not be obtained: ^{1}H NMR ($CDCl_3$) δ 3.21, 3.29 (each s, 3 each, CH_3), 4.23 (apparent s, 2, H-4), 4.43 (dd, 1, H-5′a, $J_{4',5'a}$ = 5.1 Hz, $J_{5'a,5'b}$ = 12.0 Hz), 4.56–4.65 (m, 1, H-4′), 4.68 (dd, 1, H-5′b, $J_{4',5'b}$ = 3.4 Hz), 4.77 (br s, 1, NH, exchanges with D_2O), 5.67 (dd, 1, H-3′, $J_{2',3'}$ = 5.4 Hz, $J_{3',4'}$ = 6.8 Hz), 5.83 (dd, 1, H-2′, $J_{1',2'}$ = 3.9 Hz), 5.86 (d, 1, H-1′), 6.21 (d, 1, H-2 or H-3, $J_{2,3}$ = 3.7 Hz), 6.41 (d, 1, H-2 or H-3), 7.26–8.08 (m, 15, Ar H); ^{13}C NMR ($CDCl_3$) δ 28.42, 28.90 (CH_3), 41.23 (CH_2), 64.36 (C-5′), 72.44, 74.81, 78.08, 78.46 (C-1′, C-2′, C-3′, C-4′), 98.50 (C-9a), 103.38, 108.85 (C-2, C-3), 126.01–133.50 (Ar C, C-1, C-3a), 146.87, 149.78, 156.36 (C-5a, C-7, C-9), 165.44, 165.55, 166.30 (C=O).

1,3-Dimethyl-7-(β-D-ribofuranosyl)lumazine (8) and 1,3-Dimethyl-7-(1,4-anhydro-2-deoxy-D-*erythro*-pent-1-enofuranosyl)lumazine (9). To a solution of 1,3-dimethyllumazine **3** (201 mg, 0.33 mmol) in methanol (10 mL) was added a 1 N sodium carbonate aqueous solution (2 mL) at 0 °C for 2 h, and then the reaction mixture was rendered neutral with acetic acid and evaporated to dryness in vacuo. TLC (chloroform–methanol, 9:1) showed that the colorless syrup contained two major components (R_f 0.35 and 0.32). The mixture was separated by preparative TLC with chloroform–methanol (9:1) as the eluent after three elutions.

Compound **8**: R_f 0.32; colorless needles, mp 220–222 °C; 32.7%; CIMS, m/z 325 ([M + H]$^+$, 5); ^{1}H NMR (CD_3OD) δ 3.35, 3.48 (each s, 3 each, CH_3), 3.74 (dd, 1, H-5′a, $J_{4',5'a}$ = 4.0 Hz, $J_{5'a,5'b}$ = 12.1 Hz), 3.88 (dd, 1, H-5′b, $J_{4',5'b}$ = 3.0 Hz), 4.05–4.20 (m, 2, H-3′, H-4′), 4.25 (dd, 1, H-2′, $J_{1',2'}$ = 5.1 Hz, $J_{2',3'}$ = 4.7 Hz), 5.01 (d, 1, H-1′), 8.08 (s, 1, H-6); ^{13}C NMR (CD_3SOCD_3) δ 28.31, 28.72 (CH_3), 61.25 (C-5′), 71.02, 76.64, 83.37, 84.89 (C-2′, C-3′, C-4′, C-1′), 128.30 (C-4a), 137.60 (C-6), 147.02 (C-8a), 150.41 (C-4), 152.81 (C-7), 159.01 (C-2).

Anal. Calcd for $C_{13}H_{16}N_4O_6$: C, 48.15; H, 4.97; N, 17.28. Found: C, 48.54; H, 5.30; N, 17.32.

Compound **9**: R_f 0.35; yellow needles, mp 225–226 °C; 38.6%; SIMS, m/z 307 ([M + H]$^+$, 16); ^{1}H NMR (CD_3OD) δ 3.48, 3.70 (each s, 3 each, CH_3), 3.73 (d, 2, H-5′, $J_{4',5'}$ = 5.7 Hz), 4.57 (q, 1, H-4′), 4.95 (dd, 1, H-3′, $J_{2',3'}$ = 3.0 Hz, $J_{3',4'}$ = 5.7 Hz), 6.27 (d, 1, H-2′), 8.78 (s, 1, H-6); ^{13}C NMR (CD_3OD) δ 29.95, 30.33 (CH_3), 64.12 (C-5′), 76.87, 92.86 (C-3′, C-4′), 109.98 (C-2′), 129.39 (C-4a), 138.48 (C-6), 149.44, 150.00 (C-1′, C-8a), 153.03 (C-4), 157.37 (C-7), 162.56 (C-2).

Anal. Calcd for $C_{13}H_{14}N_4O_5$: C, 50.98; H, 4.61; N, 18.29. Found: C, 50.66; H, 4.63; N, 18.06.

Methanolic sodium methoxide (16 mg, 0.3 mmol) was added to the protected *C*-nucleoside **3** (20 mg, 0.03 mmol) in 2 mL of methanol. The mixture was allowed to stand at 0 °C for 1.5 h, then rendered neutral with acetic acid, and evaporated. The residue was chromatographed over a column of silica gel with chloroform–methanol (4:1) as the eluent. This afforded 8.8 mg of **9** (82%) as yellow needles.

1,3-Dimethyl-7-(2,3-*O*-isopropylidene-β-D-ribofuranosyl)lumazine (10). To a solution of **8** (91 mg, 0.3 mmol) in acetone (5 mL) was added *p*-toluenesulfonic acid (10 mg), and the resulting solution was stirred at room temperature for 1 h. The reaction mixture was neutralized with satruated sodium bicarbonate solution and then extracted with chloroform (3 × 10 mL). The extracts were combined, washed with water, dried over magnesium sulfate, and evaporated in vacuo to a syrup. The residue was purified by preparative TLC with chloroform as the eluent. This afforded 71 mg of **10** (72%) as a colorless syrup: ^{1}H NMR ($CDCl_3$) δ 1.40, 1.65 (each s, 3 each, isopropylidene CH_3), 3.55, 3.72 (each s, 3 each, CH_3), 3.70 (dd, 1, H-5′a, $J_{4',5'a}$ = 3.0 Hz, $J_{5'a,5'b}$ = 11.7 Hz), 3.93 (dd, 1, H-5′b, $J_{4',5'b}$ = 3.0 Hz), 4.46 (apparent q, 1, H-4′), 4.88 (q, 1, H-3′, $J_{2',3'}$ = 4.1 Hz, $J_{3',4'}$ = 2.3 Hz), 4.93 (t, 1, H-2′), 5.18 (d, 1, H-1′), 8.70 (s, 1, H-6); ^{13}C NMR ($CDCl_3$ partial) δ 25.50, 27.49 (isopropylidene CH_3), 29.07, 29.49 (CH_3), 63.36 (C-5′), 82.72, 85.90, 85.94, 86.23 (C-1′, C-2′, C-3′, C-4′), 138.77 (C-6).

