N,N'-Dihydroxy-2,3-diamino-2,3-dimethylbutane (38) was synthesized from **37** in 35% yield according to the procedure of Lamchen and Mittag:[78] mp 149–150 °C (lit.[78] mp 157–159 °C); ^{1}H NMR (Me_2SO-d_6) δ 1.1 (s, 12 H), 1.8–3.1 (v br, 4 H).

3,3,4,4-Tetramethyl-1,2-diazetine 1,2-Dioxide (22).[28,79] To a stirred solution of 5.0 g (0.034 mol) of **38** in 100 mL of water was added dropwise 10.9 g (0.068 mol) of bromine (Baker). A water bath was used to keep the reaction mixture at room temperature. The solution was stirred for 1 h and extracted with four 50-mL portions of chloroform. The combined extracts were dried over anhydrous magnesium sulfate, filtered, and concentrated under reduced pressure. Recrystallization from methanol gave 2.0 g (35%) of **22**: mp 184–185 °C dec (lit.[28] mp 190–192 °C dec); ν ($CHCl_3$) 3000, 1555, 1465, 1380, 1220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.62 (s).

Acknowledgment. We wish to gratefully acknowledge financial support of this work by a Cottrell grant from the Research Corp. and Grant No. CHE-76-09566 from the National Science Foundation. We thank Professor M. A. Ratner and Dr. Karsten Krogh-Jespersen for their collaboration on the INDO/S computations. We also thank Professor N. Geacintov for helpful discussions on fluorescence and single-photon counting and Professor A. M. Halpern (Northeastern University) for the original convolution computer program which was subsequently modified as described in this paper. We also thank Professor M. Goldstein of the ERDA Courant Computational Center for a generous grant of computer time.

Registry No. 1, 1121-65-9; 3, 2235-12-3; 5, 29474-19-9; 7, 52902-51-9; 11, 34733-74-9; 15, 4668-70-6; 16, 20023-66-9; 17, 18329-20-9; 18, 38086-92-9; 19, 2363-83-9; 20, 24470-78-8; 22, 34493-89-5; 24, 57212-55-2; 27, 57212-56-3; 29, 4668-71-7; 30, 35522-47-5; 31, 1123-71-3; 32, 100-22-1; 33, 184-26-9; 34, 1728-30-9; 35, 1192-93-4; 37, 3964-18-9; 38, 14384-45-3; tropone, 539-80-0; 2,5-dihydro-2,5-dimethoxyfuran, 332-77-4; 2-iodopropane, 75-30-9; triphenylphosphine, 603-35-0; 2-nitropropane, 79-46-9.

(78) B. Lamchen and T. M. Mittag, *J. Chem. Soc. C*, 2300 (1966).
(79) P. Singh, D. G. B. Boocock, and E. F. Ullman, *Tetrahedron Lett.*, 3935 (1971).

Synthesis of the Isomeric Phenols of Benz[a]anthracene from Benz[a]anthracene

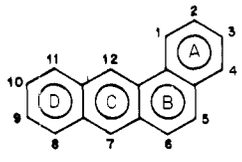
Peter P. Fu,[1] Cecilia Cortez, K. B. Sukumaran, and Ronald G. Harvey*

The Ben May Laboratory for Cancer Research, University of Chicago, Chicago, Illinois 60637

Received April 24, 1979

Novel and convenient syntheses of seven isomeric phenols of benz[a]anthracene (1-, 2-, 3-, 8-, 9-, 10-, and 11-HO-BA) from the parent polycyclic hydrocarbon are described. These syntheses demonstrate the feasibility of introduction of functional groups into polycyclic arene ring positions not prone to direct substitution through initial regioselective hydrogenation (or metal–ammonia reduction), followed by appropriate synthetic operations to introduce carbonyl or other desired functional groups into benzylic or olefinic ring positions and finally dehydrogenation. Fewer synthetic steps are generally required, and overall yields are superior to those obtained via the conventional synthetic approaches which entail total synthesis of each isomeric derivative from appropriately substituted smaller molecular units. Conversion of the aryl ketonic intermediates to phenols is accomplished by a new general method involving dehydrogenation of the corresponding enol acetate derivatives with *o*-chloranil.

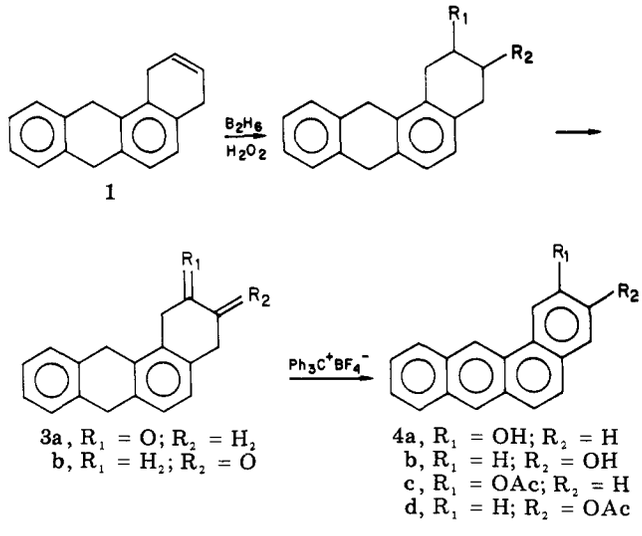
Benz[a]anthracene (BA) is an ubiquitous environmental contaminant formed through incomplete combustion of organic matter. It is present in variable concentration in



BA

the atmosphere, soil, automobile exhaust, cigarette smoke, and foods.[2] In contrast to structurally related hydrocarbons, such as 7-methyl-BA, 7,12-dimethyl-BA, dibenz[a,h]anthracene, and benzo[a]pyrene, which are potent carcinogens, BA exhibits only borderline activity as a tumor initiator.[2,3] Despite many years of investigation, the reason for this difference remains uncertain. However, recent evidence suggests that differences in the patterns of metabolism and the reactivity of diolepoxide metabolites with DNA may be critically involved.[3,4]

Chart I. Synthesis of 2- and 3-HO-BA



(1) National Center for Toxicological Research, Jefferson, Arkansas 72079.
(2) "International Agency for Research on Cancer. Monographs on the Evaluation of Carcinogenic Risk of the Chemical to Man: Certain Polycyclic Aromatic Hydrocarbons and Heterocyclic Compounds", Vol. 3, World Health Organization, Geneva, Switzerland, 1973.
(3) T. J. Slaga, E. Huberman, J. K. Selkirk, R. G. Harvey, and W. M. Bracken, *Cancer Res.*, 38, 1699 (1978); W. Levin, D. R. Thakker, A. W. Wood, R. L. Chang, R. E. Lehr, D. M. Jerina, and A. H. Conney, *ibid.*, 38, 1705 (1978).

0022-3263/79/1944-4265$01.00/0

In connection with biological studies designed to probe the nature of the differences in metabolic patterns, a complete set of the isomeric phenols of BA were required as standards for identification of the metabolites of BA. Synthesis of the B- and C-ring phenolic derivatives of BA is most conveniently achieved directly from BA through reaction with osmium tetroxide[5,6] and lead tetraacetate,[7] respectively. On the other hand, methods for the introduction of hydroxyl groups into the A and D rings of BA are lacking. Consequently, these phenolic isomers must currently be synthesized through multistep total synthesis of each isomer from appropriately substituted small molecular components.[8-10]

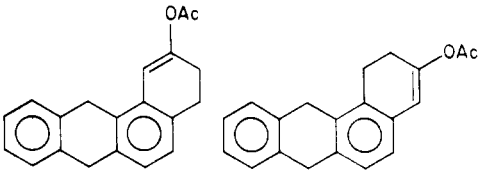
We have investigated potential synthetic approaches to the eight terminal ring phenols of BA from the parent hydrocarbon and now wish to report novel syntheses of 1-, 2-, 3-, 8-, 9-, 10-, and 11-hydroxy-BA.

