subtle unimolecular decomposition of radical cations at low temperatures.

Registry No. 2-Methyl-1,3-dioxacyclopentane, 497-26-7; 2-methyl-1,3-dioxacyclohexane, 626-68-6; 3-methyl-2,4-dioxapentane, 534-15-6; 2,4,6-trimethyl-1,3,5-trioxacyclohexane, 123-63-7; 2-ethyl-1,3-dioxacyclopentane, 2568-96-9; 2-ethyl-1,3-dioxacyclohexane, 5702-29-4; 3-ethyl-2,4-dioxapentane, 4744-10-9; 2,4,6-triethyl-1,3,5-trioxacyclohexane, 2396-42-1; dimethoxymethyl radical cation, 81027-72-7; 4,5-dihydro-1,3-dioxol-1-ium, 6680-54-2.

Analysis of Hydrocarbon Chain Conformation Using Double Quantum Coherence ^{13}C NMR

Martin A. Phillippi,[†] Richard J. Wiersema,[†]
James R. Brainard,[‡] and Robert E. London*[‡]

Clorox Technical Center, Pleasanton, California 94566
Los Alamos National Laboratory, University of California
Los Alamos, New Mexico 87545

Received June 16, 1982

An understanding of the conformational and dynamic properties of hydrocarbon chains is of interest in connection with a wide variety of problems, including the structure and function of biological membranes[1] and surfactants.[2] A full understanding of these systems requires an integrated model containing both conformational and dynamic parameters. Carbon-13 spin lattice relaxation rates have found particular application in describing the dynamics of gauche/trans isomerization.[3-5] Temperature-dependent ^{13}C chemical shifts have been suggested to reflect the gauche/trans conformational equilibrium,[6-8] but recent attempts to develop this parameter as a quantitative tool have indicated significant complications.[8] The chemical shift difference between a gauche and a trans conformation may depend strongly on the particular carbon position, in contrast to previous assumptions,[8] and in some cases of branched alkanes the model appears to break down completely. Scalar coupling constants have long been used as a basis for conformational analysis;[9] however, applications are limited by the abundances of various nuclear species and by the complexity of the spectra. The recent development of a double quantum coherence method for the observation of ^{13}C–^{13}C scalar coupling constants without the need for isotopic labeling provides an alternative approach to the hydrocarbon chain conformation problem.[10] The method is particularly suitable for this application since one-, two-, and three-bond carbon–carbon coupling constant values in hydrocarbons are typically of significantly different magnitudes,[11] and observation of coupling constants of selected magnitude may be enhanced by the appropriate choice of pulse intervals.[10] Consequently, $^3J_{CC}$ values, which are dependent on the subtended dihedral angle, can be selectively observed.

In order to evaluate the potential of this approach, we have carried out studies on a 90% octanol–10% benzene-d_6 solution, with the latter serving for the deuterium lock. A representative ^{13}C double quantum coherence spectrum of the region containing the octanol C-7 resonances with pulse intervals chosen to optimize couplings with magnitude close to 4.0 Hz is illustrated in Figure 1, and the corresponding coupling data are tabulated in Table I. For carbons near the ends of the chain there is only a single vicinal coupling interaction so that the observed coupling constant can be unequivocally associated with a particular bond conformation. Alternatively, for carbons 4 and 5 the observed coupling constants correspond to a superposition of the $^3J_{41}$ and $^3J_{47}$ values in the first case, and the $^3J_{52}$ and $^3J_{58}$ values in the second. Thus, the observed C-4 doublet should exhibit a splitting that is approximately the average of the values observed for C-1 and C-7, as is observed (Table I). For a sufficiently short chain as in the present example, it is not necessary to utilize the data obtained for the unresolved carbon splittings corresponding to C-4 and C-5.

