dioxane was mixed with 0.24 mL of 10% aqueous NaOH, and the mixture was warmed at 50 °C for 10 min.[23] After the solvents were removed, the residue was washed with diethyl ether and then water. From the ethereal solution was obtained diketone **5** (98%) as a viscous oil: mass spectrum, *m/e* 220 (M^+); IR (film) 1700, 1720 cm^{-1}; ^1H NMR 0.97, 1.15 (3 H each, s), 1.25 (6 H, s), 1.65, 1.83 (3 H each, q, J = 1 Hz), 2.19, 2.34 (1 H each, 2 d, J = 19 Hz).[6] Under the same conditions, the syn isomer of **3d** afforded the same diketone **5** in a 68% yield (see also Table IV). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 75.40; H, 9.29.

Method B. Preparation of (1,3,3,4,5,6-Hexamethyl-2-oxocyclohex-4-en-1-yl)acetic Acid (15a). When the hydrolysis by method A was performed under prolonged conditions (e.g., more than 30 min), ring-opened acid **15a** was produced. After evaporation of the solvents, the residue was washed with a mixture of water and ether, and the aqueous layer was slightly acidified with acetic acid and extracted several times with ether to give solid **15a**: 60%; mp 128–130 °C (recrystallized from 60% EtOH); mass spectrum, *m/e* 238 (M^+); ^1H NMR 1.04, 1.08, 1.17 (3 H each, s), 1.23 (3 H, d, J = 7.5 Hz), 1.77, 1.91 (3 H each, q, J = 1 Hz), 2.38 (2 H, s), 2.83 (1 H, br q, J = 7.5 Hz); ^{13}C NMR ($CDCl_3$) 11.9, 15.0, 18.0, 19.8, 21.0, 22.3, 41.7, 42.5, 42.7, 49.2, 133.7, 153.8, 178.7, 203.7. Anal. Calcd for $C_{14}H_{22}O_3$: C, 70.56; H, 9.30. Found: C, 70.30; H, 9.39.

Hydrolysis of Diketone 5. Diketone **5** (43 mg, 0.2 mmol) dissolved in 2 mL of dioxane was mixed with 0.2 mL of 10% aqueous NaOH, and the mixture was shaken at 75 °C for 20 min. After removal of the solvents, the residue was extracted with ether (no extract), the aqueous layer was acidified with AcOH, and the separated cloudy material was extracted with ether to give the acid **15a** (94%; see also Table IV).

(23) This procedure seems to convert cyanohydrin esters into the corresponding ketones better than the one reported by: DePuy, C. H.; Story, P. R. *J. Am. Chem. Soc.* **1960**, *82*, 627.

Methyl Ester of 15a. After the treatment of compound **15a** (240 mg) with an equivalent amount of ethereal diazomethane, the methyl ester formed was analyzed by VPC (Apiezon grease and PEG-20M, 2 m, 180 °C). Only a single sharp fraction peak was observed at ca. 8–10 min on both columns. No splitting or shouldering of the peak was observed: mass spectrum, *m/e* 252 (M^+); IR (film) 1730 cm^{-1}.

Alkaline Hydrolysis of 11. Adduct **11** (50 mg, 0.1 mmol) dissolved in 3 mL of $CHCl_3$ was mixed with 6 mL of 5% NaOH (7.5 mmol), and the total solution was warmed at 50 °C for 90 min. After cooling, the solution was diluted with water (20 mL), neutralized with AcOH, and extracted with ether to afford a mixture of 2,3,4,5-tetraphenylbenzonitrile (**12**, 36%) and **11** (58%). Both compounds were separated by a column chromatography (silica gel, $CHCl_3$).

Attempted Acid Hydrolysis of 11. Adduct **11** (100 mg, 0.2 mmol) dissolved in 10 mL of benzene was mixed with 2.8 mL of 30% H_2SO_4 (2.02×10^{-2} mol), and the mixture was warmed for 1.5 h under solvent reflux. After cooling, the solution was neutralized by aqueous 10% NaOH to a slightly acidic state (pH 3) and was extracted with ether three times. The extracted material (92 mg) proved to be identical with **11** by IR and NMR.

