

symmetry species of the monomer vibrations. If the sign of the coupling energy is known, the symmetric and antisymmetric bands can be identified. This identification could also follow from the polarization characteristics of the two bands, in which case the sign of the coupling energy could be deduced. The sign of the two Raman CID bands then gives the absolute configuration of the dimer; that of Figure 3 leads to a positive CID in the symmetric band.

The extension of this theory to a dimer consisting of two lower-symmetry groups in an arbitrary dissymmetric relative orientation is complicated. Extra terms involving components of intrinsic optical activity tensors of the monomers must be included to maintain origin invariance (for example,  $G'_{12} \neq -G'_{21}$  in  $C_{2v}$ ), and the polarizability tensors cannot be reduced to the simple form of (9). Nonetheless, some of the general

features of the simple dimer treatment may extend to more complicated situations. In fact, Raman CID bands have been observed<sup>6</sup> which could originate in this mechanism. In  $\alpha$ -pinene, a large  $\Delta_2$  couplet exists in two barely resolved bands centered at  $\sim 780$   $\text{cm}^{-1}$ . The relative intensities, depolarization ratios, and CID's of the two bands are of the orders deduced above. Since the bands fall in the  $\text{CH}_2$  rocking region, these CID's could originate in coupling between  $\text{CH}_2$  rocking vibrations on the two starred groups, which together constitute a rigid, highly dissymmetric structure.



Unfortunately, a detailed analysis of this situation is subject to all the fearful complexities mentioned above.

## A Study of the Distances Obtained from Nuclear Magnetic Resonance Nuclear Overhauser Effect and Relaxation Time Measurements in Organic Structure Determination. Distances Involving Internally Rotating Methyl Groups. Application to *cis*- and *trans*-Crotonaldehyde

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**Abstract:** Absolute internuclear distances between all of the protons of *cis*- and *trans*-crotonaldehyde in solution have been obtained by measuring the  $^1\text{H}\{^1\text{H}\}$  nuclear Overhauser enhancements between all of the spins and the  $^1\text{H}$  and  $^{13}\text{C}$  nuclear spin-lattice relaxation times for all of the spins. The results are compared with the reported microwave structure for *trans*-crotonaldehyde and a theoretically optimized structure (starting from the X-ray structure) for *cis*-crotonaldehyde. The internuclear distances involving the methyl protons are used to test two models for the effective position of the methyl protons when internal motions are considered.

The potential of the nuclear Overhauser effect<sup>1</sup> for providing information on the conformation of molecules in solution was first demonstrated by Anet and Bourn.<sup>2a</sup> The widespread chemical applications of the NOE which followed this initial report have recently been reviewed in detail by Noggle and Schirmer.<sup>2b</sup> Of particular interest are the paper of Bell and Saunders,<sup>3</sup> reporting a direct correlation of NOE enhancements with internuclear distance, and a series of papers by Noggle and coworkers,<sup>4</sup> demonstrating how relative internuclear distances can be quantitatively determined on systems of three or more spins from the NOE

(1) (a) Abbreviations used: nuclear Overhauser effect, NOE; nuclear magnetic resonance, nmr; nuclear spin-lattice relaxation time,  $T_1$ . (b) In this paper unless stated otherwise NOE enhancements will refer to  $^1\text{H}\{^1\text{H}\}$  double resonance experiments.

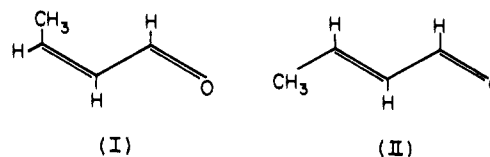
(2) (a) F. A. L. Anet and A. J. R. Bourn, *J. Amer. Chem. Soc.*, **87**, 5250 (1965); (b) J. H. Noggle and R. E. Schirmer, "The Nuclear Overhauser Effect," Academic Press, New York, N. Y., 1971.

(3) R. A. Bell and J. K. Saunders, *Can. J. Chem.*, **48**, 1114 (1970).

(4) (a) R. E. Schirmer, J. H. Noggle, J. P. Davis, and P. A. Hart, *J. Amer. Chem. Soc.*, **92**, 3266 (1970); (b) *ibid.*, **92**, 7239 (1970); (c) R. E. Schirmer, J. P. Davis, J. H. Noggle, and P. A. Hart, *ibid.*, **94**, 2561 (1972); (d) R. E. Schirmer and J. H. Noggle, *ibid.*, **94**, 2947 (1972).

measurements. Noggle and Schirmer<sup>2b</sup> have also stressed the value of an understanding of the nuclear spin-lattice relaxation.

We have been interested in the application of the NOE to the determination of the conformation in solution of the visual chromophore, 11-*cis*-retinal.<sup>5,6</sup> As a model system to test the quantitative aspects of the NOE approach, we have studied the molecules *cis*- and *trans*-crotonaldehyde, I and II below, respectively. The *cis*-



crotonaldehyde is analogous to the terminal fragment (C13-C15) of retinal. One question in particular which arose in the NOE studies of the retinals<sup>5,6</sup> was what

(5) B. Honig, B. Hudson, B. D. Sykes, and M. Karplus, *Proc. Nat. Acad. Sci. U. S.*, **68**, 1289 (1971).

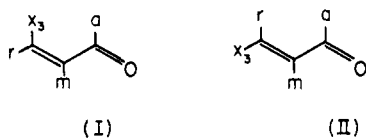
(6) R. Rowan, A. Warshel, B. D. Sykes, and M. Karplus, *Biochemistry*, **13**, 970 (1974).

effective distances were appropriate to use for the interaction of methyl protons with other protons when internal motions which modulate the internuclear distances are present.

We have calculated *absolute* internuclear distances between all of the  $^1\text{H}$ 's of *cis*- and *trans*-crotonaldehyde in solution by measuring the NOE enhancements between all of the spins<sup>2b</sup> and then measuring both the  $^1\text{H}$  and  $^{13}\text{C}$  nuclear spin-lattice relaxation times for all of the spins. These distances are then compared with the reported structures of *cis*- and *trans*-crotonaldehyde, which we have improved by theoretical geometry optimization.<sup>7,8</sup> For the rigid (nonmethyl)  $^1\text{H}$ 's the distances are in excellent agreement. The distances involving the methyl protons are used to test various models for the effective position of the methyl protons when internal motions are considered. We are then able to determine reasonable positions for the minima in the potential for methyl group internal motion.

