stand at −20 °C for 12 h, then it was added to ether (ca. 100 mL) and the solution was washed with saturated aqueous $NaHCO_3$ (20 mL) once and with water (20 mL) three times. Removal of the ether layer and evaporation afforded the crude product (210 mg, 94%) as a straw-colored powder. It was recrystallized twice from ether at −20 °C and was further purified by column chromatography using TLC grade silica gel and CH_2Cl_2 and CH_2Cl_2–acetone (9:1) as eluting solvents. The **6** isolated in this manner was recrystallized twice from Et_2O to afford light straw-colored needles of mp 113.5–114 °C. Spectral data for **6** follow: NMR ($CDCl_3$, Me_4Si) δ 3.4 (3 H, s), 5.36 (2 H, s), 7.3–8.4 (8 H, m); UV (95% EtOH) λ_{max} (ϵ_{max}) 252 nm (1.47×10^5), 343 (6.8×10^3), 359 (1.0×10^4), 384 (3.9×10^3); IR (KBr) 3060 (w), 2990 (w), 2880 (w), 1620 (w), 1605 (w), 1550 (w), 1450 (w), 1090 cm^{-1} (s); mass spectrum (70 eV) *m/e* (rel abundance) 223 (M^+, base peak), 208 (18), 192 (86), 180 (47), 178 (10). Anal. Calcd for $C_{15}H_{13}NO$: C, 80.69; H, 5.87. Found: C, 80.49; H, 5.90.

Identification of the Amine Produced in Photolysis of 3. A 50-mL flask containing **3** (43.5 mg, 0.1 mmol) in 10 mL of anhydrous CH_3OH was deoxygenated and photolyzed for 30 min. An aliquot of the reaction mixture was removed and analyzed by TLC–UV, which indicated that the reaction was 92% complete. The remaining solution was concentrated to ca. 1 mL, and 0.2 N H_2SO_4 was added.[4] The solution was allowed to stand at room temperature for 30 min. The reaction mixture was neutralized with Na_2CO_3 and extracted with hexane. This procedure extracts the amine products relatively free of acridine products. The hexane extract was concentrated to 0.5 mL and was examined by GLC (6 ft × 0.125 in., 5% Apiezon L on 3% KOH-treated Chromosorb W 100/120, 175 °C). These conditions separate *N,N*-dimethyl-3-phenylpropylamine and *N*-methyl-3-phenylpropylamine. Only *N,N*-dimethyl-3-phenylpropylamine could be detected. Its yield was estimated at 76%, based upon comparison of peak areas resulting from three 1-μL injections of the hexane solution with three 1-μL injections of a standard hexane solution of the amine (11.7 mg/0.5 mL).

Photolyses of 9-Bromomethylacridine (1) and 9-(Methoxymethyl)acridine (6). Photolyses were effected under the conditions described for preparative scale photolysis of **2**. The reaction mixtures were analyzed by TLC and NMR. The NMR spectra of the mixtures produced in the photolyses of **1** and **6** were almost identical. In each instance, 9-(methoxymethyl)acridine was identified as the major constituent by its characteristic NMR absorptions at δ 3.40 (3 H, s) and 5.36 (2 H, s) and by its TLC R_f value of 0.51 in benzene–acetone (95:5). Furthermore, no absorption characteristic of the methyl group in 9-methylacridine (ca. δ 3.0)[22] was observed. Additionally, each mixture contained minor products tentatively identified as acridans derived from **6** by their characteristic TLC behavior, namely, their spots are initially nonfluorescent but, upon standing, exhibit the fluorescence characteristic of acridines.

Registry No.—**1**, 1556-34-9; **2**, 62509-60-8; **3**, 62509-61-9; **5**, 62509-62-0; **6**, 62509-63-1; *N,N*-dimethyl-3-phenylpropylamine, 1199-99-1.

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Synthesis of 4,5:11,12-Diepoxy-4,5,11,12-tetrahydrobenzo[*a*]pyrene and Related Compounds

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The synthesis of a new diepoxide of the carcinogen benzo[*a*]pyrene is described. This "K-region" diepoxide, 4,5:11,12-diepoxy-4,5:11,12-tetrahydrobenzo[*a*]pyrene (**7**), was obtained via the osmium tetroxide oxidation of the hydrocarbon. The syn and anti tetrols along with the substituted K-region isomer, i.e., 4,5,5a,6-tetrahydroxy-4,5,5a,6-tetrahydrobenzo[*a*]pyrene (**3**), obtained from this reaction were characterized. The syn and anti tetrols yielded the diepoxide using procedures described earlier. Compound **3** yielded an internal hemiacetal, **8**, upon oxidation with lead tetraacetate.