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Registry No. 1a, 72876-47-2; **1b**, 72876-48-3; **1c**, 13427-72-0; **1d**, 3061-65-2; *Z*-**1e**, 78672-72-7; *E*-**1e**, 78672-73-8; **1f**, 72603-94-2; **2**, 3854-96-4; *anti*-**3a**, 78672-74-9; *syn*-**3a**, 78737-56-1; *anti*-**3b**, 78672-75-0; *syn*-**3b**, 78737-57-2; *anti*-**3c**, 78672-76-1; *syn*-**3c**, 78737-58-3; *anti*-**3d**, 78672-77-2; *syn*-**3d**, 78737-59-4; **3a**, 78672-78-3; **5**, 34327-63-4; **8**, 920-37-6; *anti*-**9**, 78672-79-4; *syn*-**9**, 78737-60-7; **10**, 479-33-4; *exo*-**11**, 78672-80-7; *endo*-**11**, 78672-81-8; **12**, 78672-82-9; *exo*-**14**, 78672-83-0; *endo*-**14**, 78672-84-1; **15a**, 78672-85-2; **15a** methyl ester, 78672-86-3.

Tetrabutylammonium Hydroxide: A Reagent for the Base-Catalyzed Dehydration of Vicinal Dihydro Diols of Aromatic Hydrocarbons. Implications to Ion-Pair Chromatography

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Vicinal dihydro diols of benzo[*a*]pyrene and benz[*a*]anthracene are dehydrated to their phenolic derivatives by the methanol eluate of reverse-phase (octadecylsilane) columns previously treated with tetrabutylammonium phosphate. Phenols are also produced by treating the dihydro diols with methanolic tetrabutylammonium hydroxide on removal of solvent. In most cases the regioselectivity is markedly different from the acid-catalyzed dehydration. The in situ generated tetrabutylammonium phenoxides are converted to the butyl ethers at high temperatures (150 °C) but not under the conditions of dehydration (60 °C). Tetraethylammonium and tetramethylammonium hydroxides also dehydrate dihydro diols, whereas potassium and sodium hydroxides do not. Dehydration does occur by treatment of dihydro diols with potassium hydroxide in the presence of 1,4,7,10,13,16-hexaoxacyclooctadecane (18-crown-6) and with sodium methoxide in the presence of tetrabutylammonium chloride. A mechanism is suggested.

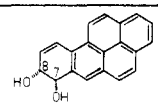
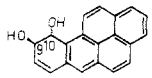
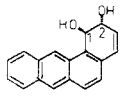
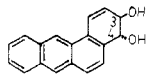
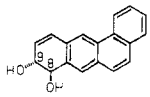
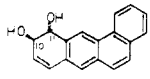
Reverse-phase ion-pair chromatography was developed to allow for separation of ionic compounds. The technique typically involves the use of tetraalkylammonium phosphate and alkyl sulfonate buffers for the analysis of weak organic acids and bases, respectively.[2]

During our studies on the analysis of vicinal dihydro diols of polycyclic aromatic hydrocarbons by reverse-phase liquid chromatography, an ODS (octadecylsilane) column previously treated with tetrabutylammonium phosphate was used. We found that the collected dihydro diol frac-

(1) Present Address: Waters Associates, Inc., 34 Maple Street, Milford, MA 01757.

(2) For an excellent review of ion-pair chromatography see: E. Tomlinson, T. M. Jefferies, and C. M. Riley, *J. Chromatogr.*, **159**, 315 (1978).

Table I. Dehydration Reactions of Benzo[a]pyrene and Benz[a]anthracene Dihydro Diols with Phosphoric Acid and with Tetrabutylammonium Hydroxide[a]

		H_3PO_4		Bu_4NOH	
	phenolic products	ratio[b]	% unreacted diol[c]	ratio[b]	% unreacted diol[c]
	7-OH/8-OH	97/3	2	13/87	4
	9-OH/10-OH	98/2	1	14/86	3
	1-OH/2-OH	13/87	1	21/79	7
	3-OH/4-OH	42/58	1	33/67	5
	8-OH/9-OH	92/8	1	58/42	25
	10-OH/11-OH	32/68	1	35/65	36

[a] Dihydro diol (0.04 μmol) was treated with H_3PO_4 (1 μmol) or Bu_4NOH (1 μmol) in methanol (0.5 mL) and then evaporated under a stream of N_2 at 60 °C for 5 min. [b] Ratio of phenolic products was determined by HPLC analysis and UV–vis spectroscopy. [c] Determined by HPLC analysis.

tions, upon evaporation under nitrogen, contained appreciable amounts of phenols. Furthermore, mass spectral analysis of these fractions by solid-probe methods indicated subsequent formation of the butyl ether derivatives. Apparently trace amounts of tetrabutylammonium salts eluting from the column effected the transformations during chemical characterization.[3]

These observations prompted the present study, which reports for the first time the use of methanolic tetrabutylammonium hydroxide as a reagent for the dehydration of vicinal dihydro diols of polycyclic aromatic hydrocarbons.

