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Aromatic Substituent Effect on the Stereoselectivity of the Condensed- and Gas-Phase Acid-Induced Methanolysis in 2-Aryloxiranes Derived from 3,4-Dihydronaphthalene and trans-1,2,3,4,4a,10a-Hexahydrophenanthrene Bearing a Tertiary Benzylic Oxirane Nucleophilic Centre

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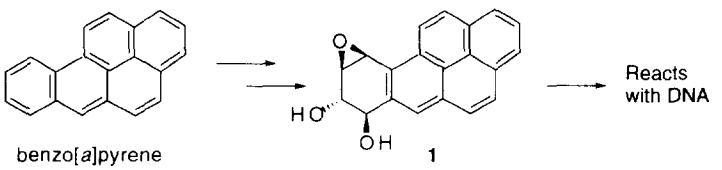
Abstract: The ring-opening reactions with MeOH of the title benzocondensed 2-aryl oxiranes **6** and **7a,b** both in the condensed (methanolysis) and in the gas phase were examined, obtaining in all cases a good Hammett-type linear correlation. Results indicate that the secondary or tertiary nature of the benzylic oxirane carbon is not responsible for the different stereochemical behavior so far encountered in different 2-aryl oxirane systems under the same operating conditions.

Introduction

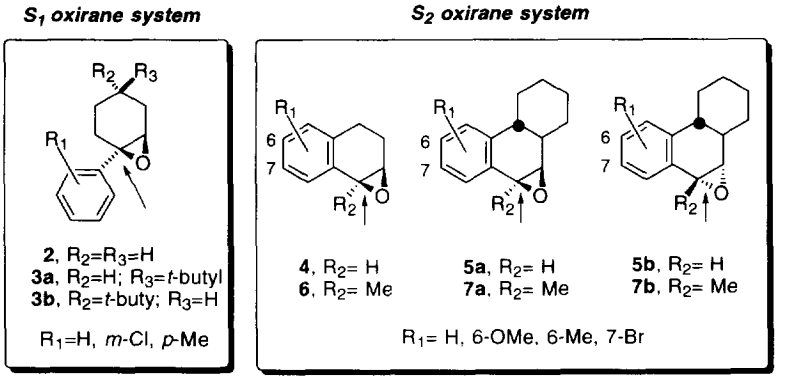
Polycyclic aromatic hydrocarbons (PAHs) are commonly encountered environmental pollutants because of their simple origin from an incomplete combustion of organic matter.[1] The mutagenic and carcinogenic activity shown by some PAHs has been linked to the formation in the course of their metabolic detoxification, of a particular type of 2-aryloxiranes, the corresponding diol epoxide such as **1** (from benzopyrene, for example) with the oxirane ring in the bay region. While the steric crowding of the surrounding bay-region protects the oxirane ring of **1** from the definitive detoxification action of the epoxide hydrase, the exceptional intrinsic reactivity of the oxirane ring itself makes possible the covalent binding of **1** to DNA by a nucleophilic ring-opening process, thus starting the mutagenic process.[1-3]



benzo[*a*]pyrene **1**

In order to get as much information as possible about the chemical behavior of complex biological oxirane systems such as **1**, simplified 2-aryloxiranes were efficaciously adopted as suitable models for studies on the stereochemical and regiochemical outcome of these systems under opening reaction conditions: the mobile **2** and the conformationally restricted **3a** and **3b** epoxides (S_1 oxirane system) derived from 1-arylcyclohexene[4a-c] and

the semirigid **4** and the rigid **5a** and **5b** benzocondensed epoxides (S_2 oxirane system) derived from 3,4-dihydronaphthalene (epoxides **4**)[5] and trans-1,2,3,4,4a,10a-hexahydrophenanthrene (epoxides **5a** and **5b**).[6]



The results obtained in the ring opening reactions of epoxides **2-5** in the condensed phase under acid conditions were interesting, but did not allow the formulation of a univocal rationalization capable of explaining the results from these systems adequately.[4-6] In particular, the decidedly unusual complete anti stereoselectivity constantly observed in the acid-promoted solvolysis of the rigid epoxides **5a**[6] appeared to be an unsurmontable obstacle in the search for a unified mechanism, to the point that the two S_1 and S_2 oxirane systems seemed to possess an unreasonably independent behavior.[4a,6] Only later, by making use of the interesting technique of gas-phase operating conditions,[7] was it possible to demonstrate that the two 2-aryloxirane model systems (S_1 and S_2) obey the same rationalization (the ion-dipole pair mechanism).[4,5a,7a]

Even admitting the validity of the studies previously carried out, a last important point had to be adequately investigated for a definitive applicability of the ion-dipole pair mechanism[4,5a,7a] to both S_1 and S_2 oxirane systems, as a consequence of an important structural difference between them: in epoxides **2-3** (S_1 system), the benzylic oxirane carbon is tertiary, while in epoxides **4-5** (S_2 system) the corresponding one is secondary. Could the different nature of the benzylic oxirane carbon in **2-3** and **4-5** be responsible for the different stereochemical behavior observed between these two systems?[4-7] In order to adequately check this point, we prepared the benzocondensed epoxides **7a** and **7b** structurally related to the previously examined **5a** and **5b**, in which the benzylic oxirane carbon was made tertiary, as in the S_1 oxirane system, by the simple introduction of a methyl group. Also in **7a,b-H**[8] appropriate substituents possessing opposite electronic effects, such as the electron-donating 6-methyl group (a *para* substitution, epoxides **7a,b-Me**)[9] and the electron-withdrawing 7-Br group (a *meta* substitution, epoxides **7a,b-Br**), were introduced on the aromatic ring, in order to evaluate whether a clear dependence of the diastereoselectivity of the opening process on the electronic properties of the aromatic substituent was present also in these tertiary benzylic benzocondensed epoxides, as previously found in the secondary ones (epoxides **5a** and **5b**).[6b,7a] For the sake of completeness, the corresponding semirigid tertiary benzylic benzocondensed epoxides **6**[8,9] bearing the same type of substituents on the aromatic ring (6-Me and 7-Br) were also prepared.

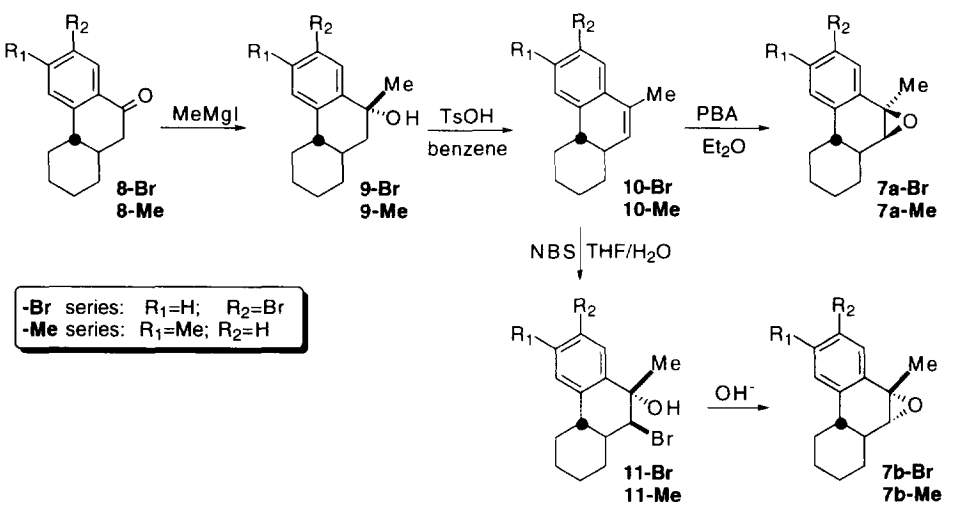
All the 2-aryloxiranes prepared were subjected to acid-catalyzed opening reaction with MeOH both under condensed phase (methanolysis in an H_2SO_4-MeOH solution) and gas-phase operating conditions (D_3^+ and MeOH in D_2 as the neutral bulk gas, see Experimental Section),[7a] in order to examine the diastereoselectivity of

the opening process (Tables 1-6). The gas phase operating conditions were likely to be particularly interesting because of the possibility of reaction pathways with more pronounced carbocationic character. As an effective comparison with the tertiary epoxides **6**, the secondary epoxides **4**, previously studied in the methanolysis,[5] were newly prepared (with the new entry of the 6-Me derivative, epoxide **4-Me**) and examined in their stereochemical behavior under the gas phase opening protocol. The overall results obtained with epoxides **4-7** were expected to give a complete, definitive outlook on the stereochemical behavior of these interesting 2-aryloxirane model systems.

Results

The known ketone **8-Me**,[10] necessary for the preparation of epoxides **7a,b-Me**, was prepared following a standard procedure (see Experimental Section).[6,11] Ketone **8-Br** was prepared as previously described.[6b,11] The olefins **10-Br** and **10-Me** and the related epoxides **7a,b-Br** and **7a,b-Me** were prepared following the procedures previously used for the synthesis of the corresponding derivatives having no substituent on the aromatic ring.[8] The Grignard reaction of ketones **8-Br** and **8-Me** with an excess of MeMgI afforded the benzylic alcohols **9-Br** and **9-Me** which were directly converted to the corresponding olefin **10-Br** and **10-Me** by their treatment with TsOH in refluxing benzene. The treatment of **10-Br** and **10-Me** with *N*-bromosuccinimide (NBS) in aqueous THF afforded the trans diaxial bromohydrins **11-Br** and **11-Me**, respectively, which were transformed under base-catalyzed conditions into the corresponding epoxides **7b-Br** and **7b-Me** (Scheme 1). The direct epoxidation of **10-Br** and **10-Me** in a two-phase system (Et_2O and saturated aqueous $NaHCO_3$ solution) with an ether solution of peroxybenzoic acid (PBA) yielded pure epoxides **7a-Br** and **7a-Me**, respectively.[8]

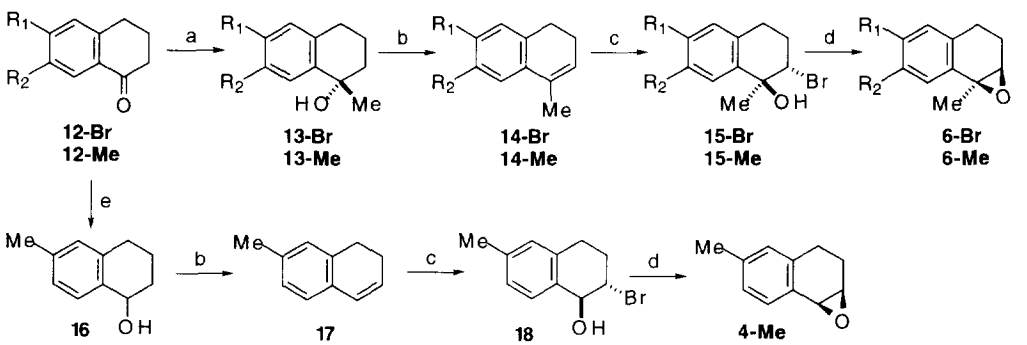
Scheme 1



The reaction of ketones **12-Br**[11] and **12-Me**[12] with an excess of MeMgI afforded the corresponding tertiary benzylic alcohols **13-Br** and **13-Me** which were dehydrated, under acid conditions, to the olefins **14-Br**[13] and **14-Me**, respectively. Their treatment with NBS in aqueous THF afforded the corresponding trans

bromohydrins **15-Br** and **15-Me** which were cyclized under basic conditions to the desired epoxides **6-Br** and **6-Me**, respectively. Following common procedures,[5] ketone **12-Me** was also used for the synthesis of epoxide **4-Me** (Scheme 2).

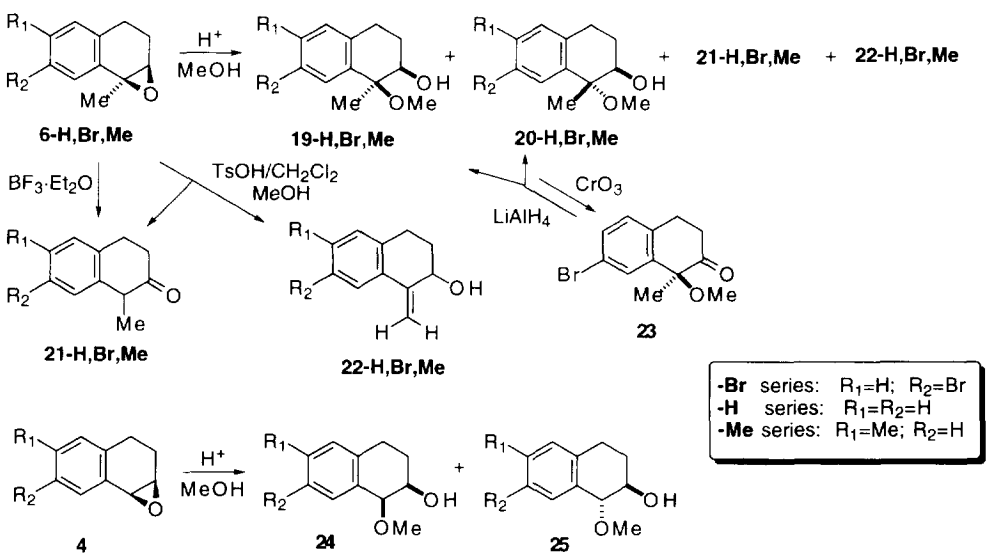
Scheme 2



a: MeMgI; b: TsOH-benzene, refluxing; c: NBS/THF-H_2O; d: *t*-BuOK-benzene; e: $NaBH_4$/EtOH.

