Synthesis of the Non-K-Region Arene Oxides and Tetrahydro Epoxides of Dibenz[*a,h*]anthracene

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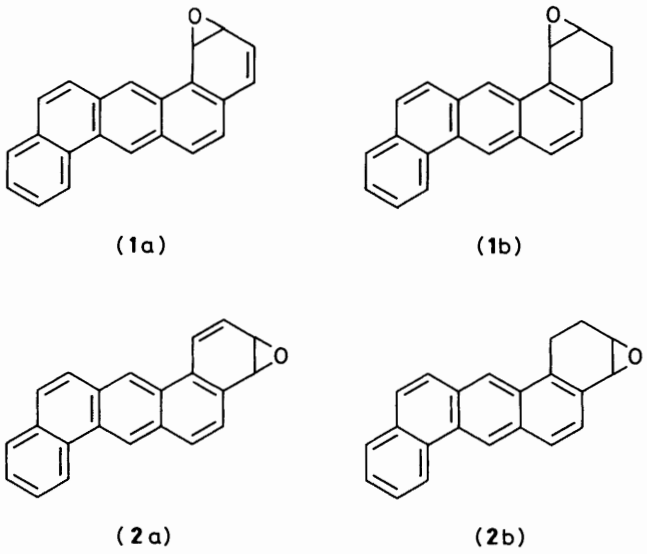
Dibenz[*a,h*]anthracene 1,2- and 3,4-oxides, (**1a**) and (**2a**), as well as the corresponding 1,2,3,4-tetrahydro epoxides, (**1b**) and (**2b**), were synthesized from 3,4-dihydro- and 1,2-dihydrodibenz[*a,h*]anthracene, (**12**) and (**17**), utilizing bromohydrin ester intermediates. Compounds (**12**) and (**17**) were prepared from 3,4-dihydrodibenz[*a,h*]anthracen-1(2*H*)-one (**10**) and 1,2-dihydrodibenz[*a,h*]anthracen-4(3*H*)-one (**15**) in almost quantitative yield. An improved synthesis of (**10**) is described. ^{1}H N.m.r. analysis revealed that (**1a**) and (**2a**) exist at room temperature predominantly as arene oxides and not as oxepines. Spontaneous aromatization of (**1a**) in aqueous solution at pH 7.4 gave a mixture of the 1- and 2-phenols, while (**2a**) yielded a mixture of the 3- and 4-phenols.

Carcinogenic polycyclic aromatic hydrocarbons (PAH) exert their cytotoxic, mutagenic and carcinogenic properties only after metabolic conversion into reactive intermediates.[1–3] The first step in this activation pathway consists of the attack of cytochrome P-450 dependent mono-oxygenases resulting in the formation of arene oxides.[4–7] Subsequent enzymatic reactions lead to *trans*-dihydro diols[4–6,8,9] and finally to dihydro diol epoxides some of which are considered the ultimate mutagenic and carcinogenic species of PAH.[10–13]

Investigations on the microsomal metabolism of the carcinogenic PAH dibenz[*a,h*]anthracene (DBA) indicate the enzymatic formation of the three possible arene oxide structures, *i.e.*, (**1a**), (**2a**) (*cf.* Scheme 1) and DBA 5,6-oxide.[14–17] These arene oxides were required in order to elucidate the mechanism of metabolic formation of phenols of DBA and to estimate their contribution to the mutagenic and carcinogenic activity of DBA. Several synthetic routes for the preparation of DBA 5,6-oxide are available,[14,18] while the synthesis of (**1a**) has not yet been reported; (**2a**) has been synthesized[7,19] for studies concerning its isomerization to oxepines[19] but experimental details on its preparation are still lacking.

We now describe syntheses of (**1a**) and (**2a**) as well as of the tetrahydro epoxides (**1b**) and (**2b**) (*cf.* Scheme 1) which can be taken as model compounds for dihydrodiol epoxides lacking the hydroxy groups.



Scheme 1.

