lowed to dry overnight. The product gave the following spectral data: ^{1}H NMR (C_6D_6) δ 1.28 (36 H), 1.30 (18 H), 1.51 (18 H), 5.16 (2 H), 7.37 (4 H), 7.67 (2 H), 7.86 (2 H); ir (CCl_4) 3600, 3550, 1600, 1580 cm^{-1}; mass spectrum *m/e* 866 (M^+), 851, 824, 809, also minor peaks at 884 (M + H_2O), 890 (3 + $2H_2O$); uv–visible λ_{max} (CCl_4) 265 nm (log ϵ 3.51), 387 (4.63), 404 sh (4.56), 440 sh (4.41). Calcd for $C_{60}H_{82}O_4$: *m/e* 866.6213. Found: 866.6206.

Electron Spin Resonance Experiments. Anion Radical of 3. A few milligrams of **3** with a small amount of $(n\text{-Bu})_4N^+ClO_4^-$ was placed in an electrolytic cell. A small piece of glass wool was placed between the electrodes to slow diffusion. The cell was evacuated and THF (distilled from $LiAlH_4$, stored over Na–K anthracene) was distilled into the cell. The solution was degassed twice and the cell was placed in the ESR cavity. A minimal current was passed through the cell and scanning was begun.

The best spectrum was obtained by electrolytic reduction at room temperature of a sample which had been reduced several times before, and observation at 0° using the line-sharpening technique devised by Glarum.[12] The spectrum showed a_H = 0.33 G and g = 2.0054, with a ratio of line intensities 70:55.6:28.3:9.1 (calcd for nine lines 70:56:29:8).

Monoradical of 4 (9). 3 as Oxidizing Agent. **3** (8.2 mg), 8.7 mg of **4** (1:1 molar ratios), and 2 g of naphthalene were ground together in a mortar and pestle and a small amount of this mixture was placed in an ESR cell. The cell was twice alternately evacuated and flushed with nitrogen, leaving 1 atm of nitrogen in the cell. (A previous experiment showed this technique was necessary to prevent loss of resolution and signal level.) No signal from this solid mixture was evident at room temperature or until it melted at about 90°. A weak five- or seven-line pattern was then observed and better resolved with the line-sharpening technique devised by Glarum.[12] The signal level increased (reversibly) with temperature up through 180°. The sample was opened to the air momentarily at 140 and 170° (with no loss of signal) to prevent undue build-up of pressure.

PbO_2 as Oxidizing Agent. **4** (6 mg) and 2 mg of PbO_2 were weighed together and manually mixed with a spatula. Approximately ⅓ of this mixture was placed in an ESR cell with about 1 ml of dry xylene. The cell was degassed twice and then nitrogen was added. A weak signal (like the signal observed with **3** as oxidizing agent) was observed at 90°. As the temperature was increased, the signal level increased reversibly up to 135° (bp of xylene 137–140°).

In both this experiment and the previous one, a_H = 1.17 G, g = 2.0051, with a ratio of line intensities 20:14.5:5.7:1.2 (calcd for seven lines, 20:15:6:1).

Base Titrations of 4. NaOH–CH_3CN Titration. A 0.04 *N* NaOH solution and a 300-ml solution of 52 mg of **4** in CH_3CN were used; 0.5-ml aliquots of base were added to the CH_3CN solution of **4**, and samples were withdrawn for uv–visible spectrum and returned after each addition. After the addition of about 1 equiv, the isosbestic point was lost and the spectrum changed, indicating that reaction had taken place.

Potassium *tert*-Butoxide–THF Titration. A solution of 20.3 mg of **4** in 300 ml of dry THF was titrated with a solution of 122.2 mg of potassium *tert*-butoxide in 100 ml of dry THF, as previously described. After addition of about 1 equiv of base the isosbestic was again lost. Evidently **4** also reacts with *tert*-butyl alcohol.

DBN–THF Titration. A solution of 22.7 mg of **4** in 300 ml of dry THF was titrated with 21.6 mg of DBN in 100 ml of THF using the same procedure. This time the isosbestic points at 522 and 300 nm persisted throughout the titration. After 2 equiv of base had been added, the new dianion peak stopped growing appreciably but the absorption due to **4** continued to diminish slightly after each addition even after five times the theoretical amount was added. The dianion has λ_{max} 640 nm (log ϵ 4.80), 393 (3.41), 370 (3.43). After standing overnight, the solution gave an altered spectrum, e.g., the main band was weaker and appeared at 630 nm instead of 640 nm indicating that the DBN–H^+ salt of the dianion is not indefinitely stable.

