

ene to afford 5.3 g (78%) of 12: mp 169–172° (dec); ir (KBr) 3320 (NH), 1710 (carbamate C=O), 1685 cm⁻¹ (acid C=O); nmr (DMSO-*d*₆) δ 1.32 (t, 2 H, ring CH₂), 1.85 (q, 1 H, CHCO₂R), 3.10 (m, 1 H, CHN), 7.10–8.10 (m, 7 H, 2-naphthyl).

Anal. Calcd for C₁₅H₁₃NO₄: C, 66.41; H, 4.83; N, 5.16. Found: C, 66.71; H, 4.95; N, 4.90.

Registry No.—2, 53229-56-4; 3, 53229-57-5; 6, 53229-58-6; 7, 53229-59-7; 8, 53229-60-0; 11, 53403-91-1; 12, 53229-62-2; 13, 6860-35-1; 14, 53229-63-3; 15, 53229-64-4; 16, 53229-65-5; 17, 53229-66-6; 18, 103-40-2; SOCl₂, 7719-09-7; *cis*-2-carbomethoxycyclopropanecarboxylic acid, 31420-47-0; *cis*-cyclopropane-1,2-dicarboxylic acid anhydride, 5617-74-3; benzyl alcohol, 100-51-6; *trans*-cyclopropanedicarboxylic acid, 696-75-3.

References and Notes

(1) This investigation was supported by Grant No. NS-06100, National Institute of Neurological Diseases and Stroke. Abstracted from a portion of

a thesis submitted by J.E.G. in partial fulfillment of the requirements for the Ph.D. degree, University of Iowa, 1974.

- (2) C. C. Shroff, W. S. Stewart, S. J. Ulm, and J. W. Wheeler, *J. Org. Chem.*, **36**, 3356 (1971).
- (3) J. Weinstock, *J. Org. Chem.*, **26**, 3511 (1961).
- (4) H. M. Walborsky and P. E. Ronman, *J. Org. Chem.*, **38**, 4213 (1973).
- (5) R. H. Rynbrandt and F. E. Dutton, *Tetrahedron Lett.*, 1937 (1972).
- (6) M. E. Kuehne and J. C. King, *J. Org. Chem.*, **38**, 304 (1973).
- (7) J. G. Cannon, A. B. Rege, T. L. Gruen, and J. P. Long, *J. Med. Chem.*, **15**, 71 (1972).
- (8) Boiling points are uncorrected; melting points were determined in open glass capillaries on a Thomas-Hoover UniMelt apparatus and are corrected. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tenn., and by the Microanalytical Service, College of Pharmacy, The University of Iowa. Nmr spectra were recorded with a Varian Associates T-60 instrument (Me₄Si) and ir spectra were obtained with a Beckman IR-10 spectrometer.
- (9) L. L. McCoy, *J. Amer. Chem. Soc.*, **80**, 6568 (1958).
- (10) T. L. Gruen, Ph.D. Thesis, University of Iowa, 1971.
- (11) C. A. Bischoff and A. Von Hedenström, *Chem. Ber.*, **35**, 4078 (1902).

Carbon-13 Nuclear Magnetic Resonance Spectroscopy Quantitative Correlations of the Carbon Chemical Shifts of Simple Epoxides¹

Donald R. Paulson,* Franklin Y. N. Tang, Gregory F. Moran, A. Spencer Murray, Benjamin P. Pelka,² and Eva M. Vasquez³

Department of Chemistry, California State University, Los Angeles, Los Angeles, California 90032

Received July 22, 1974

Fourier transform carbon-13 nuclear magnetic resonance spectra have been obtained for 42 simple epoxides. A set of additivity parameters have been developed which allow the calculation of the expected chemical shift of the carbon atoms of the epoxide functional group. The effect of adjacent unsaturation is also discussed.

Carbon-13 nuclear magnetic resonance (¹³C nmr) spectroscopy has become an extremely important research tool in the structural elucidation of organic compounds.⁴ To interpret the ¹³C nmr spectra of any particular compound it is usually required to examine the ¹³C nmr spectra of closely related compounds containing similarly substituted carbons. A number of methods have been developed to aid in the assignment of the carbon resonances. One method in particular has proved to be quite useful for the assignment of carbon resonances. Using least-squares analyses, a system of substituent parameters has been developed for a number of compound types. These parameters are then used to predict the carbon chemical shifts of related compounds. This method has been most successfully applied by Grant,⁵ Roberts,⁶ and Djerassi.⁷ We have extended this method to aliphatic epoxides and obtained a series of empirical substituent parameters which should prove very useful in the assignment of structure to molecules containing the epoxide functionality.