Results and Discussion

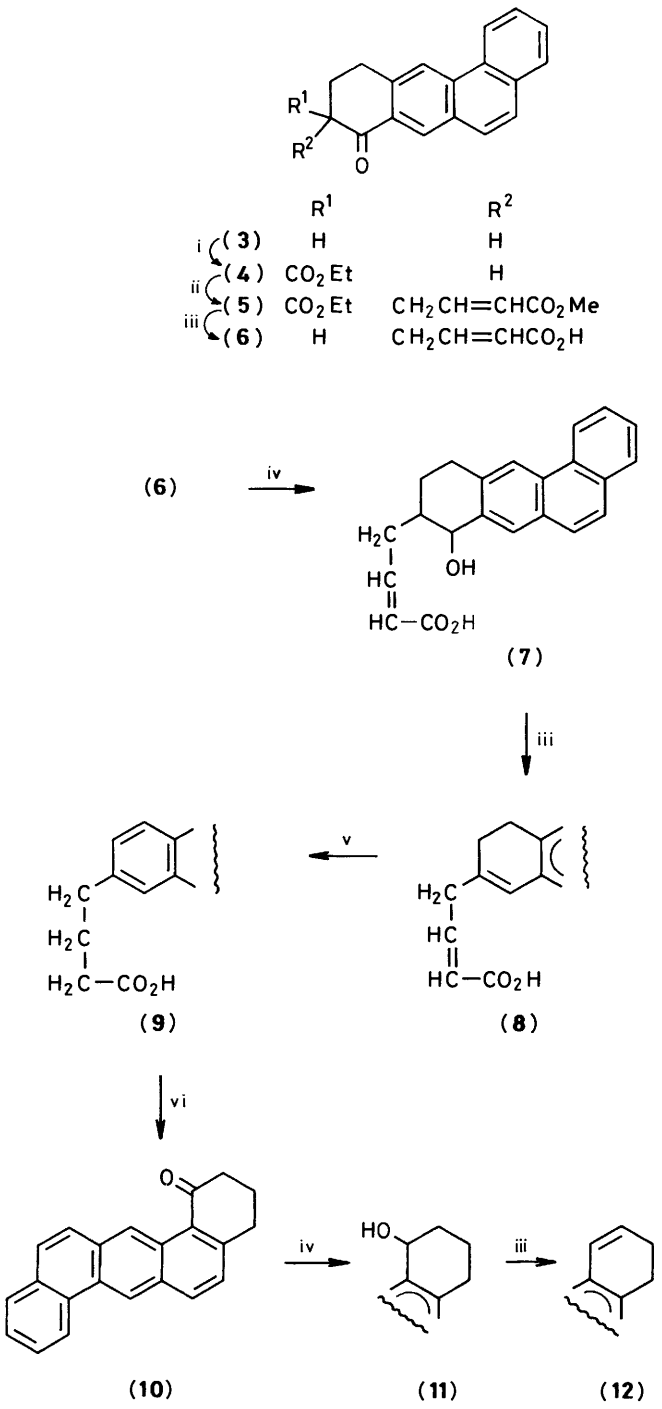
A general synthetic method for non-K-region arene oxides[20] that had been successfully applied in the case of many PAH, *i.e.*, naphthalene,[20] phenanthrene,[20] anthracene,[21] chrysene,[22,23] cyclopental[*cd*]pyrene,[24] benz[*a*]anthracene,[25–28] benzo[*c*]-phenanthrene,[29] triphenylene,[30] benzo[*g*]chrysene,[31] benzo-[*a*]pyrene,[20] benzo[*e*]pyrene[32] and dibenz[*a,c*]anthracene[33] was used for the preparation of (**1a**), (**2a**), (**1b**) and (**2b**).

The key step in the synthesis of the tetrahydro epoxides, (**1b**) and (**2b**) was the dehydrobromination of the corresponding bromohydrin acetates, (**13**) and (**18**), whereas in the case of the arene oxides, (**1a**) and (**2a**), dehydrobromination of the corresponding dibromo esters, (**14**) and (**19**), was employed.

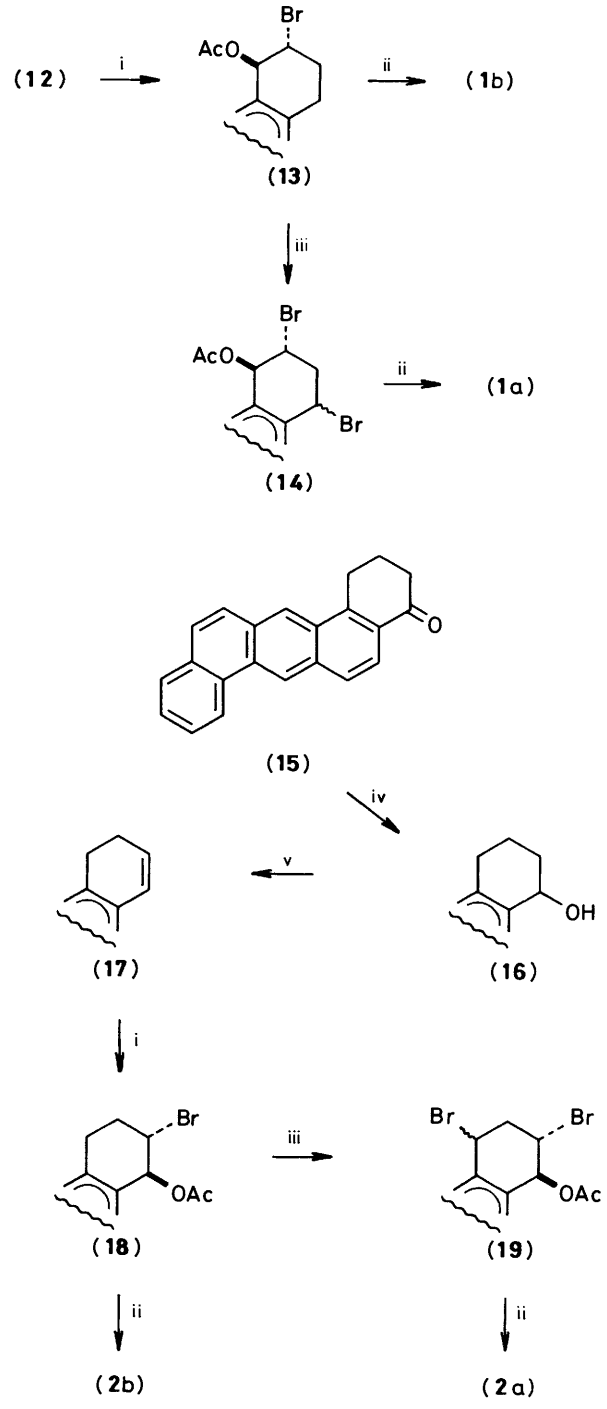
The key intermediate in each synthetic pathway (*cf.* Schemes 2 and 3) was a 1,2,3,4-tetrahydro ketone of DBA, *i.e.*, (**10**) and (**15**).

