Modeling Chemical Reactivity. 3. Stereochemistry of Michael Additions of Vinyl Sulfoxides

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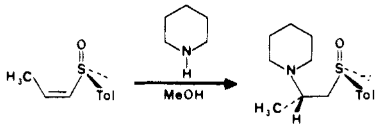
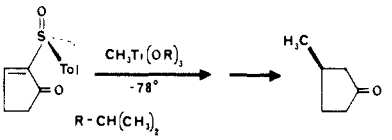
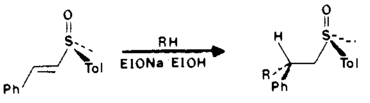
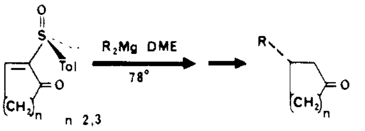
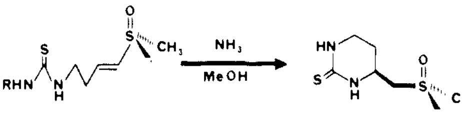
Received May 20, 1985

The synthesis of optically pure molecules represents one of the major challenges of modern organic chemistry. In order to effect the rational design of useful synthetic strategies, detailed understanding of the stereochemical course of reactions is often required. Such understanding may ultimately lead to a conceptual framework with which to extend present knowledge to as yet unexplored systems. While the determination of reaction stereochemistry remains largely the domain of the experimental science, reliable theoretical techniques continue to be developed and applied to systems of ever increasing complexity. The application of one such technique concerns us at present.

Enantiomerically pure vinyl sulfoxides have begun to find use as reagents in stereospecific syntheses. For example, they have been shown to undergo stereospecific Diels–Alder reactions with electron-rich dienes[1] and to be highly diastereoselective as Michael acceptors with a variety of nucleophiles.[2] In the latter series of reactions, the available data have generally been interpreted in terms of nucleophilic addition onto the less crowded side of the vinyl group, i.e., anti to the "bulky" phenyl or tolyl group and syn either to the sulfur oxygen or lone pair, depending on conformation.[3] Such an interpretation follows a tradition in mechanistic organic chemistry of reliance on steric arguments and underscores the fundamental lack of knowledge about the role that electronic factors are likely to play in dictating overall reactivity. Clearly, the asymmetric environment provided the vinyl group by the sulfoxide substituent will render the diastereotopic olefin faces electronically dissimilar, leading to a bias for nucleophilic addition onto one or the other. The question is whether reagents discriminate strictly on the basis of size or whether other factors might also play important roles.

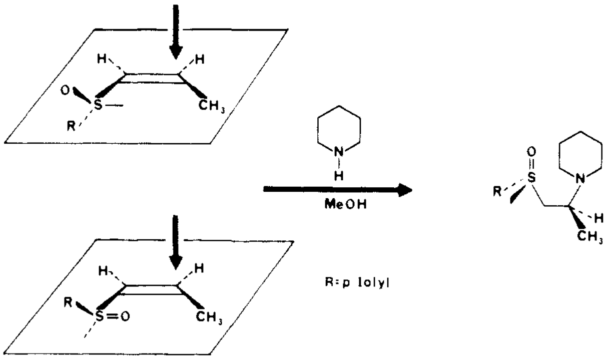
It is clear that the mode of stereodifferentiation of nucleophilic additions to vinyl sulfoxides may be determined only after the conformation of the reactive species has been established. For example, the observed stereoproduct of the Michael addition of piperidine to (−)-(*R*)-(*Z*)-propenyl *p*-tolyl sulfoxide[2b] is consistent either with approach of the nucleophile from the side of the tolyl group in a reactive conformer in which the SO and CC bonds are cis coplanar or from the side of oxygen in a conformer in which the sulfur lone pair eclipses the double bond, i.e., Here, as in other examples, (Table I), unambiguous assignment of mechanism is hindered by the possibility of two (or more) stereochemically distinct reactive conformers. We have assumed that the conformer in which CC and SO bonds are *cis* coplanar will dictate eventual product distributions, on the basis of both its high relative abundance and high reactivity (vide supra).

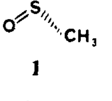
Table I. Experimental Stereochemistry of Michael Additions to Vinyl Sulfoxides[a]

reaction	ref	side of nucleophilic attack
	2b	tolyl
	2g	tolyl
	2c	lone pair
	2e	lone pair
	2c	lone pair

[a] See text for discussion.

