

recorded on a Bruker WM-250 spectrometer. Temperature measurements were based on the chemical shift separation of an ethylene glycol sample and utilization of the van Geet relationship.<sup>30</sup> Mass spectra were measured on a Kratos MS 50 RFA spectrometer. Melting points were recorded on a Thomas-Hoover melting point apparatus and are corrected. The elemental analyses were performed by Schwarzkopf Microanalytical Laboratory, Woodside, NY.

**Chloropentamethylbenzene.** To a solution of pentamethylbenzene (1 g, 6.8 mmol) in 10 mL of CCl<sub>4</sub> was added 0.6 mL of SO<sub>2</sub>Cl<sub>2</sub> (1 g, 7.4 mmol) and 0.3 g of silica gel (60–200 mesh). After the mixture stood for 12 h at room temperature (without stirring), the solvents were evaporated, and the residue was added to the top of a short silica gel column. Elution with hexane afforded 260 mg (21%) of chloropentamethylbenzene, mp 152–153 °C (lit.<sup>31</sup> mp 153–155 °C).

(30) Van Geet, A. L. *Anal. Chem.* 1968, 40, 2227; 1970, 42, 679.

(31) Andrews, L. J.; Keefer, R. M. *J. Am. Chem. Soc.* 1957, 79, 5169.

**Chloropentakis(dichloromethyl)benzene (2).** A slow stream of chlorine gas was bubbled through a refluxing solution of chloropentamethylbenzene (130 mg) in 20 mL of CCl<sub>4</sub> while the reaction mixture was irradiated with a 150-W tungsten lamp. After 24 h, the reaction mixture was cooled, and the solid that deposited in the gas inlet was collected. The product was recrystallized from 1,1,2,2-tetrachloroethane to afford 65 mg (14%) of pure 2, mp >300 °C: <sup>1</sup>H NMR (CDCl<sub>2</sub>CDCl<sub>2</sub>, room temperature) δ 7.89 (s, 1 H, *o*-CH), 8.13 (s, 1 H, *m*-CH), 8.22 (s, 1 H, *o*-CH) 8.25 (s, 1 H, *p*-CH), 8.27 (s, 1 H, *m*-CH); exact mass calcd for C<sub>11</sub>H<sub>5</sub><sup>35</sup>Cl<sub>9</sub><sup>37</sup>Cl<sub>2</sub> 525.6904, found 525.6876. Anal. Calcd for C<sub>11</sub>H<sub>5</sub>Cl<sub>11</sub>: C, 25.06; H, 0.96. Found: C, 25.12; H, 0.92.

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**Registry No.** 2, 111351-51-0; chloropentamethylbenzene, 5153-39-9.

## Interpretation of Conjugated Oxiranes Behavior toward Nucleophiles

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The behavior of conjugated oxiranes toward nucleophiles has been rationalized by means of perturbational theory and MNDO calculations. Metal ion coordination to the oxiranic oxygen seems to be important in the regioselectivity of the 1,2-addition on  $\alpha,\beta$ -epoxy esters.

Conjugated oxiranes, i.e., oxiranes directly bonded to a  $\pi$ -electron system, are synthetically important frameworks capable of sustaining regioselective reactions (1,2-addition, 1,4-conjugate addition, or 3,4-addition) depending on the reactant.<sup>1</sup> However, this rather diverse behavior toward nucleophiles in neutral or basic conditions has not yet been fully interpreted in terms of a sound theory.

We found it convenient to interpret the results by MNDO<sup>2,3</sup> calculations on several simple model compounds in terms of a combination of perturbational and hard and soft acid and base (HSAB) theories. We present herein a summary of our study qualitatively interpreted.

According to Klopman–Salem equation,<sup>4</sup> nucleophilic attack on conjugated oxiranes is governed by the combination of Coulombic interactions between reactant and substrate at the reactive site and the interactions between the occupied molecular orbitals (MO) of the nucleophile and the unoccupied MO of the substrate. In our approach reactants were classified on the basis of HSAB concept, and only the LUMO and atomic charge distribution of oxiranes (obtained by MNDO calculations on model compounds including full geometry optimization) were con-

**Table I. Four Types of Conjugate Oxiranes with LUMO and Atomic Charge Distribution Obtained by MNDO. The Experimentally Preferred Sites of Attack by Nucleophiles are Shown by the Arrows**

type	model molecule and experimental site of attack <sup>a</sup>	MNDO	
		LUMO <sup>b</sup>	charge distribution
A			
B			
C			
D			

<sup>a</sup> Open arrow for soft base and solid arrow for hard base.

<sup>b</sup> Numbers refer to  $\sum c^2$  for atomic valence orbitals on each atom.

sidered. The compounds studied were grouped into four classes, A, B, C, and D, depending on the  $\pi$ -electron system conjugated to the oxirane being the representative of each class: vinyl- (1), formyl- (2), acetyl-(enolate) (3), and (methoxycarbonyl)oxirane (4), respectively. In Table I these compounds are depicted jointly with the calculated




















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(4) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions*; Wiley: Chichester, 1978; p 27.

