eluted from the μ-Styragel GPC columns with tetrahydrofuran–methanol(95:5 v/v) flowing at 1 mL/min. A linear calibration of log $\bar{M}_N$ vs. elution volume (milliliters) was constructed from 1 ($\bar{M}_N$ = 290), 4 ($\bar{M}_N$ = 620), a tannin trimer[17] ($\bar{M}_N$ = 866), and polystyrene molecular weight standards ($\bar{M}_N$ = 3600, 17 500, and 35 000) purchased from Waters Associates (Lots No. 116, 41022, and 76, respectively). $\bar{M}_N$ was determined for the phenolic standards by VPO in acetone/water azeotrope (88.5:11.5 v/v). During GPC, distinct peaks eluted from samples of the reaction mixture at the proper elution volumes for monomer, dimer, trimer, tetramer, and, occasionally, pentamer, but higher molecular weights merged into a continuous distribution. The mass of material eluting at each molecular weight or elution volume was determined from the area under that fraction of the peak, assuming that the UV_{280} extinction coefficient was independent of molecular weight. This assumption was supported by the fact that the total peak area per mass injected remained constant throughout the reaction. For polydisperse samples, $\bar{M}_N$ was calculated as $\bar{M}_N = \sum N_i M_i / \sum N_i$, where M_i is the molecular weight of the ith fraction and N_i the moles of sample eluting in that fraction.

Isolation and Verification of Bis(8-catechinyl)methane. To improve the yield of dimers, we selected reaction times and conditions specifically. A solution of 1.1 g of 1 and 200 mL of distilled water at 22 °C was purged with N_2 and adjusted to pH 10 with 5% aqueous NaOH, and then 9.1 mL of 0.5% aqueous 2 was added, making the mole ratio of 2 to 1 equal to 1:2.5. After 5 min, the reaction was stopped by pouring the solution onto a slurry of 10 mL of 5% acetic acid, 20 mL of methanol, and 500 g of crushed ice and stirring for 5 min. The solution was filtered through glass wool, freeze–dried, redissolved in 750 mL of tetrahydrofuran, filtered through a fine-porosity Gooch crucible, diluted with water, evaporated under vacuum to a syrup, and freeze–dried again.

A 0.2% solution of this freeze–dried solid in methanol/water (1:9 v/v) was injected repeatedly into the HPLC instrument and eluted from μ-Bondapak-CN columns with methanol/water/acetic acid (10:90:5 v/v/v) flowing at 1 mL/min. This mobile phase, less polar than that used to assay 1, separated the dimer into three peaks. The major peak eluted between 9 and 11 mL and was collected in a flask wrapped in aluminum foil and chilled in ice–water. Reinjection of the isolate onto both the GPC and μ-Bondapak-CN columns verified that the fractionation was complete and that no further reaction had occurred during fractionation. A 12-mg sample of dimer was collected for VPO and proton NMR spectroscopy: $\bar{M}_N$ [$(CH_3)_2CO/H_2O$, 88.5/11.5 v/v] 620 ± 30; ^1H NMR [$(CD_3)_2CO$] δ 6.94 (s, 2, $H_{5'}$), 6.79 (s, 4, $H_{2',6'}$), 5.98 (s, 2, H_6), 4.69 (d, 2, J = 8, H_2), 4.07 (m, 2, H_3), 3.60 (s, 2, methylene bridge), 2.92 (dd, 2, J = 15, 5 Hz, H_4), 2.54 (dd, 2, J = 15, 8 Hz, H_4).

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Registry No. 1, 154-23-4; 2, 50-00-0; 4, 81555-08-0.

Supplementary Material Available: Kinetic data from which Figures 2 and 3 were constructed (3 pages). Ordering information is given on any current masthead page.

(17) The tannin trimer was provided by Dr. R. W. Hemingway, USDA Forest Service, Alexandria, LA.

Stereochemical Evidence for Aryl Participation in the Ring Opening of Oxiranes. Ring-Opening Reactions of 1-Benzyl-1,2-epoxycyclohexane under Acidic Conditions

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The reactions of 1-benzyl-1,2-epoxycyclohexane (1) have been investigated and compared with the ones of the corresponding methyl-substituted oxirane (3) in order to evaluate the possibility that an aryl group not directly linked to the oxirane ring can participate in the ring-opening processes. The acid-catalyzed ring-opening reactions of 1 are not completely anti stereoselective and give mixtures of syn and anti addition products accompanied by rearrangement compounds. The stereoselectivity and the amounts of rearrangement products vary noticeably with the reaction conditions. The results obtained and in particular the presence of substantial amounts of syn products observed in the ring-opening reactions of 1, markedly higher than those from epoxide 3, strongly suggest the incursion of aryl participation and have been rationalized through a mechanism implying the intermediacy of a phenonium-type ion.

The properties and the reactivity of some oxirane systems have been related in recent years to the carcinogenic and mutagenic activity of polycyclic arenes.[1] On the other hand, 1,2-epoxides have been found active as inhibitory agents[2] of mutagenesis and carcinogenesis. Therefore, a more detailed knowledge of the mechanism and stereochemistry of the ring opening of simple 1,2-epoxides appears to be useful in order to understand the more complex biological processes in which the more complex systems are involved.

The participation by neighboring aryl groups, and therefore the intermediacy of σ-bridged phenonium-ion-type intermediates, has been largely suggested and proved in the solvolyses of most β-arylalkyl systems.[3,4] However, the aryl participation in the ring opening of oxiranes has been put forward only in order to explain the syn stereo-

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

(2) Kupchan, S. M.; Court, W. A.; Dayley, R. G.; Gilmore, C. J.; Bryan, R. F. *J. Am. Chem. Soc.* **1972**, *94*, 7194. Kupchan, S. M.; Schubert, R. M. *Science* **1974**, *185*, 791; Kupchan, S. M.; Jarvis, B. B.; Dayley, R. G., Jr.; Bright, W.; Bryan, R. F.; Shiruri, Y. *J. Am. Chem. Soc.* **1976**, *98*, 7092.

(3) For a review, see: Lancelot, C. J.; Cram, D. J.; Schleyer, P. v. R. In "Carbenium Ions"; Olah, G. A., Schleyer, P. v. R., Eds.; Wiley-Interscience: New York, 1972; Vol. 3, p 1347.

