Solvent Effects on Conformation-Dependent Optical Rotatory Dispersion Spectra

F. M. Menger*

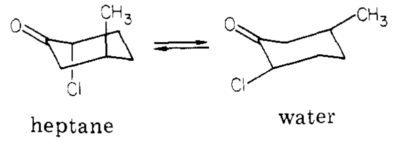
Department of Chemistry, Emory University, Atlanta, Georgia 30322

B. Boyer

Laboratoire de Chimie Organique Physique, Universite des Sciences et Techniques du Languedoc, Place E Bataillon, 34060 Montpellier Cedex, France

Received July 13, 1983

Transferring (+)-*trans*-2-chloro-5-methylcyclohexanone from water to heptane reverses the sign of the Cotton effect.[1,2] This can be ascribed to a diaxial–diequatorial equilibrium that lies further to the left in heptane than in water.[2] Since the C=O and C—Cl dipoles are poorly solvated in heptane, they tend to assume therein a less interactive perpendicular relationship even at the cost of nonbonded axial repulsions.



It seemed worthwhile to examine optical rotatory dispersion (ORD) spectra of the chloro ketone in a full array of solvents (see Table I and Figures 1 and 2) for the following reasons. (1) The molecular rotation manifests huge changes with solvent (e.g., [ϕ] at 330 nm equals +680°, +57°, and −1819° in dimethyl sulfoxide, toluene, and cyclohexane, respectively); ORD is thus a particularly sensitive reporter of solvent interactions.[3] (2) We were interested in determining how dipole–dipole interactions, as reflected in the conformational equilibria, depend on the $E_T(30)$ solvent polarity parameter. This parameter, along with the intercorrelating Z and Y values, are all derived from ionic or partially ionic systems.[4] One wonders, therefore, how well the parameters predict dipole–dipole behavior. (3) Solvent effects on the ORD spectra derive from a diaxial–diequatorial equilibrium; this is conceptually easier to grasp than excited-state or transition-state phenomena that serve as the basis for $E_T(30)$, Z, Y, and many other solvent studies.

Table I lists equilibrium constants (K = % ee/% aa) obtained from eq 1, which relates the observed molecular rotation in a particular solvent to the molecular rotations of "pure" ee and aa along with the mole fractions of each. The difficulty, of course, is to assign values to $[\phi]_{ee}$ and $[\phi]_{aa}$ at 330 nm (the wavelength used in all our calculations). For the former, we used a value of +615° obtained

$$[\phi]_{OBS} = m_f^{ee}[\phi]_{ee} + m_f^{aa}[\phi]_{aa} \qquad (1)$$

from the solvent-insensitive parent compound, (+)-3-methylcyclohexanone. (Djerassi et al.[5] showed that introducing an equatorial chlorine adjacent to a carbonyl negligibly changes the ORD curve.) For the latter, we used a value of −21 900° derived from eq 1, assuming that 11% of the chloro ketone is aa in octane.[6]

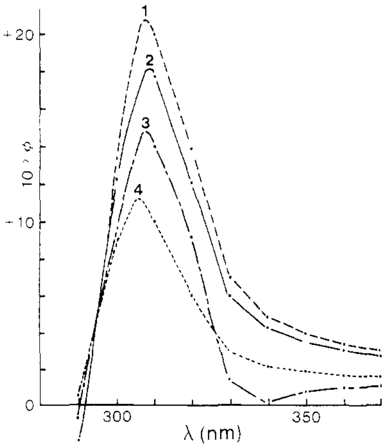


Figure 1. ORD spectra for (from top to bottom) dimethyl sulfoxide, acetonitrile, benzene, and methanol.

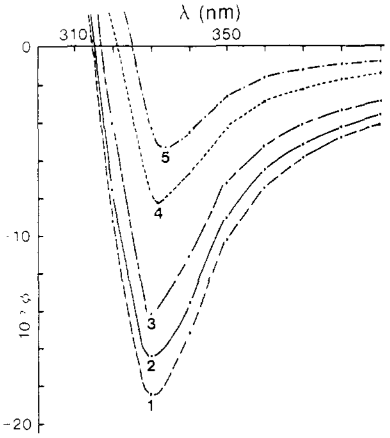


Figure 2. ORD spectra for (from bottom to top) cyclohexane, *n*-octane, carbon tetrachloride, *n*-butyl ether, and ethyl ether.

