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SUBSTITUENT EFFECTS ON THE REGIO- AND STEREOSELECTIVITY OF GAS-PHASE ACID-INDUCED RING OPENING IN 1-ARYLCYCLOHEXENE OXIDES

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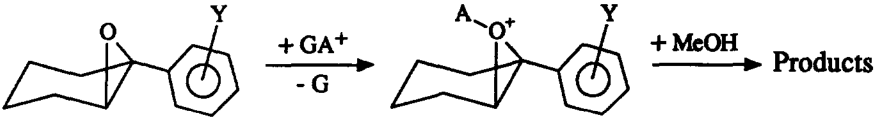
ABSTRACT: *Comparative analysis of the ratio of the isomeric monomethyl ethers of 1-arylcyclohexane-1,2-diols formed in the gas-phase and solvolytic acid-induced methanolysis of several 1-arylcyclohexene oxides indicates the intrinsic electronic factors determining the regio- and stereochemical course of the nucleophilic attack, related to the partial degree of carbocationic character at the reaction centre in the substitution transition state.*

Arene oxides have been demonstrated to be the intermediates in the carcinogenesis of the polycyclic aromatic hydrocarbons.[1] The knowledge of the mechanism and stereochemistry of the oxirane ring opening processes of such arene oxides and of their simpler models, the 2-aryl-substituted oxiranes,[2] can be of utmost importance for understanding the more complex transformations which occur under biological conditions.

Previous work carried out in our laboratories has shown the peculiar stereochemistry of acid-induced ring opening of 1-phenyl-oxirane favoring *syn* addition of a nucleophile under both gaseous and condensed phase,[3] in contrast with the normal *anti* addition observed in simple aliphatic and cycloaliphatic oxiranes.[4] A comparison between the solution data[3a,b] and the pertinent gas-phase results[3c] allowed to separate the intrinsic stereoelectronic factors governing *syn* addition in acid-catalyzed ring opening of 1-phenylcyclohexene oxide **1** from solvent and counter-ion effects, which in some instances may profoundly alter the steric course of the reaction. On these grounds, it was proposed that *syn* opening in **1** is determined by the intrinsic ability of the phenyl group in stabilizing a partial positive charge development at C_α in the transition state, promoting an entropically favored frontside rearrangement of the intimate adduct between O-protonated **1** and the nucleophile (e.g. MeOH).

Experimental support to such hypothesis is sought in this paper, which deals with the stereo- and regiochemistry of gas-phase acid-induced ring opening of 1-arylcyclohexene oxides **2** and **3**, containing electron-withdrawing groups at specific positions in the aryl ring (eq. *1*).



(I)

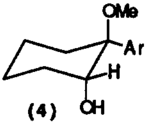
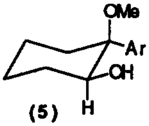
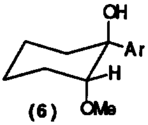
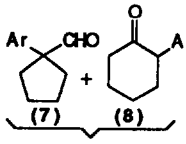
(1)

Y = H (**1**); *m*-Cl (**2**); *p*-NO_2 (**3**)

The oxonium ion derivatives (I) of the 1-arylcyclohexene oxides **2** and **3** were generated in the gas phase by attack of gaseous acid [$GA^+ = D_3^+$ or $C_nH_5^+$ (n = 1, 2)], obtained in known yields by γ-radiolysis (^{60}Co source, T = 37 °C) of the corresponding neutral precursor, *i.e.* D_2 or CH_4, respectively. Oxonium ions (I) were allowed to react with a nucleophile, such as MeOH, present in the mixture in known concentrations (0.2 - 1.5 mol %).

The relevant results are illustrated in Table I, together with earlier related data from epoxide **1** for comparison.[3c] The ionic nature of pathways *1* is demostrated by the sharp decrease of the overall product yields (over 75%) observed by addition of limited concentrations of a powerful ion interceptor, such as NMe_3 (0.4 mol%), to the gaseous mixture.

TABLE I DISTRIBUTION FROM THE GAS-PHASE RING OPENING IN 1-ARYLCYCLOHEXENE OXIDES.