Benzo[*a*]pyrene (BaP) is a potent carcinogen and one of the most ubiquitous environmental pollutants.[1] It is now generally believed that aromatic hydrocarbon carcinogens such as BaP are metabolized to activated carcinogenic intermediates that subsequently bind to cellular constituents. In the metabolism of BaP the available evidence indicates that these intermediates are epoxides or related compounds.[2] The "K-region" [3] 4,5-epoxide of BaP has recently been shown to be the principal metabolite of BaP that covalently binds to microsomal proteins.[4] Recently it was reported that BaP-4,5-epoxide and BaP-11,12-epoxide were equally potent as mutagens in Chinese hamster V79 cells.[5] However, some studies have suggested that the intermediate which binds to DNA in vivo is the diol epoxide, 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene.[6]

Since polycyclic aromatic hydrocarbons may undergo me-

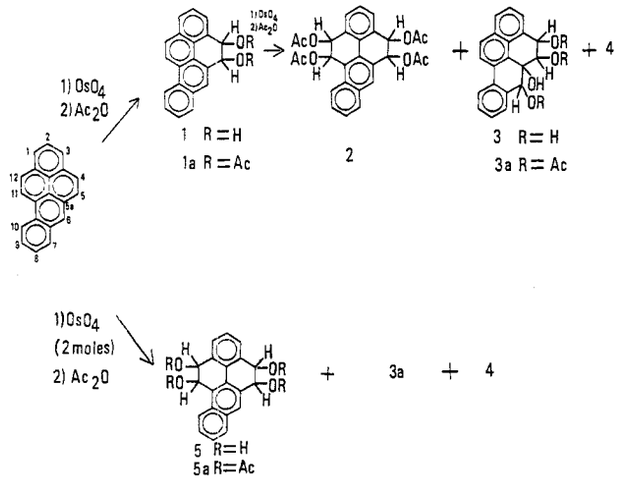
Table I. Pertinent NMR Data

Registry no.	Compound	Chemical shift, δ, ppm	No. of protons	Peak shape	Coupling constant, Hz	Assignment
56182-97-9	(1) 2-Phenylnaphthalene-1,2′,3,6′-tetracarboxaldehyde (6)	9.71	2	s		2′,6′-CHO
		9.83	1	s		3-CHO
		10.1	1	s		1-CHO
		7.7–9.2	8	m		Aromatic
56182-92-4	(2) *cis*-4,5-Diacetoxy-4,5-dihydro-BaP (1a)[11]	6.43	2	s		4 and 5
62533-85-1	(3) 4,5,11,12-Tetraacetoxy-4,5,11,12-tetrahydro-BaP (5a)	6.38	3	m	Part of AB	4,5,12
		7.08	1	d	11,12 = 4.5	11
62561-86-8	(4) 4,5,11,12-Tetraacetoxy-4,5,11,12-tetrahydro-BaP (2)	6.38	3	m	Part of AB	4,5,12
		7.17	1	d	11,12 = 4.5	11
62533-86-2	(5) 4,5,6-Triacetoxy, 5a-hydroxy-4,5,5a,6-tetrahydro-BaP (3a)	5.91	1	d	5,4 = 3	5 or 4
		6.18	1	s		6
		6.64	1	d	5,4 = 3	4 or 5
62533-87-8	(6) Internal hemiacetal (8a)	5.87	1	s		5a′ acetal H
		6.55	1	s		6 or 4
		6.67	1	s		4 or 6

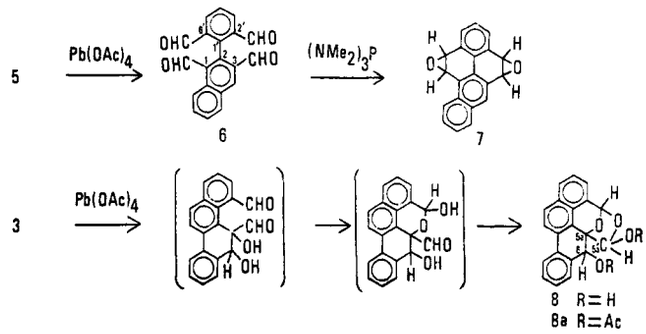
tabolism at multiple sites, one might expect that BaP and other hydrocarbons having two K regions may undergo oxidation at both sites by cytochrome P-450.[7] This report describes the synthesis of the K-region diepoxide of BaP, a bifunctional alkylating agent which is another possible activated carcinogenic intermediate of the hydrocarbon.