The reference compounds, the pairs of cis and trans hydroxy ethers (HEs) **19-20**, **26-29-H,Br,Me** and **24-25-Me** were prepared by methanolysis of the corresponding epoxides **6**, **7b**, **7a-H,Br,Me** and **4-Me** and separated by preparative TLC (Schemes 3 and 4). Only in the case of the epoxide **6-Br**, the too low

Scheme 3



amount (5%) of cis HE **19-Br** present in the reaction mixture did not allow its separation. However, the oxidation of the crude methanolysis mixture with the Jones reagent to the methoxy ketone **23** and its subsequent $LiAlH_4$ reduction yielded a 68:52 mixture of **19-Br** and **20-Br** which were separated by preparative TLC (Scheme 3). Because of the complete anti stereoselectivity of the methanolysis of epoxides **7a-**

Table 1. Stereoselectivity of the Methanolysis of Epoxides 7a,b-H,Br,Me and 5a,b-H,Br,OMe.

epoxide	syn adduct HE **28**	anti adduct HE **29**	epoxide	syn adduct	anti adduct
7a-Br[a]	0	100	**5a-Br**[b]	0	100
7a-H[a]	0	100	**5a-H**[b]	0	100
7a-Me[a]	0	100	**5a-OMe**[b]	0	100
	HE **26**	HE **27**			
7b-Br[a]	49	51	**5b-Br**[b]	23	77
7b-H[a]	65	35	**5b-H**[b]	28	72
7b-Me[a]	77	23	**5b-OMe**[b]	38	62

[a] 0.001 N H_2SO_4-MeOH. [b] 0.2 N H_2SO_4-MeOH, ref.7a.

Table 2. Stereoselectivity of the Methanolysis of Epoxides 6-H,Br,Me and 4-H,Br,Me,OMe.

epoxide	syn adduct HE **19**	anti adduct HE **20**	ketone **21**	unsatd alcohol **22**	syn/anti ratio
6-Br[a,c]	5	95			5/95
6-H[a,c]	12	72	8	8	14/86
6-Me[a,c]	17	41	25	17	29/71
6-Br[b,c]	6	18	54	22	25/75
6-H[b,c]	5	10	62	20	33/67
6-Me[b,c]			85	15	
	HE **24**	HE **25**			
4-Br[a,d]	3	97			
4-H[a,d]	8	92			
4-Me[a,c]	15	85			
4-OMe[a,d]	43	57			

[a] 0.2 N H_2SO_4-MeOH. [b] 1.6×10^{-2} N TsOH in CH_2Cl_2 containing MeOH (0.18 mmol/ml). [c] Present work. [d] Ref.5.

Table 3. Distribution of Products from the Gas-Phase Acid-Induced Ring Opening of Epoxides 7a-H,Br,Me.

system composition (Torr)[a]				product distribution[b]						
epoxide		bulk gas	CH_3OH	cis HE **28** G	cis HE **28** %	trans HE **29** G	trans HE **29** %	ketone **34** G	ketone **34** %	total abs. yield %[c]
7a-Br	(.56)	D_2 (760)	(1.61)	.35	17	1.51	74	0.18	9	68
7a-H	(.54)	D_2 (760)	(1.59)	.68	32	1.22	56	0.26	12	72
7a-Me	(.53)	D_2 (760)	(1.57)	.78	35	1.17	53	0.27	12	74
7a-Br	(.48)	D_2 (100)	(1.50)	.56	23	1.45	61	0.39	16	80
7a-H	(.51)	D_2 (100)	(1.53)	.77	28	1.25	46	0.71	26	91
7a-Me	(.52)	D_2 (100)	(1.53)	1.04	37	1.18	41	0.63	22	95
7a-Br	(.54)	D_2 (760)[d]	(1.57)	.08	12	.58	84	.03	4	23
7a-H	(.57)	D_2 (760)[d]	(1.60)	.16	21	.58	74	.04	5	26
7a-Me	(.50)	D_2 (760)[d]	(1.52)	.26	33	.49	63	.03	4	26

[a] O_2: 4 Torr, radiation dose 1.5×10^4 Gy (dose rate 1×10^4 Gy h^{-1}). [b] G values expressed as the number of molecules produced per 100eV adsorbed energy. [c] Total absolute yields (%) estimated from the ratio of the overall G(M) values of products to the $G(D^{+3})$ formation values (see ref.20). [d] 3 Torr of NMe_3 added to the gaseous mixture.

Table 4. Distribution of Products from the Gas-Phase Acid-Induced Ring Opening of Epoxides 7b-H,Br,Me.

system composition (Torr)[a]				product distribution[b]						
epoxide		bulk gas	CH_3OH	cis HE **26** G	cis HE **26** %	trans HE **27** G	trans HE **27** %	ketone **33** G	ketone **33** %	total abs. yield %[c]
7b-Br	(.55)	D_2 (760)	(1.59)	.70	44	0.65	41	0.24	15	53
7b-H	(.49)	D_2 (760)	(1.51)	.99	54	0.51	28	0.33	18	61
7b-Me	(.53)	D_2 (760)	(1.60)	1.12	58	0.44	23	0.36	19	64
7b-Br	(.48)	D_2 (100)	(1.51)	.89	39	0.93	41	0.46	20	76
7b-H	(.56)	D_2 (100)	(1.61)	1.00	42	0.70	29	0.70	29	80
7b-Me	(.51)	D_2 (100)	(1.52)	1.20	47	0.71	28	0.64	25	85
7b-Br	(.52)	D_2 (760)[d]	(1.54)	.36	58	.23	36	.04	6	21
7b-H	(.54)	D_2 (760)[d]	(1.58)	.49	68	.18	25	.05	7	24
7b-Me	(.55)	D_2 (760)[d]	(1.57)	.62	76	.16	20	.03	4	27

[a-d] See corresponding footnotes in Table 3.

Table 5. Distribution of Products from the Gas-Phase Acid-Induced Ring Opening of Epoxides 6-H,Br,Me.

system composition (Torr)[a]				product distribution[b]								
epoxide		bulk gas	MeOH	cis HE **19** G	cis HE **19** %	trans HE **20** G	trans HE **20** %	ketone **21** G	ketone **21** %	uns.alcohol **22** G	uns.alcohol **22** %	total abs. yield %[c]
6-Br	(.59)	D_2 (760)	(1.62)	.46	23.7	.94	47.8	.30	15.3	.26	13.2	65
6-H	(.46)	D_2 (760)	(1.63)	1.05	49.7	.53	25.2	.33	15.8	.19	9.2	70
6-Me	(.53)	D_2 (760)	(1.59)	1.23	56.9	.46	21.5	.28	12.9	.18	8.7	72
6-Br	(.54)	D_2 (100)	(1.57)	.73	28.1	.78	31.2	.46	18.5	.55	22.1	83
6-H	(.48)	D_2 (100)	(1.51)	.85	33.5	.77	30.3	.44	20.2	.41	16.1	85
6-Me	(.57)	D_2 (100)	(1.58)	1.04	39.1	.79	29.9	.64	16.8	.37	14.2	87
6-Br	(.52)	D_2 (760)[d]	(1.52)	.16	30.1	.26	47.3	.05	9.1	.07	13.5	19
6-H	(.55)	D_2 (760)[d]	(1.60)	.22	35.4	.28	44.6	.04	6.5	.08	13.5	22
6-Me	(.47)	D_2 (760)[d]	(1.49)	.29	41.8	.29	42.0	.04	5.6	.07	10.6	24

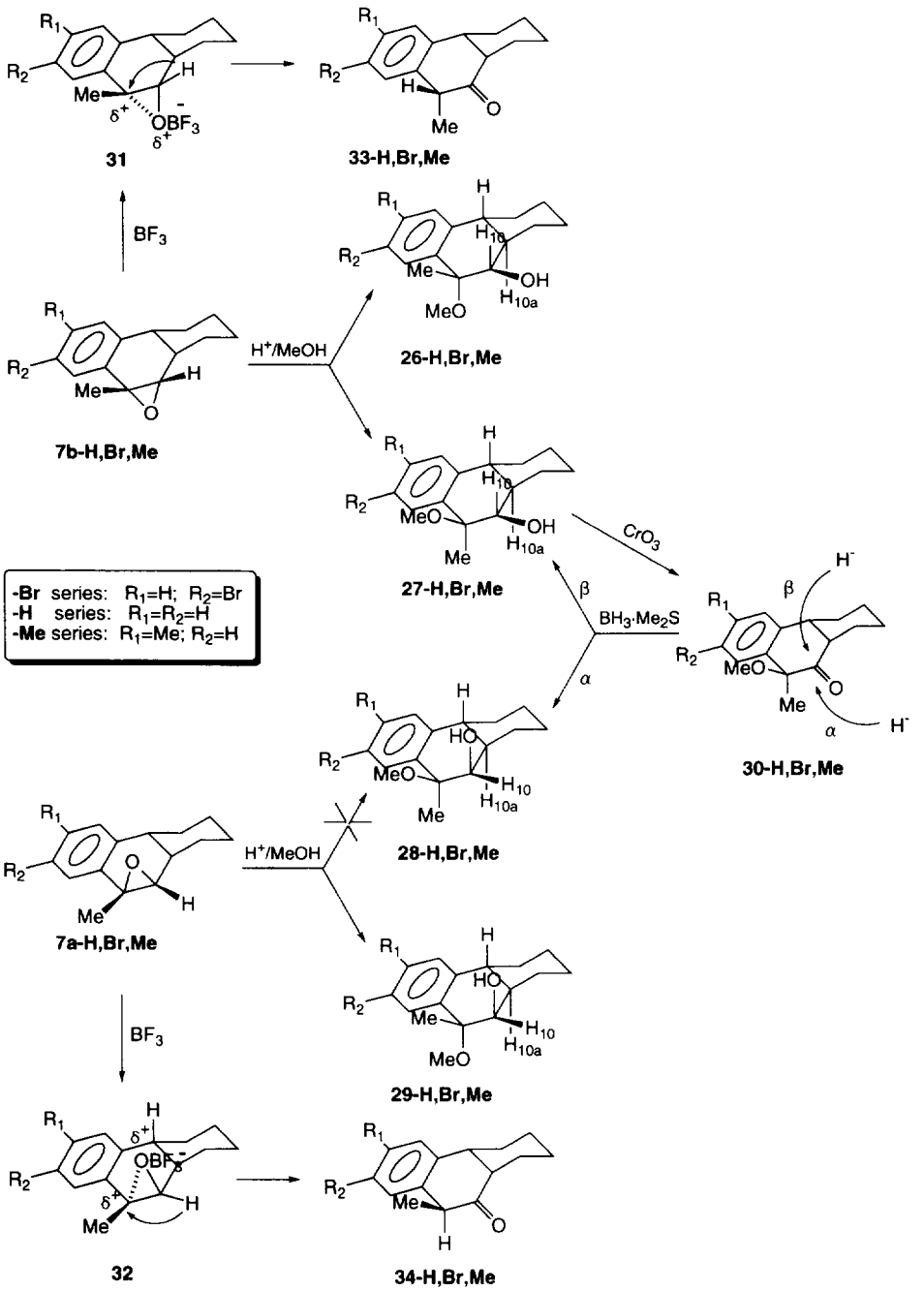
[a-d] See corresponding footnotes in Table 3.

Table 6. Distribution of Products from the Gas-Phase Acid-Induced Ring Opening of Epoxides 4-H,Br,Me,OMe.

system composition (Torr)[a]				product distribution[b]				
epoxide		bulk gas	MeOH	cis HE **24** G	cis HE **24** %	trans HE **25** G	trans HE **25** %	total abs. yield %[c]
4-Br	(.51)	D_2 (760)	(1.58)	.49	28.5	1.24	71.5	58
4-H	(.48)	D_2 (760)	(1.49)	.80	41.2	1.15	58.8	65
4-Me	(.55)	D_2 (760)	(1.61)	1.13	50.6	1.10	49.4	74
4-OMe	(.53)	D_2 (760)	(1.58)	1.29	52.7	1.15	47.3	81
4-Br	(.57)	D_2 (100)	(1.62)	.98	38.1	1.60	61.8	86
4-H	(.54)	D_2 (100)	(1.55)	1.18	43.5	1.54	56.5	91
4-Me	(.49)	D_2 (100)	(1.50)	1.44	51.4	1.36	48.6	93
4-OMe	(.43)	D_2 (100)	(1.48)	1.48	50.6	1.42	49.4	96
4-Br	(.53)	D_2 (760)[d]	(1.52)	.15	31.8	.32	68.2	16
4-H	(.56)	D_2 (760)[d]	(1.63)	.19	38.3	.31	61.7	17
4-Me	(.47)	D_2 (760)[d]	(1.51)	.25	47.2	.29	52.8	18
4-OMe	(.44)	D_2 (760)[d]	(1.53)	.36	58.8	.25	41.2	20

[a-d] See the corresponding footnotes in Table 3.