Results

Synthesis of 2- and 3-Hydroxybenz[*a*]anthracene (Chart I).[11] 1,4,7,12-Tetrahydro-BA (**1**), readily accessible through stepwise metal–ammonia reduction of BA,[12,13] provides a convenient synthetic precursor of 2- and 3-HO-BA (**4a,b**). Hydroboration of **1** and oxidation with alkaline peroxide[14] furnished a mixture of 2- and 3-hydroxy-1,2,3,4,7,12-hexahydro-BA (**2a,b**) in 91% yield.[15] Oxidation of the latter with trifluoroacetic anhydride and dimethyl sulfoxide according to the method of Swern[16] afforded the corresponding ketones, 2-oxo- and 3-oxo-1,-2,3,4,7,12-hexahydro-BA (**3a,b**). Separation of the isomeric ketones was achieved through column chromatography on Florisil. Since ketones **3a** and **3b** proved somewhat unstable on the column, minimal column residence time is recommended. Direct conversion of the ketones **3a** and **3b** to the corresponding phenols 2-HO-BA and 3-HO-BA (**4a** and **4b**) was accomplished through treatment of each with 2 molar equiv of trityl fluoroborate in refluxing acetic acid.[17,18] Purification of the crude phenols was accomplished through their acetates which proved less sensitive to decomposition in air than the phenols themselves.

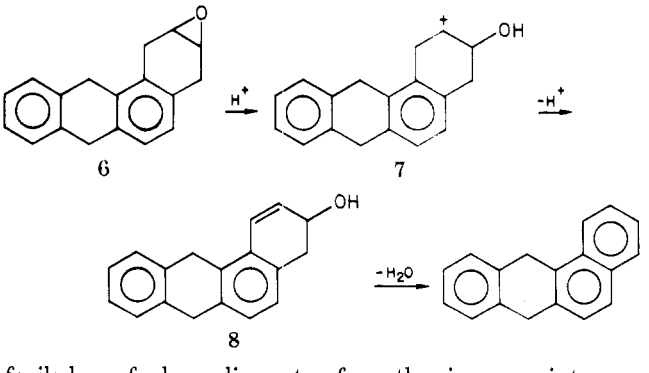
The isomeric ketones **3a** and **3b** could not be distinguished through their NMR spectra which proved virtually identical. However, the phenols arising from each of these ketones were readily characterized by NMR spectroscopy. The H_1 proton of 2-HO-BA (**4a**) dissolved in acetone-d_6 appeared at δ 8.46 as a doublet ($J_{1,3}$ = 2.5 Hz), while the analogous H_1 proton signal of 3-HO-BA (**4b**) was found at δ 8.83 as a doublet with larger coupling ($J_{1,2}$ = 8 Hz). Bartle et al.[19] report H_1 of BA in CS_2 at δ 8.63 ($J_{1,2}$ = 8.1; $J_{1,3}$ = 1.6 Hz); however, the H_1 signal of BA in acetone-d_6 was found at δ 8.8. The observed values of the H_1 protons of **4a** and **4b** relative to those of H_1 of BA are consistent only with the assignment of **4a** and **4b** as 2-HO-BA and 3-HO-BA, respectively. In addition, the upfield shift of H_1 of 2-HO-BA (δ 8.46) relative to that of H_1 of BA (δ 8.88) is indicative of the presence of this proton adjacent to the hydroxyl group. A similar characteristic upfield displacement is observed for protons ortho to the hydroxy groups of the isomeric phenols of BA, and a similar effect has been reported for the isomeric hydroxybenzo[*a*]pyrenes.[20] The isomeric identity of **4b** was further confirmed by methylation with dimethyl sulfate to afford 3-methoxy-BA, mp 159–160 °C (lit.[21] mp 161–162 °C).

Prior to development of the method for direct dehydrogenation of ketones **3a,b** to the corresponding phenols with $Ph_3C^+BF_4^-$, an alternative synthetic route involving conversion to the enol acetate (**5**), dehydrogenation with *o*-chloranil, and acid-catalyzed methanolysis was investigated. The overall yields of 2-HO-BA and 3-HO-BA via this sequence were 33 and 38%, respectively. While the latter yields were less than those obtained via the $Ph_3C^+BF_4^-$ route (70 and 73%, respectively), no attempt was made to optimize yields via the enol acetate route, and it is likely that with further experimental study they could be considerably improved.



5a 5b

Attempts to synthesize the ketones **3a,b** through epoxidation of the olefin **1** with *m*-chloroperbenzoic acid followed by acid-catalyzed isomerization of the resulting 2,3-epoxy-1,2,3,4,7,12-hexahydro-BA (**6**) were not successful. This failure is apparently a consequence of the more facile loss of a benzylic proton from the ring-open intermediate **7** (or the alternative related isomer) than of the shift of the carbinol hydrogen to form the ketone (i.e., the so-called NIH shift).[22] The resulting allylic alcohol **8** is then free to undergo acid-catalyzed dehydration–aromatization to 7,12-dihydro-BA, the only product isolated.



6 7 8

(4) (a) D. M. Jerina, H. Yagi, R. E. Lehr, D. R. Thakker, M. Schaefer-Ridder, J. M. Karle, W. Levin, A. W. Wood, R. L. Chang, and A. H. Conney in "Polycyclic Hydrocarbons and Cancer: Environment, Chemistry, and Metabolism", Vol. 1, H. V. Gelboin and P. O. P. T'so, Eds., Academic Press, 1978, p 173; (b) R. G. Harvey and P. P. Fu, *ibid.*, p 133.
(5) R. G. Harvey, S. H. Goh, and C. Cortez, *J. Am. Chem. Soc.*, **97**, 3468 (1975).
(6) J. C. Wiley, C. S. Menon, D. L. Fisher, and J. F. Engel, *Tetrahedron Lett.*, 2811 (1975).
(7) L. F. Fieser and E. B. Hershberg, *J. Am. Chem. Soc.*, **60**, 1893 (1938).
(8) R. Schoental, *J. Chem. Soc.*, 4403 (1952).
(9) L. F. Fieser and W. S. Johnson, *J. Am. Chem. Soc.*, **61**, 1647 (1939).
(10) P. Sims, *Biochem. J.*, **125**, 159 (1971).
(11) This synthesis was reported in a preliminary communication: K. B. Sukumaran and R. G. Harvey, *J. Am. Chem. Soc.*, **101**, 1353 (1979).
(12) R. G. Harvey and K. Urberg, *J. Org. Chem.*, **33**, 2206 (1968).
(13) R. G. Harvey, *Synthesis*, 161 (1970).
(14) H. C. Brown, "Hydroboration", W. A. Benjamin, New York, 1962; H. C. Brown, "Boranes in Organic Chemistry", Cornell University Press, Ithaca, NY, 1972.
(15) R. G. Harvey and K. B. Sukumaran, *Tetrahedron Lett.*, 2387 (1977).
(16) K. Omura, A. K. Sharma, and D. Swern, *J. Org. Chem.*, **41**, 957 (1976).
(17) P. P. Fu and R. G. Harvey, *Chem. Rev.*, **78**, 317 (1978).
(18) W. Bonthrone and D. H. Reid, *J. Chem. Soc.*, 2773 (1959).
(19) K. D. Bartle, D. W. Jones, and R. S. Matthews, *Spectochim. Acta*, **2**, 1603 (1969).
(20) H. Yagi, G. M. Holder, P. M. Dansette, O. Hernandez, H. J. Yeh, R. A. LeMahieu, and D. M. Jerina, *J. Org. Chem.*, **41**, 977 (1976).
(21) D. C. C. Smith, *J. Chem. Soc.*, 673 (1962).
(22) J. W. Daly, D. M. Jerina, and B. Witkop, *Experientia*, **28**, 1129 (1972), and references cited therein.