Results and Discussion

The tetraaldehydes required for the synthesis of K-region diepoxides of pyrene and dibenz[a,h]anthracene were obtained by ozonolysis of the respective hydrocarbons.[8] Ozonolysis of BaP, however, yielded a mixture of quinones rather than the required aldehydes. Moriconi et al.[9] experienced similar difficulties. In the present work the tetraaldehyde, **6**, was obtained from the corresponding tetrol **5**. BaP was oxidized sequentially first to *cis*-4,5-dihydroxy-4,5-dihydrobenzo[a]pyrene (1) which was acetylated to yield **1a**. Treatment of **1a** with a second mole of osmium tetroxide yielded



a mixture of products. The mixture, after acetylation and chromatography, yielded compounds **2**, **3a**, and a small amount of an unknown compound, **4**. Compounds **2** and **3a** were isolated in almost equal amounts, indicating that the 11,12 position (K region) and the 5a,6 position (substituted K region) were equally susceptible to oxidation after the initial substitution at 4,5 position. Direct oxidation of BaP with 2 mol of osmium tetroxide yielded an unknown compound **4**, isolated as the tetraacetate, and the tetrols **3** and **5**. Tetrol **5** was acetylated to the tetraacetate **5a**, which was the syn or anti isomer of **2**. When a benzene–pyridine solution of **5** was stirred with lead tetraacetate, 2-phenylnaphthalene-1,2′,3,6′-tetracarboxaldehyde **6** was isolated. Tetrol **3**, however, upon oxi-



dation with lead tetraacetate under identical conditions, gave the stable internal hemiacetal **8**. Freshly distilled Mark's reagent[10] (tris(dimethylamino)phosphine) cyclized the tetraaldehyde **6** to the diepoxide **7**.

The isolation of the tetraaldehyde **6** has previously been reported by Harvey et al.[11] We have verified its structure based on the following data. Structure **6** is the only possible tetraaldehyde isomer which contains no olefinic hydrogens as seen by the lack of resonance absorption characteristics of such protons in the NMR spectrum (Table I). Both the tetraacetates **2** and **5a**, after hydrolysis to tetrols and subsequent oxidation, furnished the tetraaldehyde **6**. Thus, **2** and **5a** are stereoisomers having acetoxy groups at 4,5 and 11,12 positions. Oxidation with osmium tetroxide imparts cis stereochemistry to the vicinal acetoxy groups,[12] pairs of which may be syn or anti with respect to one another. The conclusion that **2** and **5a** are syn and anti isomers is supported by their similar UV absorption and mass spectral fragmentation patterns (Table II). They had similar R_f values on TLC, but their mixed melting point was depressed. Both **2** and **5a** had a one-proton doublet in the NMR spectrum at δ 7.08 and 7.17, respectively. These signals are tentatively assigned to the 11 proton in **2** and **5a** which is downfield from the three-proton multiplet at δ 6.38 assigned to protons 4, 5, and 12. This has been reported as typical of a benzylic proton located on a bay position.[13] The coupling constant J = 4.5 Hz further confirms the cis stereochemistry of the vicinal acetoxy groups in compounds **2** and **5a**.[13d]

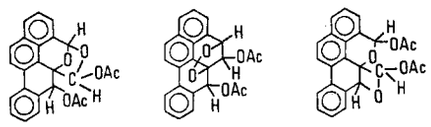
One of the hydroxyl groups of the tetrol **3** was found to be tertiary as evidenced by acetylation which yielded a triacetoxy derivative **3a**. This was confirmed by IR and NMR spectra of **3a**. The sharp singlet at δ 6.18 in the NMR indicated a benzylic proton not adjacent to another proton. This could occur only with hydroxyl substitution at position 6. The tertiary hydroxyl in compound **3** was assigned the 5a position based on the chemical-shift difference of the 4,5-benzylic protons in **3a** (0.73 ppm) as compared with those in **1a** (0.0 ppm),[11] which