Scheme 4


31
33-H,Br,Me
BF3
26-H,Br,Me
H+/MeOH
7b-H,Br,Me
27-H,Br,Me
CrO3
-Br series: R1=H; R2=Br
-H series: R1=R2=H
-Me series: R1=Me; R2=H
β
BH3·Me2S
α
30-H,Br,Me
28-H,Br,Me
H+/MeOH
7a-H,Br,Me
29-H,Br,Me
BF3
32
34-H,Br,Me

H,Br,Me, the cis HEs **28-H,Br,Me** were prepared in a similar way starting from the respective HE **27-H,Br,Me**, having the right configuration at the benzylic carbon. The oxidation of **27-H,Br,Me** yielded the corresponding ketones **30-H,Br,Me** which were reduced by BH_3·Me_2S to give an almost 1:1 mixture of the two HEs **27** and **28-H,Br,Me** which were separated by preparative TLC (Scheme 4).[14]

Because of the possible formation of non-addition products in the opening reactions of epoxides **6** and **7a,b**, the unsaturated alcohols **22**, and ketones **21**, **33** and **34-H,Br,Me** were prepared, too (Schemes 3 and 4). Ketones **21**, **33** and **34-H,Br,Me**[8] were prepared by treatment of the corresponding epoxide (**6**, **7b** and **7a-H,Br,Me**, respectively) with BF_3·Et_2O. The unsaturated alcohols **22-H,Br,Me**[8] were obtained (15-22%), together with the corresponding ketones and some amounts of the addition products (HEs) (Table 2), by treatment of the corresponding epoxides with 1.6×10^{-2} M TsOH in CH_2Cl_2 containing MeOH (0.18 mmol/ml), and were then separated by TLC.

The methanolysis reaction of epoxides **7a,b-H,Br,Me** was carried out with a 0.001 N H_2SO_4-MeOH solution instead of the 0.2 N H_2SO_4-MeOH solution commonly used in other corresponding cases.[5a,7a] This was the consequence of the observed extensive isomerization of the HEs from epoxides **7b-H,Br,Me** in the 0.2 N H_2SO_4-MeOH solution, which led to a substantial enrichment of the reaction mixture in the more stable trans isomer **27-H,Br,Me**, even after a very short reaction time (5 sec). On the contrary, HEs **26-29-H,Br,Me** turned out to be stable in the 0.001 N H_2SO_4-MeOH solution (Table 1).[15]

Structures and Configurations

The structure and configuration of the diastereoisomeric pairs of HE **19-20**, **26-27** and **28-29** were determined on the basis of their method of synthesis (acid methanolysis) from the corresponding epoxides on the reasonable assumption that in these opening conditions the nucleophilic attack occurs completely on the benzylic oxirane carbon. The trans relationship between the two functional groups in HE **20** (and consequently the cis one in the diastereoisomeric HE **19**) was firmly established by the fact that **20** is also obtained as the only product in the methanolysis of **6** under alkaline conditions (MeONa/MeOH), that is under conditions which lead to a completely anti stereoselective opening of the oxirane ring.[5a,16] As for HEs **26-29**, their structure and stereochemistry was confirmed by an examination of their ^{1}H NMR ($J_{10,10a}$) and IR spectra in dilute CCl_4 in the 3μ range (OH stretching).[6b,7a,8] The stereochemistry of ketones **33** and **34-H,Br,Me** was firmly established by their completely stereoselective method of synthesis from epoxides **7b** and **7a**, respectively, on the basis of a completely anti stereoselective hydride migration (the oxirane proton H_{10}) on the developing carbocationic benzylic centre, as shown in structures **31** and **32** of Scheme 4.[8]

Discussion

The diastereoselectivity observed in the ring-opening reaction with MeOH in the condensed (methanolysis) and in the gas-phase (see Experimental Section)[7a] of semirigid **4**[5a] and **6** and rigid epoxides **7a,b-H,Br,Me** are summarized in Tables 1-6, where some results previously obtained in the methanolysis of epoxides **5a,b**[7a] are reported too. In all cases, with the only exception of epoxides **7a** which constantly gave in the condensed phase a completely anti stereoselective result, the observed syn diastereoselectivity appears to be closely linked to the nature and electronic properties of the aryl-group substituent: the lower and the higher levels of syn stereoselectivity are obtained in the case of the 7-Br and 6-Me (or 6-OMe in the case of epoxides

4) derivatives, respectively, and a good Hammett-type linear correlation was found between the diastereoselectivity of the reaction (syn adduct/anti adduct ratio) and the σ^+ constants,[17] in accordance with equation 1.[18] The ρ_{syn}-ρ_{anti} values obtained together with their correlation coefficients (r) and standard deviations (s) are shown in Table 7 and plotted in Figures 1 (epoxides **4**[5a] and **6**) and 2 (epoxides **5**[7a] and **7**).

Table 7. ρ_{syn} - ρ_{anti} Values Obtained in the Acid Methanolysis (Condensed Phase) and in the Gas-Phase Acid-Induced Ring Opening with MeOH of Epoxides 4, 6, 7a and 7b-H,Br,Me.

$$\log \frac{[S]\,[A^\circ]}{[A]\,[S^\circ]} = (\rho_{syn} - \rho_{anti})\,\sigma^+ \qquad \text{(eq. 1)}$$

Epoxide	Reagents and reaction conditions[a]	ρ_{syn} - ρ_{anti}	Correlation coefficient (r)	Standard deviation (s)
4	MeOH-GA$^+$	-0.40	0.991	0.023
6	MeOH-H_2SO_4	-1.20	0.998	0.018
6	MeOH-GA$^+$	-0.27	0.992	0.011
7a	MeOH-GA$^+$	-0.78	0.998	0.012
7b	MeOH-H_2SO_4	-0.75	0.998	0.017
7b	MeOH-GA$^+$	-0.52	0.997	0.010

[a] MeOH-GA$^+$: gas-phase operating conditions; MeOH-H_2SO_4: condensed phase operating conditions (methanolysis).

Moreover, the syn stereoselectivity observed in the epoxides bearing a secondary benzylic carbon (epoxides **4** and **5**)[5a,7a] is on the whole lower than that observed in the epoxides bearing a tertiary benzylic carbon (epoxides **6** and **7**), both in the condensed and in the gas-phase operating opening conditions (Tables 1-6), as well-demonstrated by the graphical expression of Figures 1 and 2, in which the linear correlations relative to epoxides **4** and **5** are lower than those relative to the methyl-substituted epoxides **6** and **7**. Bearing in mind that a tertiary benzylic oxirane centre, like the one present in **6** and **7**, should reasonably be more favourable than a secondary one, as present in **4** and **5**, for the development of a partial carbocationic character in the course of the opening process, the present results obtained with epoxides **6** and **7** confirm the close relationship which must be present between syn stereoselectivity of the opening process and the stability of the intermediate benzylic carbocationic species. All this makes it possible to apply to the tertiary epoxides **6** and **7** the ion-dipole pair rationalization previously used in the case of the secondary epoxides **4** and **5** (S_2 system)[5a,7a] and tertiary epoxides **2** and **3** (S_1 system)[4] this being the only rationalization able to adequately justify the results obtained.

As previously observed in the case of epoxides **5a,b**,[7a] also the opening reactions of epoxides **4**, **6**, and **7a,b** in the gas phase are more syn stereoselective than the corresponding reactions carried out in the condensed phase (Tables 1-6). In accordance with the ion-dipole pair rationalization adopted,[7a] this points to a generally more pronounced carbocationic character of the reactions in the gas-phase than in the condensed phase because of the presence, in the gas phase, of a decidedly reduced amount of nucleophilic molecules (MeOH).[7a] As a consequence, with the only exception of epoxide **5b**,[7a] the sensitivity of the diastereoselectivity of the opening reaction to the electronic effects of the substituent on the aromatic ring (that is the ρ_{syn}-ρ_{anti} value,

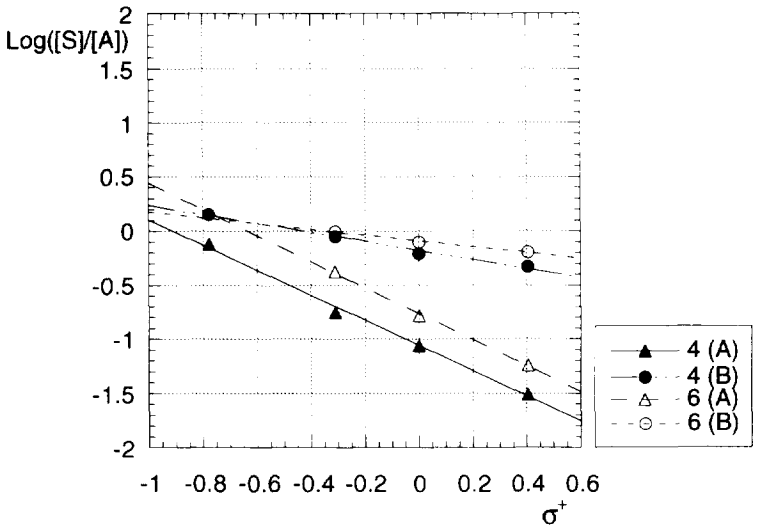


Figure 1. Hammet-Brown $\rho\sigma^+$ plot for the acid-catalyzed ring opening of epoxides **4** and **6** with MeOH. Reaction conditions: (A) condensed phase; (B) gas phase.

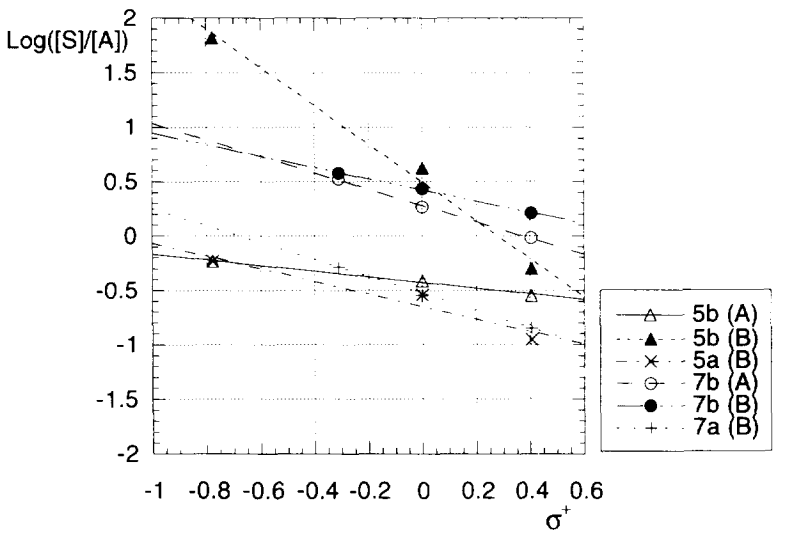


Figure 2. Hammet-Brown $\rho\sigma^+$ plot for the acid-catalyzed ring opening of epoxides **5a**, **5b**, **7a** and **7b** with MeOH. Reaction conditions: (A) condensed phase; (B) gas phase.

Table 7) is accordingly lower in the gas-phase opening conditions than in the condensed phase, as correctly shown by Figures 1 and 2.

In conclusion, the results obtained definitely confirm that both the 2-aryloxirane systems (S_1 and S_2 oxirane systems), utilized as models in stereochemical studies, obey the same rationalization (the ion-dipole mechanism)[7a] when subjected to acid-promoting opening reactions. As a consequence, the somewhat surprising different stereochemical behavior between rigid epoxides of the S_2 oxirane system (epoxides **5a** and **7a**) and conformationally restricted epoxides of the S_1 oxirane system (epoxides **3a** and **3b**), in the reaction carried out in the condensed phase, are not attributable to the different nature (secondary or tertiary) of the benzylic oxirane carbon, but to the intrinsic structural requirements of the two systems, as previously discussed.[7a]

Experimental Section

For general experimental procedures see ref. 7. Epoxides **6-H**, **7a,b-H**, ketones **8-Br**, **12-Me**, **12-Br**, **21-H**, **33-H**, and **34-H**, and unsaturated alcohol **22-H** were prepared as previously described.[8,11-12] Ketone **8-Me**[10] was prepared starting from 1-(3-methylphenyl)-cyclohexene following a standard procedure:[6,11] the physical and spectral data of the synthetic intermediates are reported down here without numbering. All new compounds gave satisfactory microanalytical results (C, H ±0.4% of the calculated value).