Chart II. Synthesis of 10-HO-BA

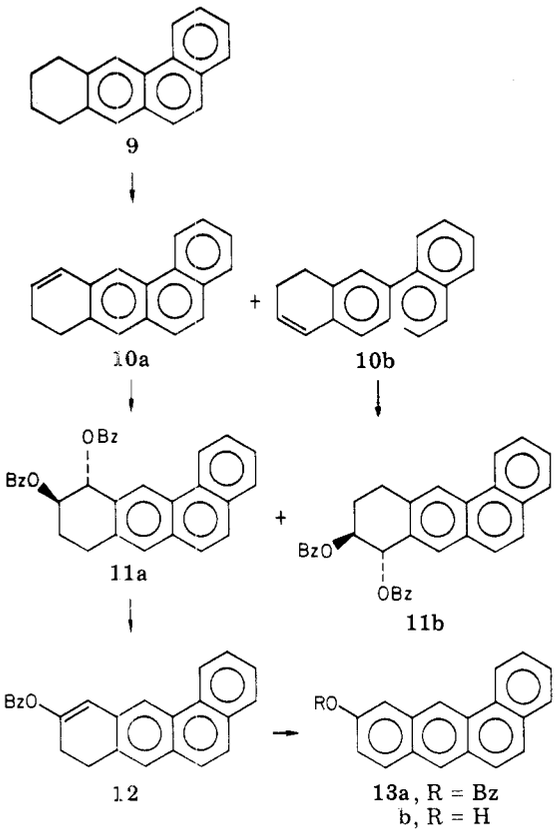
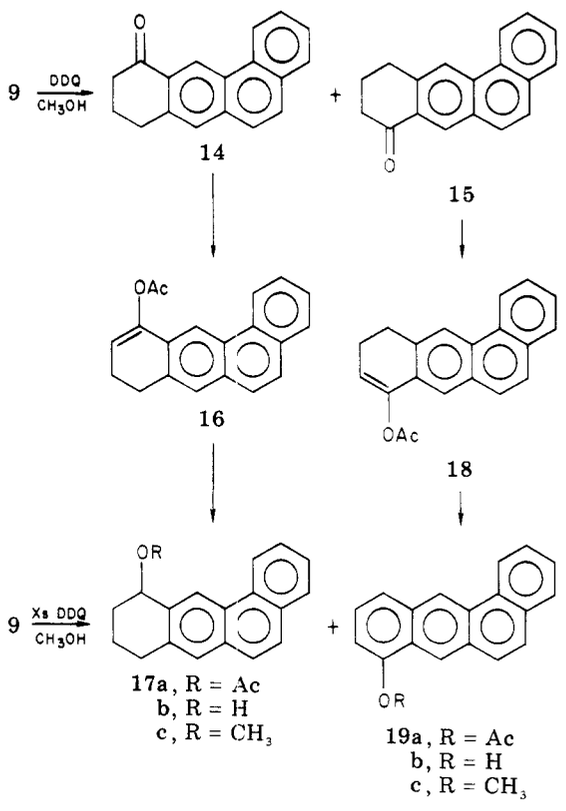


Chart III. Synthesis of 8- and 11-HO-BA



Synthesis of 10-Hydroxybenz[*a*]anthracene (Chart II). 8,9,10,11-Tetrahydro-BA (**9**), obtainable from BA through catalytic hydrogenation over PtO_2 under mild conditions,[23,24] provides a convenient starting point for the synthesis of 10-HO-BA (**13b**). As reported in a preliminary communication,[24] partial dehydrogenation of **9** with DDQ affords 8,9-dihydro-BA (**10a**) and 10,11-dihydro-BA (**10b**) in a 5:1 ratio.[17] Prevost reaction of this mixture with the silver benzoate–iodine complex furnishes the corresponding *trans*-dibenzoate esters, *trans*-10,11- and *trans*-8,9-bis(benzoyloxy)-8,9,10,11-tetrahydro-BA (**11a,b**). The latter, which are conveniently separable by fractional crystallization, are also useful synthetic intermediates in the preparation of the *trans*-10,11- and -8,9-dihydrodiols of BA.[4b,25] Treatment of **11a** with *p*-toluenesulfonic acid in refluxing benzene smoothly eliminated benzoic acid to afford 10-(benzoyloxy)-8,9-dihydro-BA (**12**) in 95% yield. Dehydrogenation of the latter with DDQ gave 10-(benzoyloxy)-BA (**13a**), acid-catalyzed methanolysis of which provided the free phenol 10-HO-BA (**13b**).

Synthesis of 8- and 11-Hydroxybenz[*a*]anthracene (Chart III). 11-Oxo-8,9,10,11-tetrahydro-BA (**14**), key intermediate in the synthesis of 11-HO-BA (**17b**), is synthesized conventionally through succinoylation of 9,10-dihydrophenanthrene, followed by either Clemmensen or Wolff–Kishner reduction of the resulting keto acid, acid-catalyzed cyclization, and dehydrogenation.[9] In the present study, two alternative potential synthetic routes to **14** from 8,9,10,11-tetrahydro-BA (**9**) were explored. In the first approach, it was reasoned that since reaction of 7,8,9,10-tetrahydrobenzo[*a*]pyrene with lead tetraacetate affords smoothly the corresponding 10-acetoxy compound,[26] analogous reaction of **9** might provide 11-acetoxy-**9**, which in turn could be oxidized to **14**. However, all attempts to prepare 11-acetoxy-**9** via this method afforded intractable mixtures containing low percentages of the desired product. However, a novel alternative route to **14** involving reaction of **9** with DDQ in refluxing methanol[17] proved more successful, providing **14** along with the 8-keto isomer **15** in a 4:1 ratio (Chart III). Minor amounts of the related phenol methyl ethers **17c** and **19c** were also produced. The latter became the major products when an excess of DDQ was employed. The ketones **14** and **15** were separable by fractional crystallization. The physical properties of **15** matched those of an authentic sample of the compound synthesized from phenanthrene by the established procedure.[27]

Conversion of the ketone **14** to 11-HO-BA (**17b**) was accomplished through formation of the enol acetate **16** by reaction with isopropenyl acetate, followed by dehydrogenation with either *o*-chloranil or DDQ to afford 11-acetoxy-BA (**17a**). Acid-catalyzed methanolysis provided pure 11-HO-BA.

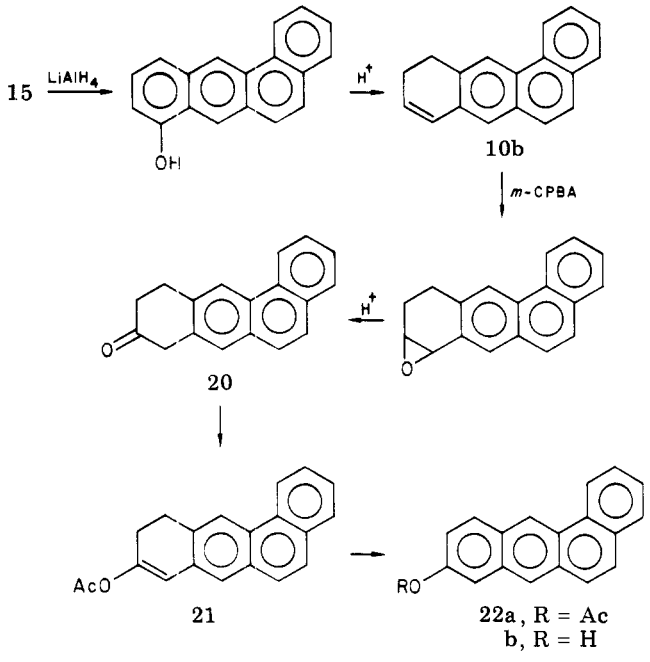
While the apparent simplicity of direct formation of the phenol methyl ethers **17c** and **19c** from **9** through reaction of the latter with excess DDQ in methanol appears attractive, this route is impractical on a preparative scale because of the difficulty of separation of these isomers.

Synthesis of 8-HO-BA (**19b**) was conveniently accomplished from 8-oxo-8,9,10,11-tetrahydro-BA (**15**) via a synthetic sequence analogous to that employed for preparation of 11-HO-BA (Chart III).

