A similar reaction employing a reaction period of 10 days as reported earlier for reduction of other keto acids to acids[4] afforded essentially the same yield of **3** (74%).

Dibenz[*a,c*]anthracene (1). (1) Dehydrogenation of 3. Reaction of **3** (4.73 g, 17 mmol) with *o*-chloranil (4.6 g, 19 mmol) was carried out in refluxing freshly distilled benzene (100 mL) for 20 h. The reaction mixture was cooled and chromatographed on a short column of neutral alumina eluted with benzene. The product was recrystallized from benzene to afford **1** as fine white needles (4.65 g, 98%): mp 205–206 °C (lit.[8] mp 200–201.5 °C); NMR ($CDCl_3$) δ 7.38–7.78 (m, 6, $H_{2,3,6,7,11,12}$), 7.86–8.20 (m, 2, $H_{10,13}$), 8.33–8.87 (m, 4, $H_{1,4,5,8}$), and 9.05 (s, 2, $H_{9,14}$).

(2) Reduction of 2 with P/HI. Reaction of **2** (1.3 g, 4 mmol) with red phosphorus (0.37 g, 12 mmol) and 50% HI (10 mL) was carried out in refluxing glacial acetic acid (80 mL) for 24 h and worked up according to the procedure employed for **3**. There was obtained essentially pure **1** (1.03 g, 93%) identical by NMR and TLC with an authentic sample.

(3) Reduction of 2 with HI. Repetition of the previous reaction with omission of P gave **1** (1.03 g, 94%). The latter was dissolved in the minimum volume of benzene and purified by passage through a short column of Florisil and recrystallized from ethanol to furnish pure **1** (932 mg, 86%) as pale yellow silky needles, mp 205–206 °C.

Dibenz[*a,c*]anthracene-9,14-dione (6). To a solution of **2** (474 mg, 1.5 mmol) and boric acid (494 mg, 8 mmol) in water (0.4 mL) was added concentrated sulfuric acid (1.5 mL). The resulting solution was heated at 80 °C for 7 h, cooled to room temperature, and sufficient 20% H_2SO_4 added to make the concentration of H_2SO_4 50%. Water (100 mL) was added and the precipitate filtered, washed with water, boiled with 2% caustic soda (10 mL), filtered, and washed with water again. There was obtained **6** (363 mg, 78%) as a yellow solid: mp 181–182 °C (lit.[9] mp 181–183 °C); NMR ($CDCl_3$) δ 7.62–7.93 (m, 6, $H_{2,3,6,7,11,12}$), 8.0–8.3 (m, 2, $H_{10,13}$), 8.52–8.82 (m, 2, $H_{4,5}$), and 9.2–9.5 (m, 2, $H_{1,8}$); IR (KBr) 1670 cm^{-1} (C=O).

In a separate experiment **2** failed to cyclize to **6** in liquid HF at room temperature for 18 h.

Reduction of Dibenz[*a,c*]anthracene-9,14-dione (6). (1) Reduction of 6 with HI. A solution of **6** (185 mg) in 1.5 mL of 50% HI and 10 mL of acetic acid was heated at reflux for 24 h. Workup following the same general procedure employed in other reactions gave pure **1** (148 mg, 89%), mp 206–207 °C.

(2) Reduction of 6 with P/HI. Reaction of **6** (285 mg) with P and HI under the conditions employed for reductive cyclization of **2** afforded a product (125 mg) shown by NMR and TLC analysis to consist of **1** and **3** in the ratio 2:1.

Wolff–Kishner Reaction of 2. The keto acid **2** (2.0 g, 6.1 mmol) was initially converted to its methyl ester in methanol (20 mL) saturated with HCl and maintained at reflux for 1.5 h. Conventional workup afforded methyl 2-(9′-phenanthroyl)benzoate: 1.72 g (83%); mp 58–60 °C; NMR ($CDCl_3$) δ 3.35 (s, 3, CH_3) and 7.48–7.80, and 8.49–9.10 (m, 12, aromatic).