6,8-Dimethyl-1-(β-D-ribofuranosyl)pyrrolo[1,2-*f*]pteridine-7,9-dione (11). To a solution of tricyclic compound **5** (50 mg, 0.07 mmol) in methanol (4 mL) was added methanolic sodium methoxide (36 mg, 0.7 mmol) at 0 °C for 1.5 h, and then the reaction mixture was rendered neutral with acetic acid and evaporated. The residue was purified by preparative TLC with chloroform–methanol (9:1) as the eluent. This afforded 15.3 mg of **11** (55%) as yellow needles: mp 236–238 °C; SIMS, m/z 363 ([M + H]$^+$, 52); ^{1}H NMR (CD_3SOCD_3) δ 3.35, 3.62 (each s, 3 each, CH_3), 3.37–3.48 (m, 2, H-5′), 3.71–3.75 (m, 2, H-2′, H-3′), 3.85 (t, 1, H-4′, $J_{3',4'}$ = $J_{4',5'}$ = 5.1 Hz), 5.74 (d, 1, H-1′), 7.25, 7.29 (each d, 1 each, H-2 or H-3, $J_{2,3}$ = 4.8 Hz), 8.99 (s, 1, H-4); ^{13}C NMR (CD_3SOCD_3) δ 28.52, 30.07 (CH_3), 61.54 (C-5′), 70.78, 74.67, 78.26, 83.75 (C-1′, C-2′, C-3′, C-4′), 105.16 (C-9a), 110.27, 116.96 (C-2, C-3), 129.29 (C-3a), 137.48 (C-1), 144.59 (C-5a), 147.75 (C-4), 150.01, 156.38 (C-7, C-9).

Anal. Calcd for $C_{16}H_{18}N_4O_6$: C, 53.03; H, 5.01; N, 15.46. Found: C, 53.37; H, 5.06; N, 15.65.

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Synthesis and Reactivity of Benzylic Epoxides Derived from 1,2,3,9,10,10a-Hexahydrophenanthrene. Search for a Unified Mechanism for the Ring Opening of 2-Aryloxiranes

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The diastereoisomeric benzylic epoxides **4a** and **4b** were synthesized, and their ring-opening reactions under acidic conditions were compared with those of the known epoxides **2** and **3**. The chemical behavior of **4** more nearly resembles that of **3**, thus suggesting that the differences in chemical behavior between **2** and **3** could be ascribed to the different conformational rigidity of the aryl in these systems. The ring opening of **4** forms significant amounts of unsaturated alcohol and ketone in addition to the diastereoisomeric diols. The results obtained in the present study are difficult to explain by means of either of the two mechanistic schemes suggested for 2-aryloxiranes.

Introduction

Studies on polycyclic aromatic hydrocarbons have indicated that diol epoxides of type **1**, with the oxirane ring in the "bay region", are the metabolites responsible for the mutagenic and carcinogenic activity of these hydrocarbons.[1] Accordingly, there is interest in the mechanism

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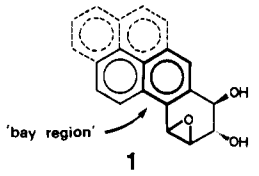

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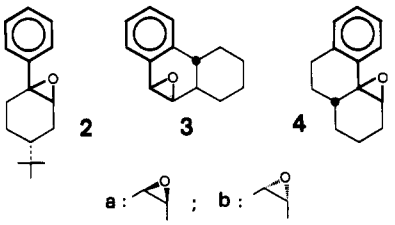
of the acid-catalyzed ring opening of 2-aryloxiranes, to which the metabolites of type 1 are related.

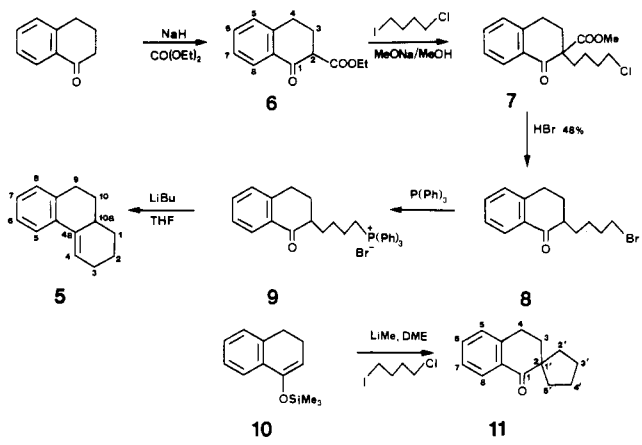


Benzylic epoxides of types **2a,b**[2] and **3a,b**[3] have been used as models of conformationally rigid 2-aryloxiranes to study the steric course of the oxirane ring opening under acidic conditions. Epoxides of types **2** and **3** exhibit significant differences in chemical behavior. These differences may stem from the conformational rigidity of the aryl of **3** compared with **2** or the fact that the benzylic oxirane carbon in **3** is secondary whereas that in **2** is tertiary. However, a recent study[4] of the 9-methyl derivatives of **3a,b** indicated that the different nature of the benzylic oxirane carbon in **2** and **3** is not responsible for the differences in chemical behavior. In order to assess the effect of conformational rigidity of the aryl on the hydrolysis of such epoxide models, we have synthesized the diastereoisomeric benzylic epoxides **4a** and **4b**, derived from 1,2,3,9,10,10a-hexahydrophenanthrene (**5**). The 1-phenylcyclohexene oxide skeleton of **2** is also found in **4**. However, in **4** the insertion of an ethylenic bridge between the aromatic ring and the 1,2-epoxycyclohexane moiety makes the aryl and the cyclohexane system conformationally restricted. Models indicate that, whereas the six-membered ring containing the epoxide group of **3** is rigid in the sense that it has only one reasonable conformation, the same ring in **4** can exist in several conformations, with one preferred. In addition the same models indicate that the benzylic carbenium ions, which may be intermediate in acid-catalyzed epoxide ring-opening reactions, are conformationally rigid in **3** but can exist in two reasonable conformations in **4**, even if one of them appears to be largely the most stable.

Results

The synthesis of **5** as a precursor for epoxides **4** was accomplished as shown in Scheme I. Reaction of 1-tetralone with diethyl carbonate in the presence of NaH yielded the ethoxycarbonyl derivative **6**. Alkylation of **6** with 1-chloro-4-iodobutane in the presence of NaOMe in MeOH was accompanied by transesterification to give the 4-chlorobutyl β-keto methyl ester **7**. This ester was hydrolyzed and decarboxylated with concentrated HBr in propionic acid at reflux temperature, which also effected nucleophilic exchange between the chlorine atom of the aliphatic side chain and bromide ion, affording 2-(4-bromobutyl)-1-tetralone (**8**). Reaction of **8** with neat triphenylphosphine at 110 °C yielded the phosphonium bromide **9**. Treatment of a suspension of crude **9** with butyllithium in anhydrous ether, followed by warming, yielded the olefin **5** through an intramolecular Wittig reaction.[5] Attempts to prepare the 4'-haloalkyl ketone of type **8** by direct alkylation of the trimethylsilyl enol ether of 1-tetralone (**10**) with 1-chloro-4-iodobutane and MeLi led to spiroketone **11**.[6]

Scheme I



6 7 8 9 10 11 5

Table I. Product Composition in the Ring Opening of Epoxides 2–4a,b

epoxide	reagents[a]	time, min	unsatd alcohol	ketone	cis diol	trans diol
2a[b]	A	5			45	55
3a[c]	A	2			0	100
4a	A	1	2	2	4	92
2a[d]	B	2			100	0
3a[c]	B	2			15	85
4a	B	1	29	6	62	3
2b[b]	A	2			24	76
3b[c]	A	2			51	49
4b	A	1	30	4	15	51
2b[d]	B	2			100	0
3b[c]	B	2			22	78
4b	B	1	20	42	8	30

[a] A: H_2SO_4, dioxane/H_2O (1:1); B: Cl_3CCO_2H, C_6H_6, followed by LAH reduction. [b] Reference 2. [c] Reference 13. [d] Unpublished results from this laboratory.

