into 50 mL of cold 10% HCl, stirred with a layer of pentane, and allowed to warm to 26 °C. After 3 h, the pentane layer was removed and the aqueous layer extracted with pentane. The combined pentane solutions were analyzed by VPC and the heptanal, benzaldehyde, and *N*-heptyl-*N*-(3-hydroxyphenyl)triflamide products were isolated by drying the pentane and removing in vacuo. The pentane extracts from the N-benzylated meta reaction contained no product; thus, the aqueous phase was extracted with $MeCl_2$. These organic extracts were then dried and concentrated to the crude product.

***N*-Heptyl-*N*-(4-acetoxyphenyl)triflamide.** The reaction gave a 76% yield of heptanal. The isolated material had spectral properties identical with an authentic sample.

***N*-Benzyl-*N*-(4-acetoxyphenyl)triflamide.** The reaction yielded 80% benzaldehyde, the material isolated having spectral properties identical with literature.

***N*-Heptyl-*N*-(3-acetoxyphenyl)triflamide.** The reaction gave *N*-heptyl-*N*-(3-hydroxyphenyl)triflamide in 100% yield after purification by preparative TLC (25% ether in petroleum ether). Spectral properties were identical to those of an authentic sample.

***N*-Benzyl-*N*-(3-acetoxyphenyl)triflamide.** The reaction yielded 97% *N*-benzyl-*N*-(3-hydroxyphenyl)triflamide after purification by preparative TLC (50% ether in petroleum ether). Spectral properties were identical to those of an authentic sample.

Acknowledgment. We wish to thank Professor James B. Hendrickson for his helpful discussion in the preparation of this manuscript. We also wish to thank McCormick & Co., Baltimore, Md. for their generous support of this work.

Registry No.—*N*-Phenyltriflamide, 456-64-4; *m*-aminophenol, 591-27-5; *p*-aminophenol, 123-30-8; triflic anhydride, 358-23-6.

References and Notes

(1) This work was done in partial fulfillment of a degree at the University of Maryland.
(2) W. W. Epstein and F. W. Sweat, *Chem. Rev.*, **67**, 247 (1967).
(3) V. J. Traynelis and R. H. Ode, *J. Org. Chem.*, **35**, 2207 (1970).
(4) A. Markovac, C. L. Stevens, A. B. Ash, and B. E. Hackley, *J. Org. Chem.*, **35**, 841 (1970).
(5) T. M. Santosusso and D. Swern, *Tetrahedron Lett.*, 4261 (1978).
(6) J. R. Pakkh and W. von E. Doering, *J. Am. Chem. Soc.*, **89**, 5505 (1967).
(7) R. E. Harman, C. V. Zenarosa, and S. K. Gupta, *J. Org. Chem.*, **35**, 1936 (1970).
(8) W. W. Epstein and J. Ollinger, *Chem. Commun.*, 1338 (1970).
(9) J. M. Epstein and J. Ollinger, *Chem. Commun.*, 1338 (1970).
(10) D. P. Bauer and R. S. Macomber, *J. Org. Chem.*, **40**, 1990 (1975).
(11) J. B. Hendrickson, R. Bergeron, A. Giga, and D. Sternbach, *J. Am. Chem. Soc.*, **95**, 3412 (1973).
(12) J. B. Hendrickson and R. Bergeron, *Tetrahedron Lett.*, 3839 (1973).
(13) J. B. Hendrickson, R. Bergeron, and D. D. Sternbach, *Tetrahedron*, **31**, 2517 (1975).
(14) J. B. Hendrickson, K. W. Bair, R. Bergeron, A. Giga, P. L. Shapper, D. D. Sternbach, and J. A. Wareing, *Org. Prep. Proced. Int.*, **9** (11), 173 (1977).
(15) J. B. Hendrickson, D. D. Sternbach, and K. W. Bair, *Acc. Chem. Res.*, **10**, 306 (1977).
(16) J. Bunnett, *Angew. Chem., Int. Ed. Engl.*, **1**, 222 (1962).
(17) T. Cuvigny, *C. R. Hebd. Seances Acad. Sci.*, **240**, 206 (1955).
(18) R. W. Wynn and A. H. Corwin, *J. Org. Chem.*, **15**, 203 (1950).