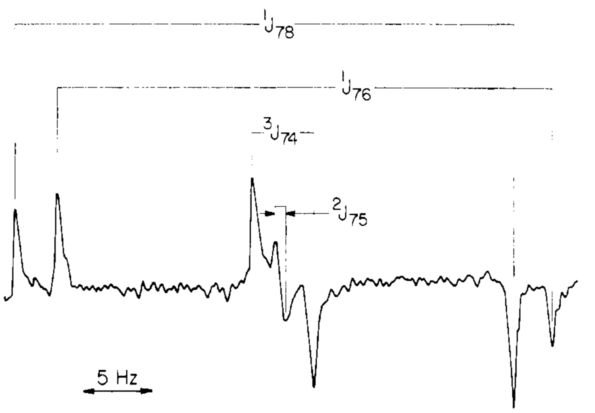

Figure 1. Double quantum coherence spectrum of the C-7 resonances of *n*-octanol in a 90% *n*-octanol–10% benzene-d_6 solution, obtained as described by Bax et al.[10] ($90°_x$-τ-$180°_y$-τ-$90°_x$-Δ-$90°(\Phi)$). Spectra were obtained on a JEOL FX 90Q NMR spectrometer in 10-mm sample tubes by using 32K time domain data points and a 1500-Hz spectral width, to provide a resolution of 0.09 Hz. This spectrum was obtained by using a τ value of 63 ms (optimizing for 4-Hz C–C coupling), a repetition rate of 15 s, and a total of 4000 scans (total accumulation time 17 h).

Table I. Vicinal Carbon–Carbon Coupling Constants in *n*-Octanol as a Function of Temperature[a]

carbon	$^3J_{CC}$ (30°)	$^3J_{CC}$ (65°)	$^3J_{CC}$ (100°)	$^3J_{CC}$ (150°)
C-1	4.30	4.21	4.12	4.04
C-2	3.76	3.57	3.67	3.58
C-3	3.94	3.85	3.75	3.67
C-4	4.12	3.93	3.94	3.85
C-5	4.03	3.75	3.66	3.67
C-6	3.94	3.85	3.76	3.66
C-7	4.03	3.85	3.75	3.66
C-8	4.03	4.03	3.84	3.67

[a] Values measured with a resolution of 0.09 Hz.

Interpretation of the coupling data in terms of chain conformation is based on a model in which the hydrocarbon chain is described as an equilibrium mixture of rapidly interconverting trans and gauche conformers about each bond. Two approaches have been utilized to estimate the pure trans and gauche coupling constants. In the first, a theoretical self-consistent field, finite perturbation theory treatment at the INDO level of approximation was used.[12] In previous studies with ^{13}C-enriched amino acids, we have found that these calculations give qualitatively reasonable predictions for $^1J_{CC}$ and $^3J_{CC}$ but relatively poor agreement for $^2J_{CC}$.[13] For reasons of time and convenience, calculations were carried out on *n*-heptanol, and the results for trans and gauche coupling constants along the chain are summarized in Figure 2a. With the exception of $^3J_{14}$, for which a significant substituent effect

---

[†] Clorox Technical Center.

[‡] Los Alamos National Laboratory.

(1) Lee, A. G.; Birdsall, N. J. M.; Metcalfe, J. C. In "Methods in Membrane Biology"; Plenum Press: New York, 1974.

(2) Tanford, C. "The Hydrophobic Effect"; Wiley: New York, 1973.

(3) Gent, M. P. N.; Prestegard, J. H. *J. Magn. Reson.* **1977**, *25*, 243.

(4) London, R. E.; Avitabile, J. *J. Am. Chem. Soc.* **1977**, *99*, 7765.

(5) Edholm, O.; Blomberg, C. *Chem. Phys.* **1981**, *53*, 185.

(6) Batchelor, J. G.; Prestegard, J. H.; Cushley, R. J.; Lipsky, S. R. *Biochem. Biophys. Res. Commun.* **1972**, *48*, 70.

(7) Rosenholm, J. B.; Drakenberg, T.; Lindman, B. *J. Colloid Interface Sci.* **1978**, *63*, 538.

(8) Cheng, H. N.; Bovey, F. A. *Org. Magn. Reson.* **1978**, *11*, 457.

(9) Feeney, J. *Proc. R. Soc. London, Ser. A* **1975**, *343*, 61.

(10) Bax, A.; Freeman, R.; Kempsell, S. P. *J. Am. Chem. Soc.* **1980**, *102*, 4849.

(11) (a) Marshall, J. L.; Ihrig, A. M. *Tetrahedron Lett.* **1972**, *21*, 2139. (b) Marshall, J. L.; Miiller, D. E. *Org. Magn. Reson.* **1974**, *6*, 395.