A solution of the methyl ester of **2** (1.53 g, 4.5 mmol) in *n*-butyl alcohol (20 mL) was added to a solution of hydrazine hydrate (5.7 mL) in the same solvent (20 mL) and the resulting solution was heated at reflux for 18 h. Reaction was quenched with ice water and neutralized with HCl. Conventional workup gave **7** as a white crystalline solid (1.25 g, 86%): mp 260–262 °C; NMR (Me_2SO-d_6) δ 7.16 (dd, 1, $J_{5,6}$ = 7 Hz, $J_{5,7}$ = 3 Hz, H_5), 7.4–8.1 (m, 8, aromatic), 7.95 (s, 1, $H_{10'}$), 8.33 (dd, 1, $J_{7,8}$ = 7 Hz, $J_{6,8}$ = 3 Hz, H_8), 8.95 (m, 2, $H_{4',5'}$), and 11.35 (s, 1, NH); the NH peak underwent exchange with D_2O.

Anal. Calcd for $C_{22}H_{14}N_2O$: C, 81.97; H, 4.38; N, 8.69. Found: C, 81.95; H, 4.41; N, 8.68.

Acetylation of **7** (250 mg, 0.77 mmol) with pyridine (3 mL) and acetic anhydride (30 mL) at room temperature overnight furnished the *N*-acetate of **7** (262 mg, 89%) as a white solid: mp 224–226 °C; NMR ($CDCl_3$) δ 2.78 (s, 3, OAc), 7.19 (dd, 1, $J_{5,6}$ = 7 Hz, $J_{5,7}$ = 3 Hz, H_5), 7.4–8.0 (m, 8, aromatic), 7.87 (s, 1, $H_{10'}$), 8.42–9.05 (m, 3, $H_{8,4',5'}$); IR ($CHCl_3$) 1690 (C=O) and 1770 cm^{-1} (CH_3C=O).

Attempted conversion of **7** to **4** by heating a solution of the former and KOH in refluxing diethylene glycol for 3 days according to the general procedure described by Fieser and Fieser[9] furnished only recovered **7**.

Acknowledgment. This investigation was supported by research Grants CA 11968 and CA 19448 and contract CP 033385 from the National Cancer Institute, DHEW.

Registry No.—**1**, 215-58-7; **2**, 66859-11-8; **2** methyl ester, 66859-12-9; **3**, 35281-25-5; **6**, 3228-74-8; **7**, 66859-13-0; **7** *N*-acetate, 66859-14-1.

References and Notes

(1) E. Clar, "Polycyclic Hydrocarbons", Vol. 1, Academic Press, New York, N.Y., 1964, p 322; compound **1** is named 1,2,3,4-dibenzanthracene in the obsolete nomenclature system employed in this volume.
(2) J. D. Scribner, *J. Natl. Cancer Instit.*, **50**, 1717 (1973).
(3) C. Weizmann, E. Bergmann, and F. Bergmann, *J. Chem. Soc.*, 1367 (1935).
(4) L. L. Ansell, T. Rangarajan, W. M. Burgess, E. J. Eisenbraun, G. W. Keen, and M. C. Hamming, *Org. Prep. Proced. Int.*, **8**, 133 (1976).
(5) R. N. Renaud and J. C. Stephens, *Can. J. Chem.*, **52**, 1229 (1974).
(6) E. Bergmann and T. Berlin, *J. Chem. Soc.*, 493 (1939).
(7) P. P. Fu, H. M. Lee, and R. G. Harvey, *Tetrahedron Lett.*, 551 (1978).
(8) R. G. Harvey and P. P. Fu in "Polycyclic Hydrocarbons and Cancer: Chemistry, Molecular, Biology and Environment", Vol. 1, H. V. Gelboin and P. O. P. T'so, Ed., Academic Press, New York, N.Y., 1978, p 131; P. P. Fu and R. G. Harvey, *Tetrahedron Lett.*, 2059 (1977); R. G. Harvey and K. Sukumaran, *Ibid.*, 2387 (1977); R. G. Harvey, P. P. Fu, C. Cortez, and J. Pataki, *Ibid.*, 3533 (1977).
(9) L. F. Fieser and M. Fieser, "Reagents in Organic Synthesis", Vol. I, Wiley, New York, N.Y., 1967, p 435.

