MHz, $CDCl_3$) δ 12.04 (carboxyl, s, 1 H) and 1.41–0.62 (methyl and cyclopropyl, m, 9 H)] and IR spectra [(neat film) $\bar{\nu}_{OH}$ 3520–3160, $\bar{\nu}_{C-H}$ 2880, $\bar{\nu}_{C=O}$ 1695, and $\bar{\nu}_{C-O}$ 1240 cm^{-1}], as well as from the electron impact mass spectrum (70 eV) of the corresponding methyl ester (from a diazomethane treatment) [*m/e* 128 (M^+), 113 ($M^+ - CH_3$), 97 ($M^+ - CH_3O$), and 69 ($M^+ - CH_3CO_2$)].

(−)-*c*-2,*t*-3-Dimethyl-*r*-1-cyclopropanecarboxylic Acid [(−)-3]. Diastereomeric salts were prepared from (±)-*c*-2,*t*-3-dimethyl-*r*-1-cyclopropanecarboxylic acid (**3**; 32.0 g, 280 mmol) and quinine monohydrate (50.0 g, 150 mmol) in 400 mL of absolute ethanol in a 3-L round-bottom flask. The mixture was heated at reflux for 1 h before 1.6 L of water was added. After 24 h, the crystals were collected (60.5 g; mp 124–126 °C) and redissolved in 2:1 water/ethanol. After an additional 60 h, the crystals were collected (36.0 g; mp 134–136 °C), redissolved in 1:1 water/ethanol, and allowed to stand for an additional 48 h. The collected crystals (34.4 g; mp 137–138 °C) were heated with aqueous methanol at 70 °C. After removing the methanol by distillation, the aqueous solution was made acid with dilute hydrochloric acid. The product was extracted into ether (5 × 50 mL), washed with water (3 × 30 mL), dried ($MgSO_4$), filtered, and distilled [bp 74–76 °C (6–8 Torr)] to give 5.5 g (17%) of (−)-*c*-2,*t*-3-dimethyl-*r*-1-cyclopropanecarboxylic acid (**3**), $[\alpha]^{22}_{589}$ −23.72° (*c* 0.0137, C_2H_5OH).[12,19]

(−)-*c*-2,*t*-3-Dimethyl-*r*-1-cyclopropane Methyl Ketone [(−)-4]. To a 2-L three-neck round-bottom flask fitted with a magnetic stirring bar, addition funnel, and reflux condenser was added (−)-*c*-2,*t*-3-dimethyl-*r*-1-cyclopropanecarboxylic acid [(−)-**3**; 6.1 g, 54 mmol] and 250 mL of anhydrous ether. Methyllithium (370 mmol) in ethyl ether was rapidly added, and the reaction mixture was subsequently heated at reflux for 1 h. The reaction was quenched with saturated ammonium chloride solution and extracted into ether. After washing with water (3 × 50 mL), drying ($MgSO_4$), and filtering, the optically active product[20] (4.68 g, 82%) was isolated by distillation: bp 44–48 °C (32 torr); $[\alpha]^{22}_{589}$ −27.17° (*c* 0.0138, C_2H_5OH). The structure of the product was confirmed from its ^1H NMR [(60 MHz, $CDCl_3$) δ 2.08 (methyl, s, 3 H), 1.57 (methine, m, 1 H), and 1.28–0.90 (methyl and cyclopropyl, m, 8 H)], IR [(neat film) $\bar{\nu}_{C-H}$ 3010–2880 and $\bar{\nu}_{C=O}$ 1685 cm^{-1}], and electron impact mass spectra [(70 eV) *m/e* 112 (M^+), 97 ($M^+ - CH_3$), and 69 ($M^+ - CH_3CO$)].