Acknowledgment. This work was supported by Grant GP32081 from the National Science Foundation.

Registry No.—**3**, 34879-70-4; **3** radical ion, 55255-32-8; **4**, 55255-35-1; **5**, 14106-40-2; **6a**, 55281-78-2; **6b**, 55255-36-2; **9**, 55255-37-3; **10**, 55255-31-7.

References and Notes

(1) R. West and D. C. Zecher, *J. Am. Chem. Soc.*, **92**, 155 (1970).
(2) D. C. Zecher and R. West, *J. Am. Chem. Soc.*, **89**, 153 (1967).
(3) S. Koster and R. West, *Chem. Commun.*, 1380 (1971).
(4) H. O. Hartzler, *J. Am. Chem. Soc.*, **88**, 1966 (1966).
(5) B. Heinrich and A. Roedig, *Angew. Chem., Int. Ed. Engl.*, **7**, 375 (1968).
(6) V. N. M. Rao, J. Calabrese, S. Koster, and R. West, *Acta Crystallogr.*, in press.
(7) J. Calabrese, A. Tullnsky, R. Vandlen, V. N. M. Rao, and R. West, *Acta Crystallogr.*, in press.
(8) S. Hauff and A. Rieker, *Tetrahedron Lett.*, 1451 (1972).
(9) R. West and D. C. Zecher, *J. Am. Chem. Soc.*, **92**, 161 (1970).
(10) Preceding paper in this issue: R. West, S. K. Koster, D. C. Zecher, and D. Eggerding.
(11) D. C. Zecher, Ph.D. Thesis, University of Wisconsin, Madison, Wis., 1967.
(12) S. H. Glarum, *Rev. Sci. Instrum.*, **36**, 771 (1965).

Synthesis of Heterofulvenes—Derivatives of 9-Alkylenexanthenes by the Friedel–Crafts Reaction, Accompanied by Halide Exchange

Itshak Granoth,* Lea Gradovski, and Rivka Alkabets

Israel Institute for Biological Research, Ness-Ziona, Israel

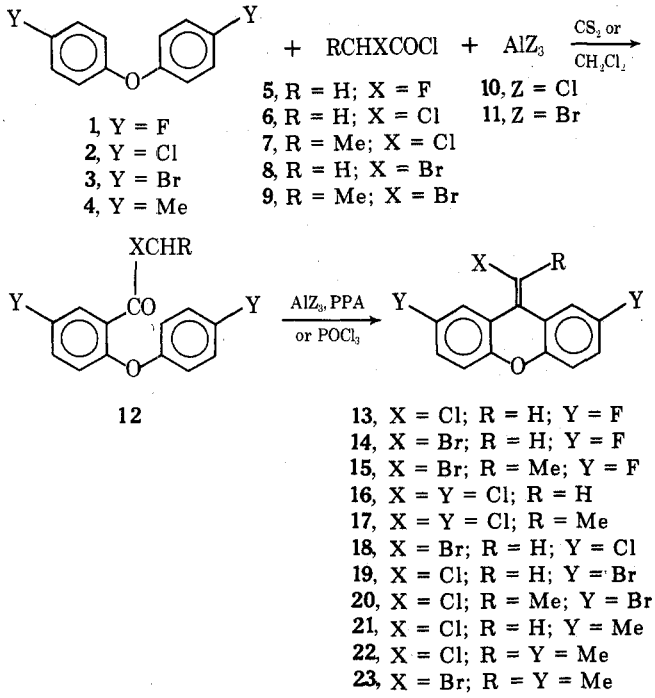
Received December 10, 1974

11-Chloro- and 11-bromo-9-alkylenexanthenes can be prepared from aromatic ethers and 2-haloacyl chlorides in the presence of aluminum halides. In some cases, halide exchange occurs between the haloacyl compounds and the aluminum halides. Occasionally, intermediate ketones are obtained and can be transformed to the final products by heating with phosphorus oxychloride or polyphosphoric acid. 9-Methylenexanthenes can be similarly synthesized.