According to 3-21G$^{(*)}$//3-21G$^{(*)}$ calculations,[4,5] the conformational energy profile for methyl vinyl sulfoxide incorporates two potential minima; these are forms in which the SO bond and the sulfur lone pair are (approximately) syn to C=C. Structure **1** is 3.5 kcal mol^{-1} more stable than **2** at this level. 6-31G*//3-21G$^{(*)}$ calculations[6] show the same ordering of stabilities but a smaller difference of 1.6 kcal mol^{-1}. The calculated conformational energy profiles for (*Z*)-1-propenyl sulfoxide and (*Z*)-1-propenyl methyl sulfoxide are qualitatively similar. Again only two minima exist (corresponding to structures in which the SO linkage and the sulfur lone pair eclipse the CC bond), and again those in which

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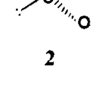
2

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(1) [4 + 2] cycloadditions: (a) DeLucchi, O.; Marchioro, C.; Valle, G.; Modena G. *J. Chem. Soc., Chem. Commun.* **1985**, 878. (b) Koizumi, T.; Hakamada, I.; Yoshii, E. *Tetrahedron Lett.* **1984**, *25*, 87. (c) Maigan, C.; Raphael, R. A. *Tetrahedron* **1983**, *39*, 3245. [3 + 2] cycloadditions: (d) Marino, J. P.; Perez, A. D. *J. Am. Chem. Soc.* **1984**, *106*, 7643.

(2) (a) Posner, G. H. In "Asymmetric Synthesis"; Morrison, J. O., Ed.; Acadmic Press, New York, 1983; Vol. 2, p 225. (b) Abbott, D. J.; Colonna, S.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1971**, *471*. (c) Tsuchihashi, G.; Mitamura, S. M.; Inoue, S.; Oguro, K. *Tetrahedron Lett.* **1973**, 323. (d) Hansen, J. J.; Kjaer, A. *Acta Chem. Scand., Ser. B* **1974**, *B28*, 418. (e) Posner, G. H.; Hulce, M. *Tetrahedron Lett.* **1984**, 379. (f) Iwata, C.; Hattori, K.; Uchida, S.; Imanishi, T. *Ibid.* **1984**, 2995. (g) Posner, G. H.; Frye, L. L.; Hulce, M. *Tetrahedron* **1984**, *40*, 1401. (h) Iwata, C.; Fujita, M.; Hattori, K.; Uchida, S.; Imanishi, T. *Tetrahedron Lett.* **1985**, 2221.

(3) Vinyl sulfoxides for which conformation may be dictated by chelation via an added Lewis acid will be discussed in a forthcoming full paper.

(4) All calculations were run by using GAUSSIAN 85 as implemented on a Harris H800 computer. Hout, R. F., Jr.; Francl, M. M.; Kahn, S. D.; Dobbs, K. D.; Blurock, E. S.; Pietro, W. J.; McGrath, M. P.; Steckler, R.; Hehre, W. J., unpublished.

(5) 3-21G basis set for first-row elements: (a) Binkley, J. S.; Pople, J. A.; Hehre, W. J. *J. Am. Chem. Soc.* **1980**, *102*, 939. 3-21G$^{(*)}$ basis set for second-row elements: (b) Pietro, W. J.; Francl, M. M.; Hehre, W. J.; DeFrees, D. J.; Pople, J. A.; Binkley, J. S. *Ibid.* **1982**, *104*, 5039.

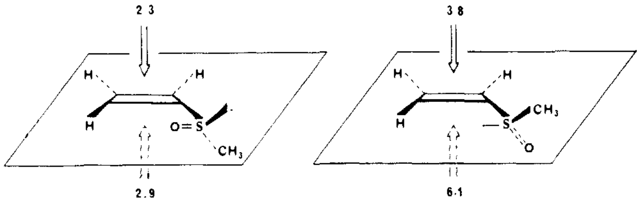
(6) 6-31G* basis set. First-row elements: (a) Hariharan, P. C.; Pople, J. A. *Chem. Phys. Lett.* **1972**, *66*, 217. Second-row elements: (b) Francl, M. M.; Pietro, W. J.; Hehre, W. J.; Binkley, J. S.; Gordon, M. S.; DeFrees, D. J.; Pople, J. A. *J. Chem. Phys.* **1982**, *77*, 3654.