(−)-*c*-2,*t*-3-Dimethyl-*r*-1-cyclopropyl Acetate [(−)-5]. In a 250-mL three-neck round-bottom flask fitted with a magnetic stirring bar, addition funnel, and reflux condenser was placed (−)-*c*-2,*t*-3-dimethyl-*r*-1-cyclopropyl methyl ketone (4.7 g, 42 mmol), sodium hydrogen phosphate (28.3 g, 200 mmol), and methylene chloride (50 mL). Freshly prepared trifluoroperacetic acid [from freshly distilled trifluoroacetic anhydride (20.8 g, 104 mmol) and 90% hydrogen peroxide (4 mL)] was added to the mixture at a rate which produced a steady reflux. The reaction mixture was stirred and heated at reflux for 8 h. After washing with saturated ammonium chloride (3 × 15 mL) and water (3 × 15 mL), the product was extracted into ether (5 × 25 mL), dried ($MgSO_4$), filtered, and distilled [bp 46–48 °C (30 torr)] to yield 3.6 g (67%) of the optically active acetate, $[\alpha]^{22}_{589}$ −44.88° (*c* 0.0088, C_2H_5OH). The product structure was confirmed from its ^1H NMR [(60 MHz, $CDCl_3$) δ 3.65 (methine, m, 1 H), 1.98 (acetate methyl, s, 3 H), 1.2–0.9 (ring methyls, m, 6 H), and 0.9–0.4 (cyclopropyl, m, 2 H)], IR [(neat film) $\bar{\nu}_{C-H}$ 3020–2890, $\bar{\nu}_{C=O}$ 1755, and $\bar{\nu}_{C-O}$ 1240 cm^{-1}], and electron impact mass spectra [(70 eV) *m/e* 128 (M^+), 113 ($M^+ - CH_3$), and 69 ($M^+ - CH_3CO_2$)].

(+)-*c*-2,*t*-3-Dimethyl-*r*-1-methoxycyclopropane (7). To a 250-mL three-neck round-bottom flask fitted with a magnetic stirring bar and an addition funnel containing (−)-*c*-2,*t*-3-dimethyl-*r*-1-cyclopropyl acetate (**5**; 3.0 g, 24 mmol) in 100 mL of anhydrous ether was added freshly prepared methyllithium (52 mmol) in ether. After stirring the reaction mixture for 1 h at room temperature, saturated boric acid solution was added (30 mL) and the organic phase was dried ($MgSO_4$), filtered, and analyzed by infrared spectroscopy; $\bar{\nu}_{C=O}$ at 1755 cm^{-1} had disappeared and a $\bar{\nu}_{O-H}$ at 3650–3150 cm^{-1} had appeared, indicating the presence of the cyclopropanol **6**. Aluminum chloride (50 mg) was added to the ethereal solution before diazomethane[18] was bubbled through in a stream of nitrogen. The reaction was followed by infrared spectroscopy, where the disappearance of $\bar{\nu}_{O-H}$ after 10 h signaled the end of the reaction. (+)-*c*-2,*t*-3-Dimethyl-*r*-1-methoxycyclopropane was isolated in 18% yield by preparative gas chromatography utilizing a 4.6 m × 3.2 mm, 10% SE-30 on Chromosorb W stainless steel column operated at 75 °C, $[\alpha]^{22}_{237}$ +13.4° (*c* 0.095, C_2H_5OH). The optically active product was found to be identical both chromatographically and spectroscopically with authentic racemic material.[15]

(±)-*c*-2,*t*-3-Dimethyl-*r*-1-methoxycyclopropane (7). An authentic sample of the cyclopropyl ether was prepared by the method of Schöllkopf.[15]

Acknowledgment. Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, to the Research Corporation under a Frederick Gardner Cottrell Grant, and to The Cleveland State University under a Senior Research Award for partial support of this research.

Registry No.—**1**, 624-64-6; **2**, 56711-67-2; (±)-**3**, 02431-63-4; (−)-**3**, 20431-71-4; (−)-**3** quinine salt, 66791-91-1; (+)-**3**, 20431-72-5; (+)-**3** quinine salt, 66791-92-2; (−)-**4**, 66769-48-0; (+)-**4**, 66791-93-3; (−)-**5**, 66769-49-1; **6**, 13830-35-8; (+)-**7**, 66791-94-4; cupric trifluoromethanesulfonate, 34946-82-2; cupric carbonate, 36386-77-3; trifluoromethanesulfonic acid, 1493-13-6; ethyl diazoacetate, 623-73-4; quinine, 130-95-0.

