# Conformational Analysis of 1-Substituted 2,3-Epoxypropanes. A Carbon-13 Nuclear Magnetic Resonance Study

Michael J. Shapiro

*Department of Chemistry, Texas Christian University, Fort Worth, Texas 76129*

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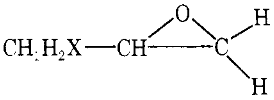
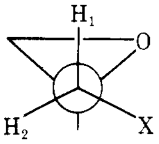
The $^{13}C$ NMR shift data for nine 1-substituted-2,3-epoxypropanes were obtained and analyzed. It was found that the $\gamma$ shift was useful in evaluating rotational preferences of the $CH_2X$ moiety. Comparison with 1-substituted propane data is also presented. Solvent effects on rotational populations were found to be unimportant.

The 1-substituted 2,3-epoxypropanes, of general formula I, pose an interesting problem in conformational analysis



I

because the barrier to rotation of the $CH_2X$ moiety is expected to be small. The problem involving rotational populations can be more simply analyzed if all eclipsed conformations are ignored, leaving only rotamers A, B, and C to be considered.



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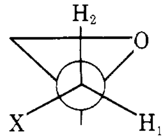

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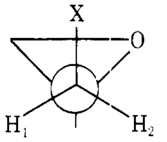

C

The stereochemistry of the epoxypropanes, particularly the halogenated derivatives, has been previously investigated using electron diffraction spectroscopy,[1] ab initio calculations,[2] dipole moments,[3] and $^1H$ NMR spectroscopy.[3,4] However, the conclusions concerning the relative importance of conformations A, B, and C are not in complete agreement. For instance, Thomas[4b] concluded that rotamer C was the least populated state for X = fluorine, while Reynolds[3] reported that B is the minor conformer. The gas-phase diffraction data apparently indicate that for X = chlorine and bromine A and B are of equal importance,[1] while Reynolds states that A is the major conformation.[3] In view of this controversy, it was felt that $^{13}C$ NMR shift data would provide useful information such that the above situation could be clarified.

The application of $^{13}C$ NMR spectroscopy to the assessment of molecular structure and stereochemical assignment is well documented.[5] These applications are facilitated by empirical correlations of substituent effects generated from systematic studies of closely related compounds.[6] Of particular utility for obtaining stereochemical assignments is the induced upfield shift observed for the resonance of a carbon which is in a gauche disposition to another carbon or heteroatom at the $\gamma$ position.[7] The "$\gamma$ effect" is ascribed to induced polarization of the charge along the $^{13}C$–H bond caused by nonbonded interactions, through space, such that the carbon in question becomes more electron rich.[8] Some caution must be exercised in this type of evaluation when the compound contains N, O, or F, since these heteroatoms also induce upfield shifts when $\gamma$-antiperiplanar to a particular carbon.[9] The proposed mechanism for this effect is amply described elsewhere.[9] Owing to the sensitivity of the carbon-13 chemical shift to this stereochemical probe, the importance of the rotamer populations for the 1-substituted 2,3-epoxypropanes can be evaluated.

## Experimental Section

All of the compounds, except where X = I, were commercially available and of high purity. These compounds were used as received. The iodo derivative was prepared by literature procedures.[3] The carbon-13 magnetic resonance spectra were obtained in the Fourier transform mode on a JEOL FX-60 spectrometer system equipped with a Texas Instruments computer with a 24K memory. The spectra were obtained at an observing frequency of 15.03 MHz. Sample concentrations were ca. 10% w/v in the appropriate solvent in 10-mm o.d. sample tubes. General NMR spectral and instrumental parameters employed follow: internal deuterium lock to solvent; spectral width of 2500 Hz; a pulse width of 4 $\mu$s, corresponding to a 36° pulse angle; and a pulse repetition time of 1.8 s. All shifts reported are estimated to be accurate to ±0.05 ppm.