Experimental Section

A. Preparation of the Epoxides. The epoxides were either obtained commercially or synthesized by peracetic acid oxidation of the appropriate olefin. The structures of the epoxides were confirmed by proton magnetic resonance spectroscopy.

B. ¹³C Spectra. The carbon-13 chemical shifts were obtained on a Bruker HX-90-E instrument equipped with a Bruker-Nicolet Data System, Model B-NC-12. The spectra were recorded at 22.6 MHz with 5-μsec pulse widths applied at 1-sec intervals. All of the chemical shifts were measured relative to 10% internal TMS using 45% CDCl₃ as solvent. At these concentrations 1000 pulses were used to obtain a reasonable signal-to-noise ratio. Complete proton decoupling was used to obtain the chemical shifts and single-frequency-off-resonance decoupled spectra were used to assign the resonances of the epoxy carbons in questionable cases. No attempts were made to assign the other carbons in the molecules.

C. Least-Squares Solutions. The least-squares solutions were obtained by using a modification of the BMD03R⁸ regression anal-

ysis program for the CDC 3151 computer at California State University, Los Angeles. The program computed the least-squares empirical value for the substituent parameter, the 96% confidence limits for the parameters, the deviation between each calculated and experimental chemical shift, the standard error of prediction, and the multiple correlation coefficient.⁹

Results and Discussion

Recently several papers have appeared on the subject of the ¹³C spectra of epoxides. Tori and Komeno¹⁰ have studied the conformational effects in steroidal epoxides. Anet and Servis have investigated the conformational analysis of cycloheptane oxide by ¹³C spectroscopy¹¹ and Anet has also studied the ¹³C spectra of a series of di-, tri-, and tetra-epoxides¹² and assigned additivity parameters to these classes of polyepoxides. However, there has not been a detailed study of simple epoxides. We now wish to report such a study.

In calculating the chemical shifts of the epoxy carbon atoms, substituent effects shown in Chart Ia were used. These are defined in the same manner as those defined by Roberts in his study of acyclic alkenes.⁶ Using this method, the substituent effects for carbon 3 of *trans*-3,4-epoxy-5-methylheptane are given as $\alpha + \beta + \alpha' + 2\beta' + \gamma'$ (Chart Ib). In addition to the substituent parameters α , β , γ , α' , β' , and γ' , it was found that better results were obtained if a *cis* correction factor was included when α and α' were located *cis* to one another. Finally a gem correction factor was also included when a system contained two α parameters. Thus the substituent effects of carbon 4 of *cis*-4,5-epoxy-4-methyloctane are given as $2\alpha + \beta + \gamma + \alpha' + \beta' + \gamma' + \text{gem factor} + \text{cis factor}$ (Chart Ic). The ¹³C nmr shift of any epoxide can be calculated by addition of the appropriate substituent parameters to the chemical shift of ethylene oxide. The values obtained for the substituent parameters are given in Table I.

Table I
Substituent Parameters for Epoxide Carbons

α (48) ^a	8.3 ± 0.5^b
β (32)	4.4 ± 0.2
γ (19)	-0.9 ± 0.2
α' (48)	7.1 ± 0.3
β' (32)	-0.9 ± 0.2
γ' (19)	0.2 ± 0.2
cis factor (15)	-2.7 ± 0.4
gem factor (9)	-4.3 ± 0.6

Standard error of estimate 0.85

Multiple correlation coefficient 0.99

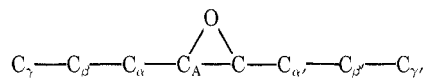
^a The numbers in parentheses represent the number of occurrences of that parameter. ^b Values are given in parts per million (ppm).

In Table II the observed chemical shifts are given for 10 of the 30 simple epoxides used to generate the parameters shown in Table I. The calculated chemical shifts for each of these 10 epoxides are also given in Table II along with the residuals. The complete carbon nuclear magnetic resonance spectra of all 30 compounds are available as supplementary material. See paragraph on supplementary material at the end of this paper.

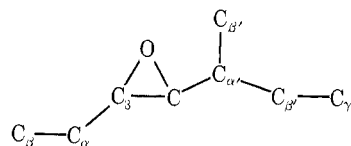
These substituent parameters generally parallel but are somewhat lower in magnitude than the parameters found by Roberts in his study of acyclic alkenes.⁶ The α and β substituent parameters are deshielding as they are for the alkanes studied by Grant.⁵ The α' parameter is deshielding as expected since the substituent is actually β to the carbon atom in question. However, this contrasts with the alkene series where the α' parameter was found to be shielding.⁶ The γ and β' parameters are all shielding. They are small in magnitude and may be of only minor significance. The γ' parameter is the same value as the error in the γ' parameter and thus this parameter can be excluded.