0002-7863/86/1508-7399$01.50/0

the SO and CC bonds are approximately syn are the more stable.[7,8]

Relative reactivities and stereochemical preferences of the two stable conformers of methyl vinyl sulfoxide have been obtained by direct comparison of the affinities of the diastereotopic faces of the incorporated olefin toward a test nucleophile, in our case hydride anion.[9] Information relating to the relative nucleophilic reactivities of the diastereotopic olefin faces may then be "extracted" either visually, by direct inspection of the reactivity information as superimposed onto the substrate electron-density surface, or by constructing average potentials.[13a-c]

Average hydride potentials for the diastereotopic faces of the two stable conformers of methyl vinyl sulfoxide are provided below.



These show that the favored direction of approach in both conformers is from the side of the methyl group, i.e., away from the sulfur lone pair in the ground-state structure, and anti to the SO bond in the higher energy form. While it is entirely reasonable that an approaching nucleophile would prefer to avoid areas of high electron density, this is contrary to steric considerations. The small difference in reactivities between the more reactive faces of the two conformers is not likely to be significant in view of the large conformational bias in favor of form **1**. Thus, we have interpreted the experimental data explicitly in terms of conformers analogous to **1**.[3,8]

The observed stereochemistry of the first two reactions illustrated in Table I are in accord with the results of the theory; that is, nucleophilic attack occurs preferentially anti to the sulfur lone pair. On the other hand, the experimental stereochemistry for the remaining three examples appears to disagree with the models. Note, however, that these are situations in which the reagent contains an electrophilic site, i.e., the metal of an organometallic reagent (entries 3 and 4 in Table I) or an acidic proton (entry 5 in Table I), which would allow for the possibility of ion pairing between the sulfur lone pair (or sulfoxide oxygen), and therefore lead to an overiding of the fundamental preference for the nucleophile to avoid centers of electron density.[14]

Acknowledgment. We thank Professor G. H. Posner (John Hopkins University) for helpful discussions during the course of preparation of this manuscript.

Registry No. 1, 10258-86-3; hydride anion, 12184-88-2.

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(7) Conformational preferences in vinyl sulfoxides have previously been rationalized on the basis of dipole minimization: Trost, B. M.; Salzmann, T. N.; Hiroi, K. *J. Am. Chem. Soc.* **1976**, *98*, 4887.

(8) Preliminary results indicate that substitution may destabilize forms such as **2**. Details will be presented in a full paper.

(9) Application follows in three stages from an appropriate quantum mechanical wave function.[10] First, a surface of constant electron density, corresponding to $\psi^2 = 0.002$ electrons/bohr^3, is defined.[11] Next, the test reagent, as defined by the radius of its electron-density surface,[12] is rolled upon the substrate density surface, to generate a series of points elevated above this surface (at the reagent/substrate "contact" distance). Finally, the energy of interaction between reagent and substrate is evaluated at each of these locations. In the simplest model, this energy accounts only for Coulombic interactions between the fixed charge distrubtions on the substrate and reagent. Reorganization of the electron distribution of the substrate, charge transfer between reagent and substrate, and geometrical relaxation have not been allowed for. Full details of the numerical procedures involved, as well as further examples of applications, have been presented elsewhere.[13]

(10) 3-21G$^{(*)}$ wave functions[5] have been used throughout.

(11) See: Francl, M. M.; Hout, R. F., Jr.; Hehre, W. J. *J. Am. Chem. Soc.* **1984**, *106*, 563.

(12) 1.547 Å at the 3-21G level. See ref 11.

(13) (a) Pau, C. F.; Hehre, W. J. *J. Comput. Chem.*, submitted for publication. (b) Hehre, W. J.; Pau, C. F.; Hout, R. F., Jr.; Francl, M. M. "Molecular Modeling. Computer-Aided Descriptions of Molecular Structure and Reactivity"; Wiley: New York, 1987. (c) Kahn, S. D.; Pau, C. F.; Overman, L. E.; Hehre, W. J. *J. Am. Chem. Soc.*, in press. (d) Kahn, S. D.; Pau, C. F.; Hehre, W. J. *Ibid.*, in press.