## Results

The carbon-13 chemical shift data for the 1-substituted 2,3-epoxypropanes are given in Table I. The shift assignments were readily determined by examination of the proton-coupled spectra. The methylene carbons were readily differentiated by the size of the one-bond coupling constants, that for the ring methylene carbon being invariably larger than the substituted methylene carbon.[5] All of the one-bond coupling constants are given in Table II. Complete analysis of the coupled spectrum was not attempted because the splitting patterns were highly second order.

## Discussion

Conformations A, B, and C can be described in terms of the $\gamma$ interaction of the substitutent X with the oxygen and methylene carbon, respectively. (These interactions can be classified as either $\gamma$-syn, $\gamma$-syn′, or $\gamma$-anti.) For example, in rotamer A the substituent X is $\gamma$-syn to oxygen and $\gamma$-anti to the methylene moiety. Judging from molecular models and consideration of the angle and distance factors, which control the magnitude of the "$\gamma$ effect",[8] the $\gamma$-syn′ interaction with the methylene should cause larger upfield shifts than the $\gamma$-syn interaction. Based upon the simplistic fundamentals of conformational analysis,[10] rotamer C ($\gamma$-syn′,$\gamma$-syn′) is expected to make the smallest relative contribution to the observed geometry of the epoxypropanes. However, this rotamer should prove important to the observed $\gamma$ shift because of the large interaction of the substituent X and the methylene carbon. In the instance of X = OH rotamer C could be stabilized by hydrogen bonding and thus be the major conformation.[4d] In cyclopropylcarbinol, a similar compound, the $\gamma$-syn′,$\gamma$-syn′ conformation was found to present to about 25% of the rotamer population.[11] Conformations A and B are seen to be similar to the two dominant conformations of 1-substituted propanes. Thus it may prove instructive to compare the data obtained for the epoxypropanes with that found for 1-halopropanes. (See Table III.)

Preliminary comparison of the propane and epoxypropane data indicates that the $\alpha$ shift is similar for both systems while the $\beta$ and $\gamma$ shifts in the epoxypropanes are much smaller in magnitude. The reduction in the $\beta$ shift is probably a consequence of "saturation" phenomena previously noted in other systems.[12] The smaller magnitude of the $\gamma$ shift may also be associated with "saturation" effects; however, in those cases

**Table I. Carbon-13 Chemical Shift and Substituent Shift Data for the 1-Substituted 2,3-Epoxypropanes[a]**

| Registry no. | | $C_1$ | $C_2$ | $C_3$ | α | β | γ |
|---|---|---|---|---|---|---|---|
| 75-56-9 | H | 18.1[b] | 47.9 | 48.1 | | | |
| | | (18.3)[c] | (47.7) | (48.1) | 0.2 | −0.2 | 0.0 |
| 503-09-3 | F | 83.6 | 49.8 | 43.6 | 65.5 | 1.9 | −4.5 |
| | | (85.1) | (50.3) | (43.5) | (67.0 | (2.4) | (−4.6) |
| 106-89-8 | Cl | 45.2 | 51.3 | 46.9 | 27.1 | 3.4 | −1.2 |
| | | (46.5) | (51.9) | (46.9) | (28.4) | (4.0) | (−1.2) |
| 3132-64-7 | Br | 32.8 | 51.3 | 48.5 | 14.7 | 3.4 | 0.4 |
| | | (34.4) | (51.8) | (48.6) | (16.3) | (3.9) | (0.5) |
| 624-57-7 | I | 5.2 | 52.3 | 50.5 | −12.9 | 4.4 | 2.4 |
| 556-52-5 | OH | 62.4 | 52.6 | 44.4 | 44.3 | 4.7 | −3.7 |
| | | (63.3) | (52.9) | (44.3) | (45.2) | (5.0) | (−3.8) |
| 122-60-1 | OPh | 69.6 | 50.2 | 44.5 | 51.5 | 2.3 | −3.6 |
| | | (70.6) | (50.6) | (44.3) | (52.5) | (2.7) | (−3.8) |
| 106-88-7 | $CH_3$ | 25.5 | 53.3 | 46.7 | 7.4 | 5.4 | −1.4 |
| 4436-24-2 | Ph | 38.8 | 52.5 | 46.9 | 20.7 | 4.6 | −1.2 |

[a] In parts per million from $Me_4Si$. [b] 10% w/v in $CDCl_3$. [c] 10% w/v in acetone-$d_6$.