(4) Schadt, F. L.; Lancelot, C. J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1978**, *100*, 228 and references therein cited.

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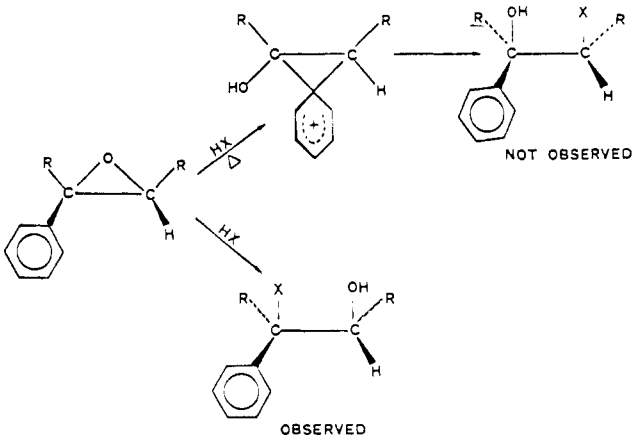
Table I. Product Composition in the Ring Opening of Epoxide 1 in Acidic Methanol

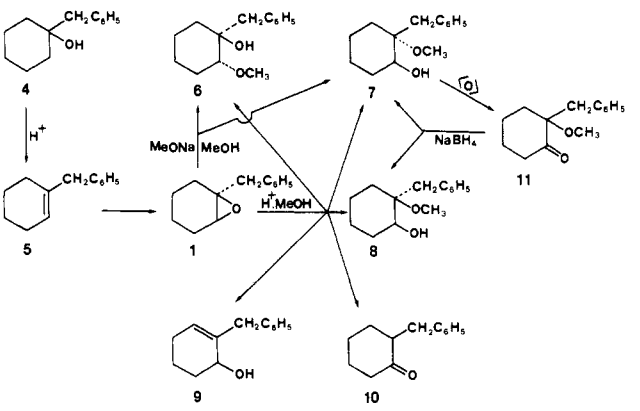
reagents	composition, % 7	8	6	9	10	15	syn/anti[a] ratio
MeOH, H_2SO_4	71.5	0.5	20.0	5.0	3.0		0.5/99.5
MeOH-$LiClO_4$,[b] TsOH	62.5	1.5	19.0	3.5	13.5		1.8/98.2
MeOH-CH_2Cl_2,[c] TsOH	33.5	1.5	16.0	8.0	26.0	15.0	2.9/97.1

[a] Anti adducts are 6 and 7. [b] 0.5 M solution. [c] Molar ratio of 1:0.1:6 epoxide/acid/MeOH.

Scheme I

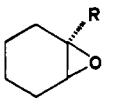


Scheme II



chemistry observed in the acid-catalyzed ring opening of a particular case of oxiranes bearing aryl groups directly linked to the epoxide ring, that is in the case of stilbene oxides[5] (see Scheme I). This mechanism has, however, never been proved, and alternative explanations of the results, implying intermediates with high carbocationic character, have been given.[5-7] In the case of oxiranes bearing only one phenyl directly linked to the epoxide ring, the aryl participation can be unequivocally excluded on the basis of considerations of the regiochemistry of the products obtained.

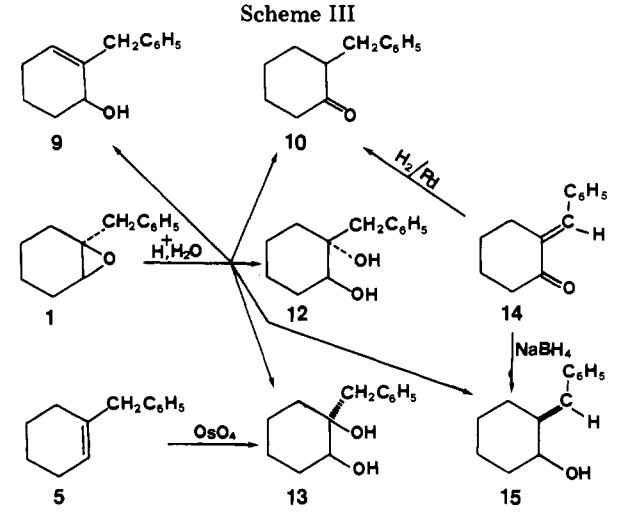
In connection with our studies on the mechanism and stereochemistry of the reaction of oxirane derivatives bearing particular substituents linked to the ring,[7,8] we have extended our research to 2-benzyloxiranes. These studies were aimed at evaluating the possibility that an aryl group not directly linked to the oxirane ring can participate in the ring-opening reactions. The aryl participation could modify[3] the essentially anti stereochemistry observed in the ring opening of oxiranes bearing neither aryl nor other unsaturated systems directly bonded to the ring.[8-10] Here we report on the ring-opening reactions of 1-benzyl-1,2-epoxycyclohexane (1), a structural



1, R=$CH_2C_6H_5$
2 R=C_6H_5
3, R=CH_3

analogue of the epoxides 2 and 3, whose reactions have been largely studied in our laboratory.[7,10] Also in these cases mechanisms proceeding through carbocationic species have been proposed.[7]

Scheme III



Results

The epoxide 1 was obtained from olefin 5 by treatment with NBA in aqueous dioxane followed by dehydrohalogenation with KOH[11] or by direct epoxidation with peroxybenzoic acid. Pure olefin 5 was prepared by acid-catalyzed dehydration of 1-benzylcyclohexanol (4) and purified by fractional distillation.

Pure reference compounds were obtained in the following manner (see Schemes II and III). The acid-catalyzed reaction of 1 with methanol gave a mixture consisting mainly of the two trans regioisomeric hydroxy ethers 6 and 7 in a ratio of 1:3.5 accompanied (see Table I) by small amounts of the cis ether 8 and of the rearrangement products 9 and 10. From this mixture, 7 can be obtained by crystallization, whereas 6 was purified by preparative TLC. The latter compound, 6, was also obtained as the main product in the reaction of 1 with sodium methoxide in methanol. Oxidation of 7 gave 11 which on reduction with $NaBH_4$ gave a 28:72 mixture of 7 and 8, from which

(5) Parker, R. E.; Isaacs, S. *Chem. Rev.* **1959**, *59*, 737.
(6) Brewster, J. H. *J. Am. Chem. Soc.* **1956**, *78*, 4061.
(7) See for example: Battistini, C.; Crotti, P.; Damiani, D.; Macchia, F. *J. Org. Chem.* **1979**, *44*, 1643 and references cited therein.
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(9) Buchanan, J. G.; Sable, H. Z. In "Selective Organic Transformations"; Thyagarajan, B. S., Ed.; Wiley-Interscience: New York, 1972; Vol. 1, p 1.
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(11) Balsamo, A.; Battistini, C.; Crotti, P.; Macchia, B.; Macchia, F. *Gazz. Chim. Ital.* **1976**, *106*, 77.

