Novel Annelation Reaction: Synthesis of Polycyclic Hydrocarbons from *o*-Quinones

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A novel general synthesis of polycyclic aromatic ring systems involving initial reaction of a polycyclic *o*-quinone with lithium acetylide, reduction of the resulting diacetylenic diol with $LiAlH_4$ to the corresponding divinyl diol, and finally cyclization and dehydration with HI or $POCl_3$ to a polyarene having one more aromatic ring is reported. Syntheses of triphenylene, dibenz[*a*,*c*]anthracene, benzo[*e*]pyrene, and benzo[*g*]chrysene by this means from phenanthrene-9,10-dione, benz[*a*]anthracene-5,6-dione, pyrene-4,5-dione, and chrysene-5,6-dione, respectively, are described. Yields are high (94–97%) in the initial two steps and good (52–74%) in the final stage. The divinyl diol intermediates may be generated directly, though in lower yield, via direct reaction of the quinones with vinylmagnesium bromide or vinyllithium reagents. Various related reactions are also explored, and evidence concerning the stereochemistries of the intermediates and the mechanisms of these reactions is discussed.

A revival of interest in the chemistry of polycyclic aromatic hydrocarbons has been stimulated recently by the finding that diol epoxide metabolites are ultimate[1] carcinogenic forms of benzo[*a*]pyrene and other carcinogenic hydrocarbons.[2-4] Chemical and biological studies in this area are hampered, however, by the relative synthetic inaccessibility of many polycyclic hydrocarbons and their substituted derivatives, except through complex multistep syntheses.[8] There is a clear need for the development of a greater diversity of synthetic approaches to polycyclic aromatic ring systems as well as for more direct methods for the introduction of functional groups anywhere in the polycyclic ring system.

We report now a convenient new synthesis of polycyclic aromatic hydrocarbons, utilizing a novel annelation reaction. In essence, this method involves initial reaction of an appropriate polycyclic *o*-quinone with lithium acetylide, reduction of the resulting diacetylenic diol to the corresponding divinyl diol, and catalyzed cyclization and concurrent dehydration of the latter directly to a polyarene having one additional ring (Scheme I). Alternatively, the divinyl diol may be generated directly, albeit in lower yield, by reaction of the quinone with vinylmagnesium bromide or vinyllithium.

Scheme I

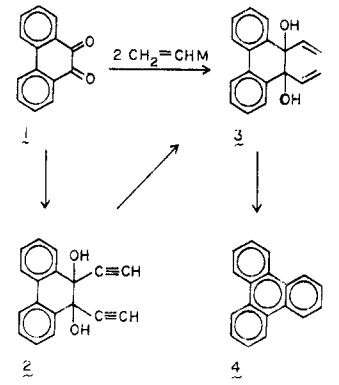
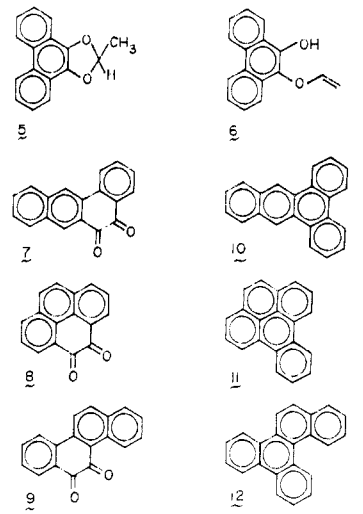


Chart I



Results

Initial studies were conducted with phenanthrene-9,10-dione (1). Treatment of 1 with vinylmagnesium bromide afforded smoothly the divinyl diol **3** (50–55%) accompanied by 2-methylphenanthro[9,10-*d*][1,3]dioxole (**5**, 15%). The latter is believed to arise during chromatography on Florisil through cyclization of the vinyl ether **6** (Chart I) which is the second primary product. A similar reaction was reported earlier by Wege,[9] who obtained **3** and **6** in yields of 35% and 50%, respectively. Direct conversion of **3** to triphenylene (**4**) took place on treatment of **3** with $POCl_3$ in pyridine or with HI in acetic acid. Somewhat surprisingly, no reaction occurs with **3** and HCl in ethyl acetate[10] or *p*-toluenesulfonic acid in refluxing

(1) The *ultimate carcinogen* in current terminology is the metabolically activated form of a carcinogen which interacts with the critical cellular target, generally believed to be DNA, to induce tumor formation; *proximate carcinogens* are metabolic intermediate precursors of the ultimate carcinogens such as arene oxides and dihydro diols: Miller, J. *Cancer Res.* **1970**, *30*, 559.

(2) Reviews: (a) Harvey, R. G., Fu. P. P. In "Polycyclic Hydrocarbons and Cancer: Environment, Chemistry, and Metabolism"; Gelboin, H. V., T'so, P. O. P., Eds.; Academic Press: New York, 1978; Vol. 1, Chapter 6, p 133; (b) Yang, S. K.; Deutsch, J.; Gelboin, H. V. *Ibid.*, Chapter 10, p 205; (c) Levin, W.; Wood, A. W.; Wislocki, P. G.; Chang, R. L.; Kapitulnik, J.; Mah, H. D.; Yagi, H.; Jerina, D. M.; Conney, A. H. *Ibid.*, Chapter 9, p 189; (d) Harvey, R. G. In "Safe Handling of Chemical Carcinogens, Mutagens, Teratogens and Highly Toxic Substances"; Walters, D. B., Ed.; Ann Arbor Science Publishers, Inc.: Ann Arbor, MI, 1980; Vol. 2, Chapter 23, p 439.

(3) For recent references cf.: Slaga, T. J.; Gleason, G. L.; DiGiovanni, J.; Sukumaran, K. B.; Harvey, R. G. *Cancer Res.* **1979**, *39*, 1934.

(4) Arene oxide metabolites[5] are also found to exhibit significant activity as mutagens, carcinogens, inducers of cellular transformation, and inhibitors of viral replication[6] and are suspected to be ultimate carcinogens in certain cases.[7]

(5) Sims, P.; Grover, P. *Adv. Cancer Res.* **1974**, *20*, 165.