**Table II. One-Bond Carbon–Hydrogen Coupling Constants for the 1-Substituted 2,3-Epoxypropanes[a]**

| | H | F | Cl | Br | OH | OPh | $CH_3$ |
|---|---|---|---|---|---|---|---|
| $J_{11}$ | 126.2 | 165.3 | 151.5 | 153.1 | 142.5 | 142.8 | 128.3 |
| $J_{22}$ | 166.3 | 181.2 | 183.7 | 181.2 | 174.9 | 170.6 | 173.0 |
| $J_{33}$ | 173.3 | 176.2 | 177.1 | 176.2 | 175.5 | 170.5 | 173.3 |

[a] ±0.3 Hz.

**Table III. Carbon-13 Chemical Shift and Substituent Shift Data for 1-Substituted Propanes**

| | $C_1$ | $C_2$ | $C_3$ | α | β | γ |
|---|---|---|---|---|---|---|
| H[a] | 15.6 | 16.1 | 15.6 | | | |
| Cl[b] | 46.6 | 26.5 | 11.4 | 31.0 | 10.4 | −4.2 |
| Br[b] | 35.7 | 26.8 | 13.2 | 20.1 | 10.7 | −2.4 |
| I[c] | 9.2 | 26.8 | 15.3 | −6.4 | 10.7 | −0.3 |
| OH[c] | 64.0 | 26.3 | 10.5 | 48.4 | 10.2 | −5.1 |
| $OCH_3$[d] | 75.5 | 24.1 | 11.0 | 59.9 | 8.0 | −4.6 |
| $CH_3$[d] | 25.0 | 25.0 | 13.2 | 9.4 | 8.9 | −2.4 |
| Ph[b] | 39.0 | 25.2 | 14.1 | 23.4 | 9.1 | −1.5 |

[a] E. G. Paul and D. M. Grant, *J. Am. Chem. Soc.*, **86**, 2984 (1964). Original data converted using $\delta_c{}^{C_6H_6}$ 128.7. [b] J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972. [c] L. F. Johnson and W. C. Jankowski, "Carbon-13 NMR Spectra", Wiley-Interscience, New York, N.Y., 1972. [d] T. Yonemoto, *J. Magn. Reson.*, **13**, 153 (1974).

where there is a *sign* difference, changes in conformational populations are probably in operation.

As previously mentioned, the nature of the γ shift should give indication to the rotational preference of the $CH_2X$ fragment. In the instance of the 1-halopropanes it has been noticed that as the halogen becomes larger the relative population of the gauche rotamer decreases. Concomitant with this change is a decrease of the "γ effect".

Unfortunately, no clear correlation of the "γ effect" and substituent size has been established. Since the propane data analysis may be crucial in determining the rotamer populations in the epoxypropanes, the conclusions concerning group size should be examined more closely. The propane shift data can be evaluated by consideration of the carbon-13 substituent effects obtained from low-temperature spectra of appropriate monosubstituted cyclohexanes.[13] When the substituent is in an axial disposition, corresponding to the gauche interaction in the propanes, the γ shifts for Cl, Br, and I are −6.6, −5.5, and −4.2 ppm, respectively. For the equatorial disposition, corresponding to the anti interaction, the γ shifts are −0.1, 1.4, and 2.3 ppm, respectively. Based on these data, the relative population of the gauche and anti conformation in the propanes can be obtained. In the case of chloropropane, a close to statistical population of conformers is observed (63% gauche). For bromopropane and iodopropane, the gauche population decreases to 55 and 35%, respectively. These calculations confirm the accepted results.