Phenylcinnamalones. 4. An Oxidation Reaction[1]

Robert G. Brown,[2b,3] L. Guy Donaruma,* [2a–c,3] Ronald A. Kropf,[2b,3] and Philip L. Southwick[2c]

Departments of Chemistry, Carnegie-Mellon University, Pittsburgh, Pennsylvania 15213,
Clarkson College of Technology, Potsdam, New York 13676,
and New Mexico Institute of Mining and Technology, Socorro, New Mexico 87801

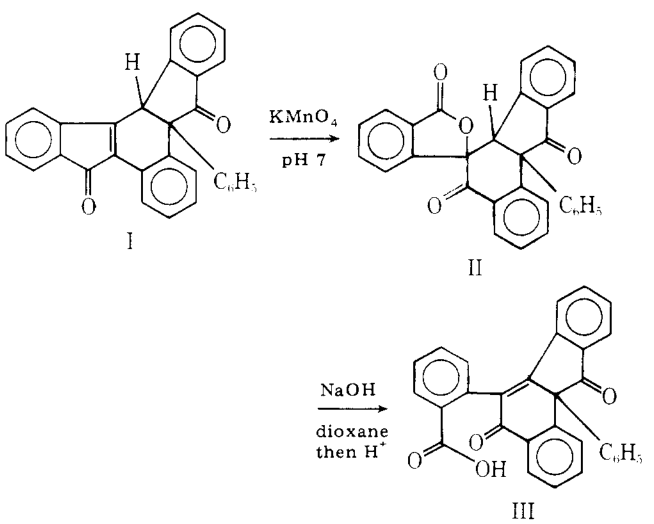
Received May 11, 1978

Mild oxidation of phenylcinnamalone (I) with neutral potassium permanganate gave the spiro lactone 6a′-hydro-11a′-phenylspiro[isobenzofuran-3(1*H*),6′-benzo[*a*]fluorene]-1,5′,11′-trione (II). Hydrolysis of II yielded 6-(*o*-carboxyphenyl)-11a-phenyl-5*H*-benzo[*a*]fluorene-5,11-dione (III) rather than the hydroxy acid which might be expected. The characterization of II and III is reported along with some ideas concerning possible reaction mechanisms.

Prior reports in this series have been concerned with the preparation and characterization of I,[4] its analogues and derivatives,[4,5] the scope of the preparative reaction,[5] and the nature of the potential reaction intermediates.[5] One of the intriguing aspects of the phenylcinnamalone (I) ring system is the ease with which it can be converted into other complex polycyclic compounds by simple single-step gentle procedures. In the most recent of the previous publications,[6] we described one method of entry into the benzo[*a*]fluorene system from phenylcinnamalone via an initial hydrolytic cleavage of one of the five-membered rings. In this report we shall describe an oxidative cleavage of the other five-membered ring of phenylcinnamalone to yield additional derivatives of benzo[*a*]fluorene (see Scheme I).

Reaction of phenylcinnamalone (I) with neutral potassium permanganate leads to a single white crystalline material (II) in good yield. A molecular formula of $C_{30}H_{18}O_4$ is consistent with the elemental analysis and with the isotopic analysis of the mass spectrum of II. Also, the infrared spectrum of II displays no hydroxyl-stretching band. These data rule out the possible formation of a glycol such as IV.