SYSTEM COMPOSITION (Torr)[a]			PRODUCT DISTRIBUTION[b]								
SUBSTRATE	BULK GAS	MeOH	 (4)		 (5)		 (6)		 (7) + (8)		TOTAL ABS. YIELD[c] %
			G	%rel.	G	%rel.	G	%rel.	G	%rel.	
1 (0.55)	D_2(760)	(1.54)[d]	traces[e]	-	0.14	28	n.d.[f]	-	0.36	72	16
1 (0.64)	D_2(760)	(1.97)	0.17	6	2.62	94	n.d.	-	traces	-	93
1 (0.52)	D_2(100)	(1.37)	0.05	2	2.56	85	n.d.	-	0.40	13	100
1 (0.46)	CH_4(760)	(1.58)[d]	traces	-	traces	-	n.d.	-	0.12	100	4
1 (0.42)	CH_4(760)	(1.49)	0.01	3	0.30	88	n.d.	-	0.03	9	12
1 (0.49)	CH_4(100)	(1.48)	0.15	5	2.44	87	n.d.	-	0.21	8	100
2 (0.56)	D_2(760)	(1.76)[d]	traces	-	traces	-	n.d.	-	traces	-	-
2 (0.50)	D_2(760)	(1.50)	0.15	13	0.86	53	n.d.	-	0.60	37	54
2 (0.52)	D_2(100)	(1.56)	0.28	9	1.75	59	n.d.	-	0.96	32	100
2 (0.48)	CH_4(760)	(1.25)[d]	traces	-	traces	-	n.d.	-	traces	-	-
2 (0.51)	CH_4(760)	(1.51)	0.06	11	0.36	63	n.d.	-	0.15	26	20
2 (0.54)	CH_4(100)	(1.55)	0.49	17	1.12	40	n.d.	-	1.19	43	100
3 (0.42)	D_2(760)	(1.53)[d]	0.02	100	n.d.	-	traces	-	traces	-	1
3 (0.46)	D_2(760)	(1.61)	0.10	62	n.d.	-	0.02	13	0.04	25	5
3 (0.42)	D_2(100)	(1.50)	1.74	60	n.d.	-	0.57	19	0.61	21	97
3 (0.49)	CH_4(760)	(1.53)[d]	0.01	100	n.d.	-	traces	-	traces	-	1
3 (0.49)	CH_4(760)	(1.58)	0.05	50	n.d.	-	0.01	10	0.04	40	4
3 (0.45)	CH_4(100)	(1.51)	0.29	49	n.d.	-	0.07	12	0.23	39	21

Ar = C_6H_5, *m*-Cl-C_6H_4, *p*-NO_2-C_6H_4.

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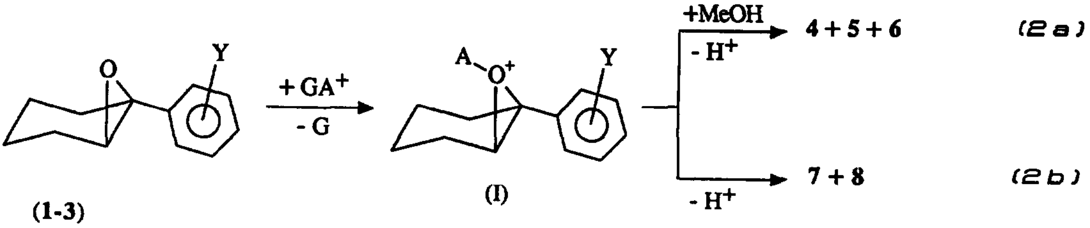
a) O_2: 4 Torr, Radiation dose $2{\cdot}10^4$ Gy (dose rate: $1{\cdot}10^4$ Gy h^{-1}). b) G values expressed as the number of molecules produced per 100 eV absorbed energy. The data reported have a 10% range of uncertainty. c) Total absolute yields estimated from the ratio of the overall G (M) values of products to the G (D_3^+) and G ($C_nH_5^+$) formation values (see refs. 4b, c). d) 3 Torr of NMe_3 added to gaseous mixture. e) $1{\cdot}10^{-4} <$ G (M) $< 1{\cdot}10^{-3}$. f) n.d. : below detection limit [G (M) $\leq 1{\cdot}10^{-4}$].