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(20) An identical procedure from (+)-**3** gave (+)-**4**,[19] $[\alpha]^{22}_{589}$ +5.38°.

A Novel and Convenient Synthesis of Dibenz[*a*,*c*]anthracene

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Dibenz[*a*,*c*]anthracene (**1**) is a relatively rare and expensive polycyclic hydrocarbon available synthetically only through complex multistep procedures.[1] Consequently, relatively little is known concerning its chemistry or that of its derivatives, few of which are known.[1] However, **1** has been found to be a weak tumor initiator,[2] stimulating interest in its chemical and biological properties and the nature of its potentially activated metabolite(s).

We now wish to report an unexpectedly simple and conve-

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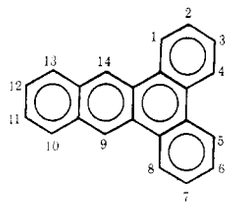
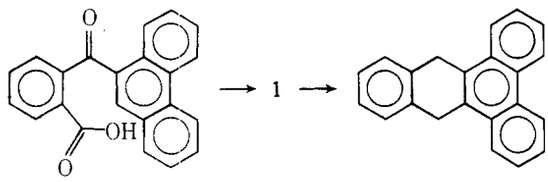


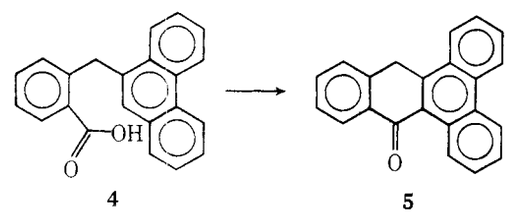
1

nient synthesis of **1**. The method involves direct reductive cyclization of 2-(9′-phenanthroyl)benzoic acid (**2**) to **1** with hydroiodic acid in refluxing acetic acid. The keto acid **2** is readily available through reaction of phthalic anhydride with the Grignard reagent of 9-bromophenanthrene.[3]

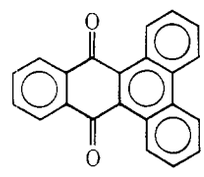


2 **3**

Initial experiments with **2** were carried out with red phosphorus and HI with the expectation that the product would be the reduced acid **4**. The conditions employed were patterned after those described for reduction of other aryl keto acids, utilizing a large excess of P and a reaction period of 10 days.[4] The major product (75%), obtained as fine white needles, mp 205.5–206.5 °C, showed no carbonyl absorption in the infrared region, while the integrated proton NMR spectrum exhibited a benzylic peak as a sharp singlet at δ 4.50 and aromatic protons consistent with the 9,14-dihydrodibenz[*a*,*c*]anthracene structure **3**. In confirmation of this assignment, treatment of **3** with *o*-chloranil in refluxing benzene gave **1** essentially quantitatively. Compound **1** was also obtained as a minor product (15%) of reductive cyclization of **2**, affording a 90% net overall yield of **1**. When reaction time was decreased to 1 day, **1** was obtained as essentially the sole product (90%). When the proportion of red phosphorus was decreased or this element eliminated entirely, **1** was also obtained as the sole product in excellent yield. It appears, therefore, that **1** is the primary product of reduction of **2** by HI, and **3** is formed through relatively slower further reduction of **1**.



4 **5**



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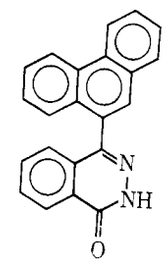
Formation of **1** from **2** is explicable through either (A) reduction to **4** followed by HI catalyzed cyclization to the ketone **5** and reduction of the latter to **1** or (B) initial cyclization of **2** to the quinone **6** followed by reduction of the latter to **1**. Reduction of quinones by P and HI to dihydro and further hydrogenated derivatives is a known reaction, although vigorous conditions (200 °C, long reaction periods) are generally employed.[1,4,5] To test the latter possibility, the quinone **6** was synthesized by cyclization of **2** with sulfuric acid and treated with HI under the optimum conditions employed for reduction of **2**. Dibenz[*a*,*c*]anthracene was obtained in good yield, supporting the feasibility of path B. Attempted synthesis of the reduced acid **4** by Clemmensen or Wolff–Kishner reduction afforded only recovered **2** and 4-(9-phenanthryl)-phthalazinone (**7**), respectively. Although Bergmann and Berlin[6] report Clemmensen reduction of **2** to **4**, they provide only minimal detail and this reaction could not be repeated. Incidentally, cyclization of **2** to the quinone did not take place under the strongly acid conditions of this reaction nor in liquid HF, suggesting that path B is less likely than path A. That reduction of **2** by HI most likely precedes cyclization is further supported by reactions carried out for shorter reaction periods (7–10 h) which furnished mixtures of products shown to contain as much as 60% of **4** by NMR spectroscopy (characteristic benzylic peak at δ 4.9). It appears likely, therefore, that while both paths A and B are feasible, that A predominates because of the greater facility of reduction than cyclization of **2**.