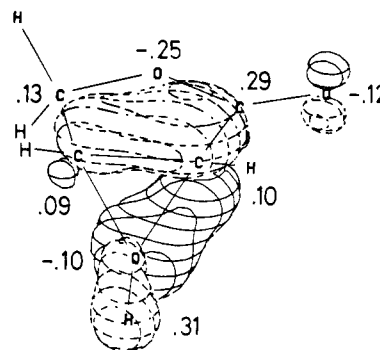
**Table II. Typical Examples of Nucleophilic Addition to Conjugate Oxiranes**

type	oxirane	nucleophile	major product	
			addition	% yield (ref)
A		Me <sub>2</sub> CuLi	1,4	 96 (5)
		Me <sub>2</sub> Mg	1,2	 81
		Me <sub>2</sub> CuLi	1,4 + 1,2	 42 + 49 (6)
		MeLi	1,2	 100
B		NaBH <sub>4</sub>	3,4	 100 (7b)
		RMgBr	3,4	 88 (8,9)
C		MeLi	1,2	 93 (11a)
		Me <sub>2</sub> CuLi	1,4	 80
		(MeCuCN)-Li	1,4	 75 (11b)
D		Me <sub>2</sub> CuLi	1,2	 67 (13)
		MeLi	1,2	 1 (13)
		Me <sub>2</sub> CuLi	1,2	 18 (14)

atomic orbital contributions and charges.

Type A oxiranes show no contribution of the C-1 and C-2 atomic orbitals in their LUMO, but the largest coefficient is at the C-4 carbon atom. Then, a soft nucleophile is most likely to react at this point (*orbital control*) leading to 1,4-addition with ring opening, while a hard nucleophile will attack under *charge control* seeking the most positive center (ring carbon atoms). Indeed, Me<sub>2</sub>CuLi (soft reagent) reacts with 3,4-epoxy-1-butene (1)<sup>5</sup> and with 3,4-epoxycyclohexene (5)<sup>6</sup> under orbital control (although the later also reacts through charge control). On the other hand, hard nucleophiles always attack the ring carbon atoms, and more precisely the C-2 carbon atom (the results of typical additions to a variety of epoxides are referred on Table II and have been obtained from the literature).

In contrast, type B oxiranes usually do not give ring-opened products when treated with a nucleophile.<sup>7</sup> As shown with a simple model, formyloxirane (2), theory predicts that both hard and soft bases will attack C-3 in preference to any other carbon atoms: C-3 has the largest contribution to the LUMO, as well as the largest atomic charge. Again, experiments reinforce theory, and most of the examples agree with these arguments. For instance, the reaction of  $\alpha,\beta$ -epoxy ketones with hydrides<sup>7</sup> and Grignard reagents<sup>8</sup> afford epoxy alcohols instead of hy-



**Figure 1.** LUMO drawing<sup>15</sup> of the protonated lactone 12 as obtained by MNDO calculations. Atomic charges are as follows: C-1 = 0.09, C-2 = 0.10, C-3 = 0.29, and O-4 = -0.12.

droxy ketones, as occurs in 6 and 7 ( $\alpha,\beta$ -epoxycyclopentanones), and if conditions are forced, diols are obtained.<sup>9</sup> The contrasting behavior between types A and B is formally the result of replacing the C-4 methylene of 1 by an oxygen atom.

Types C and D are formally obtained when an oxygen atom is introduced into the C-3 position of types A and B, respectively; the behavior of the resulting conjugated oxiranes is influenced accordingly. Type C, modeled by the enolate anion of acetyloxirane (3), shows a very high LUMO (6.8275 eV) with a large electron density on the C-1 and C-2 atoms (Table I). Moreover, the largest charge density is on the C-3 position (bearing both the oxygen and the oxirane ring). However, C-1 and C-2 are also positively charged. Then, a soft nucleophile would react, yielding 1,4-addition products with ring opening, and a hard reactant will probably find difficulties in approaching the most positive C-atom due to the nearby negative charge on oxygen. Experimental results on this type of oxirane can be found in literature,<sup>10</sup> and it has been stated that their behavior is similar to that of allylic oxiranes. The umpolung of C-3 alkyl substituted type B oxiranes converting them into the type C class has been successfully used in natural product synthesis,<sup>11</sup> and products show mainly addition at the  $\alpha'$ -carbon atom of the alkyl substituent. This is indeed the case of the enolate ion 8<sup>11a</sup> and of the trimethylsilyl enol ether 9<sup>11b</sup> of the  $\alpha,\beta$ -epoxycyclohexanone.