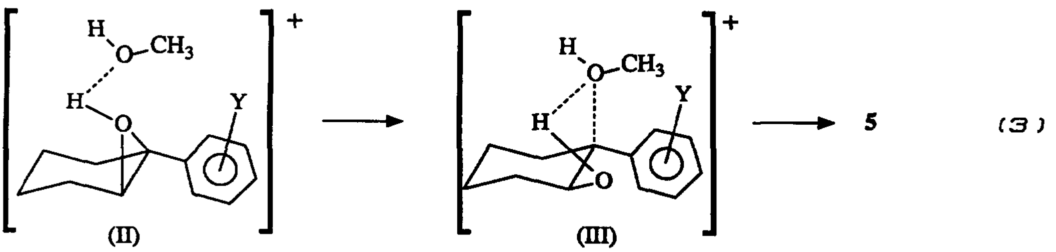
Analysis of Table I reveals formation of addition products 4-6, together with variable amounts of the carbonilic compounds 7 and 8. In general the combined relative yield of 7 and 8 is rather unaffected by an over seven-fold decrease of the system pressure (from 760 to 100 Torr). In addition, they do not appear to change much for the same substrate, in passing from $GA^+ = D_3^+$ to $GA^+ = C_nH_5^+$ (n = 1, 2). These observations point to the occurrence of two independent competitive channels (eqs.2a, and 2b), whose relative extent is rather insensitive to the energy excess of the common intermediate (I), but rather depending essentially on the MeOH concentration, *i.e.* the ion (I) lifetime.

Concerning the substitution product pattern of Table I, *i.e.* 4-6, a significant variation of the stereo- and regiochemistry of the acid-induced nucleophilic displacement processes by MeOH as a function of the phenyl-ring substituent is observed. In fact, irrespective of the experimental conditions adopted, by increasing the electron-withdrawing properties of the ring substituent [from H (1) to *m*-Cl (2) and to *p*-NO_2 (3)], the stereoselectivity of the MeOH nucleophilic attack changes dramatically from predominant frontside *syn* [91-100% of 5 (Y = H) from 1 and 70-87% of 5 (Y = *m*-Cl) from 2] to exclusive backside *anti* attack [100% of 4 (Y = *p*-NO_2) from 3]. Besides, the regioselectivity of the MeOH attack on (I) is modified as well by the presence of the powerful electron-withdrawing NO_2 group at the *para* position of the phenyl ring. Indeed, while the displacement takes place exclusilvely at the C_α atom of (I) from 1 and 2, partial attack of the nucleophile occurs at the C_β centre of (I) from 3 as well (from 20% to 32%).

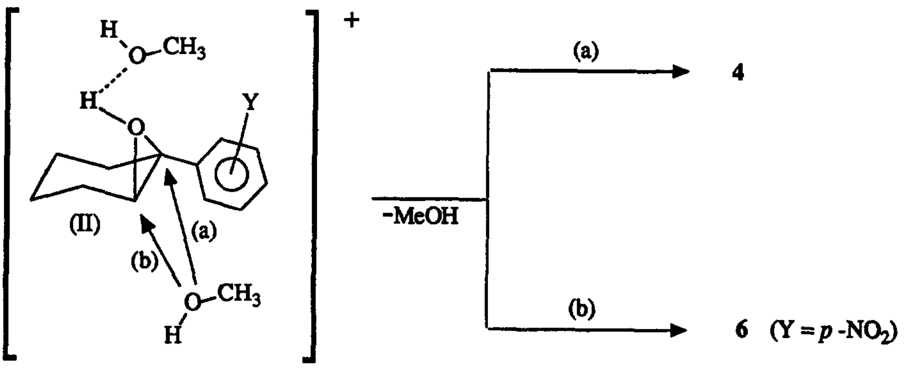
As pointed out in a previous paper,[3c] the pronounced stereoselectivity of eq. 2a excludes intervention of a planar carbocationic intermediate from unimolecular epoxy-ring opening within (I).



Rather, the predominant frontside nucleophilic *syn* addition in (I) from 1 was thought to be due to the development of a sufficient degree of positive charge at the C_α atom of (I), which promotes isomerization of its adduct with MeOH (II; Y = H) to the entropically-favored structure (III; Y = H), followed by a collapse to the syn adduct 5 (eq.3).