Synthesis of 9-Hydroxybenz[*a*]anthracene (Chart IV). Synthetic access to 9-HO-BA (**22b**) is provided through 9-oxo-8,9,10,11-tetrahydro-BA (**20**) previously synthesized from the 8-oxo compound **15** by Sims[10] through reduction with $NaBH_4$ to the alcohol, acid-catalyzed dehydration to 10,11-dihydro-BA, reaction of the

(23) P. P. Fu and R. G. Harvey, *Tetrahedron Lett.*, 415 (1977).
(24) P. P. Fu, H. M. Lee, and R. G. Harvey, *Tetrahedron Lett.*, 551 (1978).
(25) P. P. Fu and R. G. Harvey, *Tetrahedron Lett.*, 2059 (1977).
(26) G. A. Kon and E. M. Roe, *J. Chem. Soc.*, 143 (1945).
(27) W. E. Bachmann, *J. Org. Chem.*, 3, 434 (1939).

Chart IV. Synthesis of 9-HO-BA



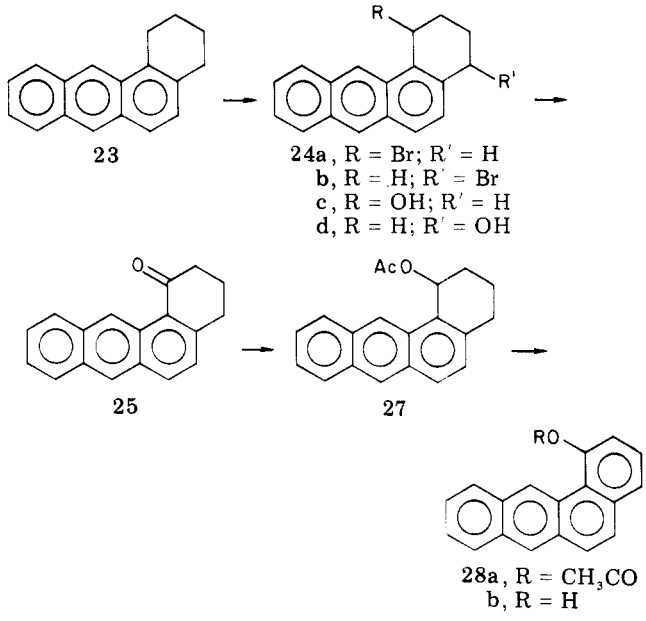
latter with osmium tetroxide, and acid-catalyzed dehydration of the resulting *cis*-7,8-dihydrodiol. An improved synthetic approach (Chart IV) was employed in these studies. It differed principally in that conversion of 10,11-dihydro-BA to the 9-oxo compound was accomplished through epoxidation and acid-catalyzed rearrangement of the resulting epoxide to **20**, eliminating the use of the hazardous OsO_4 reagent. The overall yield of **20** from 10,11-dihydro-BA via this route was 84%, which compares favorably with that reported (70%) by the older procedure.[10]

Transformation of the ketone **20** to 9-HO-BA (**22b**) was achieved through conversion of **20** to the enol acetate derivative **21**, dehydrogenation with *o*-chloranil, and acidic hydrolysis. The overall yield of **22b** (53%) obtained by this method was superior to that previously reported (25%) from dehydrogenation of **20** with sulfur.[10]

Synthesis of 1- and 4-Hydroxybenz[*a*]anthracene (Chart V). 1,2,3,4-Tetrahydro-BA (**23**), the key intermediate in this sequence, was found to be conveniently accessible through dehydrogenation with *o*-chloranil of 1,2,3,4,7,12-hexahydro-BA. The latter was readily synthesized from BA by reduction with sodium and isoamyl alcohol by a modification of the method described originally by Fieser and Hershberg[28] using approximately half the proportion of sodium metal and providing 1,2,3,4,7,12-hexahydro-BA in higher yield (78%) than that obtained by the earlier workers (53%). Bromination of **23** with NBS afforded a mixture of 1- and 4-bromo-1,2,3,4-tetrahydro-BA (~2:1 **24a** and **24b**). These isomers were readily distinguishable by NMR spectroscopy by the low-field appearance of the H_1 methine signal of **24a** (δ 6.20) relative to the analogous H_4 proton of **24b** (δ 5.63); downfield displacement of the H_1 signal of **24a** is anticipated as a consequence of steric interaction with the H_{12} aromatic proton in the bay region. The structures of **24a** and **24b** were further confirmed by subsequent conversion (described below) to 1- and 4-oxo-1,2,3,4-tetrahydro-BA (**25** and **29**), the physical properties and spectra of which proved identical with those of authentic samples.

(28) L. F. Fieser and E. B. Hershberg, *J. Am. Chem. Soc.*, **59**, 2502 (1937).

Chart V. Synthesis of 1- and 4-HO-BA



Transformation of the bromo compounds to the corresponding ketones was accomplished to two steps via the alcohol intermediates **24c** and **24d**. Treatment of **24a** and **24b** with silver carbonate and sodium carbonate in aqueous dioxane afforded 1- and 4-hydroxy-1,2,3,4-tetrahydro-BA (**24c** and **24d**). Oxidation of the latter with dimethyl sulfoxide and py–SO_3 complex afforded 1- and 4-oxo-1,2,3,4-tetrahydro-BA (**25** and **26**). Conversion of **25** to 1-HO-BA (**28b**) was achieved through dehydrogenation of the corresponding enol acetate with *o*-chloranil. Analogous synthesis of 4-HO-BA (**29**), though feasible in principle, offered no significant advantage over the alternative synthetic route from BA-7,12-dione via sulfonation, reduction, and alkali fusion.[29]

Discussion

Development of practical syntheses of the full range of oxidized metabolites of BA and other polycyclic arenes has been seriously hampered by the lack of methods for the introduction of functional groups regioselectively into ring positions not normally prone to direct substitution. This includes most positions of polycyclic aromatic ring systems. Consequently, laborious total synthesis of each isomeric derivative from appropriately substituted smaller molecular units currently provides the only synthetic access to the preponderance of such substituted polycyclic arenes.[30]

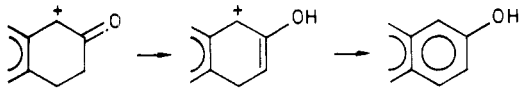
The syntheses described in the preceding section provide practical synthetic methods for the preparation of the isomeric A- and D-ring phenols of BA. They also demonstrate the feasibility of methods for the introduction of functional groups regioselectively into the polycyclic ring system through initial partial saturation (by catalytic hydrogenation, metal–ammonia reduction, etc.) of one or more aromatic rings followed by appropriate synthetic operations on olefinic bonds or at benzylic positions to introduce the desired group and finally dehydrogenation. In the syntheses reported herein (Charts I–V) generally fewer synthetic steps are required, and overall yields are superior to those obtained or anticipated from conventional

(29) J. Cason and L. Fieser, *J. Am. Chem. Soc.*, **62**, 2681 (1940); A. Sempronj, *Gazz. Chim. Ital.*, **69**, 28 (1939).

(30) E. Clar, "Polycyclic Hydrocarbons", Vol. 1 and 2, Academic Press, New York, 1964; benz[*a*]anthracene is named tetraphene in the obsolete nomenclature system used in this book.

total synthetic methods. Application of these methods to the synthesis of the related phenols of 7,12-dimethyl-BA,[11] 7-methyl-BA,[31] and dibenz[a,h]anthracene[31] is described in related papers. It is likely that these methods are more generally applicable, since procedures for the regiospecific hydrogenation[23,24] or metal–ammonia reduction[13,32-37] of numerous polycyclic hydrocarbons have already been reported.