Table II. Ultraviolet Absorption Spectra

Registry no.	Compd	λ_{max}, nm (EtOH) (ϵ)
	2-Phenylnaphthalene-1,2′,3,6′-tetracarboxaldehyde (6)	231 (sh), 254, 310, 326 (sh) (41 712, 34 570, 6952, 6510)
62533-88-4	4,5,11,12-Tetrahydroxy-4,5,11,12-tetrahydro-BaP (5)	236 (sh), 244, 253, 262, 272, 297, 308, 322, 347 (21 120, 18 176, 21 184, 36 672, 47 424, 9856, 12 864, 11 392, 1024)
	4,5,11,12-Tetraacetoxy-4,5,11,12-tetrahydro-BaP (5a)	220, 243 (sh), 253, 262, 273, 297, 309, 322 (29 475, 20 008, 25 083, 45 188, 58 169, 11 419, 14 054, 11 810)
	4,5,11,12-Tetraacetoxy-4,5,11,12-tetrahydro-BaP (2)	234 (sh), 243 (sh), 251, 260, 270, 297 (sh), 308, 322, 346 (49 483, 40 992, 45 823, 84 765, 116 534, 24 448, 30 451, 26 205, 2050)
62533-89-5	4,5,5a,6-Tetrahydroxy-4,5,5a,6-tetrahydro-BaP (3)	230, 240 (sh), 250 (sh), 259, 269, 286, 298, 310, 323 (21 248, 20 352, 24 832, 39 680, 52 864, 8192, 10 880, 12 864, 10 240)
	4,5,6-Triacetoxy,5a-hydroxy-4,5,5a,6-tetrahydro-BaP (3a)	230, 238 (sh), 249 (sh), 258, 268, 285 (sh), 297, 309, 321 (26 314, 21 586, 24 976, 47 454, 67 792, 8741, 12 309, 15 075, 11 685)
62586-45-2	BaP tetraacetate (4)	228, 237, 249 (sh), 258, 268, 301 (sh), 312, 325, 341 (sh) (25 473, 22 155, 24 888, 44 017, 57 779, 10 345, 12 395, 9076, 1464)
62533-90-8	Internal hemiacetal (8)	228 (sh), 239, 249, 258, 268, 286 (sh), 297, 309, 322 (21 465, 19 795, 23 452, 47 541, 65 269, 7314, 10 494, 13 594, 11 368)
	Diacetoxy derivative of internal hemiacetal (8a)	226, 238, 248, 257, 267, 297, 308, 322 (27 175, 23 557, 27 175, 54 833, 73 807, 11 577, 15 517, 12 783)
62533-91-9	4,5,11,12-Diepoxy-4,5,11,12-tetrahydro-BaP (7) (solvent CH_2Cl_2)	256, 266, 277, 310, 315, 321, 329, 354 (22 720, 40 157, 55 436, 10 337, 11 189, 10 678, 10 394, 1136)

indicates an inductive effect of a proximate hydroxyl group on the 5 proton. Furthermore, **1a** may be viewed as a substituted chrysene and, as such, osmium tetroxide oxidation would be expected at the K-region positions 5a and 6 as well as 11, 12. Similar results have been reported by Jerina et al. in the oxidation of 4,5-dihydrobenzo[*a*]pyrene with osmium tetroxide.[12b]

Compound **8**, obtained by lead tetraacetate oxidation of tetrol **3**, had no carbonyl absorptions in the IR. The UV spectrum of the acetylated product **8a** was similar to that of **2** and **3a** and remained unchanged upon addition of dilute acid or base. It had two acetoxy groups as confirmed by its mass spectrum and NMR, and did not show OH absorption in the IR. Examination of its NMR spectrum revealed the presence of three sharp singlets at δ 5.87, 6.55, and 6.67. These data are consistent with the three possible structures **8a, 8b,** and **8c.**



The diacetate of **8** gave a negative peroxide test. This fact along with its acid stability rules out a peroxide function group such as **8b.** Structure **8c** contains a four-membered cyclic acetal which is less likely to be formed compared with the five-membered cyclic acetal in **8a.** Thus, the chemical and spectral data are satisfactorily explained by structure **8a.** Such internal acetals, for example, the internal dimethyl acetal from 4,5-chrysenedicarboxaldehyde, are quite stable to acid,[11] a behavior common to that observed for **8a.**

Compound **4** exhibited a mass spectral parent ion at *m/e* 488 as well as four methyl peaks in the NMR, indicating that it is an isomer of **2** and **5a.** Its complete structure remains to be elucidated.

The structure of the diepoxide **7** was established by the presence of a mass spectral parent ion, *m/e* 284, the absence of hydroxyl and carbonyl absorptions in the IR, UV absorption pattern comparable to that of **5a,** its NMR spectrum, and C,H analysis. This compound was found to be photochemically unstable. Analogous behavior was observed earlier for the DBA diepoxide[8] as well as the pyrene mono- and diepoxide.[8,14]

The diepoxide, **7**, has not yet been detected in metabolic studies of BaP. However, development of improved chromatographic techniques and the availability of pure reference compounds has led to the isolation and definitive identification of many metabolites, such as benzo[*a*]pyrene 4,5-epoxide[15] and 7,8,9,10-tetrahydroxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene.[16] The synthesis and characterization of new potentially activated intermediates such as **7** and its derivatives described here are useful in the further elucidation of BaP metabolism and the mode of action of this carcinogen.