### Theory

(I)  $^1\text{H}$  Nmr. The  $^1\text{H}$  nmr spectra of both *cis*- and *trans*-crotonaldehyde are loosely coupled ( $J_{ij} \ll |\delta_i - \delta_j|$ ) amrx<sub>3</sub> systems. While the  $\alpha$  proton is in fact upfield of the  $\beta$  proton, we will use the following convention; the aldehyde proton a, the  $\alpha$  proton m, the  $\beta$  proton r, and the methyl protons x (see Table I).



(1) **Nuclear Overhauser Enhancements.** The fractional NOE enhancement of a detected spin *d* when spin *s* is saturated ( $f_d(s)$ ) is given by Noggle and Schirmer<sup>2b</sup> for loosely coupled spin  $1/2$  systems at sufficient dilution that intramolecular dipole-dipole interactions dominate the relaxation, and neglecting cross correlation, as

$$f_d(s) = 0.5 \frac{\rho_{ds}}{R_d} - 0.5 \sum_{n \neq d, s} \frac{\rho_{dn} f_n(s)}{R_d} \quad (1)$$

where

$$R_i = \sum_{j \neq i} \rho_{ij} + \rho_i^*$$

$$\rho_{ij} = \gamma_i^2 \gamma_j^2 \hbar^2 \tau_c(ij) / r_{ij}^6$$

$\tau_c(ij)$  is the correlation time of the vector  $r_{ij}$  between spins *i* and *j*, and  $\rho_i^*$  is the relaxation rate of spin *i* due to other relaxation paths (e.g., interaction with solvent nuclei, spin-rotation, etc.)

For an amrx<sub>3</sub> spin system eq 1 becomes

$$\begin{aligned} R_a f_a(m) &= 0.5 \rho_{am} - 0.5 \rho_{ar} f_r(m) - 3(0.5) \rho_{ax} f_x(m) \\ R_o f_a(r) &= -0.5 \rho_{am} f_m(r) + 0.5 \rho_{ar} - 3(0.5) \rho_{ax} f_x(r) \quad (2a) \\ R_a f_a(x) &= -0.5 \rho_{am} f_m(x) - 0.5 \rho_{ar} f_r(x) + 3(0.5) \rho_{ax} \end{aligned}$$

$$\begin{aligned} R_m f_m(a) &= 0.5 \rho_{am} - 0.5 \rho_{mr} f_r(a) - 3(0.5) \rho_{mx} f_x(a) \\ R_m f_m(r) &= -0.5 \rho_{am} f_a(r) + 0.5 \rho_{mr} - 3(0.5) \rho_{mx} f_x(r) \quad (2b) \\ R_m f_m(x) &= -0.5 \rho_{am} f_a(x) - 0.5 \rho_{mr} f_r(x) + 3(0.5) \rho_{mx} \end{aligned}$$

$$\begin{aligned} R_r f_r(a) &= 0.5 \rho_{ar} - 0.5 \rho_{mr} f_m(a) - 3(0.5) \rho_{rx} f_x(a) \\ R_r f_r(m) &= -0.5 \rho_{ar} f_a(m) + 0.5 \rho_{mr} - 3(0.5) \rho_{rx} f_x(m) \quad (2c) \\ R_r f_r(x) &= -0.5 \rho_{ar} f_a(x) - 0.5 \rho_{mr} f_m(x) + 3(0.5) \rho_{rx} \end{aligned}$$

(7) J. E. Williams, P. J. Stang, and P. Schleyer, *Annu. Rev. Phys. Chem.*, **19**, 531 (1968).

(8) H. A. Scheraga, *Advan. Phys. Org. Chem.*, **6**, 103 (1968).

$$\begin{aligned} R_{xx} f_x(a) &= 0.5 \rho_{ax} - 0.5 \rho_{mx} f_m(a) - 0.5 \rho_{rx} f_r(a) \\ R_{xx} f_x(m) &= -0.5 \rho_{ax} f_a(m) + 0.5 \rho_{mx} - 0.5 \rho_{rx} f_r(m) \quad (2d) \\ R_{xx} f_x(r) &= -0.5 \rho_{ax} f_a(r) - 0.5 \rho_{mx} f_m(r) + 0.5 \rho_{rx} \end{aligned}$$

where

$$\begin{aligned} R_a &= 3\rho_{ax} + \rho_{am} + \rho_{ar} + \rho_a^* \\ R_m &= 3\rho_{mx} + \rho_{am} + \rho_{mr} + \rho_m^* \\ R_r &= 3\rho_{rx} + \rho_{ar} + \rho_{mr} + \rho_r^* \\ R_{xx} &= \rho_{ax} + \rho_{mx} + \rho_{rx} + 3\rho_{xx} + \rho_x^* \end{aligned} \quad (2e)$$

Equation 2 can be solved to determine the ratio of  $\rho_{ij}$ 's; for example

$$\frac{\rho_{ar}}{\rho_{am}} = \frac{\begin{vmatrix} 1 & f_a(m) & -3f_x(m) \\ -f_m(r) & f_a(r) & -3f_x(r) \\ -f_m(x) & f_a(x) & 3 \end{vmatrix}}{\begin{vmatrix} f_a(m) & -f_r(m) & -3f_x(m) \\ f_a(r) & 1 & -3f_x(r) \\ f_a(x) & -f_r(x) & 3 \end{vmatrix}} \quad (3)$$

Alternatively, if the  $R_i$ 's are known, eq 2 can be solved for the individual  $\rho_{ij}$ 's; for example

$$\rho_{ar} = 2R_a \frac{\begin{vmatrix} 1 & f_a(m) & -3f_x(m) \\ -f_m(r) & f_a(r) & -3f_x(r) \\ -f_m(x) & f_a(x) & 3 \end{vmatrix}}{\begin{vmatrix} 1 & -f_r(m) & -3f_x(m) \\ -f_m(r) & 1 & -3f_x(r) \\ -f_m(x) & -f_r(x) & 3 \end{vmatrix}} \quad (4)$$