Results and Discussion

Dehydration of *trans*-7,8-Dihydroxy-7,8-dihydrobenzo[*a*]pyrene (1) by Methanolic Tetrabutylammonium Hydroxide. Compound 1 was treated with a 10 times molar excess of tetrabutylammonium hydroxide as described in the experimental section, and the formation of 2 was confirmed by HPLC analysis and UV–vis spectroscopy. This reaction was temperature dependent, the yields from 1 being 2% when the solvent evaporation temperature was 21 °C, 25% at 32 °C, 51% at 42 °C, 70% at 50 °C, and 89% at 61 °C. The reaction was independent of the configuration of the dihydro diol; for example, *cis*-7,8-dihydroxy-7,8-dihydrobenzo[*a*]pyrene was also dehydrated to 2 by tetrabutylammonium hydroxide.

Dehydration of Dihydro Diols of Benzo[*a*]pyrene and Benz[*a*]anthracene by Phosphoric Acid and Methanolic Tetrabutylammonium Hydroxide. A series of trans dihydro diols of benzo[*a*]pyrene and benz[*a*]anthracene were treated with H_3PO_4 and Bu_4NOH to compare regioselectivities. Yields and product distributions are shown in Table I. The method of acid dehydration we describe is milder than the method of Cook and Schoental[5] and may prevent decomposition of heat-sensitive material.

Mechanism. March[6] presents a mechanism for the base-catalyzed 1,4 conjugate elimination of water from 9,10-dihydroxy-9,10-dihydroanthracene by means of sodium hydroxide.[7] In our case, when 1 was treated with sodium or potassium hydroxide in methanol, no dehydration occurred. On the other hand, when 1 was treated with tetraethylammonium hydroxide or with tetramethylammonium hydroxide, dehydration was observed with formation of 2. Some additional observations and the following discussion help in delineating the factors involved in the 1,2-elimination reaction of concern here.

The ion association is substantially weaker for salts of tetraalkylammonium ions than for metal ions. One ob-

(3) A Du Pont Zorbax ODS column (6.2 mm × 25 cm) was used in the ion-pair mode with 0.005 M tetrabutylammonium phosphate (PIC A, Waters Associates, or H_3PO_4 + Bu_4NOH) in methanol/water. The column was washed with 50% methanol in water to remove the salts and then used to purify a small amount (0.05 μmol) of *trans*-7,8-dihydroxy-7,8-dihydrobenzo[*a*]pyrene (1). The absorption spectrum of the major fraction was identical with the pure dihydro diol [λ_{max} 225, 245, 281, 293, 332 sh, 348, 366 nm (ε 50 500 at 366 nm)].[4] The sample was evaporated to dryness at 55 °C under a stream of dry nitrogen, leaving a dark red residue. The absorption spectrum indicated that the diol had decomposed and was later found to be nearly identical with a spectrum of 8-hydroxybenzo[*a*]pyrene [2; λ_{max} 263 sh, 278, 303 sh, 345 sh, 368, 381, 408 nm (ε 43 540 at 278 nm)]. Analysis of the residue by high-pressure liquid chromatography (HPLC) confirmed the presence of 2 as the major component along with smaller amounts of 7-hydroxybenzo[*a*]pyrene and unreacted 1. Retention times (*k'* values) were all identical with the standard synthetic derivatives. Mass spectral analysis of the residue gave a major ion at *m/z* 324, indicating butylation of the phenols (molecular ion at *m/z* 268). Analysis of the evaporation residue of the methanol wash (in the absence of the dihydro diol) gave a major ion at *m/z* 242, the molecular weight of the tetrabutylammonium ion. These same observations were made with the following columns: Spectra-Physics Spherisorb ODS (3 mm × 25 cm), Whatman Partisil ODS-2 (4.6 mm × 25 cm), and Waters μBondapak C_{18} (4 mm × 30 cm).