Experimental Section

Melting points were taken on a Thomas-Hoover capillary apparatus and are uncorrected. Infrared spectra were determined on a Perkin-Elmer Model 421 spectrophotometer as KBr pellets, and ultraviolet spectra with a Cary Model 14. Proton magnetic resonance spectra were recorded on Varian Associates Models T-60A and EM-390 spectrometers with Me_4Si as an internal standard and $CDCl_3$ as solvent unless otherwise indicated. High-resolution ^1H NMR spectra were recorded with a Varian SC-300 spectrometer. Mass spectra were obtained with a Du Pont Model 21-492 double-focusing high-resolution mass spectrometer. The samples were introduced through a direct inlet. Microanalyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. TLC was carried out on precoated silica gel G plates in solvent systems A (CH_2Cl_2:acetone, 24:1) and B (CH_2Cl_2:CH_3OH, 9:1); spots were visualized with short- and long-wavelength UV lamps. Most of the compounds reported are sensitive to photooxidation and precautions were taken to prevent such degradation.

4,5,11,12-Tetrahydroxy-4,5,11,12-tetrahydrobenzo[*a*]pyrene (5), 4,5,5a,6-Tetrahydroxy-4,5,5a,6-tetrahydrobenzo[*a*]pyrene (3), and Compound 4. OsO_4 (2.0 g, 2 mmol) dissolved in 15 mL of freshly distilled dry pyridine was added to a solution of BaP (1.0 g, 1 mmol) in 25 mL of pyridine. The resulting dark-brown solution was stirred for 12 days under N_2. An additional amount of OsO_4 (0.35 g) was added and stirring was continued for another 4 days. A solution of sodium bisulfite (4 g) in 60 mL of water was then added to the reaction mixture and stirred for 4 h. The resulting mixture was extracted several times with CH_2Cl_2 (500 mL), and the organic layer was then washed with water and flash evaporated under reduced pressure to remove CH_2Cl_2 and pyridine. The residue (residue A), when macerated with 75 mL of CH_2Cl_2, gave a reddish solid (0.87 g) which was filtered and the filtrate was discarded. The reddish solid (0.2 g) was then refluxed with 300 mL of CH_2Cl_2 and filtered. The residue and the filtrate (filtrate B) thus obtained were worked up separately. Repeated crystallization of the residue from THF and hexane yielded white compound **5** (0.05 g): mp 246–248 °C dec; IR 3340 cm^{-1} (OH, vs); mass spectrum *m/e* (rel intensity) 320 (5), 255 (2), 71 (89), 32 (24), 28 (100); TLC R_f 0.43 in solvent-system B. Its acetylation with an Ac_2O–pyridine mixture for 18 h at room temperature followed by Florisil chromatography employing CH_2Cl_2/hexane (9:1) as the eluent afforded colorless prisms **5a** (from CH_2Cl_2–hexane): mp 240–242 °C; IR 1748, 1731 cm^{-1} (C=O); NMR δ 1.91 (s, 6 H), 2.26 (s, 6 H), ($C_{4,5}$

and $C_{11,12}$ $COCH_3$), 6.38 (m, 3, $H_{4,5,12}$), 7.08 (d, 1H,H_{11}; $J_{H_{11,12}}$ = 4.5 Hz), 7.27–8.0 ppm (m, 8 H, aromatic); mass spectrum (rel intensity) 488 (56), 386 (54), 327 (26), 326 (25), 285 (100), 284 (98), 268 (23), 267 (26), 255 (23), 239 (22), 143 (12). Anal. Calcd for $C_{28}H_{24}O_8$: C, 68.85; H, 4.95. Found: C, 68.68; H, 4.81. TLC R_f 0.71 in solvent system A.

The filtrate B on concentration to a small volume followed by filtration gave a residue which crystallized from excess CH_2Cl_2 as colorless needles, **3** (0.07 g): mp 153–155 °C dec; IR 3540, 3350 (vs), 3050, 1585, 1470 cm^{-1}; mass spectrum *m/e* (rel intensity) 320 (39), 302 (15), 285 (37), 256 (15), 255 (45), 86 (39), 84 (73), 49 (100). TLC R_f 0.37 in solvent system B. It was acetylated with an Ac_2O–pyridine mixture.[11] The product **3a** was purified by Florisil chromatography with CH_2Cl_2/CH_3OH (1:1) as eluent. The acetate **3a** crystallized from CH_2Cl_2–hexane as colorless flakes: mp 230–232 °C dec; IR 1750 cm^{-1} (C=O); NMR δ 1.80 (s, 3 H), 2.20 (s, 3 H), 2.30 (s, 3 H) ($C_{5,6,4}COCH_3$), 2.60 (s, 1 H, $C_{5a}OH$, chemical shift variable, exchangeable with D_2O), 5.91 (d, 1 H, H_5; $J_{4,5}$ = 3 Hz), 6.18 (s, 1 H, H_6), 6.64 (d, 1 H, H_4; $J_{5,4}$ = 3 Hz), 7.13–7.91 ppm (m, 9 H, aromatic); mass spectrum *m/e* (rel intensity) 446 (10), 369 (11), 327 (43), 326 (14), 285 (49), 284 (100), 268 (57), 267 (20), 255 (40), 239 (26). Anal. Calcd for $C_{26}H_{22}O_7$: C, 69.95; H, 4.97. Found: C, 69.92; H, 4.91. TLC R_f 0.38 in solvent system A.

