

**Figure 1.** Variation of zero-point energy differences between isotopic transition states,  $\delta(\text{ZPE})^*$ , with transition-state symmetry,  $\alpha$ , in accordance with the Melander–Westheimer principle.

difference of the initial state,  $\delta(\text{ZPE})_{\text{IS}}$ ; in the absence of an equilibrium isotope effect, the product-like limit will be the same.

These ideas may be quantified by introducing a parameter  $\alpha$  to denote transition-state symmetry:  $\alpha = 0$  for a completely reactant-like transition state,  $\alpha = 1/2$  for a symmetrical transition state, and  $\alpha = 1$  for a completely product-like transition state.<sup>8</sup> The simplest continuous function relating  $\alpha$  and  $\delta(\text{ZPE})^*$  consistent with the limits imposed by the Melander–Westheimer principle is then the parabolic one shown in Figure 1 and stated by eq 4.

$$\delta(\text{ZPE})^* = \delta(\text{ZPE})_{\text{min}}^* + [\delta(\text{ZPE})_{\text{IS}} - \delta(\text{ZPE})_{\text{min}}^*](2\alpha - 1)^2 \quad (4)$$

Marcus theory provides an expression for  $\alpha$  in terms of  $\Delta G^\circ$  and  $\Delta G_0^\ddagger$ , eq 5, and insertion of this into eq 4 leads to eq 6. For-

$$\alpha = (1 + \Delta G^\circ / 4\Delta G_0^\ddagger) / 2 \quad (5)$$

$$\delta(\text{ZPE})^* = \delta(\text{ZPE})_{\text{min}}^* + [\delta(\text{ZPE})_{\text{IS}} - \delta(\text{ZPE})_{\text{min}}^*](\Delta G^\circ / 4\Delta G_0^\ddagger)^2 \quad (6)$$

mulation of the kinetic isotope effect in the usual way as the difference between transition-state and initial-state zero-point energy differences then leads to eq 7.

$$\Delta G_{\text{H}}^* - \Delta G_{\text{D}}^* = \delta(\text{ZPE})^* - \delta(\text{ZPE})_{\text{IS}} = [\delta(\text{ZPE})_{\text{min}}^* - \delta(\text{ZPE})_{\text{IS}}][1 - (\Delta G^\circ / 4\Delta G_0^\ddagger)^2] \quad (7)$$

Comparison of this expression with eq 2 shows that the two are identical in form. The maximum isotope effect which occurs at  $\Delta G^\circ = 0$  is now  $\delta(\text{ZPE})_{\text{min}}^* - \delta(\text{ZPE})_{\text{IS}}$  rather than  $\Delta G_{0,\text{H}}^* - \Delta G_{0,\text{D}}^*$  and the quantity  $\Delta G_{0,\text{H}}^* \Delta G_{0,\text{D}}^*$ , which governs how rapidly the isotope effect changes with changing  $\Delta G^\circ$ , is now replaced by a single intrinsic barrier,  $\Delta G_0^\ddagger$ . The presence of only one intrinsic barrier in eq 7 is an advantage in that it avoids any implication that two reaction series which differ only by an isotopic substitution may take place on different potential energy surfaces.

Although this expression was derived from the Melander–Westheimer principle, it is not incompatible with the alternative idea that it is not this principle but rather the tunnel effect which produces isotopic effect maxima at  $\Delta G^\circ = 0$ .<sup>5a</sup> Tunneling, and its influence on isotope effects, is expected to be greatest when  $\Delta G^\circ = 0$  and to fall off on either side of this value, becoming negligible for systems with reactant-like or product-like transition states.<sup>5a</sup> A parabolic dependence of the tunneling isotope effect on  $\alpha$  consistent with this expectation will then lead to a relationship of the same form as eq 7. Such a simple parabolic dependence is, of course, an oversimplification, for the tunnel effect is a complex phenomenon; but the factors which determine isotopic zero-point energy differences are complex as well, and eq 4 must also be an oversimplification. These approximations, however, crude though they may be, do lead to a simple expression which

(8) The parameter  $\alpha$  could be the exponent in the Brønsted relation or the order of the forming bond; in simple Marcus theory these two quantities are equal.

allows easy correlation of experimental data.