(6) Hsu, W. T.; Harvey, R. G.; Lin, E. J.; Weiss, S. B. *Proc. Natl. Acad. Sci. U.S.A.* **1977**, *74*, 1378; *Biochem. Biophys. Res. Commun.* **1979**, *88*, 251.

(7) Harvey, R. G.; Dunne, F. B. *Nature (London)* **1978**, *273*, 566.

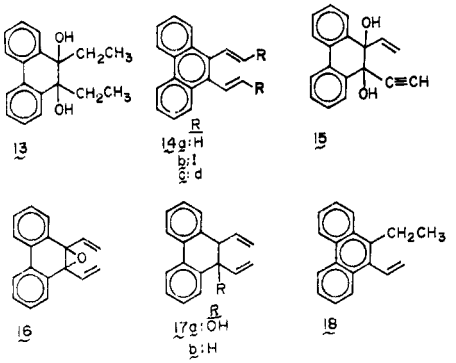
(8) Clar, E. "Polycyclic Hydrocarbons"; Academic Press, New York, 1964; Vol. I, II.

(9) Wege, D. *Aust. J. Chem.* **1971**, *24*, 1531.

(10) Newman, M. S.; Sankaran, V. *Tetrahedron Lett.* **1977**, 2067.

0022-3263/81/1946-2740$01.25/0

Chart II



benzene. The isolated yield of pure triphenylene via this route was 70–75%.

Analogous reactions of benz[a]anthracene-5,6-dione (7), pyrene-4,5-dione (8), and chrysene-5,6-dione (9) furnished the related divinyl diols which underwent conversion on treatment with $POCl_3$ in pyridine to dibenz[a,c]anthracene (10), benzo[e]pyrene (11), and benzo[g]chrysene (12), respectively. A vinyl ether analogous to 6 was isolated as a coproduct only in the case of 7. These syntheses constitute practical synthetic approaches to these polycyclic aromatic ring systems.

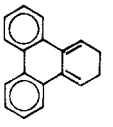
Substitution of vinyllithium for vinylmagnesium bromide in the reaction of 1 suppressed formation of the vinyl ether 6 as reported by Beak.[11] However, the isolated yield of the divinyl diol 3 was lower (34%) than via the Grignard route (51%), and the diacetylenic diol 2 was obtained as a side product (20%). The latter very likely arises from lithium acetylide present in the vinyllithium which was made by exchange between vinyl bromide and *sec*-butyllithium.

As a potential alternative route to the divinyl diol intermediates, the analogous reactions of polycyclic *o*-quinones with lithium acetylide were also investigated. Reaction of phenanthrene-9,10-dione with this reagent in THF afforded 2 smoothly and virtually quantitatively, with no detectable traces of products analogous to 5 and 6 arising from attack on oxygen. The analogous reaction of 1 with sodium acetylide in liquid ammonia was reported by Ried and Schmidt[12] to furnish 2 in 50% yield. Three methods for the potential reduction of the diethynyl diol 2 to the divinyl diol 3 were investigated. Hydrogenation of 2 over a palladium catalyst in quinoline afforded only the saturated diethyl diol 13 (Chart II). Reduction of 2 with chromous chloride in ammonia solution[13] furnished the desired 3 along with 9,10-divinylphenanthrene (14a). Although the ratio of these two products could be partially controlled through adjustment of the stoichiometry and reaction time, the maximum yields attained of either product were approximately 60%. Addition of 1 mol of hydrogen to each of the acetylenic groups of 2 was most efficiently achieved through reduction with $LiAlH_4$. Treatment of 2 with excess $LiAlH_4$ in refluxing ether for 18 h afforded 3 in excellent yield (95%). With a shorter reaction time (4 h) the intermediate vinyl acetylenic diol 15 was recoverable as the major product.

Similar results were observed with quinones 7–9. Reactions of the latter with lithium acetylide afforded smoothly the related diacetylenic diol derivatives of benz[a]anthracene, pyrene, and chrysene analogous to 2 in generally high yields. Reduction of these diacetylenic diols with chromous chloride in ammonia furnished the corresponding divinyl diols (5,6-dihydroxy-5,6-divinyl-5,6-dihydrobenz[a]anthracene, 4,5-dihydroxy-4,5-divinyl-4,5-dihydropyrene, and 5,6-dihydroxy-5,6-divinyl-5,6-dihydrochrysene) in moderate yields accompanied by lesser amounts of the related *o*-divinylpolyarenes (5,6-divinylbenz[a]anthracene, 4,5-divinylpyrene, and 5,6-divinylchrysene). Reduction of the same diacetylenic diols with $LiAlH_4$ provided cleanly the corresponding divinyl diols in uniformly excellent yields.

Since *o*-divinylarenes such as 9,10-divinylphenanthrene (14a) are also potential synthetic precursors of polycyclic aromatic ring systems, the synthesis and reactions of 14a were examined in greater detail. For this purpose, a convenient synthetic route to 14a was developed from the divinyl diol 3. Reaction of 3 with the dimethyl acetal of dimethylformamide by the method of Harvey et al.[14] afforded the divinylarene oxide 16. The latter on treatment with $LiAlH_4$ in ether underwent quantitative reduction to the divinyl monoalcohol 17a. Dehydration of 17a catalyzed with *p*-toluenesulfonic acid in refluxing benzene or with phosphorus oxychloride in pyridine gave 14a. Attempted conversion of the divinyl diol 3 directly to divinylphenanthrene with $LiAlH_4$–$AlCl_3$ in ether furnished instead 9-ethyl-10-vinylphenanthrene (18). Conceivably 18 arises from initial reduction of 3 to 9,10-divinyl-9,10-dihydrophenanthrene (17b) followed by successive 1,3-prototropic rearrangement.

Attempts to cyclize 9,10-divinylphenanthrene thermally or photochemically have met with only limited success. Photochemical reactions under a variety of conditions furnished predominantly polymeric products. Thermal reaction of 14a at 210 °C afforded mainly triphenylene (~35%), apparently arising through cyclization to the relatively unstable dihydro intermediate 19 followed by loss of hydrogen.