2-(3-Methylphenyl)-2-cyclohexenone oxime, a solid m.p. 90-91°C: ^{1}H NMR δ 7.80-8.09 (m, 1H), 7.00-7.35 (m, 4H), 6.17 (t, 1H, *J*=4.4 Hz), 2.70 (t, 2H, *J*=4.4 Hz), 2.34 (s, 3H), 2.25-2.51 (m, 2H), 1.64-1.95 (m, 2H). ^{13}C NMR δ 156.79, 139.78, 138.09, 137.56, 136.28, 130.32, 128.50, 128.55, 126.61, 26.12, 23.21, 22.07, 21.53.

2-(3-Methylphenyl)-2-cyclohexenone, a liquid: ^{1}H NMR δ 7.16-7.30 (m, 1H), 7.05-7.15 (m, 3H), 7.00 (t, 1H, *J*=4.3 Hz), 2.45-2.65 (m, 4H), 2.35 (s, 3H), 2.00-2.18 (m, 2H). ^{13}C NMR δ 198.61, 148.47, 141.04, 138.02, 137.10, 129.91, 128.88, 128.46, 126.27, 39.65, 27.14, 23.51, 22.02.

Diethyl trans-2-(3-methylphenyl)-3-oxo-1-cyclohexanemalonate, a liquid: ^{1}H NMR δ 7.16-7.30 (m, 1H), 7.05-7.15 (m, 3H), 7.00 (t, 1H, *J*=4.3 Hz), 2.45-2.65 (m, 4H), 2.35 (s, 3H), 2.00-2.18 (m, 2H). ^{13}C NMR δ 198.61, 148.47, 141.04, 138.02, 137.10, 129.91, 128.88, 128.46, 126.27, 39.65, 27.14, 23.51, 22.02.

Diethyl trans-2-(3-methylphenyl)-3,3-diethoxy-1-cyclohexanemalonate, a liquid: ^{1}H NMR δ 7.16-7.30 (m, 1H), 7.05-7.15 (m, 3H), 7.00 (t, 1H, *J*=4.3 Hz), 2.45-2.65 (m, 4H), 2.35 (s, 3H), 2.00-2.18 (m, 2H). ^{13}C NMR δ 198.61, 148.47, 141.04, 138.02, 137.10, 129.91, 128.88, 128.46, 126.27, 39.65, 27.14, 23.51, 22.02.

trans-2-(3-Methylphenyl)-3-oxo-1-cyclohexanemalonic acid, a liquid: ^{1}H NMR δ 8.83 (m, 2H), 6.97-7.21 (m, 2H), (m, 1H), 6.79-6.88 (m, 2H), 3.71 (d, 1H, *J*=12.4 Hz), 3.16 (d, 1H, *J*=2.8 Hz), 2.37-2.79 (m, 2H), 2.24 (s, 3H), 2.00-2.20 (m, 2H), 1.64-1.98 (m, 2H). ^{13}C NMR δ 210.16, 174.35, 173.16, 138.95, 136.09, 130.93, 129.23, 129.18, 127.21, 60.90, 52.83, 45.28, 42.28, 27.78, 25.58, 22.14.

trans-2-(3-Methylphenyl)-1-cyclohexaneacetic acid, a solid m.p. 93-96°C (from hexane): ^{1}H NMR δ 7.01-7.12 (m, 2H), 6.81-6.93 (m, 2H), 2.02-2.31 (m, 4H), 2.24 (s, 3H), 1.63-1.99 (m, 5H), 1.12-1.50 (m, 3H). ^{13}C NMR δ 180.50, 145.88, 138.66, 129.10, 129.05, 127.74, 125.83, 50.82, 40.21, 40.16, 36.21, 33.29, 27.36, 26.82, 22.14.

trans-2-(3-Methylphenyl)-3-oxo-1-cyclohexaneacetic acid, a liquid: ^{1}H NMR δ 7.02-7.30 (m, 2H), 6.83-6.98 (m, 2H), 3.35 (d, 1H, *J*=12.0 Hz), 2.42-2.70 (m, 3H); 2.33 (s, 3H), 2.04-2.28 (m, 4H),

1.52-2.00 (m, 2H). ^{13}C NMR δ 209.70, 178.83, 138.75, 136.75, 130.77, 129.10, 128.84, 127.02, 63.08, 42.38, 42.21, 39.84, 31.79, 26.00, 22.14.

6-Methyl-trans-1,2,3,4,4a,10a-hexahydro-9(10*H*)-phenanthrenone (8-Me),[10] a solid m.p. 78-81°C (from hexane): ^{1}H NMR δ 7.88 (d, 1H, *J*=7.9 Hz), 7.14 (s, 1H), 7.03 (d, 1H, *J*=7.9 Hz), 2.31 (s, 3H), 2.13-2.65 (m, 3H), 1.82-1.98 (m, 1H), 1.57-1.79 (m, 3H), 1.04-1.50 (m, 5H). ^{13}C NMR δ 198.61, 147.94, 144.90, 130.92, 127.93, 127.89, 126.36, 47.29, 43.31, 41.30, 34.30, 30.36, 26.94, 26.19, 22.64.

6-Methyl-trans-1,2,3,4,4a,10a-hexahydro-4,9(10*H*)-phenanthrendione,[10] a solid m.p. 92-95°C (from hexane): ^{1}H NMR δ 7.90 (d, 1H, *J*=8.0 Hz), 7.12 (d, 1H, *J*=8.0 Hz), 6.82 (s, 1H), 3.87 (d, 1H, *J*=5.1 Hz), 2.78-2.96 (m, 1H), 2.50 (d, 2H, *J*=7.4 Hz), 2.32-2.46 (m, 2H), 1.78-2.03 (m, 3H), 1.60-1.77 (m, 1H). ^{13}C NMR δ 210.78, 197.15, 148.98, 145.45, 140.22, 130.31, 129.45, 128.01, 55.90, 42.16, 41.12, 39.28, 28.92, 24.68, 22.41.

6-Methyl-1,2,3,4-tetrahydronaphthalen-1-ol (16). A solution of ketone **12-Me** (2.0 g, 12.5 mmol) in EtOH 95% (90 ml) was treated with $NaBH_4$ (0.43 g, 11.3 mmol) and the resulting reaction mixture was stirred for 3 h at r.t.. Acidification with 10% aqueous H_2SO_4, dilution with saturated aqueous NaCl, extraction with ether and evaporation of the washed (satured aqueous $NaHCO_3$ and brine) ether extracts afforded a solid residue (1.9 g) which was recrystallized from hexane to give pure **16** (1.5 g, 75% yield), as a solid m.p. 38-40 °C: ^{1}H NMR δ 7.31 (d, 1H, *J*=7.7 Hz), 7.02 (d, 1H, *J*=7.9 Hz), 6.93 (s, 1H), 4.72-4.84 (m, 1H), 2.58-2.90 (m, 2H), 2.31 (s, 3H), 1.63-2.11 (m, 4H). ^{13}C NMR δ 137.95, 137.66, 136.59, 130.20, 129.33, 127.71, 68.60, 33.03, 29.90, 21.76, 19.43.

Alcohols 9-Br,Me, 13-Br,Me and Olefins 10-Br,Me, 14-Br,Me and 17. The following procedure is typical. A solution of ketone **8-Me** (3.50 g, 16.4 mmol) in anhydrous Et_2O (25 ml) was added dropwise to a stirred solution of MeMgI [from MeI (5.8 g, 41 mmol) and Mg (1.03 g, 43.0 gatoms)] in anhydrous Et_2O (30 ml) and the resulting reaction mixture was refluxed for 4 h under stirring. The usual work up afforded a crude solid product (2.8 g) which was recrystallized from hexane to give pure alcohol **9-Me** (2.1 g, 56% yield), as a solid, m.p. 119-121°C: ^{1}H NMR δ 7.42 (d,1H, *J*=7.8 Hz), 6.88-7.04 (m, 2H), 2.24 (s, 3H), 1.98-2.47 (m, 2H), 1.51-1.93 (m, 6H), 1.45 (s, 3H), 1.03-1.40 (m, 4H). ^{13}C NMR δ 141.61, 139.87, 137.27, 127.80, 127.25, 126.18, 72.68, 48.79, 45.13, 40.16, 34.59, 32.91, 31.35, 27.48, 26.76, 21.94. A solution of alcohol **9-Me** (2.75 g, 12.0 mmol) in anhydrous benzene (78 ml) was refluxed for 1h in the presence of *p*-toluenesulfonic acid (TsOH) (0.092 g). Evaporation of the washed (saturated aqueous $NaHCO_3$) benzene solution afforded a liquid residue (2.5 g) which was filtered through a short silica gel column. Elution with hexane yielded pure **6,9-dimethyl-trans-1,2,3,4,4a,10a-hexahydrophenanthrene (10-Me)**, as a liquid (2.10 g, 83% yield): ^{1}H NMR δ 6.90-7.60 (m, 3H), 5.42-5.53 (m, 1H), 2.33 (s, 3H), 2.23-2.43 (m, 2H), 2.01 (d, 3H, *J*=1.5 Hz), 1.67-1.95 (m, 4H), 1.20-1.43 (m, 4H). ^{13}C NMR δ 140.48, 136.99, 134.20, 131.96, 131.84, 127.03, 124.74, 123.38, 42.78, 40.07, 33.52, 29.20, 27.04, 26.93, 22.14, 19.83.

Alcohol **9-Br** (2.49 g, 41% yield), a solid m.p. 136-138°C: ^{1}H NMR δ 7.73 (d, 1H, *J*=2.1 Hz), 7.30 (dd,1H, *J*=8.4 and 2.2 Hz), 7.12 (d, 1H, *J*=8.6 Hz), 2.33-2.47 (m, 1H), 2.17-2.31 (m, 1H), 1.86-2.00 (m, 2H), 1.58-1.85 (m, 4H), 1.52 (s, 3H), 1.05-1.50 (m, 4H). ^{13}C NMR δ 146.76, 138.86, 130.71, 130.37, 127.56, 120.69, 72.53, 48.22, 44.73, 39.87, 34.35, 32.99, 31.20, 27.32, 26.65.

7-Bromo-9-methyl-trans-1,2,3,4,4a,10a-hexahydrophenanthrene (10-Br), a liquid (2.15 g, 7.75 mmol, 92% yield): ^{1}H NMR δ 7.26-7.35 (m, 3H), 7.09 (d, 1H, *J*=7.7 Hz), 5.58-5.66 (m, 1H), 2.17-2.45 (m, 2H), 2.01 (d, 3H, *J*=1.5 Hz), 1.77-1.97 (m, 4H), 1.19-1.48 (m, 4H). ^{13}C NMR δ 139.30, 138.92, 134.33, 130.95, 129.92, 126.31, 125.49, 120.69, 42.29, 39.67, 33.20, 28.97, 26.80, 26.74, 19.63.

1,6-Dimethyl-1,2,3,4-tetrahydronaphthalen-1-ol (13-Me), (3.7 g, 77% yield), a solid m.p.72-74°C. ^{1}H NMR δ 7.47 (d, 1H, *J*=8.0 Hz), 7.03 (d, 1H, *J*=8.4 Hz), 6.89 (s, 1H), 2.67-2.80 (m, 2H), 2.29 (s, 3H), 1.72-1.98 (m, 2H), 1.54 (s, 3H).^{13}C NMR δ 140.59, 137.40, 136.84, 129.97, 127.90, 126.91, 71.06, 40.56, 31.32, 30.58, 21.62, 21.08.

1,6-Dimethyl-3,4-dihydronaphthalene (14-Me) (2.1 g, 88 % yield), a liquid: ^{1}H NMR δ 7.09 (d, 1H, *J*=7.7 Hz), 6.97 (d, 1H, *J*=7.9 Hz), 6.92 (s, 1H), 5.70-5.80 (m, 1H), 2.69 (t, 2H, *J*=8.0 Hz), 2.29 (s, 3H), 2.13-2.27 (m, 2H), 1.95-2.04 (m, 3H).

7-Bromo-1-methyl-1,2,3,4-tetrahydronaphthalen-1-ol (13-Br) (2.5 g, 78% yield), a solid m.p.76-80°C: ^{1}H NMR δ 7.71 (d, 1H, *J*=2.1 Hz), 7.27 (dd, 1H, *J*=7.9 and 2.1 Hz), 6.94 (d, 1H, *J*=7.9 Hz), 2.68-2.77 (m, 2H), 1.82-1.95 (m, 4H), 1.53 (s, 3H). ^{13}C NMR δ 145.73, 135.69, 131.16, 130.70, 130.04, 120.43, 71.15, 40.00 31.41, 29.92, 20.86.

7-Bromo-1-methyl-3,4-dihydronaphthalene (14-Br)[13] (1.18 g, 91% yield), a liquid: ^{1}H NMR δ 7.30 (d,1H, *J*=2.0Hz), 7.22 (dd, 1H, *J*=7.9 and 2.0 Hz), 5.82-6.01 (m, 1H), 2.61-2.69 (m, 2H), 2.12-2.26 (m, 2H), 1.98 (d, 3H, *J*=1.7 Hz). ^{13}C NMR δ 138.45, 135.60, 131.93, 129.87, 129.44, 127.39, 126.39, 120.67, 28.32, 23.63, 19.82.