According to such hypothesis, the presence of an electron-withdrawing Y group on the phenyl ring of (II) is expected to reduce the efficiency of process (3), owing to its destabilizing effect in the development, in the transition state, of a partial positive charge at the C$_\alpha$ and, therefore, significant C$_\alpha$-O bond rupture in (II). Indeed, when a relatively slightly electron-withdrawing group is present on the aromatic ring of (II) (Y = *m*-Cl), the relative yield of the frontside *syn* adduct 5 decreases from 91-100% to 70-87%, the remainder being the backside *anti* adduct 4. In this case, in fact, the isomerization channel 3 is slowed down enough to become comparable to the collision frequency (ca. 10^8 - 10^7 s^{-1})[5] of the attack of external MeOH at the unshielded side of (II), leading to the backside substitution product 4 (eq. 4, route a).



(4)

In the case of 3 (Y = *p*-NO_2), the highly destabilizing effect of the *p*-NO_2 group toward partial positive charge development at C$_\alpha$ of (II) makes process 3 much slower than backside attack from an external MeOH to the point that the backside displacement derivatives 4 and 6 are exclusively formed. Here, recovery of minor amounts (20-32%) of 6 from the gas-phase experiments, points to a dramatic decrease of the ability of the aryl substituent (*p*-NO_2) in stabilizing partial positive charge development at adjacent benzylic C$_\alpha$ carbon. As a consequence, nucleophilic *anti* attack at the less sterically hindered C$_\beta$ carbon effectively becomes competitive (route a *vs* route b in eq. 4), yielding some amounts of adduct 6 (Y= *p*-NO_2).

The present gas-phase results find interesting analogies with those of analogous solvolytic experiments carried out in 0.2 N H_2SO_4-MeOH. In fact, under such conditions, the 4/5 yield ratio increases from 1.6 (Y = H)[6,7] to 11.3 (Y = *m*-Cl) and up to infinity, when Y = *p*-NO_2. The agreement is extended as well as regards to the regioselectivity of the MeOH attack on (II) in the case of 3, being 0.4% of 6 recovered together with the predominant isomer 4 (99.6%) from the relevant reaction mixture.

In conclusion, comparative analysis of the present gas-phase and solvolytic experiments further supports the intrinsic electronic nature of the directing properties of (II) toward nucleophilic attack by MeOH. The intrinsic factors determining the stereochemical course of the nucleophilic addition, related primarily to the stabilizing effect of the aryl moiety on the C$_\alpha$ centre of the substrate, are fully confirmed in the present study.

EXPERIMENTAL SECTION

Melting points were determined on a Kofler apparatus and are uncorrected. IR spectra for comparison between compounds were taken on paraffin oil mulls on a Perkin-Elmer Infrared Model 137. ^1H NMR spectra were determined on 10% $CDCl_3$ solutions with a Varian EM 360 spectrometer using Me_4Si as an internal standard. GLC analyses were run on a Hewlett-Packard 5730 gas chromatograph equipped with a flame ionization detector. The following columns were employed: (i) - an 8 ft x 0.25 in glass column packed with 3% OV-17 on 80-100 mesh Chromosorb W-HP, operated between 130 and 200 °C (8 °C min^{-1}); (ii) - an 8ft x 0.25 in glass column packed with 3% SE-30 on 80-100 mesh Chromosorb GAW-DMCS, operated at 130 °C. Preparative and semipreparative TLC were performed on 2 mm and 0.5 mm, respectively, layer silica gel plates containing a fluorescent indicator. All comparisons between compounds were made on the basis of IR and ^1H NMR spectra and GLC. Petroleum ether refers to the fraction boiling at 40-70 °C.

Materials

Deuterim, methane, oxygen, and trimethylamine were high-purity gases from Matheson Co., used without further purification. Methanol, used as reactant, was research-grade chemical from Fluka A. G. Compounds 2[8], 3[9], 7 (Y = *p*-NO_2)[10], and 8 (Y = *p*-NO_2)[10], were prepared as previously described. The racemic mixtures of 2 and 3 were used in all experiments, however for clarity only one enantiometer is depicted. No conformatinal implications is given to formulas. The samples used in the radiolytic experiments were assayed by GLC on the same columns subsequently employed for the analysis of the products, and, when required, purified by preparative GLC.