Table II. Product Composition in the Hydrolysis, Trichloroacetolysis, and Acetolysis of Epoxide 1

reagents	composition, % 12	13	9	10	15	syn/anti ratio
H_2O, H_2SO_4	86.5	1.0	7.5	2.0	3.0	1.2/98.8
H_2O-$LiClO_4$,[a] H_2SO_4	48.5	1.0	9.0	39.0	2.5	2.0/98.0
cyclohexane, CCl_3COOH[b]	88.5	2.5	5.0	1.0	3.0	2.7/97.3
CCl_4, CCl_3COOH[b]	85.5	4.5	6.5	0.5	3.0	5.0/95.0
benzene, CCl_3COOH[b]	61.5	18.5	15.0	1.0	4.0	23.1/76.9
$CHCl_3$, CCl_3COOH[b]	50.5	28.5	16.5	1.0	3.5	36.1/63.9
CH_2Cl_2, CCl_3COOH[b]	36.0	40.5	19.5	1.0	3.0	52.9/47.1
CH_3COOH, TsOH[b]	42.0	2.0	10.0	46.0		4.5/95.5
CH_3COOH-$LiClO_4$,[a] TsOH[b]	15.0	2.5	5.0	77.5		14.3/85.7

[a] 0.5 M solution in $LiClO_4$. [b] After saponification of the crude reaction mixture.

8 was obtained by preparative TLC. The *trans*-diol 12 was obtained by acid-catalyzed hydrolysis of 1 together with minor amounts of the *cis*-diol 13 and of 9, 10, and 15 (see Table II). The *cis*-diol 13 was prepared by OsO_4-catalyzed dihydroxilation[12] of olefin 5. The unsaturated alcohol 9 was obtained through preparative TLC of the mixture obtained by trichloroacetolysis of 1 in CH_2Cl_2 followed by saponification (see Table II). Ketone 10 and *trans*-2-benzylidenecyclohexanol (15) were obtained by Pd-catalyzed reduction and $NaBH_4$ reduction of *trans*-2-benzylidenecyclohexanone (14),[31,32] respectively.

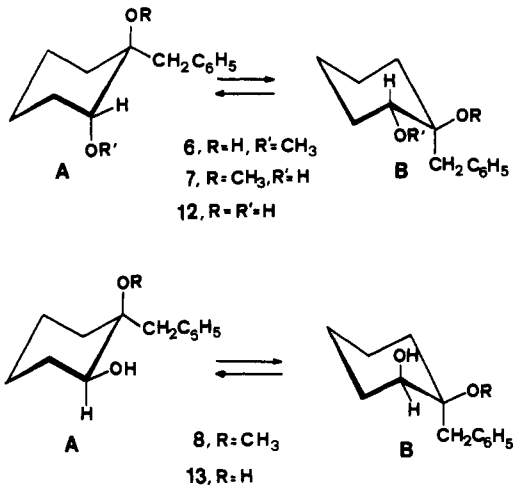
Table I shows the product compositions of the acid-catalyzed methanolysis of 1 in methanol and CH_2Cl_2, and Table II shows the acid-catalyzed hydrolysis, the acetolysis, and the trichloroacetolysis of the same epoxide 1 in several aprotic solvents. The products of the two last reactions have been analyzed after saponification of the monoesters obtained. Several experiments were carried out to verify the stability of the products obtained in the ring-opening reactions.

Structures and Configurations

The structures of the starting products 1 and 5 and of the rearrangement products 9, 10, and 15 were confirmed by NMR spectroscopy. The structures and configurations of the addition products 6–8, 12, and 13 were deduced from their methods of preparation and confirmed by NMR spectroscopy and by IR studies in dilute solutions of CCl_4 in the 3000–3600-cm^{-1} range. In particular, the formation of 6 and 7 in the base-catalyzed methanolysis of 1 defines their trans configuration, in accordance with an S_N2-type substitution in the ring opening of oxiranes under strongly basic conditions.[5-7] On the other hand, the structures of 6–8 were inferred both by the oxidation of 7 to the ketone 11, whose reduction gives a mixture of 7 and 8, and by the stability of 6 to the same oxidation conditions. The relative configurations of the diols 12 and 13 were deduced by the formation of the diol 13 in the cis dihydroxylation of olefin 5 with OsO_4.[13]

As for the conformational equilibrium in compounds 6–8, 12, and 13, both the trans compounds 6, 7, and 12 and the cis compounds 8 and 13 exist as an equilibrium mixture of the conformers A and B (Scheme IV). The results can be inferred from the values of the half-bandwidth of the signal of the methynyl proton β to the benzyl group in the NMR spectra: 6 ($W_{1/2}$ = 9.5 Hz), 7 ($W_{1/2}$ = 10.6 Hz), 8 ($W_{1/2}$ = 9.8 Hz), 12 ($W_{1/2}$ = 14.2 Hz), 13 ($W_{1/2}$ = 16.0 Hz). These values are intermediate between those of an axial proton ($W_{1/2}$ > 16.5 Hz) and those of an equatorial one ($W_{1/2}$ < 7.5 Hz).[7,14,15a] In the case of unsubstituted cyclohexane-1,2-diols and 2-methoxycyclohexanols the trans derivatives prefer the diequatorial conformation due to the formation of an OH···O bond.[15b] However, when a substituent larger than hydrogen is present on carbon 1 or 2 (e.g., a methyl), an equilibrium mixture of the two possible conformers is obtained,[15b,c] whereas larger substituents (e.g., phenyl) favor the unbonded conformer. In the unsubstituted cis derivatives the two possible conformations are equivalent (diol) or roughly equivalent (methoxy alcohol) (the hydrogen bond is possible in both of them).[15b] However, the presence of a substituent on carbon 1 or 2 shifts the equilibrium toward the conformation in which the substituent is equatorial to an extent depending on the size of the substituent itself (e.g., phenyl derivatives exist largely in this last conformation).[7,15c] The conformational equilibria observed in the present compounds are in accordance with the expected relatively low conformational *A* value for a substituted methylene[16] such as benzyl.[17] This value does not differ significantly from the one of the unsubstituted CH_3.[17] The equilibria are, however, influenced by the substituents. The conformation B with the axial benzyl group is more favored in the methoxy alcohols 6–8 than in the corresponding diol derivatives 12 and 13.