Synthesis of Aryloxiranes

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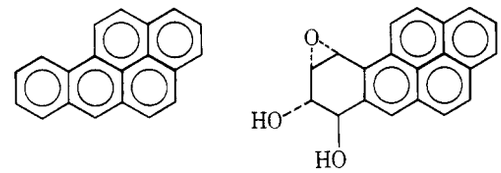
Received March 21, 1978

Polynuclear aromatic hydrocarbons are metabolically converted into derivatives of oxiranes which are implicated as the ultimate carcinogens in chemical carcinogenesis.[1] The in vitro and in vivo conversions of the ubiquitous benzo[*a*]pyrene (**1**) to the derivatives of isomeric 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrenes, commonly known as BP diolepoxides (BPDE, such as **2**), have been



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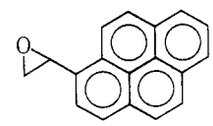

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shown to be an important event in the mechanism of chemical carcinogenesis in benzo[*a*]pyrene.[2] Isomeric BPDEs are chemically reactive compounds via their oxiranyl function to cellular macromolecules[3] and are highly biologically active in a variety of testing systems including Ames' bacteria and cell cultures.[1,4] Simple aryloxiranes which contain both the aromatic π system as well as the reactive oxiranyl group of these activated carcinogens are a group of interesting compounds. A few of these compounds have been found to possess both carcinogenic and mutagenic activities.[5] Since BPDEs and related compounds are usually prepared by multistep synthesis and the metabolically activated forms of many other polynuclear aromatic hydrocarbons are not yet established, in order to carry out a structure–activity relationship study in chemical mutagenesis and carcinogenesis, aryloxiranes may serve well as model substances for metabolically activated forms of polynuclear aromatic hydrocarbons. This note deals with the synthesis of a group of aryloxiranes by three different methods.

We first attempted and failed to synthesize 9-anthryloxirane by the epoxidation of 9-vinylanthracene with *m*-chlo-

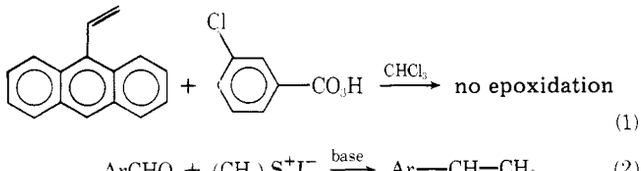
0022-3263/78/1943-3425$01.00/0

Table I

compd	registry no.	method	yield,[a] %	physical constant [lit. value]
1-pyrenyloxirane	61695-74-7	A	69	mp 66–68 °C (ethanol) [oil][b]
		B	82	mp 67–68 °C (ethanol)
9-anthryloxirane	61695-73-6	A	94	mp 68–69 °C (ethanol) [mp 76.5–78.0 °C (CCl_4)][b]
		B	65	mp 68–69°
1-naphthyloxirane	62222-40-6	A	82	bp 80–82 °C (0.075 mm) [bp 90–96 °C (0.10–0.13 mm)][c]
2-naphthyloxirane	20861-99-8	A	94	mp 57–58 °C (methanol) [mp 55.5–56.5 °C, 58–59 °C][b,d]
7-benzanthryloxirane	61695-72-5	A	81	mp 116–118 °C (ethanol) [mp 116–118 °C][b]
6-chrysenyloxirane	66842-41-9	B	85	mp 155–156 °C (acetone–petroleum ether)
10-methyl-9-anthryloxirane	66842-42-0	B	90	mp 100–101 °C (ethanol)
9-phenanthryloxirane	33424-05-4	B	90	mp 65–67 °C (ethanol)
9,10-bis(oxiranylanthracene)	66842-43-1	B	92	mp 200–201 °C (acetone)
9,10-dimethyl-2-anthryloxirane	66842-44-2	C	82[e]	mp 134–135 °C (aqueous ethanol)