t-2-Methoxy-2-(*p*-nitrophenyl)-*r*-1-cyclohexanol (4, Y = *p*-NO_2)

A solution of epoxide 3 (0.40 g, 1.82 mmol) in a 0.2N H_2SO_4/MeOH solution was stirred at room temperature for 4 h; then the reaction mixture was diluted with water and extracted with ether. Evaporation of the washed (water, saturated aqueous $NaHCO_3$, and water) ether extracts afforded a solid residue (0.43 g) consisting of *trans* hydroxyether 4 (Y = *p*-NO_2) practically pure. Recrystallization from petroleum ether afforded pure 4 (Y = *p*-NO_2) (0.25 g) as a solid, mp 146-147 °C. IR λ 2.84 (OH), and 9.30 μ (OCH_3); ^1H NMR δ 8.46-7.56 (2d, 4H, J = 9.0 Hz each, aromatic protons), 3.80 (m, 1H, $w_{1/2}$ = 7.0 Hz, C<u>H</u>OH), 3.00 (s, 3H, OCH_3). Anal. Calcd. for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.81. Found: C, 62.35; H, 6.94.

c-2-Methoxy-2-(*p*-nitrophenyl)-*r*-1-cyclohexanol (5, Y = *p*-NO_2)

Trans hydroxyether 4 (Y = *p*-NO_2) (0.37 g, 1.47 mmol) in acetone (50 mL) was treated under stirring at room temperature with 8N CrO_3 (0.4 mL). After 5 min, dilution with water, extraction with ether and evaporation of the washed (water, saturated aqueous $NaHCO_3$) ether extracts afforded a solid product (0.36 g) consisting of ketone 8 (Y = *p*-NO_2) [IR λ 5.81 μ (C=O)] which was dissolved in EtOH (20 mL) and treated with $NaBH_4$ (0.20 g). After 2 h stirring at room temperature the reacion mixture was diluted with water and extracted with ether. Evaporation of the washed (water) ether extracts afforded a solid residue (0.36 g) consisting of a 37 : 63 mixture of *trans* hydroxyether 4 (Y = *p*-NO_2) and *cis* hydroxyether 5 (Y = *p*-NO_2) (^1H NMR) which was subjected to preparative TLC (a 6 : 4 mixture of petroleum ether and ether was used as the eluent; elution was repeated twice). Extraction of the two most intense bands, the faster moving band contained 4 (Y = *p*-NO_2), afforded pure 4 (Y = *p*-NO_2) (0.050 g) and pure 5 (Y = *p*-NO_2) (0.12 g) as a solid, mp 144-145 °C; IR λ 2.89 (OH), and 9.43 μ (OCH_3); ^1H NMR δ 8.46-7.50 (2d, 4H, J = 8.0 Hz each, aromatic protons), 3.40 [m, 1H, $w_{1/2} \geq$ 16.0 Hz (the signal is partially overlapped with the one of the methoxy group), C<u>H</u>OH], 3.20 (s, 3H, OCH_3). Anal. Calcd. for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.81. Found: C, 62.40; H, 6.73.

t-2-Methoxy-1-(*p*-nitrophenyl)-*r*-1-cyclohexanol (6, Y = *p*-NO_2)

Epoxide 3 (0.15 g) in anhydrous methanol (5 mL) was added dropwise to a MeONa solution (from 0.3 g of Na) in anhydrous methanol (7 mL) and the resulting reaction mixture was refluxed for 24 h. After cooling the reaction mixture was diluted with water and extracted with ether. Evaporation of the washed (water) ether extracts afforded a solid residue consisting of a mixture of the two *trans* regioisomers 6 (Y = *p*-NO_2) and 4 (Y = *p*-NO_2) in the ratio 85 : 15 (GLC) which was subjected to semipreparative TLC (a 6 : 4 mixture of petroleum ether and ether was used as the eluent; elution was repeated twice). Extraction of the most intense band afforded pure 6 (Y = *p*-NO_2) (0.080 g) as a solid mp114-115 °C; IR λ 2.98 (OH) and 9.09 μ (OCH_3); ^1H NMR δ 8.36-7.66 (2d, 4H, J = 8.0 Hz each, aromatic protons), 3.26 (m, 1H, $w_{1/2}$ = 7.0 Hz, $C\underline{H}OH$), 3.06 (s, 3H, OCH_3). Anal. Calcd. for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.81. Found: C, 62.10; H, 6.55;

t-2-Methoxy-2-(*m*-chlorophenyl)-*r*-1-cyclohexanol (4, Y = *m*-Cl)