(12) Maciel, G. E.; McIver, J. W.; Ostlund, N. S.; Pople, J. A. *J. Am. Chem. Soc.* **1970**, *92*, 1; **1970**, *92*, 11.

(13) (a) London, R. E.; Walker, T. E.; Kollman, V. H.; Matwiyoff, N. A. *J. Am. Chem. Soc.* **1978**, *100*, 3723. (b) London, R. E. *J. Chem. Soc., Chem. Commun.* **1978**, 1070. (c) London, R. E. *Org. Magn. Reson.* **1981**, *17*, 134.

0002-7863/82/1504-7333$01.25/0 © 1982 American Chemical Society

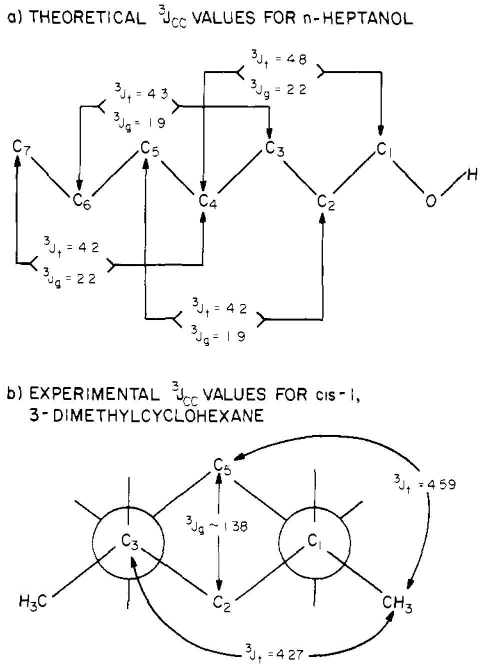

Figure 2. (a) Theoretical vicinal carbon–carbon coupling constants in *n*-heptanol obtained by using a finite perturbation theory, self-consistent field molecular orbital calculation at the INDO level of approximation. Standard bond geometries (C–C = 1.53 Å, C–H = 1.09 Å, C–O = 1.44 Å, tetrahedral bond angles) were used in the calculations. The hydroxyl proton was fixed trans to C-2. Coupling constants were obtained with each bond individually constrained in a trans or gauche conformation and all other bonds trans. (b) Experimental coupling constants obtained for *cis*-1,2-dimethylcyclohexane by using the double quantum coherence technique. Since the gauche coupling constants in the cyclohexyl ring are quantitatively similar in magnitude to the geminal ^{13}C–^{13}C coupling constants, the assignment of the 1.38-Hz value to the vicinal C-2–C-5 coupling is tentative.

Table II. Conformational Analysis of *n*-Octanol

bond	P_{trans}[a] 30 °C	65 °C	100 °C	150 °C	ΔH,[b] kcal/mol
2–3	0.59	0.56	0.54	0.51	0.68
3–4	0.59	0.52	0.56	0.53	*c*
4–5	0.65	0.62	0.58	0.56	0.84
5–6	0.68	0.62	0.58	0.55	1.19
6–7	0.68	0.68	0.61	0.56	1.18

[a] Fractional trans probabilities calculated from the data in Table I by using J_t = 5.7 Hz, J_g = 2.3 Hz for the C-2-C-3 bond, J_t = 5.0 Hz, J_g = 2.0 Hz for all other bonds. [b] Derived from a least-squares fit of the data to the equation $P_{\text{trans}}/P_{\text{gauche}} = A \exp(-\Delta H/kT)$. The correlation coefficient for all values given was ≥0.88. [c] Correlation coefficient for these data was 0.36.

is predicted, the results show little variation along the chain and are in close agreement with reported theoretical results for butane.[14] However, these theoretical values for J_t and J_g predict extremely high trans probabilities for all bonds, which are doubtful on the basis of relaxation data.[4]