Scheme I

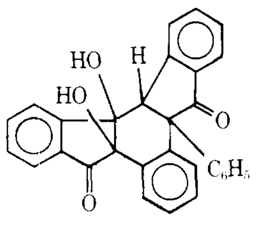


A tetraketone (V), analogous to the triketone (VI) prepared by Daleo[7] from 2,3-diphenylindone, does fit the observed molecular formula. However, the infrared spectrum of II shows, in addition to two strong carbonyl absorptions at 1710

---

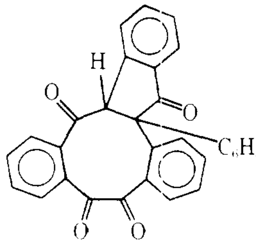
* Address correspondence to New Mexico Institute of Mining and Technology.

0022-3263/79/1944-1839$01.00/0

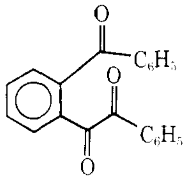


IV

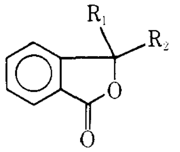
and 1725 cm^{-1}, a very strong carbonyl band at 1780 cm^{-1}. These data raise serious objection to structure V. The α-diketo moiety of V, incorporated in a nine-numbered ring, would have been expected to absorb at a lower infrared frequency, not a higher one, than the 1750 cm^{-1} observed for the *s-cis*-α-diketo function in unenolized cyclopentane-1,2-dione derivatives[8a] or the 1740 cm^{-1} observed for camphorquinone.[8b] Likewise, the indanone carbonyl band would not be expected to appear as high as 1780 cm^{-1}. In view of this high-frequency carbonyl absorption in II, it became necessary to conclude that an acid anhydride structure or a five-membered lactone ring had been introduced.



V



VI



VII

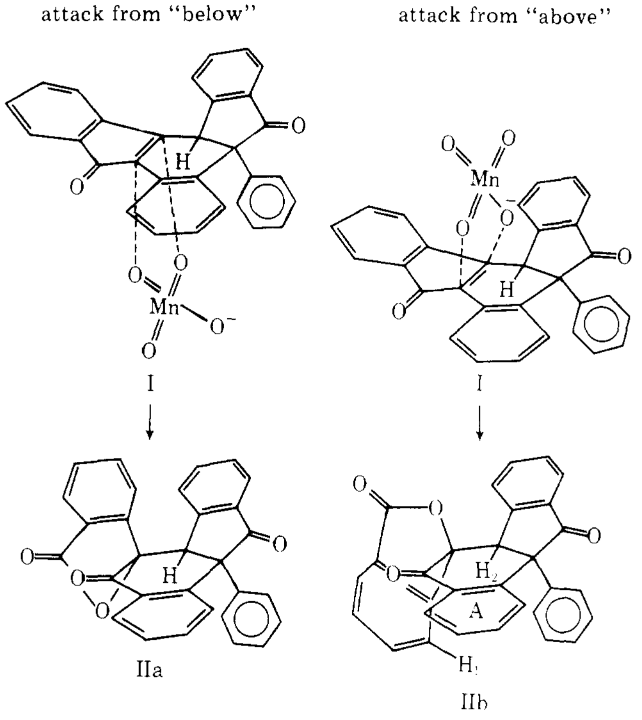
A variety of 3-substituted phthalides (VII) have carbonyl absorptions in their infrared spectra in the region under examination,[8c-f] and the range of absorption frequencies for a wide variety of 3 substituents ranges from 1749 to 1780 cm^{-1}.

Also, Jacobsen and Wyant[8c] studied a series of 3,3-disubstituted phthalides (VII) and classified two additional strong bands common to each derivative. One band appears in the region between 1279 and 1289 cm^{-1}. The other appears in the region between 1100 and 1117 cm^{-1}. The authors ascribed the two bands to the -CO-O- grouping of the lactone ring. Compound II has a strong band in both regions. Phenylcinnamalone, the starting material, does not exhibit strong absorption in either region.