19

Treatment of the diacetylenic diol 2 with hydriodic acid in acetic acid afforded in good yield (92%) an iodinated hydrocarbon identified as 9,10-bis(β-iodovinyl)-phenanthrene (14b). The structure of 14b was confirmed by deiodination with *sec*-butyllithium at −100 °C. The NMR spectrum of the 9,10-divinylphenanthrene product was identical with that of authentic 14a. In a separate deiodination experiment, the reaction was quenched with deuterium oxide instead of water to furnish the deuterated analogue 14c. The NMR spectrum of the latter clearly showed the deuterium label to be in the terminal β,γ-positions.

Discussion

These experimental results demonstrate the feasibility of the synthetic scheme outlined in Scheme I for the synthesis of polycyclic aromatic ring systems. Optimal yields are obtained via the synthetic sequence which involves reaction of the appropriate polycyclic *o*-quinone with lithium acetylide, reduction of the resulting diacetylenic diol with $LiAlH_4$ to the related divinyl diol, and cyclization of the latter with $POCl_3$ in pyridine directly to

(11) Beak, P.; Yamamoto, J.; Upton, D. J. *J. Org. Chem.* **1975**, *40*, 3052.
(12) Ried, W.; Schmidt, H. H. *Chem. Ber.* **1957**, *90*, 2553.
(13) Ho, T. L. *Synthesis* **1979**, 1; Hanson, J. R. *Synthesis* **1974**, 1.
(14) Harvey, R. G.; Goh, S. H.; Cortez, C. *J. Am. Chem. Soc.*, **1975**, *97*, 3468.

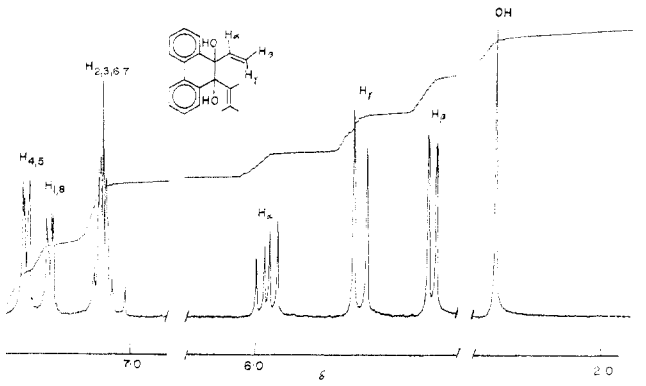
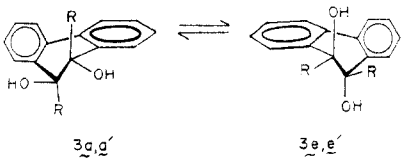


Figure 1. 270-MHz NMR spectrum of 3.

a polyarene having one additional aromatic ring. Isolated yields of the intermediate diacetylenic and divinyl diols are high (94–97%), and yields of the polycyclic hydrocarbon products obtained in the final step are generally good (52–74%). While only the four hydrocarbons, triphenylene (**4**), dibenz[*a*,*c*]anthracene (**10**), benzo[*e*]pyrene (**11**), and benzo[*g*]chrysene (**12**), have been synthesized via this route to date, the method appears quite general. Since only relatively simple experimental procedures and readily available reagents are involved, this method provides a convenient new synthetic approach to polycyclic aromatic ring systems.

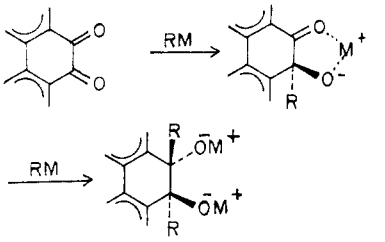
The stereochemistries of the divinyl and diacetylenic diols **3** and **2** were previously established to be trans[9,12] by their hydrogenation to the known *trans*-9,10-diethyl-9,10-dihydroxy-9,10-dihydrophenanthrene (**13**).[15] The trans stereochemical assignment of **3** was further confirmed in these studies by its conversion to the epoxide derivative **16** through reaction with the dimethyl acetal of dimethylformamide.[14,16] NMR studies on the structurally related 9-alkyl- and 9,10-dialkyl-9,10-dihydrophenanthrenes have demonstrated molecules of this type to exist in twisted boat-like structures which undergo relatively facile conformational interconversion.[17,18] As a consequence of steric interactions, substituents are known to adopt preferentially the pseudoaxial orientation (**3a,a′**). The 270-MHz NMR spectrum (Figure 1) of the divinyl diol **3** exhibits characteristic vinylic, aryl, and hydroxyl peaks in the anticipated ratios, further confirming its identity as a single stereoisomer. While rapid equilibration between trans-diaxial and trans-diequatorial conformations (**3a,a′** and **3e,e′**) cannot be entirely ruled out,



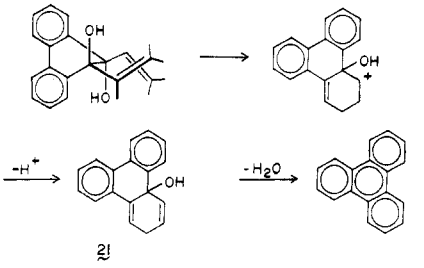
3a,a′ **3e,e′**

the sharpness of the spectrum strongly suggests existence in a fixed conformation. While a preferred diaxial orientation of the vinyl groups might be anticipated on steric grounds, the diequatorial assignment (**3e,e′**) is indicated by the apparent absence of hydrogen bonding between the hydroxyl groups, as evidenced by the sharpness of the

Scheme II



Scheme III. Mechanism of Cyclization



21

hydroxyl proton peaks in the NMR spectrum, independent of solvent polarity ($CDCl_3$ or Me_2SO-d_6). Hydrogen bonding is a characteristic feature of the diequatorial diols of polycyclic hydrocarbons.[19,20] The proton NMR spectra of all of the additional divinyl and diacetylenic diols synthesized in this study were similarly consistent with their assignment as the trans stereoisomers existing predominantly as a single conformer, most probably the diequatorial form analogous to **3e,e′**.

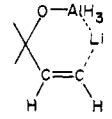
While the trans stereospecificity of dialkylation of *o*-quinones with organomagnesium and -lithium reagents has been previously observed,[9,11,15] no explanation has been advanced for this strong steric preference. We propose that stereospecificity is a consequence of the steric requirements of the initially formed intermediate (e.g., **20**, Scheme II). As a consequence of bonding between the metal cation and the oxygen atom of the adjacent carbonyl of **20**, the alkyl group preferentially adopts a pseudoaxial orientation approximately normal to the plane of the molecule. The resulting steric interference to nucleophilic attack from the same face of the molecule directs subsequent reaction with a second reagent molecule exclusively to the opposite face, affording the trans stereoisomeric product.

