prior to use. The NMR spectra were obtained on a Varian T60 or Bruker HX 270 spectrometers with tetramethylsilane as internal standard in $CDCl_3$ unless specified otherwise. UV spectra were obtained on a Perkin–Elmer, Model 512 spectrometer. Melting points are uncorrected. All new compounds gave satisfactory microanalyses for C, H within ±0.3% and/or mass spectra consistent with the assigned structures.

7H-Benzanthrene (**8a**). To a soln of LAH (380 mg, 10 mmol) in 10 ml anhyd ether under N_2 was added over a 10–15 min period a soln of $AlCl_3$ (1.33 g, 10 mmol) in 10 ml ether. To this mixture was added a soln of benzanthrone (2.3 g, 10 mmol) in 20 ml anhyd ether over 30 min at a rate to produce gentle reflux. The mixture was heated at reflux for an additional 1 hr, then 5 ml EtOAc was added slowly to the cooled mixture to destroy the excess reagent. Conventional workup followed by chromatographic purification on a column of Florisil eluted with hexane gave pure **8a** (2 g, 90%), m.p. 81–82° (lit.[1] 81–82°C): NMR δ 4.3 (*s*, 2, benzylic), 7.0 ~ 8.05 (*m*, 10, aromatic).

3-Methylbenzo[e]pyrene (**11a**)

(A) *From 3-bromobenzo[e]pyrene* (**7**). A soln of *n*-BuLi (2 mmol) in hexane was added to a suspension of **7** (165 mg, 0.5 mmol) in dry ether (40 ml) under N_2. The mixture was heated at reflux for 30 min, then was cooled to room temp and excess MeI was added. Stirring was continued for 10 min, then the product was worked up conventionally to afford **11a** (135 mg, 80%). Consecutive recrystallization from EtOH and from $CHCl_3$–hexane gave the analytical sample of **11a** (68 mg, 58%), m.p. 121–123°: NMR (270 MHz, $CDCl_3$)δ 2.84 (s, 3, CH_3), 7.69 (m, 2, $H_{10,11}$), 7.83 (d, 1, H_2), 7.98 (t, 1, H_7), 8.03 (d, 1, H_5), 8.14 (d, 1, H_6), 8.17 (d, 1, H_4), 8.73 (d, 1, H_1), 8.78 (m, 2, $H_{9,12}$), 8.84 (d, 1, H_8).

(B) *From benzanthrene* (**8a**). A soln of **8a** (320 mg, 1.5 mmol), $NaOCH_3$ (89 mg, 1.65 mmol), and 1, 3- bis(dimethylamino)-3-methyltrimethinium perchlorate (362 mg, 1.5 mmol) in pyridine (7 ml) was heated at 100° for 6 hr under N_2. The pyridine was then replaced by quinoline (5 ml), and the soln was heated at reflux overnight. The usual workup gave a residue which was taken up in minimal benzene and passed through a column of Florisil eluted with benzene-hexane (1:4) to provide **11a** (100 mg, 25%) identical with the above sample.

2-Methylbenzo[e]pyrene (**11b**). A soln of **8a** (454 mg, 2.1 mmol), $NaOCH_3$ (135 mg, 2.5 mmol), and 1,3-bis(dimethylamino)-2-methyltrimethinium perchlorate (543 mg, 2.3 mmol) in pyridine (15 ml) was heated at 100° for 5 hr under N_2. The pyridine was replaced by quinoline (10 ml) and the soln was heated at reflux overnight. Workup by the method for **11a** gave **11b** (220 mg, 40%). Recrystallization from benzene-EtOH afforded pure **11b**, m.p. 180–182°: NMR (270 MHz, $CDCl_3$) δ 2.82 (s, 3, CH_3), 7.72 (m, 2, $H_{10,11}$), 7.95 (d, 1, $H_{4 \text{ or } 5}$), 7.96 (t, 1, H_7), 7.96 (s, 1, H_3), 7.98 (d, 1, $H_{4 \text{ or } 5}$), 8.14 (d, 1, H_6), 8.69 (s, 1, H_1), 8.82 (m, 2, $H_{9,12}$), 8.86 (d, 1, H_8).

β-(9-anthryl)butyric acid (**13**). To a soln of *t*-BuOK (12.32 g, 110 mmol) in *t*-BuOH (100 ml) under N_2 was added anthrone (19.4 g, 100 mmol). The soln was heated at reflux for 30 min, then ethyl crotonate (12.54 g, 110 mmol) was added from an addition funnel over 1 hr. The soln was refluxed for an additional hour and worked up in the usual manner to furnish a semisolid residue of **12** (32 g). A mixture of **12** (5 g, 16 mmol) and Zn dust (5 g activated with 1 g $CuSO_4$) in 240 ml of 10% KOH and 36 ml pyridine was maintained at reflux overnight. The product was filtered and worked up conventionally to afford crude **13**. Recrystallization from EtOHc gave pure **13** (3.4 g, 80%), m.p. 149–150° (lit.[19] 138–140°): NMR δ 1.75 (d, 3, CH_3), 3.15 (m, 2, CH_2), 4.9 (m, 1, CH), 7.2–8.6 (m, 9, aromatic).