Resynthesis of the ketone (**10**)[34,35] resulted in very low overall yield mainly caused by the inefficient transformation of (**3**) to 9-methoxycarbonyl-10,11-dihydrobenz[*a*]anthracen-8(9*H*)-one[36] by condensation with dimethyl oxalate followed by thermal decarbonylation. This difficulty was circumvented by activation of C-9 in (**3**) *via* diethyl carbonate condensation,[37] transformation of (**4**) into the potassium salt, alkylation with methyl 4-bromocrotonate[35] and removal of the activating substituent at C-9 of (**5**) with conc. HCl leading to (**6**) in 62% overall yield. The subsequent synthetic steps to (**9**) proceeded smoothly, essentially as described.[35] For the cyclization of the benz[*a*]anthrylbutyric acid (**9**), methanesulphonic acid[38] proved to be superior to other reagents. Thus ketone (**10**) was obtained after chromatographic purification in 13% overall yield from (**3**). Reduction of (**10**) to the alcohol (**11**) and dehydration to the olefin (**12**) proceeded almost quantitatively. Compound (**12**) was transformed, in glacial acetic acid, into the bromohydrin acetate (**13**) with NBS† in the presence of lithium acetate.[20,21] Upon treatment of (**13**) with sodium methoxide, an alcoholate ion is formed which closes the oxirane ring of the tetrahydro epoxide (**1b**) *via* an intramolecular nucleophilic

† *N*-Bromoacetamide, usually employed for the transformation of a PAH olefin to the corresponding bromohydrin acetate,[20,21] can conveniently be replaced by *N*-bromosuccinimide (NBS).



Scheme 2. *Reagents:* i, NaH, $CO(OEt)_2$; ii, K, methyl 4-bromocrotonate; iii, HCl; iv, $NaBH_4$; v, KOH, 220 °C; vi, $MeSO_3H$



Scheme 3. *Reagents:* i, LiOAc, NBS; ii, NaOMe; iii, NBS, UV; iv, $NaBH_4$; v, HCl

substitution. Benzylic bromination of (**13**) with NBS leads to a labile dibromo ester (**14**) whose treatment with sodium methoxide forms the olefinic double bond and the oxirane ring of the arene oxide (**1a**) simultaneously. Complete purification of (**1a**) by low temperature recrystallization was unsuccessful; purification by chromatography on deactivated alumina failed also because of complete aromatization to a mixture of the 1- and 2-phenols of DBA; finally digestion with acetone yielded a satisfactorily pure product as judged by ^1H n.m.r. analysis.

For the synthesis of the epoxides of DBA in the 3,4-position ketone (**15**) was the key intermediate; it was obtained by direct alkylation of (**3**) with methyl 4-bromocrotonate *via* a Reformatsky reaction[35,39] followed by synthetic steps similar to the ones mentioned above for the transformation of (**7**) to (**10**). Preparation of (**2a**) and (**2b**) from (**15**) proceeded in essentially the same way as described for (**1a**) and (**1b**). Arene oxide (**2a**) in contrast to (**1a**) could be purified by recrystallization at −70 °C without decomposition.

The ^1H n.m.r. spectrum of (**1a**) shows great similarity to that of 1,2-dihydro-1,2-epoxybenz[*a*]anthracene,[28] as far as the signals of protons in the 1,2,3,4-position are concerned, thus proving that (**1a**) exists as the arene oxide as theoretically

predicted[40] and not as an areno[*c*]oxepine. The same holds true for (**2a**) whose ^{1}H n.m.r. spectrum confirms predictions[40] of its existence at ambient temperature as an arene oxide.

Recently it has been shown[19,32,33] that several arene oxides including (**2a**)[19] prepared by the same reaction sequence as used in this study can be transformed *via* a photochemical oxygen walk pathway into the corresponding areno[*b*]oxepines. However ^{1}H n.m.r. analysis of purified samples of (**1a**) and (**2a**) provided no indication of the presence of areno[*b*]oxepines. Nevertheless the formation of areno[*b*]oxepines as by-products during synthesis of (**1a**) and (**2a**) cannot be excluded since they may have been removed during purification of the arene oxides and therefore escaped detection.