(2) **Nuclear Spin-Lattice Relaxation.** The nuclear spin-lattice relaxation of an amrx<sub>3</sub> system (loosely coupled) is described by the following equations with the notation of Noggle and Schirmer<sup>2b</sup> and assuming dipole-dipole relaxation

$$\begin{aligned} \frac{d\langle I_z^a \rangle}{dt} &= -R_a[\langle I_z^a \rangle - I_0^a] - (0.5)\{\rho_{am}[\langle I_z^m \rangle - I_0^m] + \rho_{ar}[\langle I_z^r \rangle - I_0^r] + \rho_{ax}[\langle I_z^x \rangle - I_0^x]\} \\ \frac{d\langle I_z^m \rangle}{dt} &= -R_m[\langle I_z^m \rangle - I_0^m] - (0.5)\{\rho_{am}[\langle I_z^a \rangle - I_0^a] + \rho_{mr}[\langle I_z^r \rangle - I_0^r] + \rho_{mx}[\langle I_z^x \rangle - I_0^x]\} \end{aligned} \quad (5)$$

$$\frac{d\langle I_z^r \rangle}{dt} = -R_r[\langle I_z^r \rangle - I_0^r] - (0.5)\{\rho_{ar}[\langle I_z^a \rangle - I_0^a] + \rho_{mr}[\langle I_z^m \rangle - I_0^m] + \rho_{rx}[\langle I_z^x \rangle - I_0^x]\}$$

$$\frac{d\langle I_z^x \rangle}{dt} = -R_{xx}[\langle I_z^x \rangle - I_0^x] - 3(0.5)\{\rho_{ax}[\langle I_z^a \rangle - I_0^a] + \rho_{mx}[\langle I_z^m \rangle - I_0^m] + \rho_{rx}[\langle I_z^r \rangle - I_0^r]\}$$

with  $I_0^a = I_0^m = I_0^r = I_0^x/3$  and  $R_i$ 's defined as above. The relaxation of any given spin is complex. However, after a nonselective  $180^\circ$  pulse such that at  $t = 0$

$$\begin{aligned} \langle I_z^x \rangle - I_0^x &= -2I_0^x \\ \langle I_z^i \rangle - I_0^i &= -2/3 I_0^x \quad i = a, m, r \end{aligned} \quad (6)$$

we can define an initial relaxation rate which will describe the relaxation before significant cross relaxation occurs

$$\begin{aligned} R_a^0 &= 3/2[3\rho_{ax} + \rho_{am} + \rho_{ar}] + \rho_a^* \\ R_m^0 &= 3/2[3\rho_{mx} + \rho_{am} + \rho_{mr}] + \rho_m^* \\ R_r^0 &= 3/2[3\rho_{rx} + \rho_{ar} + \rho_{mr}] + \rho_r^* \\ R_{xx}^0 &= 3/2[\rho_{ax} + \rho_{mx} + \rho_{rx} + 2\rho_{xx}] + \rho_x^* \end{aligned} \quad (7)$$

The time for which this relaxation rate describes the relaxation is long if the relaxation rates are approximately equal. To the extent that  $\rho_i^* \ll \sum_j \rho_{ij}$ , then

$$\begin{aligned} R_a^0 &= \frac{3}{2}R_a \\ R_m^0 &= \frac{3}{2}R_m \\ R_r^0 &= \frac{3}{2}R_r \end{aligned} \quad (8)$$

### (3) Determination of Distances in Rigid Systems.

Given the individual  $\rho_{ij}$ 's determined from the measured NOE's and spin-lattice relaxation rates, internuclear distances ( $r_{ij}$ ) can be calculated in rigid systems from

$$\rho_{ij} = \frac{\gamma_i^2 \gamma_j^2 \hbar^2 \tau_c(ij)}{r_{ij}^6} \quad (9)$$

if the  $\tau_c(ij)$ 's are known. This formula assumes dipole-dipole relaxation, isotropic motion, extreme narrowing, and no internal motions and neglects cross correlation. The values for  $\tau_c(ij)$  can be determined from the  $^{13}\text{C}$   $T_1$ 's under conditions of  $^1\text{H}$  noise decoupling since the appropriate  $r_{ij}$ 's are known (see below).

**(4) Determination of Distances When Internal Motions Are Involved.** The presence of internal motion where the  $r_{ij}$  remains constant (e.g., the internuclear vector between the protons of the methyl group) has been treated by several workers. For the protons of a methyl group jumping between three potential wells separated by  $120^\circ$ ,  $\tau_c(ij)$  can be replaced by an effective correlation time<sup>9</sup>

$$\tau_{\text{eff}} = \frac{(3 \cos^2 \Delta - 1)^2}{4} \tau_c + \frac{3(\sin^2 2\Delta)}{4} \tau_1 + \frac{3(\sin^4 \Delta)}{4} \tau_1 \quad (10)$$

where  $\tau_c$  is the correlation time for the overall rotation of the molecule (assumed isotropic)

$$\tau_1 = \left( \frac{1}{\tau_c} + \frac{1}{\tau_j} \right)^{-1}$$

( $2/3\tau_j$ ) is the jump rate per unit time for a given methyl proton and  $\Delta$  is the angle that the internuclear vector makes with the axis of internal rotation.

We are also interested in  $^1\text{H}$  relaxation in the presence of internal motion where  $r_{ij}$  is not constant. For example, the methyl proton-aldehyde proton internuclear vector for each methyl proton is changed in length and direction upon internal rotation of the methyl group. Starting from the general approach of Woessner<sup>9,10</sup> we can then calculate that the relaxation is given by (see Appendix)

$$\rho_{ij} = \gamma_i^2 \gamma_j^2 \hbar^2 \tau_c \left( A + B \frac{\tau_j}{\tau_c + \tau_j} \right) \quad (11)$$

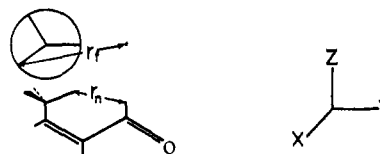
where  $\tau_c$  and  $\tau_j$  are defined as above and where

$$\begin{aligned} A &= \frac{2}{9} \left\{ \left( \frac{1}{r_i^6} + \frac{0.5}{r_n^6} \right) + \left[ \frac{(1 - 6l_i^2 + 6l_i^4)}{r_i^6} + \frac{3(m_n m_i + n_n n_i)^2 - 1}{r_n^3 r_i^3} \right] \right\} \\ B &= \frac{2}{9} \left\{ \left( \frac{2}{r_i^6} + \frac{1}{r_n^6} \right) - \left[ \frac{(1 - 6l_i^2 + 6l_i^4)}{r_i^6} + \frac{3(m_n m_i + n_n n_i)^2 - 1}{r_n^3 r_i^3} \right] \right\} \end{aligned} \quad (12)$$

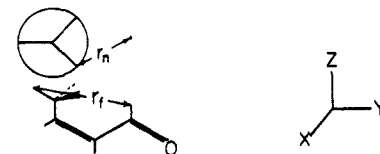
(9) D. E. Woessner, *J. Chem. Phys.*, **36**, 1 (1962).