Scheme IV

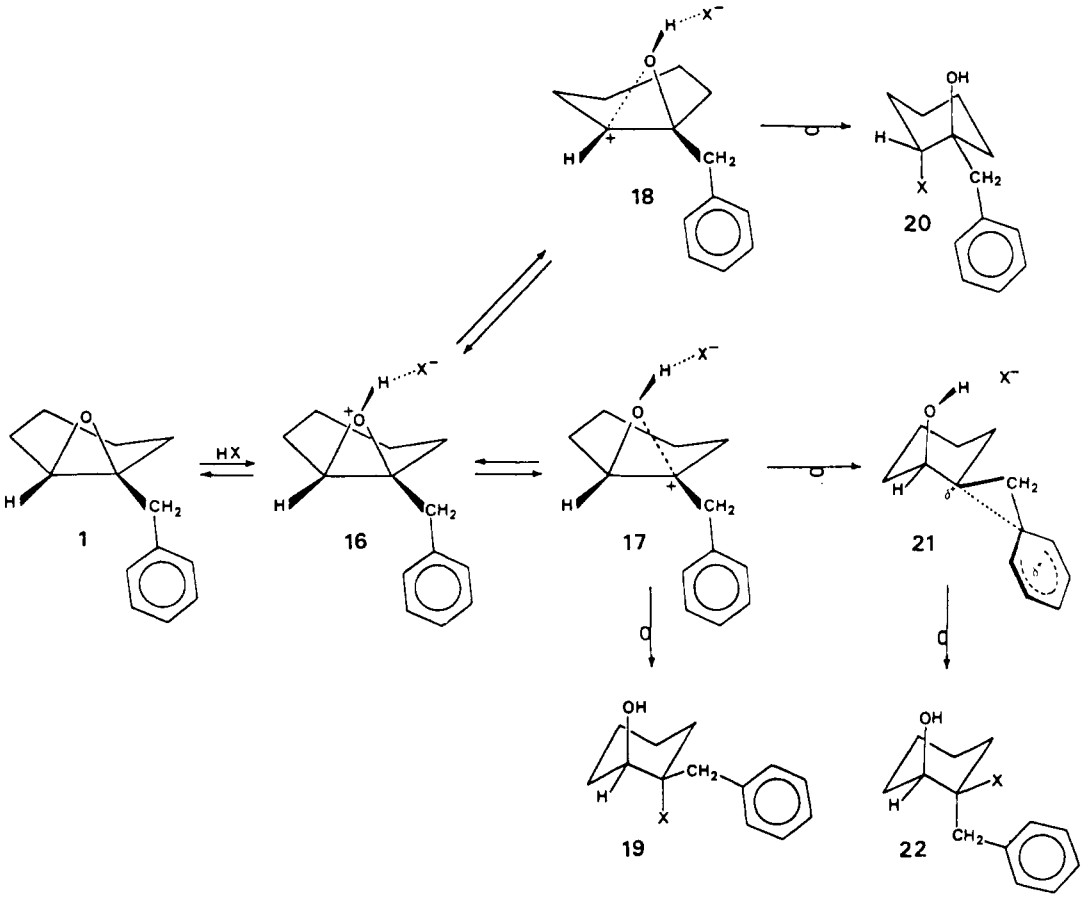


Discussion

The acid-catalyzed ring-opening reactions of 1 are not completely anti stereoselective (see Tables I and II) and

(12) VanRheenan, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973.
(13) Schroder, M. *Chem. Rev.* **1980**, *80*, 187.
(14) Jackman, L. M.; Sternell, S. "Application of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: Oxford, 1969; p 288.
(15) (a) Berti, G.; Macchia, B.; Macchia, F. *Tetrahedron* **1968**, *24*, 1755; **1972**, *28*, 1299. (b) Cole, A. R. H.; Jefferies, P. R. *J. Chem. Soc.* **1956**, 4391. (c) Ceccarelli, G.; Macchia, B.; Macchia, F.; Monti, L. *Org. Magn. Reson.* **1975**, *7*, 548.
(16) Kitching, W.; Olszowy, H.; Adcock, W. *Org. Magn. Reson.* **1981**, *15*, 230.
(17) Anderson, J. E. *J. Chem. Soc., Perkin Trans. 2* **1974**, 10.

Scheme V



give mixtures of syn and anti addition products accompanied by rearrangement compounds (9, 10, and 15). The percentages of syn addition observed in the acid methanolysis and hydrolysis are not negligible, even though they are not exciting. However, their amounts increase noticeably in the trichloroacetolysis in aprotic solvents and in the acetolysis. The relative amounts of rearrangement products formed in the ring-opening reactions of 1 vary markedly according to the type of reaction and to the reaction conditions in general.

The data of the acid-catalyzed methanolyses of 1 show that these reactions, and very probably the other reactions under acidic conditions (even if for the latter reactions a direct proof is still lacking), are not completely regioselective. However, most of the oxirane ring opening (ca. 80%) occurs between the oxygen and the tertiary carbon.