1-Methyl-1, 11b-dihydro-7H-benzanthrene (**16**). The ketone **15** required for this synthesis was prepared from **13** through reduction with Na and amyl alcohol and cyclization with HF according to the reported procedures.[19]

To a soln of **15** (600 mg, 2.4 mmol) in THF (10 ml) and MeOH (40 ml) was added $NaBH_4$ (380 mg). The mixture was stirred at room temp for 2.5 hr, then worked up conventionally to provide 1-methyl-3-hydroxy-1, 2, 3, 11b-tetrahydrobenzanthrene (600 mg). A soln of this alcohol (500 mg) and *p*-toluenesulfonic acid (70 mg) in benzene (25 ml) was refluxed for 1 hr. The usual workup followed by chromatography on Florisil gave **16** (400 mg, 72%) as a white oil: NMR δ 0.5 (d, 3, CH_3), 3.05 (m, 1, H_1), 4.1 (m, 3, $H_{7,11b}$), 6.2 (q, 1, H_2, $J_{1,2} = 6$, $J_{2,3} = 9$ Hz), 6.5 (d, 1, H_3), 6.9–7.6 (m, 7, aromatic).

1-Methyl-7H-benzanthrene (**8b**). A soln of **16** (310 mg, 1.35 mmol) and DDQ (386 mg, 1.7 mmol) in benzene (10 ml) was refluxed overnight under N_2. The usual workup followed by chromatography on Florisil eluted with hexane-benzene (4:1) afforded **8b** (250 mg, 81%) as an oil: NMR δ 2.9 (s, 3, CH_3), 4.25 (s, 2, H_7), 7.0–7.9 (m, 9, aromatic).

1-Methylbenzo[e]pyrene (**11c**). Reaction of **8b** (320 mg, 1.3 mmol) with **9c** was conducted according to the procedure for the synthesis of **11a** to afford **11c** (221 mg, 64%). Recrystallization from benzene–EtOH furnished the analytical sample of **11c**, m.p. 178–180°: NMR (270 MHz, $CDCl_3$) δ 3.27 (s, 3, CH_3), 7.67 (m, 1, $H_{10 \text{ or } 11}$), 7.70 (m, 1, $H_{10 \text{ or } 11}$), 7.85 (d, 1, H_2), 7.96 (t, 1, H_7), 7.96 (s, 2, $H_{4,5}$), 8.03 (d, 1, H_3), 8.12 (d, 1, H_6), 8.78 (d, 1, H_9), 8.82 (m, 2, $H_{8,12}$).

1-(1,2,3,4-Tetrahydrotriphenylenyl)acetic acid (**17b**). Hydrolysis of **17a** (500 mg) in 5% alcoholic KOH soln overnight furnished the crude acid. Recrystallization from EtOH gave pure **17b** (400 mg, 86%), m.p. 185–186°.

5-Oxo-1, 2, 3, 3a, 4, 5-hexahydrobenzo[e]pyrene (**18**). Cyclization of **17b**(1 g) in liquid HF (20 ml) gave the crude ketone (900 mg). Chromatography on Florisil eluted with benzene followed by recrystallization from EtOH afforded pure **18** (780 mg, 83%), m.p. 130–131°, $M^+ = 272$: NMR (60 MHz, $CDCl_3$)δ 1.5 ~ 2.3 (m, 4, $H_{2,3}$), 2.7 (d, 2, H_4), 2.9 ~ 3.3 (m, 3, $H_{1,3a}$), 7.4 ~ 8.8 (m, 7, aromatic).

4-Methylbenzo[e]pyrene (**19**). A soln of **18** (200 mg, 0.73 mmol) in ether (15 ml) and MeMgI (4 mmol) was stirred overnight under N_2. Usual workup afforded the crude intermediate alcohol (210 mg) which was dissolved in dry benzene (20 ml). DDQ (770 mg) was added, and the resulting soln was refluxed for 3 hr under N_2 and worked in the usual manner. The crude **17** was passed through a column of Florisil eluted with hexane and recrystallized from benzene–alcohol to provide pure **19** (150 mg, 77%) as pale yellow needles, m.p. 206°: NMR (270 MHz, $CDCl_3$) δ 2.88 (s, 3, CH_3), 7.73 (m, 2, $H_{10,11}$), 7.88 (s, 1, H_5), 7.99 (t, 1, H_7), 8.05 (t, 1, H_2), 8.09 (d, 1, H_6), 8.31 (d, 1, H_3), 8.85 (d, 2, $H_{9,12}$), 8.85 (d, 1, $H_{1 \text{ or } 8}$), 8.91 (d, 1, $H_{1 \text{ or } 8}$).