(10) D. E. Woessner, *J. Chem. Phys.*, **42**, 1855 (1965).

in which  $r_n$  and  $r_i$  are defined by the configuration shown below viewing the molecule from the top (e.g., looking down on methyl and aldehyde protons) and  $l_n, m_n, n_n$



and  $l_i, m_i, n_i$  are the direction cosines of  $\mathbf{r}_n$  and  $\mathbf{r}_i$  respectively with respect to the  $x, y,$  and  $z$  axes shown. The indices for  $\mathbf{r}_n$  and  $\mathbf{r}_i$  in the definitions of  $A$  and  $B$  are reversed for the alternate methyl group torsional conformation shown below.



**(II)  $^{13}\text{C}$  Nmr. (1) Nuclear Spin Relaxation.** The  $^{13}\text{C}$  relaxation under conditions of proton noise decoupling is given by

$$\frac{1}{T_1(^{13}\text{C})} = \frac{N_H \gamma_C^2 \gamma_H^2 \hbar^2 \tau_c(\text{CH})}{r_{\text{CH}}^6} \quad (13)$$

in the extreme narrowing limit and assuming that dipole-dipole interactions dominate, where  $N_H$  is the number of directly bonded protons (at distance  $r_{\text{CH}}$ ) and  $\tau_c(\text{CH})$  is the rotational correlation time for the CH internuclear vector. Since the C-H distances are generally known, this allows the determination of  $\tau_c(\text{CH})$ . Internal motion which does not change the magnitude of  $r_{\text{CH}}$  has the same effect as for the  $^1\text{H}$  relaxation; e.g.,  $\tau_c(\text{CH})$  is replaced by an effective correlation time (see section I.4).

**(III) Geometry Optimization.** Details of the *trans*-crotonaldehyde geometry and those of the simpler compound acrolein as determined by microwave spectroscopy are available,<sup>11,12</sup> but we are unaware of any similar data on *cis*-crotonaldehyde with which the results of our work might be compared. We have therefore taken the known geometry of the aldehyde end of *all-trans*-retinal<sup>13</sup> as a rough approximation to the geometry of *cis*-crotonaldehyde and tried to improve this approximation by minimizing the conformational energy of the molecule.<sup>7,8</sup>

The conformational energy expression is given by

$$E = E_b + E_\theta + E_\phi + E_e + E_{LJ}$$

where

$$E_b = \sum_{\text{bonds}} K_B (b - b_0)^2$$

$$E_\theta = \sum_{\text{bond angles}} K_\theta (\theta - \theta_0)^2$$

$$E_\phi = \sum_{\text{torsional angles}} K_\phi [1 + \cos(n\phi - \delta)]$$

(11) M. Suzuki and K. Koziyam, *Bull. Chem. Soc. Jap.*, **42**, 2183 (1969).

(12) E. A. Cherniak and C. C. Costain, *J. Chem. Phys.*, **45**, 104 (1966).

(13) T. Hamanaka, T. Mitsui, T. Ashida, and M. Kadudo, *Acta Crystallogr., Sect. B*, **28**, 214 (1972).

$$E_{el} = \frac{1}{\epsilon} \sum_{i < j} \frac{q_i q_j}{r_{ij}}$$

$$E_{LJ} = \sum_{i < j} \left( \frac{A_{ij}}{r_{ij}^{12}} - \frac{B_{ij}}{r_{ij}^6} \right)$$

The terms in the energy expression represent respectively the bond length and bond angle deformation energies, the torsional energy, the electrostatic energy between partial charges on the atoms in the molecule, and the Lennard-Jones interactions between atoms in the molecule. Electrostatic and Lennard-Jones interactions are evaluated only for atoms separated by three or more bonds.

The bond length and bond angle functions were only roughly parameterized, using estimates for the force constants ( $K_B$  ranged from 150 kcal/(mol Å<sup>2</sup>) for C(sp<sup>2</sup>)-C(sp<sup>3</sup>) to 700 kcal/(mol Å<sup>2</sup>) for C=O;  $K_\theta = 35$  kcal/(mol rad<sup>2</sup>) for bond angles including hydrogen atoms,  $K_\theta = 60$  kcal/(mol rad<sup>2</sup>) for all other bond angles), standard values for the unstrained bond lengths  $b_0$ , and average bond angles from the retinals and *trans*-crotonaldehyde for the unstrained bond angles  $\theta_0$ . Values for  $K_\phi$ ,  $n$ , and  $\delta$  were taken from the literature on internal rotation.<sup>14,15</sup> Partial charges were determined by a CNDO/2 molecular orbital calculation<sup>16</sup> and a dielectric constant  $\epsilon = 3.0$  was assumed. Lennard-Jones parameters were determined using the Slater-Kirkwood formula as discussed by Scheraga.<sup>8</sup>

Coordinates of all the atoms in the molecule were varied in each cycle of a steepest descent routine until the conformational energy was minimized.

## Experimental Section

A mixture of *cis*- and *trans*-crotonaldehyde was prepared photochemically, as suggested by McCreer and Page.<sup>17</sup> Reagent grade *trans*-crotonaldehyde was distilled under argon; the low-boiling (less than 100°) fraction was collected for photolysis. The fraction (100 ml) was placed in an Ace Glass Co. water-cooled photoreactor cell, employing a 500-W mercury arc lamp held in a quartz sleeve. The free volume of the cell was flushed with N<sub>2</sub>. The course of the reaction was followed by nmr, using the ratio of the peak heights of the respective aldehyde resonances to determine the isomeric ratios. After 24 hr of photolysis, the reaction was stopped, having reached a *cis*:*trans* isomeric ratio of 24:76. During the course of the reaction the reagent mixture, which started out clear, turned increasingly darker yellow, indicating that polymerization had occurred on the glass and quartz surfaces around the atmosphere-liquid interface. Consequently, the photolysis mixture was distilled at reduced temperature and pressure and the clear, low-boiling fraction was retained. This fraction was free of visible impurity peaks in the <sup>1</sup>H or <sup>13</sup>C nmr spectra, and the isomeric ratio was unchanged from before distillation.