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## Hydroxymercuration of Nonconjugated Dienes in Aqueous Micelles<sup>1</sup>

Sir:

Among the reports of micellar catalysis of organic reactions,<sup>2</sup> there are only a few examples of a micelle partitioning a reaction among a variety of pathways<sup>3</sup> and none have demonstrated a general synthetic utility for selective micellar catalysis. We would like to report preliminary results of our attempts to use an anionic surfactant in aqueous medium to (a) catalyze the mercuration of simple olefins, (b) control the selective monofunctionalization of nonconjugated dienes, and (c) promote effective partitioning of a reaction intermediate into a disfavored manifold, in a predictable and synthetically useful way.

The hydroxymercuration of olefins is a reaction that is compatible with aqueous medium and ambient temperatures.<sup>4</sup> Its products (olefins, alcohols, and ethers) can be readily analyzed, and it is a system of proven synthetic utility.<sup>4b</sup> The standard mercuration procedure, involving  $\text{Hg}(\text{OAc})_2$  in  $\text{THF}/\text{H}_2\text{O}$ ,<sup>4a</sup> was modified by replacing the THF with a solution of sodium lauryl sulfate (SLS) at concentrations  $\geq 2.5$  times its critical micelle concentration. This allowed the conversion of 1-octene to 2-octanol, with both the hydroxymercuration of the olefin and the  $\text{NaBH}_4$  reduction of the alkylmercurial proceeding smoothly in the micellar medium. The exclusive formation of the Markovnikoff alcohol was comparable to the specificity of the  $\text{THF}/\text{H}_2\text{O}$  system. The SLS reaction was somewhat faster than that in  $\text{THF}/\text{H}_2\text{O}$ , but no attempt was made to precisely compare rates. Interestingly, the corresponding reaction using a cationic surfactant (hexadecyltrimethylammonium bromide) in place of SLS resulted in almost no reaction, even after extended reaction times. Our observation of the enhanced approach of mercurating agent to olefin in an anionic system and severely retarded reaction with cationic micelles is consistent with a well-precedented Coulombic attraction or repulsion at the micelle surface.<sup>2,5</sup>

We next turned our attention to the hydroxymercuration of nonconjugated dienes. Random attack on two noninteracting

(1) Portions of this work were presented at the International Symposium on Solution Behavior of Surfactants, June 30–July 3, 1980, Potsdam, NY.

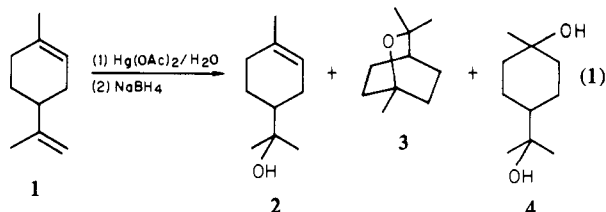
(2) An excellent review of the literature on micellar catalysis can be found in: Fendler, J. H.; Fendler, E. J. "Catalysis in Micellar and Macromolecular Systems"; Academic Press: New York, 1975. Two useful recent symposia are: "Micellization, Solubilization and Microemulsions"; Mittal, K. L., Ed.; Plenum: New York, 1977; and "Solution Chemistry of Surfactants"; Mittal, K. L., Ed.; Plenum: New York, 1979.

(3) (a) Fendler, J. H.; Fendler, E. J.; Smith, L. W. *J. Chem. Soc., Perkin Trans 2* 1972, 2097. (b) Moss, R. A.; Talkowski, C. J.; Reger, D. W.; Powell, C. E. *J. Am. Chem. Soc.* 1973, 95, 5215 and references therein. (c) Kirmse, W.; Rauleder, G.; Ratajczak, H. *J. Ibid.* 1975, 97, 4141. (d) Lapinte, C.; Viout, P. *Tetrahedron Lett.* 1974, 2401 and references therein. (e) Sukenik, C. N.; Bergman, R. G. *J. Am. Chem. Soc.* 1976, 98, 6613. (f) Bunton, C. A.; Kamengo, A. A.; Ng, P. *J. Org. Chem.* 1974, 39, 3469. (g) Jaeger, D. A.; Robertson, R. E. *J. Org. Chem.* 1977, 42, 3298. (h) Recent examples of stereochemical selectivity can be found in: Moss, R. A.; Lee, Y. S.; Lukas, T. J. *J. Am. Chem. Soc.* 1979, 101, 2499 and references therein; and in: Nakamura, Y.; Kato, T.; Morita, Y.; American Chemical Society/Chemical Society of Japan Chemical Congress, Hawaii, 1979; American Chemical Society: Washington, DC, 1979; Abstract No. ORGN-147.