Following the procedure previously described for the preparation of 4 (Y = *p*-NO_2), reaction of epoxide 2 (0.30 g) with 0.2N H_2SO_4 in anhydrous methanol (30 mL) for 10 s at 25°C afforded a solid residue consisting of a 91.9 : 8.1[3] mixture of *trans* hydroxyether 4 (Y = *m*-Cl) and *cis* hydroxyether 5 (Y = *m*-Cl) which was subjected to preparative TLC (a 8 : 2 mixture of petroleum ether and ether was used as the eluent; elution was repeated twice). Extraction of the most intense band afforded pure 4 (Y = *m*-Cl) (0.20 g) as a solid, mp 67-68 °C; IR λ 2.94 (OH) and 9.25 μ (OCH_3); ^1H NMR δ 7.60-7.23 (m, 4H, aromatic protons), 3.73 (m, 1H, $w_{1/2}$ = 7.0 Hz, $C\underline{H}OH$), 3.00 (s, 3H, OCH_3). Anal. Calcd. for $C_{13}H_{17}ClO_2$: C, 64.88; H, 7.07. Found: C, 64.59; H, 7.35.

c-2-Methoxy-2-(*m*-chorophenyl)-*r*-1-cyclohexanol (5, Y = *m*-Cl)

As previously described for the preparation of 5 (Y = *p*-NO_2), Jones oxidation of 4 (0.25 g) afforded the ketone 8 (Y = *m*-Cl) [IR λ 5.79 μ (C=O)] which was treated with $NaBH_4$ in EtOH to give a 45 : 55 mixture of 4 (Y = *m*-Cl) and 5 (Y = *m*-Cl) (^1H NMR). Preparative TLC on this reaction mixture (a 8 : 2 mixture of petroleum ether and ether was used as the eluent; elution was repeated twice) afforded, after extraction of the two most intense bands [the faster moving band contained 4 (Y = *m*-Cl)], 4 (Y = *m*-Cl) (0.060 g) and 5 (Y = *m*-Cl) (0.070 g) as a solid, mp 68-70 °C; IR λ 2.89 (OH), and 9.34 μ (OCH_3); ^1H NMR δ 7.53-7.40 (m, 4H, aromatic protons), 3.50 (m, 1H, $w_{1/2}$ = 18.0 Hz, $C\underline{H}OH$), 3.17 (s, 3H, OCH_3). Anal. Calcd. for $C_{13}H_{17}ClO_2$: C, 64.88; H, 7.07. Found: C, 64.60; H, 7.15.

t-2-Methoxy-1-(*m*-chlorophenyl)-*r*-1-cyclohexanol (6, Y = *m*-Cl)

As above for the preparation of 6 (Y = *p*-NO_2), treatment of epoxide 2 (O.15 g) with MeONa in refluxing anhydrous methanol afforded a crude residue consisting of 6 (Y = *m*-Cl) practically pure which was subjected to semipreparative TLC (a 8 : 2 mixture of petroleum ether and ether was used as the eluent; elution was repeated twice). Extraction of the most intense band afforded pure 6 (Y = *m*-Cl) as a liquid; IR λ 2.90 (OH), 9.17 μ (C=O); ^1H NMR 7.66-7.16 (m, 4H, aromatic protons), 3.23 (m, 1H, $w_{1/2}$ = 8.0 Hz, $C\underline{H}OH$), 3.06 (s, 3H, OCH_3). Anal. Calcd. for $C_{13}H_{17}ClO_2$: C, 64.88; H, 7.07. Found: C, 64.70; H, 7.40.