[a] All yields given are for isolated products. All compounds exhibit the typical ABX pattern for oxirane in their NMR spectra, proper UV and IR spectra, and correct elemental analysis. [b] R. G. Harvey, J. Pataki, R. N. Wilke, J. W. Flesher, and S. Soedigdo, *Cancer Lett.*, **1**, 339 (1976). [c] S. L. Shapiro, H. Soloway, and L. Freedman, *J. Am. Chem. Soc.*, **80**, 6060 (1958). [d] R. Howe, A. F. Crowther, J. S. Stephenson, B. S. Rao, and L. H. Smith, *J. Med. Chem.*, **11**, 1000 (1968). [e] The yield is for the conversion of α-bromo-9,10-dimethyl-2-acetylanthracene to the oxirane.

roperbenzoic acid (reaction 1). At elevated temperatures, anthraquinone was isolated as the major product, and no oxirane was detected in the reaction mixture. Since the vinyl derivatives of many polynuclear aromatic hydrocarbons were unknown or not readily available at that time,[5] this approach was abandoned. In a preliminary communication, Harvey and his co-workers reported the synthesis of a few aryloxiranes by the reaction of aromatic aldehydes and Corey's dimethylsulfonium methylide reagent[6] generated from the sulfonium iodide and *n*-butyllithium.[5] The products were isolated by chromatography and no yields were reported. Independently, we also applied this method for the synthesis but used sodium hydride as the base; the products were formed in high purity and were isolated in good yields directly by recrystallization (method A, reaction 2). Subsequently, we found that these oxiranes may be prepared conveniently in comparable yields by the application of phase transfer catalysis technique to the Corey's reaction without the use of the moisture and air sensitive reagents (method B).[7] In the synthesis of 9,10-dimethyl-2-anthryloxirane, the starting material of the Corey reaction, 9,10-dimethylanthracene-2-carboxaldehyde, is not known and our attempt to prepare this compound via the Vilsmeier reaction was not successful.[8] Therefore, an alternative synthesis from 2-acetyl-9,10-dimethylanthracene via the α-bromo derivative was developed (method C, reaction 3). The results are tabulated in Table I.



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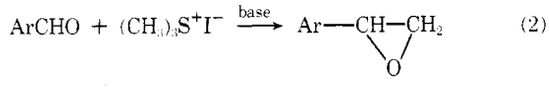

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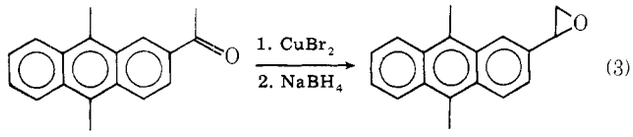

(3)

Preliminary investigation on the mutagenicity of these aryloxiranes by Miller, Miller, and Drinkwater with the Ames' systems, Salmonella typhimurium TA-98 and TA-100, indicated that these oxiranes are highly active mutagens.[9] Particularly, 1-pyrenyloxirane (**3**) exhibits mutagenicity at a level comparable to 7β,8α-dihydroxy-9α,10α-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrene (**2**), the common isomer of BPDE. Therefore, these aryloxiranes not only exhibit interesting biological properties but also may serve as model compounds for the activated forms of polynuclear hydrocarbons.

Experimental Section

All ultraviolet spectra were obtained with a Cary-14 spectrophotometer, infrared spectra with a Perkin-Elmer 737 spectrophotometer, and NMR spectra with a Bruker HX-270 (270 MHz) spectrometer with tetramethylsilane (Me_4Si) as the internal standard. Melting points were determined on a Fisher–Jones melting point apparatus and were uncorrected.