In the evaluation of the γ shifts observed for the halogenated epoxypropanes (Cl, Br, and I) an interesting, although not unpredictable, pattern emerges. As the substituent becomes larger the γ shift passes from an upfield to a downfield value. This observation appears quite analogous to the propane situation. The conclusion concerning the rotational preference of the $CH_2X$ moiety structured on this result can be best explained if rotamer C makes a significant contribution to the γ shift. As the substituent becomes larger, rotamer A increases at the expense of rotamer C and probably to a small extent at the expense of rotamer B. For X = Cl, the relatively small "γ effect" indicates that A is the major conformation. Using the cyclohexane data, as was done for the simple propanes, a minimum value (saturation effects unimportant) for the sum of rotamers B and C is about 20%. Similarly, for X = Br a value of 15% is obtained. Judging from the magnitude of the γ shift, it appears that when X = $CH_3$ or phenyl, the rotational populations are similar to the chlorine derivative.

**Table IV. Solvent Effects on the Carbon–Fluorine Coupling Constants in 1-Fluoro-2,3-epoxypropane.**[a]

| Solvent | $J_{1F}$ | $J_{2F}$ | $J_{3F}$ |
|---|---|---|---|
| Benzene | 169.6 | 23.8 | 8.6 |
| Chloroform | 170.3 | 23.8 | 8.6 |
| Acetone | 166.6 | 23.2 | 9.2 |
| Acetonitrite | 166.0 | 22.6 | 9.2 |

[a] ±0.6 Hz.

An analysis similar to that used above can not be used when X = F, OH, or OPh because these groups induce upfield shifts from both $\gamma$-syn and $\gamma$-anti orientations. The evaluation of the rotamer populations when X = F was made on the basis of solvent shifts and long-range $^{13}$C–F coupling constants (Table IV).

It was indicated by Thomas (X = F) that as the solvent polarity is increased, the relative population of conformation A increases at the expense of B.[4b] This conclusion was based partly on the analysis of the proton chemical shifts. However, reevaluation of that data indicates an inconsistency in the reasoning. As the population of rotamers changes from B to A, the proton chemical shift of $H_1$ should move to higher field, owing to this proton being in the face of the oxirane ring for a greater fraction of the time.[14] This is observed. In concert, the proton chemical shift of $H_2$ should move to lower field. However, this does not occur, suggesting that the conclusions regarding solvent effects are not correct.

Solvent effects on the carbon-13 chemical shifts in many of the compounds were studied in order to ascertain if rotamer populations could be changed. Except for the $C_1$ carbon shifts, no substantial solvent effects were observed. These results indicate that the solvent plays at best a minor role in determining rotamer populations. Further insight regarding the role of solvent can be obtained from the $^3J$ $^{13}$C–F coupling constant. The geometrical dependence upon the three-bond $^{13}$C–F coupling constants can be seen in the low-temperature spectrum of fluorocyclohexane.[13] In the fluorine axial conformation (dihedral angle 60°) the $^3J_{CF}$ coupling constant is about 1 Hz, while in the fluorine equatorial conformation (dihedral angle 180°) the $^3J_{CF}$ is 11.5 Hz. A population change from conformation B to conformation A in polar solvents would require an increase in $^3J_{CF}$. Similarly, a change from rotamer B to C should increase $^3J_{CF}$ if a Karplus-like equation were to operate. From a consideration of the constancy of $^3J_{CF}$ with solvent polarity and the magnitude of the coupling constant value, it is concluded that the major conformation when X = F is A with C being the next most populated. This result is in complete agreement with Reynolds $^1$H NMR investigation.

The remaining substituents to be considered are X = OH and X = OPh. From $^1$H NMR studies it was concluded that for X = OH, the order of rotamer population is C > A > B.[4d] A major consideration in determining the relative populations of A and B was the ease of hydrogen bonding. Since hydrogen bonding cannot occur for X = OPh, the comparison of the $\gamma$ shift should be informative. In the propane series, where hydrogen bonding is unimportant, the $\gamma$ shift for X = OH and X = $OCH_3$ is similar in magnitude. The same observation applies to the epoxypropanes. Unless one assumes that the similar $\gamma$ shifts in the epoxypropanes are fortuitous, an accident of the averaging of various conformations, a reasonable conclusion is that both X = OH and OPh reside in similar environments. It is concluded from the carbon-13 shift data that the order of conformational stability for X = OH and OPh is A > C > B.

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