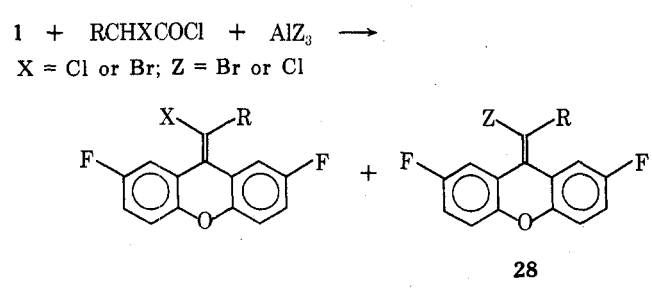
9-Alkylenexanthenes, such as **13**, are π-isoelectronic with the corresponding thioxanthenes and dibenzoheptafulvenes,[1,2] and consequently are of both biological and theoretical interest. In fact, it has been suggested that the 9-alkylenexanthenes are more "heptafulvenic" in nature than the dibenzoheptafulvenes.[3,4] Only one general approach to the synthesis of these olefins exists to date, namely, the reaction of xanthen-9-one with Grignard reagents, followed by dehydration.[5] However, this and the Wittig reaction[6] were found unsatisfactory for the preparation of 9-methylenexanthene.

We would like to report a convenient procedure for the synthesis of 9-alkylenexanthenes, such as **13** or **25**, using the aluminum halide catalyzed condensation of aromatic ethers **1–4** and acyl chlorides[7] illustrated in Scheme I. This approach is especially suited for the preparation of 11-chloro- and 11-bromo-9-alkylenexanthenes **13–23**. Halide exchange between the 2-haloacyl compounds **5–9** or **12** and

Scheme I



Scheme II



the aluminum halides **10** and **11** occurs when X ≠ Z. (See Scheme II.)

The intermediate ketones **12** (R = H) were usually not isolated, as they cyclized in situ, giving the final products. Occasionally, these ketones were obtained and converted to the product olefins by brief boiling with phosphorus oxychloride. The same treatment, or alternatively heating with polyphosphoric acid (PPA), completed the cyclization of **12** (R = Me), in which case **10** is usually ineffective for the cyclization. Aluminum bromide (**11**) is superior for this latter step. It appears that the halide X in **12** facilitates the aluminum halide induced cyclization of these ketones, possibly by enhancing the enolization of **12** as compared with **24**. Thus, acetyl chloride yields mainly (80–98%) the ketones **24** when employed according to Scheme I. The latter ketones are best transformed to the appropriate 9-methylenexanthenes **25–27** by heating them for 1 hr with freshly prepared PPA at 100–110° under N_2. The lack of an 11 substituent in these heterofulvenes[8] renders them highly sensitive to air oxidation,[9] yielding eventually the corresponding xanthen-9-ones.

Surprisingly, the 11-fluoro analog of **13** could not be obtained. Whenever fluoroacetyl chloride (**5**) was used according to Scheme I, total fluoride exchange with **10** or **11** took place, leading finally to **13** and **14**, respectively. This phenomenon is independent of the solvent. Partial chlorination during Friedel–Crafts fluoroacetylation of benzene in the presence of aluminum chloride has been recorded.[10] However, this has been a side reaction which could be eliminated[10] by use of dichloromethane as the solvent. The halide exchange observed in all the other reactions studied, i.e., where X ≠ F or Z, was incomplete, giving a mixture of 11-halo-9-alkylenexanthenes, as shown in Scheme II.

Generally, bromination by **11** proceeds to a greater extent than chlorination by **10** (see Table I). In two reactions, those of **1** and **2** with **8** in the presence of **10**, the chlorination is negligible. The halide exchange involves **5–9** or possibly **12**, but not the final products, since prolonged heating of the reaction mixture does not increase the halide exchange degree. In conclusion, pure **13–23** must be prepared from 2-haloacyl chlorides and aluminum halides containing the same halogens. Halide exchange degrees during the Friedel–Crafts haloacylations of **1** are given in Table I.