The following compounds were purchased from the Aldrich Chemical Co. and purified by recrystallization from the solvent indicated: trimethylsulfonium iodide (ethanol, mp 215 °C), anthracene-9-carboxaldehyde (ethanol, mp 103 °C), 2-naphthaldehyde (methanol, mp 60 °C), and 9,10-dimethylanthracene (ethanol, mp 182 °C). The following compounds were purchased from the respective suppliers and used without further purification: sodium hydride (50% oil dispersion, Ventron), sodium borohydride (Ventron), cupric bromide (Mallinckrodt), acetyl chloride (Baker and Adamson), tetrabutylammonium iodide (Aldrich), phenanthrene-9-carboxaldehyde (Aldrich), and 10-methylanthracene-9-carboxaldehyde (Aldrich). 1-Naphthaldehyde (Aldrich) was purified by chromatography over neutral alumina. Dimethyl sulfoxide was purified by vacuum distillation over calcium hydride, bp 35–36 °C (0.15 mm). Benzene and tetrahydrofuran were purified by distillation over lithium aluminum hydride.

Pyrene-1-carboxaldehyde was prepared by the method of Tanikawa and co-workers, mp 125–127 °C((ethanol);[10] benzanthracene-7-carboxaldehyde was prepared by the method of Fieser and Hartwell, mp 146–148 °C (ethanol);[8] chrysene-6-carboxaldehyde was prepared by the method of Buu-Hoi and co-workers, mp 166–168 °C (benzene);[11] anthracene-9,10-dicarboxaldehyde was prepared from 9,10-bis(chloromethylanthracene) by the method of Klanderman, mp 241–244 °C dec (dichloromethane);[12,13] 9,10-dimethyl-2-acetylanthracene was prepared by the method of Van Hove, mp 164–165 °C (ethanol).[14]

Method A. 1-Pyrenyloxirane. All operations before the addition of water were carried out under an atmosphere of dry nitrogen. Sodium hydride in 50% oil dispersion (1.055 g, 22 mmol) was placed in a 250-mL round-bottomed flask with a magnetic stirrer and was washed with 40 mL of petroleum ether (bp 30–60 °C). The mixture was stirred, the hydride was allowed to settle, the solvent was decanted, and the hydride was dried under reduced pressure. A 1:1 (v/v) mixture of prepurified Me_2SO and tetrahydrofuran (20 mL) was added to the hydride, and the whole system was cooled in a salt–ice bath (bath temperature, −5 °C). With magnetic stirring, a solution of 4.59 g (22.5 mmol) of recrystallized trimethylsulfonium iodide in 15 mL of purified Me_2SO was added dropwise to the mixture. Some gas evolution was noted. A solution of 3.83 g (16.6 mmol) of pyrene-1-carboxaldehyde in 10 mL of purified tetrahydrofuran was added dropwise next. Stirring was continued with cooling for 10 more min after the addition and then for another 60 min after the bath was removed.

The reaction mixture was then decomposed with 180 mL of water, extracted with 150 mL of ethyl ether, washed with water, and dried

over magnesium sulfate. Removal of the solvent under reduced pressure gave a yellow oily residue which solidified upon trituation with methanol. Crystallization of the residue from methanol afforded 2.83 g (69% yield) of pale yellow crystals, 1-pyrenyloxirane: mp 66–68 °C; IR (KBr) 3050 (m), 1220 (m), 1180 (m), 1030 (m), 880 (s), 840 (s), 820 (s), 735 (s), and 715 cm^{-1} (s); UV_{max} (methanol) 342 (48 900), 325 (31 300), 312 (12 600), 275 (52 800), 264 (26 400), 254 (11 400), 241 (80 700), and 232 nm (43 600); NMR δ_{Me_4Si} ($CDCl_3$) 2.88 (dd, 1 H, J = 6 and 3 Hz), 3.37 (dd, 1 H, J = 6 and 4 Hz), 4.70 (broad t, 1 H, J = 3 and 4 Hz), 7.88–8.13 (m, 8 H), and 8.27 (d, 1 H, J = 9 Hz).