(14) The stereochemical role of the metal in organometallic additions to chiral vinyl sulfoxides, among other substrates, is currently under study in our laboratory.

A New Group of Ruthenium Complexes: Structure and Catalysis

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Received December 10, 1985

The isolation and structural characterization of intermediate transition-metal complexes that participate in catalytic processes are of prime importance in elucidating and understanding mechanistic features of homogeneous catalysis. Herein we report on the structure and catalytic aspects of a new class of ruthenium complexes.

Recently we have reported that complexes **1** and **2** are both active in the following catalytic reactions: (a) bimolecular dehydrogenation of primary alcohols to esters in the presence or absence of H acceptors;[1] (b) dehydrogenation of secondary alcohols to ketones;[1] (c) hydrogenation of ketones, olefins, and acetylenes under moderate hydrogen pressure and temperature.[2]

$$(\eta^4\text{-}\mathrm{Ph_4C_4C{=}O})(\mathrm{CO})_3\mathrm{Ru} \qquad [(\eta^4\text{-}\mathrm{C_4H_4C{=}O})(\mathrm{CO})_2\mathrm{Fe}]_2$$

1 **2a**

$$[(\eta^4\text{-}\mathrm{Ph_4C_4C{=}O})(\mathrm{CO})_2\mathrm{Ru}]_2$$

2

X-ray crystallography has revealed a η^4-bonding of the cyclopentadienone (CPD) ligand to ruthenium in complex **1**.[3] Refluxing **1** in propanol results in an orange crystalline solid (85%) for which we have previously proposed the dimeric formula **2**,[1,2] in analogy with the isoelectronic iron complex **2a**[4,5] and on the basis of analytical, spectral, and chemical data. Hubel et al.[4] proposed a centrosymmetric structure with two $>\mathrm{C{=}O}\rightarrow\mathrm{Fe}$ coordination bonds for the dimer **2a**. Since complex **2** plays a central role in our catalytic schemes, it is extremely important to ascertain its molecular structure. We could not crystallographically characterize **2**, as crystals were unsuitable for diffraction analysis.

Now we have reinvestigated the NMR spectrum of **2** which was found to exhibit a signal at δ −17.75, integrating as one hydrogen (hydride) relative to 40 aromatic hydrogens atoms, i.e., two Ru atoms. Obviously, structure **2** is incompatible with this finding. Therefore, we prepared several isoelectronic–isostructural derivatives complexes (Table I). Only **3** gave crystals which were suitable for X-ray crystallography (Figure 1).[6]

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(1) Blum, Y.; Shvo, Y. *Isr. J. Chem.* **1984**, *24*, 144.

(2) Blum, Y.; Czarkie, D.; Rahamim, Y.; Shvo, Y. *Organometallics* **1985**, *4*, 1459.

(3) Blum, Y.; Shvo, Y.; Chodosh, D. F. *Inorg. Chim. Acta* **1985**, *97*, L25.

(4) Weiss, E.; Merenyl, R. G.; Hubel, W. *Chem. Ind.* (*London*) **1960**, 407.

(5) Reppe, W.; Vetter, H. *Justus Liebigs Ann. Chem.* **1953**, *582*, 133.

(6) Crystal data for $\mathrm{Ru_2Cl_4O_6C_{62}H_{38}}$ $M = 1222.94$: monoclinic, space group $C2/c$, with $a = 26.961$ (7) Å, $b = 9.613$ (3) Å, $c = 20.367$ (5) Å, $\beta = 101.44$ (2)°, $V = 5174.0$ Å^3, $D_{\text{calcd}} = 1.570$ g·cm^{-3} for $Z = 4$; Mo Kα $\lambda = 0.71073$ Å. A total of 6433 reflections were collected using Enraf-Nonius automated diffractometer. The structure was solved by direct methods (Program MULTAN80) Fourier techniques and refined by using full-matrix least-squares methods (SDP program library with local modifications). Least-square refinement of 36 atoms (anisotropic), 18 hydrogen atoms (fixed isotropic), 390 variables, and 4572 observations converged to yield final $R = 3.09\%$ and $R_w = 4.06\%$ with $I \geq 3\sigma(I)$ and $2° \leq 2\theta \leq 55°$. A full description of the data collection and structure solution and refinement is provided in the supplementary material.

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