Table I
Halide Exchange Degrees during Haloacylations of 1

Starting materials		
RCHXCOCl	AlZ_3	Exchange degree, %
5	10	100
5	11	100
6	11	37
8	10	0
9	10	25
7	11	50

The relatively facile fluoride exchange with the aluminum halides could be due to the Lewis acid induced polarization of the carbon–fluorine bond.[11] Alternatively, simple metathesis reaction could have occurred between the aluminum halides and the haloacyl compounds, competing with the Friedel–Crafts acylation. This is in accord with the soft–hard acid–base concept,[12] since the harder the base (the smaller the halide), the greater its affinity to the hard Lewis acid **10** or **11**. Consequently, the observed relative reactivities of the halides in the haloacyl groups studies (F > Cl > Br) could be expected.

The 9-halomethylenexanthenes, e.g., **14**, are partly decomposed by light or heating at ca. 150° into intense red products which have not been identified. The homologs, such as **15**, are more stable. All these exocyclic olefins are oxidized by potassium permanganate, yielding the corresponding xanthen-9-ones.[7]

Product mixtures (Scheme II) were identified by NMR spectroscopy, using the different chemical shifts of H-8 and H-11 in the 11-chloro- and 11-bromo-9-alkylenexanthenes. The deshielding of H-8, arising from the long-range electrical effect[13] of the vinylic halide, is greater for Br than for Cl. Consequently, H-8 in **14**, e.g., resonates at a lower field than H-8 in **13**. (See Experimental Section.) A similar effect is observed for R = H (H-11) or Me in **13–23**. The differences in the corresponding chemical shifts of the latter protons, which are influenced directly by the vinylic halides, are greater than those associated with H-8.

All the new compounds obtained in this study were also characterized by mass spectrometry. The molecular ions

are always observed as the typical isotope peak patterns. In some of the mass spectra they are not the most intense peaks.

Experimental Section

Melting points were taken with a Thomas-Hoover Unimelt apparatus and are uncorrected. Uv spectra were recorded for solutions in 96% ethanol with a Bausch and Lomb Spectronic 505 instrument. NMR spectra were run for solutions in $CDCl_3$ with Me_4Si as internal standard with a Jeol C-60 HL high resolution spectrometer. Mass spectra were obtained with a Hitachi Perkin-Elmer RMU 6 spectrometer at 70 eV, using the direct insertion probe and a source temperature of 120–180°. The aromatic ethers and haloacyl chlorides used in this study were either commercially available or prepared as described elsewhere.[14,15]

General Procedure for the Condensation of Aromatic Ethers with Haloacyl Chlorides. The haloacyl chloride **5–9** (0.11 mol) was added rapidly to a mechanically stirred mixture of carbon disulfide (or dichloromethane) (250 ml), the aromatic ether (**1–4**) (0.1 mol), and the aluminum halide (**10** or **11**) (0.13 mol). The mixture was refluxed for 5 hr, cooled, and decomposed with ice–water. The organic layer and a $CHCl_3$ extract (if needed) yielded, after evaporation, a crude product which was examined by NMR. The mixture obtained upon incomplete cyclization was heated for 1 hr with phosphorus oxychloride (150 ml) (R = H; X = Cl or Br) or PPA (200 ml) at 100–110°. Finally, decomposition of the reaction mixture with ice–water and extraction with $CHCl_3$ afforded the appropriate 9-alkylenexanthene **13–23.**

2,7-Difluoro-9-chloromethylenexanthene[7] **(13)** was prepared from **1, 5,** and **10** (60%): mp and mmp 147°; NMR δ 6.48 (1 H, s, H-11), 7.05 (5 H, m, HAr), 8.09 (1 H, m, H-8).

Anal. Calcd for $C_{14}H_7ClF_2O$: C, 63.5; H, 2.6; Cl, 13.4. Found: C, 63.6; H, 2.6; Cl, 13.5.

2,7-Difluoro-9-bromomethylenexanthene (14) was prepared from **1, 8,** and **10** (40%) and also from **1, 5,** and **11** (45%): mp 142° (EtOH); NMR δ 6.61 (1 H, s, H-11), 7.10 (5 H, m, HAr), 8.17 (1 H, m, H-8); λ_{max} 240 nm (sh, ε 11,300), 263 (5600), 290 (sh, 3300), 338 (9500).

Anal. Calcd for $C_{14}H_7BrF_2O$: C, 54.4; H, 2.3; Br, 25.9; F, 12.3. Found: C, 54.6; H, 2.5; Br, 25.4; F, 12.6.