9-Methylbenzo[e]pyrene (**22**). A soln of MeMgI was prepared from Mg (100 mg, 4 mmol) and excess MeI in ether (10 ml), and to this a soln of **20**(200 mg, 0.72 mmol) in ether was added. The resulting soln was stirred overnight at room temp., then worked up conventionally to afford the intermediate alcohol. The latter was dissolved in benzene (20 ml) along with DDQ (0.91 g), and the mixture was refluxed for 3 hr under N_2. The unusual workup gave **22** (137 mg, 72%), m.p. 123–124°: NMR (270 MHz, $CDCl_3$) δ 3.17 (s, 3, CH_3), 7.58 (d, 1, H_{10}), 7.60 (m, 1, H_{11}), 7.95 (t, 2, $H_{2,7}$), 8.01 (s, 2, $H_{4,5}$), 8.13 (d, 2, $H_{3,6}$), 8.75 (m, 1, H_{12}), 8.85 (d, 1, H_1), 8.92 (m, 1, H_8).

10-Oxo-1, 2, 3, 6, 7, 8, 9, 10, 11, 12-decahydrobenzo[e]pyrene (**23**). To a soln of **21a** (1 g, 2 mmol) in THF (30 ml) and MeOH (15 ml) under N_2 was added NaOMe (200 mg), and the soln was heated at reflux for 1 hr. Conventional workup gave the crude product which was triturated with ether–hexane (1:1) and filtered to yield **21b**(600 mg, 100%). The diol was dissolved in glacial AcOH (20 ml). Conc. HCl (0.5) ml) was added and the soln refluxed for 30 min. Usual workup gave the crude ketone (450 mg) which was chromatographed on Florisil eluted with benzene to yield pure **23** (350 mg, 63%): NMR (60 MHz, $CDCl_3$) δ

1.8–2.2 (m, 6, aliphatic), 3.2–3.0 (m, 10, benzylic), 3.6 (s, 2, H_9), 7.0 (br s, 2, aromatic).

10-Methylbenzo[e]pyrene (**24**). Reaction of **23** (350 mg, 1.3 mmol) with MeMgI was conducted by the procedure employed for **20**. The crude alcohol (350 mg) was dissolved in benzene (40 ml), DDQ (1.65 g) was added, and the mixture was heated at reflux for 24 hr under N_2. The product was chromatographed on Florisil. Elution with hexane gave pure **24** (250 mg, 73%) m.p. 106–108°: NMR (270 MHz, $CDCl_3$) δ 2.60 (s, 3, CH_3), 7.51 (d, 1, H_{11}), 7.97 (t, 1, $H_{2,7}$), 7.99 (s, 2, $H_{4,5}$), 8.11 (d, 1, $H_{3 \text{ or } 6}$), 8.13 (d, 1, $H_{3 \text{ or } 6}$), 8.52 (s, 1, H_9), 8.66 (d, 1, H_{12}), 8.80 (d, 1, H_8), 8.84 (d, 1, H_1).

3,6-Dimethylbenzo[e]pyrene (**25**). To a suspension of 3,6-dibromobenzo[e]pyrene (200 mg, 0.5 ml) in anhyd ether (10 ml) was added *n*-BuLi (2 ml of 2.1 M, 4 mmol) under N_2. The suspension was stirred at reflux for 30 min, then cooled, and MeI (568 mg, 4 mmol) was added. The usual workup followed by chromatography on Florisil (benzene–hexane, 4:1) afforded **25** (126 mg, 90%), m.p. 178–180° (benzene-hexane): NMR (270 MHz, $CDCl_3$) δ 2.90 (s, 6, CH_3), 7.65 (dd, 2, $H_{10,11}$), 7.79 (d, 2, $H_{2,7}$), 8.14 (s, 2, $H_{4,5}$), 8.69 (d, 2, $H_{1,8}$), 8.71 (m, 2, $H_{9,12}$).

4,5-Dimethylbenzo[e]pyrene (**26**). To a suspension of benzo[e]pyrene-4, 5-dione (150 mg, 0.53 mmol) in benzene (10 ml) under N_2 was added MeLi (5.3 mmol). The suspension was stirred at ambient temp. overnight, then worked up in the usual way to afford 4,5-dihydroxy-4, 5-dimethylbenzo[e]pyrene (165 mg, 99%) as a white solid, m.p. 128–130°: NMR (60 MHz, acetone-d_6) δ 2.85 (s, 6, CH_3), 7.5 ~ 9.05 (m, 10, aromatic).