To prepare epoxides **4**, we tried the reaction of **5** with *N*-bromoacetamide (NBA) in aqueous THF (Scheme II), which gave only the *trans*-bromohydrin **12**, accompanied by a small amount of the unsaturated alcohol **13**.[7] Treatment of **12** with potassium *tert*-butoxide in benzene afforded the epoxide **4b**. However, direct epoxidation of **5** with peroxybenzoic acid in ether afforded a 60:40 mixture (^{1}H NMR) of epoxides **4a** and **4b**, which were separated by flash chromatography.

(1) (a) Jerina, D. M.; Daly, J. W. *Science* **1974**, *185*, 573. (b) Sims, P.; Grover, P. L. *Adv. Cancer Res.* **1974**, *20*, 165. (c) Daly, J. W.; Jerina, D. M.; Witkop, B. *Experientia* **1972**, *28*, 1129.

(2) Crotti, P.; Dell'Omodarme, G.; Ferretti, M.; Macchia, F. *J. Am. Chem. Soc.* **1987**, *109*, 1463.

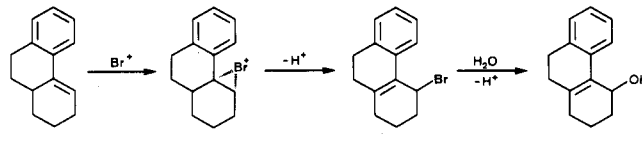
(3) Sayer, J. M.; Yagi, H.; Silverton, J. Y.; Friedman, S. L.; Whalen, D. L.; Jerina, D. M. *J. Am. Chem. Soc.* **1982**, *104*, 1972.

(4) Chini, M.; Crotti, P.; Macchia, F. *Gazz. Chim. Ital.* **1988**, *118*, 827.

(5) Becker, B. K. *Tetrahedron* **1980**, *36*, 1717.

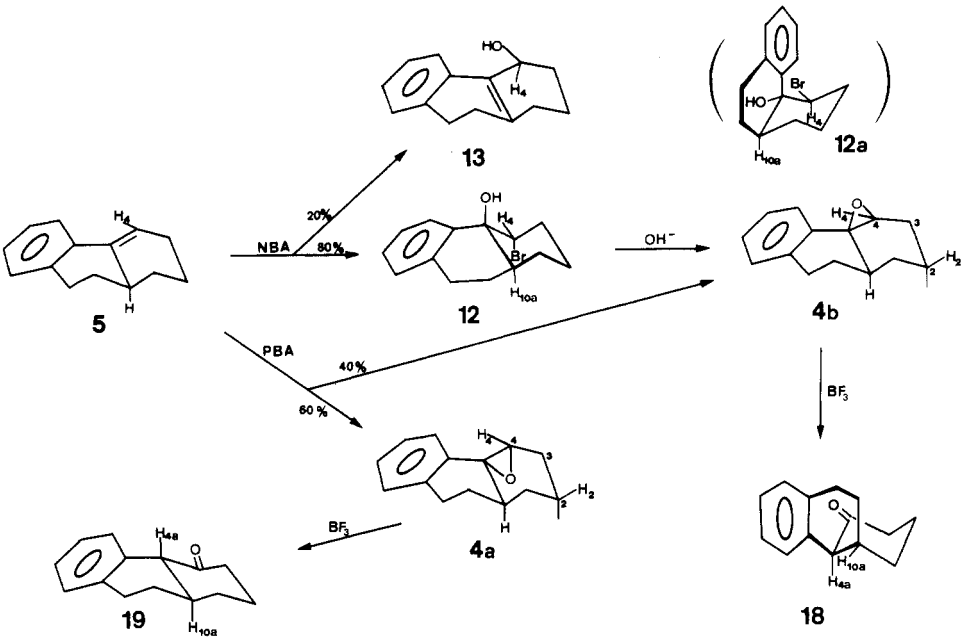
(6) Zimmerman, H. E.; Tolbert, L. M. *J. Am. Chem. Soc.* **1975**, *97*, 5497.

(7) The unsaturated alcohol **13** is not a likely primary product of the reaction. It could arise from the bromonium ion **24** obtained from **5**, which on loss of a proton would afford the allylic bromide **25**, which easily solvolyzes to **13**.

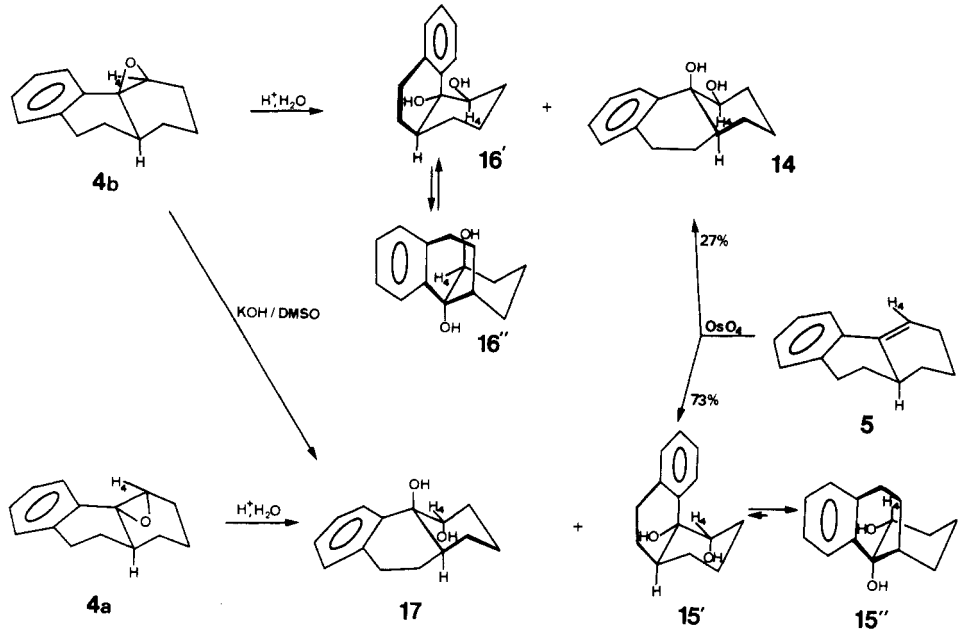


5 24 25 13

Scheme II



Scheme III



The reference diols **14–17** were prepared as shown in Scheme III. Osmium tetraoxide cis dihydroxylation of **5** yielded a 27:73 mixture of the two cis diols **14** and **15**, which were separated by preparative TLC. Hydrolysis of **4b** gave *trans*-**16** and *cis*-**14**, which were separated from the crude reaction mixture by preparative TLC. On the contrary, only *trans*-**16** was obtained by trichloroacetolysis of **4b** followed by hydrolysis of the trichloroacetates (Table I). Reaction of **4a** with trichloroacetic acid followed by hydrolysis gave primarily cis diol **15** with a minor amount of trans diol **17**, whereas hydrolysis of **4a** with H_2SO_4 in aqueous dioxane gave primarily trans diol **17** with a little **15** (Table I). On the other hand, reaction of epoxide **4b** with KOH in aqueous DMSO[8] afforded exclusively the trans diol **17**. The structures and configurations of diols **14–17** and epoxides **4a,b** were inferred from their methods of synthesis, spectroscopic data, and conformational considerations. Table II shows pertinent spectroscopic data for diols **14–17** and bromohydrin **12**. Whereas diols **14** and **17** are conformationally rigid because of the trans fusion of the two cyclohexane rings, diols **15** and **16** may exist, in principle, in two interconvertible chair conformations