The steric course of the acid-catalyzed ring opening of oxiranes bearing aryl or other unsaturated systems directly linked to the ring can range from complete retention to complete inversion of configuration depending on the structure of the epoxide and on the reaction conditions.[7-9] On the other hand, the ring opening of simple aliphatic and cycloaliphatic oxiranes is almost exclusively anti stereoselective:[5-10] e.g., a maximum value of 8% of syn addition has been observed (see Table III) in the trichloroacetolysis of epoxide 3 in CH_2Cl_2.[10] The syn products formed in these reactions have been rationalized through the intermediacy of structures with some carbocation character, and their amounts were shown, at least in the case of 1-aryloxiranes,[18] to be directly linked to the stability of the carbocationic intermediate following the breaking of the C–O bond of the protonated oxirane.[7,8,10] According

Table III. Stereoselectivity of the Trichloroacetolysis and of the Hydrolysis of Epoxides 1 and 3

epoxide	reagents	composition, % syn adduct	composition, % anti adduct
1	CCl_3COOH, benzene	23.2	76.8
3[a]	CCl_3COOH, benzene	6.0	94.0
1	CCl_3COOH, CH_2Cl_2	52.9	47.1
3[a]	CCl_3COOH, CH_2Cl_2	8.0	92.0
1	H_2SO_4, H_2O	1.2	98.8
3[b]	H_2SO_4, H_2O	<0.2	100

[a] Reference 10. [b] Reference 8.

to this, benzyloxirane 1 should be expected to give lower amounts of syn addition than those of methyloxirane 3, because of the electron-withdrawing inductive effect usually resulting from the replacement of a hydrogen by a phenyl, due to the sp^2–sp^3 bond dipole between the phenyl ring and the methylene group.[19] The substantial amounts of syn products found in the reactions of the benzyl epoxide 1, markedly higher than those observed in the corresponding reactions of the methyl one, 3,[10] strongly suggest the incursion of aryl participation and therefore the intermediacy of a phenonium-type ion in the ring opening of 1.

The nucleophilic addition to 1,2-epoxides in acid media is a peculiar type of substitution which implies a preliminary proton transfer to the oxirane oxygen and in which the leaving group is neutral and remains closely linked to the reaction center.[7-9] The results obtained in the ring-opening reactions of 1 can be rationalized on the basis of a modification, which implies neighboring aryl participa-

(18) Battistini, C.; Balsamo, A.; Berti, G.; Crotti, P.; Macchia, B.; Macchia, F. J. Chem. Soc., Chem. Commun. 1974, 712.

(19) Reference 3, p 1370.

tion (see Scheme V; no conformational implication is given to the formulas), of a mechanism previously proposed for the ring opening of 1-aryl-substituted and other oxiranes.[7,8,18] This mechanistic scheme[7,8,18] can be strictly related to the "ion–dipole pair" mechanism,[20] a close analogue of the Winstein ion-pair scheme of nucleophilic substitutions and eliminations.[21-23] According to this interpretation[7,8,18] the protonated oxirane **16** can lead to two intramolecular intimate ion–dipole pairs, **17** and **18**, which on attack of the nucleophile from the back side, because of the strong shielding at the front, afford the anti products **19** and **20**, respectively. The preferential formation of addition products of type **19** (methanolysis reactions) can be ascribed to the higher stability of the intermediate **17** due to the presence of the tertiary carbocationic center. Neighboring group participation by the β-phenyl on the ion–dipole pair **17** can lead to a discrete, but unsymmetrically bridged, phenonium-like ion, **21**. A symmetrical phenonium ion would be less likely because the distribution of the positive charge on the primary carbon would be expected to reduce the stability of the intermediate[24] (no trace of products arising from phenyl migration can be detected in the reaction mixtures). Attack of the nucleophile on **21** from the side opposite the phenonium bridge gives the syn adduct **22** with overall retention of configuration. It may be pointed out that the only syn addition product found in the acid-catalyzed methanolysis of **1** (**8**) corresponds structurally to **22**. In such a mechanistic scheme the stereoselectivity of the ring opening of **1** could be linked to the competition between the aryl-assisted vs. the aryl-unassisted pathways.[3,4]

Tertiary β-arylalkyl substrates are usually considered to react through very weak or no aryl participation because the stability of the tertiary carbenium ions reduces the electron demand for additional stabilization via aryl-assisted routes.[24] However, in the present case, the presence of the electron-withdrawing former oxirane oxygen on the carbon adjacent to the tertiary carbocationic center of **21** increases the electron demand at the reactive site itself and therefore enhances the phenyl participation,[25,26] thus justifying the substantial amounts of syn products formed in some reactions of **1**.

According to the mechanism suggested, the highest amounts of syn adduct (**22**) are observed in the trichloroacetolysis carried out in the low-polarity nonnucleophilic aprotic solvents. In the other reactions (acetolysis, hydrolysis, and methanolysis) the nucleophilic solvents compete considerably with neighboring participation shifting the mechanism from aryl assisted to aryl unassisted and yielding mainly anti adducts. The addition of salt ($LiClO_4$), which should increase the polarity of the medium, causes only a small increase of the syn/anti ratio and a substantial increase of the amounts of ketone **10**. However, the increase of the syn/anti ratio in these reactions appears to be due more to a decrease of the amounts of the anti adduct in favor of the ketone **10** than to a real speeding up of the aryl participation route. A much more definite dependence on the solvent both of the syn/anti ratio and of product composition in general is observed in the trichloroacetolysis. In this case, however, an actual marked increase of the percentage of the syn products accompanied by a corresponding decrease of the anti adducts is observed in the following solvent series: cyclohexane, CCl_4, benzene, $CHCl_3$, CH_2Cl_2. The amounts of the unsaturated alcohol **9** also increase in the same solvent series, whereas, on the contrary, the amount of ketone **10** does not change appreciably. An analogous solvent–stereoselectivity dependence has been observed in the trichloroacetolysis of 1-aryl- and 1-ethynylcyclohexene oxides.[8] However, the rationalization previously given[8] does not appear to be appropriate for the present case.