The K values in Table I involve a number of approximations that must be stated explicitly. (1) The chloro ketone conformation is assumed (certainly with an abundance of precedent[7]) to obey a two-state model. (2) ORD data at 330 nm are treated as if they arise from an n–π* transition uncomplicated by shorter wavelength transitions. This seems reasonable particularly since rotations at 330 nm and those at an even higher wavelength, 350 nm, correlate linearly with a coefficient of 0.9989. (3) As stated above, eq 1 utilizes literature constants. Although the absolute value of K are thus uncertain, the *changes* in K as a function of solvent remain useful. In summary, K values are best viewed as apparent equilibrium constants whose solvent sensitivity reflects qualitatively the intramolecular dipole–dipole relationships.

A poor agreement is evident in Table I between the K values and the dielectric constants of the corresponding solvents. Thus, chloroform (ϵ = 4.8) and ethyl ether (ϵ = 4.3) have quite different K values (48 and 21, respectively). A much better correlation is secured with the $E_T(30)$ solvent polarity scale[4] (Figure 3). Even here there exists two distinct families of solvents: protic and aprotic. The protic solvents lie well below the least-squares line drawn through the aprotic group; it is as if water and alcohols do

---

[1] Menger, F. M.; Boyer, B. *J. Am. Chem. Soc.* **1980**, *102*, 5936.

[2] Djerassi, C.; Geller, L. E.; Eisenbraun, E. J. *J. Org. Chem.* **1960**, *25*, 1.

[3] Contrast the data in Table I with the small solvent effects on the n → π* of acetone or the Cotton effects of steroidal ketones: Hayes, W. P.; Timmons, C. J. *Spectrochim. Acta* **1965**, *21*, 529. Kirk, D. N.; Klyne, W.; Wallis, S. R. *J. Chem. Soc. C* **1970**, 350.

[4] Reichardt, C. "Solvent Effects in Organic Chemistry"; Verlag Chemie: Weinheim/Bergstr., Germany, 1979.

[5] Allinger, N. L.; Allinger, J.; Geller, L. E.; Djerassi, C. *J. Org. Chem.* **1960**, *25*, 6.

[6] Wellman, K.; Djerassi, C. *J. Am. Chem. Soc.* **1963**, *85*, 3515.

[7] Eliel, E. L. "Stereochemistry of Carbon Compounds"; McGraw-Hill: New York, 1962.

0022-3263/84/1949-1826$01.50/0

Table I. Molecular Rotations at 330 nm and Equilibrium Constants K = % ee/% aa for the Conformationally Mobile (+)-*trans*-2-Chloro-5-methylcyclohexanone in Various Solvents[a,b]

solvent	[ϕ]	K	solvent	[ϕ]	K
1. dimethyl sulfoxide	680	*c*	15. benzene	108	43
2. *N,N*-dimethylformamide	614	*c*	16. toluene	57	39
3. acetonitrile	573	*c*	17. 2-propanol	34	38
4. benzonitrile	466	150	18. chlorocyclohexane	−247	25
5. anisole	396	102	19. ethyl ether	−428	21
6. methylene chloride	388	98	20. trichloroethylene	−442	20
7. water	382	95	21. *n*-butyl ether	−738	6
8. valeronitrile	370	91	22. cyclohexene	−1124	12
9. ethanol	291	68	23. carbon tetrachloride	−1386	10
10. methanol	269	64	24. heptane	−1486	9.7
11. dioxane	185	51	25. tetrachloroethylene	−1513	9.6
12. chloroform	157	48	26. hexadecane	−1537	9.5
13. fluorobenzene	151	48	27. *n*-decane	−1599	9.2
14. chlorobenzene	149	47	28. cyclohexane	−1819	8.3

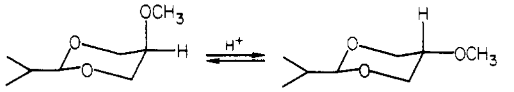
[a] Concentrations of ketone = 0.0068 M. T = 25.0 ± 0.1 °C. [b] Log K values correlate with the solvatochromic parameter π^* with a correlation coefficient of 0.89. See: Kamlet, M. J.; Abboud, J. M.; Abraham, M. H.; Taft, R. W. *J. Org. Chem.*, **1983**, *48*, 2877. [c] Too large to measure accurately.