Anal. Calcd for $C_{18}H_{12}O$: C, 88.50; H, 4.95. Found: C, 88.35; H, 4.84.

Method B. 1-Pyrenyloxirane. In a 500-mL round-bottomed flask were placed 5.915 g (25.7 mmol) of pyrene-1-carboxaldehyde and 0.676 g (1.83 mmol) of tetrabutylammonium iodide in 100 mL of dichloromethane. A layer (100 mL) of 50% (w/w) aqueous sodium hydroxide was introduced underneath this solution. Trimethylsulfonium iodide (6.067 g, 29.7 mmol) was then added and the whole mixture was warmed up to 60 °C with vigorous stirring under nitrogen atmosphere for 72 h until the originally undissolved sulfonium salt entered the solution.

The reaction mixture was next poured into 200 mL of an ice–water mixture, and the organic phase was separated, washed with water, and dried over magnesium sulfate. Dichloromethane was removed under reduced pressure to give an oily yellow residue. Crystallization of the oily residue from ethanol gave 5.15 g (82% yield) of pale yellow prisms of 1-pyrenyloxirane, mp 67–68 °C.

α-Bromo-2-acetyl-9,10-dimethylanthracene. Finely ground cupric bromide (1.165 g, 5.22 mmol) and 8 mL of ethyl acatate were placed in a 50-mL round-bottomed flask fitted with a reflux condenser and a magnetic stirrer. The solution was brought to reflux in an oil bath. 2-Acetyl-9,10-dimethylanthracene (0.619 g, 2.50 mmol) was dissolved in 8 mL of hot chloroform and introduced into the flask. The resulting reaction mixture was refluxed for 5 h with vigorous stirring to ensure complete exposure of the cupric bromide to the reaction medium. The completion of the reaction could be judged from the color change of the solution from green to amber, disappearance of all black solid, and cessation of hydrogen bromide evolution. After removal of cuprous bromide by filtration, the solution was treated with Norite A. Concentration of the filtrate under reduced pressure gave a greenish brown solid. Recrystallization from benzene afforded 0.521 g (64% yield) of a yellow compound, α-bromo-2-acetyl-9,10-dimethylanthracene: mp 176–178 °C dec; IR (KBr) 1665 (s), 1615 (m), 1290 (m), 1260 (s), 1020 (m), and 750 cm^{-1} (s); UV_{max} (methanol) 426 (3800), 375 (3690), 355 (3400), 338 (2480), 270 (36 700), and 245 nm (29 600); NMR δ_{Me_4Si} ($CDCl_3$) 3.09 (s, 3 H), 3.18 (s, 3 H), 4.61 (s, 2 H), 7.60 (m, 2 H), 7.98 (d, 1 H, J = 9 Hz), 8.36 (m, 3 H), and 9.07 (s, 1 H).

Anal. Calcd for $C_{18}H_{15}OBr$: C, 66.07; H, 4.62; Br, 24.42. Found: C, 66.11; H, 4.70; Br, 24.36.