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 Infracord Model 137, and those for the determination of OH-stretching bands were taken with a Perkin-Elmer Model 225 double-beam grating spectrophotometer in dried (P_2O_5) CCl_4, and the indene band at 3110 cm^{-1} was used as calibration standard; a quartz cell of 2-cm optical length was employed, and the concentration of the solution was 5×10^{-3} M or lower to prevent intermolecular association. ^1H NMR spectra were determined on 10% $CDCl_3$ solutions with a JEOL C 60 HL spectrometer using Me_4Si as an internal standard. In the case of compounds **6** and **8** the ^1H NMR spectra were also measured with a CFT-20 spectrometer in order to get a better separation of the signal of the methynyl proton from that of the methoxy group. GLC analyses of the mixtures of diols **12** and **13**, alcohol **9**, ketone **10**, and benzylidenecyclohexanol (**15**) were run on a Carlo Erba Fractovap 2300 apparatus with a flame-ionization detector with a glass column (1.5 m × 2.5 mm) packed with 10% diethyleneglycol succinate on 80–100-mesh silanized Chromosorb W (column 195 °C, evaporator and detector 250 °C; nitrogen flow rate 40 mL/min); the order of increasing retention times was **10** < **9** < **15** < **13** < **12**. GLC analyses of mixtures of hydroxy ethers **6–8** and of **9**, **10**, and **15** were performed on a Carlo Erba Fractovap GV apparatus with a flame-ionization detector and a glass column (2 m × 2.5 mm) packed with 10% Carbowax 20M on 80–100-mesh silanized Chromosorb W (column 180 °C, evaporator and detector 220 °C; nitrogen flow rate 40 mL/min); the order of increasing retention times was **10** < **6** < **9** < **8** < **15** < **7**. Preparative TLC was performed on 2-mm-layer silica gel plates (Merck F_{254}) containing a fluorescent indicator. All comparisons between compounds were made on the basis of IR and NMR spectra and GLC. Magnesium sulfate was always used as the drying agent. Evaporations were done in vacuo (rotating evaporator). Cyclohexane, CCl_4, $CHCl_3$, and CH_2Cl_2 were refluxed over P_2O_5 and rectified. Benzene was washed with concentrated sulfuric acid, kept at reflux over sodium, and distilled.

1-Benzylcyclohexanol (4) was prepared as previously described;[27] mp 55–57 °C (lit.[27] mp 53–55 °C).

1-Benzylcyclohexene (5). Compound **4** (20 g) was added to a freshly prepared solution of H_2SO_4 in glacial AcOH (2:8 v/v, 100 mL). The mixture was stirred at room temperature for 10 min and then poured into a separatory funnel containing petroleum ether (bp 40–70 °C, 200 mL) and H_2O (400 mL). The organic layer was washed (H_2O, 10% Na_2CO_3 aqueous solution, H_2O), dried, and evaporated to give a liquid (18 g) which was fractionated to yield pure **5**: 13.0 g; bp 87 °C (0.7 mm) [lit.[28] bp 127.2–128.4 °C (15 mm)].

1-Benzylcyclohexene Oxide (1). A solution of **5** (7.0 g, 40.6 mmol) in 75% (v/v) aqueous dioxane (160 mL) was treated with NBA (6.32 g, 45.8 mmol) in 50% (v/v) aqueous dioxane (80 mL) and warmed on a steam bath for 5 min. After cooling, the reaction mixture was titrated while being stirred with 1 N aqueous NaOH

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(phenolphthalein), diluted with water, and extracted with ether. Evaporation of the washed (H_2O) and dried ether extracts gave crude 1 (7.1 g) which was distilled to yield pure 1: 3.5 g; bp 94–96 °C (0.3 mm); NMR δ 3.05 (m, 1, $W_{1/2}$ = 9.0 Hz, CHO), 2.87 (s, 2, CH_2Ph). Anal. Calcd for $C_{13}H_{16}O$: C, 82.93; H, 8.56. Found: C, 82.71; H, 8.39.

Reaction of 1 with Sodium Methoxide in Methanol. A solution of sodium methoxide (6.5 g) in anhydrous methanol (50 mL) was added to a solution of 1 (0.40 g) in anhydrous methanol (10 mL), and the resulting mixture was maintained at gentle reflux for 24 h, diluted with water, and extracted with ether. Evaporation of the washed (H_2O) ether extracts yielded a residue (0.4 g) mainly consisting (GLC) of ether **6** (98%) with a small amount of ether **7** (2%). The crude mixture was subjected to preparative TLC (a 9:1 mixture of petroleum ether and ether was used as the eluent; elution was repeated three times): extraction of the main band yielded pure **1-benzyl-*trans*-2-methoxy-*r*-1-cyclohexanol (6)** as a solid: 0.220 g; mp 50–51 °C; IR (CCl_4) 3587 (sh, OH···Ph), 3580 cm^{-1} (OH···O); NMR δ 3.00 (m, 1, $W_{1/2}$ = 9.5 Hz, $CHOCH_3$), 2.94 and 2.74 (AB system, 2, J = 13.6 Hz, CH_2Ph). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.14. Found: C, 76.64; H, 9.40.

Compound **6** was stable to oxidation in the Jones reagent[29] conditions.

2-Benzyl-*trans*-2-methoxy-*r*-1-cyclohexanol (7). A solution of 1 (1.0 g) in 0.2 N H_2SO_4 in anhydrous methanol (200 mL) was left at room temperature overnight, quenched with solid $NaHCO_3$ and saturated aqueous $NaHCO_3$, and extracted with ether. Evaporation of the washed (H_2O) and dried ether extracts yielded a residue (1.12 g) which on crystallization at −10 °C from petroleum ether (bp 40–70 °C) afforded pure **7** as a solid: 0.62 g; mp 50.5–52 °C; IR (CCl_4) 3587 (OH···O), 3628 cm^{-1} (OH free); NMR δ 3.62 (m, 1, $W_{1/2}$ = 10.6 Hz, CHOH), 2.92 (s, 2, CH_2Ph). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.14. Found: C, 76.16; H, 9.35.

The crude product (0.49 g), obtained in an analogous reaction of 1 (0.50 g) in 0.2 N H_2SO_4–MeOH solution (50 mL), was subjected to preparative TLC (a 9:1 mixture of petroleum ether and ether was used as the eluent, and elution was repeated four times). Extraction of the two main bands (the faster moving band contained **6**) afforded **6** (0.060 g) and **7** (0.250 g).

2-Benzyl-2-methoxycyclohexanone (11). A stirred solution of **7** (0.58 g, 2.63 mmol) in acetone (55 mL) was treated dropwise with Jones reagent[29] (0.65 mL). After 10 min at room temperature the mixture was diluted with water and extracted with ether. Evaporation of the washed (H_2O, saturated aqueous $NaHCO_3$, and H_2O) and dried ether extracts gave an oily reside (0.49 g) of crude **11** which was 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 band with the highest R_f yielded pure **11**: 0.38 g; IR 5.94 μm (C=O); NMR δ 3.35 (s, 3, OCH_3), 3.20 and 2.92 (AB system, 2, J = 15.0 Hz, CH_2Ph). Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.14; H, 8.54.