Table II. Molecular Rotations of 17α-Hydroxy-5α-pregnan-20-one at 330 nm in Various Solvents[a]

solvent	[ϕ]	solvent	[ϕ]
1. dimethyl sulfoxide	3950	15. benzene	1930
2. *N,N*-dimethylformamide	3920	16. toluene	2210
3. acetonitrile	3110	17. 2-propanol	4150
4. benzonitrile	3480	18. chlorocyclohexane	*b*
5. anisole	2950	19. ethyl ether	3840
6. methylene chloride	991	20. trichloroethylene	707
7. water	*b*	21. *n*-butyl ether	3790
8. valeronitrile	3480	22. cyclohexene	1150
9. ethanol	3560	23. carbon tetrachloride	465
10. methanol	4180	24. heptane	334
11. dioxane	4190	25. tetrachlorethylene	341
12. chloroform	652	26. hexadecane	366
13. fluorobenzene	1780	27. *n*-decane	*b*
14. chlorobenzene	1290	28. cyclohexane	*b*

[a] [Steroid] = 5 × 10^{-4} M; T = 25.0 ± 0.1 °C. [b] Not measured.

not stabilize the ee conformation (with its parallel C=O and C—Cl dipoles) as successfully as the aprotic solvents relative to their effects on the phenoxypyridinium dye used to obtain the E_T(30) scale. Note also that among the aprotic solvents, three aromatics (anisole, benzene, and toluene) lie somewhat above the line.



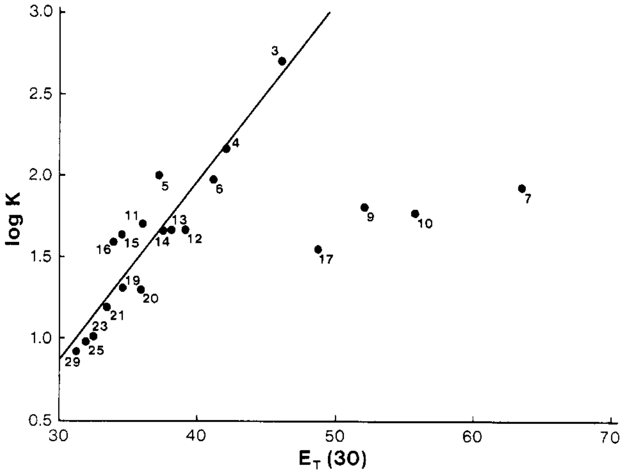


Figure 3. Plot of log K vs. E_T(30) values. Log K values and solvent numbers are based on data in Table I. Least-squares plot does not include the protic solvents (points 7, 9, 10, and 17).

Our results are strongly reminiscent of those of Eliel and Hofer,[8] who examined the solvent effects on conformational equilibria of 1,3-dioxanes. They found, as we did with our system, that benzene deviates from the E_T(30) correlation line (i.e., it behaves as a more polar solvent than one would anticipate from its E_T(30) value). This was attributed to solute dipole stabilization by solvent polarizability.[8] A much more striking deviation from the E_T(30) correlation, however, was observed for methanol.[8] We, too, find that three alcohols and water (points 7, 9, 10, and 17 in Figure 3) do not manifest the polarity implied by their E_T(30) values. Indeed, water is associated with a K orders of magnitude "too low".[9] Since the 1,3-dioxane and our chloro ketone are structurally unrelated, one might presume that the protic solvent behavior is general rather than an attribute of one particular system. The data thus lead to an important conclusion: Hydrogen bonding solvents stabilize weak dipoles much less than one would expect. Thus, *solvent polarity scales based on ionic species (E_T(30), Z, and Y) exaggerate the polarity of protic solvents when small dipole changes are involved.* Owing to their own strong solvent–solvent interactions, protic media may not properly fulfill the solvations needs of the C=O and C—Cl dipoles. We will resist the temptation to devise yet

---

[8] Eliel, E. L.; Hofer, O. *J. Am. Chem. Soc.* **1973**, *95*, 8041.