The mechanism of cyclization of **3** and other divinyl diols (Scheme III) is suggested to involve initial loss of an hydroxyl group with more or less concurrent bond formation between the terminal vinylic carbon atoms, followed by loss of a proton to furnish a dienyl alcohol (**21**). Facile dehydration of the latter is thermodynamically favored to provide the fully aromatic hydrocarbon.

Reduction of **2** and other diacetylenic diols cleanly to the corresponding diols with $LiAlH_4$ is somewhat surprising in view of the known facility of reduction of allylic alcohols with this reagent.[21] Indeed, when **3** was treated with $LiAlH_4$ in refluxing ether, it underwent reduction to the corresponding saturated derivative **13**. These findings are explicable as a consequence of resistance to addition of a second hydride to the negatively charged olefinic bond of the cyclic intermediate **22** formed initially. An additional

(15) Criegee, R.; Hoger, E.; Huber, G.; Kruck, F.; Marktscheffel, F.; Schellenberger, H. *Justus Liebigs Ann. Chem.* **1956**, *599*, 81.
(16) Cis diols furnish cyclic dioxolanes on treatment with this reagent: Neumann, H. *Chimia* **1969**, *23*, 267.
(17) Harvey, R. G.; Fu, P. P.; Rabideau, P. W. *J. Org. Chem.* **1976**, *41*, 3722.
(18) Rabideau, P. W.; Harvey, R. G.; Stothers, J. B. *Chem. Commun.* **1969**, 1005.
(19) Jeffrey, A. M.; Yeh, H. J.; Jerina, D. M.; Patel, T. R.; Davey, J. F.; Gibson, D. T. *Biochemistry* **1975**, *14*, 575.
(20) Zacharias, D.; Glusker, J. P.; Fu, P. P.; Harvey, R. G. *J. Am. Chem. Soc.* **1979**, *101*, 4043.
(21) Snyder, E. *J. Org. Chem.* **1967**, *32*, 3531. Bordon, W. T. *J. Am. Chem. Soc.*, **1968**, *90*, 2197.

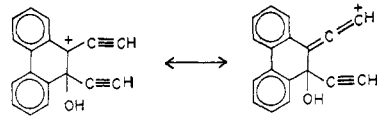
factor is the relative insolubility of the adduct **22** which precipitates from solution during reaction.



22

Decomposition of **22** with deuterium oxide furnished **14c**, the NMR spectrum of which showed the deuterium label to be situated in the terminal position, consistent with expectation.

The mechanism of formation of the diiodinated compound **14b** is not immediately obvious. It is unlikely that **14b** arises through initial reduction of **2** to 9,10-diethynylphenanthrene, since subsequent addition of HI would be anticipated to proceed in the Markovnikov manner to furnish the α-iodinated analogue of **14b**. The origin of **14b** can be rationalized as proceeding via initial HI-catalyzed loss of hydroxyl with more or less simultaneous addition of iodide to the resulting carbocation intermediate **23** to generate the bis(iodoallenic) intermediate **24**, followed by reduction of the latter with HI to furnish **14b** and I_2.



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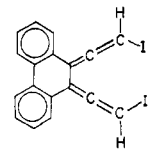

24

Experimental Section

General Methods. Phenanthrene-9,10-dione was purchased from the Aldrich Chemical Co. and purified by chromatography on Florisil and crystallization from benzene. Benz[*a*]anthracene-5,6-dione,[22] pyrene-4,5-dione,[22] and chrysene-5,6-dione[23] were synthesized from the parent hydrocarbons by the methods previously described. Vinylmagnesium bromide (1.1 M in THF) was purchased from Alfa-Ventron Corp., and vinyl bromide and acetylene were purchased from Matheson Gas. Pyridine, THF, and ether were distilled from $LiAlH_4$ immediately prior to use. The NMR spectra were recorded on Varian EM 360 A or Bruker HX 270-MHz spectrometers with tetramethylsilane as an internal standard in $CDCl_3$, unless otherwise specified. UV spectra were obtained on a Varian Techtron 635 spectrometer. Melting points are uncorrected. All new compounds gave satisfactory analyses for C and H within ±0.3% and/or mass spectra consistent with the assigned structures.

Reaction of Phenanthrene-9,10-dione with Vinylmagnesium Bromide. Into a stirred solution of **1** (2 g, 9.6 mmol) in THF (150 mL) was added dropwise a solution of vinylmagnesium bromide (1 M, 30 mmol in THF) at ambient temperature under N_2. The excess Grignard reagent was decomposed after 2 h by careful addition of a saturated solution of ammonium chloride (5 mL) followed by water (200 mL) and poured into ether (300 mL). The ether layer was separated, dried, and evaporated under reduced pressure. The residue was taken up in methylene chloride and adsorbed on Florisil (~20 g), and the solvent was removed in vacuo. The adsorbed product was placed on the top of a column of Florisil. Elution with hexane gave **5**: 350 mg (15%); mp 62 °C (lit.[9,24] mp 63–65 °C). Further elution with benzene and benzene–CH_2Cl_2 (1:1) gave **3** [1.3 g (51%); mp 78 °C (ether–hexane) (lit.[9] mp 84–86 °C)] and unreacted **1** (320 mg 16%). For **5**: NMR (270 MHz, $CDCl_3$) δ 1.40 (d, 3, CH_3), 5.0 (q, 1, CH, J = 5 Hz), 7.0–8.0 (m, 6, aryl), 8.55 (m, 2, aryl). For **3**: NMR (270 MHz, $CDCl_3$) δ 2.6 (s, 2, OH), 5.18 (dd, 2, H_β), 5.52 (dd, 2, H_γ), 5.95 (dd, 2, H_α), $J_{\alpha,\beta}$ = 9.5, $J_{\alpha,\gamma}$ = 15, $J_{\beta,\gamma}$ = 1.8 Hz); mass spectrum, m/e 264 (P).