Method C. 9,10-Dimethyl-2-anthryloxirane. A solution of 0.186 g (0.569 mmol) of α-bromo-2-acetyl-9,10-dimethylanthracene in 10 mL of ethanol was placed in a 25-mL round-bottomed flask with a magnetic stirrer and heated on an oil bath. Into the hot alcoholic solution was added dropwise a solution of 0.0245 g (0.648 mmol) of sodium borohydride in 1 mL of water. The resulting solution was allowed to reflux for 3–5 min and then filtered while still hot. When the volume of the solution was reduced by a gentle stream of nitrogen, light yellow crystals began to appear. The light yellow platelets were collected by filtration to give 0.116 g (82% yield) of 9,10-dimethyl-2-anthryloxirane: mp 134–135 °C; IR (KBr) 1380 (s), 1390 (s), 1250 (m), 870 (s), 815 (s), 800 (s), and 750 cm^{-1} (s); UV_{max} (methanol) 397 (7500), 376 (8200), 357 (5210), and 262 (191 000); NMR δ_{Me_4Si} ($CDCl_3$) 2.98 (dd, 1 H, J = 6 and 3 Hz), 3.08 (s, 3 H), 3.10 (s, 3 H), 3.26 (t, 1 H, J = 6 and 4 Hz), 4.11 (t, 1 H, J = 3 and 4 Hz), 7.32 (d, 1 H, J = 8 HZ(= 7/5[(dd, 2 H, J = 8 and 4 Hz), and 8.28–8.32 ppm (broad d, 4 H).

Anal. Calcd for $C_{18}H_{16}O$: C, 87.06; H, 6.49. Found: C, 86.63; H. 6.51.

Acknowledgment. The authors wish to acknowledge the National Cancer Institute (Grant CA-10220) and the National Institute of General Medical Sciences (Grant GM-20329) for the support of this work. They also wish to thank Professors J. A. Miller, E. C. Miller, and R. K. Boutwell of the McArdle Laboratory for Cancer Research, the University of Wisconsin, for their interest, encouragement, and biological essays of these oxiranes.

Registry No.—Pyrene-1-carboxaldehyde, 3029-19-4; anthracene-9-carboxaldehyde, 642-31-9; 1-naphthaldehyde, 66-77-3; 2-naphthaldehyde, 66-99-9; benz[a]anthracene-7-carboxaldehyde, 7505-62-6; chrysene-6-carboxaldehyde, 22138-85-8; 10-methyanthracene-9-carboxaldehyde, 7072-00-6; phenanthrene-9-carboxaldehyde, 4707-71-5; anthracene-9,10-dicarboxaldehyde, 7044-91-9; α-bromo-9,10-dimethyl-2-acetylanthracene, 66842-45-3; trimethylsulfonium iodide, 2181-42-2; tetrabutylammonium iodide, 311-28-4; 2-acetyl-9,10-dimethylanthracene, 15254-37-2; 9,10-dimethylanthracene, 781-43-1.