Spontaneous aromatization of (**1a**) in aqueous solution at pH 7.4 resulted in a mixture of the 1- and 2-phenols of DBA in the ratio of 1:3.9 while (**2a**) yielded a mixture of the 3- and 4-phenols of DBA, under the same conditions, in the ratio of 1:6.3.[17] For the prediction of, preferential formation of the phenol from (**1a**) the index N_i proposed by Szentpály[17,41] was better suited than the reactivity number, N_t.[42]

The biological activities of (**1a**), (**2a**), (**1b**) and (**2b**) were investigated using reversion of histidine-dependent mutants of *Salmonella typhimurium* (TA100) to histidine prototrophy as the test system. Compounds (**1a**) and (**2a**) showed only very weak mutagenic effects[43] probably due to their fast spontaneous aromatization to phenols which are not direct bacterial mutagens in the case of DBA.[43]

Tetrahydro epoxides (**1b**) and (**2b**) can be considered model compounds for dihydrodiol epoxides of DBA lacking the hydroxy groups. The chemical reactivity of tetrahydro epoxides of PAH can be calculated by the ease of carbonium ion formation at the benzylic carbon atom of the oxirane ring and is expressed as values of $\Delta E_{deloc}/\beta$.[44] These values are 0.738 for (**1b**) and 0.593 for (**2b**).[43,44] The different chemical reactivities of (**1b**) and (**2b**) are reflected by their specific bacterial mutagenicity in as far as (**1b**) leads to about 30 times more his$^+$ revertants per nmol as compared to (**2b**).[43]

Experimental

N-Bromosuccinimide (NBS), α,α′-azoisobutyronitrile (AIBN) and sodium methoxide were supplied by Aldrich-Chemie, lithium acetate dihydrate by Fluka. Silica gel 60, 0.06—0.2 mm, was obtained from Macherey-Nagel, and neutral alumina from Merck. Light petroleum used as mobile phase in column chromatography had b.p. 40—60 °C. ^{1}H N.m.r. spectra were recorded on a Varian EM 360 or a Bruker WH 90 or a Bruker AM 400 spectrometer. Chemical shifts (σ_H) are given in p.p.m. with Me_4Si as an internal standard. Electron impact mass spectra were performed on a Varian CH 7A system at 70 eV. U.v. spectra were measured on a Shimadzu spectrophotometer MPS 2000. M.p.s were determined with a Büchi 510 melting point apparatus and are uncorrected.

Ethyl 8-Oxo-8,9,10,11-tetrahydrobenz[a]*anthracene-9-carboxylate* (**4**).—A solution of 10,11-dihydrobenz[*a*]anthracen-8(9*H*)-one, (**3**)[45] (67.6 g, 0.275 mol) in dry 1,2-dimethoxyethane (1.2 l) was treated with oil-free sodium hydride (18.7 g, 0.78 mol) and diethyl carbonate (64.9 g, 0.55 mol) and heated to 100 °C for 2h. The cooled reaction mixture was diluted with water (3 l), made acidic with glacial acetic acid, and extracted with CH_2Cl_2. The extract was dried ($MgSO_4$) and evaporated and the residue washed with hexane and recrystallized from acetone to yield the *title compound* (**4**) (58.6 g, 67%) as pale brown crystals, m.p. 118—119 °C (Found: C, 78.95; H, 5.6. $C_{21}H_{18}O_3$ requires C, 79.23; H, 5.70%); δ_H(60 MHz; $CDCl_3$) 1.37 (3 H, t, CH_3CH_2), 2.50—3.20 (5 H, m, 9—11-H), 4.30 (2 H, q, CH_3CH_2), 7.47—7.90 (5 H, m, 2—6-H), and 8.27—8.63 (3 H, m, 1-, 7-, 12-H); *m/z* 318 (M^+, 75%), 272 ($M - C_2H_5OH$, 100), 244 (47), and 215 (33).

9-(3-Carboxyallyl)-10,11-dihydrobenz[a]*anthracen-8(9H)-one* (**6**).—A solution of (**4**) (67.0 g, 0.21 mol) in toluene (340 ml) was treated with finely cut potassium (8.2 g, 0.21 mol) under argon and stirred at 100 °C for 4h. Methyl 4-bromocrotonate[46] (38.3 g, 0.214 mol) was then added slowly and the mixture heated to reflux. After 48 h under reflux the mixture was distributed between 8% (v/v) HCl and CH_2Cl_2. The latter phase was separated, dried ($MgSO_4$), and evaporated to afford the crude intermediate (**5**) (85 g); *m/z* 416 (M^+, 42%), 343 ($M - C_2H_5CO_2$, 13), 284 (27), and 244 (42).

Crude (**5**) (85 g) in a mixture of glacial acetic acid (250 ml) and conc. HCl (250 ml) was heated to reflux for 5 h. Upon cooling a solid precipitated which was filtered off, washed with water, and dried. The *title compound* (**6**) (64.6 g, 93% from (**4**)) was obtained as an off-white powder, m.p. 148 °C (Found: C, 79.75; H, 5.40. $C_{22}H_{18}O_3$ requires C, 79.98; H, 5.49%); δ_H(60 MHz; [$^2H_6$]-DMSO) 2.00—2.43 (2 H, m, 10-H), 2.58—2.97 (2 H, m, $CH_2CH=CH$), 3.07—3.47 (3 H, m, 9- and 11-H), 5.83 (1 H, d, $CH=CHCO_2H$), 6.67—7.15 (1 H, m, $CH=CHCO_2H$), 7.41—8.07 (5 H, m, 2—6-H), 8.45 (1 H, s, 12-H), 8.67 (1 H, s, 7-H), and 8.55—8.91 (1 H, m, 1-H); *m/z* 330 (M^+, 36%), 286 ($M - CO_2$, 13), 271 ($M - CH_2CO_2H$, 67), 245 (38), and 189 (100).