Table II. Spectroscopic Data for Bromohydrin 12 and Diols 14–17

	^{1}H NMR, δ		IR (CCl_4), OH stretching band, cm^{-1}		
compd	H_4[a]	$W_{1/2}$, Hz	OH···O	OH···π	OH_{free}
12	4.93	5.0		3610	
14	3.96	16.0	3588		3616
15	4.13	13.0	3578 (br)		3610
16	3.86	11.0		3604 (br)	
17	4.50	6.0		3602 (sh)	3617

[a] All peaks are multiplets.

(8) Berti, G.; Macchia, B.; Macchia, F. *Tetrahedron* **1968**, *24*, 1755.

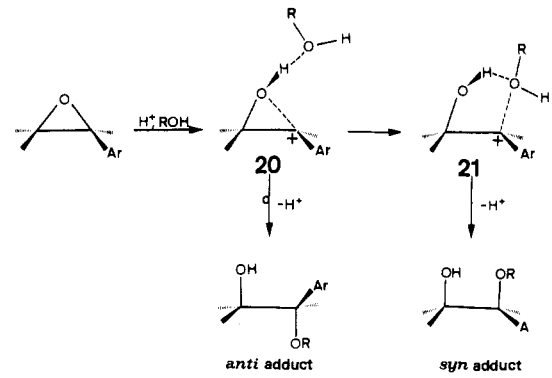
(Scheme III).[9] The relative cis configuration of diols **14** and **15**, and consequently the trans configuration of **16** and **17**, is inferred from the formation of **14** and **15** by the cis dihydroxylation of **5** with OsO_4.[10] Furthermore, the higher half-bandwidth of the ^1H NMR peak of the methynyl proton α to the secondary OH group in one of the two cis diols ($W_{1/2}$ = 16.0 Hz) with respect to the same peak in the other cis isomer ($W_{1/2}$ = 13.0 Hz)[11a] led us to assign to the former the rigid structure **14** and to the latter the conformationally mobile structure **15**. The $W_{1/2}$ value of **15** indicated that conformation **15″** should be preferred over **15′**. The hydroxy stretching bands of **14** and **15** indicate strong OH···O interactions, which are possible in both the cis derivatives (Table II).[12] The conformationally rigid structure **17** was assigned to the trans diol exhibiting the lower $W_{1/2}$ value (6.0 Hz), consistent with an equatorial proton.[11a] On the other hand, the conformationally mobile structure **16** must correspond to the trans diol showing a half-bandwidth value (11.0 Hz) that is between the common values for axial and equatorial protons.[11a] A conformational equilibrium (**16′** ⇄ **16″**) is possible only in this structure.

The IR data for diols **16** and **17** confirm the trans relationship between the two OH groups,[12] which is consistent with the lack of strong OH···O interactions (Table II). The configurational assignments are also in agreement with the formation of **16** and **17** from epoxide **4b** and **4a**, respectively, under acid conditions. In these conditions the opening process should involve breaking of the benzylic C–O bond and subsequent attack of the nucleophile (H_2O) on the benzylic carbon.

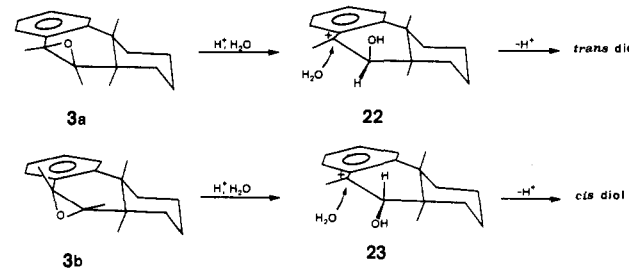
The configurations of **4a** and **4b** were assigned on the basis that they should be the same as those of the cis diols **15** and **14**, which were derived from them. Confirmation of the configurations assigned to **4a** and **4b** was obtained by comparison of the chemical shifts and the multiplicities of the ^1H NMR signals of their oxirane protons H_4. The H_4 proton resonates at lower field (δ 3.97) in **4b** than in **4a** (δ 3.19). Examination of molecular models shows that in **4b** H_4 is more nearly coplanar with the aromatic ring than it is in **4a**, thus being exposed to the deshielding ring currents. In addition, the signal of H_4 (comparable to the X of an ABX system)[11b] in **4a** is much more complex (seven lines) than that in **4b** (three lines), indicating long-range coupling (J = 0.8 Hz) in **4a** but not in **4b**. Molecular models show that the H_4 proton of **4a** can have appreciable long-range coupling with the equatorial H_2 proton, the fully saturated system H_{2eq}–C_2–C_3–C_4–H_4 being in the planar zig-zag configuration required by the "W" rule on coupling across four single bonds.[11c] On the contrary, in **4b** the required planar W configuration of the four σ bonds joining H_4 to H_{2eq} does not exist.

Further confirmation of the configuration assigned to epoxide **4b** derives from its synthesis by base-catalyzed dehydrohalogenation of the conformationally rigid *trans*-bromohydrin **12**. The trans configuration of **12** was inferred from its stability to oxidation by CrO_3 and from the very low half-bandwidth of the signal of the proton α to the bromine atom ($W_{1/2}$ = 5.0 Hz), which is consistent with its equatorial position. A much higher $W_{1/2}$ value would be expected for the alternative conformationally mobile trans configuration **12a** (Scheme II). The IR data for **12** are also in agreement with an antiperiplanar OH/Br relationship: OH···Br interactions are completely absent in the spectrum (Table II).

Scheme IV



Scheme V



Ketones **18** and **19** were prepared by reaction of epoxides **4b** and **4a** with BF_3·Et_2O in anhydrous benzene (Scheme II). The ^1H NMR spectra of the two ketones showed a small $J_{H4a,H10a}$ coupling constant (5.2 Hz in **18**) and a large half-bandwidth (16.0 Hz in the signal of H_{4a} in **19**). These features are consistent with a cis (**18**) and a diaxial trans (**19**) relationship[11a] between H_{4a} and H_{10a} and confirm the structures shown in Scheme II.

Table I shows the relative amounts of cis and trans diols obtained by acid hydrolysis and trichloroacetolysis of **2–4a** and **2–4b**. While the hydrolysis mixtures were analyzed directly, the trichloroacetolysis mixtures were examined after LAH reduction of the monoester initially formed.