Additional evidence consistent with a lactone structure is supplied by the mass spectrum of II. The spectrum displays peaks at both *m/e* 398 and 44. Cleavage of II to release carbon dioxide could give rise to these peaks. It is not unreasonable to expect a lactone to display this type of behavior. The only lactone of the phthalide type containing two other carbonyl groups which might reasonably result from an oxidation of phenylcinnamalone would be the spiro lactone (II). Thus, it appears that the five- to six-membered spiro lactone, 6a′-hydro-11a′-phenylspiro[isobenzofuran-3(1*H*),6′-benzo[*a*]-fluorene]-1,5′,11′-trione (II), is formed in preference to the tetraketone (V) which should be the expected product in view of the known behavior[7] of 2,3-disubstituted indones with permanganate ion. It may be that the reaction path is governed by an energy barrier to formation of the final product, with the two small rings of the spiro configuration being preferred to the single large ring of structure V.

Initial attack on phenylcinnamalone (I) by permanganate ion to form II can occur in two ways. These two modes of attack are illustrated schematically in Scheme II. Examination of framework molecular models of both the reactant (I) and the possible products (IIa and IIb) indicates that attack from above I by permanganate ion to form II is the most likely of the two modes of attack.

Scheme II. Schematic of the Two Possible Modes of Permanganate Ion Attack on Phenylcinnamalone (I) and the Resultant Products IIa and IIb



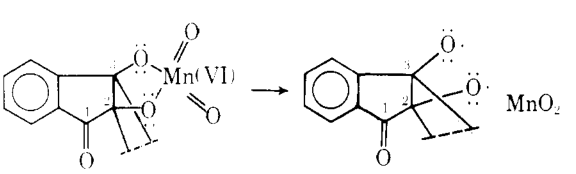
The model of phenylcinnamalone indicates that the ortho hydrogens of the nonfused phenyl ring would hinder attack from below. Additionally, the model of structure IIa, the result of such attack, is severely crowded in any conformation. The model of structure IIb, the resultant product of attack from above phenylcinnamalone, shows it to be considerably less crowded. This is particularly so in one conformation.

The conformation, in which IIb appears to be best situated, places the aromatic proton H$_1$ (see Scheme II) in the positive ^{1}H NMR shielding zone of aromatic ring A. Thus positioned, proton H$_1$ may be expected to give rise to a multiplet analogous to those which have been assigned to resonance of the shielded aromatic protons of the previously reported 6-(*o*-carboxyphenyl)-5-phenyl-11*H*-benzo[*a*]fluoren-11-one[6] and 14b,14c-dihydro-5a-phenyl-10-(α-phenyl-*trans*-cinnamoxy)benz[*a*]indeno[2,1-*c*]fluoren-5-one.[5] The ^{1}H NMR spectrum of II has such a multiplet centered at δ 6.34. Integration indicates it to be the result of one proton. The analogous multiplets noted above appear at δ 5.75[6] and 6.35[5] respectively. Splitting patterns of all three multiplets are very similar.

In no other conformation does the model of II so place a proton. Furthermore, no aromatic proton of the model of structure II may be so placed.

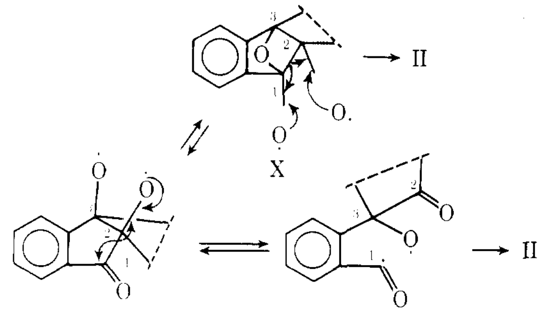
The remaining peaks of the ^{1}H NMR spectrum of II also are consistent for the proposed structure. A singlet, the result of resonance of one proton, appears at δ 5.12; this is very reasonable for proton H$_2$ (Scheme II). The remainder of the signals in the ^{1}H NMR spectrum are part of an intense complex multiplet centered at δ 7.50. These may be reasonably assigned as being due to resonance of the remaining aromatic protons of II. Thus, the pair of enantiomers represented by IIb (Scheme II) is consistent with the spectral and chemical data obtained from II.