Chart I

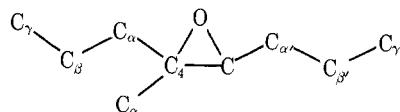
A. Definition of the Substituent Effects Used in Calculation of the Chemical Shift of Carbon A



B. Substituent Effects of Carbon 3 of *trans*-3,4-Epoxy-5-methylheptane

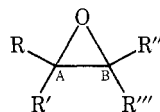


C. Substituent Effects of Carbon 4 of *cis*-4,5-Epoxy-4-methyloctane



The *cis* and *gem* parameters point up the great importance of steric factors in these systems. They are probably due to the so-called "steric compression shift" introduced by Grant.¹³ This steric effect is shielding in nature and is directly related to the force component along the H-¹³C bond associated with nonbonded hydrogen-hydrogen interactions. It is apparently due to an induced polarization of charge along the H-¹³C bond. One could also rationalize the γ and β' parameters as steric compression shifts. It should also be pointed out that compounds which contain the *gem* factor give the largest deviation between calculated and observed chemical shift values. This could be due to either the smaller number of examples which contain the *gem* factor or to a nonlinear nature of steric effects.

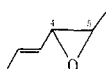
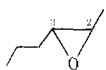
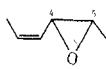
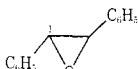
Table II
Calculated and Observed ¹³C Chemical Shifts for a Series of Simple Epoxides^{a,b}



Compd	R	R'	R''	R'''	Carbon	Obsd	Calcd	Residual
1	H	H	H	H	A	40.6		
2	CH ₃	H	H	H	A	47.5	48.4	-0.9
					B	47.2	47.1	0.1
3	<i>n</i> -C ₃ H ₇	H	H	H	A	51.9	51.9	0.0
					B	46.7	46.5	0.2
4	<i>i</i> -C ₄ H ₉	H	H	H	A	51.1	51.0	0.1
					B	47.0	46.8	0.2
5	<i>sec</i> -C ₅ H ₁₁	H	H	H	A	57.0	56.3	0.7
					B	46.7	45.7	1.0
6	<i>n</i> -C ₃ H ₇	CH ₃	H	H	A	56.5	55.9	0.6
					B	53.5	53.6	-0.1
7	C ₂ H ₅	C ₂ H ₅	H	H	A	60.6	61.2	-0.6
					B	51.5	52.5	-1.0
8	C ₂ H ₅	H	H	CH ₃	A	60.7	59.8	0.9
					B	54.1	54.6	-0.5
9	C ₂ H ₅	H	CH ₃	H	A	58.1	57.2	0.9
					B	52.4	51.9	0.5
10	C ₂ H ₅	C ₂ H ₅	CH ₃	H	A	64.4	65.7	0.3
					B	58.5	58.2	0.3
11	CH ₃	CH ₃	CH ₃	CH ₃	A	61.2	61.2	0.0

^a The chemical shift data are relative to internal TMS and are given in ppm. ^b The complete ¹³C nmr data for these and other similar compounds are given in the supplementary material.

Table III
Effect on Unsaturation on ^{13}C Chemical Shift of Epoxides^{a,b}

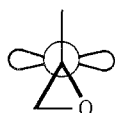
Compound	Carbon	Obsd	Calcd
	4	59.3	59.2
	5	55.8	54.4
	3	59.6	59.2
	2	54.3	54.4
	4	53.7	56.0
	5	52.4	52.2
	1	62.6	61.5

^a The chemical shift data are relative to internal TMS and are given in ppm. ^b The complete carbon magnetic resonance spectra for these and similar compounds are included in the supplementary material.

The effect of adjacent unsaturation on the ^{13}C chemical shift of the epoxy carbons is minimal as is shown in Table III. Even the effect of an aromatic ring can be approximated by our additivity parameters. This has also been observed with alkenes. Allylic carbons usually have a chemical shift very close to the analogous saturated molecule. Cycloheptatriene is a striking example of the insensitivity of ^{13}C chemical shift to the hybridization of the adjacent carbons.¹⁴ The lone sp^3 hybridized carbon appears at 28.8 ppm downfield from TMS while the chemical shift for cycloheptane is 28.5 ppm.







Table IV presents evidence that adjacent unsaturation can have a pronounced effect if the epoxy group and the olefinic group are oriented properly. The saturated cyclopentyl and cyclooctyl epoxides come very close to the calculated value using our additivity parameters for acyclic epoxides. The cyclohexyl system deviates significantly from the calculated value. This may be due to a steric compression shift caused by interaction between the epoxy group and the proton on carbon 4 of the ring. The approximately 4-ppm upfield shift from the calculated value in cyclohexene oxide is consistent with this argument. The conjugated alicyclic epoxides show a pronounced upfield shift for the epoxy carbon atom adjacent to the unsaturation as compared to the other epoxy carbon atom. This effect is largest in the 3,4-epoxycyclohexene system where the difference in chemical shift between the two epoxy carbons is 7.8 ppm.