11-Bromo-2,7-difluoro-9-ethylidenexanthene (15) was prepared from **1, 9,** and **11** (45%): mp 163° (EtOAc); NMR δ 2.8 (3 H, s, Me), 7.37 (5 H, m, HAr), 8.09 (1 H, m, H-8); λ_{max} 254 nm (sh, ε 7100), 286 (2580), 321 (7750).

Anal. Calcd for $C_{15}H_9BrF_2O$: C, 55.7; H, 2.8; Br, 24.8; F, 11.8. Found: C, 55.5; H, 2.7; Br, 24.6; F, 12.0.

2,7,11-Trichloro-9-methylenexanthene (16) was prepared from **2, 6,** and **10** (42%): mp 105° (EtOH); NMR δ 6.55 (1 H, s, H-11), 7.32 (5 H, m, HAr), 8.34 (1 H, d, H-8).

Anal. Calcd for $C_{14}H_7Cl_3O$: C, 56.5; H, 2.4; Cl, 35.8. Found: C, 56.4; H, 2.4; Cl, 35.5.

2,7,11-Trichloro-9-ethylidenexanthene (17) was prepared from **2, 7,** and **10** (40%): mp 173° (EtOAc); NMR δ 2.49 (3 H, s, Me), 7.15 (5 H, m, HAr), 7.90 (1 H, d, H-8); mass spectrum *m/e* (rel intensity) 310 (87, M^+), 275 (44), 250 (60), 239 (100), 205 (53).

Anal. Calcd for $C_{15}H_9Cl_3O$: C, 57.8; H, 2.9; Cl, 34.1. Found: C, 57.8; H, 3.0; Cl, 34.1.

2,7-Dichloro-9-bromomethylenexanthene (18) was prepared from **2, 8,** and **10** (52%): mp 113° (EtOH); NMR δ 6.61 (1 H, s, H-11), 7.20 (5 H, m, HAr), 8.49 (1 H, d, H-8); mass spectrum *m/e* (rel intensity) 340 (64, M^+), 233 (13), 226 (26), 197 (10), 164 (13).

Anal. Calcd for $C_{14}H_7BrCl_2O$: C, 49.1; H, 2.1. Found: C, 49.2; H, 2.3.

2,7-Dibromo-9-chloromethylenexanthene (19) was prepared from **3, 6,** and **10** (45%) mp 128° (EtOAc); NMR δ 6.52 (1 H, s, H-11), 7.27 (5 H, m, HAr), 8.55 (1 H, d, H-8); λ_{max} 250 nm (sh, ε 11,200), 264 (sh, 7760), 294 (sh, 3100), 339 (6900); mass spectrum *m/e* (rel intensity) 384 (45, M^+), 270 (16), 163 (47), 162 (14), 113 (16).

Anal. Calcd for $C_{14}H_7Br_2ClO$: C, 43.5; H, 1.8. Found: C, 43.4; H, 1.8.

11-Chloro-2,7-dibromo-9-ethylidenexanthene (20) was prepared from **3, 7,** and **10** (35%): mp 163° (EtOH–EtOAc); NMR δ 2.50 (3 H, s, Me), 7.30 (5 H, m, HAr), 8.16 (1 H, d, H-8); λ_{max} 255 nm (ε 12,050), 290 (2720), 323 (6220); mass spectrum *m/e* (rel intensity) 398 (33 M^+), 284 (30), 283 (48), 205 (100), 176 (32).

Anal. Calcd for $C_{15}H_9Br_2ClO$: C, 44.9; H, 2.3. Found: C, 44.7; H, 2.3.

2,7-Dimethyl-9-chloromethylenexanthene (21) was prepared from **4, 6,** and **10** (70%): oil; NMR δ 2.14 (3 H, s, Me-2), 2.20 (3 H, s, Me-7); 6.07 (1 H, s, H-11), 6.72 (5 H, m, HAr), 7.85 (1 H, m, H-8).

This compound was further characterized by oxidation[7] with $KMnO_4$ to 2,7-dimethylxanthen-9-one, which was identical with an authentic sample,[16] mp and mmp 140°.