Formation of a lactone, from the type of intermediate (VIII) expected to result from permanganate oxidation of an olefin in neutral solution,[9,10] is not unreasonable. Such an intermediate could disproportionate to form the diradical IX and



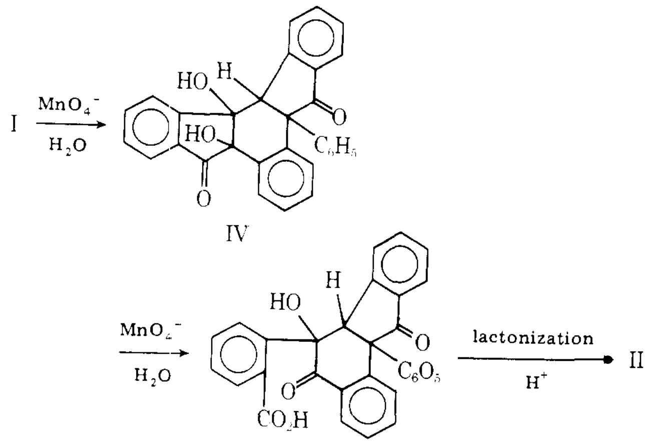
VIII IX

manganese dioxide. Simple homolytic cleavage of the 2,3 bond of diradical IX would lead to the unobserved tetraketone V. A five-membered lactone (II) could result if the oxygen radical of carbon 3 in IX attacked carbonyl carbon 1, followed by homolytic cleavage of the resultant diradical X. This route, however, may be unlikely on steric grounds, and a more plausible explanation of the outcome would assume cleavage of the 1,2 bond to form XI, followed by lactone formation.



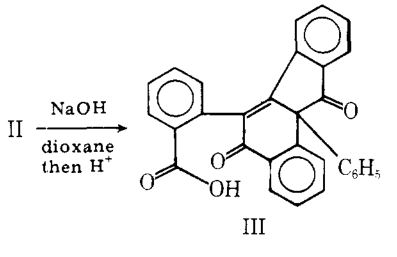
IX XI

Another explanation of the formation of the spiro lactone II would assume that the permanganate oxidation is a two-stage process in which an initially formed diketo diol (IV) is attacked preferentially in the second stage at the α-hydroxy ketone moiety, with cleavage to the diketo hydroxy acid IVa. Compound IVa would then undergo spontaneous lactonization to II. The site of attack at the second stage of the oxidation might be controlled by steric effects. Baeyer–Villiger oxidations of some cyclic α,β-unsaturated ketones have been found to yield epoxy lactones,[11] but it is not clear that the reaction processes involved or the type of product formed relate these oxidations at all closely with the permanganate oxidation under consideration here.



IVa

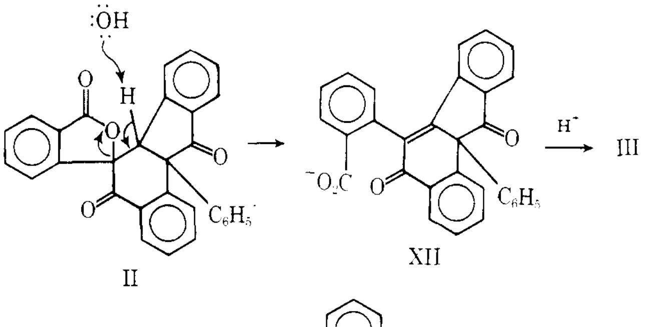
The spiro lactone (II) undergoes basic hydrolysis in aqueous sodium hydroxide to form a single white crystalline product (III). Elemental analyses are in agreement with the molecular formula $C_{30}H_{18}O_4$, which is the same as that of the starting material. III was soluble in aqueous sodium bicarbonate.

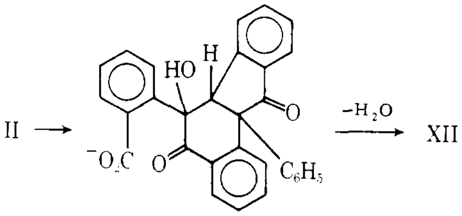


III

Spectral comparison of the starting material (II) and the product indicated that structure III, that of 6-(*o*-carboxyphenyl)-11a-phenyl-5*H*-benzo[*a*]fluorene-5,11-dione, might be correct.