The largest conjugative interaction between the epoxy group and the olefinic π bond would be expected in the bisected conformation shown below. This prediction is based



on a comparison with the corresponding cyclopropyl system.¹⁵ In this conformation the overlap between the darkened σ orbitals of the epoxy group and the π system would be the greatest. Models indicate that the cyclohexenyl system most closely approximates this bisected geometry, and thus one would expect a significant conjugative interaction in this case. Such an interaction would lead to an electron deficiency at the carbon in question and give the observed upfield shift. The geometry in the other cases is much different from the bisected geometry needed for maximum overlap and a smaller effect would be expected.

Table IV
Unsaturated Cyclic Epoxides^{a,b}

Compound	Carbon	Obsd	$\Delta\delta$
	1	56.6	
	3	55.8	2.4
	4	58.2	
	1	51.3	
	3	46.2	7.8
	4	54.0	
	1	55.1	
	3	52.8	4.4
	4	57.2	

^a The chemical shift data are relative to internal TMS and are given in ppm. ^b Complete ^{13}C data for these and similar compounds are found in the supplementary material.

Acknowledgment. The authors wish to express their appreciation to Mr. T. Murillo and Mr. R. Perrigan for their valuable assistance in obtaining the ^{13}C spectra.

Registry No.—1, 75-21-8; 2, 75-56-9; 3, 1003-14-1; 4, 23850-78-4; 5, 53229-39-3; 6, 3657-41-8; 7, 1192-17-2; 8, 3203-98-3; 9, 3203-99-4; 10, 53229-40-6; 11, 5076-20-0; 12, 1436-34-6; 13, 2984-50-1; 14, 2855-19-8; 15, 53229-41-7; 16, 53229-42-8; 17, 15359-10-1; 18, 53229-43-9; 19, 2390-95-6; 20, 6124-91-0; 21, 17612-35-0; 22, 1192-22-9; 23, 2245-30-9; 24, 1758-33-4; 25, 21490-63-1; 26, 106-88-7; 27, 2245-29-6; 28, 5076-19-7; 29, 16262-93-4; 30, 10353-53-4; 31, 286-62-4; 32, 286-20-4; 33, 285-67-6; 34, 31598-71-7; 35, 6690-12-6; 36, 6253-27-6; 37, 6705-51-7; 38, 7129-41-1; 39, 36808-01-2; 40, 36808-00-1; 41, 34485-82-0; 42, 1439-07-2.

Supplementary Material Available. Full ^{13}C nmr data for all of the compounds used in this study (42 compounds) appear following this article in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all the supplementary material for the papers in this issue may be obtained from the Journals Department, American Chemical Society, 1155 16th Street, N.W., Washington, D.C. 20036. Remit check or money order for \$3.00 for photocopy or \$2.00 for microfiche, referring to code number JOC-75-184.

References and Notes

- (1) Supported by a grant from the California State University Foundation, Los Angeles, Calif.
- (2) National Science Foundation Undergraduate Research Program, Summer 1973.
- (3) American Chemical Society, Project Catalyst Program, Summer 1973.
- (4) (a) G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists," Wiley-Interscience, New York, N.Y., 1972; (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.
- (5) D. K. Dalling, D. M. Grant, and E. G. Paul, *J. Amer. Chem. Soc.*, **95**, 3718 (1973), and earlier papers in this series.
- (6) D. E. Dorman, M. Jautelat, and J. D. Roberts, *J. Org. Chem.*, **36**, 2757 (1971), and references contained therein.
- (7) H. Egger and C. Djerassi, *J. Amer. Chem. Soc.*, **95**, 3710 (1973).
- (8) "BMD Biomedical Computer Program," W. J. Dixon, Ed., University of California Press, Berkeley, Calif.
- (9) J. Mandel, "The Statistical Analysis of Experimental Data," Wiley-Interscience, New York, N.Y., 1964, Chapter 7.
- (10) K. Tori and T. Komeno, *Tetrahedron Lett.*, 1157 (1974).
- (11) K. L. Servis, E. A. Nal, N. R. Easton, and F. A. L. Anet, *J. Amer. Chem. Soc.*, **96**, 4185 (1974).
- (12) N. R. Easton, F. A. L. Anet, P. A. Burns, and C. S. Foote, *J. Amer. Chem. Soc.*, **96**, 3945 (1974).
- (13) D. M. Grant and B. V. Cheney, *J. Amer. Chem. Soc.*, **89**, 5315 (1967).
- (14) Reference 4a, p 59.
- (15) S. A. Monti, *J. Org. Chem.*, **35**, 380 (1970), and references contained therein.