11-Chloro-2,7-dimethyl-9-ethylidenexanthene (22) was prepared from **4, 7,** and **10** (40%): mp 94° (EtOH); NMR δ 2.38 (6 H, s, MeAr), 2.52 (3 H, s, Me-11), 7.16 (5 H, m, HAr), 7.88 (1 H, m, H-8); mass spectrum *m/e* (rel intensity) 270 (100, M^+), 255 (31), 235 (45), 220 (24), 219 (54).

Anal. Calcd for $C_{17}H_{15}ClO$: C, 75.4; H, 5.5; Cl, 13.1. Found: C, 75.4; H, 5.7; Cl, 13.1.

11-Bromo-2,7-dimethyl-9-ethylidenexanthene (23) was prepared from **4, 9,** and **11** (45%): mp 93° (EtOH); NMR δ 2.37 (3 H, s, Me-2), 2.38 (3 H, s, Me-7), 2.73 (3 H, s, Me-11), 7.10 (5 H, m, HAr), 7.93 (1 H, m, H-8); mass spectrum *m/e* (rel intensity) 314 (80, M^+), 235 (79), 234 (40), 220 (52), 219 (100).

Anal. Calcd for $C_{17}H_{15}BrO$: C, 64.8; H, 4.8; Br, 25.4. Found: C, 64.9; H, 4.8; Br, 25.4.

Preparation of Substituted 9-Methylenexanthenes (25–27). These olefins were prepared as described above for the 11-halogenated derivatives, using aluminum chloride and acetyl chloride instead of the haloacyl chloride. However, the primary products were mixtures of the ketones **24** (80–98%) and the desired olefins (20–2%). These ketones were characterized by ^1H NMR, and then heated for 1 hr with a freshly prepared solution of P_2O_5 (160 g) and H_3PO_4 (200 ml) at 100–110° under N_2. Hydrolysis with ice–water (600 ml) followed by filtration yielded the appropriate **25–27.** When the cyclization reaction was conducted without an inert atmosphere, the 9-methylenexanthenes were heavily contaminated with the corresponding xanthen-9-ones. These olefins could not be recrystallized without partial oxidation, excluding the 2,7-dibromo derivative. Consequently, only the latter gave satisfactory combustion analysis. The other derivatives were characterized by their NMR and mass spectra, and by oxidation to the corresponding xanthen-9-ones by $KMnO_4$.[7]

2,7-Difluoro-9-methylenexanthene (25). The ketone **24** (Y = F) contained 20% of the desired **25,** when prepared from **1** and AcCl: NMR δ 2.65 (3 H, s, Me), 7.20 (7 H, m, HAr). Cyclization of this mixture afforded **25** (Y = F) (60%): mp 84–86°; NMR δ 5.50 (2 H, s, H-11), 7.10 (4 H, m, HAr), 7.40 (2 H, m, H-1 and 8). Oxidation of this olefin with $KMnO_4$[7] yielded 2,7-difluoroxanthen-9-one, mp and mmp[7] 170° (EtOH).

2,7-Dimethyl-9-methylenexanthene (27). The ketone **24** (Y = Me) had NMR δ 2.30 (6 H, s, MeAr), 2.64 (3 H, s, MeCO), 7.22 (7 H, m, HAr).

This ketone was transformed to the olefin (50%): mp 85° (EtOH); NMR δ 2.31 (6 H, s, Me), 5.48 (2 H, s, H-11), 7.05 (4 H, m, HAr), 7.50 (2 H, m, H-1 and -8). $KMnO_4$ oxidation[7] of this compound gave 2,7-dimethylxanthen-9-one, mp and mmp 140° (EtOH).[15]

2,7-Dibromo-9-methylenexanthene (26). The ketone **24** (Y = Br) was prepared from **3** and AcCl. The NMR spectrum showed peaks at δ 2.65 and 2.68 (3 H, two s, Me), 7.70 (7 H, m, HAr).

The desired olefin was obtained after the polyphosphoric acid treatment (50%): mp 150° (EtOAc); NMR δ 5.68 (2 H, s, H-11), 7.22 (2 H, d, H-4 and -5), 7.68 (2 H, dd, H-3 and -6), 8.10 (2 H, d, H-1 and -8); mass spectrum *m/e* (rel intensity) 350 (50, $M^{\cdot+}$), 192 (46), 164 (29), 163 (69), 162 (12). Anal. Calcd for $C_{14}H_8Br_2O$: C, 47.7; H, 2.3; Br, 45.5. Found: C, 47.5; H, 2.4; Br, 45.7.