Type D, modeled by methyl  $\alpha,\beta$ -epoxypropionate (4) is expected to react with a nucleophile always at the C-3 position. Only one example, 10, has been reported<sup>12</sup> which records a high yield of 1,2-adduct by reaction with the soft Me<sub>2</sub>CuLi but a very poor yield with the hard MeLi. A related compound, lactone 11, also undergoes only 1,2-addition by soft nucleophiles, albeit in somewhat low yield.<sup>13</sup>

In all known examples of 1,2-addition of nucleophiles to conjugated oxiranes (only a part of these is given in Table II), the base always attaches to the C-2 atom instead of to the C-1 atom. This observation is rather surprising

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since the difference between these two positions regarding orbital coefficients in the LUMO and atomic charge densities is not large enough to warrant such a high selectivity on C-2 carbon atom, at least on model compounds of types C and D. We suspect that coordination of a metal ion as a Lewis acid with the oxirane oxygen preceding the nucleophilic attack of the base may be the cause. In order to simulate metal ion coordination at the oxirane oxygen in the simplest possible way, the approach of a proton to the oxirane oxygen of  $\alpha,\beta$ -epoxy- $\gamma$ -butyrolactone (**12**) was simulated with the MOPAC program. An intermediate was obtained at a O...H distance of 0.96 Å. Full geometry minimization on this intermediate was carried out and the final results denoted a molecule having an almost symmetrical oxirane ring. The atomic orbital contributions to the calculated LUMO of this cationic intermediate showed that the most reactive center toward a soft nucleophile will be the C-2 atom,<sup>14</sup> while the C-3 position is still the hardest carbon atom (charge control; Figure 1).

(14) IUPAC numbering was not maintained, to keep consistency with in Table I compounds.

(15) Molecular orbital representation obtained by PSI/77 program: Jorgensen, W. L. QCPE program 340.

In summary, we conclude that a consistent explanation for the mode of addition of a base to conjugated oxiranes can be obtained by performing theoretical diagnosis based on the LUMO electron densities and charge distribution that result from molecular orbital calculations on simple model compounds on a semiempirical level like MNDO. It may be noted that the HSAB theory alone failed to correctly interpret the behavior of type B compounds toward ring opening with soft bases. The intervention of metal ion coordination seems to be important in the regioselectivity of the 1,2-addition in  $\alpha,\beta$ -epoxy esters or lactones, as deduced from MNDO calculation on the simplest possible model.

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**Registry No.** 1, 930-22-3; 2, 765-34-4; 3, 111410-09-4; 4, 4538-50-5; 12, 111410-10-7.

**Supplementary Material Available:** Full computer print out for the MNDO calculations on compounds 1-4 and 12 (43 pages). Ordering information is given on any current masthead page.

## Application of Mechanistic and Transition-State Indicators to *endo*- and *exo*-2-Norbornyl Arenesulfonates. Definition of a New Mechanistic Indicator

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We have mechanistically classified *endo*- and *exo*-2-norbornyl arenesulfonates by using two common probes: the effect on rate of added thiourea and rate correlation in aqueous ethanol and trifluoroethanol. Interestingly, the *exo* isomer is improperly classified by each of these probes because of medium-dependent ion-pair return. In search of better mechanistic indicators, pseudo-first-order solvolytic rates and products have been determined for a series of *endo*- and *exo*-2-norbornyl arenesulfonates. Using these and literature data, we have compared these substrates with others by plotting  $\alpha$ -deuterium isotope effects against  $\beta_{1g}^{Me}$  values determined for a series of arenesulfonates in the same or a similar solvent. The use of this type of plot as a heuristic method for distinguishing  $k_s$  and  $k_{\Delta}$  substrates is discussed. Finally, our product studies are consistent with the involvement of solvent-separated ion pairs in the solvolysis of 2-norbornyl arenesulfonates. Different alcohol-ether product ratios for the isomeric esters is consistent with dual pathways for product formation with the *endo* substrates.

The quite different solvolytic behavior of isomeric 2-norbornyl halides and esters has attracted considerable attention and sparked controversy.<sup>1,2</sup> A prime contributor to the controversy is the unfortunate fact that most mechanistic indicators are too imprecise to deal with the reactivity of substrates that show any complexity; clearly the 2-norbornyl substrates are not simple. Although there is no longer a controversy,<sup>2</sup> an unequivocal method for mechanistic characterization of substrates that are *weakly* solvent assisted ( $k_s$  substrates), *weakly* neighboring group assisted ( $k_{\Delta}$  substrates), and nucleophilically unassisted ( $k_c$  substrates) would still be welcome.<sup>3</sup> In this paper we evaluate *exo*- and *endo*-2-norbornyl arenesulfonates with

the use of common probes that are readily applicable to most substrates, and we discuss the results in terms of the solvolytic mechanisms and transition states. Our data further illustrates the problems with quantifying these substrates by qualitative probes.

### Results and Discussion

**Mechanistic Characterization.** Three distinct mechanisms have been identified for solvolysis reactions:<sup>3</sup> backside nucleophilic assistance by the solvent is important with the greatest number of substrates, called  $k_s$  substrates; another group of substrates ( $k_{\Delta}$  substrates) undergoes

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