6-Methyl-3,4-dihydronaphthalene (17)[19] (1.1 g, 80% yield), a liquid: ^{1}H NMR δ 6.80-6.99 (m, 3H), 6.40 (d, 1H, *J*=9.6 Hz), 5.92 (dt, 1H, *J*=9.6 and 4.6 Hz), 2.72 (t, 2H, *J*=8.1 Hz), 2.20-2.34 (m, 2H), 2.28 (s, 3H).

Bromohydrins 11-Br,Me, 15-Br,Me and 18. The following procedure is typical. A solution of olefin **10-Me** (0.50 g, 2.4 mmol) in a 75:25 THF/H_2O mixture (50 ml) was treated with NBS (0.47 g, 2.64 mmol) for 10 min at r.t. in the dark. Dilution with water, extraction with ether and evaporation of the washed (water and brine) ether extracts afforded practically pure **(4aβ,10β)-*t*-10-Bromo-6,9-dimethyl-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-9-ol (11-Me)** (0.49 g, 1.56 mmol), as a liquid, which was directly utilized in the next step without any further purification: ^{1}H NMR δ 7.35 (d, 1H, *J*=8.0 Hz), 7.09 (s, 1H), 6.97 (d, 1H, *J*=7.9 Hz), 4.04 (d, 1H, *J*=1.6 Hz), 2.36-2.72 (m, 8H), 2.25 (s, 3H), 1.18-2.08 (m, 8H), 1.79 (s, 3H). ^{13}C NMR δ 139.59, 138.48, 135.54, 128.14, 127.34, 127.24, 72.94, 67.58, 40.60, 39.63, 32.33, 31.66, 29.53, 27.29, 26.29, 26.18.

(4aβ,10β)-7,*t*-10-Dibromo-9-methyl-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-9-ol (11-Br) (0.90 g, 61% yield), as a solid, m.p. 92-94°C: ^{1}H NMR δ 7.65 (d,1 H, *J*=2.1 Hz), 7.40 (dd, 1H, *J*=8.5 and 2.1 Hz), 7.24 (d, 1H, *J*=8.5 Hz), 4.12 (d, 1H, *J*=1.5 Hz), 3.87-4.10 (m, 1H), 3.66-3.79 (m, 2H), 2.65-2.81 (m, 1H), 2.17-2.53 (m, 3H), 1.89 (s, 3H), 1.15-2.12 (m, 3H). ^{13}C NMR δ 140.76, 138.94, 132.02, 130.39, 128.88, 121.03, 73.05, 66.75, 40.53, 39.51, 32.23, 31.61, 29.70, 27.24, 26.26.

***t*-2,7-Dibromo-1-methyl-1,2,3,4-tetrahydronaphthalen-*r*-1-ol (15-Br)** (1.4 g, 76% yield), a solid m.p. 68-70°C: ^{1}H NMR δ 7.78 (d, 1H, *J*=2.1 Hz), 7.31 (dd, 1H, *J*=8.2 and 2.1 Hz), 6.93 (d, 1H, *J*=8.3 Hz), 4.50 (dd, 1H, *J*=11.8 and 3.9 Hz), 2.85-2.98 (m, 2H), 2.24-2.51 (m, 2H), 1.61 (s, 3H). ^{13}C NMR δ 143.24, 133.18, 131.29, 130.78, 130.10, 120.90, 73.76, 62.99, 31.33, 29.41, 28.78.

***t*-2-Bromo-1,6-dimethyl-1,2,3,4-tetrahydronaphthalen-*r*-1-ol (15-Me)** (2.7g, 84% yield), a liquid: ^{1}H NMR δ 7.53 (d, 1H, *J*=8.0 Hz), 7.06 (d, 1H, *J*=7.1 Hz), 6.89 (s, 1H), 4.50 (dd, 1H, *J*=11.6 and 3.7 Hz); 2.82-3.00 (m, 2H), 2.22-2.64 (m, 2H), 2.31 (s, 3H), 1.64 (s, 3H). ^{13}C NMR δ 138.65, 137.96, 134.19, 129.51, 128.29, 127.08, 73.95, 64.21, 31.73, 29.93, 28.94, 21.65.

trans-2-Bromo-6-methyl-1,2,3,4-tetrahydronaphthalen-1-ol (18) (1.6 g), a solid m.p. 108-110°C (from hexane): ^{1}H NMR δ 7.40 (d, 1H, *J*=7.9 Hz), 7.07 (d, 1H, *J*=8.1 Hz), 6.94 (s, 1H), 4.89 (d, 1H, *J*=6.6 Hz), 4.30-4.43 (m, 1H), 2.84-2.98 (m, 2H), 2.40-2.60 (m, 2H), 2.32 (s, 3H).

Epoxides 6-Br,Me, 7b-Br,Me, and 4-Me. The following procedure is typical. A solution of bromohydrin **11-Me** (0.20 g, 0.64 mmol) in anhydrous benzene (20 ml) was treated under stirring at r.t. with two portions of *t*-BuOK (0.146 g x 2, 2.60 mmol). Evaporation of the filtered (celite) organic solution afforded pure **(4aβ,10α)-6,9-dimethyl-9,10-epoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (7b-Me)** (0.125 g, 85% yield), as a liquid: ^{1}H NMR δ 7.42 (d, 1H, *J*=7.6 Hz), 6.90-7.08 (m, 2H), 2.96 (s, 1H), 2.25 (s, 3H), 1.96-2.13 (m, 1H), 1.63-1.95 (m, 4H), 1.59 (s, 3H), 1.06-1.54 (m, 5H). ^{13}C NMR δ

141.52, 138.60, 133.86, 128.20, 127.55, 125.64, 66.41, 54.50, 43.40, 40.14, 33.25, 29.68, 26.64, 26.50, 22.23, 22.03.

(4aβ,10α)-7-Bromo-9,10-epoxy-9-methyl-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (7b-Br) (0.44 g, 76% yield) as a solid, m.p. 94-97°C: ^{1}H NMR δ 7.70 (d, 1H, *J*=2.0 Hz), 7.39 (dd, 1H, *J*=8.3 and 2.1 Hz), 7.07 (d, 1H, *J*=8.3 Hz), 3.05 (s, 1H), 2.26-2.52 (m, 2H), 2.09-2.19 (m, 1H), 1.77-2.01 (m, 2H), 1.66 (s, 3H), 1.12-1.50 (m, 5H). ^{13}C NMR δ 140.67, 139.12, 131.90, 126.85, 120.87, 66.30, 54.18, 43.16, 40.01, 33.08, 29.58, 26.49, 26.38, 21.71.

7-Bromo-1,2-epoxy-1-methyl-1,2,3,4-tetrahydronaphthalene (6-Br) (0.45 g, 78% yield), a solid m.p. 37-39°C: ^{1}H NMR δ 7.61 (d, 1H, *J*=2.0 Hz), 7.34 (dd, 1H, *J*=8.0 and 2.0 Hz), 6.96 (d, 1H, *J*=8.1 Hz), 3.49 (d, 1H, *J*=3.0 Hz), 2.76 (ddd, 1H, *J*=14.4 and 6.5 Hz), 2.50 (dd, 1H, *J*=15.5 and 5.5 Hz), 2.30-2.43 (m, 1H), 1.72-1.88 (m, 1H), 1.75 (s, 3H). ^{13}C NMR δ 138.34, 136.52, 131.35, 130.77, 130.67, 126.70, 62.97, 55.35, 25.62, 22.51, 20.50.

1,6-Dimethyl-1,2-epoxy-1,2,3,4-tetrahydronaphthalene (6-Me) (1.5 g, 81% yield) as a yellow liquid: ^{1}H NMR δ 7.38 (d, 1H, *J*=7.8 Hz), 7.00 (d, 1H, *J*=7.8 Hz), 6.90 (s, 1H), 3.45 (d, 1H, *J*=3.1 Hz), 2.82 (ddd, 1H, *J*=14.4 and 6.4 Hz), 2.48 (dd, 1H, *J*=15.5 and 5.5 Hz), 2.29 (s, 3H), 1.70-1.90 (m, 1H), 1.73 (s, 3H). ^{13}C NMR δ 138.12, 137.32, 132.82, 129.88, 127.53, 127.29, 63.14, 55.73, 25.97, 22.82, 21.61, 20.65.

1,2-Epoxy-6-methyl-1,2,3,4-tetrahydronaphthalene (4-Me) (0.65 g, 66% yield), a solid m.p. 40-42°C: ^{1}H NMR δ 7.28 (d, 1H, *J*=7.6 Hz), 7.01 (d, 1H, *J*=7.8 Hz), 6.91 (s, 1H), 3.82 (d, 1H, *J*=4.2 Hz), 3.68-3.73 (m, 1H), 2.76 (ddd, 1H, *J*=14.4 and 6.4 Hz), 2.34-2.58 (m, 2H), 2.31 (s, 3H), 1.65-1.85 (m, 2H). ^{13}C NMR δ 138.89, 137.16, 130.20, 130.11, 129.91, 127.40, 55.76, 53.33, 24.99, 22.61, 21.91.

Epoxides 7a-Br,Me. The following procedure is typical. A two-phase system composed of a solution of olefin **10-Me** (0.500 g, 2.36 mmol) in Et_2O (30 ml) and saturated aqueous $NaHCO_3$ (30 ml) was treated at 0°C, under vigorous stirring, with a 0.16 M peroxybenzoic acid solution in Et_2O (14.5 ml, 2.32 mmol). The reaction mixture was stirred for 1h at 0°C, then two portions (2 x 14.5 ml) of 0.16 M peroxybenzoic acid solution were added at 1 h intervals. The reaction was quenched with 10% aqueous $Na_2S_2O_3$ solution (30 ml) and stirring was continued at r.t. for 10 min. Evaporation of the washed (saturated aqueous $NaHCO_3$, and water) ether extracts afforded pure **(4aβ,10β)-6,9-dimethyl-9,10-epoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (7a-Me)**, as a liquid (0.38 g, 76% yield): ^{1}H NMR δ 7.30 (d, 1H, *J*=7.7 Hz), 6.88-7.01 (m, 2H), 3.10 (s, 1H), 2.29-2.47 (m, 2H), 2.25 (s, 3H), 1.77-1.98 (m, 4H), 1.65 (s, 3H), 1.15-1.45 (m, 4H). ^{13}C NMR δ 140.89, 138.14, 132.82, 127.66, 126.96, 125.62, 67.53, 56.74, 39.38, 37.53, 31.56, 29.23, 27.02, 26.65, 22.05, 21.13.

(4aβ,10β)-7-Bromo-9,10-epoxy-9-methyl-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (7a-Br), a solid (0.450 g, 62% yield), m.p. 53-56°C: ^{1}H NMR δ 7.61 (d, 1H, *J*=2.1 Hz), 7.40 (dd, 1H, *J*=8.3 and 2.1 Hz), 7.12 (d, 1H, *J*=8.5 Hz), 3.22 (s, 1H), 2.32-2.51 (m, 2H), 2.01-2.10 (m, 1H), 1.74 (s, 3H), 1.85-1.97 (m, 2H), 1.15-1.68 (m, 5H). ^{13}C NMR δ 140.10, 138.40, 131.39, 130.70, 126.61, 120.25, 67.36, 56.28, 39.07, 37.31, 31.43, 29.18, 26.94, 26.53, 20.94.

Acid-Catalyzed Methanolysis of Epoxides 6-H,Br,Me, 7a,b-H,Br,Me and 4-Me. The following procedure is typcal. A solution of epoxide **7b-Me** (0.150 g, 0.707 mmol) in a 0.001 N (0.2 N in the case of **6** and **4**) solution of H_2SO_4 in anhydrous MeOH (15 ml) was stirred at r.t. for 1 min. Dilution with saturated aqueous $NaHCO_3$ solution, extraction with ether and evaporation of the washed (brine) ether extracts, afforded a liquid residue (0.160 g) consisting of a mixture of HE **26-Me** and **27-Me** (^{1}H NMR and HPLC) (Table 1) which was subjected to preparative TLC (hexane/AcOEt 9:1). Extraction of the two most intense bands (the faster moving band contained **26-Me**) afforded pure **26-Me** (0.105 g) and **27-Me** (0.030 g).

(4aβ,10α)-6,9-dimethyl-*c*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (26-Me), a solid, m.p. 42-44°C (from hexane): IR 3565 cm^{-1} (OH···O); ^{1}H NMR δ 7.30 (d, 1H, *J*=8.0

Hz), 7.12 (s, 1H); 7.00 (d, 1H, *J*=7.8 Hz), 3.26 (t, 1H, *J*=10.7), 3.06 (s, 3H), 2.36-2.54 (m, 2H), 2.27 (s, 3H), 2.09-2.22 (m, 1H), 1.72-1.83 (m, 2H), 1.57-1.71 (m, 1H), 1.53 (s, 3H), 0.92-1.42 (m, 4H). ^{13}C NMR δ 141.11, 138.28, 133.61, 128.93, 127.17, 126.83, 79.21, 76.41, 51.98, 42.98, 42.88, 31.27, 29.88, 27.17, 26.25, 23.61, 21.99.