(4) S. K. Yang, H. V. Gelboin, J. D. Weber, V. Sankaran, D. L. Fischer, and J. F. Engel, *Anal. Biochem.*, 78, 520 (1977).

(5) J. W. Cook and R. Schoental, *J. Chem. Soc.*, 170–173 (1948).

(6) J. March, "Advanced Organic Chemistry: Reactions, Mechanisms, and Structure", McGraw-Hill, New York, 1968, p 753.

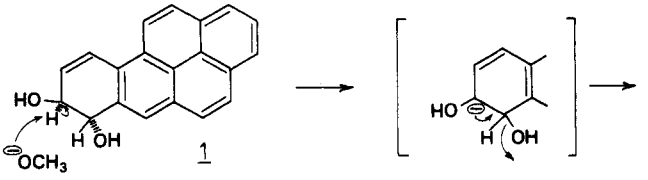
(7) S. J. Cristol, W. Barasch, and C. H. Tieman, *J. Am. Chem. Soc.*, 77, 583 (1955).

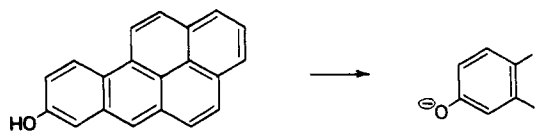
servation which supported this view was that dehydration was not observed when 1 (0.02 μmol) was treated with Bu_4NOH (0.2 μmol) in the presence of KCl (0.2 μmol). Upon evaporation, the potassium ions form strong ion pairs with hydroxide, as is the case with KOH. Thus, the concentration of "free" hydroxide is too low for dehydration to proceed. When the concentration of Bu_4NOH was increased, dehydration occurred. Winstein et al.[8] compared the reactivities of lithium and tetrabutylammonium halides in nucleophilic substitution reactions in acetone. Reaction rates for the latter were considerably higher due to less associated ion pairs.

There have been several reports on the use of crown ethers to solubilize alkali metal salts in solvents of low polarity.[9] When 1 (0.02 μmol) was treated with KOH (0.2 μmol) in the presence of 18-crown-6 (0.2 μmol), dehydration occurred, and the formation of 2 was confirmed by HPLC analysis and UV–vis spectroscopy. Sodium hydroxide did not dehydrate 1 in the presence of 18-crown-6. This is in agreement with the known fact that this particular crown ether complexes the sodium ion less efficiently.[10]

In contrast to acid-catalyzed dehydration, reactions with Bu_4NOH are dependent on the solvent. For example, when 1 was treated with Bu_4NOH in acetonitrile, dichloromethane, or tetrahydrofuran, dehydration was not observed. Addition of MeOH to these residues followed by evaporation at 60 °C resulted in dehydration. It is suggested that methoxide ion is formed from the reaction of hydroxide with MeOH and that methoxide ion is the actual dehydrating species. The formation of methoxide from KOH and MeOH has been reported.[9b] The absence of "free" anion (methoxide) can still be used to explain the lack of dehydration when the metal hydroxides are used. No dehydration occurred when 1 was treated with sodium methoxide in MeOH. Chemical characterization of methoxide ion was not performed. However, there was indirect evidence for its formation. For example, when 1 was treated with excess $NaOCH_3$ in the presence of Bu_4NCl, dehydration was observed.

It is suggested that the mechanism for this 1,2-elimination is analogous to that for the 1,4-elimination reported by Cristol.[7] In the case of 1, a proton is abstracted from





C(8) by methoxide ion with subsequent loss of the hydroxyl group from C(7) and formation of an aromatized molecule. The 8-benzo[a]pyrenolate ion is immediately formed in the presence of base, and since this anion is also dissociated, a highly visible chromophore is produced. The important requirement is that the methoxide ion be relatively dissociated. This obviously places limits on the type of cation that can be used. Thus this reaction would require a tetraalkylammonium methoxide or potassium methoxide/18-crown-6 in a nonpolar or aprotic solvent, resulting in dissociated ion pairs with little solvation of methoxide ion. It is relevant to note that earlier workers used crown ethers and quaternary ammonium salts in the phase-transfer-catalyzed dehydration of benzaldoxime with potassium salts, yielding benzonitrile and benzamide.[11]