Acetylation of residue A with Ac_2O–pyridine afforded on repeated chromatography and fractional crystallizations **5a** and **3a** in almost equal amounts as the major components. A very small amount of another tetraacetate, **4**, was also isolated along with **5a**. They were separated by preparative thick-layer chromatography in solvent system A. Compound **4** crystallized from CH_2Cl_2–hexane as colorless thin plates: mp 202–205 °C dec; IR 1752, 1740 (sh) cm^{-1} (C=O); NMR δ 1.62 (s, 3 H), 1.83 (s, 3 H), 2.20 (s, 3 H), 2.30 (s, 3 H) ($C_{4,5}COCH_3$ and 2 $COCH_3$), 5.25 (d, 1 H; *J* = 2 Hz), 6.14 (d, 1 H; *J* = 3.5 Hz), 6.46 (m, 2 H), 7.11–7.92 ppm (m, 8 H, aromatic); mass spectrum *m/e* (rel intensity) 488 (0.4), 370 (25), 369 (14), 327 (41), 326 (18), 285 (34), 284 (100), 269 (33), 268 (98), 267 (17), 239 (25); TLC R_f 0.59 in solvent-system A.

4,5,11,12-Tetraacetoxy-4,5,11,12-tetrahydrobenzo[a]pyrene (2), 3a, and 4. Osmium tetroxide (0.484 g) dissolved in 3 mL of pyridine was added to a solution of 1a[11] (0.712 g) in 15 mL of dry pyridine. The brown solution was stirred at room temperature for 5 days under nitrogen atmosphere. It was then treated with a solution of sodium bisulfite (2 g) in 40 mL of water and the mixture stirred for 4 h. Ice-cold water was added and the precipitate that separated was filtered and washed with water. The filtrate was extracted with chloroform and the residue obtained on evaporation of the solvent was combined with the precipitate. The combined dried product was acetylated using acetic anhydride (40 mL) and dry pyridine (5 mL) and worked up as usual. The residue thus obtained was dissolved in benzene and chromatographed on Florisil. Initial fractions eluted with benzene/hexane (7:3) contained mostly the unreacted diacetate (0.3 g). Benzene eluted tetraacetate **2** (0.18 g) along with orange-colored quinones. Finally, benzene/methanol (1:3) eluted a colorless compound (0.1 g) which, on further purification, was found to be identical with **3a** (mixture melting point, IR, UV).

Rechromatography of the benzene fraction on Florisil and elution with benzene/methanol (19:1) afforded the tetraacetate **2** along with a small amount of **4**: mp 202–205 °C dec. The two compounds were separated by preparative thick-layer chromatography in solvent-system A. The tetraacetate **2** was crystallized from CH_2Cl_2–hexane as colorless prisms: mp 258–260 °C; IR 1750, 1735 cm^{-1} (C=O); NMR δ 1.93 (s, 3 H), 1.97 (s, 3 H), 2.28 (s, 3 H), 2.34 (s, 3 H) ($C_{4,5,12,11}COCH_3$), 6.38 (m, 3 H, $H_{4,5,12}$), 7.17 (d, 1 H, H_{11}; $J_{11,12}$ = 4.5 Hz), 7.32–8.28 ppm (m, 8 H, aromatic); mass spectrum *m/e* (rel intensity) 488 (82), 428 (20), 387 (26), 386 (91), 327 (21), 326 (27), 285 (97), 284 (100), 268 (30), 255 (18). Anal. Calcd for $C_{28}H_{24}O_8$: C, 68.85; H, 4.95. Found: C, 68.98; H, 4.90. TLC R_f 0.63 in solvent-system A. Its mixture melting point with **5a** was depressed to 223–226 °C and also its cochromatography with **5a** resulted in two spots in the above solvent system.