(4aβ,10α)-6,9-dimethyl-*t*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (27-Me), a solid, m.p. 76-80°C (from hexane): IR 3619 (shoulder, free OH) and 3591 cm^{-1} (OH···O); ^{1}H NMR δ 7.33 (d, 1H, *J*=7.8 Hz), 7.06-7.18 (m, 2H), 3.99 (d, 1H, *J*=11.0 Hz), 3.04 (s, 3H), 2.34 (s, 3H), 2.18-2.64 (m, 3H), 1.77-2.08 (m, 4H), 1.44 (s, 3H), 1.12-1.75 (m, 3H). ^{13}C NMR δ 140.48, 137.54, 136.52, 128.88, 128.69, 126.32, 82.09, 71.64, 50.56, 44.11, 43.68, 31.30, 29.43, 27.14, 26.38, 26.19, 23.50, 21.95.

The crude product (0.120 g) from epoxide **7b-Br** was subjected to preparative TLC (hexane/AcOEt/MeOH 6:4:0.2). Extraction of the two most intense bands afforded HEs **26-Br** (0.048 g) and **27-Br** (0.052 g).

(4aβ,10α)-7-bromo-9-methyl-*c*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (26-Br), a solid, m.p. 151-154°C (from hexane): IR 3564 cm^{-1} (OH···O); ^{1}H NMR δ 7.59 (d, 1H, *J*=2.1Hz), 7.40 (dd, 1H, *J*=8.5 and 2.1 Hz), 7.24 (d, 1H, *J*=8.5 Hz). 3.34 (t , 1H, *J*=10.5 Hz); 3.16 (s, 3H), 2.13-2.52 (m, 4H), 1.77-2.01 (m, 1H), 1.60 (s, 3H), 1.52-1.78 (m, 1H), 0.94-1.50 (m, 4H). ^{13}C NMR δ 140.28, 139.27, 131.66, 131.69, 128.14, 120.33, 78.98, 76.41, 52.18, 42.85, 42.55, 31.20, 29.82, 27.02, 26.13, 23.64.

(4aβ,10α)-7-bromo-9-methyl-*t*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (27-Br), a solid, m.p. 118-121°C: IR 3619 (shoulder, free OH) and 3591 cm^{-1} (OH···O); ^{1}H NMR δ 7.56 (d, 1H, *J*=2.2 Hz), 7.34 (dd, 1H, *J*=8.4 and 2.1 Hz); 7.15 (d, 1H, *J*=8.4 Hz), 3.98 (dd, 1H, *J*=11.0 and 2.2 Hz), 3.05 (s, 3H), 2.20-2.52 (m, 3H), 2.03 (d, 1H, *J*=2.3 Hz), 1.54-1.74 (m, 1H), 1.42 (s, 3H), 1.07-1.53 (m, 3H). ^{13}C NMR δ 142.21, 139.62, 131.64, 130.17, 127.82, 121.13, 81.82, 71.34, 50.90, 43.98, 43.45, 31.27, 29.79, 27.02, 26.40, 26.10.

The crude product (0.160 g) from epoxide **7b-H** was subjected to preparative TLC (hexane/AcOEt 9:1). Extraction of the two most intense bands afforded HEs **26-H** (0.089 g) and **27-H** (0.028 g).

(4aβ,10α)-9-methyl-*c*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (26-H), a solid m.p. 47-51°C (from hexane): IR 3564 cm^{-1} (OH···O); ^{1}H NMR δ 7.43-7.54 (m, 1H), 7.20-7.42 (m, 3H), 3.34 (t, 1H, *J*=10.7), 3.14 (s, 3H), 2.45-2.62 (m, 2H), 2.20-2.42 (m, 2H), 1.78-2.02 (m, 2H), 1.62 (s, 3H), 1.02-1.58 (m, 4H). ^{13}C NMR δ 141.26, 136.62, 128.91, 128.64, 126.34, 126.14, 79.19, 76.57, 52.12, 43.00, 42.88, 31.21, 29.89, 27.14, 26.22, 23.78.

(4aβ,10α)-9-methyl-*t*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (27-H), a solid m.p. 110-115°C (from hexane): IR 3618 (shoulder, free OH) and 3591 cm^{-1} (OH···O); ^{1}H NMR δ 7.37-7.49 (m, 1H), 7.20-7.36 (m, 3H), 4.00 (d, 1H, *J*=11 Hz), 3.04 (s, 3H), 2.36-2.56 (m, 2H), 2.21-2.35 (m, 1H), 2.02-2.14 (m, 1H), 1.82-2.01 (m, 2H); 1.54-1.77 (m, 2H), 1.44 (s, 3H), 1.04-1.42 (m, 2H). ^{13}C NMR δ 140.58, 139.55, 128.01, 127.40, 127.08, 125.72, 82.17, 71.53, 50.67, 44.06, 43.76, 31.27, 29.41, 27.13, 26.40, 26.17.

The crude solid product (0.148 g) from epoxide **7a-Me** was recrystallized from hexane to give pure **(4aβ,10β)-6,9-dimethyl-*t*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (29-Me)** (0.095 g), a solid m.p. 87-90°C (from hexane): IR 3619 (free OH) and 3596 cm^{-1} (OH···Π); ^{1}H NMR δ 7.33 (d, 1H, *J*=7.9 Hz), 7.20 (s, 1H); 6.97-7.16 (m, 2H), 3.60 (s, 1H), 3.11 (s, 3H), 2.43-2.68 (m, 2H), 2.32 (s, 3H), 2.00-2.16 (m, 1H), 1.77-1.95 (m, 2H), 1.61 (s, 3H), 1.13-1.76 (m, 5H). ^{13}C NMR δ 140.82, 138.15, 132.75, 129.43, 127.50, 127.05, 78.12, 76.66, 50.76, 40.06, 38.17, 32.02, 30.71, 27.67, 26.93, 21.92, 21.06.

The crude solid product (0.080 g) from epoxide **7a-Br** was recrystallized from hexane to give pure **(4aβ,10β)-7-bromo-9-methyl-*t*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (29-Br)** (0.058 g), m.p. 125-130°C (from hexane): IR 3621 (free OH) and 3600 cm^{-1} (OH···Π); ^1H NMR δ 7.54 (d, 1H, *J*=2.1 Hz), 7.38 (dd, 1H, *J*=8.5 and 2.1 Hz), 7.25 (d, 1H, *J*=8.3 Hz), 3.63 (s, 1H), 3.15 (s, 3H), 2.36-2.63 (m, 2H), 1.78-2.13 (m, 2H), 1.61 (s, 3H), 1.55-1.77 (m, 1H), 1.11-1.54 (m, 5H). ^{13}C NMR δ 140.11, 138.81, 132.06, 131.53, 129.51, 120.12, 77.37, 76.51, 50.88, 39.87, 37.77, 31.80, 30.57, 27.52, 26.84, 20.94.

The crude product (0.110 g) from epoxide **7a-H** was recrystallized from hexane to give pure **(4aβ,10β)-9-methyl-*t*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (29-H)** (0.088), m.p. 83-85°C (from hexane): IR 3620 (free OH) and 3600 cm^{-1} (OH···Π); ^1H NMR δ 7.38-7.62 (m, 2H), 7.18-7.35 (m, 2H); 3.64 (s, 1H), 3.14 (s, 3H), 2.45-2.68 (m, 2H), 2.03-2.19 (m, 1H); 1.77-2.00 (m, 2H), 1.64 (s, 3H), 1.19-1.76 (m, 5H). ^{13}C NMR δ 140.97, 135.91, 129.40, 128.58, 126.79, 126.21, 77.88, 76.77, 50.81, 40.01, 38.14, 31.93, 30.68, 27.64, 26.91, 21.03.

The crude reaction product (0.130 g) from epoxide **6-Me** was subjected to semipreparative TLC (hexane/AcOEt 7:3). Extraction of the two most intense bands afforded pure HEs **19-Me** (0.034 g) and **20-Me** (0.089 g).

1,6-dimethyl-*c*-1-methoxy-1,2,3,4-tetrahydronaphthalen-*r*-2-ol (19-Me), a liquid: ^1H NMR δ 7.40 (d, 1H, *J*=8.0 Hz), 7.04 (d, 1H, *J*=8.2 Hz), 6.95 (s, 1H), 3.90-3.96 (m, 1H), 3.29 (s, 3H), 2.95-3.09 (m, 1H), 2.63-2.78 (m, 2H), 2.31 (s, 3H), 2.06-2.23 (m, 1H), 1.85-2.01 (m, 1H), 1.53 (s, 3H). ^{13}C NMR δ 137.65, 136.67, 135.74, 129.90, 128.27, 127.28, 76.71, 71.77, 50.79, 27.14, 26.50, 23.30.

1,6-dimethyl-*t*-1-methoxy-1,2,3,4-tetrahydronaphthalen-*r*-2-ol (20-Me), a soild m.p. 41-43°C (from hexane): ^1H NMR δ 7.22 (d, 1H, *J*=7.9 Hz), 6.97 (d, 1H, *J*=7.9 Hz), 6.83 (s, 3H), 4.17 (dd, 1H, *J*=11.8 and 3.9 Hz), 3.00 (s, 3H), 2.72-2.87 (m, 2H), 2.23 (s, 3H), 1.70-2.14 (m, 3H), 1.33 (s, 3H). ^{13}C NMR δ 137.53, 137.16, 136.53, 129.74, 127.87, 127.22, 81.33, 68.75, 50.65, 28.56, 28.14, 25.05, 21.65.

The crude reaction product (0.150 g) from epoxide **6-H** was subjected to semipreparative TLC (hexane/AcOEt 7:3). Extraction of the two most intense bands afforded pure HEs **19-H** (0.019 g) and **20-H** (0.121 g).

1 methyl-*c*-1-methoxy-1,2,3,4-tetrahydronaphthalen-*r*-2-ol (19-H), a solid m.p. 57-59°C (from hexane): ^1H NMR δ 7.44-7.52 (m, 1H), 7.03-7.28 (m, 3H), 3.92-4.01 (m, 1H), 3.30 (s, 1H), 2.97-3.18 (m, 1H), 2.61-2.82 (m, 2H), 1.83-2.25 (m, 2H), 1.53 (s, 3H). ^{13}C NMR δ 138.94, 136.74, 129.37, 128.27, 128.02, 126.45, 77.03, 71.32, 50.82, 27.02, 26.33, 23.58.

1-methyl-*t*-1-methoxy-1,2,3,4-tetrahydronaphthalen-*r*-2-ol (20-H), a liquid: ^1H NMR δ 7.34 (d, 1H, *J*=7.8 Hz), 7.00-7.20 (m, 3H), 4.20 (dd, 1H, *J*=11.8 and 3.9 Hz), 3.02 (s, 3H), 2.80-2.92 (m, 2H), 2.24-2.38 (m, 1H), 2.02-2.17 (m, 1H), 1.88 (dt, 1H, *J*=11.5 and 7.0 Hz), 1.36 (s, 3H). ^{13}C NMR δ 139.60, 137.24, 129.25, 127.90, 127.24, 126.94, 81.44, 68.60, 50.78, 28.66, 28.09, 25.09.

The crude reaction product (0.120 g) from epoxide **4-Me** was subjected to semipreparative TLC (hexane/AcOEt 7:3). Extraction of the two most intense bands afforded HEs **24-Me** (0.018 g) and **25-Me** (0.094 g).

6-methyl-*c*-1-methoxy-1,2,3,4-tetrahydronaphthalen-*r*-2-ol (24-Me), a liquid: ^1H NMR δ 7.16 (d, 1H, *J*=7.8 Hz), 6.88-6.97 (m, 2H), 4.12 (d, 1H, *J*=3.4 Hz), 3.92-4.06 (m, 1H), 3.43 (s, 3H), 2.54-3.00 (m, 2H), 2.24 (s, 3H), 1.72-2.16 (m, 2H). ^{13}C NMR δ 138.63, 137.16, 130.39, 129.52, 127.12, 80.19, 68.29, 57.66, 30.38, 27.23, 21.79.

6-methyl-*t*-1-methoxy-1,2,3,4-tetrahydronaphthalen-*r*-2-ol (25-Me), a liquid: ^1H NMR δ 7.21 (d, 1H, *J*=7.9 Hz), 6.96 (d, 1H, *J*=7.9 Hz), 6.87 (s, 1H), 4.22 (d, 1H, *J*=6.8 Hz), 3.93-4.07 (m, 1H), 3.42 (s, 3H), 2.76 (t, 2H, *J*=6.6 Hz), 2.36-2.57 (m, 1H); 2.24 (s, 3H), 1.67-2.17 (m, 2H). ^{13}C NMR δ 137.93, 137.16, 132.20, 129.74, 128.90, 127.62, 83.26, 69.76, 57.13, 28.52, 26.97, 21.69.