Tetrabutylammonium 8-Benzo[*a*]pyrenolate. Compound 2 (0.02 μmol) was evaporated to dryness in the presence of Bu_4NOH (0.2 μmol) to leave a red residue. The absorption spectrum of the redissolved residue in MeOH is identical with that of 2 with the major absorption band at 277 nm. The addition of 0.02 mL of 1 N KOH or 1 N Bu_4NOH to this MeOH solution resulted in anion formation and a bathochromic shift (λ_{max} 294 nm). A spectrum of the residue in CH_2Cl_2 was also of the anion but with a further bathochromic shift (λ_{max} 323 nm). The color of the solutions was very light yellow, dark yellow, and light brown, respectively. The spectrum in MeOH/KOH is thought to be that of the solvated anion or solvent-separated ion pair, and the spectrum in CH_2Cl_2 is that of the unsolvated anion or contact ion pair.[12] The absorption spectra of other phenols in the presence of the same three solvents and reagents showed similar shifts of the major absorption band in the ultraviolet region. Some examples are 7-hydroxybenzo[a]pyrene (302, 317, 338 nm), 9-hydroxybenzo[a]pyrene (266, 268, 275 nm), 10-hydroxybenzo[a]pyrene (302, 323, 346 nm), 1-hydroxybenz[a]anthracene (308, 324, 336 nm), 3-hydroxybenz[a]anthracene (287, 303, 319 nm), and 9-hydroxybenz[a]anthracene (286, 296, 305 nm). Methylene chloride solutions of 1 or of benzo[a]pyrene in the presence of Bu_4NOH had spectra identical with those without Bu_4NOH. These spectra indicated that Bu_4NOH did not alter the absorption spectra of aromatic hydrocarbons by possible interaction with the extensive aromatic system. Shifts in absorption spectra of alkali salts of phenols have been observed,[13] and the use of solvents containing the tetrabutylammonium ion in the extraction of phenols has also been reported.[14]

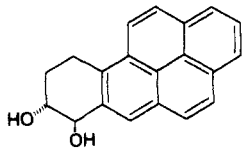
Decomposition of Tetrabutylammonium 8-Benzo[*a*]pyrenolate. As noted in the introduction, direct-probe mass spectral analysis of the unpurified dehydration residues of benzo[a]pyrene and of benz[a]anthracene dihydro diols gave major ions (m/z) that conformed well with butyl aryl ether structures. Separately, authentic 8-butoxybenzo[a]pyrene was prepared by treating 2 with *N,N*-dimethylformamide di-*n*-butyl acetal,[15] and this material was used for comparison.

Thus when 1 or 2 were treated with a methanolic solution of Bu_4NOH, followed by evaporation to dryness at 60 °C under a stream of dry nitrogen, 8-butoxybenzo[a]pyrene was not detected in either sample on analysis by HPLC. The residues were then heated at 150 °C for 15 min and analyzed. 8-Butoxybenzo[a]pyrene was now detected as

(8) S. Winstein, L. G. Savedoff, S. Smith, I. D. R. Stevens, and J. S. Gall, *Tetrahedron Lett.*, 24 (1960).
(9) (a) C. J. Pedersen, *J. Am. Chem. Soc.*, **92**, 391 (1970); (b) D. J. Sam and H. E. Simmons, *ibid.*, **96**, 252 (1974); (c) C. L. Liotta and H. P. Harris, *ibid.*, **96**, 2250 (1974).
(10) C. J. Pedersen and H. K. Frensdorff, *Agnew. Chem., Int. Ed. Engl.*, 11, 16 (1972).
(11) J. K. Rassmussen, *Chem. Lett.*, 11, 1295 (1977).
(12) T. E. Hogen-Esch and J. Smid, *J. Am. Chem. Soc.*, **88**, 307 (1966). The terms "contact" and "solvent separated" were used here to describe carbanion salts in solution.
(13) H. E. Zaugg and D. A. Schaefer, *J. Am. Chem. Soc.*, **87**, 1857 (1965).
(14) T. D. Doyle and J. B. Proctor, *J. Assoc. Off. Anal. Chem.*, **59**, 1175 (1976).
(15) H. Vorbruggen, *Angew. Chem. Int. Ed. Engl.*, **2**, 211 (1963).