[9] Monochloroacetone is roughly one-third hydrated in water according to Bell and McDougall: Bell, R. P.; McDougall, A. O. *Trans. Faraday Soc.* **1960**, *56*, 1281. Although (+)-3-methylcyclohexanol gives a normal ORD in water (relative to other solvents), we cannot exclude the possibility that the water value in Table I is affected by hydration. The possible complication would seem insignificant in the alcohol solvents.

[10] Danilewicz, J. C.; Klyne, W. *J. Chem. Soc.* **1965**, 1306.

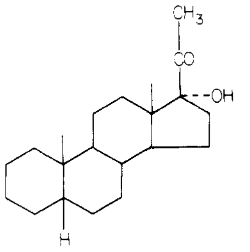
Table III. Molecular Rotations of 17α-Hydroxy-5α-pregnan-20-one at 330 nm in Mixtures of Heptane and Dioxane[a]

solvent	$[\phi]_{330}$	solvent	$[\phi]_{330}$
heptane	334	5% dioxane	2240
1% dioxane[b]	1140	10% dioxane	2960
3% dioxane	1690	dioxane	4190

[a] [Steroid] = 5×10^{-4} M; $T = 25.0 \pm 0.1$ °C. [b] Volume/volume.

another polarity scale with the data in Table I, but it can be reasonably predicted that such a scale would provide better correlations over the entire solvent range for systems not containing ionic, basic, or acidic functionalities (e.g., NR_3^+, COOH, OH, NH_2, and R_3C^+).

In related work, we examined the conformationally mobile 17α-hydroxy-5α-pregnan-20-one whose ORD spectra likewise respond markedly to the solvent (Table II). Thus, $[\phi]_{330}$ equals 4.2×10^3 in dioxane but only 0.33×10^3 in heptane. Interestingly, the molecular rotations of the steroid in Table II correlate miserably with those of the cyclohexanone in Table I (coefficient = 0.64). In particular, the steroid finds the oxygen-containing solvents (methanol, 2-propanol, dioxane, ether) much more polar relative to their effect on the cyclohexanone system. Hydrogen bonding by the steroidal hydroxy group, where the conformational mobility is centered, must play a key role. Chlorocarbons (methylene chloride, chloroform, and chlorobenzene) rank low in polarity in Table II but not so in Table I. In contrast to the protic solvents, the chlorocarbons are relatively efficient in stabilizing the opposed dipoles that exist in the ee configuration of the cyclohexanone system.



Addition of only 5% dioxane to heptane elevates the molecular rotation of the steroid from 0.33×10^3 to 2.3×10^3 (Table III). In other words, the steroid in 5% dioxane–95% heptane behaves similarly to steroid in pure dioxane, a clear indication of a solvent-sorting phenomenon.[11] ORD would seem to provide a particularly sensitive method for assessing specific solvent effects.

Experimental Section

(+)-*trans*-2-Chloro-5-methylcyclohexanone was prepared by chlorinating (+)-3-methylcyclohexanone (Aldrich).[5] Synthesis of the steroid followed known procedures.[12] All ORD spectra were obtained with a Perkin-Elmer 241 MC polarimeter and a 10-cm quartz cell thermostated at 25.0 ± 0.1 °C. Solvents were either spectrophotometric grade or distilled immediately before use.

Acknowledgment. This work was supported by the National Science Foundation and the North Atlantic Treaty Organization.

Registry No. (+)-*trans*-2-Chloro-5-methylcyclohexanone, 89616-30-8; 17α-hydroxy-5α-pregnan-20-one, 2301-91-9.