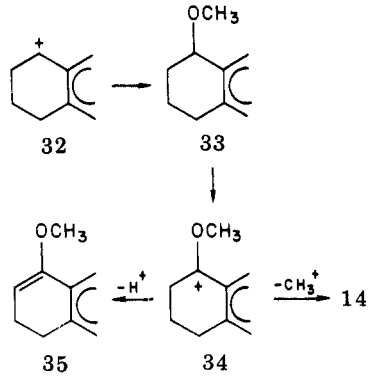
Aromatization of the intermediate polycyclic aromatic ketones to phenols was achieved in the present studies through direct dehydrogenation with trityl fluoroborate (in the case of **4a** and **4b**) or through two-step conversion to the enol acetate and dehydrogenation with *o*-chloranil or DDQ. While both methods are novel, the latter is most general in its applicability, providing good yields of phenols from both α- and β-aryl ketones (i.e., analogues of α- and β-tetralone). The trityl fluoroborate reagent, while highly effective in the conversion of the β-ketones **3a** and **3b** to phenols, failed to similarly transform α-ketones, e.g., 7-oxo-7,8,9,10-tetrahydrobenzo[a]pyrene.[38] This difference may be a consequence of the greater facility of hydride abstraction from the benzylic site of a β-ketone to afford an intermediate such as **30**; loss of a benzylic proton from



30 31

the related enol structure **31** affords directly the phenolic product. Aromatization of polycyclic aromatic ketones to phenols has in the past been most commonly achieved through catalytic dehydrogenation or by treatment with sulfur or selenium at elevated temperatures.[17] Yields from these methods are variable as a consequence of deoxygenation and other secondary reactions.[17] The enol acetate method is apparently uncomplicated by significant secondary processes, and in view of its relative simplicity and convenience, it can be recommended as the method of choice for the synthesis of phenols from polycyclic aromatic ketones.

Another relatively novel reaction is the oxidation of 8,9,10,11-tetrahydro-BA (**9**) with DDQ in refluxing methanol to the related 11- and 8-ketones (**14** and **15**) in a 4:1 ratio (Chart III). This reaction has precedent in the reported oxidation of 6-hydroxytetralin to 6-hydroxytetral-1-one with this reagent.[39] Formation of **14** is rationalized as proceeding through reaction of the carbocation intermediate **32** with solvent to afford the methyl ether **33**. Reaction of the latter with a second equivalent of DDQ provides carbocation **34** which may undergo demethylation to the ketone **14** or deprotonation to the enol methyl ether **35**. Further reaction of the latter with DDQ affords the phenol methyl ether **17c**. Attempted analogous reaction of 1,2,3,4-tetrahydro-BA (**23**) with DDQ in methanol furnished only recovered **23**. On the other hand,



32 33 35 34

reaction of 7-methyl-BA with this reagent was found in other studies to afford smoothly 7-formyl-BA,[17] while 4-methylpyrene failed to react under similar conditions.[40] The reason for these differences in reactivity is unknown. Despite this limitation, the DDQ–methanol reagent appears potentially useful for the synthesis of other aryl ketones and aldehydes.

The isomeric phenols of benz[a]anthracene synthesized herein have been furnished to the Chemical Repository at Illinois Institute of Technology Research Institute (IITRI) for distribution to qualified investigators for biological studies in carcinogenesis and related areas.

Experimental Section

General Methods. Benz[a]anthracene was purchased from Research Organic/Inorganic Chemical Corp. and also synthesized through reduction of BA-7,12-dione with HI in acetic acid.[40] 1,4,7,12-Tetrahydro-BA (**1**),[12,13] 8,9,10,11-tetrahydro-BA (**9**),[4b,23,24] and *trans*-10,11-bis(benzoyloxy)-8,9,10,11-tetrahydro-BA (**11a**)[4b,23] were prepared by the procedures previously described. *m*-Chloroperbenzoic acid, BA-7,12-dione, 1-oxo-1,2,3,4-tetrahydro-BA, and borane–tetrahydrofuran complex (1 M solution in THF) were purchased from Aldrich Chemical Co. The peracid was purified by washing with pH 7.5 phosphate buffer and drying under reduced pressure. Pyridine–sulfur trioxide complex was purchased from Eastman. 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) and *o*-chloranil were purchased from Arapahoe Chemical Inc. and the Upjohn Co., respectively, and purified by recrystallization from benzene before use. Triphenylmethyl fluoroborate was purchased from Willow Brook Laboratory, Inc. Benzene, THF, triethylamine, and Me_2SO were distilled prior to use. The NMR spectra were obtained on Varian T 60 or Bruker HX 270 spectrometers with tetramethylsilane as internal standard in $CDCl_3$ unless specified otherwise. Ultraviolet spectra were obtained on a Varian Techtron 635 spectrometer. Melting points are uncorrected. All new compounds gave satisfactory microanalyses for C and H within ±0.3% and/or mass spectra consistent with the assigned structure.

Synthesis of 2- and 3-HO-BA (4a and 4b). (1) 2- and 3-Hydroxy-1,2,3,4,7,12-hexahydro-BA (2a and 2b). A 1 M solution of boron hydride (50 mmol) in THF was added to a solution of 1,4,7,12-tetrahydro-BA[12,13] (**1**; 5.7 g, 24.6 mmol) in freshly distilled THF, and the resulting solution was stirred at ambient temperature under N_2 for 3 h and then quenched carefully with water. Solutions of 5% NaOH (75 mmol) and 70% H_2O_2 (75 mmol) were then added, and the reaction mixture was heated at 50 °C for 25 min. The resulting solution was treated with K_2CO_3 and worked up conventionally to afford a crude product which was chromatographed on silica gel. Initial elution with 10% benzene in hexane gave a few milligrams of 1,2,3,4,7,12-hexa- and polyhydro-BA; further elution with benzene afforded a mixture of **2a** and **2b** (5.6 g, 91%). The NMR spectra of these isomers exhibited apparently similar patterns: δ 1.75–2.22 (m, 2, H_3 or H_2), 2.75–3.21 (m, 2, H_1 or H_4), 3.90 (s, 4, $H_{7,12}$), 4.1–4.35 (m, 2, H_2 or H_3), 6.94–7.30 (m, 6, aromatic). The mixture of **2a,b** was employed directly in the next step.

(31) H. M. Lee and R. G. Harvey, *J. Org. Chem.*, in press.
(32) R. G. Harvey and P. W. Rabideau, *Tetrahedron Lett.*, 3695 (1970).
(33) R. G. Harvey, *J. Org. Chem.*, **36**, 3306 (1971).
(34) D. F. Lindow, C. N. Cortez, and R. G. Harvey, *J. Am. Chem. Soc.*, **94**, 5406 (1972).
(35) R. G. Harvey, D. F. Lindow, and P. W. Rabideau, *J. Am. Chem. Soc.*, **94**, 5412 (1972).
(36) R. G. Harvey, D. F. Lindow, and P. W. Rabideau, *Tetrahedron*, **28**, 2909 (1972).
(37) R. G. Harvey, P. P. Fu, and P. W. Rabideau, *J. Org. Chem.*, **41**, 2706 (1976).
(38) P. P. Fu and R. G. Harvey, unpublished studies.
(39) J. W. A. Findlay and A. B. Turner, *Chem. Ind. (N.Y.)*, 158 (1970).
(40) M. Konieczny and R. G. Harvey, *J. Org. Chem.*, in press.

(2) 2- and 3-Oxo-1,2,3,4,7,12-hexahydro-BA (3a and 3b). A solution of trifluoroacetic anhydride (41 mmol) in CH_2Cl_2 (50 mL) was added dropwise to a solution of Me_2SO (56 mmol) in CH_2Cl_2 (5 mL) at −50 °C in a period of 10 min. To the resulting solution was added a solution of **2a,b** (6.9 g, 27.6 mmol) in CH_2Cl_2 (150 mL) over 20 min. This solution was stirred at −50 °C for 5 min, warmed to room temperature over a 40-min period, and stirred at ambient temperature another 20 min. Triethylamine (12 mL) was then added over 10 min, and stirring was continued for an additional 60 min. Conventional workup furnished a mixture of **3a** and **3b** (6.1 g, 88%). Separation of the mixed ketones was achieved by chromatography on Florisil. Elution with benzene gave virtually pure **3a** (2.65 g) as a waxy white solid: NMR δ 2.5–2.67 (m, 2), 2.8–3.2 (m, 2), 3.47 (s, 2, H_1), 3.88 (apparent s, 4, $H_{7,12}$), 6.8–7.3 (m, 6, aromatic). Further elution with benzene provided **3b** (1.72 g) as a waxy white solid; the NMR spectrum of **3b** closely matched that of **3a** except the H_4 peak of **3b** appeared at δ 3.51, displaced slightly upfield from the H_1 signal of **3a**.