the major compound in both samples. Therefore, the ethers are not formed under the conditions of dehydration but under conditions of solid-probe sample evaporation in the mass spectrometer. Similarly, the analogous alkyl aryl ethers were prepared by treating **2** with Et_4NOH for Me_4NOH at 150 °C for 20 min. Indeed, the thermal decompositon of tetrasubstituted ammonium aryl oxides to ethers has been reported previously,[16] and this type of alkylation has been utilized in the in situ derivatization of phenols and of carboxylic acids in gas chromatographic analyses.[17]

Treatment of Benzo[a]pyrene Tetrahydro Diols with Methanolic Tetrabutylammonium Hydroxide and Phosphoric Acid. *trans*-7,8-Dihydroxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene (**3**) and *trans*-9,10-dihydroxy-



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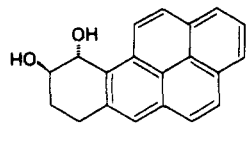

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7,8,9,10-tetrahydrobenzo[*a*]pyrene (**4**) were treated with Bu_4NOH followed by solvent evaporation at 60 °C, and dehydration was not observed. This suggested that methanolic Bu_4NOH would only dehydrate those diols which yield phenolic products. It is suggested that the methoxide-mediated dehydration of dihydro diols is facilitated by the formation of an energetically favorable aromatic system. Base dehydration of β-hydroxy ketones is a common reaction, again yielding a stable conjugated system. However, the conditions under which the hydroxy ketones are dehydrated (e.g., alcoholic $NaOCH_3$)[18] would not be suitable for dehydration of the dihydro diols as exemplified in Table I.

Conclusion

Methanolic tetrabutylammonium hydroxide is a potentially useful dehydrating reagent. The fact that regioselectivity may differ from acid dehydration would make Bu_4NOH a useful reagent in the analysis of dihydro diols of polycyclic aromatic hydrocarbons. In a recent study of benzo[*a*]pyrene metabolism, acid dehydration was highly regioselective.[19] Bu_4NOH would have provided sufficient amounts of all phenols for subsequent mass spectral analysis.

The lack of dehydration upon treatment of the tetrahydro diols with methanolic Bu_4NOH places limitations on the usefulness of the reagent. Some reactions such as dehydration of alcohols to alkenes may not be possible. However, this area requires more investigation.

The solubility of tetrabutylammonium phenoxides in dichloromethane could provide another use for the reagent as a qualitative tool in identifying phenols. Since spectral shifts are quite significant, its application in structure determination studies may be important.

The use of phosphoric acid provides an easy method for dehydration of dihydro diols since high yields of phenols are obtained under relatively mild conditions.

It is not clearly understood why the tetrabutylammonium ion continues to elute from reverse-phase HPLC columns long after washing with methanol/water.[3] There may be some type of adsorption or partitioning of the ion onto the packing material followed by gradual elution over a long period of time. The present study underscores the cautionary advice that mass spectrometry may give false structural information on chromatography eluates from liquid chromatography columns that had been pretreated with the tetraalkylammonium type of ion-pair reagents. In such instances phenols and aromatic dihydro diols may be falsely identified as alkyl aryl ethers.

Experimental Section

Materials. Synthetic benzo[*a*]pyrene and benz[*a*]anthracene derivatives were obtained through the National Cancer Institute Carcinogenesis Research Program and were synthesized under National Cancer Institute Contracts No. NO1-CP-33387 and NO1-CP-33385. Information on the availability of the derivatives can be obtained from the Information and Resources Segment.[21] Tetrabutylammonium phosphate (PIC A) was purchased from Waters Associates, Inc., tetraalkylammonium hydroxides (Bu_4NOH, Et_4NOH, and Me_4NOH) and spectroquality methanol and dichloromethane were purchased from Matheson Coleman and Bell, Co., *N,N*-dimethylformamide di-*n*-butyl acetal was purchased from Pierce Chemical Co., phosphoric acid and sodium methoxide were purchased from Fisher Scientific, and 18-crown-6 was purchased from Aldrich Chemical Co.