9-(3-Carboxyallyl)-8,9,10,11-tetrahydrobenz[a]*anthracen-8-ol* (**7**).—A solution of (**6**) (64.0 g, 0.194 mol) in EtOH (700 ml) was treated with $NaBH_4$ (15.2 g, 0.4 mol) in small portions and then stirred at room temperature for 20 h. The reaction mixture was neutralized with glacial acetic acid and the solvent removed by evaporation under reduced pressure. The residue was acidified conc. HCl, and the precipitate was filtered off, washed with water, and dried to give the *title compound* (**7**) (62.1 g, 96%) as a white solid, m.p. 233—234 °C (Found: C, 79.2; H, 5.95. $C_{22}H_{20}O_3$ requires C, 79.50; H, 6.06%); δ_H(60 MHz; [$^2H_8$]THF) 2.12—2.45 (3 H, m, 9-, 10-H), 2.83—3.27 (5 H, m, $CH_2CH=CH$, 8-, 11-H), 5.87 (1 H, d, $CH=CHCO_2H$), 6.67—7.23 (1 H, m, $CH=CHCO_2H$), 7.42—7.98 (6 H, m, 2—7-H), 8.50 (1 H, s, 12-H), and 8.58—8.83 (1 H, m, 1-H); *m/z* 314 ($M - H_2O$, 44%) and 229 (29).

4-(9-Benz[a]*anthryl)butyric Acid* (**9**).[34]—A solution of (**7**) (61.0 g, 0.184 mol) in glacial acetic acid (500 ml) was treated with conc. HCl (5 ml) and stirred under reflux for 1 h. After cooling the mixture was poured into water. The precipitate was filtered off, washed with water, and dried to afford the crude intermediate (**8**) (52.8 g) as an off-white solid; *m/z* 314 (M^+, 73%), and 229 ($M - CH_2CH=CHCO_2H$, 100).

A solution of the crude intermediate (**8**) (52.0 g) and KOH (70 g, 1.25 mol) in ethylene glycol (600 ml) was stirred at 220 °C for 3 h. The resulting mixture was diluted with water (1 l) and then 10% (v/v) HCl (1 l) was added with vigorous stirring. The precipitate was filtered off, washed with water, and dried to yield crude (**9**) [43.3 g, *ca.* 76% from (**7**)] as a brownish solid. Attempts to purify (**9**) by recrystallization resulted in considerable loss of material; therefore only a small sample of the crude product was recrystallized from benzene for spectroscopic verification of its structure. Compound (**9**) was obtained as off-white crystals, m.p. 188—190 °C (lit.,[34] 192—193 °C); δ_H(60 MHz; [$^2H_6$] DMSO) 1.93—2.52 (4 H, m, $ArCH_2CH_2$), 2.63—2.97 (2 H, m, CH_2CO_2H), 7.33—8.08 (8 H, m, 2—6-, 8, 10-, 11-H), 8.32 (1 H, s, 7-H), 8.67—8.97 (1 H, m, 1-H), and 9.25 (1 H, s, 12-H); *m/z* 314 (M^+, 100%), 270 ($M - CO_2$, 11), and 241 ($M - CH_2CH_2CO_2H$, 76).

3,4-Dihydrodibenz[a,h]*anthracen-1(2H)-one* (**10**).[34,35]—Crude (**9**) (43.0 g) in methanesulphonic acid (310 ml) was heated to 80 °C for 1.5 h. The resulting mixture was poured onto ice

and extracted with CH_2Cl_2. The organic phase was washed with saturated aqueous $NaHCO_3$ and water, dried ($MgSO_4$), and evaporated to afford a solid which was put on neutral alumina (activity 2—3; 600 g) in a dropping funnel (8 × 12 cm) and continuously extracted with hot benzene. The extract was brought to dryness and the resulting solid purified by chromatography on a silica gel column (5 × 50 cm) with $CHCl_3$–light petroleum (4:1, v/v) to yield compound (**10**) (11.5 g, *ca.* 28%) as yellow crystals, m.p. 164—165 °C (lit.,[34] 168—169 °C); δ_H(60 MHz; $CDCl_3$) 2.07—2.37 (2 H, m, 3-H), 2.80 (2 H, t, 2-H), 3.07 (2 H, t, 4-H), 7.13—8.10 (7 H, m, 5-, 6-, 9—13-H), 8.57—8.80 (1 H, m, 8-H), 8.93 (1 H, s, 7-H), and 9.97 (1 H, s, 14-H); *m/z* 296 (M^+, 100%), 268 (M − CO, 16), and 240 (55).

1,2,3,4-*Tetrahydrodibenz*[a,h]*anthracen*-1-*ol* (**11**).—A suspension of (**10**) (4.4 g, 14.9 mmol) in 95% (v/v) EtOH (100 ml) was treated with $NaBH_4$ (2.0 g, 53 mmol) and stirred under reflux for 3 h. The cooled reaction mixture was neutralized with HOAc and diluted with water (500 ml). The precipitate was filtered off, washed with water, saturated aqueous $NaHCO_3$, and again water, and then dried to afford the *title compound* (**11**) (4.3 g, 97%) as a white solid, m.p. 181—182 °C (Found: C, 88.3; H, 5.95. $C_{22}H_{18}O$ requires C, 88.56; H, 6.08%); δ_H(60 MHz; $CDCl_3$) 1.83—2.13 (4 H, m, 2-, 3-H), 2.73—3.00 (2 H, m, 4-H), 5.50—5.63 (1 H, m, 1-H), 7.53—8.00 (7 H, m, 5-, 6-, 9—13-H), 8.73 (1 H, s, 14-H), 8.77—8.93 (1 H, m, 8-H), and 9.07 (1 H, s, 7-H); *m/z* 298 (M^+, 100%), 280 (M − H_2O, 13), and 278 (6).