Two nmr samples of the crotonaldehyde isomeric mixture, using acetone-*d*<sub>6</sub> as the solvent, were prepared: one relatively dilute (0.612 M in total crotonaldehyde) for <sup>1</sup>H  $T_1$  and NOE measurements, and one more concentrated (50% v/v) for <sup>13</sup>C measurements. The former sample also contained 1% v/v HMDS for an internal reference standard. Each sample was carefully degassed using at least five freeze-pump-thaw cycles and sealed.

All NOE and  $T_1$  measurements were made on a Varian XL-100-15 nmr spectrometer operating in the Fourier transform mode and interfaced to a Varian 620-i computer equipped with a magnetic tape unit. Under <sup>1</sup>H homonuclear double resonance conditions, the  $\pi$  pulse of the spectrometer was 104  $\mu$ sec. NOE's were determined by comparison of the relative intensities of the observed

peak with the irradiating radiofrequency field first on the resonance for the irradiated nucleus ("irradiated spectrum") and then far off-resonance ("control spectrum"). Irradiated and control transients were collected alternately and stored on magnetic tape. For each experiment (a row in Tables IVA or IVB), at least four irradiated and four control transients were averaged. To protect the receiver from overload, the H<sub>2</sub> power was gated off during the pulse and the acquisition of the free induction decay. Long delays (greater than five times the longest  $T_1$  of the observed nuclei) were used between pulses to assure the recovery of the spin system to its steady state under conditions of on-resonance or control irradiation. The H<sub>2</sub> power was chosen as the minimum needed to effectively saturate the resonance of the irradiated nucleus, as determined by the disappearance of that resonance from the irradiated spectrum. When the resonances of irradiated and observed nuclei were (a) fairly close in frequency and (b) spread out in frequency due to spin-spin coupling, as in the case of  $\alpha$  H and  $\beta$  H (separated by about 0.85 ppm in both isomers), the high H<sub>2</sub> power level necessary to saturate the irradiated nucleus also affected the magnetization of the observed nucleus. To compensate in these situations, the control irradiating frequency was placed exactly equidistant in the spectrum from the resonance frequency of the observed nucleus but in the opposite direction from the on-resonance irradiating frequency. Since the decoupler was gated off during the acquisition of the free induction decay, the irradiated spectra showed no change in line width, and peak heights were used as the intensities for the well-separated lines measured.

<sup>13</sup>C  $T_1$  measurements were made at 25.16 MHz under conditions of full <sup>1</sup>H noise decoupling, using the method of progressive saturation ( $\pi/2 - \tau$ )<sub>N</sub>.<sup>18</sup> The measured peak heights were fit to the recovery curve by a two-parameter (fitting to  $T_1$  and  $M_0$ , the equilibrium magnetization) nonlinear least-squares program. The error limits (given in Table III) are the standard deviations of the fit. The  $\pi$  pulse for <sup>13</sup>C was 72  $\mu$ sec corresponding to  $\gamma_C H_1$  about equal to 6900 Hz.

<sup>1</sup>H  $T_1$ 's were measured by the inversion-recovery technique ( $P_p - \tau - P_0 - T$ )<sub>N</sub>.<sup>19</sup> A waiting time  $T$  of 350 sec was used. Incorrect calibration of the pulse strength resulted in a poor fit to the ideal inversion-recovery curve, which assumes that the preparatory pulse  $P_p$  is exactly 180°. Consequently, a three-parameter (to  $M_0$ ,  $T_1$ , and  $\alpha$ ) fit<sup>20</sup> was used for each peak to obtain the tip angle of the pulse  $P_p$ . This tip angle (the mean of the tip angles for all spins,  $135.9 \pm 2.7^\circ$ ) was then used in the same function for a two-parameter fit to  $M_0$  and  $T_1$ . These  $T_1$  values, together with the standard deviations of the two-parameter fit, are listed in Tables I and II.

**Table I.** Chemical Shifts and Coupling Constants for Crotonaldehyde Spectra in Acetone-*d*<sub>6</sub> (Chemical Shifts Relative to HMDS, ppm)

Proton	<i>cis</i> -crotonaldehyde	<i>trans</i> -crotonaldehyde
Chemical Shifts		
A	10.054	9.417
$\alpha$	5.809	6.017
$\beta$	6.696	6.907
Methyl (M)	2.097	1.932
Coupling Constant, Hz		
A- $\alpha$	7.80	7.80
A- $\beta$	<0.25	<0.25
A-methyl	<0.25	<0.25
$\alpha$ - $\beta$	11.3	15.55
$\alpha$ -methyl	1.7	1.5
$\beta$ -methyl	7.5	6.8

(18) R. Freeman and H. D. W. Hill, *J. Chem. Phys.*, **54**, 3367 (1971).

(19) R. L. Vold, J. S. Waugh, M. P. Klein, and D. E. Phelps, *J. Chem. Phys.*, **48**, 3831 (1968).

(20) The function used for fits was  $M_z(\tau) = M_0(1 - (1 - \cos \alpha) \exp(-\tau/T_1))$ , where  $M_0$  = the reduced equilibrium magnetization =  $M_0 \sin(\alpha/2)$ ,  $M_z(\tau)$  = peak height =  $M_z(\tau) \sin(\alpha/2)$ ,  $\alpha$  = tip angle,  $\tau$  = delay between the preparatory pulse  $P_p$  and the observational pulse  $P_0$ , and  $T_1$  = the longitudinal relaxation time. This function is valid as long as the transverse magnetization created by the preparatory pulse ( $\alpha$ ) decays away before the observational pulse ( $\alpha/2$ ). In these experiments the magnetic field inhomogeneity was 0.3 Hz, which sets the upper limit on  $T_2^*$ , the effective transverse relaxation time, of about 1s. Thus the transverse magnetization should be at least 95% decayed by  $\tau = 3s$ , the shortest time point used in the fit.

(14) E. B. Wilson, Jr., *Advan. Chem. Phys.*, **2**, 367 (1959).

(15) J. P. Lowe, *Progr. Phys. Org. Chem.*, **6**, 1 (1968).

(16) J. A. Pople and D. L. Beveridge, "Approximate Molecular Orbital Theory," McGraw-Hill, New York, N. Y., 1970.