2-Phenylnaphthalene-1,2′,3,6′-tetracarboxaldehyde (6) and Compound (8). A solution of the tetrol **5** (0.32 g, 1 mmol) in 100 mL of 1:1 benzene/pyridine was stirred with $Pb(OAc)_4$ (1.0 g, 2 mmol) at room temperature for 4 h. Water (50 mL) was added and the solution extracted with 250 mL of CH_2Cl_2. The extract was dried and flash evaporated to remove all the solvents. The residue was chromatographed over Florisil and eluted with CH_2Cl_2/hexane (4:1). The eluate, on concentration and addition of hexane, furnished creamy-white flakes, **6** (0.22 g): mp 191–192 °C (lit.[11] mp 191–192 °C); IR 2855, 2752 (C–H stretch), 1697, 1672 cm^{-1} (C=O); NMR δ 7.7–9.2 (m, 8 H, aromatic), 9.71 (s, 2 H, 2′,6′-CHO), 9.83 (s, 1 H, 3-CHO), 10.1 ppm (s, 1 H, 1-CHO); mass spectrum 316 (parent ion). Anal. Calcd for $C_{20}H_{12}O_4$: C, 75.94; H, 3.82. Found: C, 75.83; H, 3.88. TLC R_f 0.63 in solvent-system A.

4,5,11,12-Tetraacetoxy-4,5,11,12-tetrahydrobenzo[a]pyrene (2) when hydrolyzed with NH_4OH in THF–CH_3OH for 48 h with stirring and the dried residue subsequently oxidized with $Pb(OAc)_4$ as given above, also yielded the tetraaldehyde **6** (TLC, IR, UV, mixture melting point).

The tetrol **3** (0.32 g) on oxidation with $Pb(OAc)_4$ under identical conditions and workup gave a white residue which was purified by eluting the Florisil column with CH_2Cl_2. It crystallized from THF–hexane as tiny clusters of colorless needles, **8** (0.21 g): 211–213 °C dec; IR 3375, 3270 (vs), 1480, 1437 cm^{-1}; mass spectrum *m/e* (rel intensity) 318 (12), 288 (21), 287 (100), 271 (12), 270 (34). TLC R_f 0.08 in solvent-system A and R_f 0.65 in solvent system B. Its acetylation with an acetic anhydride–pyridine mixture followed by Florisil chromatography with CH_2Cl_2 as the eluent afforded colorless flakes, **8a** (from CH_2Cl_2–hexane): mp 219–221 °C; IR 1754, 1731 cm^{-1} (C=O); NMR δ 1.83 (s, 3 H), 2.14 (s, 3 H) ($C_{5a'}$ acetal CH_3 and C_6COCH_3), 5.87 (s, 1 H), 6.55 (s, 1 H), 6.67 (s, 1 H) ($H_{5a'}$ acetal, H_6, H_4), 7.18–7.98 ppm (m, 9 H, aromatic); mass spectrum *m/e* (rel intensity) 402 (2), 315 (5), 314 (27), 256 (42), 255 (100), 226 (19), 128 (20). Anal. Calcd for $C_{24}H_{18}O_6$: C, 71.64; H, 4.54. Found: C, 71.11; H, 4.48. TLC R_f 0.76 in solvent system A. Its solution in methanol gave no color with aqueous potassium iodide.

4,5:11,12-Diepoxy-4,5,11,12-tetrahydrobenzo[a]pyrene (7). The tetraaldehyde **6** (0.15 g) in 8 mL of dry benzene was refluxed with 0.5 mL of freshly distilled tris(dimethylamino)phosphine for 1 h. The brown solution was concentrated by N_2 stream to 4 mL. On addition of a few drops of hexane, greenish-yellow crystals separated out. The diepoxide was recrystallized from a dioxane–hexane mixture as tiny pale-yellow needles (0.015 g, 11.2%): mp 207–209 °C dec; IR 1470, 1233, 1208, 1062, 812, 781, 753 cm^{-1}; NMR (CD_2Cl_2) 4.56 (d, 1 H), 4.68 (q, 2 H), 5.16 (d, 1 H) (oxirane $H_{4,5,11,12}$; *J* = 4 Hz), 7.47–8.5 ppm (m, 8 H, aromatic); mass spectrum *m/e* (rel intensity) 284 (85), 269 (25), 268 (100), 255 (12), 239 (33), 142 (12), 134 (16), 119 (28), 118 (15). Anal. Calcd for $C_{20}H_{12}O_2$: C, 84.49; H, 4.25. Found: C, 84.33; H, 4.27. TLC R_f 0.63 in cyclohexane/dioxane (6:4).