(3) 2-Acetoxy-BA (4c). Method 1. A solution of **3a** (3.7 g, 14.9 mmol) and trityl fluoroborate (30 mmol) in glacial acetic acid was heated at reflux for 3 h, poured into ice water, and extracted with ether. Conventional workup followed by acetylation with acetic anhydride–pyridine at room temperature overnight furnished the crude **4c** which was purified by chromatography on a column of Florisil. Elution with benzene afforded 2-acetoxy-BA as a white solid (3.0 g, 70%): mp 156–157 °C (benzene–hexane) (lit.[41] mp 156.5–158.5 °C); NMR δ 2.40 (s, 3, CH_3), 7.29 (dd, 1, $J_{3,4}$ = 7 Hz, $J_{1,3}$ = 2 Hz, H_3), 7.32–8.20 (m, 7, aromatic), 8.28 (s, 1, H_7), 8.45 (d, 1, $J_{1,3}$ = 2 Hz, H_1), 8.95 (s, 1, H_{12}).

Method 2. A solution of **3a** (4 mmol), *p*-toluenesulfonic acid (60 mg), and acetic anhydride (5 mL) in isopropenyl acetate (50 mL) was heated at reflux for 1 day. Partition between ether and water and conventional workup provided the crude product which was purified by chromatography on Florisil. Elution with benzene afforded the enol acetate **5a** (60%) employed directly in the next step. A solution of **5a** and *o*-chloranil (2.4 mmol) in benzene (30 mL) was heated at reflux under N_2 for 1 h. Evaporation of the solvent and chromatography of the resulting residue on Florisil gave 2-acetoxy-BA (72%) as a white solid, mp 156–157 °C, identical by NMR with **4c** above.

(4) 2-HO-BA (4a). A solution of 2-acetoxy-BA (200 mg, 7 mmol) and *p*-toluenesulfonic acid (60 mg) in methanol (20 mL) was heated at reflux for 5 h, cooled, and poured into ice–water. The crude product was collected by filtration and purified by chromatography on Florisil. Elution with benzene afforded **4a** (150 mg, 89%): mp 193–194 °C (benzene–hexane) (lit.[41] mp 191.5–193.5 °C); NMR (acetone-d_6) δ 7.28 (dd, 1, $J_{3,4}$ = 9 Hz, $J_{1,3}$ = 2.5 Hz, H_3), 7.54–8.32 (m, 7, aromatic), 8.46 (d, 1, $J_{1,3}$ = 2.5 Hz, H_1), 8.52 (s, 1, H_7), 8.82 (s, 1, H_{12}).

(5) 3-Acetoxy-BA (4d). Synthesis of 3-acetoxy-BA from **3b** was carried out by the procedure (method 1) described for the preparation of 2-acetoxy-BA. 3-Acetoxy-BA was obtained in 73% yield: mp 165–166 °C (benzene–hexane); NMR δ 7.28–8.23 (m, 8, aromatic), 8.32 (s, 1, H_7), 8.78 (d, 1, $H_{1,2}$ = 8 Hz, H_1), 9.05 (s, 1, H_{12}). Method 2 provided the enol acetate **5b** in 65% yield in the first step and 3-acetoxy-BA in 71% yield in the second step.

(6) 3-HO-BA (4b) and 3-Methoxy-BA (4f). Acidic methanolysis of 3-acetoxy-BA by the procedure described for synthesis of 2-HO-BA gave 3-HO-BA in 82% yield: mp 209–210 °C (benzene–hexane); NMR (acetone-d_6) δ 7.23 (dd, 1, $J_{1,2}$ = 7 Hz, $J_{2,4}$ = 2.5 Hz, H_2), 7.25–8.2 (m, 7, aromatic), 8.33 (s, 1, H_7), 8.75 (m, 1, H_1), 9.13 (s, 1, H_{12}). Treatment of **4b** with dimethyl sulfate and sodium methoxide in methanol gave **4b**, mp 159–161 °C (lit.[21] mp 156.5–158.5 °C).

Synthesis of 10-HO-BA (13b). (1) 10-(Benzoyloxy)-8,9-dihydro-BA (12). *trans*-10,11-Bis(benzoyloxy)-8,9,10,11-tetrahydro-BA (**11a**) was prepared from 8,9,10,11-tetrahydro-BA (**9**) as previously described.[4b] A solution of **11a** (1.58 g, 3.0 mmol) and *p*-toluenesulfonic acid (80 mg) in benzene (150 mL) was heated at reflux for 10 h. Partition of the product between ether and water and conventional workup afforded crude **12** (1.00 g, 95%) as a pale yellow solid: NMR δ 2.6–2.98 (m, 2, H_9), 2.18–3.40 (m, 2, H_8), 6.78 (s, 1, H_{11}), 7.3–8.85 (m, 8, aromatic). Compound **12** was employed directly in the following step.

(2) 10-(Benzoyloxy)-BA (13a). Dehydrogenation of **12** (2.06 g, 6 mmol) with DDQ (2.04 g, 9 mmol) in refluxing benzene (300 mL) for 4 h under N_2 furnished crude **13a**. Chromatography on Florisil gave on elution with benzene **13a** (1.10 g, 75%) as pale yellow needles: mp 174–176 °C (benzene–hexane); NMR δ 7.3–8.45 (m, 13, aromatic), 8.37 (s, 1, H_7), 8.7–8.98 (s, 1, H_1), 9.16 (s, 1, H_{12}).

(3) 10-HO-BA (13b). A solution of **13a** (1.1 g, 3.16 mmol) and hydrochloric acid (45 mL) in acetic acid (90 mL) was heated at reflux for 24 h. The product obtained on conventional workup was chromatographed on Florisil. Elution with benzene gave 10-HO-BA (670 mg, 87%) as a pale yellow solid, mp 218–222 °C dec (lit.[9] mp 151.3–151.8 °C).

Synthesis of 11-HO-BA (17b). (1) 11-Oxo-8,9,10,11-tetrahydro-BA (14). 8,9,10,11-Tetrahydro-BA (**9**; 3.48 g, 15 mmol) and DDQ (5.11 g, 22 mmol) in methanol (70 mL) were stirred at ambient temperature for 4 h and then heated at reflux for 24 h under N_2. The product obtained on conventional workup was chromatographed on Florisil. Elution with benzene–hexane (1:1) gave 302 mg of a mixture of 8-methoxy- and 11-methoxy-BA (**19c** and **17c**) in a ratio of 1:4. Further elution with benzene gave a mixture of the ketones **14** and **15** (1.68 g, 80% based on conversion of **9**) in the ratio of 4:1. Pure **14** was obtained as colorless needles: mp 116–118 °C (lit.[9] mp 117.8–118.5 °C); NMR δ 2.03–2.48 (m, 2, CH_2), 2.60–2.90 (m, 2, CH_2), 2.99–3.28 (m, 2, CH_2), 7.50–7.98 (m, 5, H_{2-6}), 8.48–8.9 (m, 2, $H_{1,7}$), 9.40 (s, 1, H_{12}).

(2) 11-Acetoxy-BA (17a). Conversion of **14** to the corresponding enol acetate (**16**) was carried out by the procedure utilized for preparation of **5a**. The NMR spectrum of **16** exhibited δ 2.40 (s, 3, CH_3), 2.23–2.65 (m, 2, H_9), 2.80–3.20 (m, 2, H_8), 5.80 (t, 1, $J_{9,10}$ = 5 Hz, H_{10}), 7.4–7.9 (m, 6, H_{2-7}), 8.35 (s, 1, H_{12}), and 8.38–8.7 (m, 1, H_1). The compound was used directly in the next reaction. Reaction of **16** with *o*-chloranil by a procedure analogous to that employed for synthesis of **4c** gave **17a** (95%): mp 121–124 °C; NMR δ 2.54 (s, 3, CH_3), 7.2–7.82 (m, 8, aromatic), 8.10 (s, 1, H_7), 8.52–8.80 (m, 1, H_1), 9.0 (s, 1, H_{12}).