HEs 28-H,Br,Me. The following procedure is typical. A solution of HE **27-Me** (0.180 g, 0.692 mmol) in 20 ml of acetone (distilled over $KMnO_4$) was treated with 8N CrO_3 in a 1:1 H_2SO_4/H_2O solution (0.20 ml). After 30 min at r.t., the reaction mixture was diluted with water and extracted with Et_2O. Evaporation of the washed (saturated aqueous $NaHCO_3$ and water) ether extracts afforded a liquid residue (0.110 g) consisting of pure quite unstable ketone **30-Me**: ^{1}H NMR δ 7.02-7.37 (m, 3H), 2.80 (s, 3H), 2.40-2.63 (m, 3H), 2.30 (s, 3H), 1.61-1.93 (m, 3H), 1.55 (s, 3H), 1.16-1.49 (m, 4H). ^{13}C NMR δ 211.15, 141.17, 138.51, 136.49, 128.96, 128.06, 125.58, 98.25, 82.41, 53.04, 51.47, 42.70, 31.67, 29.53, 26.13, 25.98, 25.22. Ketone **30-Me** was immediately utilized in the next step without any further purification. A 10 M solution of BH_3·Me_2S (0.3 ml) was added dropwise at 0°C to a stirred solution of ketone **30-Me** (0.110 g, 0.43 mmol) in anhydrous Et_2O (10 ml) and stirring was prolonged for 3 h at r.t. After cooling at 0°C, methanol (4 ml) was added and the reaction mixture was stirred at r.t. overnight. Evaporation of the solvent afforded an oily product (0.090 g) consisting of a 44:56 mixture of HE **27-Me** and **28-Me** (^{1}H NMR) which was subjected to semipreparative TLC (hexane/AcOEt 8:2). Extraction of the two most intense bands (the faster moving band contained **28-Me**) afforded pure HEs **27-Me** (0.035 g) and **(4aβ,10β)-6,9-dimethyl-*c*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol** (**28-Me**) (0.058 g), as a liquid: IR 3570 cm^{-1} (OH···O); ^{1}H NMR δ 7.41 (d, 1H, *J*=8.0 Hz), 7.10 (s, 1H), 7.04 (d, 1H, *J*=7.8 Hz), 3.83 (s, 1H), 3.42 (s, 3H), 2.63-2.86 (m, 2H), 2.46-2.62 (m, 2H), 2.31 (m, 3H), 1.80-2.02 (m, 3H), 1.48 (s, 3H), 1.04-1.79 (m, 3H). ^{13}C NMR δ 139.36, 137.85, 137.42, 128.27, 127.72, 126.24, 78.34, 73.05, 50.32, 43.18, 37.36, 31.66, 31.55, 27.40, 27.19, 25.87, 21.97.

Ketone **30-Br** (0.152 g): ^{1}H NMR δ 7.55 (d, 1H, *J*=2.2 Hz), 7.36 (dd, 1H, *J*=8.4 and 2.0 Hz), 7.13 (d, 1H, *J*=8.4 Hz), 2.84 (s, 3H), 2.40-2.67 (m, 3H), 1.75-2.04 (m, 4H), 1.55 (s, 3H), 1.15-1.43 (m, 3H). ^{13}C NMR δ 209.98, 142.09, 140.36, 132.01, 131.04, 126.96, 82.30, 53.41, 51.37, 42.44, 31.71, 29.64, 26.05, 25.91, 25.14.

(4aβ,10β)-7-bromo-9-methyl-*c*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (**28-Br**) (0.110 g), a solid m.p. 69-73°C (from hexane): IR 3569 cm^{-1} (OH···O); ^{1}H NMR δ 7.57 (d, 1H, *J*=2.2 Hz), 7.24 (dd, 1H, *J*=8.4 and 2.2 Hz), 7.08 (d, 1H, *J*=8.4 Hz), 3.76 (s, 1H), 3.35 (s, 3H), 2.32-2.73 (m, 4H), 1.73-1.94 (m, 1H), 1.56-1.72 (m, 1H), 1.40 (s, 3H), 1.05-1.48 (m, 4H). ^{13}C NMR δ 143.25, 138.45, 131.59, 131.25, 127.64, 120.57, 78.12, 72.70, 50.32, 42.92, 37.56, 37.27, 27.29, 27.08, 25.89.

Ketone **30-H** (0.135 g), a liquid: ^{1}H NMR δ 7.46-7.57 (m, 1H), 7.30-7.40 (m, 3H), 2.90 (s, 3H), 2.51-2.79 (m, 3H), 1.84-2.06 (m, 3H), 1.66 (s, 3H), 1.20-1.54 (m, 4H). ^{13}C NMR δ 210.93, 141.38, 139.67, 128.87, 128.18, 125.02, 82.60, 53.23, 51.54, 42.88, 31.73, 29.70, 26.18, 26.00, 25.26.

(4aβ,10β)-9-methyl-*c*-9-methoxy-trans-1,2,3,4,4a,9,10,10a-octahydrophenanthren-*r*-10-ol (**28-H**) (0.058 g), a solid m.p. 132-140°C (from hexane): IR 3570 cm^{-1} (OH···O); ^{1}H NMR δ 7.48-7.57 (m, 1H), 7.17-7.34 (m, 3H), 3.85 (s, 1H), 3.44 (s, 3H), 2.67-2.90 (m, 2H), 2.48-2.58 (m, 1H), 1.82-2.00 (m, 2H), 1.68-1.80 (m,2H), 1.50 (s,3H), 1.23-1.67 (m,3H). ^{13}C NMR δ 140.79, 139.47, 128.30, 127.90, 126.82, 125.64, 78.33, 73.01, 50.33, 43.11, 37.46, 31.62, 31.53, 27.40, 27.18, 25.90.

HE 19-Br and 20-Br. The oxidation with Jones reagent of the 95:5 mixture of HEs **19-Br** and **20-Br** (0.200 g, 0.74 mmol) derived from the acid-catalyzed ring opening of epoxide **6-Br** (see above) afforded a liquid residue (0.18 g) consisting of pure, quite unstable ketone **23** which was utilized in the next step without any further purification: ^{1}H NMR δ 7.56 (d, 1H, *J*=2.1 Hz), 7.33 (dd, 1H, *J*=8.2 and 2.1 Hz), 7.02 (d, 1H, *J*=8.1 Hz), 2.95-3.09 (m, 2H), 3.00 (s, 3H), 2.69-2.84 (m, 1H), 2.40-2.59 (m, 1H), 1.48 (s, 3H). ^{13}C NMR δ 210.10, 141.60, 136.30, 131.71, 130.43, 130.22, 121.92, 81.53, 53.72, 37.90, 28.34, 27.29. Following standard procedures, the LAH reduction of **23** at 0°C afforded a 49:55 mixture of HEs **19-Br** and **20-Br** (0.16 g) which were separated by preparative TLC (petroleum ether/*i*-PrOH/AcOEt 6:3:1). Extraction of

the two most intense bands (the faster moving band contained **19-Br**) afforded pure **19-Br** (0.067 g) and **20-Br** (0.074 g).

7-Bromo-1-methyl-*c*-1-methoxy-1,2,3,4-tetrahydronaphthalen-*r*-2-ol (19-Br), a liquid: ^{1}H NMR δ 7.63 (d, 1H, *J*=2.1 Hz), 7.30 (dd, 1H, *J*=8.2 and 2.1 Hz), 6.97 (d, 1H, *J*=8.2 Hz), 3.99-4.08 (m, 1H), 3.35 (s, 3H), 2.92-3.09 (m, 1H), 2.58-2.72 (m, 2H), 1.99-2.22 (m, 1H), 1.78-1.98 (m, 1H), 1.47 (s, 3H). ^{13}C NMR δ 141.87, 135.38, 131.01, 130.95, 77.41, 69.92, 50.67, 26.39, 25.17, 23.99.

7-Bromo-1-methyl-*t*-1-methoxy-1,2,3,4-tetrahydronaphthalen-*r*-2-ol (20-Br), a solid m.p. 70-72°C (from hexane): ^{1}H NMR δ 7.46 (d, 1H, *J* =1.9 Hz), 7.20 (dd, 1H, *J*=8.2 and 2.0 Hz), 6.87 (d, 1H, *J*=8.2 Hz), 4.15 (dd, 1H, *J*=11.7 and 3.9 Hz), 3.01 (s, 3H), 2.62-2.79 (m, 3H), 1.69-2.08 (m, 2H), 1.32 (s, 3H). ^{13}C NMR δ 142.04, 136.10, 130.93, 129.91, 120.68, 81.08, 68.10, 50.82, 28.06, 27.88, 24.91.

Methanolysis of Epoxides 6-H,Br,Me with MeONa/MeOH. General procedure. A solution of the epoxide **6** (0.10 g) in 10% MeONa in anhydrous MeOH was refluxed for 24 h. After cooling, dilution with saturated aqueous NaCl, extraction with ether and evaporation of the ether extracts afforded a solid residue consisting of practically pure HE **20** (95-98%, ^{1}H NMR and GC).

Ketones 33-Br,Me, 34-Br,Me and 21-Br,Me. The following procedure is typical. A solution of epoxide **7b-Me** (0.050 g, 0.170 mmol) in anhydrous benzene (5 ml) was treated at r.t. with BF_3·Et_2O (0.025 ml, 0.2 mmol). The reaction mixture was stirred 3 min at the same temperature, then poured into saturated aqueous $NaHCO_3$. Evaporation of the washed (brine) organic solution afforded a liquid (0.042 g, 84 % yield) consisting of **(4aβ, 9β)-6,9-dimethyl-trans-1,2,3,4,4a,10a-hexahydro-10(9*H*)-phenanthrenone (33-Me)**, practically pure as a liquid: ^{1}H NMR δ 7.06-7.13 (m, 3H), 3.49 (q, 1H, *J*=13.5 and 6.7 Hz), 2.37 (s, 3H), 1.64-2.03 (m, 6H), 1.50 (d, 3H, *J*=6.8 Hz), 1.28-1.42 (m, 4H). ^{13}C NMR δ 214.17, 141.29, 136.77, 134.49, 127.94, 125.28, 124.73, 50.81, 46.72, 40.90, 29.53, 28.72, 26.43, 21.97, 12.59.

The same procedure on epoxide **7a-Me** afforded pure **(4aβ,9α)-6,9-dimethyl-trans-1,2,3,4,4a,10a-hexahydro-10(9*H*)-phenanthrenone (34-Me)** (0.038g, yield 76%), as a liquid: ^{1}H NMR δ 6.92-7.07 (m, 3H), 3.50 (q, 1H, *J*=14.9 and 7.6 Hz), 2.36 (s, 3H), 2.09-1.62 (m, 7H), 1.37 (d, 3H, *J*=7.6 Hz), 1.18-1.57 (m, 3H). ^{13}C NMR δ 214.58, 144.58, 139.70, 133.55, 128.69, 127.00, 124.72, 52.13, 47.99, 42.76, 30.96, 29.18, 27.02, 26.21, 21.99, 20.15.

The same procedure on epoxide **7b-Br** afforded pure **(4aβ, 9β)-7-bromo-9-methyl-trans-1,2,3,4,4a,10a-hexahydro-10(9*H*)-phenanthrenone (33-Br)** (0.045 g), as a solid, m.p. 90-93°C (from hexane): ^{1}H NMR δ 7.25-7.39 (m, 2H), 7.06 (d, 1H, *J*=8.2 Hz), 3.44 (q, 1H, *J*=6.7 Hz), 2.48-2.67 (m, 1H), 2.30-2.42 (m, 1H), 2.13-2.25 (m, 1H), 1.80-1.98 (m, 2H), 1.57-1.72 (m, 1H), 1.15-1.50 (m, 4H), 1.42 (d, 3H, *J*=6.7 Hz). ^{13}C NMR δ 212.83, 140.43, 139.78, 130.20, 128.42, 125.63, 121.37, 50.44, 46.86, 40.49, 29.40, 28.59, 26.26, 26.30, 12.21.

The same procedure on epoxide **7a-Br** afforded pure **(4aβ,9α)-7-Bromo-9-methyl-trans-1,2,3,4,4a,10a-hexahydro-10(9*H*)-phenanthrenone (34-Br)** (0.048 g), as a solid m.p. 41-43°C (from hexane): ^{1}H NMR δ 7.17-7.42 (m, 3H), 3.50 (q, 1H, *J*=7.6 Hz), 2.46-2.77 (m, 2H), 2.20-2.37 (m, 1H), 1.40 (d, 3H, *J*=7.7 Hz), 1.20-2.02 (m, 7H). ^{13}C NMR δ 213.19, 142.33, 138.96, 131.58, 130.34, 126.94, 121.29, 51.92, 48.07, 39.69, 30.95, 27.13, 26.06, 25.60, 20.12.

The same procedure on epoxide **6-Me** afforded a liquid residue (0.092 g) consisting of ketone **21-Me** (85%) and unidentified by products (^{1}H NMR) which was subjected to semipreparative TLC (hexane/AcOEt 7:3). Extraction of the most intense band afforded pure **1,6-dimethyl-3,4-dihydro-2-(1*H*)-naphthalenone (21-Me)**, as a liquid (0.078 g, 78% yield): ^{1}H NMR δ 7.00-7.12 (m, 3H), 3.49 (q, 1H, *J*=7.0 Hz), 2.98-3.18 (m, 2H), 2.45-2.71 (m, 2H), 2.34 (s, 3H), 1.46 (d, 3H, *J*=7.0 Hz).