Discussion

Diastereoselectivity in the hydrolysis of epoxides of type **2a,b** has been rationalized by a mechanism (schematically represented in Scheme IV), which involves two different benzylic carbocationic species (the less carbocationic-like **20** and the more carbocationic-like **21**), on the assumption that the axial opening pathway is energetically favored.[2] On the contrary, the steric course of the hydrolysis of epoxides of type **3a,b** was explained as in Scheme V by assuming completely developed benzylic carbenium ions **22** and **23**, which are preferentially attacked by the nucleophile in a pseudoaxial fasion.[2,3] The trichloroacetolysis reactions of epoxides **2** and **3** also have different stereochemical outcomes, and the results are better rationalized by the mechanism summarized in Scheme IV.[13]

Comparison of the relative amounts of products formed in acid hydrolysis and trichloroacetolysis of epoxides **2–4** underlines the differences in chemical behavior among these structures (Table I). The results of the ring opening

(9) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962; pp 279–280.
(10) Schröder, M. *Chem. Rev.* **1980**, *80*, 187.
(11) (a) Jackman, L. M.; Sternhell, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon Press: London, 1969; p 286. (b) Reference 11a, p 132. (c) Reference 11a, p 334.
(12) Macchia, B.; Macchia, F.; Monti, L. *Gazz. Chim. Ital.* **1970**, *100*, 35.
(13) Chini, M.; Crotti, P.; Ferretti, M.; Macchia, F. *Tetrahedron* **1988**, *44*, 2001.

Table III. Syn Diastereoselectivity in Acid Opening of 2-Aryloxiranes

epoxide	syn adduct,[a] %	
	H_2SO_4, dioxane/H_2O (1:1)	Cl_3CCO_2H, C_6H_6
2a	45[b]	100[d]
2b	24[b]	100[d]
3a	0[c]	15[c]
3b	51[c]	22[c]
4a	4[e]	95[e]
4b	23[e]	21[e]

[a] Percent syn adduct from the syn/anti ratio. [b] Reference 2. [c] Reference 13. [d] Unpublished results from this laboratory. [e] This work.

of **4a** and **4b** do not appear to clarify the mechanistic puzzle of the ring opening of 2-aryloxiranes under acidic conditions. The acid hydrolysis of **4** is not completely anti stereoselective, thus resembling the behavior of epoxides **2** but not epoxides **3**. The trichloroacetolysis of **4**, unlike that of **2**, is not completely syn stereoselective. Table III evidences the variation in the syn diastereoselectivity observed on passing from acid hydrolysis to trichloroacetolysis for all the epoxides **2–4a,b**: the amounts of syn adducts increase in the case of epoxides **2–4a**, whereas for **2–4b** the syn stereoselectivity increases only for epoxides **2** and decreases for epoxides **3** and **4**. Thus the chemical behavior of **4** appears to be closer to that of **3** than to **2**, although a complete parallel cannot be established because there is less anti stereoselectivity in the hydrolysis of **4a** compared to **3a**. In addition, the ring opening of **4a** and **4b** produces significant amounts of unsaturated alcohol and ketone (Table I), which are not formed from epoxides **2** and **3**.[2,3] As a consequence the mentioned differences in chemical behavior between epoxides **2** and **3** could be ascribed to the different conformational rigidity of the aryl in the two systems. Anyway, apart from the similarity in chemical behavior between epoxides **3** and **4**, the results obtained with epoxides **4** are difficult to explain by the mechanistic scheme suggested for the hydrolysis of **3** (Scheme V),[3] which implies the formation of a completely developed carbenium ion pseudoaxially attacked by the nucleophile. In the hydrolysis of **4a**, there is 96% axial attack, compared with only 23% axial attack in **4b**. The results of the trichloroacetolysis of **4** are in even more disagreement with such a mechanism:[3] only 4% and 21% axial attack is observed for **4a** and **4b**, respectively. However, the trichloroacetolysis of **3** could not be explained by such a mechanism, either.[13] A mechanism analogous to the one proposed for epoxides **2**[2] (Scheme IV) could rationalize the formation of both cis and trans diols in the reactions of **4a** and **4b**. However, the hypothesis that in this mechanism one of the main factors determining stereoselectivity is the preferential axial cleavage of the epoxide ring is absolutely untenable. The difficulty in explaining the ring opening of **4** by either mechanism may be due to the lack of rigidity of these epoxides and their benzylic carbenium ions.

Experimental Section

Melting points were determined on a Kofler apparatus and are uncorrected. IR spectra for the comparison of compounds were taken on paraffin oil mulls on a Perkin-Elmer Infracord Model 137 and those for the determination of OH-stretching bands were taken with a Perkin-Elmer Model 257 double-beam grating spectrophotometer in dried (P_2O_5) CCl_4, using the indene band at 3110 cm^{-1} as a calibration standard; a quartz cell of 2-cm optical length was employed, and the concentration of the solutions was 5×10^{-3} M or lower to prevent intramolecular association. ^1H NMR spectra were determined in ca. 10% $CDCl_3$ solution with a Varian EM 360 spectrometer using Me_4Si as the internal standard; ^1H NMR spectra for compounds **4a** and **4e** were also measured with a Varian CFT 20 spectrometer. GLC analyses were performed on a Dani Model 3800 gas chromatograph with a flame ionization detector and a glass column (2 m × 2.5 mm) packed with 10% OV 17 on 80–100-mesh silanized Chromosorb W; column 180 °C, evaporator and detector 250 °C, nitrogen flow 40 mL/min. Preparative and semipreparative TLC were performed on 2- and 0.5-mm silica gel plates (Merck F_{254}), respectively, containing a fluorescent indicator. Petroleum ether refers to the fraction with bp 40–70 °C.

2-(Ethoxycarbonyl)-1-tetralone (6). Following a described procedure,[14] reaction of 1-tetralone (73.0 g, 0.50 mol) in anhydrous toluene (400 mL) with diethyl carbonate (177.0 g, 1.50 mol) in the presence of NaH (30.0 g of an 80% dispersion in oil, 1.0 mol) afforded crude **6** as a solid (88.0 g, 80%), which on recrystallization from petroleum ether at −20 °C afforded pure **6** (79.0 g), mp 31–32 °C: IR 5.79 and 6.15 μm (C=O); ^1H NMR δ 11.5 (s, 0.5 H, C=COH), 8.16–7.70 (m, 1 H, H_8), 7.50–6.93 (m, 3 H, H_5, H_6, and H_7), 4.26 (q, 2 H, J = 7.0 Hz, $COOCH_2$), 3.50 (m, 0.5 H, CHCOO), 3.13–2.16 (m, 4 H, $ArCH_2CH_2COO$), 1.30 (t, 3 H, J = 7.0 Hz, $COOCH_2CH_3$). Anal. Calcd for $C_{13}H_{14}O_3$: C, 71.54; H, 6.46. Found: C, 71.49; H, 6.71.