---

(11) Menger, F. M.; Singh, T. D. *J. Org. Chem.* **1980**, *45*, 183.
(12) Danilewicz, J. C.; Klyne, W. *J. Chem. Soc.* **1962**, 4950.

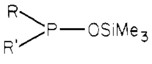
Reactions of (Silylamino)phosphines with Epoxides and Episulfides

John D. Buynak,* Nancy McKenzie Graff, and Kiran P. Jadhav

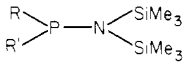
Department of Chemistry, Southern Methodist University, Dallas, Texas 75275

Received October 28, 1983

Recently, several authors[1-4] have reported the synthesis of *O*- and *N*-trimethylsilyl derivatives of phosphorus(III) compounds. Most prominent among these are the trimethylsilyl phosphites (**1**) and the [bis(trimethylsilyl)amino]phosphines (**2**). The silyl phosphites have proven useful in various synthetic and mechanistic studies. For example, the reaction of diethyl trimethylsilyl phosphite with α-halo carbonyl compounds[5] has helped to clarify the mechanism of the Perkow reaction. 1,2-Adducts of silyl phosphites with α,β-unsaturated carbonyls have also been used as homoenolate equivalents.[6]



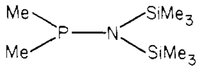
1



2

Recently, similar reactions of [(trimethylsilyl)amino]phosphines have been reported.[7] In view of their ease of preparation,[8] relatively high reactivity, and the affinity of both silicon and phosphorus for oxygen, we decided to explore the reactions of these compounds with epoxides.

The deoxygenation of epoxides was first reported by Boskin and Denny,[9] who found that (*E*)- and (*Z*)-but-2-ene epoxides are deoxygenated by triphenylphosphine at 150 °C with inversion of configuration. The mechanism of this process is believed to involve a nucleophilic ring opening, rotation, and collapse of the betaine intermediate.[10] We herein report the results of our study of the reactions of [bis(trimethylsilyl)amino]dimethylphosphine (**3**) with epoxides.



3

Results and Discussion

When **3** was heated with 1 equiv of propylene oxide in a pressure tube to temperatures as high as 150 °C, no reaction occurred. However, on the addition of 5 mol % of $ZnBr_2$, a reaction occurred at 90 °C, as observed by ^{31}P NMR, to produce a 81% yield of trimethylsiloxy phosphine imide **4** as an easily distillable air- and moisture-sensitive liquid. This reaction was repeated with several other epoxides to produce the products shown in Table I.

A survey of the products obtained shows that, despite the zinc catalysis, the phosphorus exhibits a strong preference for attack at the least sterically hindered position. With butadiene monoxide, **3** reacted with attack of

---

(1) Voronkov, M. G.; Skorik, Y. I. *Zh. Obshch. Khim.* **1965**, *35*, 106.
(2) Hata, T.; Sekine, M. *J. Am. Chem. Soc.* **1974**, *96*, 7363.
(3) Podovik, A. N.; Batyeva, E. S.; Al'fonsov, V. A. *J. Gen. Chem. USSR* **1975**, *45*, 921.
(4) Evans, D. A.; Hurst, K. M.; Truesdale, L. K.; Takacs, J. M. *Tetrahedran Lett.* **1977**, 2495.
(5) Sekine, M.; Okimoto, K.; Yamada, K.; Hata, T. *J. Org. Chem.* **1981**, *46*, 2097.
(6) Evans, D. A.; Takacs, J. M.; Hurst, K. M. *J. Am. Chem. Soc.* **1979**, *101*, 371.
(7) Neilson, R. H.; Morton, D. W. *Organometallics* **1982**, *1*, 289.
(8) Neilson, R. H.; Wilburn, J. C. *Inorg. Chem.* **1979**, *18*, 347.
(9) Boskin, M. J.; Denny, D. B. *Chem. Ind.* **1959**, 330.
(10) Bissing, D. E.; Speziale, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 2683.

0022-3263/84/1949-1828$01.50/0