3,4-*Dihydrodibenz*[a,h]*anthracene* (**12**).—A solution of (**11**) (4.2 g, 14.1 mmol) in glacial acetic acid (170 ml) was treated with conc. HCl (100 µl) and then stirred at reflux under argon for 0.5 h. The cooled reaction mixture was diluted with water (1 l), and the precipitate filtered off, washed with water, saturated aqueous $NaHCO_3$, and again with water and then dried to furnish the *title compound* (**12**) (3.7 g, 94%) as a white powder, m.p. 203—205 °C (Found: C, 94.0; H, 5.95. $C_{22}H_{16}$ requires C, 94.25; H, 5.75%); δ_H(60 MHz; $CDCl_3$) 2.23—2.67 (2 H, m, 3-H), 2.87—3.17 (2 H, m, 4-H), 6.27—6.53 (1 H, m, 2-H), 7.43—8.07 (8 H, m, 1-, 5-, 6-, 9—13 H), 8.63 (1 H, s, 14-H), 8.73—8.93 (1 H, m, 8-H), and 9.13 (1 H, s, 7-H); *m/z* 280 (M^+, 100%), 279 (M − H, 32), and 278 (M − H_2, 29).

(±)-trans-1-*Acetoxy*-2-*bromo*-1,2,3,4-*tetrahydrodibenz*[a,h]*anthracene* (**13**).—A suspension of (**12**) (4.2, 15 mmol), LiOAc·$2H_2O$ (8.5 g, 83 mmol) and NBS (3.6 g, 20 mmol) in glacial acetic acid (425 ml) was stirred at room temperature under argon in the dark for 5 h and then poured into water (1 l). The precipitate was filtered off, washed with saturated aqueous $NaHCO_3$ and water to afford crude (**13**) which was purified by chromatography on a silica gel column (5 × 50 cm) with $CHCl_3$-light petroleum (4:1, v/v) to yield the *title compound* (**13**) (2.0 g, 32%) as a yellowish solid, m.p. 170—172 °C (decomp.) (Found: C, 68.45; H, 4.5; Br, 20.9. $C_{24}H_{19}BrO_2$ requires C, 68.75; H, 4.57; Br, 19.06%); δ_H(90 MHz; $CDCl_3$) 2.09 (3 H, s, H-acetate), 2.23—2.55 (2 H, m, 3-H), 2.98—3.36 (2 H, m, 4-H), 4.66—4.77 (1 H, m, 2-H), 6.92 (1 H, d, 1-H, $J_{1,2}$ 2.64 Hz), 7.34 (1 H, d, $J_{5,6}$ 8.8 Hz, 5-H), 7.60—7.86 (5 H, m, 6-, 9—12-H), 8.07 (1 H, d, $J_{12,13}$ 8.8 H, 13-H), 8.27 (1 H, s, 14-H), 8.71—8.84 (1 H, m, 8-H), and 9.13 (1 H, s, 7-H); *m/z* 420 (M^+ [^{81}Br], 24%), 418 (M^+ [^{79}Br], 23), 338 (M − HBr, 13), 296 (M − HBr − CH_2CO, 36), 280 (M − HBr − CH_2CO_2, 100), and 278 (M − HBr − CH_3CO_2H, 51).

(±)-1,2,3,4-*Tetrahydro*-1,2-*epoxydibenz*[a,h]*anthracene* (**1b**).—A solution of (**13**) (0.2 g, 0.48 mmol) in dry THF (10 ml) was treated with NaOMe (52 mg, 0.96 mmol) and stirred under argon at 0 °C for 6 h. The mixture was then diluted with water (50 ml), extracted with CH_2Cl_2 and the extract dried (K_2CO_3) and evaporated, and the residue recrystallized from CH_2Cl_2–light petroleum to give the *title compound* (**1b**) (73.4 mg, 52%) as a white solid, m.p. 190—191 °C (Found: C, 88.9; H, 5.4. $C_{22}H_{16}O$ requires C, 89.16; H, 5.44%); δ_H(90 MHz; CD_2Cl_2) 1.73—2.10 (1 H, m, 3-H), 2.42—2.68 (1 H, m, 3-H), 2.80—3.01 (2 H, m, 4-H), 3.87—3.95 (1 H, m, 2-H), 4.85 (1 H, d, $J_{1,2}$ 4.4 Hz, 1-H), 7.30 (1 H, d, $J_{5,6}$ 8.51 Hz, 5-H), 7.59—7.92 (5 H, m, 6-, 9—12-H), 8.06 (1 H, d, $J_{12,13}$ 8.8 Hz, 13-H), 8.80 (1 H, s, 14-H), 8.81—8.88 (1 H, m, 8-H), and 9.17 (1 H, s, 7-H); *m/z* 296 (M^+, 100%), 268 (M − CO, 22), and 267 (M − CHO, 20); $\lambda_{max.}$ (EtOH), 371 (ε 5 800 dm^3 mol^{-1} cm^{-1}), 353 (8 800), 336 (7 700), 322 (5 300), 291 (102 000), 281 (88 100), 271 (54 200), 263 (44 700), 237 (33 400), and 223 nm (40 200).