III could be most simply formed via hydrogen abstraction and subsequent opening of the lactone ring to form the carboxylate anion XII. Alternately, the lactone ring could be opened first and followed by dehydration.





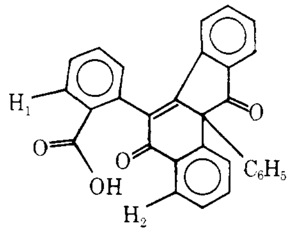
The infrared spectrum of III displays a strong broad band centered at 3000 cm^{-1}, indicative of the O–H stretching frequency of a carboxylic acid group. Also consistent with a carboxylic acid group is the presence of a strong carbonyl band at 1690 cm^{-1}, as is the observed aciditiy of the compound.

That the lactone ring of II has been opened is evidenced by the disappearance of the strong carbonyl absorption at 1780 cm^{-1}. The only carbonyl band above 1700 cm^{-1} in the spectrum of III appears at 1730 cm^{-1}, and it is attributable to the carbonyl group of the five-membered ring.

Both the singlet at δ 5.12 and the multiplet centered at δ 6.34 of the ^{1}H NMR spectrum of II are absent in the spectrum of III. Elimination of the methine proton of II would account for the absence of the former. Absence of the multiplet is reasonable since its appearance is dependent on the configuration of II (See Scheme II).

The ^{1}H NMR spectrum of II is composed entirely of signals which can be easily rationalized as resulting from resonance of aromatic protons. Two nearly identical multiplets appear, centered at δ 8.40 and 8.68. These two multiplets are well separated from an intense complex multiplet centered at δ 7.40. The ratio of integration is 1:1:15, respectively.

The multiplets centered at δ 8.40 may be reasonably assigned as the result of resonance of protons H_1 and H_2 of structure III (see below). Both protons are ortho to carbonyl groups, which would deshield the protons in question. Both protons may couple with an ortho, a para, and a meta proton. Thus, the nearly identical splitting patterns are reasonable. The intense multiplet centered at δ 7.40 is reasonable for the remainder of the aromatic protons of III.



III

Experimental Section

Infrared spectra were recorded in potassium bromide wafers using a Perkin-Elmer Model 237 spectrophotometer. ^{1}H NMR spectra were recorded on a Varian A60A spectrophotometer. Melting points were taken on a Reichert polarizing hot stage. Elemental analyses were done by Galbraith Laboratories, Knoxville, Tenn. Mass spectra were taken by Morgan and Schaeffer, Montreal, Canada.

Phenylcinnamalone (I) was prepared as reported previously.[4]

Oxidation of Phenylcinnamalone (I) with Neutral Potassium Permanganate. Preparation of 6a′-Hydro-11a′-phenylspiro[isobenzofuran-3(1*H*),6′-benzo[*a*]fluorene]-1,5′,11′-trione (II). I (2 g) was dissolved in 200 mL of acetone. A saturated aqueous solution of potassium permanganate was added dropwise until the purple color persisted. The excess permanganate ion was destroyed with concentrated HCl. The manganese dioxide was removed by filtration, and the filtrate was evaporated until crystallization began. The solution was filtered after standing overnight. The collected solids were recrystallized from glacial acetic acid to yield 1.0 g (50%) of product: mp 270–272 °C; IR (cm^{-1})[12a] 3065 w, 2950 w, 1780 s, 1725 w, 1710 s, 1600 m, 1495 w, 1465 m, 1450 m, 1335 w, 1315 w, 1285 m, 1275 w, 1250 m, 1235 m, 1215 w, 1200 vw, 1190 w, 1165 w, 1130 w, 1105 m, 1075 vw, 1060 vw, 1035 m, 1000 m, 975 vw, 965 vw, 930 w, 925 m, 900 w, 895 w, 890 w, 875 vw, 830 w, 805 vw, 800 w, 780 m, 775 ms, 755 m, 750 m, 720 m 715 m, 700 m, 660 w, 650 w; ^{1}H NMR (Me$_2$SO-d_6, 120 °C) (δ)[12b] 5.12 (s, 1), 634 (m, 1), 7.50 (m, 16); mass spectrum, (m/e) 442 (P), 424, 414, 398, 397, 396, 386, 385, 252, 193, 165, 104, 77, 76. Isotopic analysis[12c] Calcd for $C_{30}H_{18}O_4$: P, 100; P + 1, 32.8; P + 2, 6.0. Found: P, 100; P + 1, 32.8; P + 2, 6.0. Anal. Calcd for $C_{30}H_{18}O_4$: C, 81.44; H, 4.09. Found: C, 81.10; H, 4.25.