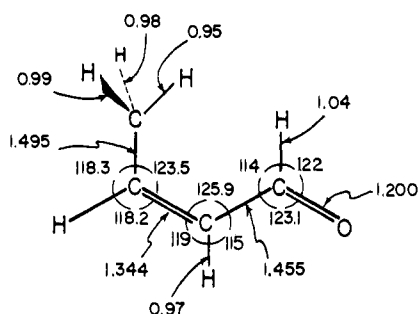
(17) D. E. McCreer and B. D. Page, *Can. J. Chem.*, **47**, 866 (1969).

**Table II.**  $^1\text{H}$  Nuclear Spin-Lattice Relaxation Times  $T_1$  for *cis*- and *trans*-Crotonaldehyde

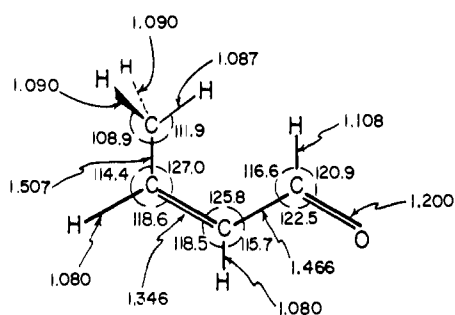
<i>cis</i> -Crotonaldehyde			<i>trans</i> -Crotonaldehyde		
Line	$T_1$ , sec	Av $T_1$ , sec	Line	$T_1$ , sec	Av $T_1$ , sec
A1	$78.4 \pm 0.6$	$78.2 \pm 1.0$	A1	$63.8 \pm 0.6$	$64.0 \pm 0.6$
A2	$78.1 \pm 0.8$		A2	$64.2 \pm 0.3$	
$\beta$ 1	$65.8 \pm 0.8$		$\beta$ 1	$38.0 \pm 0.9$	
$\beta$ 2	$53.3 \pm 2.2$	$60.4 \pm 0.8$	$\beta$ 2	$45.0 \pm 0.8$	$42.6 \pm 0.5$
$\beta$ 3	$64.5 \pm 0.3$		$\beta$ 3	$44.8 \pm 0.6$	
$\beta$ 4	$57.7 \pm 0.6$		$\beta$ 4	$42.6 \pm 0.7$	
$\alpha$ 1	$78.6 \pm 1.2$		$\alpha$ 1	$90.7 \pm 0.4$	
$\alpha$ 2	$77.8 \pm 0.6$		$\alpha$ 2	$91.1 \pm 0.5$	$91.4 \pm 0.3$
$\alpha$ 3	$79.8 \pm 1.1$	$79.0 \pm 0.6$	$\alpha$ 3	$92.1 \pm 0.5$	
$\alpha$ 4	$79.4 \pm 1.4$		$\alpha$ 4	$91.6 \pm 0.4$	
$\alpha$ 5	$79.2 \pm 1.2$				
M1	$26.9 \pm 0.4$		M1	$23.7 \pm 0.2$	$23.5 \pm 0.4$
M2	$26.8 \pm 0.5$	$26.9 \pm 0.4$	M2	$23.3 \pm 0.4$	
M3	$27.0 \pm 0.6$				

## Results

(I) **Molecular Geometries.** The retinal terminal geometry for *cis*-crotonaldehyde is<sup>13</sup>

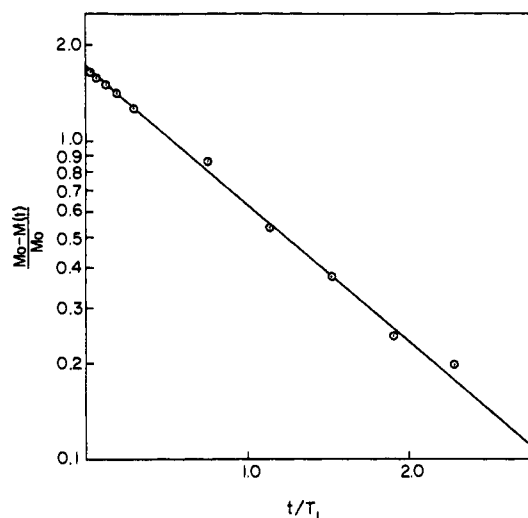


After conformational energy minimization, we obtained the geometry



Nonbonded repulsion between the aldehyde proton and the methyl group has moved these groups apart, but energy minimizations with the methyl group held staggered with respect to the double bond indicate that the eclipsed methyl geometry shown is still the more stable structure by 1.1 kcal/mol. Corresponding calculations on *trans*-crotonaldehyde indicate that the geometry with a methyl proton eclipsing the double bond is more stable than a staggered geometry by 1.9 kcal/mol.

(II) **Nmr.** The recovery of the magnetization for each line in the  $^1\text{H}$  nmr spectrum of *cis*- and *trans*-crotonaldehyde (Table I) after the application of a non-selective inverting pulse could be described by a single exponential (see Figure 1). The time constants  $T_1$  obtained are listed in Table II. The  $^{13}\text{C}$  relaxation times measured under conditions of  $^1\text{H}$  noise decoupling are listed in Table III. The nuclear Overhauser enhancements<sup>2</sup> obtained for *cis*- and *trans*-crotonaldehyde are listed in Table IV.



**Figure 1.** Semilogarithmic  $T_1$  plot for *cis*-crotonaldehyde  $\beta$ 1 peak (see Tables I and II for notation and Experimental Section for details),  $T_1 = 65.8 \pm 0.8$  sec.