Reaction of Benz[*a*]anthracene-5,6-dione with Vinylmagnesium Bromide. Reaction of **7** (900 mg, 3.5 mmol) with vinylmagnesium bromide (12 mmol) was carried out by the above procedure to afford 350 mg (35%) of 2-methylbenz[*a*]anthro[5,6-*d*][1,3]dioxole (mp 79 °C) and 600 mg (55%) of 5,6-dihydroxy-5,6-divinyl-5,6-dihydrobenz[*a*]anthracene: mp 92–93 °C (ethanol). For the dioxole NMR (270 MHz, $CDCl_3$) δ 1.90 (d, 3, CH_3, J = 4.78 Hz), 6.62 (q, 1, CH), 7.50–8.10 (m, 7, aryl), 8.32 (s, 1, H_7), 8.81 (d, 1, H_1), 9.15 (s, 1, H_{12}). For the divinyl diol: NMR (60 MHz, $CDCl_3$) δ 2.7 (br s, 2, OH), 5.0–6.30 (m, 6, vinylic), 7.30–8.25 (m, 10, aryl); mass spectrum, m/e 314 (P).

Reaction of Chrysene-5,6-dione with Vinylmagnesium Bromide. A similar reaction of chrysene-5,6-dione (900 mg, 3.5 mmol) with vinylmagnesium bromide (12 mmol) gave 610 mg (56%) of 5,6-dihydroxy-5,6-divinyl-5,6-dihydrochrysene as a waxy solid and 360 mg of unreacted **9**. A sample of the diol which crystallized from ethanol after 2 weeks melted at 97 °C: NMR (60 MHz, $CDCl_3$) δ 2.80 (br s, 2, OH), 5.0–6.2 (m, 6, vinyl), 7.20–8.0 (m, 7, aromatic), 8.3–9.1 (m, 3, aromatic); mass spectrum, m/e 314 (P).

Reaction of Pyrene-4,5-dione with Vinylmagnesium Bromide. Analogous reaction of **8** (400 mg, 1.7 mmol) with vinylmagnesium bromide (8 mmol) gave 270 mg (54%) of 4,5-dihydroxy-4,5-divinyl-4,5-dihydropyrene, mp 89 °C, and 137 mg of unreacted **8**: NMR (60 MHz, $CDCl_3$) δ 2.6 (br s, 1, OH) 4.95–6.00 (m, 6, vinyl), 7.40–8.10 (m, 8, aromatic); mass spectrum, m/e 288 (P).

Reaction of Phenanthrene-9,10-dione with Vinyllithium. A solution of vinyl bromide (0.642 g, 6 mmol) in a mixture of anhydrous THF, ether, and pentane (4:1:1, 100 mL; Trapp mixture)[25] was cooled to −120 °C. *sec*-Butyllithium (5 mL of 1.3 M solution) was added dropwise, maintaining the temperature below 115 °C. The solution was stirred at −120 °C for 2 h, and then a solution of **1** (620 mg, 298 mmol) in THF (50 mL) was added dropwise, maintaining the temperature below −110 °C. The solution was subsequently allowed to warm up to room temperature (3 h) and stirred at this temperature overnight. Workup in the usual manner and chromatography on Florisil gave on elution with benzene 430 mg of **3** (34%). Further elution with a mixture of benzene and CH_2Cl_2 (1:1) gave 370 mg (20%) of a colorless product (mp 210 °C) which has been identified as 9,10-diethynyl-9,10-dihydroxy-9,10-dihydrophenanthrene (**2**): NMR (60 MHz, $CDCl_3$) δ 2.40 (s, 2, acetylenic), 3.10 (s, 2, OH), 7.35–7.90 (m, 8, aromatic).

An analogous reaction stirred overnight at 100 °C gave only unreacted **1**.

Triphenylene (4). (A) $POCl_3$ in Pyridine. A solution of **3** (900 mg, 3.4 mmol) in pyridine (25 mL) was treated with $POCl_3$ (0.6 g, 3.9 mmol). The reaction mixture was heated at reflux for 10 min, decomposed by pouring onto crushed ice, and stirred until the ice had melted. The dark precipitate that separated was dissolved in CH_2Cl_2 and chromatographed on Florisil. Elution with hexane gave **4**: 575 mg (74%), mp 194–196 °C (lit.[8] mp 196.5 °C); NMR (60 MHz, $CDCl_3$) δ 7.50 (m, 6, $H_{2,3,6,7,10,11}$), 8.60 (m, 6, $H_{1,4,5,8,9,12}$).

(B) HI in Acetic Acid. A solution of **3** (300 mg, 1.1 mmol) and 1 mL of hydriodic acid (57%) in glacial acetic acid (5 mL) was refluxed for 10 min and then poured onto ice. The ice was allowed to melt, and sufficient sodium bisulfite was added to decolorize the iodine. The precipitated solid was filtered, dissolved in CH_2Cl_2, and chromatographed on Florisil. Elution with 5% benzene in hexane furnished **4**: 185 mg (71%); mp 196 °C.

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Dibenz[a,c]anthracene (10). Reaction of 7 (625 mg, 2 mmol) with $POCl_3$ (690 mg, 3.9 mmol) in pyridine (20 mL) by use of the procedure used for 4 gave 10: 310 mg (56%); mp 198–200 °C (lit.[8] mp 205 °C); NMR (270 MHz, $CDCl_3$) δ 7.54 (m, 2, $H_{11,12}$), 7.62 (m, 6, $H_{2,3,6,7}$), 8.05 (m, 2, $H_{10,13}$), 8.59 (m, 2, $H_{1,8}$), 8.73 (m, 2, $H_{4,5}$), 9.03 (s, 2, $H_{9,14}$).

Benzo[e]pyrene (11). Analogous reaction of 8 (270 mg, 0.94 mmol) with $POCl_3$ (500 mg, 3.25 mmol) in refluxing pyridine (20 mL) afforded 11: 124 mg (52%); mp 178 °C (lit.[8] mp 178–79 °C); NMR (60 MHz, $CDCl_3$) δ 7.5–8.1 (m, 8), 8.6–9.0 (m, 4, $H_{1,8,9,12}$).