Registry No.—**1,** 330-93-8; **2,** 2444-89-5; **3,** 2050-47-7; **4,** 1579-40-4; **5,** 359-06-8; **6,** 79-04-9; **7,** 7623-09-8; **8,** 22118-09-8; **9,** 7148-74-5; **10,** 7446-70-0; **11,** 7727-15-3; **13,** 37611-30-6; **14,** 55517-16-3; **15,** 55517-17-4; **16,** 55517-18-5; **17,** 55517-19-6; **18,** 55517-20-9; **19,** 55517-21-0; **20,** 55517-22-1; **21,** 55517-23-2; **22,** 55517-24-3; **23,** 55517-25-4; **24** (Y = F), 55517-26-5; **24** (Y = Me), 55517-27-6; **24** (Y = Br), 55517-28-7; **25,** 55164-23-3; **26,** 55164-25-5; **27,** 55164-24-4.

References and Notes

(1) E. D. Bergmann, *Chem. Rev.*, **68,** 41 (1968).
(2) J. F. Liebman, *J. Chem. Educ.*, **48,** 188 (1971).
(3) E. D. Bergmann, E. Fischer, Y. Hirschberg, D. Lavie, B. Pullman, and D. Shapiro, *Bull. Soc. Chim. Fr.*, **19,** 262 (1952).
(4) H. C. Longuet-Higgins, *Trans. Faraday Soc.*, **45,** 173 (1949).
(5) E. D. Bergmann, G. Berthier, E. Fischer, Y. Hirschberg, D. Lavie, A. Pullman, and B. Pullman, *Bull. Soc. Chim. Fr.*, **18,** 693 (1951).
(6) I. Granoth, unpublished results.

(7) I. Granoth and A. Kalir, *J. Org. Chem.*, **38**, 841 (1973).
(8) I. Belsky, H. Dodiuk, and Y. Shvo, *J. Org. Chem.*, **39**, 989 (1974).
(9) E. D. Bergmann and M. Rabinovitz, *J. Org. Chem.*, **25**, 828 (1960).
(10) F. Bergmann and A. Kalmus, *J. Am. Chem. Soc.*, **76**, 4137 (1954).
(11) J. F. Liebman and T. H. Vanderspurt, *J. Fluorine Chem.*, **2**, 413 (1972–1973).
(12) T-L. Ho, *Chem. Rev.*, **75**, 1 (1975).
(13) R. F. Zurcher in "Nuclear Magnetic Resonance in Chemistry", B. Pesce, Ed., Academic Press, New York, N.Y., 1965, p 45.
(14) I. Granoth, A. Kalir, Z. Pelah, and E. D. Bergmann, *Tetrahedron*, **26**, 813 (1970).
(15) F. L. Pattison, R. R. Fraser, J. C. Middleton, J. C. Schneider, and J. B. Stothers, *Can. J. Technol.*, **34**, 21 (1956).
(16) I. Granoth and H. J. Pownall, *J. Org. Chem.*, **40**, 2088 (1975).

Synthesis of Diepoxides and Diphenol Ethers of Pyrene and Dibenz[*a,h*]anthracene

S. C. Agarwal and B. L. Van Duuren*

Laboratory of Organic Chemistry and Carcinogenesis, Institute of Environmental Medicine, New York University Medical Center, New York, New York 10016

Received March 18, 1975

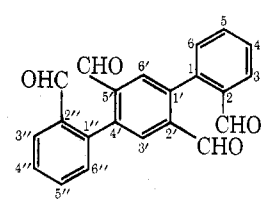
The diepoxides, 4,5,9,10-diepoxytetrahydropyrene and 5,6,12,13-diepoxytetrahydrodibenz[a,h]anthracene, were synthesized from the parent hydrocarbons via their respective diozonides and tetraaldehydes. Both epoxides were converted to diphenols; because of the instability of the diphenols they were converted to and characterized as phenol ethers. The two diphenol ethers derived from diepoxydibenz[a,h]anthracene were characterized as 5,12-dimethoxydibenz[a,h]anthracene and 6,13-dimethoxydibenz[a,h]anthracene. All of these compounds are new with the exception of 5,12-dimethoxydibenz[a,h]anthracene. These epoxides and their diphenols are important in chemical carcinogenesis studies.