**Table III.**  $^{13}\text{C}$  Nuclear Spin-Lattice Relaxation Times  $T_1$  for *cis*- and *trans*-Crotonaldehyde

Carbon	<i>cis</i> -Crotonaldehyde $T_1$ , sec	<i>trans</i> -Crotonaldehyde $T_1$ , sec
CHO	$33.0 \pm 3.1$	$25.7 \pm 3.8$
$\alpha$	$27.2 \pm 4.2$	$28.7 \pm 2.9$
$\beta$	$29.2 \pm 1.4$	$22.5 \pm 1.5$
$\text{CH}_3$	$46.3 \pm 20.9$	$36.2 \pm 3.0$

**Table IV.** Nuclear Overhauser Enhancements for (A) *cis*- and (B) *trans*-Crotonaldehyde (in Per Cent, all  $\pm 2\%$ )

Irradiated	(A) Obsd			
	a	m	r	x
a		4.4	0.8	4.7
m	1.5		23.3	1.5
r	1.3	32.8		1.5
x	32.6	3.8	18.6	
Irradiated	(B) Obsd			
	a	m	r	x
a		2.4	17.4	-2.1
m	2.3		-2.0	3.8
r	25.7	4.0		0.6
x	0.1	24.2	11.6	

The time constants listed in Tables I and II can be identified with the initial relaxation rates ( $T_1(i)^{-1} = R_i^0$ ) since no nonexponential character developed in the recovery of the magnetization. Using eq 8, values for  $R_a$ ,  $R_m$ , and  $R_r$  can then be obtained. By substituting these values and the experimental NOE's into the nine equations of the form of eq 4 which can be obtained from eq 2a-c, values for the various  $\rho_{ij}$ 's were obtained (two determinations for  $\rho_{ij}$ ,  $i, j \neq x$ , one determination for  $\rho_{ij}$ ,  $i$  or  $j = x$ ). The values obtained for the  $\rho_{ij}$ 's for *cis*- and *trans*-crotonaldehyde are listed in Table V. The error limits quoted in Table V were calculated by a propagation of the errors in the relaxation rates and NOE's through the calculation and reflect how accurately the different  $\rho_{ij}$ 's are known.

The  $^{13}\text{C}$  relaxation times for the  $\alpha$  and  $\beta$  carbons can be used to calculate the rotational correlation times for *cis*- and *trans*-crotonaldehyde using eq 13 and a CH

**Table V.** Relaxation Rates  $\rho_{ij}$  for *cis*- and *trans*-Crotonaldehyde

(i,j)	Cis	Trans
	$\rho_{ij} \times 10^4$ <sup>a</sup>	$\rho_{ij} \times 10^4$ <sup>a</sup>
am	4.46 ± 4.00	4.00 ± 3.96
	8.80 ± 3.63	3.97 ± 3.18
ar	4.53 ± 4.11	53.42 ± 4.25
	5.95 ± 4.53	53.62 ± 6.36
rm	55.76 ± 3.52	7.08 ± 3.26
	50.28 ± 4.42	
ax	18.86 ± 1.38	2.47 ± 1.50
mx	6.55 ± 1.29	12.04 ± 1.07
rx	14.47 ± 1.59	11.83 ± 2.19

<sup>a</sup> In sec<sup>-1</sup>.

distance of 1.08 Å. The results are: for *cis*-crotonaldehyde,  $\tau_c = (1.56 \pm 0.12) \times 10^{-12}$  sec; for *trans*-crotonaldehyde,  $\tau_c = (1.72 \pm 0.11) \times 10^{-12}$  sec.

Using the  $\tau_c$ 's calculated from the <sup>13</sup>C relaxation times and the  $\rho_{ij}$ 's listed in Table V, the internuclear distances  $r_{ij}$  were calculated. These are listed in Table VI, again with two determinations for  $r_{ij}$ ,  $i, j \neq x$  and

**Table VI.** Experimental and Calculated Internuclear Distances  $r_{ij}$  for (A) *cis*- and (B) *trans*-Crotonaldehyde (Å)

A			
(i,j)	Exptl $r_{ij}$	$r_{ij}$ from optimal geom (eclipsed)	Methyl proton centroid optimized geom (eclipsed)
am	3.54 ± 1.20	3.12	3.12
	3.16 ± 0.33		
ar	3.54 ± 1.24	3.82	3.82
	3.38 ± 0.80		
mr	2.33 ± 0.05	2.38	2.38
	2.37 ± 0.07		
ax	2.97 ± 0.07	2.65	2.91
mx	3.32 ± 0.16	4.12	3.87
rx	2.91 ± 0.09	2.89	2.52
B			
(i,j)	Exptl $r_{ij}$	$r_{ij}$ from microwave geom (eclipsed)	Methyl proton centroid microwave geom (eclipsed)
am	3.66 ± 2.13	3.13	3.13
	3.66 ± 0.95		
ar	2.37 ± 0.06	2.31	2.31
	2.37 ± 0.08		
mr	3.32 ± 0.40	3.08	3.08
ax	3.96 ± 0.67	4.71	4.48
mx	3.04 ± 0.08	3.10	3.08
rx	3.04 ± 0.14	2.90	2.54

one determination for  $r_{ij}$ ,  $i$ , or  $j = x$ . The errors again reflect the propagation of the errors in the  $\rho_{ij}$ 's and the  $\tau_c$ 's through the calculation. The ax, mx, and rx distances shown in Table VI are "effective" distances calculated using eq 9. For these internuclear distances involving the methyl protons, eq 11 shows that the effective distances  $r_{ix}$  are identified in our theory with the quantity  $(A + B\tau_j/(\tau_c + \tau_j))^{-1/6}$ . Values of this latter quantity calculated using distances taken from the microwave and optimized X-ray geometries and the experimentally determined ratio of  $\tau_c$  to  $\tau_j$  (see below) are shown in the second column of Table VI. In the third column of Table VI we give the distances from a, m, and r to the centroid of the methyl protons calculated from the microwave and optimized geometries.

The values of  $\rho_{ij}$  listed in Table V along with the equation for  $R_{xx}$ <sup>0</sup> of the form of eq 7 can be used to calculate  $\rho_{xx}$ , again with the assumption  $\rho_x^* \ll \sum_j \rho_{xj}$ . The results are: for *cis*-crotonaldehyde,  $\rho_{xx} = 104 \times 10^{-4}$  sec<sup>-1</sup>; for *trans*-crotonaldehyde,  $\rho_{xx} = 129 \times 10^{-4}$  sec<sup>-1</sup>. These values, and the <sup>13</sup>C  $T_1$ 's for the methyl carbons, can both be used to calculate the correlation time for the internal rotation of the methyl group using eq 10. The results from the  $\rho_{xx}$ 's are: for *cis*-crotonaldehyde,  $\tau_j = 0.19 \times 10^{-12}$  sec; for *trans*-crotonaldehyde,  $\tau_j = 0.30 \times 10^{-12}$  sec. The results from the <sup>13</sup>C  $T_1$ 's for the methyl carbons are: for *cis*-crotonaldehyde,  $\tau_j = 0.12 \times 10^{-12}$  sec; for *trans*-crotonaldehyde,  $\tau_j = 0.17 \times 10^{-12}$  sec.