2-(4-Chlorobutyl)-2-(methoxycarbonyl)-1-tetralone (7). A solution of **6** (38.0 g, 0.174 mol) in anhydrous MeOH (130 mL) was added over 30 min, at room temperature, to a solution of MeONa (from 7.0 g of Na, 0.302 g-atoms, in anhydrous MeOH, 440 mL). The mixture was stirred at room temperature for 90 min and then pure 1-chloro-4-iodobutane (59.5 g, 0.273 mol) was added over 3 h: stirring was continued for 18 h and then the reaction mixture was refluxed for 3 h. After cooling, most of the solvent was distilled off at reduced pressure, and the liquid residue was diluted with water and extracted with ether. Evaporation of the washed (water) ether extracts afforded an oily residue (39.5 g) consisting mostly of **7** (^1H NMR), which was purified by flash chromatography (eluant hexane/diisopropyl ether 7:3) to give pure **7** (32.9 g, 61%) as an oil: IR 5.71 and 5.88 μm (C=O); ^1H NMR δ 8.17–7.93 (m, 1 H, H_8), 7.56–7.10 (m, 3 H, H_5, H_6, and H_7), 3.66 (s, 3 H, $COOCH_3$), 3.53 (t, 2 H, J = 6.0 Hz, CH_2Cl), 3.33–2.87 (m, 2 H, benzylic CH_2). Anal. Calcd for $C_{16}H_{19}ClO_3$: C, 65.19; H, 6.49. Found: C, 65.28; H, 6.60.

2-(4-Bromobutyl)-1-tetralone (8). A solution of **7** (19.7 g, 63.5 mmol) in propionic acid (160 mL) containing 48% aqueous HBr (19.7 mL) was refluxed under stirring for 4 h while a slow stream of gaseous HBr was bubbled into the reaction mixture. After cooling, water was added and the mixture was repeatedly extracted with petroleum ether. Evaporation of the washed (saturated aqueous $NaHCO_3$, then water) organic solvent afforded an oily residue (18.0 g) consisting mostly of **8** (^1H NMR), which was purified by filtration on a silica gel column (eluant petroleum ether/ether 85:15) to give pure **8** as an oil (16.0 g, 89%): IR 5.88 μm (C=O); ^1H NMR δ 8.16–7.98 (m, 1 H, H_8), 7.53–7.13 (m, 3 H, H_5, H_6, and H_7), 3.43 (t, 2 H, J = 6.0 Hz, CH_2Br), 3.05 and 2.93 (2 d, 2 H, J = 5.0 Hz each, benzylic CH_2). Anal. Calcd for $C_{14}H_{17}BrO$: C, 59.80; H, 6.08. Found: C, 59.62; H, 6.29.

1,2,3,9,10,10a-Hexahydrophenanthrene (5). A mixture of **8** (6.40 g, 22.8 mmol) and PPh_3 (6.60 g, 25.2 mmol) was warmed at 110 °C for 2 h. The glassy reaction product was triturated with anhydrous ether and then dried in vacuo. The crystalline crude phosphonium salt **9** so obtained (12.6 g) was used directly for the next reaction. A stirred solution of **9** (12.6 g, 23.3 mmol) in anhydrous THF (200 mL) was treated under N_2 at 0 °C with 1.6 M BuLi (25.5 mmol) during a 40-min period. The mixture was stirred for 1 h at room temperature and then refluxed for 5 h. After cooling, the mixture was filtered; then most of the THF was distilled off at reduced pressure. The liquid residue was diluted with water and extracted with hexane. Evaporation of the washed (water) organic extracts afforded crude **5** as an oil (3.20 g), which was filtered on a silica gel column (hexane eluant). From the first eluted fractions pure olefin **5** (2.85 g, 67%) was obtained as a liquid: ^1H NMR δ 7.76–7.53 (m, 1 H, H_5), 7.33–7.00 (m, 3 H, H_6, H_7, and H_8), 6.33 (m, 1 H, =CH), 3.07–2.57 (m, 2 H, benzylic CH_2). Anal. Calcd for $C_{14}H_{16}$: C, 91.25; H, 8.75. Found: C, 91.30; H, 8.61.

(14) Frew, A. J.; Proctor, G. R. *J. Chem. Soc., Perkin Trans. I* **1980**, *1245*.

Attempted Direct Alkylation of 1-Tetralone. Following a described method,[15] 1-tetralone (7.3 g, 0.05 mol) was transformed into the trimethylsilyl enol ether **10** by treatment with chlorotrimethylsilane (6.48 g, 0.06 mol) and triethylamine (12.1 g, 0.12 mol) in DMF (20 mL). The crude enol ether **10** (10.2 g) [^{1}H NMR δ 5.2 (t, 1 H, J = 4.0 Hz, =CH), 0.23 (s, 9 H, $SiMe_3$)] contained only about 10% of the starting ketone (GLC) and was used directly for the next reaction.

A mixture of enol ether **10** (1.97 g, 9.0 mmol) and 1.6 M MeLi (5.7 mL, 9.1 mmol) was stirred at 0 °C for 30 min and then the organic solvent was carefully evaporated by a slow stream of dry N_2. The residue was taken up in dry glyme (6 mL) and treated at room temperature under stirring with pure 1-chloro-4-iodobutane (2.07 g, 9.5 mmol) added dropwise. GLC analyses at different times indicated that after 3 h the alkylation reaction did not proceed any more; water was added and the mixture was extracted with ether. Evaporation of the washed (water) ether extracts afforded an oily residue (1.58 g) consisting of a mixture of enol ether **10** (17%), 1-tetralone (38%), and another compound (45%). This mixture (0.6 g) was subjected to preparative TLC (eluant petroleum ether/ether 9:1). Extraction of the slower moving band afforded an oily product which turned out to be **1-tetralone-2-spiro-1′-cyclopentane (11)** (0.18 g): IR 5.97 μm (C=O); ^{1}H NMR δ 8.17–7.97 (m, 1 H, H_8), 7.63–7.07 (m, 3 H, H_5, H_6, and H_7), 3.00 (t, 2 H, J = 6.0 Hz, benzylic CH_2), 2.03 (t, 4 H, J = 6.0 Hz, 2′ and 5′ CH_2). Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.04. Found: C, 84.10; H, 8.25.

Reaction of Olefin 5 with *N*-Bromoacetamide in THF/H_2O. Treatment of olefin **5** (0.92 g, 5.0 mmol) in a 75:25 THF/H_2O mixture (90 mL) with NBA (0.76 g, 5.5 mmol) for 30 min at room temperature afforded an oily residue (1.30 g) consisting of an 80:20 mixture (^{1}H NMR) of bromohydrin **12** and unsaturated alcohol **13**, which were separated by fractional crystallization from petroleum ether at −15 °C. The first fraction afforded pure **1,2,3,4,9,10-hexahydrophenanthren-4-ol (13)** (0.14 g)as a solid, mp 137–138 °C: IR 3.17 μm (OH); ^{1}H NMR δ 7.77–7.47 (m, 1 H, H_5), 7.40–7.10 (m, 3 H, H_6, H_7, and H_8), 4.70 (m, 1 H, $W_{1/2}$ = 7.0 Hz, C*H*OH), 3.00–2.56 (m, 2 H, benzylic CH_2). Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.05. Found: C, 83.65; H, 8.34. From the mother liquors pure **(4α,4aβ,10aα)-*t*-4-bromo-*trans*-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-4a-ol (12)** (0.46 g) was obtained as a solid, mp 82–83 °C: IR, see Table II; ^{1}H NMR δ 7.66–7.06 (m, 4 H, aromatic protons), 3.00–2.73 (m, 2 H, benzylic CH_2), and see Table II. Anal. Calcd for $C_{14}H_{17}BrO$: C, 59.80; H, 6.08. Found: C, 59.47; H, 6.01. Alternatively, bromohydrin **12** can be separated from alcohol **13** by preparative TLC (eluant hexane/ether 9:1). Extraction of the fastest moving band afforded pure **12**, while extraction of the slowest moving band afforded pure **13**.