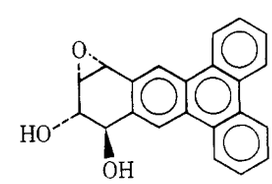


7

The unexpected ease of cyclization of **4** and/or **2** in comparison with analogous keto acids is ascribed to the relatively high olefinic character of the phenanthrene 9,10 bond in these compounds. Analogous reaction with P and HI of *o*-(1-naphthoyl)benzoic acid, which lacks such a bond, furnished only the product of carbonyl reduction, *o*-(1-naphthylmethyl)benzoic acid.

These experiments suggest that HI may be a generally useful reagent for selective reduction of quinones directly to the corresponding aromatic hydrocarbons and for selective reduction of the carbonyl groups of keto acids, an important step in the synthesis of polycyclic arenes.[1] Research is in progress to examine these possibilities.

Conversion of dibenz[*a*,*c*]anthracene to 10,11-dihydrodibenz[*a*,*c*]anthracene, a key intermediate in the synthesis of the diolepoxide derivative **8**, a potential biologically active metabolite[8] of **1**, has been described recently;[7] synthesis of **8** will be reported separately.



8

Experimental Section

9,14-Dihydrodibenz[*a*,*c*]anthracene (3). A heterogeneous solution of **2**[3] (5.2 g, 16 mmol), red phosphorus (4.5 g, 144 mmol), and 50% HI (30 mL) in glacial acetic acid (240 mL) was refluxed for 3 days and then cooled and poured into water. The precipitate was filtered, washed consecutively with water and ethanol, then dried under vacuum. The product was crystallized from benzene to provide **3** (3.0 g) as silky needles: mp 205.5–206.5 °C; NMR ($CDCl_3$) δ 4.50 (s, 4, benzylic), 7.15–7.48 (m, 4, H_{10-13}), 7.48–7.80 (m, 4, $H_{2,3,6,7}$), 7.98–8.40 (m, 2, $H_{1,8}$), and 8.57–8.90 (m, 2, $H_{4,5}$). The second crop contained a mixture of **1** and **3** (1.0 g) in the ratio of 1:2. Overall yields of **3** and **1** are 75 and 15%, respectively.

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.

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Synthesis of Aryloxiranes

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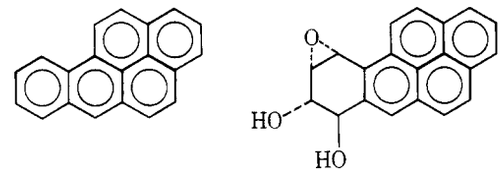
Polynuclear aromatic hydrocarbons are metabolically converted into derivatives of oxiranes which are implicated as the ultimate carcinogens in chemical carcinogenesis.[1] The in vitro and in vivo conversions of the ubiquitous benzo[*a*]pyrene (**1**) to the derivatives of isomeric 7,8-dihydroxy-9,10-epoxy-7,8,9,10-tetrahydrobenzo[*a*]pyrenes,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



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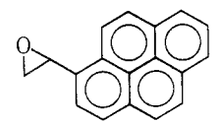

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shown to be an important event in the mechanism of chemical carcinogenesis in benzo[*a*]pyrene.[2] Isomeric BPDEs are chemically reactive compounds via their oxiranyl function to cellular macromolecules[3] and are highly biologically active in a variety 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-

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