(±)-1,2-*Dihydro*-1,2-*epoxydibenz*[a,h]*anthracene* (**1a**).—To a solution of (**13**) (0.525 g, 1.25 mmol) in dry CCl_4 (100 ml) was added NBS (0.260 g, 1.46 mmol) and AIBN (15 mg). The suspension was irradiated with a heat lamp (Osram Vitalux, 300 W) and stirred under argon at 60 °C for 25 min. Precipitated succinimide was filtered off and the solvent evaporated under reduced pressure. The residue containing (**14**) was dissolved in dry THF (7.5 ml), treated with NaOMe (0.435 g, 8.1 mmol) and stirred under argon at room temperature in the dark for 2 days. The resulting turbid solution was filtered and the filtrate evaporated at 0 °C under reduced pressure. Digestion of the residue with acetone yielded the *title compound* (**1a**) [131 mg, 36% from (**13**)] as a yellowish solid, m.p. 170 °C (decomp.). (Found: C, 89.45; H, 5.0. $C_{22}H_{14}O$ requires C, 89.77; H, 4.79%); δ_H(400 MHz; [$^2H_8$]-THF) 4.28—4.32 (1 H, m, 2-H), 5.48 (1 H, d, $J_{1,2}$ 3.88 Hz, 1-H), 6.61—6.64 (1 H, dd, $J_{3,4}$ 9.48 Hz, $J_{2,3}$ 3.71 Hz, 3-H), 6.93—6.96 (1 H, dd, $J_{3,4}$ 9.48 Hz, $J_{2,4}$ 1.65 Hz, 4-H), 7.53 (1 H, d, $J_{5,6}$ 8.58 Hz, 5-H), 7.66—7.75 (3 H, m, 6-, 9-, 10-H), 7.89—7.96 (2 H, m, 11-, 12-H), 8.17 (1 H, d, $J_{12,13}$ 8.53 Hz, 13-H), 8.92—8.97 (1 H, m, 8-H), 9.08 (1 H, s, 14-H), and 9.33 (1 H, s, 7-H); *m/z* 294 (M^+, 100%), 278 (M − O, 7), 266 (M − CO, 23), and 265 (M − CHO, 70); $\lambda_{max.}$ (EtOH) 351 (ε 7 800 dm^3 mol^{-1} cm^{-1}), 324sh, 308 (37 700), 293 (56 000), 283sh, and 225 nm (29 800).

1,2,3,4-*Tetrahydrodibenz*[a,h]*anthracen*-4-*ol* (**16**).—A suspension of 1,2-dihydrodibenz[*a,h*]anthracen-4(3*H*)-one (**15**)[35] (10.4 g, 35 mmol) in absolute EtOH (500 ml) was treated with $NaBH_4$ (1.8 g, 48 mmol) and stirred at 80 °C for 4 h. Work-up as described for compound (**11**) yielded the *title compound* (**16**) (10.0 g, 96%) as a pale yellow solid, m.p. 228—229 °C (Found: C, 88.3; H, 6.2. $C_{22}H_{18}O$ requires C, 88.56; H, 6.08%); δ_H(60 MHz; [$^2H_6$] DMSO) 1.63—2.23 (4 H, m, 2-, 3-H), 2.90—3.23 (2 H, m, 1-H), 4.60—4.90 (1 H, m, 4-H); 5.13—5.37 (1 H, m, OH), 7.50—8.13 (7 H, m, 5, 6, 9—13H), 8.53 (1 H, s, 14-H), 8.80—9.03 (1 H, m, 8-H), and 9.30 (1 H, s, 7-H); *m/z* 298 (M^+, 100%), 280 (M − H_2O, 32), and 278 (10).

1,2-*Dihydrodibenz*[a,h]*anthracene* (**17**).—A solution of (**16**) (4.2 g, 14.1 mmol) in glacial acetic acid (140 ml) was stirred under reflux when conc. HCl (0.3 ml) in glacial acetic acid (20 ml) was slowly added and stirring continued for 0.5 h. Work-up as described for compound (**12**) yielded the *title compound* (**17**) (3.8 g, 96%) as an off-white solid, m.p. 237—238 °C (Found: C, 93.95; H, 5.85. $C_{22}H_{16}$ requires C, 94.25; H, 5.75%); δ_H(60 MHz; [$^2H_6$] benzene) 2.15—2.40 (2 H, m, 2-H), 2.90—3.22 (2 H, m, 1-H), 5.80—6.18 (1 H, m, 3-H) 6.45—6.70 (1 H, m, 4-H), 7.20—7.95 (7 H, m, 5-, 6-, 9—13-H), 8.32 (1 H, s, 14–H), 8.45—8.68 (1 H, m, 8-H), and 9.00 (1 H, s, 7-H); *m/z* 280 (M^+, 100%), 279 (M − H, 53), and 278 (M − H_2, 49).