General Methods. HPLC analyses were performed on a Spectra-Physics Model 3500 liquid chromatograph and a Waters Associates Model 204 liquid chromatograph, both fitted with a Du Pont Zorbax ODS column (6.2 mm × 25 cm). Benzo[*a*]pyrene phenols were separated with $MeOH/H_2O$ (85/15) at 1.0 mL/min and benz[*a*]anthracene phenols with $MeOH/H_2O$ (75/25) at 1.0 mL/min. The alkyl aryl ethers were analyzed with 100% MeOH at 1.0 mL/min. UV–vis spectra were recorded with a Cary Model 15 spectrophotometer and mass spectra with a JEOL JMS-01SG-2 instrument at a 70-eV ionizing voltage in the electron-impact mode and using a solid probe at a temperature of 130–180 °C.

General Dehydration Procedure. To a methanol solution of Bu_4NOH (or H_3PO_4) was added the dihydro diol in MeOH, and the solution was evaporated to dryness in a tube (13 mm × 100 mm) at 60 °C under a stream of dry nitrogen. The nitrogen was left on for 1 min after the MeOH had evaporated to guarantee sufficient yield.[20]

8-Butoxybenzo[a]pyrene. To a solution of **2** (10.3 mg, 0.038 mmol) in dry pyridine (9 mL) was added *N,N*-dimethylformamide di-*n*-butyl acetal (1 mL at 2 mequiv/mL in pyridine) and the mixture refluxed for 1 h. After cooling, the solvent was evaporated under dry nitrogen, and the residue was purified by HPLC as described above: UV (MeOH) λ_{max} 261 sh, 277, 304 sh, 347, 379, 407 nm); mass spectrum, *m/z* (relative intensity) 325 (9), 324.1524 (34, m^+ calcd for $C_{24}H_{20}O_1$ 324.1514), 269 (15), 268 (61), 267 (4), 251 (4), 250 (10), 240 (25), 239 (100), 238 (18), 237 (24).

8-Alkoxybenzo[a]pyrenes from 8-Hydroxybenzo[a]pyrene. To a solution of R_4NOH (0.2 μmol) in MeOH was added **2** (0.02 μmol) in MeOH and the solution evaporated to dryness at 60 °C under a stream of dry nitrogen. The residue (tetraalkylammonium 8-benzo[*a*]pyrenolate) was heated at 150 °C for 20 min. The ethers were analyzed by HPLC as described.

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Registry No. **1**, 57404-88-3; **2**, 13345-26-1; 7-hydroxybenzo[*a*]pyrene, 37994-82-4; *trans*-9,10-dihydroxy-9,10-dihydrobenzo[*a*]pyrene, 58886-98-9; 9-hydroxybenzo[*a*]pyrene, 17573-21-6; 10-hydroxybenzo[*a*]pyrene, 56892-31-0; *trans*-1,2-dihydroxy-1,2-dihydrobenzo-

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(20) Dehydration did not occur until all of the solvent had evaporated. Therefore, the reaction is independent of the initial volume of the MeOH solution containing the reagent and dihydro diol.
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[a]anthracene, 60967-88-6; 1-hydroxybenzo[a]anthracene, 69847-26-3; 2-hydroxybenzo[a]anthracene, 69847-27-4; *trans*-3,4-dihydroxy-3,4-dihydrobenzo[a]anthracene, 60967-89-7; 3-hydroxybenzo[a]-anthracene, 4834-35-9; 4-hydroxybenzo[a]anthracene, 5133-12-0; *trans*-8,9-dihydroxy-8,9-dihydrobenzo[a]anthracene, 34501-24-1; 8-hydroxybenzo[a]anthracene, 34501-23-0; 9-hydroxybenzo[a]-anthracene, 34570-62-2; *trans*-10,11-dihydroxy-10,11-dihydrobenzo-[a]anthracene, 60967-90-0; 10-hydroxybenzo[a]anthracene, 69884-53-3; 11-hydroxybenzo[a]anthracene, 63019-35-2; 8-butoxybenzo-[a]pyrene, 78673-06-0; Bu_4NOH, 2052-49-5.