Basic Hydrolysis of II. Formation of 6-(*o*-Carboxyphenyl)-11a-phenyl-5*H*-benzo[*a*]fluorene-5,10-dione (III). II (1 g) was dissolved in 20 mL of 1,4-dioxane. The solution was brought to reflux. 10% NaOH (20 mL) was added. The resultant mixture was refluxed for 4 h. Upon cooling, the solution was acidified with concentrated HCl. The precipitate was collected and crystallized from glacial acetic acid. The yield of product, mp 322–323 °C, was 0.7 g (70%): IR (cm^{-1}) 3060 w, 2900 s (broad), 1730 s, 1690 s, 1615 m, 1580 w, 1510 w, 1485 m, 1465 w, 1420 w, 1375 m, 1330 w, 1305 m, 1280 m, 1255 m, 1205 m, 1180 m, 1155 m, 1125 s, 1075 m, 1045 m, 975 w, 885 w, 875 w, 830 w, 810 w, 805 w, 785 w, 765 s, 740 m, 720 m, 700 w, 685 w, 675 w, 665 w, 640 w; ^{1}H NMR (Me$_2$SO-d_6, 37 °C) (δ) 7.40 (m, 15), 8.40 (m, 1), 8.68 (m, 1). Anal. Calcd for $C_{30}H_{18}O_4$: C, 81.44; H, 4.09. Found: C, 81.24; H, 3.94.

Registry No.—I, 18585-55-2; II, 69622-44-2; III, 69622-33-9.

References and Notes

(1) Research performed in part under the auspices of the Research Corporation.

(2) (a) New Mexico Institute of Mining and Technology; (b) Clarkson College of Technology; (c) Carnegie-Mellon University.

(3) Taken in part from the dissertations submitted by Drs. R. G. Brown, L. G. Donaruma, and R. A. Kropf in partial fulfillment of the requirements for a Ph.D. degree.

(4) A. L. Bednowitz, W. C. Hamilton, R. G. Brown, L. G. Donaruma, P. L. Southwick, R. A. Kropf, and R. E. Stansfield, *J. Am. Chem. Soc.*, **90**, 291 (1968).

(5) A. L. Bednowitz, R. G. Brown, L. G. Donaruma, P. L. Southwick, R. A. Kropf, and R. E. Stansfield, *J. Org. Chem.*, **39**, 3537 (1974).

(6) R. G. Brown, L. G. Donaruma, R. A. Kropf, P. L. Southwick, R. E. Stansfield, A. L. Bednowitz, and W. C. Hamilton, *J. Org. Chem.*, **41**, 3622 (1976).

(7) P. Daleo, *Nauchni. Tr. Vissh. Med. Inst., Sofia*, **5** (3), 1 (1958).