Naphthalene epoxide is the first aromatic hydrocarbon epoxide to be synthesized and shown to be a metabolite in a biological system.[1] Since then a number of monoepoxides of carcinogenic hydrocarbons have been synthesized;[2] recently the synthesis of the monoepoxide of the noncarcinogenic hydrocarbon, pyrene, was also reported.[3] The metabolism of both pyrene and the carcinogen dibenz[a,h]anthracene has been studied in detail[4] and several phenolic metabolites of both hydrocarbons have been reported.[4] The definitive isolation of their mono- or diepoxides from in vivo or in vitro biological systems has, however, not been accomplished.[5] It has been shown, however, that 5,6-epoxydibenz[a,h]anthracene has weak tumor-inducing activity.[6]

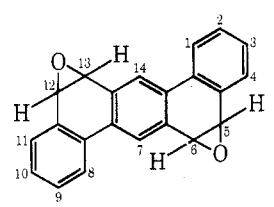
The continued interest in mechanism of action and metabolism of aromatic hydrocarbons[7] prompted the synthesis of diepoxides of pyrene and of the carcinogen dibenz[a,h]anthracene, since these diepoxides are expected to play a role in the biologic activity of the hydrocarbons. In the present work, the phenol ethers formed from the diepoxides upon acid-catalyzed rearrangement and methylation are described and compared with the known metabolic products.

The general procedure of Newman and Blum[8] was used to convert the dialdehydes to the epoxides using Mark's reagent,[9] i.e., tris(dimethylamino)phosphine. The required precursor for the synthesis of 5,6,12,13-diepoxytetrahydrodibenz[a,h]anthracene is *p*-terphenyl-2,2′,5′,2″-tetracarboxaldehyde (1), which has been reported.[10] However, the reported product was not identical with the completely characterized product obtained in this work. Ozonization of a dilute solution of dibenz[a,h]anthracene in anhydrous CH_2Cl_2 at −70° with 2 molar equiv of ozone gave predominantly the 5,6,12,13-diozonide of the parent hydrocarbon. This was shown by the alkaline hydrogen peroxide oxidation of the diozonide to the known 2,2′,5′2″-tetracarboxy-*p*-terphenyl.[10] The diozonide on reduction with sodium iodide in acetic acid afforded an aldehyde, mp 234–236°, in good yield. The product reported earlier[10] had mp >360°. Based on its uv absorption at 296 and 233 nm, ir bands at 3.46, 3.61, and 5.93 μ, mass spectrum and C, H analysis it was characterized as the tetraaldehyde **1**. When refluxed with tris(dimethylamino)phosphine in dry benzene, the tetraaldehyde was converted to the diepoxide **2**, the structure of which was confirmed by spectral and combustion analyses. Additional support for its structure was provided by the comparison of its ultraviolet spectrum with that of 5,6,12,13-tetrahydrodibenz[a,h]anthracene.[11] In both compounds there is restricted rotation of the benzene rings and therefore they have similar uv absorption spectra which are, however, quite different from that of *p*-terphenyl.

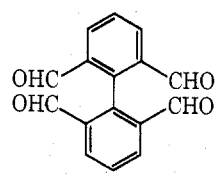
The acid-catalyzed rearrangement of the diepoxide **2** could lead to three isomeric diphenols, i.e., 6,13-dihydroxy, 5,13-dihydroxy-, and 5,12-dihydroxydibenz[a,h]anthracene. Two of the methyl ethers derived from these phe-



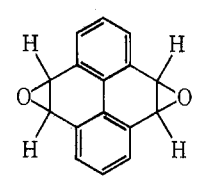
1



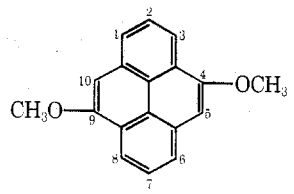
2



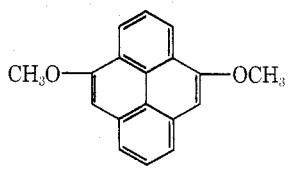
3



4



5



6