1-(*m*-chlorophenyl)-*r*-1-cyclopentancarbaldehyde (7, Y = *m*-Cl)

A solution of epoxide 2 (0.214 g, 1.03 mmol) in anhydrous benzene (20 mL) was treated at 0 °C with $BF_3\cdot Et_2O$ (0.14 mL, 1.13 mmol) then stirred at the same temperature for 1 min. Evaporation of the washed (saturated aqueous

$NaHCO_3$, and water) afforded a liquid residue only consisting of aldehyde **7** (Y = *m*-Cl) with no trace of ketone **8** (Y = *m*-Cl). Semipreparative TLC (a 3 : 1 mixture of petroleum ether and ether was used as the eluent; elution was repeated twice), afforded, after extraction of the most intense band, pure aldehyde **7** (Y = *m*-Cl) as a liquid: IR λ 3.59 and 3.70 (CHO) and 5.84 μ (C=O); ^1H NMR δ 9.46 (s,1H, CHO), 7.46-7.16 (m, 4H, aromatic protons). Anal. Calcd for $C_{12}H_{13}ClO$: C, 69.06; H, 6.27. Found: C, 68.75; H, 6.08.

2-(*m*-chlorophenyl)-cyclohexanone (8, Y = *m*-Cl)

Cyclohexene oxide (1.96 g, 20 mmol) was added to *m*-chlorophenylmagnesium bromide (from 3.82 g of 1-bromo-3-chlorobenzene and 0.48 g of Mg) in anhydrous ether (30 mL), and the reaction mixture was then refluxed for 2 h. After cooling ice-water and cool saturated aqueous NH_4Cl was added to hydrolize organic salt. Evaporation of the washed (water, saturated aqueous $NaHCO_3$, and water) ether solution afforded an oily residue (3.5 g) consisting of 2-(*m*-chlorophenyl)-cyclohexanol [IR λ 2.99 μ (OH)] which was directly oxidized by Jones reagent to crude ketone **8** (Y = *m*-Cl). Then purified by preparative TLC (a 9 : 1 mixture of petroleum ether and ether was used as the eluent; elution was repeated twice). Extraction of the most intense band afforded pure **8** (Y = *m*-Cl) as a liquid: IR λ 5.91 μ (C=O); ^1H NMR δ 8.13-7.40 (m, 4H, aromatic protons), 3.66 (m, 1H, ArCH). Anal. Calcd for $C_{12}H_{13}ClO$: C, 69.06; H, 6.27. Found: C, 69.15; H, 6.40.

Opening Reaction of Epoxide 2 and 3 with 0.2N H_2SO_4 in Anhydrous MeOH under Standard Conditions.

A thermostatted (25 °C) 0.2N H_2SO_4-anhydrous MeOH solution (5 mL) was added to epoxides (0.050 g) kept at the same temperature. After 10 s, in the case of **3**, or 2 h, in the case of **2**, stirring at 25 °C, the reaction mixture was diluted with water and extracted with ether. Usual work-up[6] afforded a crude residue which showed the composition as reported in table II. Experiments were carried out in order to check that the reaction products are stable under the opening reaction conditions used.

TABLE II STEREOSELECTIVITY OF THE RING OPENING REACTION IN 0.2N H_2SO_4-MEOH OF EPOXIDES 2 AND 3.

Epoxides	*syn* adduct	*anti* adduct
2	8.1 [a]	91.9 [b, c]
3	0 [d]	100 [e, f]

a) 5 (Y = *m*-Cl)
b) 4 (Y = *m*-Cl)
c) See Ref. 6
d) 5 (Y = *p*-NO_2)
e) 4 (Y = *p*-NO_2)
f) 0.4% of 6 (Y = *p*-NO_2) is also present.

Radiolytic Experiments

The gaseous samples were prepared by conventional tecniques, using a greaseless vacuum line and enclosed into carefully outgassed 500-mL Pyrex bulbs, each equipped with a break-seal tip. The bulbs were filled with the required amont of appropriate bulk gas (D_2 or CH_4), cooled to liquid nitrogen temperature, and sealed-off. The irradiations were carried out at 37.5 °C in a 220 Gammacell (Nuclear Canada Ltd), to a dose of 2 x 10^4 Gy at a rate of 10^4 Gy h^{-1}, as determined by a neopentane dosimeter. The radiolytic products were analyzed by GLC, identified by comparison of their retention volumes with those of authentic samples and were further confirmed by GLC/MS, using a Hewlett-Packard 5982 A quadrupole mass-spectrometer. The yields of the products were deduced from the areas of the corresponding elution peaks, using the internal standard calibration method.

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