Compound **12** was the only bromohydrin present in the crude NBA reaction mixture from olefin **5**, and no trace of the stereoisomeric bromohydrin **12a** was detected; the ^{1}H NMR spectra of the crude NBA reaction product showed only two lower field signals (δ 4.70, 4.93) corresponding to the ones found in the spectra of pure alcohol **13** and pure bromohydrin **12**, respectively.

Bromohydrin **12** is completely stable under the Jones oxidation conditions.

(4β,4aβ,10aα)-4,4a-Epoxy-*trans*-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (4b). Base-catalyzed cyclization of bromohydrin **12** (0.48 g, 1.71 mmol) with *t*-BuOK (0.19 g, 1.71 mmol) in anhydrous benzene (20 mL) at room temperature for 1 h afforded a crude reaction mixture consisting of epoxide **4b**, which was purified by crystallization from hexane at −20 °C to give pure **4b** (0.26 g) as a solid, mp 44–45 °C: ^{1}H NMR δ 7.24–7.12 (m, 4 H, aromatic protons), 4.01–3.94 (unresolved m, three lines, X part of the ABX system, $J_{AX} + J_{BX}$ = 4.9 Hz, CHO), 3.01–2.87 (m, 2 H, benzylic CH_2). Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.04. Found: C, 83.90; H, 8.15.

Reaction of Olefin 5 with PBA in Et_2O. A stirred two-phase system of a solution of olefin **5** (0.92 g, 5.0 mmol) in Et_2O (60 mL) and saturated aqueous $NaHCO_3$ solution (60 mL) was treated at 0 °C with a 0.195 M peroxybenzoic (PBA) solution in Et_2O (25 mL). The same amount of PBA was added at 1-h intervals with the temperature kept at 0 °C. After three additions, the TLC analysis showed only traces of the starting olefin; the mixture was quenched with 10% aqueous $Na_2S_2O_3$ solution and then stirred for 10 min. The ether phase was washed (water, 5% aqueous NaOH solution, and water) dried, and evaporated to give an oily residue (0.90 g) consisting of a 60:40 mixture (^{1}H NMR) of **4a** and **4b**, which was subjected to flash chromatography (eluant hexane/ethyl acetate 96:4) to give **4b** (0.13 g) and **(4α,4aα,10aα)-4,4a-epoxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (4a)** (0.25 g) as a liquid: ^{1}H NMR δ 7.24–7.0 (m, 4 H, aromatic protons), 3.22–3.16 (m, seven lines, comparable to the X part of an ABX system, $J_{AX} + J_{BX}$ = 4.0 Hz, $J_{H4,H2eq}$ = 0.8 Hz, CHO, see text), 2.95–2.79 (m, 2 H, benzylic CH_2). Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.04. Found: C, 83.75; H, 8.20.

Reaction of Olefin 5 with OsO_4. OsO_4 (0.254 g, 1.0 mmol) was added to a solution of olefin **5** (0.184 g, 1.0 mmol) in anhydrous pyridine (4 mL) and the resulting mixture was kept in the dark for 24 h. Usual workup[13] afforded a crude solid residue consisting of a 27:73 mixture of *cis*-diols **14** and **15** (GLC). Recrystallization from hexane afforded pure **(4α,4aα,10aα)-*cis*-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-*r*-4,*c*-4a-diol (15)** as a solid, mp 142–143 °C; IR, see Table II; ^{1}H NMR δ 7.66–7.43 (m, 1 H, H_5), 7.40–7.10 (m, 3 H, H_6, H_7, and H_8), 3.03–2.76 (m, 2 H, benzylic CH_2), and see Table II. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.30. Found: C, 77.35; H, 8.15.

Reaction of Epoxide 4b with KOH–DMSO. A solution of epoxide **4b** in DMSO (7 mL) was treated with aqueous 2 N KOH (1.4 mL) and then kept at 100 °C for 20 h. After cooling, the mixture was diluted with water and extracted with ether. Evaporation of the washed (water) ether extracts afforded a solid residue (0.095 g), which was recrystallized from hexane to give pure **(4α,4aβ,10aα)-*trans*-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-*r*-4,*t*-4a-diol (17)** (0.035 g) as a solid, mp 127–128 °C: IR, see Table II; ^{1}H NMR δ 7.76–7.43 (m, 1 H, H_5), 7.41–7.14 (m, 3 H, H_6, H_7, and H_8), 3.03–2.70 (m, 2 H, benzylic CH_2), and see Table II. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.30. Found: C, 77.17; H, 8.60.

Reaction of Epoxide 4b with 0.2 N H_2SO_4 in 1:1 Dioxane/H_2O. A solution of epoxide **4b** (0.30 g) in a 1:1 aqueous 0.2 N H_2SO_4/dioxane (100 mL) was stirred at 25 °C for 1 min. Usual workup[13] afforded a crude solid reaction product (0.31 g) consisting of a mixture of *trans*-diol **16**, *cis*-diol **14**, unsaturated alcohol **13**, and ketone **18** (Table I), which was subjected to semipreprative TLC (eluant petroleum ether/ether 9:1). Extraction of the two main slower moving bands afforded **(4β,4aα,10aα)-*cis*-1,2,3,4,4a,9,10,10a-octahydrophenanthrene-*r*-4,*t*-4a-diol (16)** (0.095 g, R_f = 0.22) as a dense liquid which did not crystallize; IR, see Table II; ^{1}H NMR δ 8.10–7.66 (m, 1 H, H_5), 7.46–7.06 (m, 3 H, H_6, H_7, and H_8), 3.13–2.70 (m, 2 H, benzylic CH_2), and see Table II. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.30. Found: C, 77.25; H, 8.43. **(4β,4aβ,10aα)-*trans*-1,2,3,4,4a,9,10,10a-Octahydrophenanthrene-*r*-4,*c*-4a-diol (14)** (0.025 g, R_f = 0.28) as a solid, mp 135–136 °C; IR, see Table II; ^{1}H NMR δ 8.56–8.26 (m, 1 H, H_5), 7.40–7.00 (m, 3 H, H_6, H_7, and H_8), 3.13–2.70 (m, 2 H, benzylic CH_2), and see Table II. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.30. Found: C, 77.09; H, 8.52. Extraction of the faster moving band afforded a solid residue consisting of unsaturated alcohol **13** (0.040 g).

Reaction of Epoxide 4a with 0.2 N H_2SO_4 in 1:1 Dioxane/H_2O. Proceeding as previously described for **4b**, the opening reaction of **4a** (0.050 g) in a 1:1 aqueous 0.2 N H_2SO_4/dioxane (20 mL) at 25 °C for 1 min afforded a solid residue consisting of a 96:4 mixture of *trans*-diol **17** and *cis*-diol **15**, together with small amounts of unsaturated alcohol **13** and ketone **19** (GLC), (Table I), from which pure *trans*-diol **17** (0.025 g) was obtained by crystallization from hexane.