A second approach that we have used to estimate the trans and gauche couplings involved a model system, *cis*-1,3-dimethylcyclohexane, which can be viewed as essentially locked into a single conformation with both methyl groups in equatorial positions (ΔE = 5.4 kcal/mol). Double quantum coherence studies analogous to those used in the *n*-octanol system indicate that the two types of trans couplings involving exocyclic methyls have values of 4.27 and 4.59 Hz, as illustrated in Figure 2b. The use of cyclic, conformationally constrained models for obtaining coupling constants applicable to linear systems has recently been questioned[15] on the basis of the occurrence of multiply impinging rear lobes of bond orbitals in the latter systems[15a] and on the additional β substituents which characterize the cyclic analogues.[15b] The theoretical calculations for the cyclic systems indicate significantly reduced trans couplings in comparison with linear analogues. However, the theoretical trans coupling predicted by Barfield et al. for methyl cyclohexane[15a] is substantially below the 4.3-Hz value reported for this compound[16] and below the experimental results obtained here for the conformationally locked *cis*-1,3-dimethylcyclohexane. The qualitative trend theoretically predicted for the series butane, methylcyclohexane, methyladamantane, as well as the predicted magnitude of the trans $^3J_{CC}$ for the latter compound, are all in agreement with experiment; however, the experimentally observed magnitudes for the former two cases are significantly greater than the theoretical predictions. Using the trans couplings for the *cis*-1,3-dimethylcyclohexane measured here together with the observation that the theoretical trans coupling in methylcyclohexane is 0.55 Hz below the theoretical trans coupling for butane, we have estimated the trans $^3J_{CC}$ for a linear hydrocarbon as 5.0 Hz. Reasonable values for the gauche coupling constants in linear hydrocarbons are more difficult to determine. In addition to problems of the type noted above inherent in the use of cyclic model systems, the possibility of coupling via multiple pathways further limits the value of these systems as models. In the absence of a reasonable experimental model, we have utilized the theoretical value of 2.0 Hz for the analysis. Finally, the theoretical results for *n*-heptanol presented here indicate that the hydroxyl substituent at C-1 is associated with an increase of about 14% in the couplings so that for analysis of the conformation about the 2–3 bond we have used J_t = 5.7 Hz and J_g = 2.3 Hz. This correction leads to similar fractional trans probabilities for bonds 2–3 and 3–4.

Fractional trans probabilities calculated based on the estimates for the coupling constants discussed above are summarized in Table II. In all cases, the trans probabilities are found to decrease at higher temperatures, as expected. An Arrhenius treatment of these data indicates an average gauche–trans enthalpy difference of 1.0 kcal/mol for the chain. This value is in excellent agreement with recently obtained theoretical[17] and experimental[18] values for butane, in contrast with earlier estimates of 0.5 kcal/mol.[19] This result suggests that intermolecular interactions make a negligible contribution to the gauche/trans enthalpy difference for the 90% octanol solution. Both P_{trans} and ΔH appear to increase toward the methyl end of the chain. The signficance of this observation is unclear, and these apparent trends may reflect the need to use variable values for J_t and J_g as a function of chain position, although no significant variation is predicted by the theoretical calculations on *n*-heptanol. These results might also be related to the existence of coupled gauche conformations as are proposed to occur in liquid crystalline systems. A small dependence of the $^3J_{CC}$ value on parameters other than the subtended dihedral angle is predicted theoretically.[15] The utility of this approach for the evaluation of hydrocarbon chain conformation should increase as additional theoretical data and data for model systems become available. Uniformly ^{13}C-enriched molecules are expected to find particular application in studies requiring enhanced sensitivity.

Acknowledgment. This work was carried out in part under the auspices of the U.S. Dept. of Energy and supported in part by the NIH Division of Research Resources Grant RR00962-07 (J.R.B.).

Registry No. *n*-Octanol, 111-87-5.

---

(14) Barfield, M.; Burfitt, I.; Doddrell, D. *J. Am. Chem. Soc.* **1975**, *97*, 2631.

(15) (a) Barfield, M.; Conn, S. A.; Marshall, J. L.; Miiller, D. E. *J. Am. Chem. Soc.* **1976**, *98*, 6253. (b) Wray, V. *Ibid.* **1978**, *100*, 768.

(16) Hansen, P. E. *Org. Magn. Reson.* **1978**, *11*, 215.

(17) Bartell, L. S. *J. Am. Chem. Soc.* **1977**, *99*, 3279.

(18) Verma, A. L.; Murphy, W. F.; Bernstein, H. J. *J. Chem. Phys.* **1974**, *60*, 1540.

(19) Flory, P. J. "Statistical Mechanics of Chain Molecules"; Interscience: New York, 1969.