Reactions of Ketene Acetals. 13.[1] Synthesis of Contiguously Trihydroxylated Naphtho- and Anthraquinones

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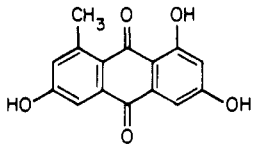
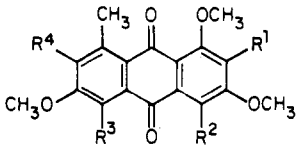
A regiospecific method of obtaining various quinones bearing at least three adjacent hydroxyl groups has been devised by using a new vinylketene acetal, 2-methoxy-1,1,3-tris(trimethylsiloxy)-1,3-butadiene (**9b**). In this way the first total syntheses of dermoglaucin (**50**) and ceroalbolinic acid, as its pentamethyl derivative **49**, have been achieved. The structure of another natural product, copareolatin dimethyl ether, was established indirectly by the unambiguous formation of one of the two possible isomers. Advantageous preparations of "7-hydroxyemodin", copareolatin, and isoerythrolaccin derivatives **32**, **38**, and **2**, as well as those of useful intermediates such as 2- and 3-chloro-5,7-dihydroxy-6-methoxynaphthoquinones or their dimethyl ethers, are described.

Some 1,2,3-trihydroxyanthraquinones such as "7-hydroxyemodin"[2] (**27**), isoerythrolaccin[2] (**44**) and copareolatin[3] (**37**) have been prepared by Friedel–Crafts-type condensations of the appropriate substrates; however, these reactions provide no regiochemical control over products and, except in the case of the parent compound anthragallol,[4] give complex mixtures in low yield. The method has limited value in establishing proof of structure, particularly if partially methylated substances are considered, and in one attempted synthesis[5] of ceroalbolinic acid gave only the wrong isomer.

A solution to some of the problems was proposed[6] recently and consists of the persulfate oxidation of a corresponding 1,3-dihydroxyanthraquinone. In this way "7-hydroxyemodin" was obtained from emodin with 20–33% conversion. When this method was applied to deoxyerythrolaccin (**1**), at least six products, besides starting



1



2 $R^1 = OCH_3$, $R^2 = R^3 = R^4 = H$

3 $R^1 = R^2 = H$, $R^3 = R^4 = OCH_3$

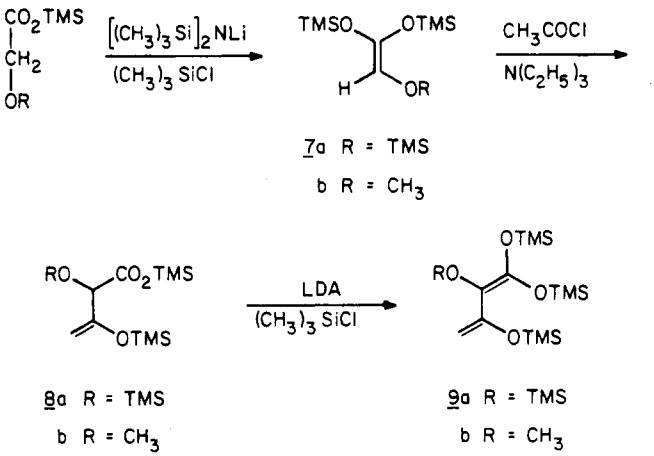
4 $R^1 = R^2 = R^4 = H$, $R^3 = OCH_3$

5 $R^1 = R^3 = R^4 = H$, $R^2 = OCH_3$

6 $R^1 = R^4 = H$, $R^2 = R^3 = OCH_3$

material (2%), were isolated after methylation of the crude mixture. Five of the compounds (as their permethylated derivatives) could be recognized as known substances or could readily be identified from their spectral characteristics: isoerythrolaccin, the desired product (**2**, 3%), 7-hydroxyerythrolaccin (**3**, 5%), erythrolaccin (**4**, 7%), 4-hydroxydeoxyethrythrolaccin (**5**, 8%), 4-hydroxyerythrolaccin (**6**, 3%), and a small amount of an unidentified compound. Since this reaction was carried out, the originators of the procedure have also applied it to deoxyerythrolaccin with unsatisfactory results.[6b]

Scheme I



7a R = TMS

b R = CH_3

8a R = TMS

b R = CH_3

9a R = TMS

b R = CH_3

An advantageous method of synthesis seemed available through the appropriate derivatives of vinylketene acetal since such dienes have recently been used efficiently, and in some cases regiospecifically, in reactions with quinones[7] and other dienophiles.[8] Various approaches to the elaboration of this type of synthon such as the preparation and dienolization of 2,3-dioxobutanal dimethyl acetal, the formation and electrocyclic ring opening of 1,2-bis(trimethylsiloxy)-3,3-dimethoxycyclobutene, or the synthesis and enolization of 2-oxo-3-methoxy-3-butenal dimethyl

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