(8) (a) C. N. R. Rao, "Chemical Applications of Infrared Spectroscopy", Academic Press, New York, 1963, p 211; (b) J. Modiano, *Ann. Chim.*, (Paris), **12**, 574 (1955); (c) R. K. Jacobsen and R. E. Wyant, *Appl. Spectrosc.*, **14**, 61 (1960); (d) L. A. Duncanson, J. F. Grove, and J. Zeally, *J. Chem. Soc.*, 1331 (1953); (e) P. R. Jones and S. L. Congdon, *J. Am. Chem. Soc.*, **81**, 4291 (1959); (f) P. Venturella and A. Bellino, *Ann. Chim. (Rome)*, **50**, 875 (1960).

(9) K. B. Wiberg and K. A. Saegebarth, *J. Am. Chem. Soc.*, **79**, 2882 (1957).

(10) R. Stewart, "Oxidation in Organic Chemistry", K. B. Wiberg, Ed., Academic Press, New York, 1965, p 1.

(11) A. DeBoer and R. E. Ellwanger, *J. Org. Chem.*, **39**, 77 (1974).

(12) (a) s = strong absorption, m = medium absorption, w = weak absorption, and vw = very weak absorption. (b) First number is chemical shift; s = singlet and m = multiplet. (c) Isotopic analysis: P = parent peak, P + 1 = parent peak + 1, and P + 2 = parent peak + 2; numbers are relative intensities.

Radiation-Induced Oxidation of Benzo[*a*]pyrene[1]

Thomas L. Gibson and Leland L. Smith*[2]

Division of Biochemistry, Department of Human Biological Chemistry and Genetics,
University of Texas Medical Branch, Galveston, Texas 77550

Received October 24, 1978

The oxidation in air of benzo[*a*]pyrene induced by ^{60}Co γ radiation gave over two dozen products, of which half have been identified. Products include three isomeric 7,8,9,10-tetrahydrobenzo[*a*]pyrene-7,8,9,10-tetraols, 9,10-dihydrobenzo[*a*]pyrene-*trans*-9,10-diol, a 7,8-dihydrobenzo[*a*]pyrene-7,8-diol, a 4,5-dihydrobenzo[*a*]pyrene-4,5-diol, benzo[*a*]pyrene-1,6-dione, benzo[*a*]pyrene-3,6-dione, benzo[*a*]pyrene-6,12-dione, 9-(2′formylphenyl)phenalen-1-one, and tentatively benzo[*a*]pyren-3-ol, benzo[*a*]pyren-6-ol, and benzo[*a*]pyren-9-ol. These results establish that air oxidation of benzo[*a*]pyrene yields products similar to those found as mammalian metabolites, with oxidative attack at the K region, bay region, and the 6 position. Some of the air oxidation products are weakly mutagenic toward *Salmonella typhimurium* test strains.

Mammalian metabolism of the common environmental pollutant benzo[*a*]pyrene (**1**) produces phenol, dihydrodiol, tetrahydrotetrol, epoxide, and dihydrodiol epoxide derivatives, some of which are powerful mutagens suspected of being proximate or ultimate carcinogens. Benzo[*a*]pyrene is also sensitive to radiation-induced air oxidation in solution,[3] as pure crystals,[4] and adsorbed on particulate matter.[4,5] Moreover, we have demonstrated that radiation-induced air oxidations of benzo[*a*]pyrene and of several other polycyclic aromatic hydrocarbons yield preparations mutagenic toward strains of *Salmonella typhimurium* without preliminary metabolic activation.[4]

We describe here the isolation and identification of oxidation products recovered from mutagenic preparations of oxidized benzo[*a*]pyrene and demonstrate thereby close similarities between air oxidation and oxidative metabolism of benzo[*a*]pyrene.

Results

Of the several irradiation conditions previously shown to transform benzo[*a*]pyrene into mutagenic material,[4] we chose for ease of product recovery the ^{60}Co γ irradiation of benzo[*a*]pyrene adsorbed on silica gel. Over two-dozen products were detected chromatographically, of which half have been isolated and identified by chromatographic and spectral data.

The major products were the well-known benzo[*a*]pyrene-1,6-, -3,6-, and -6,12-diones, **2**, **3**, and **4**, respectively.

0022-3263/79/1944-1842$01.00/0