Reaction of Epoxide 4b with CCl_3COOH in Anhydrous Benzene. A solution of epoxide **4b** (0.10 g, 0.50 mmol) in anhydrous benzene (10 mL) was treated at room temperature with a 1 M CCl_3COOH solution in anhydrous benzene (0.60 mL). After 1 min, evaporation of the washed (saturated aqueous $NaHCO_3$ solution, and water) organic solvent afforded an oily residue (0.12 g), which was dissolved in THF (8 mL), treated with 1 M KOH in EtOH (2.5 mL), and then left for 5 h at room temperature. Dilution with water, extraction with ether, and evaporation of

(15) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

the washed (water) ether extracts afforded an oily residue, which was subjected to semipreparative TLC (eluant petroleum ether/ether 9:1). Extraction of the slower moving band afforded *trans*-diol **16** (0.015 g).

Reaction of Epoxide 4a with CCl_3COOH in Anhydrous Benzene. A solution of epoxide **4a** (0.10 g) in anhydrous benzene was treated with CCl_3COOH, and then the crude reaction mixture was hydrolyzed as described for the corresponding reaction on **4b**. The crude solid reaction product was recrystallized from hexane to give pure *cis*-diol **15** (0.020 g).

Reaction of Epoxide 4b with $BF_3 \cdot Et_2O$. A solution of epoxide **4b** (0.10 g, 0.50 mmol) in anhydrous benzene (10 mL) was treated at 0 °C with $BF_3 \cdot Et_2O$ (0.07 mL, 0.55 mmol) and then stirred 1 min at room temperature. Evaporation of the washed (saturated aqueous $NaHCO_3$ and water) organic solution afforded a solid residue (0.090 g) mostly consisting of ketone **18** (^1H NMR), which was subjected to semipreparative TLC (eluant petroleum ether/ether 85:15). Extraction of the most intense band afforded pure **(4aα,10aα)-*cis*-1,2,3,9,10,10a-hexahydro-4(4a*H*)-phenanthrenone (18)** (0.030 g) as a solid, mp 47-48 °C: IR 5.88 μm (C=O); ^1H NMR δ 7.40-6.83 (m, 4 H, aromatic protons), 3.76 (d, 1 H, J = 5.2 Hz, H_{4a}), 3.06-2.73 (m, 2 H, benzylic CH_2). Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.04. Found: C, 84.05; H, 8.20.

Reaction of Epoxide 4a with $BF_3 \cdot Et_2O$. A solution of epoxide **4a** (0.040 g, 0.2 mmol) was treated with $BF_3 \cdot Et_2O$ as previously described for **4b** to give an oily residue mostly consisting of ketone **19** (^1H NMR, and GLC), which was subjected to semipreparative TLC (eluant petroleum ether/ether, 8:2). Extraction of the most intense band afforded pure **(4aβ,10aα)-*trans*-1,2,3,9,10,10a-hexahydro-4(4a*H*)-phenanthrenone (19)** (0.020 g) as a solid, mp 88-90 °C: IR 5.84 μm (C=O); ^1H NMR δ 7.40-7.00 (m, 4 H, aromatic protons), 3.66 (unresolved multiplet, 1 H, $W_{1/2}$ = 16.0 Hz, H_{4a}), 2.90-2.50 (m, 2 H, benzylic CH_2). Anal. Calcd for $C_{14}H_{16}O$: C, 83.96; H, 8.04. Found: C, 83.75; H, 7.90.

Reaction of Epoxides 4a and 4b in 1:1 Dioxane/H_2O in the Presence of Acid. A solution of the epoxide (0.020 g) in thermostatted (25 °C) 1:1 0.2 N aqueous H_2SO_4/dioxane (20 mL) was stirred for 1 min, then quenched with solid $NaHCO_3$ and saturated aqueous $NaHCO_3$, and extracted with ether. Evaporation of the washed (water) and dried ether extracts yielded mixtures consisting of diols **16** and **14**, of alcohol **13** and ketone **18** from **4b**, and of diols **17** and **15**, of alcohol **13** and ketone **19** from **4a** (see Table I).

Reaction of Epoxides 4a and 4b with Trichloroacetic Acid in Anhydrous Benzene. A solution of the epoxide (0.030 g, 0.15 mmol) in anhydrous benzene (3 mL) was treated at 25 °C with a 1 M solution of CCl_3COOH in the same solvent (0.165 mL) and left for 1 min at the same temperature. The reaction mixture was then washed (saturated aqueous $NaHCO_3$ and water), dried, and evaporated to give an oily residue consisting of monotrichloroacetates of the corresponding diols (**16** and **14** from **4b** and **17** and **15** from **4a**) together with consistent amounts of rearrangement products (alcohol **13** and ketone **18** from **4b** and alcohol **13** and ketone **19** from **4a**, GLC). The crude mixture was dissolved in anhydrous ether (10 mL) and then treated at room temperature with $LiAlH_4$ (0.050 g) under stirring. After 30 min, the excess hydride was destroyed with water and 10% aqueous NaOH, and the organic solution was filtered and evaporated to give a residue that was directly analyzed by GLC. Because of the reduction of the ketone present in the crude reaction product from each epoxide, the percentages of the ketone relative to the diols and to alcohol **13** were determined by measuring (GLC) the peaks of diols and alcohol **13** relative to the only two other peaks present. These latter were attributed to the reduced ketones by comparison with an analytical sample of the ketones reduced under the same conditions. The monotrichloroacetates of diols **14-17**, alcohol **13**, and ketones **18** and **19** were completely stable under the reaction conditions used.

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The Wittig-Horner Reaction in Weakly Hydrated Solid/Liquid Media: Structure and Reactivity of Carbanionic Species Formed from Ethyl (Diethylphosphono)acetate by Adsorption on Solid Inorganic Bases

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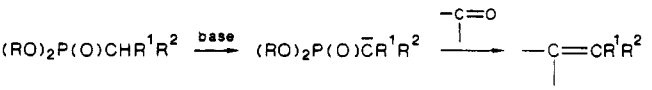
The rate and yield of the Wittig-Horner reaction of furfural with ethyl (diethylphosphono)acetate (**1**) in dioxane in the presence of solid $Ba(OH)_2 \cdot H_2O$, $K_2CO_3 \cdot 1.5H_2O$, or $Cs_2CO_3 \cdot 3H_2O$ depended on the quantity of water added to the reaction medium. Different configurations of phosphorus anionic species formed and adsorbed at the surface of each base account for the difference in reactivity of phosphonate with inorganic solids. The formation of phosphonate carbanion and the decomposition of the oxaphosphetane intermediate into diethylphosphoric acid depend on the action of water molecules added to the aprotic organic medium, indicating novel acid-base interactions at the solid/liquid interface. The rate of reaction of several substituted benzaldehydes with **1** in dioxane in the presence of $K_2CO_3 \cdot 1.5H_2O$, and the yield of ethyl cinnamates, increases with increasing electrophilic character of the aldehyde.

Introduction

A useful modification of the Wittig reaction, known as the Wittig-Horner (or Horner-Wadsworth-Emmons) reaction[1] involves the base-catalyzed condensation of a phosphonate ylide with a carbonyl compound. The use of a weak base in a heterogeneous solid/liquid system[2] has led to improve yields and selectivity in these reactions. Thus Foucaud and Texier-Boullet[3] used solid KOH/THF to transform aromatic aldehydes and ketones into α,β-unsaturated esters and nitriles and obtained better yields than those obtained in reactions carried out under liquid/liquid transfer conditions.[4] These authors also found



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