(3) 11-HO-BA (17b). Acidic methanolysis of **17a** by the procedure employed for synthesis of 2-HO-BA gave **17b**: mp 120–124 °C dec (lit.[42] mp 217–218 °C); NMR (acetone-d_6) δ 6.92 (dd, 1, $J_{9,10}$ = 8 Hz, $J_{8,10}$ = 2 Hz, H_{10}), 7.3–8.0 (m, 7, aromatic), 8.3 (s, 1, H_7), 8.45–8.99 (m, 1, H_1), 9.12 (s, 1, H_{12}).

Synthesis of 8-HO-BA (19b). (1) 8-Acetoxy-BA (19a). Due to a tendency toward cocrystallization of the 8- and 11-ketones, **14** and **15**, pure 8-oxo-8,9,10,11-tetrahydro-BA (**15**) could be recovered only in low yield from fractional crystallization of the mother liquor of **14**. Larger quantities of **15** were more conveniently prepared by synthesis from phenanthrene.[10,27] The enol acetate **18** was synthesized from **15** (1.0 g, 4.35 mmol) by the procedure employed for preparation of the enol acetate **5a**. Compound **18** (1.14 g, 92%) was obtained as a pale yellow solid: NMR δ 2.32 (s, 3, CH_3), 2.20–2.60 (m, 2, H_{10}), 2.82–3.20 (apparent t, 2, H_{11}), 5.80 (t, 1, $J_{9,10}$ = 4.5 Hz, H_9), 7.4–7.85 (m, 6, aromatic), 8.32 (s, 1, H_{12}), 8.42–8.70 (m, 1, H_1).

A solution of **18** (1.14 g, 3.95 mmol) and *o*-chloranil (971 mg, 3.95 mmol) in benzene (50 mL) was heated at reflux under N_2 for 1 h. The residue obtained after evaporation of the solvent was chromatographed on Florisil. Elution with benzene afforded **19a**, recrystallized from benzene–hexane as white needles (1.10 g, 97%): mp 146–148 °C; NMR δ 2.46 (s, 3, CH_3), 7.1–8.0 (m, 8, aromatic), 8.30 (s, 1, H_7), 8.53–8.66 (m, 1, H_1), 8.90 (s, 1, H_{12}).

(2) 8-HO-BA (19b). A solution of **19a** (5.72 mg, 2 mmol) and *p*-toluenesulfonic acid (190 mg) in methanol (30 mL) was heated at reflux under N_2 for 5 h. The resulting solution was poured into ice–water with stirring, and the product was collected by filtration and purified by chromatography on Florisil. Elution with benzene provided **19b** (449 mg, 92%) as an off-white solid: mp 239 °C dec (lit.[10] mp 217–218 °C); NMR (Me_2SO-d_6) δ 6.82–8.50 (m, 8, aromatic), 8.65–9.0 (m, 1, H_1), 8.70 (s, 1, H_7), 9.15 (s, 1, H_{12}).

Synthesis of 9-HO-BA (22b). (1) 10,11-Dihydro-BA (10b). 8-Oxo-8,9,10,11-tetrahydro-BA[10,27] (**15**; 2.5 g, 10 mmol) in a glass Soxhlet thimble (medium porosity) was extracted by refluxing ethyl ether (300 mL) into a suspension of $LiAlH_4$ (2.31 g). The

(41) L. Fieser and M. Fieser, *J. Am. Chem. Soc.*, **55**, 3342 (1933); G. M. Badger, *J. Chem. Soc.*, 940 (1947).

(42) J. W. Cook and R. Schoental, *J. Chem. Soc.*, 9 (1952).

reaction mixture was heated at reflux for 8 h and then quenched with water. Conventional workup afforded practically pure 8-hydroxy-8,9,10,11-tetrahydro-BA as a white solid: mp 121–122 °C (lit.[10] mp 122–123 °C); NMR δ 1.73–2.30 (m, 4, $H_{9,10}$), 2.96–3.33 (m, 2, H_{11}), 4.86–5.24 (m, 1, H_8), 7.4–8.13 (m, 6, H_{2-7}), 8.37 (s, 1, H_{12}), 8.42–8.70 (m, 1, H_1). The alcohol underwent dehydration smoothly on refluxing in benzene (100 mL) with *p*-toluenesulfonic acid (253 mg) for 1 h. Conventional workup gave **10b** (2.25 g, 97% based on **15**): mp 112–113 °C (benzene–hexane) (lit.[10] mp 112–113 °C); NMR δ 1.97–2.42 (m, 2, H_{10}), 2.62–3.03 (apparent t, 2, H_{11}), 5.73–6.13 (m, 1, H_9), 6.50 (apparent s, 1, H_8), 7.02–7.80 (m, 6, H_{2-7}), 8.12 (s, 1, H_{12}), 8.30–8.60 (m, 1, H_1).

(2) 9-Oxo-8,9,10,11-tetrahydro-BA (20). *m*-Chloroperbenzoic acid (3.0 g) was added to a two-phase solution of **10b** (2.25 g, 9.8 mmol) in 250 mL of CH_2Cl_2 and $NaHCO_3$ (5.04 g) in 120 mL of H_2O. The resulting binary solution was stirred at ambient temperature for 3 h under N_2. Conventional workup avoiding heating during solvent evaporation furnished the crude 8,9-epoxy-8,9,10,11-tetrahydro-BA (2.81 g) as an orange solid. Chromatography of the crude epoxide on neutral alumina (activity IV) eluted with 4% dioxane in hexane (v/v) gave the purified epoxide (2.4 g, 99%). The latter isomerized to **20** upon treatment with *p*-toluenesulfonic acid (20% by weight) in refluxing benzene for 2 h. Conventional workup gave **20** (85%): mp 146–148 °C (lit.[10] mp 146–148 °C); NMR δ 2.40–2.75 (m, 2), 3.05–3.37 (m, 2), 3.70 (s, 2, H_8), 7.30–8.00 (m, 6, H_{2-7}), 8.46 (s, 1, H_{12}), 8.56–8.76 (m, 1, H_1).

(3) 9-Acetoxy-BA (22a). The enol acetate **21** was synthesized from **20** following the procedure employed for synthesis of the enol acetate **5a**. Compound **21** was obtained in 86% yield: NMR δ 2.01 (s, 3, CH_3), 2.18–2.58 (m, 2, H_{10}), 2.68–3.27 (m, 2, H_{11}), 6.30 (s, 1, H_8), 7.2–8.58 (m, 8, aromatic). Dehydrogenation of **21** with *o*-chloranil following the procedure employed for the synthesis of **19a** gave **22a** (70%): mp 147–149 °C; NMR δ 2.40 (s, 3, CH_3), 7.28 (dd, 1, $J_{10,11}$ = 9 Hz, $J_{8,10}$ = 2 Hz, H_{10}), 7.6–8.02 (m, 8, aromatic), 8.26 (s, 1, H_7), 8.83 (m, 1 H_1), 9.11 (s, 1, H_{12}).

(4) 9-HO-BA (22b). Hydrolysis of **22a** (480 mg, 1.68 mmol) by the method employed for synthesis of **10b** (2-h reaction time) gave **22b** (361 mg, 88%) as a white solid: mp 205–206.5 °C (lit.[10] mp 212–215 °C); NMR δ 7.2–8.1 (m, 9, aromatic), 8.08 (s, 1, H_6), 8.61 (m, 1, H_1), 8.98 (s, 1, H_{12}).

Synthesis of 1-HO-BA (28b). (1) 1,2,3,4,7,12-Hexahydro-BA. Sodium metal (60 g) was added in small pieces over a 4-h period to a solution of BA (9.2 g, 40.4 mmol) in refluxing isoamyl alcohol (700 mL). The solution was allowed to cool and then decomposed by cautious addition of water followed by ethyl ether. The organic layer was washed with water and dilute HCl, dried ($MgSO_4$), and evaporated to dryness. The residue was chromatographed on Florisil and eluted with hexane to afford 1,2,3,4,-7,12-hexahydro-BA (7.2 g, 78%) as colorless plates: mp 69–71 °C (methanol) (lit.[28] mp 69–71 °C); NMR (CCl_4) δ 1.65–2.03 (m, 4, $H_{2,3}$), 2.60–2.98 (m, 4, $H_{1,4}$), 3.70–3.92 (m, 4, $H_{7,12}$), 6.70–7.45 (m, 6, aromatic).