(±)-trans-4-*Acetoxy*-3-*bromo*-1,2,3,4-*tetrahydrodibenz*[a,h]*anthracene* (**18**).—A suspension of (**17**) (3.4 g, 12.1 mmol), LiOAc·$2H_2O$ (6.8 g, 67 mmol) and NBS (2.2 g, 12.4 mmol)

in glacial acetic acid (340 ml) was treated, worked up and purified as described for compound (**13**) to yield the *title compound* (**18**) (3.1 g, 61%) as a white solid, m.p. 176—177 °C (decomp.). Found: C, 68.5; H, 4.85; Br, 21.0. $C_{24}H_{19}BrO_2$ requires C, 68.75; H, 4.57; Br, 19.06%); δ_H(90 MHz; $CDCl_3$) 2.16 (3 H, s, H-acetate), 2.43—2.69 (2 H, m, 2-H), 3.38—3.55 (2 H, m, 1-H), 4.52—4.67 (1 H, m, 3-H), 6.34 (1 H, d, $J_{3,4}$ 4.4 Hz, 4-H), 7.34 (1 H, d, $J_{5,6}$ 8.8 Hz, 5-H), 7.56—7.87 (5 H, m, 6-, 9—12-H), 7.98 (1 H, d, $J_{12,13}$ 8.8 Hz, 13-H), 8.48 (1 H, s, 14-H), 8.76—8.86 (1 H, m, 8-H), and 9.10 (1 H, s, 7-H); *m/z* 420 (M^+[^{81}Br], 21%), 418 (M^+[^{79}Br], 21), 338 (M − HBr, 25), 296 (M − HBr − CH_2CO, 59), 280 (M − HBr − CH_2CO_2, 75), 279 (M − HBr − CH_3CO_2, 100), and 278 (M − HBr − CH_3CO_2H, 42).

(±)-1,2,3,4-*Tetrahydro*-3,4-*epoxydibenz*[a,h]*anthracene* (**2b**).—A solution of (**13**) (0.2 g, 0.48 mmol) in dry THF (10 ml) was treated with NaOMe (52 mg, 0.96 mmol) and stirred under argon at 0 °C for 6 h. Work-up and purification as described for compound (**1b**) resulted in the *title compound* (**2b**) (72.7 mg, 51%) as a white solid, m.p. 231—232 °C (decomp). (Found: C, 88.9; H, 5.6. $C_{22}H_{16}O$ requires C, 89.16; H, 5.44%); δ_H(90 MHz; CD_2Cl_2) 1.86—2.11 (1 H, m, 2-H), 2.54—3.07 (2 H, m, 1-H), 3.47—3.86 (2 H, m, 2-, 3-H), 4.04 (1 H, d, $J_{3,4}$ 4.11 Hz, 4-H), 7.56—7.90 (6 H, m, 5-, 6-, 9—12-H), 8.04 (1 H, d, $J_{12,13}$ 8.5 Hz, 13-H), 8.56 (1 H, s, 14-H), 8.77—8.88 (1 H, m, 8-H), 9.17 (1 H, s, 7-H); *m/z* 296 (M^+,100%), 268 (M − CO, 16), 267 (M − CHO, 16); $\lambda_{max.}$ (EtOH) 370 (ε 3 500 dm^3 mol^{-1} cm^{-1}), 354 (6 000), 337 (5 900), 323 (4 400), 294 (103 000), 282 (82 300), 272 (46 000), 263 (37 100), 239 (27 100), and 222 nm (28 500).

(±)-3,4-*Dihydro*-3,4-*epoxydibenz*[a,h]*anthracene* (**2a**).—To a solution of (**18**) (0.525 g, 1.25 mmol) in dry CCl_4 (100 ml) was added NBS (0.260 g, 1.46 mmol) and AIBN (15 mg). Reaction conditions and further treatment were exactly as described for the preparation of (**1a**). Crude (**2a**) was recrystallized from THF–pentane at −78 °C, filtered off under argon, and dried to yield the *title compound* (**2a**) (36.8 mg, 10% from (**18**)) as a yellowish solid, m.p. 245 °C (decomp.). (Found: C, 89.5; H, 4.7. $C_{22}H_{14}O$ requires C, 89.77; H, 4.79%); δ_H(400 MHz; [$^2H_8$]THF) 4.26—4.28 (1 H, m, 3-H), 4.69 (1 H, d, $J_{3,4}$ 3.73 Hz. 4-H), 6.72—6.75 (1 H, dd, $J_{1,2}$ 9.83 Hz, $J_{2,3}$ 3.69 Hz, 2-H), 7.59—7.63 (1 H, m, 1-H), 7.66—7.70 (2 H, m, 9-, 10-H), 7.82—7.94 (4 H, m, 5-, 6-, 11-, 12-H), 8.81 (1 H, d, $J_{12,13}$ 8.51 Hz, 13-H), 8.92 (1 H, d, $J_{8,9}$ 6.97 Hz, 8-H), 8.93 (1 H, s, 14-H), and 9.33 (1 H, s, 7-H); *m/z* 294 (M^+, 100%), 278 (M − O, 4), 266 (M − CO, 9), and 265 (M − CHO, 34); $\lambda_{max.}$ (EtOH) 377 (ε 2 800 dm^3 mol^{-1} cm^{-1}), 354 (3 800), 337 (3 100), 298 (85 000), 288 (82 200), 248 (26 000), and 229 nm (34 400).

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