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Thermal Isomerization of Heterofulvenes. Dynamic Nuclear Magnetic Resonance Study

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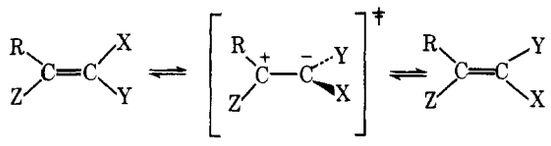
The dynamic behavior of heterofulvenes, derivatives of 2,6-dimethyl-γ-pyrone, -γ-thiopyrone, and *N*-butyl-2,6-dimethyl-γ-pyridone (IV), were investigated by variable temperature NMR technique. The observed process is the thermal isomerization about the exocyclic double bond of the above compounds. In each case the substituents on the exocyclic double bond are two different electron-withdrawing groups (NO_2, $COCH_3$, CO_2CH_3, $CONH_2$, CN) and H. The NMR line shape of the chemically nonequivalent H-3 and H-5 was studied. Complete line analysis was carried out on methyl 2,6-dimethyl-d_6-4*H*-pyran-4-ylidenenitroacetate (2) in HMPT-d_{18} and acetonitrile-d_3. A pronounced decrease in the enthalpy of activation ($\Delta\Delta H^{\ddagger}$ = 3.2 kcal/mol) was found in acetonitrile as compared to HMPT. The low entropies of activation (−21.7 and −27.4 eu) indicate extensive charge separation in the transition state for the isomerization process. The rate constants at the coalescence temperature for 22 additional compounds were determined, and the corresponding rate constants at 298 K were evaluated by applying the entropies found in the total line shape analysis experiments. This allows for the comparison of rate and activation data for the various compounds at a standard temperature. The isomerization was found to be moderately accelerated by polar solvents with a maximum rate enhancement factor of 80. The reaction rate is sensitive to the nature of the exocyclic substituents in three measurable series. The rates are enhanced in the order of the σ_R^- values of the substituents with a ρ value of ca. 8. The hetero ring atoms were found to accelerate the isomerization in the decreasing order of N > S > O which is at variance with previous results in similar, but acyclic, systems.

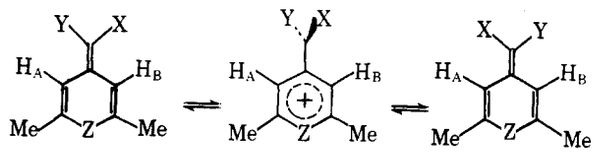
It has been demonstrated by us,[1] and also by others,[2,3] that some olefins may be thermally isomerized at rates which are on the NMR time scale. The double bond of such an olefin (I) is polarized by electron-withdrawing groups (X, Y), and an electron-releasing group (Z). The rates of the isomerization about the C=C double bond (I ⇌ III) were found to be ex-



I II III

tremely sensitive to structural factors.[1] Generally, this was taken as an indication that a charged transition state of type II is involved in the process. Approximate structure–reactivity relationships support the dipolar nature of the transition state (II).[1]

The present work concerns the dynamic behavior of an interesting structural variant of I, namely, the heterofulvene of type IV. If IV isomerizes by the same mechanism as I, then the

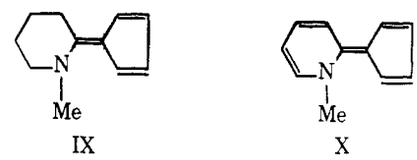


IV V VI

X, Y = CN, CO_2Me, COMe, $CONH_2$, NO_2, H
Z = S, O, N-Bu

thermal transition state V, analgous to II, may be invoked. Such a transition state is unique in that it creates an empty p orbital on C-4 which may now induce a cyclic delocalization of the 6π electrons of the heterocyclic ring. Since the corresponding charged heterocycles, pyrylium, pyridinium, and thiopyrylium cations exhibit extra stability, it would be of interest to find out whether the transition state (V) would respond to the potential stabilization of the 6π electrons, absent in the acyclic transition state II. Calculations (MINDO/2) by Dewar[4] of rotational barriers about the carbon–carbon double bond in methylenecyclopropene systems also bear on the above-mentioned point.

Experimental results which shed light on this phenomenon can be found in the NMR work of Crabtree and Bartelli.[5] These authors have studied the systems IX and X where both



IX X

E_a = 19.6 kcal/mol E_a = 11.4 kcal/mol

termini of the double bond are incorporated into rings, which, in the transition state for isomerization about the C=C double bond, can be described as aromatic. Thus the difference in E_a for the thermal isomerization about the exocyclic double bond between IX and X reflects, in the author's opinion, the extra stability which is due to the formation of the pyridinium ring in the transition state. Although the difference (8.2 kcal/mol) is substantial, it amounts to only ca. ¼ of the resonance energy of pyridinium. This deficiency in stabilization was attributed to the extra energy required for charge separation in the transition state.

The work which is most closely related to the present one, although limited in scope, is that of Seitz et al.[6] and Jackman et al.[3] The results are summarized in Table I. For both XIb