(2) 1,2,3,4-Tetrahydro-BA (23). Dehydrogenation of 1,2,3,-4,7,12-hexahydro-BA (1.75 g, 7.5 mmol) was achieved through treatment with *p*-chloranil (1.84 g, 7.5 mmol) in refluxing benzene (30 mL) for 4 h under N_2. The residue obtained following evaporation of the solvent was chromatographed on Florisil. Elution with hexane gave **23** which was crystallized from chloroform–ethanol to provide pure **23** (1.55 g, 89%) as colorless plates: mp 103–105 °C (lit.[28] mp 102–104 °C); NMR (CCl_4) δ 1.36–1.77 (m, 4, $H_{2,3}$), 2.32–2.63 (m, 2, H_4), 2.63–2.98 (m, 2, H_1), 6.60 (d, 1, $J_{5,6}$ = 9 Hz, H_5), 6.80–7.08 (m, 2, $H_{9,10}$), 7.07 (d, 1, $J_{5,6}$ = 9 Hz, H_6), 7.22–7.62 (m, 2, $H_{8,11}$), 7.80 (s, 1, H_7), 7.95 (s, 1, H_{12}).

(3) 1- and 4-Bromo-1,2,3,4-tetrahydro-BA (24a,b). Bromination of **23** (880 mg, 3.8 mmol) with NBS (694 mg, 3.9 mmol) and benzoyl peroxide (10 mg) was conducted in refluxing CCl_4 (50 mL) under N_2 for 30 min. The resulting solution was washed with water, dried, and evaporated to dryness (avoiding excessive heating) to afford crude **24a** and **24b** (1.14 g) in a 2:1 ratio by NMR analysis (cf. Results). This mixture was employed directly without further purification in subsequent reactions.

(4) 1- and 4-Oxo-1,2,3,4-tetrahydro-BA (25 and 26). The mixed bromo compounds **24a** and **24b** (557 mg, 1.8 mmol) were heated with $AgCO_3$ (500 mg) and Na_2CO_3 (500 mg) in aqueous dioxane (60 mL, 1:1) at reflux for 50 min. The product was partitioned between ether and water, washed with water, dried, and evaporated. The residue was taken up in THF and passed through a short column of Florisil eluted with ether–ethyl acetate. Evaporation gave a mixture of 1- and 4-hydroxy-1,2,3,4-tetrahydro-BA (**24c** and **24d**, 352 mg) containing a small amount of BA and **23**. These compounds were identified by TLC on silica gel and NMR analysis in comparison with standard samples of pure **24c** and **24d** obtained by reduction of authentic 1- and 4-oxo-1,2,3,4-tetrahydro-BA and $NaBH_4$ in methanol.[43]

Oxidation of **24c** and **24d** (176 mg) was achieved with py-SO_3 complex (425 mg) and triethylamine (2 mL) in Me_2SO (3 mL) at ambient temperature under N_2 for 30 min.[44] The product obtained following conventional workup was dissolved in benzene and chromatographed on a column of Florisil. Elution with benzene provided pure **25** (19 mg): mp 112–115 °C (lit.[8] mp 114 °C); NMR δ 1.93–2.40 (m, 2), 2.60–3.25 (m, 4), 7.14–7.57 (m, 3, $H_{5,9,10}$), 7.73–8.20 (m, 3, $H_{6,8,11}$), 8.31 (s, 1, H_7), 10.03 (s, 1, H_{12}). Further elution with benzene gave an approximately 1:1 mixture of **25** and **26** (35 mg). Further elution with the same solvent furnished pure **26** (7 mg): mp 195–196 °C (lit.[8] mp 196–197 °C); NMR δ 2.23–2.97 (m, 4), 3.40–3.70 (m, 2), 7.40–8.65 (m, 2, $H_{9,10}$), 7.82–8.20 (m, 4, $H_{5,6,8,11}$), 8.37 (s, 1, H_7), 8.70 (s, 1, H_{12}).

(5) 1-Acetoxy-BA (27a). A solution of **25** (3 g, 12.3 mmol), *p*-toluenesulfonic acid (300 mg), and acetic anhydride (15 mL) in isopropenyl acetate (150 mL) was heated at reflux for 6 days. Partition of the crude product between ether and water, followed by conventional workup, provided crude 1-acetoxy-3,4-dihydro-BA (**27**, 3 g). Compound **27** was dehydrogenated by refluxing with *o*-chloranil (3.0 g, 12.6 mmol) in benzene (80 mL) for 2 h. Conventional workup followed by passage through a column of Florisil eluted with benzene furnished **28a** (1.2 g, 40%): NMR δ 2.6 (s, 3, CH_3), 7.28–8.29 (m, 9, aromatic), 8.32 (s, 1, H_7), 9.60 (s, 1, H_{12}).

(6) 1-HO-BA (27b). A solution of **28a** (1.0 g, 3.5 mmol) in acetic acid (100 mL), water (3 mL), and concentrated HCl (3 mL) was heated at reflux for 30 h. Conventional workup followed by passage through a column of silica gel eluted with benzene gave **28b** (300 mg, 30%): mp 169–170 °C (lit.[8] mp 168–170 °C); NMR δ 7.2–8.18 (m, 9, aromatic), 8.27 (s, 1, H_7), 9.56 (s, 1, H_{12}).

Acknowledgment. This research was supported by Grant No. CA 11968 and Research Contract No. CP 033385 from the National Cancer Institute, DHEW. The HX 270 Bruker NMR spectrometer was funded through the University of Chicago Cancer Research Center Grant No. CA 14599.

Registry No. **1**, 16434-60-9; **2a**, 70092-07-8; **2b**, 70092-08-9; **3a**, 70092-09-0; **3b**, 70092-11-4; **4a**, 69847-27-4; **4b**, 4834-35-9; **4c**, 70092-12-5; **4d**, 70092-10-3; **4f**, 69847-25-2; **5a**, 71685-64-8; **5b**, 71685-65-9; **9**, 67064-62-4; **10b**, 34501-50-3; **11a**, 60968-18-5; **12**, 71685-66-0; **13a**, 71685-67-1; **13b**, 69884-53-3; **14**, 60968-15-2; **15**, 5472-20-8; **16**, 71685-68-2; **17a**, 71685-69-3; **17b**, 63019-35-2; **17c**, 68757-80-2; **18**, 71685-70-6; **19a**, 71685-71-7; **19b**, 34501-23-0; **19c**, 63019-69-2; **20**, 34501-58-1; **21**, 71685-72-8; **22a**, 71685-73-9; **22b**, 34570-62-2; **23**, 4483-98-1; **24a**, 71685-74-0; **24b**, 71685-75-1; **24c**, 60968-00-5; **24d**, 60968-07-2; **25**, 57652-74-1; **26**, 38393-90-7; **27**, 71685-76-2; **28a**, 71685-77-3; **28b**, 69847-26-3; BA, 56-55-3; acetic acid, 64-19-7; isopropenyl acetate, 108-22-5; dimethyl sulfate, 77-78-1; 8-hydroxy-8,9,10,11-tetrahydrobenz[*a*]anthracene, 34520-44-0; 8,9-epoxy-8,9,10,11-tetrahydrobenz-[*a*]anthracene, 34501-53-6; 1,2,3,4,7,12-hexahydrobenz[*a*]anthracene, 16434-62-1.

(43) S. K. Yang, P. P. Fu, R. G. Harvey, P. P. Roller, and H. V. Gelboin, *Mol. Pharmacol.*, in press.

(44) J. R. Parikh and W. von E. Doering, *J. Am. Chem. Soc.*, **89**, 5505 (1967); R. G. Harvey, S. H. Goh, and C. Cortez, *ibid.*, **97**, 3468 (1975).