Reduction of 11 with $NaBH_4$. A solution of **11** (0.37 g, 1.69 mmol) in 95% ethanol (37 mL) was treated with $NaBH_4$ (0.287 g, 7.60 mmol) and stirred at room temperature for 3 h. The reaction mixture was acidified with 2 N H_2SO_4, diluted with water, and extracted with ether. Evaporation of the washed (saturated aqueous $NaHCO_3$ and H_2O) ether extracts gave a residue (0.35 g) consisting of a 28:72 mixture of **7** and **8** (GLC) which was subjected to preparative TLC (a 9:1 mixture of petroleum ether and ether was used as the eluent; elution was repeated six times). Extraction of the two main bands (the faster moving band contained **8**) gave **7** (0.55 g) and **2-benzyl-*cis*-2-methoxy-*r*-1-cyclohexanol (8)** as a solid: 0.10 g; mp 56–58 °C; IR (CCl_4) 3580 cm^{-1} (OH···O); NMR δ 3.29 (m, 1, $W_{1/2}$ = 9.8 Hz, CHOH), 3.07 and 2.74 (AB system, 2, J = 13.0 Hz, CH_2Ph). Anal. Calcd for $C_{14}H_{20}O_2$: C, 76.32; H, 9.14. Found: C, 76.05; H, 9.26.

1-Benzyl-*r*-1,*t*-2-cyclohexane-1,2-diol (12). A suspension of 1 (0.20 g) in 0.2 N aqueous H_2SO_4 was stirred at room temperature for 2 days, treated with solid $NaHCO_3$, and extracted with ether. Evaporation of the washed (H_2O) and dried ether extracts yielded a solid residue (0.21 g) which was crystallized from petroleum ether (bp 40–70 °C) to give pure **12**: 0.11 g; mp 95–96 °C; IR (CCl_4) 3587 (OH···O), 3623 cm^{-1} (OH free); NMR δ 3.68 (m, 1, $W_{1/2}$ = 14.2 Hz, CHOH), 3.07 and 2.88 (AB system, 2, J = 14.25 Hz, CH_2Ph). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.86; H, 8.90.

1-Benzyl-*r*-1,*c*-2-cyclohexane-1,2-diol (13). A mixture of *N*-methylmorpholine *N*-oxide monohydrate (1.51 g, 11.2 mmol), water (4.5 mL), acetone (1 mL), and OsO_4 (0.010 g) in *tert*-butyl alcohol (1 mL) was treated with **5** (1.0 g, 5.8 mmol) in acetone (2 mL). The resulting mixture was maintained at room temperature with a water bath for 1 h and then stirred overnight at room temperature under nitrogen. After this time the reaction mixture was added with a slurry of $NaHSO_3$ (0.10 g), magnesium silicate (1.15 g), and water (12 mL), and then the magnesium silicate was filtered. The filtrate was acidified (pH 2) with 1 N H_2SO_4, saturated with NaCl, and extracted with ether. The ether extracts were washed with water, dried, and evaporated to yield a solid residue (0.60 g) which was crystallized from petroleum ether (bp 40–70 °C) to give pure **13**: 0.45 g; mp 107–108 °C; IR (CCl_4) 3587 (sh, OH···O), 3620 cm^{-1} (OH free); NMR δ 3.43 (m, 1, $W_{1/2}$ = 16.0 Hz, CHOH), 2.87 (s, 2, CH_2Ph). Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found C, 75.56; H, 8.80.

Isolation of 2-Benzylcyclohex-3-en-1-ol (9) and of Diols 12 and 13 in the Reaction of 1 with Trichloroacetic Acid in Anhydrous CH_2Cl_2. A solution of 1 (0.50 g, 2.65 mmol) in anhydrous CH_2Cl_2 (50 mL) was treated with 1 N solution of CCl_3COOH in anhydrous CH_2Cl_2 (2.91 mL), and the resulting mixture was left overnight at room temperature. The organic solution was washed (H_2O, saturated aqueous $NaHCO_3$) filtered, and evaporated; the crude reaction product was dissolved in THF (40 mL), treated with 1 M KOH aqueous solution (12.5 mL), left at room temperature for 5 h, diluted with water, and extracted with ether. Evaporation of the washed (H_2O) and dried ether extracts yielded an oily residue (0.48 g) which was subjected to preparative TLC (petroleum ether was used as the eluent; elution was repeated six times). Extraction of the main band with an R_f of about 0.5 gave **9** (0.050 g), slightly impure due to carbonylic products (IR), which was further purified through a semipreparative TLC on 0.5-mm silica gel plates (petroleum ether was used as the eluent; elution was repeated four times). Extraction of the main band afforded pure **9** as an oil:[30] 0.040 g; IR 3.0 μm (OH); NMR δ 5.70 (m, 1, CH=), 4.08 (m, 1, CHOH), 3.52 (large s, 2, CH_2Ph).

The crude product (0.060 g) obtained in an analogous reaction of 1 (0.050 g), but stopping before saponification, was dissolved in anhydrous ether and treated, under stirring, with $LiAlH_4$ (0.070 g). When the addition was complete, the mixture was stirred for 20 min and treated with water and 2 N aqueous NaOH. Evaporation of the dried ether yielded a crude product (0.050 g) which was subjected to TLC analysis on 0.2-mm silica gel plates (a 8:2 mixture of petroleum ether and ether was used as the eluent; elution was repeated five times). Extraction of the two main bands (the faster moving band contained **13**) afforded **12** (0.010 g) and **13** (0.010 g).

***trans*-2-Benzylidenecyclohexanol (15).** A solution of **14**[31,32] (0.120 g, 0.64 mmol) in EtOH (12 mL) was treated with $NaBH_4$ (0.125 g, 3.30 mmol), and the resulting mixture was left at room temperature under stirring for 3 h. After acidification with 10% aqueous H_2SO_4, the reaction mixture was extracted with ether. Evaporation of the washed (H_2O, saturated aqueous $NaHCO_3$, H_2O) and dried ether extracts afforded a crude solid product which on recrystallization from petroleum ether (bp 40–70 °C) at 5 °C gave pure **15**: 0.040 g; mp 62.5–63.5 °C (lit.[33] mp 63–64 °C).