Benzo[g]chrysene (12). Analogous reaction of 9 (550 mg, 1.75 mmol) with $POCl_3$ (500 mg, 3.25 mmol) in pyridine provided benzo[g]chrysene: 360 mg (74%); mp 116 °C (lit.[8] mp 114.5–115 °C); NMR (270 MHz, $CDCl_3$) δ 7.55 (m, 6, $H_{2,3,6,7,10,11}$), 7.93 (m, 2, $H_{1,14}$), 8.55 (m, 4, $H_{8,9,12,13}$), 8.87 (m, 2, $H_{4,5}$).

Reaction of Phenanthrene-9,10-dione with Lithium Acetylide. Anhydrous THF (25 mL) was saturated with acetylene at −20 °C. The solution was diluted with 225 mL of anhydrous THF and cooled to −78 °C in a dry ice/acetone bath under dry argon. *n*-Butyllithium (40 mL of 2.2 M solution in hexane, 88 mmol) was added dropwise, while maintaining the temperature below −75 °C (45 min). The solution was stirred for an additional 15 min, and then a solution of 1 (5.29 g, 25 mmol) in THF (250 mL) was added dropwise with stirring, while maintaining the temperature below −70 °C (40 min). The dark color of the quinone disappeared immediately, indicating instantaneous reaction. The solution was stirred for an additional 30 min, and then the reaction was quenched by the addition of a saturated aqueous solution of NH_4Cl (20 mL). The product was partitioned between ether (600 mL) and water (300 mL) and worked up conventionally to provide 9,10-diethynyl-9,10-dihydroxy-9,10-dihydrophenanthrene (2; 6.3 g, 97%). A sample of 2 crystallized from benzene melted at 205–207 °C (lit.[12] mp 196 °C): NMR (60 MHz, $CDCl_3$) δ 2.40 (s, 2, acetylenic), 3.1 (s, 2, OH), 7.35–7.95 (m, 8, aromatic).

Reaction of Benz[a]anthracene-5,6-dione with Lithium Acetylide. Analogous reaction of 7 (5.2 g, 20 mmol) with lithium acetylide (80 mmol) gave 5,6-diethynyl-5,6-dihydroxy-5,6-dihydrobenz[a]anthracene: 5.9 g (95%); mp 208–210 °C (softens at 193 °C); NMR (60 MHz, $CDCl_3$) δ 2.30 (2 s, 2, acetylenic), 3.20 (2 s, 2, OH), 7.30–7.60 and 7.7–8.05 (m, 8, aromatic), 8.20 (s, 1, H_7 or H_{12}), 8.30 (s, 1, H_{12} or H_7) ; mass spectrum, *m/e* 310 (P).

Anal. Calcd for $C_{22}H_{14}O_2$: C, 85.16; H, 4.52. Found: C, 84.92; H, 4.68.

Reaction of Pyrene-4,5-dione with Lithium Acetylide. Analogous reaction of 8 (2.1 g, 9.05 mmol) with lithium acetylide (35 mmol) yielded 4,5-diethynyl-4,5-dihydroxy-4,5-dihydropyrene: 2.41 g (94%); mp 245–247 °C; NMR (60 MHz, $CDCl_3$) δ 2.60 (s, 2, acetylenic), 3.20 (s, 2, OH), 7.70–8.50 (m, 8, aromatic); mass spectrum, *m/e* 284 (P).

Reaction of Chrysene-5,6-dione with Lithium Acetylide. Similar reaction of 9 (4.0 g, 15.5 mmol) with lithium acetylide (62 mmol) afforded 5,6-diethynyl-5,6-dihydroxy-5,6-dihydrochrysene: 4.6 g (96%); mp 186–88 °C; NMR (60 MHz, $CDCl_3$) δ 2.20 and 2.35 (2 s, 2, acetylenic), 3.15 and 3.25 (2 s, 2, OH), 7.20–7.90 (m, 9, aromatic), 8.90–9.20 (m, 1, H_4); mass spectrum, *m/e* 310 (P).

Reduction of Diacetylenic Diols with Chromous Chloride. (1) Phenanthrene. A solution of 2 (1.3 g, 5 mmol) in THF was degassed under vacuum and then added to a freshly prepared ammoniacal solution of chromous chloride (1 M, 20 mL) under argon. The resulting solution was stirred overnight, acidified with concentrated HCl to pH ~1, and stirred for an additional 1 h. Extraction with ether, evaporation of the solvent, and chromatography of the residue (1.18 g) on Florisil provided 9,10-divinylphenanthrene (14a): 0.62 g (54%); mp 58–60 °C: NMR (60 MHz, $CDCl_3$) δ 5.25, 5.55, and 5.80 (m, 4, β-vinylic), 6.7–7.3 (dd, 2, α-vinylic), 7.40–7.70 (m, 4, $H_{2,3,6,7}$), 8.1–8.4 (m, 2, $H_{1,8}$), 8.55–8.80 (m, 2 $H_{4,5}$). Further elution gave 3 (480 mg, 37.5%) identical by NMR with an authentic sample.

(2) Benz[a]anthracene. Reduction of 5,6-diethynyl-5,6-dihydroxy-5,6-dihydrobenz[a]anthracene (1 g, 3.2 mmol) with ammoniacal Cr(II) by the preceding procedure yielded 5,6-dihydroxy-5,6-divinyl-5,6-dihydrobenz[a]anthracene (560 mg, 56%; mp 96–97 °C), identical by NMR with an authentic sample, and 5,6-divinylbenz[a]anthracene: 400 mg (45%); mp 118–121 °C; NMR (60 MHz, $CDCl_3$) δ 5.30, 5.60, and 5.80 (m, 4, β-vinylic), 6.70–6.90 (m, 12, α-vinylic and aromatic).

(3) Pyrene. Analogous reduction of 4,5-diethynyl-4,5-dihydroxy-4,5-dihydropyrene (1.2 g, 4.2 mmol) with Cr(II) gave 4,5-divinylpyrene [570 mg (53%); mp 94–96 °C; NMR (60 MHz, $CDCl_3$) δ 5.5, 5.70, and 5.95 (m, 4, β-vinylic), 7.0–7.3 (dd, 2, α-vinylic), 7.8–8.4 (m, 8, aromatic)] and 4,5-dihydroxy-4,5-divinyl-4,5-dihydropyrene (320 mg, 26%) identical by NMR with an authentic sample.