(4) (a) Brown, H. C.; Geoghegan, P. J. *J. Org. Chem.* 1970, 35, 1844. (b) Selected reviews of the mercuration of olefins: Kitching, W. *Organomet. Chem. Rev.* 1968, 3, 61. Seyferth, D. *J. Organomet. Chem.* 1972, 41, 155. Larock, R. C. *Angew. Chem., Int. Ed. Engl.* 1978, 17, 27.

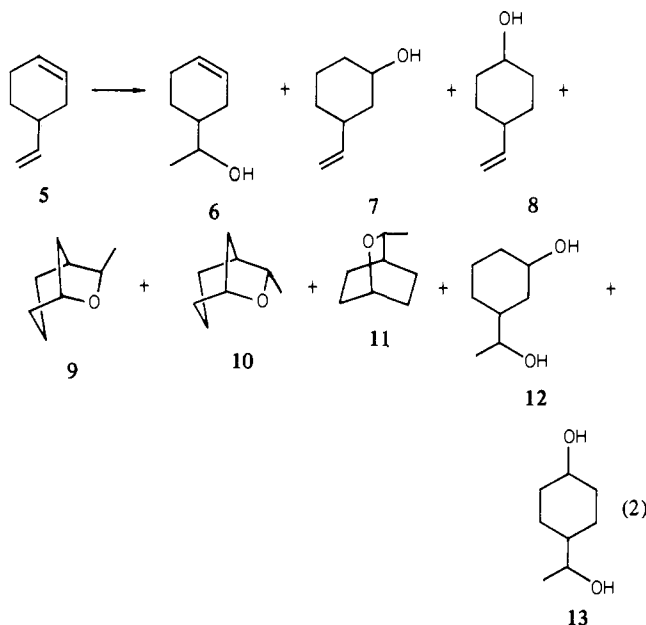
(5) Particularly for divalent cations, see: (a) Robb, I. D. *J. Colloid Interface Sci.* 1971, 37, 521. (b) Larsen, J. W.; Magid, L. *J. Am. Chem. Soc.* 1974, 96, 5774.

double bonds in a molecule with 1 equiv of  $\text{Hg}(\text{OAc})_2$  would predict a product mixture of 1:2:1 (starting diene-enol-diol). Reaction at the second double bond could lead to diol by reaction with  $\text{H}_2\text{O}$  or to cyclic ether by intramolecular trapping by the first formed alcohol. These problems are made less severe in some systems with nonequivalent double bonds by selective mercuration based on electronic and steric factors.<sup>4</sup> An example of such a competition is seen<sup>6</sup> in the conversion of limonene to a mixture of a monool, cyclic ether, and a diol (eq 1). The reaction of 1



equiv of  $\text{Hg}(\text{OAc})_2$  with limonene in  $\text{THF}/\text{H}_2\text{O}$  yields a mixture of 70% monool (2), 14% ether and diol (3 and 4), and 19% recovered starting material. We have found that this same reaction in aqueous SLS solution produces a 97% yield of monool (2).<sup>7,8</sup>

In an even more dramatic example, we have reinvestigated the mercuration of 4-vinylcyclohexene. Under standard  $\text{THF}/\text{H}_2\text{O}$  reaction conditions, 1 equiv of  $\text{Hg}(\text{OAc})_2$  yields the complex mixture shown in eq 2. The major monool product (6) never



exceeds a 20–25% yield, and the monoools are formed along with an equimolar amount of diols.<sup>6</sup> When this reaction is done in aqueous SLS, it produces 90% pure monool (6).<sup>9</sup>

A simple explanation of this selective mono reaction is that, despite the dynamic nature of the micellar aggregate and its solubilizates, there is some net anisotropy imparted to the substrate by the micelle. We would suggest that on a time-average basis there is a net orientation of the newly created polar end of the

(6) Brown, H. C.; Geoghegan, P. J.; Lynch, G. J.; Kurek, J. T. *J. Org. Chem.* **1972**, *37*, 1941.