2-Benzylcyclohexanone (10). A solution of **14**[31,32] (0.10 g, 0.53 mmol) was hydrogenated at 25 °C under room pressure in the presence of 10% Pd/C (0.010 g). After the theoretical amount of hydrogen was absorbed, the solution was filtered and carefully evaporated to give pure **10** (0.090 g) as an oil.[32,34,35]

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Acid-Catalyzed Reactions of 1 in Water, Methanol, and Acetic Acid. A suspension (water) or a solution (methanol and acetic acid) of the epoxide 1 (0.10 g, 0.53 mmol) in a 0.2 N solution of the acid (H_2SO_4 for the reactions in water and *p*-toluenesulfonic acid monohydrate for the reactions in methanol and acetic acid) in the solvent (10 mL) was stirred at 25 °C for 24 h (reaction in water), 7 h (reaction in methanol), or 1 h (reaction in acetic acid), quenched with solid $NaHCO_3$ and saturated aqueous $NaHCO_3$ (in the case of the reaction in acetic acid the mixture was previously diluted with water), and thoroughly extracted with ether. Evaporation of the washed (H_2O) ether extracts yielded mixtures consisting of diols **12** and **13** (reaction in water), hydroxy ethers **6–8** (reaction in methanol), or monoacetates (reaction in acetic acid) together with different amounts of the rearrangement products **9**, **10**, and **15** which were analyzed by GLC (see Tables I and II), except for the reaction carried out in acetic acid. The crude product obtained from the reaction in acetic acid was analyzed by GLC after saponification of the monoacetates to the corresponding diols **12** and **13** as described later for the reactions of 1 with trichloroacetic acid. The reaction of 1 in methanol and that in acetic acid were also performed in the presence of anhydrous $LiClO_4$ (0.5 M) to give the results reported in Tables I and II.

The solvolysis addition products of these reactions were completely stable under the reaction conditions used.

Reaction of 1 with Methanol in CH_2Cl_2 in the Presence of *p*-Toluenesulfonic Acid. To the epoxide 1 (0.65 g, 3.45 mmol) was added a solution of *p*-toluenesulfonic acid monohydrate and methanol in a molar ratio (epoxide/acid/methanol) of 1:0.1:6 in anhydrous CH_2Cl_2 (65 mL) at 25 °C. The resulting mixture was stirred for 12 h at the same temperature and then treated with solid $NaHCO_3$ and saturated aqueous $NaHCO_3$. Evaporation of the washed (H_2O) organic solvent gave a residue (0.70 g) which was analyzed by GLC (see Table I) and at the same time subjected to preparative TLC (a 9:1 mixture of petroleum ether and ether was used as the eluent; elution was repeated six times). Extraction of the observed bands afforded the following: **15** (R_f 0.27, 0.045 g), **7** (R_f 0.38, 0.078 g), **6** (R_f 0.52, 0.012 g), **10** (R_f 0.65, 0.053 g), 1 (R_f 0.86, 0.045 g). GLC analysis of the crude products obtained by the same reaction of 1, but stopping after different reaction times, showed the same product composition within experimental error.

Reactions of the Epoxide 1 with Trichloroacetic Acid in Several Solvents. The reactions were carried out in anhydrous benzene, cyclohexane, CCl_4, $CHCl_3$, and CH_2Cl_2 in the following way. A solution of 1 (0.10 g, 0.53 mmol) in the solvent (10 mL) at 25 °C was treated with a 1 M solution of trichloroacetic acid in the same solvent (0.58 mL), stirred for 1 h at the same temperature, washed with saturated aqueous $NaHCO_3$ and water, and evaporated to dryness. The residue obtained, consisting of mixtures of monotrichloroacetates and rearrangement products, was hydrolyzed in the following way. The crude product was dissolved in freshly distilled THF (8 mL), treated with 1 M KOH in ethanol (2.5 mL), and then left 5 h at room temperature. Dilution with water, extraction with ether, and evaporation of the washed (H_2O) and dried ether extracts yielded a mixture of **12** and **13** together with **9**, **10**, and **15** which was analyzed by GLC (see Table II). Reaction of 1 in each solvent carried out under the same conditions, but stopping after a longer reaction time of contact with the acid, yielded the same product composition within the experimental error. Experiments showed that the diols **12** and **13** are stable under the saponification conditions and that the method of saponification used does not alter the stereoselectivity of the reactions.

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Solubilization of Picric Acid by Reversed Micelles of a Double-Chained *N*-Methylpyridinium Chloride Amphiphile

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A spectrophotometric study was made of the binding of picric acid (HP) to reversed micelles of 17-(*N*-methyl-4-pyridinio)tritriacontane chloride (1) in cyclohexane and chloroform. Vapor pressure osmometric (VPO) measurements on solutions of 1 in cyclohexane at 50 °C indicate that the apparent number averaged aggregation number ($\bar{N}_{NA}$) is 16 down to surfactant concentrations of at least 3×10^{-3} *m*. Similar measurements (at 37 °C) on 1 in chloroform indicate a much smaller tendency to aggregate ($\bar{N}_{NA} \leq 2$ up to $[1] = 9 \times 10^{-2}$ *m*). When solutions of 1 in cyclohexane or chloroform were mixed with solutions of HP in the same solvents, a yellow color developed, and the features of the absorption spectrum can be reconciled with the formation of an ion pair. A similar ion pair is formed in solutions of HP in solvents of sufficient polarity and proton-acceptor ability. The spectral behavior of the HP indicator in cyclohexane at varying surfactant concentrations at 37 °C was quantitatively described in terms of simple association equilibria between HP and the surfactant aggregates. The VPO data were incorporated into this analysis. It appears that the results provide a quite realistic picture of the aggregation process, the mean aggregation number increasing with surfactant concentration and gradually reaching a limiting value. A similar treatment of the data for chloroform as the solvent also gave satisfactory results, but at low surfactant concentrations dissociation of the surfactant monomer should be invoked to rationalize the optical absorption measurements.

Many surfactant molecules are known to aggregate in apolar, aprotic solvents.[1-4] These aggregates, called reversed or inverted micelles, are stabilized by dipole–dipole and ion-pair interactions and are capable of solubilizing

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