(4) Chrysene. Analogous reduction of 5,6-diethynyl-5,6-dihydroxy-5,6-dihydrochrysene (1.1 g, 3.5 mmol) with Cr(II) furnished 5,6-dihydroxy-5,6-divinyl-5,6-dihydrochrysene [660 mg (59%); mp 96 °C], identical by NMR with an authentic sample, along with unreacted starting material (340 mg, 32%).

Reaction of 9,10-Dihydro-9,10-dihydroxy-9,10-divinylphenanthrene (3) with Dimethylformamide Dimethyl Acetal. A solution of the divinyl diol 3 (500 mg, 1.89 mmol) in dimethylformamide dimethyl acetal (1 mL) was held at reflux for 16 h, poured into a 5% aqueous solution of sodium chloride, and stirred for 0.5 h. Extraction with ether, removal of the solvent, and chromatography of the residue on Florisil with benzene and hexane (1:1) as eluant gave 356 mg (76%) of 9,10-divinylphenanthrene 9,10-oxide (16) as a waxy solid: mass spectrum, *m/e* 246 (P); NMR (270 MHz, $CDCl_3$) δ 5.02 (d, 2, H_β), 5.36 (d, 2, H_γ), 6.00 (dd, 2 H_α, $J_{\alpha,\beta}$ = 10.35 Hz, $J_{\alpha,\gamma}$ = 17.11 Hz), 7.36–8.04 (m, 8, aryl).

Reduction of 16 with $LiAlH_4$. A solution of 16 (250 mg, 1 mmol) and $LiAlH_4$ (225 mg, 6 mmol) in ether (200 mL) was heated at reflux for 4 h and then cooled, and the excess hydride was decomposed by careful addition of water (1 mL) and stirring for 30 min. Filtration of the inorganic residue and removal of the solvent gave 9-hydroxy-9,10-dihydro-9,10-divinylphenanthrene (17a) as a waxy solid: 190 mg (75%); NMR (60 MHz, $CDCl_3$) δ 2.40 (br s, 1, OH), 4.40–6.3 (m, 7, vinylic and benzylic), 7.00–7.8 (m, 8, aryl).

Dehydration of 9-Hydroxy-9,10-dihydro-9,10-divinylphenanthrene (17a). A solution of 17a (120 mg, 0.5 mmol) and *p*-toluenesulfonic acid (50 mg) in benzene (20 mL) was refluxed for 1 h. Removal of the solvent and chromatography of the product on Florisil with hexane gave 9,10-divinylphenanthrene 14a: 90 mg (81%); mp 60 °C.

Reduction of Diacetylenic Diols with $LiAlH_4$. (1) Phenanthrene. A solution of 2 (550 mg, 2 mmol) and $LiAlH_4$ (500 mg, 13.5 mmol) in anhydrous ether (300 mL) was refluxed for 18 h. The excess hydride was decomposed by careful addition of water (5 mL) followed by 10% HCl (100 mL). Separation of the ether layer, successive extraction with water (2 × 100 mL), 5% $NaHCO_3$ solution (1 × 100 mL), and water (1 × 100 mL), and removal of the solvent gave 3 (535 mg, 96%) identical by NMR and melting point with an authentic sample. A similar experiment with 2.09 g (7.7 mmol) of 2 heated at reflux for 4 h gave a crude product which was purified by chromatography on Florisil. Elution with benzene gave 3 (480 mg, 24%). Continued elution with methylene chloride gave 15: 1.20 g (60%); mp 110 °C (crystallized from 1:1 benzene–hexane); NMR (60 MHz, $CDCl_3$) δ 2.33 (s, 1, acetylenic), 2.60 (s, 1, OH), 3.05 (s, 1, OH), 5.00–6.00 (m, 3, vinylic), 7.20–7.90 (m, 8, aryl).

Anal. Calcd for $C_{18}H_{14}O_2$: C, 82.42; H, 5.38. Found: C, 82.31; H, 5.42.

(2) Benz[a]anthracene. Reduction of 5,6-diethynyl-5,6-dihydroxy-5,6-dihydrobenz[a]anthracene (400 mg, 1.3 mmol) with $LiAlH_4$ (200 mg, 5.4 mmol) by the above procedure (18 h reflux) gave 5,6-dihydro-5,6-dihydroxy-5,6-divinylbenz[a]anthracene (380 mg, 94%), identical by NMR with an authentic sample.

(3) Chrysene. Analogous reduction of 5,6-diethynyl-5,6-dihydro-5,6-dihydroxychrysene (300 mg, 0.96 mmol) with $LiAlH_4$ (200 mg, 5.4 mmol) gave 5,6-dihydro-5,6-dihydroxy-5,6-divinylchrysene (220 mg, 72%), identical by NMR with an authentic sample.

(4) Pyrene. Reduction of 4,5-diethynyl-4,5-dihydro-4,5-dihydroxypyrene (500 mg, 1.8 mmol) with $LiAlH_4$ (240 mg, 6.5 mmol) gave after chromatography 4,5-dihydro-4,5-dihydroxy-4,5-divinylpyrene (420 mg, 83%), identical by NMR with an authentic sample.

Reduction of 9,10-Dihydro-9,10-dihydroxy-9,10-divinylphenanthrene with $LiAlH_4$–$AlCl_3$. Into a solution of $LiAlH_4$ (300 mg, 8.1 mmol) in ether (300 mL) at 0 °C under argon was added anhydrous $AlCl_3$ (360 mg, 2.7 mmol) with stirring during

10 min. The solution was stirred for an additional 30 min, a solution of **3** (400 mg, 1.5 mmol) in anhydrous ether (50 mL) was added, and the resulting solutiuon was stirred at room temperature for 6 h. The excess hydride was decomposed with water (3 mL) followed by dilute HCl (50 mL), and the product was worked up in the conventional manner and chromatographed on Florisil. Elution with hexane gave 9-vinyl-10-ethylphenanthrene (**18**): 280 mg (79%); colorless oil; NMR (60 MHz, $CDCl_3$) δ 1.40 (t, 3, CH_3), 3.25 (q, 2, CH_2), 5.30–6.00 (m, 2, vinylic), 7.00–7.50 (m, 1, vinylic), 7.60–8.95 (m, 8, aryl).