References and Notes

(1) For a review, see D. M. Jerina, etc., in "Origin of Human Cancer", H. H. Hiatt, J. D. Watson, and J. A. Winsten, Ed., Cold Spring Harbor Laboratory, Cold Spring Harbor, N.Y., 1977, Book B, pp 639–659; W. Levin, etc., *ibid.*, pp 659–682.
(2) (a) A. Borgen, H. Dawey, N. Castagnoli, T. T. Crocker, R. E. Rasmussen and I. Y. Wang, *J. Med. Chem.*, **16**, 503 (1973); (b) P. Sims, P. L. Grover, A. Swaisland, K. Pal, and A. Hewer, *Nature* (London), **252**, 326 (1974); (c) P. Daudel, M. Duquesne, P. Vigny, P. L. Grover, and P. Sims, *FEBS Lett.*, **57**, 250, (1975); (d) S. K. Yang, D. W. McCourt, P. P. Roller, and H. V. Gelboin, *Proc. Natl. Acad. Sci. U.S.A.*, **73**, 2594 (1976); (e) D. R. Thakker, H. Yagi, Y. H. Lu, W. Levin, A. H. Conney, and D. M. Jerina, *ibid.*, **73**, 3381 (1976).
(3) (a) I. B. Weinstein, A. M. Jeffrey, K. W. Jennette, S. H. Blobstein, R. G. Harvey, C. Harris, H. Autrup, H. Kasai, and K. Nakanishi, *Science*, **193**, 592 (1976); (b) K. M. Straub, T. Meehan, A. L. Burlingane, and M. Calvin, *Proc. Natl. Acad. Sci. U.S.A.*, **74**, 5285 (1977); (c) M. Koreeda, P. G. Wislocki, P. Moore, W. Levin, A. H. Conney, H. Yagi, and D. M. Jerina, *Science*, **199**, 778 (1978).
(4) (a) C. Malaveille, H. Bartsch, P. L. Grover, and P. Sims, *Biochem. Biophys. Res. Commun.*, **66**, 693 (1975); (b) E. Huberman, L. Sachs, S. K. Yang, and H. V. Gelboin, *Proc. Natl. Acad. Sci. U.S.A.*, **73**, 607 (1976); (c) R. F. Newbold and P. Brookes, *Nature* (*London*), **261**, 52 (1976); (d) A. W. Wood, P. G. Wislocki, R. L. Chang, W. Levin, H. Yagi, O. Hernandez, D. M. Jerina, and A. H. Conney, *Cancer Res.*, **36**, 3358 (1976); (e) T. J. Slaga, W. M. Bracken, A. Viaje, W. Levin, H. Yagi, D. M. Jerina, and A. H. Conney, *Ibid.*, **37**, 4130 (1977).
(5) R. G. Harvey, J. Pataki, R. N. Wilke, J. W. Flesher, and S. Soedigdo, *Cancer Lett.*, **1**, 339 (1976).
(6) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **87**, 1353 (1965).
(7) A. Merz and G. Märkl, *Angew. Chem. Int. Ed. Engl.*, **12**, 845 (1973).
(8) L. F. Fieser and J. L. Hartwell, *J. Am. Chem. Soc.*, **60**, 2555 (1938); L. F. Fieser, J. L. Hartwell, and J. E. Jones, "Organic Syntheses", Collect. Vol. III, Wiley, New York, N.Y., 1955, p 98.
(9) (a) N. Drinkwater, J. A. Miller, E. C. Miller, and N. C. Yang, *Proc. Am. Assoc. Cancer Res.*, **19**, 97 (1978); (b) *Cancer Res.*, in press.
(10) K. Tanikawa, T. Ishizuka, K. Suzuki, S. Kusabayashi, and H. Mikawa, *Bull. Chem. Soc. Jpn.* **41**, 2719 (1968).
(11) N. P. Buu-Hoi, J. P. Hoeffinger, and P. Jacquignon, *Bull. Soc. Chim. Fr.*, 3808 (1968).
(12) M. W. Miller, R. W. Amidon, and P. O. Tawney, *J. Am. Chem. Soc.*, **77**, 2845 (1955).
(13) B. H. Klanderman, *J. Org. Chem.*, **31**, 2618 (1961).
(14) L. Van Hove, *Bull. Soc. Chim. Belg.*, **66**, 413 (1957).

A Unique Ring Contraction of 1,4-Dihydro-5*H*-1,3,4-benzotriazepin-5-ones to 1-Methyl-2-(methylamino)-4(1*H*)-quinazolinones via an Intermediate Dimroth Rearrangement[1]

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Received April 14, 1978

We have previously reported the synthesis of substituted 3,4-dihydro- and 1,4-dihydro-5*H*-1,3,4-benzotriazepin-5-ones[2] from *o*-aminobenzoyl hydrazides[3] and the discovery of a new alkoxide-induced ring contraction of the former compounds to 3-(methylamino)-4(3*H*)-quinazolinones.[4] We now wish to report a unique, base-catalyzed, ring contraction of the 1,4-dihydro-5*H*-1,3,4-benzotriazepin-5-ones in which the rearrangement takes place through a Dimroth-like intermediate (Scheme I).

The reaction is believed to proceed via abstraction of the C_2 proton by the ethoxide to yield the highly stable 2-cyanamidobenzamide anion (**4**). This anion then cyclizes by intramolecular attack of the amide nitrogen on the cyano carbon to give the 1,3-dimethyl-2-imino-4(3*H*)-quinazolinones (**2**) (Scheme II). These quinazolinones can be isolated from

0022-3263/78/1943-3427$01.00/0