A mixture of the dimethyl diol (187 mg, 0.6 mmol) and 57% HI (0.6 ml) in AcOH (10 ml) was heated at reflux for 4 hr. The hot soln was poured in $NaHSO_3$aq and the ppt was collected by filtration, worked with water and air-dried. Purification on a column of Florisil eluted with benzene–hexane (1:1) gave **26** (120 mg, 71%) as a white solid, m.p. 249–250° (benzene): NMR (270 MHz, $CDCl_3$) δ 2.88 (s, 6, CH_3), 7.73 (m, 2, $H_{10,11}$), 8.03 (t, 2, $H_{2,7}$), 8.38 (d, 2, $H_{2,6}$), 8.85 (dd, 2, $H_{9,12}$), 8.88 (d, 2, $H_{1,8}$).

6H-Benanthra-6-one (**30**). Oxidation of **27** (950 mg, 4.36 mmol) with DDQ (4.0 g, 17.4 mmol) was conducted in refluxing 10% aqueous dioxane (150 ml) overnight. The reaction mixture was poured onto a column of alumina and eluted with dioxane to afford **30** (750 mg, 70%), m.p. 137–139°: NMR (270 MHz, $CDCl_3$) δ 6.67 (d, 1, H_5), 7.63 ~ 7.78 (m, 5, $H_{2,3,4,9,10}$), 8.06 (d, 1, H_8), 8.62 (q, 2, $H_{1,11}$), 8.85 (s, 1, H_7).

4,5-Dihydro-6H-benzanthra-6-one (**29**). Oxidation of **27** (11.88 g, 54 mmol) with lead tetraacetate (26.6 g, 60 mmol) was carried out in glacial AcOH at 100° for 30 min. After the usual workup, the product was purified by chromatography on Florisil. Elution with benzene gave **28a** (9.58 g, 64%) as an oil: NMR (60 MHz, $CDCl_3$) δ 2.1 (s, 3, CH_3), 2.35 (m, 2, H_5), 3.2 (m, 2, H_4), 6.32 (t, 1, H_6), 7.3 ~ 7.9 (m, 6, aromatic), 8.4 ~ 8.8 (m, 2, $H_{1,11}$).

Methanolysis of **28a** (9.58 g, 34.6 mmol) in 5% KOH in MeOH (120 ml) at reflux over 40 min gave **28b** (7.43 g, 92%) as a yellow solid, m.p. 156–158°: NMR δ 2.2 (q, 2, H_5), 3.2 (m, 2, H_4), 4.6 (s, 1, OH), 5.1 (t, 1, H_6), 7.3 ~ 8.0 (m, 6, aromatic), 8.4 ~ 8.8 (m, 2, $H_{1,11}$).

Oxidation of **28b** (80 mg, 0.34 mmol) with DDQ (84 mg, 0.37 mmol) was carried out in dioxane (100 ml) at room temp. for 17 hr. The soln was passed through a column of neutral alumina eluted with dioxane to furnish 29 (76 mg. 97%), m.p. 158–159°: NMR (270 MHz, $CDCl_3$), δ 2.98 (t, 2, H_5), 3.41 (t, 2, H_4), 7.49 (d, 1, H_3), 7.60 (t, 2, $H_{9,11}$), 7.71 (t, 1, H_2), 7.99 (d, 1, H_8), 8.46 (s, 1, H_7), 8.52 (d, 1, $H_{1 \text{ or } 11}$), 8.62 (d, 1, $H_{1 \text{ or } 11}$).

Ethyl 2-(6-7H-benzanthryl)acetate (**32**). Zn (30 mg, 0.6 mmol) was placed in a flame dried flask equipped with condenser. To this was added a soln of **29** (141 mg, 0.6 mmol) and ethyl bromoacetate (100 mg, 0.6 mmol) in benzene (5 ml). A few crystals of I_2 were added, and the soln was heated at reflux for 3 hr. Dilute HCl was then added, and the product extracted with ether to afford the Reformatski addition product **31** (192 mg, ~ 100%) as an oil: NMR δ 1.2 (t, 3, CH_3), 2.35 (m, 2, H_5), 2.8 (s, 2,–CH_2C–), 3.2 (m, 2, H_4), 4.1 (q, 2, $C\underline{H}_2CH_3$), 7.2–8.1 (m, 6, aromatic), 8.4–8.8 (m, 2, $H_{1,11}$).

A solution of **31** (60 mg, 0.19 mmol) and *p*-tosic acid (12mg) in benzene (20 ml) was refluxed for 2 hr. The usual workup gave **32** (50 mg, 81%) as an oil which crystallized from ether–EtOH as a white solid, m.p. 65–66°: NMR δ 1.2 (t, 3, CH_3), 3.72 (s, 2, CH_2), 4.15 (q, 2, $\underline{CH}_2CH_3$), 4.4 (s, 2, H_7), 7.2 ~ 8.15 (m, 9, aromatic).

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