The crude reaction product (0.140 g) from epoxide **6-Br**, was subjected to semipreparative TLC (hexane/AcOEt 7:3). Extraction of the most intense band afforded pure **7-bromo-1-methyl-3,4-dihydro-**

2-(1*H*)-naphthalenone (21-Br), as a liquid: ^{1}H NMR δ 7.29-7.38 (m, 2H), 7.09 (d, 1H, *J*=8.5 Hz), 3.50 (q, 1H, *J*=7.0 Hz), 2.36-2.71 (m, 2H), 1.46 (d, 3H, *J*=7.2 Hz).

Reaction of Epoxides 6-Me and 6-Br with TsOH in CH_2Cl_2-MeOH. The following procedure is typcal. A solution of epoxide **6-Me** (0.15 g, 0.86 mmol) in a 1.6 x 10^{-2} M TsOH solution in CH_2Cl_2 containing MeOH (0.18 mmol/ml) (10 ml) was stirred for 10 min at r.t.. Evaporation of the washed (saturated aqueous $NaHCO_3$ and water) ether extracts afforded a liquid residue (0.115 g) (Table 2) which was subjected to semipreparative TLC (hexane/AcOEt 7:3). Extraction of the two most intense bands (the slower moving band contained **21-Me**) afforded ketone **21-Me** (0.070 g) and **6-methyl-1-methylen-1,2,3,4-tetrahydronaphthalen-2-ol (22-Me)** (0.015 g), as a liquid: ^{1}H NMR δ 7.01-7.13 (m, 3H), 5.55 (s, 1H), 5.23 (s, 1H), 4.47-4.53 (m, 1H), 2.98-3.12 (m, 2H), 2.50-2.73 (m, 2H), 2.33 (s, 3H).

The crude reaction product (0.135 g) from epoxide **6-Br** (Table 2) was subjected to semipreparative TLC (toluene/Et_2O 8:2). Extraction of the two most intense bands (the slower moving band contained **21-Br**) afforded ketone **21-Br** (0.060 g) and **7-bromo-1-methylen-1,2,3,4-tetrahydronaphthalen-2-ol (22-Br)**, as a liquid: ^{1}H NMR δ 7.75 (d, 1H, *J*=2.0 Hz), 7.31 (dd, 1H, *J*=8.2 and 2.0 Hz), 7.01 (d, 1H, *J*=8.2 Hz), 5.60 (d, 1H, *J*=1.1 Hz), 5.34 (d, 1H, *J*=1.1 Hz), 4.51 (dd, 1H, *J*=6.7 and 4.0 Hz), 2.91-3.10 (m, 1H), 2.70-2.87 (m, 1H), 1.95-2.08 (m, 2H).

Radiolytic Experiments

General. The approach adopted in the radiolytic experiments was based upon the generation of stationary concentrations of gaseous acid, D_3^+, obtained in the gas phase by γ-radiolysis (^{60}Co source, T= 37.5°C) of the corresponding neutral precursor, D_2 (100-760 Torr), and its attack on the *n*-centre (the oxygen atom) of the selected epoxide. The excess internal energy of the protonated intermediates was dissipated by unreactive impacts with the bulk gas molecules. Furthermore, the charged intermediates were rapidly trapped by suitable nucleophile, MeOH, and converted into neutral end products. The conditions typical of the present experiments, in particular the low concentrations of epoxides **4-7** (<0.6 mol%) diluted with a large excess of the bulk gas, exclude direct radiolysis of the epoxidic substrate as a significant route to the products of Tables 3-6. The presence of an efficient thermal radical scavenger, O_2, in about tenfold excess over the substrate inhibited possible free-radical pathways to products in favor of the corresponding ionic ones, whose large predominance is demonstrated by the marked effect of an ion trap such as NMe_3 on the overall yields of products (Tables 3-6).

Materials. Deuterium, oxygen and NMe_3 were supplied as high purity gases by Matheson and used without further purification. The epoxides **4**, **6** and **7** were repeatedly purified by preparative GC with a 5 m x 4 mm (i.d.) stainless steel column packed with 5% FFAP on 80-100 mesh Chromosorb G-AW-DMCS at 120°C. Their final purity exceeded 99.93%.

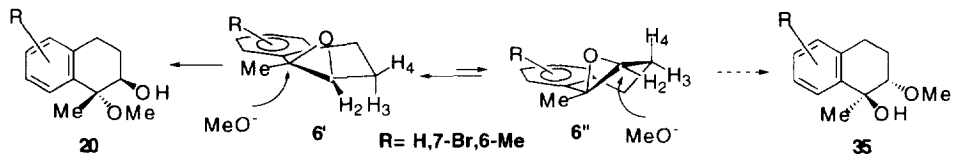
Procedure. A greaseless vacuum line was used to prepare the gaseous mixtures. The reagents and the additives were enclosed in evacuated and carefully outgassed 250 ml Pyrex bulbs equipped with a fragile tip. The bulbs were filled with the appropriate amounts of the bulk gas (D_2), cooled to the liquid nitrogen temperature and sealed off. The irradiation was carried out at 37.5°C in a 220 Gammacell from Nuclear Canada Ltd. at a dose of 1.5x10^4 Gy and at a rate of 10^4 Gy h^{-1}, as determined by a neopentane dosimeter. The analysis of the irradiated mixtures from epoxides **4** was performed with a Hewlett-Packard 5890/II gas chromatograph equipped with a flame ionization detector. The following columns were employed: (*i*) a 30 m x 0.32 mm (i.d.) Supelcowax 10 fused silica capillary column operating at temperatures ranging from 80 to 180°C; (*ii*) a 25 m x 0.2 mm (i.d.) Carbowax 20 M ULTRA performance capillary column operating at 160°C.

The analysis of the irradiated mixtures from epoxides **6** and **7** were performed with a Hewlett-Packard 1090/II high performance liquid chromatograph equipped with a diode array detector, auto-injector and HPLC chemstation Pascal series. All analyses were run at r.t. under isocratic conditions (MeOH:water 75:25) with a 25 cm x 4 mm (i.d.) stainless stell column Spherisorb ODS-2.5 μm packing. The radiolytic products were identified by coincidence of their retention volumes with those of authentic reference compounds and their identity confirmed by GC/MS with a Hewlett-Packard 5971A mass-spectrometer and by a Hewlett-Packard 59980 Particle Beam LC-MS interface connect with a Hewlett-Packard 5971A mass spectrometer. The yields of the products were deduced from the areas of the corresponding elution peaks, using the internal standard calibration method. The results given in Tables 3-6 are the average of at least three measurements taken on at least two different runs for each point.

References and Notes

1. Harvey, R.G. *Polycyclic Aromatic Hydrocarbons: Chemistry and Carcinogenicity*, Cambridge University Press: Cambridge, England, 1991.
2. Lehr, R.E.; Kumar, S.; Levin, W.; Wood, A,W.; Chang, R.L.; Conney, A.-H.; Yagi, H.; Sayer, J.M.; Jerina, D.M. in *Polycyclic Hydrocarbons and Carcinogenesis*, Harvey,R.G., Ed., ACS Symposium Series n. 283, American Chemical Society: Washington, D.C., 1985, p 63-84 and references therein.
3. Harvey, R.G. *Acc.Chem.Res.* **1981**, *14*, 218-226.
4. a) Crotti, P.; Dell'Omodarme, G.; Ferretti, M.; Macchia, F. *J.Am.Chem.Soc.* **1987**, *109*, 1463-1469. b) Battistini, C.; Crotti, P.; Damiani, D.; Macchia, F. *J.Org.Chem.* **1979**, *44*, 1643-1469. c) Battistini, C.; Balsamo, A.; Berti, G.; Crotti, P.; Macchia, B.; Macchia, F. *J.Chem.Soc.Chem.Commun.* **1974**, 712-713.
5. a) Chini, M.; Crotti, P.; Minutolo, F.; Martinelli, A.; Micali, E. *Gazz.Chim.Ital.* **1994**, *124*, 27-33. b) Gillilan, R.E.; Pohl, T.M.; Whalen, D.L. *J.Am.Chem.Soc.* **1982**, *104*, 4481-4482.
6. a) Sayer, J.M.; Yagi, H.; Silverton, J.V.; Friedman, S.L.; Whalen, D.L.; Jerina, D.M. *J.Am.Chem.Soc.* **1982**, *104*, 1972-1978. b) Chini, M.; Crotti, P.; Ferretti, M.; Macchia,F. *Tetrahedron* **1988**, *44*, 2001-2014.
7. a) Chini, M.; Crotti, P.; Minutolo, F.; Dezi, A.; Lombardozzi, A.; Pizzabiocca, A.; Renzi, G. *Tetrahedron* **1993**, *49*, 5845-5858. b) Cecchi, P.; Chini, M.; Crotti, P.; Pizzabiocca, A.; Renzi,G.; Speranza,M. *Tetrahedron* **1991**, *47*, 4683-4692. c) Crotti, P.; Macchia, F.; Pizzabiocca, A.; Renzi, G.; Speranza, M. *Tetrahedron Lett.* **1987**, *28*, 3393-3396.
8. Epoxides **6-H** and **7a,b-H**, ketones **21-H**, **33-H** and **34-H** and unsaturated alcohol **22-H** have previously been prepared: Chini, M.; Crotti, P.; Macchia, F. *Gazz.Chim.Ital.* **1988**, *118*, 827-836.
9. In the presently studied tertiary epoxides **6** and **7a,b**, we chose the 6-Me substitution as the electron-donating group instead of the 6-OMe one utilized in the secondary epoxides **4**[5a] and **5a,b**[6b,7a] because of the reasonable suspicion that the corresponding epoxides **6-OMe** and **7a,b-OMe** could be too reactive and difficult to handle.
10. Bien, S.; Boazi, M. *J.Chem.Soc.* **1959**, 1727-1730.
11. Chini, M.; Crotti, P.; Macchia, F.; Domiano, P. *Gazz.Chim.Ital.* **1988**, *118*, 369-374.
12. Chini, M.; Crotti, P. *Gazz.Chim.Ital.* **1990**, *120*, 733-739 and references therein.
13. Fieser, L.F.; Selignan, A.M. *J.Am.Chem.Soc.* **1938**, *60*, 170-176.

14. When the reduction of ketones **30-H,Br,Me** was carried out with $LiAlH_4$, the corresponding HE **27-H,Br,Me** (exclusive β-attack of the hydride, Scheme 4) was the only reaction product, in each case. As the β attack:α attack selectivity was 9:1 in the $LiAlH_4$ reduction of the corresponding ketones without the benzylic Me group,[7a] the present results indicate that the pseudoaxial 9-methyl group definitely hinders the α face in ketones **30** towards the rather voluminous AlH_4^- reducing species. In this case, only the smaller BH_3 is able to give consistent amount of α-attack.
15. For example, in the case of the epoxide **7b-Me** a 5:95 mixture of HE cis **26-Me** and trans **27-Me** was obtained with the 0.2 N H_2SO_4-MeOH solution, quenching the reaction after 5 sec. The same reaction repeated with a 0.001 N H_2SO_4-MeOH solution gave a 77:23 cis **26-Me**:trans **27-Me** ratio (5 sec) which turned out to be stable even after a rather prolonged reaction time (1 min, Table 1).
16. The somewhat surprising exclusive formation of HE **20** in the alkaline methanolysis of **6** (no trace of the regioisomeric HE **35** being found), by attack of the nucleophile (MeO^-) on the sterically hindered



tertiary oxirane carbon, appears to be the consequence of the preferential reactivity of **6** through its more stable conformation **6'**. In **6'** no eclipsed interactions are present between hydrogens H_2, H_3 and H_4, as in the alternative conformer **6"**.[5] A conformational study on epoxide **6-H**, through molecular mechanics and quantum mechanical ab initio calculations, confirmed conformer **6'** to be favored over **6"** by 2.25 Kcal/mol.[5]

17. Brown,H.C.; Okamoto,Y. *J.Am.Chem.Soc.* **1958**, *80*, 4979-4987.
18. Equation 1 (Table 7) can be obtained[4a,4c,6b] by term by term subtraction of the Hammett equation relative to the formation of the anti adduct (A) from the one relative to the syn adduct (S), under the very likely assumption that the two parallel reactions follow the same kinetic equation and therefore the rate ratios k_{syn}/k_{anti} can be equated to the concentration ratios [S]/[A]. This type of correlation affords the difference $\rho_{syn}-\rho_{anti}$.
19. Paquette, L.A.; Henzel, K.A. *J.Am.Chem.Soc.* **1975**, *97*, 4649-4658.
20. a) Ausloos, P.; Lias, S.G.; Gorden Jr., R. *J.Chem.Phys.* **1963**, *39*, 3341-3348. b) Weiss, J.; Bernstein, W. *Radiat.Res.* **1957**, *6*, 603-610.

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