Reaction of 2 with HI. A solution of **2** (1.2 g, 4.6 mmol) in acetic acid (15 mL) containing HI (57%, 2 mL) was refluxed for 15 min. The dark reaction mixture was poured into a stirred solution of 10% sodium bisulfite (200 mL), and the precipitate was collected by filtration. Chromatography on Florisil and elution with 1:3 benzene–hexane gave **14b**: 2.05 g (92%); mp 183 °C; mass spectrum, *m/e* 482 (P); NMR (60 MHz, $CDCl_3$) δ 6.35 (m, 2, vinyl), 7.40–8.60 (m, 10, aryl and vinyl). The 270-MHz spectrum is better resolved and shows the presence of two isomers in approximately a 1:3 ratio; however, specific assignments of isomer structures could not be made.

Deiodination of 9,10-Bis(β-iodovinyl)phenanthrene. A solution of **14b** (300 mg, 0.6 mmol) in anhydrous THF at −100 °C (acetone, liquid N_2) was treated with a solution (5 mL, 1.4 M in hexane) of *sec*-butyllithium. The resulting solution was stirred at −100 °C for 3 h, and then the reaction was quenched by addition of saturated aqueous solution of ammonium chloride. Conventional workup and chromatography of the product on Florisil gave **14a** (90 mg, 63%) eluted with hexane.

In a similar experiment the reaction mixture was quenched with deuterium oxide to afford **14c** (~85% with 15% of **14a**): NMR (270 MHz, $CDCl_3$) δ 5.60–6.00 (m, 2, β (or α) vinylic), 7.10–7.60 (dd, 1, α-vinylic), 7.70–8.90 (m, 8, aryl).

Hydrogenation of 2. A solution of **2** (600 mg, 2.3 mmol) and 800 mg (6.3 mmol) of quinoline in ethyl acetate (20 mL) containing 100 mg of Pd/C (10%) was stirred under H_2 (15 psi) for 6 h. Filtration to remove the catalyst and removal of the solvent gave 560 mg of **13** identical by NMR with an authentic sample prepared by a reported procedure:[9] NMR (60 MHz, $CDCl_3$) δ 0.7 (t, 6, CH_3), 1.20–1.85 (q, 4, CH_2) 2.90 (br s, 2, OH), 7.10–7.70 (m, 8, aryl).

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Registry No. **1**, 84-11-7; *trans*-**2**, 66415-21-2; *trans*-**3**, 33367-03-2; **4**, 217-59-4; **5**, 17529-30-5; **7**, 18508-00-4; **8**, 6217-22-7; **9**, 2051-10-7; **10**, 215-58-7; **11**, 192-97-2; **12**, 196-78-1; *trans*-**13**, 33367-04-3; **14a**, 77320-67-3; **14b**, 77320-68-4; **14c**, 77320-69-5; *trans*-**15**, 77341-74-3; **16**, 77320-70-8; **17a**, 77320-71-9; **18**, 77320-72-0; 2-methylbenz[*a*]anthro[5,6-*d*][1,3]dioxole, 77320-73-1; *trans*-5,6-dihydroxy-5,6-divinyl-5,6-dihydrobenz[*a*]anthracene, 77320-74-2; *trans*-5,6-dihydroxy-5,6-divinyl-5,6-dihydrochrysene, 77320-75-3; *trans*-4,5-dihydroxy-4,5-divinyl-4,5-dihydropyrene, 77320-76-4; *trans*-5,6-diethynyl-5,6-dihydroxy-5,6-dihydrobenz[*a*]anthracene, 77320-77-5; *trans*-4,5-diethynyl-4,5-dihydroxy-4,5-dihydropyrene, 77320-78-6; *trans*-5,6-diethynyl-5,6-dihydroxy-5,6-dihydrochrysene, 77320-79-7; 5,6-divinylbenz[*a*]anthracene, 77320-80-0; 4,5-divinylpyrene, 77320-81-1.

Amine Addition to Unsymmetrical Benzoquinones

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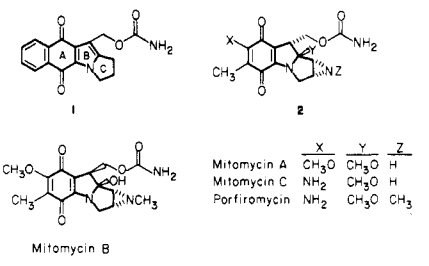
New routes to 2-methoxy-3-methyl-1,4-benzoquinone and 4-methoxy-3-methyl-1,2-benzoquinone have been developed. Both quinones undergo highly regioselective oxidative amination with pyrrolidine and copper acetate, yielding aminoquinones related to the mitomycin antibiotics. The corresponding dibromoquinones have also been prepared and both readily undergo regioselective addition–elimination reactions to give monoamine adducts with the same relative orientation. The regiochemistry has been determined unambiguously by correlation to adducts derived from specificially deuterated quinone intermediates.

Recently the synthesis of the naphthoquinone mitosene analogue **1** was reported[1] as part of a study of synthetic approaches to the mitomycin antibiotics **2** (Chart I). The convergent route developed first joined the A ring (as a quinone) and the C ring (as an amine) and then cyclized to form the B ring. For the purpose of applying this and related methodology to unsymmetrical benzoquinone systems, we have considered the *o*- and *p*-quinones **5**, **8**, **20**, and **25** as potential substrates, bearing substitution patterns which are found in or are convertible to the parent mitomycin system. In this report, we present the syntheses of these substrates and their addition reactions with pyrrolidine as a model amine.

Unlike the naphthoquinone model, the benzenoid system potentially can form isomers, thereby creating a regiochemical problem in the initial amine addition step. We were encouraged, however, to anticipate that this addition might be highly selective by the report that homoproline ethyl ester reacted with quinone **5**, giving addition only at C-5.[2]

Chart I



Quinone **5** has been synthesized many times, invariably in low yield.[2-5] Initial examination of the literature routes suggested that the most facile synthesis would arise from Fremy's salt (potassium nitrosodisulfonate) oxidation of phenol **4**,[3] best obtained by monoether cleavage of **3**.[6]

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