(7) (a) Bambagiotti et al.<sup>7b</sup> report that this reaction yields a 1:1 mixture of monool and diol. This discrepancy with the results in ref 6 is not commented on. We have, however, been able to reproduce the results in ref 6 and are thus content to compare our SLS system to the  $\text{THF}/\text{H}_2\text{O}$  systems reported in ref 6. If anything, comparison of our results in SLS with the results in ref 7b would make for an even more impressive contrast. (b) Bambagiotti, M.; Vincieri, F. F.; Coran, S. A. *J. Org. Chem.* **1974**, *39*, 680.

(8) All yields are by calibrated GLC analysis. Concentrations of both olefin and surfactant were 20–100 mM.

(9) Selected controls, with added sodium methyl sulfate instead of the SLS and with  $\text{HgSO}_4$  instead of  $\text{Hg}(\text{OAc})_2$ , confirmed that the results reported both in these systems and in those discussed below could not be achieved without micellar SLS.

monoreacted molecule toward a hydrophilic environment, forcing the more hydrophobic portion of the molecule into a less favorable environment for reaction. Further support for this hypothesis was obtained from the mercuration of 1,7-octadiene in SLS. This flexible, linear substrate yielded an almost statistical mixture of diene, monool, and diol. This is consistent with the independent reaction of the two chain ends and the inability of the micelle to constrain an unreacted end of a flexible chain in a hydrophobic environment. This test is revealing both in limiting the synthetic scope of the micelle-mediated reaction and in its concurrence with our explanation for the micellar perturbation of the more rigid systems.

A second problem in the mercuration of nonconjugated dienes is that in systems where intramolecular cyclic ether formation is possible, doubly reacted material will typically partition between diols and cyclic ethers. While earlier investigation of both limonene and 4-vinylcyclohexene did not precisely identify and quantify the ether products,<sup>6</sup> we have done so.<sup>10</sup> We find that upon reaction with either 2 or 3 equiv of  $\text{Hg}(\text{OAc})_2$  in  $\text{THF}/\text{H}_2\text{O}$ , limonene gives an ether-diol ratio of 1:3. Similarly, the 4-vinylcyclohexene produces three ethers, 9, 10, and 11 (9 is the major isomer), and the ratio of ethers (9 + 10 + 11) to diols (12 + 13) is slightly less than 1:1. In contrast, when either substrate is reacted in SLS medium, the products are drastically shifted in favor of ether formation. Using 2 or 3 equiv of  $\text{Hg}(\text{OAc})_2$  in aqueous SLS solution changes the limonene products from predominant diol to ~95% cyclic ether and the vinylcyclohexene reaction from a slight preference for diol to an 8:1 ether-diol ratio.<sup>11</sup>

We suggest that while mercuration in bulk aqueous medium allows attack by solvent to compete with, and even overwhelm, intramolecular alcohol attack, mercuration at the surface of an anionic micelle takes advantage of the strong stabilization of the cationic mercury species by the anionic surfactant head groups and thus forces out the water that would have otherwise solvated the cationic complex. This effectively lowers the water concentration in the immediate vicinity of the reaction site<sup>12</sup> and allows much more favorable competition by the intramolecular nucleophile than is otherwise possible.<sup>13</sup>

We are exploring the scope of this micelle-mediated mercuration and of related systems in terms of both kinds of reaction selectively discussed here. Extensions of this work to other reagents and other cyclization reactions are also in progress. The implications of these results for theories of micellar organization<sup>14</sup> will be discussed in a full paper.

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(10) Assignments in the limonene system are based on comparison to known compounds. The vinylcyclohexenemonools were assigned on the basis of comparison with authentic material and diols were assigned by their spectral properties and by analogy to the monoools. Structures 9, 10, and 11 were assigned on the basis of spectral data and analogy to model compounds.

(11) Despite the shift in ether-diol ratio, 9 always accounts for 75–85% of the ether products.

(12) This explanation finds some analogy in the explanation of micellar rate retardation in ref 3e and in micellar control of deamination stereochemistry in ref 3b.

(13) Support for this explanation can be inferred from the quantitative conversion of terpineol (2) to cineole (3) by mercuration in anhydrous THF. See: Coxon, J. M.; Hartshorn, M. P.; Mitchell, J. W.; Richards, K. E. *Chem. Ind. (London)* **1968**, 652.

(14) Menger, F. M. *Acc. Chem. Res.* **1979**, *12*, 111.

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