## Discussion

For the internuclear distances between the rigid protons of *cis*- and *trans*-crotonaldehyde, the agreement between the numbers determined from the combined NOE and <sup>1</sup>H and <sup>13</sup>C  $T_1$  measurements and either the microwave or theoretically optimized X-ray structure is really quite good. This is especially true for the distances which are small (*cf.*  $r_{mr}$  in *cis*-crotonaldehyde, exptl = 2.35 ± 0.06 Å, optimized structure = 2.38 Å; and  $r_{ar}$  in *trans*-crotonaldehyde, exptl = 2.37 ± 0.07 Å, microwave structure = 2.31 Å). Going back through the calculations, one finds that these protons dominate each other's relaxation so that even when all of the errors in the individual NOE's and relaxation rates are propagated through the calculation the  $\rho_{ij}$ 's in question are well determined. Longer distances ( $\geq 3.5$  Å), on the other hand, correspond to  $\rho_{ij}$ 's which are not at all well determined.

The fact that the absolute distances come out correctly (in fact, all of the distances are determined relative to the assumed <sup>13</sup>CH bond distance) indicates that the assumptions involved in the relaxation and NOE measurements and their interpretation are valid. The largest errors might be expected in the <sup>1</sup>H relaxation. First, while the longitudinal relaxation on theoretical grounds can be very complex,<sup>21</sup> all of the resonances could be characterized experimentally by single exponential relaxation. This results from the fact that all of the <sup>1</sup>H relaxation times, except for the methyl group, are roughly equal so that cross relaxation is ineffectual and that the fast relaxing methyl group with which the other protons interact has an efficient relaxation pathway of its own ( $\rho_{xx}$ ).<sup>21</sup> The spectrum was also sufficiently loosely coupled so that all of the resonances associated with a given spin relaxed equally. The assumption of dominating dipole-dipole relaxation for protons can be checked directly. The  $\rho_{ij}$ 's determined from eq 4 can be summed for a given spin and divided by  $R_i$ . How close this ratio comes to unity is then an independent indication from the NOE measurements of the contribution of other relaxation pathways. As a typical example we can do this calculation for the  $\beta$  proton in *cis*-crotonaldehyde. The result is  $(\sum_j \rho_{j\beta})/R_\beta = 0.88 \pm 0.10$ , indicating that within experimental error the relaxation is almost completely dominated by dipole-dipole interactions.

The appropriateness of the  $\tau_c$ 's determined from the <sup>13</sup>C  $T_1$ 's is open to some question. While many workers

(21) (a) R. Freeman, S. Wittekoek, and R. R. Ernst, *J. Chem. Phys.*, **52**, 1529 (1970); (b) I. D. Campbell and R. Freeman, *J. Magn. Resonance*, **11**, 143 (1973).

have verified that  $^{13}\text{C}$  relaxation is dominated by dipole-dipole interactions with directly bonded protons,<sup>22</sup> one could question whether the tumbling of either *cis*- or *trans*-crotonaldehyde in solution is isotropic. The aldehyde,  $\alpha$ , and  $\beta$  CH bonds are oriented differently with respect to the principle diffusion axes (not known) of either molecule, but not one is oriented out of the plane of the molecule. Therefore, the approximate equality of their  $^{13}\text{C}$   $T_1$ 's really only indicates that with respect to axes in the plane of the molecule the diffusion is relatively isotropic. However, since all of the internuclear vectors in question are either in the plane of the molecule or only slightly out of it, any errors involved in using the  $\tau_c$ 's determined from the  $^{13}\text{C}$   $T_1$ 's are expected to be small. It is interesting that the more compact *cis*-crotonaldehyde seems to diffuse slightly faster than the more extended *trans* isomer. The  $\tau_j$ 's determined from the  $^1\text{H}$  and  $^{13}\text{C}$   $T_1$ 's are approximately equal and always shorter for *cis*-crotonaldehyde. This is consistent with the lower torsional barrier in the *cis* molecule because the steric interactions of the methyl and aldehyde protons raise the energy of the eclipsed minimum.

The internuclear distances involving a methyl proton determined from the nmr measurements cannot be as directly compared to the structures involved because of the internal rotation of the methyl groups. On the other hand, ideally the "effective" nmr distances determined can be used to probe the methyl group torsional potential. The "effective" internuclear distances were best reproduced using eq 11 and the distances from the optimized or microwave structure which have the methyl proton eclipsed over the double bond. If the more open, optimized, *cis*-crotonaldehyde structure was not used, the theoretical ax distance was far too short for all models for the torsional conformers of the methyl group. The remaining difference between measured and calculated  $r_{\text{eff}}$  for a-x in *cis*-crotonaldehyde could be due either to inadequacy of the "optimized" geometry of *cis*-crotonaldehyde or to inadequacy of the jumping model for internal rotation (nonbonded repulsion between the methyl group and the aldehyde proton "levels" the effective torsional potential; the internal motion may be something between a jumping motion and simple stochastic diffusion).

While the "methyl proton centroid" model does not seem much worse when expressed as effective internuclear distances, two of the distances are quite short ( $\sim 2.5 \text{ \AA}$ ), which would lead to unacceptably large  $\rho_{ij}$ 's when predicting NOE's. For all protons except those directly adjacent to the methyl group (for which the calculated NOE will be predicted too large but the observed NOE will be large and obvious anyway), neglecting internal motion of the methyl group and using the "centroid" model will not introduce serious errors (e.g., see ref 5 and 6).

## Conclusion

Internuclear distances between all of the protons of *cis*- and *trans*-crotonaldehyde in solution have been obtained. While this is an extension of the normal conclusion that NOE's can only be used to obtain relative internuclear distances, all of the distances obtained

herein are in fact measured relative to the CH bond length of 1.08  $\text{\AA}$ . In general the CH bond lengths in typical organic compounds do not vary and can be assumed known. NOE measurements can then be applied to a wide range of problems in structure determination. For molecules with internal motions, once a model for the internal motion has been selected, the effective internuclear distances obtained to the spins involved can be used to determine the parameters of the motional model and therefore to choose between the various proposals for the internal dynamics.

An especially interesting feature of the crotonaldehyde study is the configuration of the methyl groups in the two isomers. It has been known for some time that methyl groups which are singly bonded to an  $\text{sp}^2$  carbon generally have stable conformations in which one of the methyl protons eclipses the double bond to the unsaturated carbon.<sup>14,15</sup>



Some theoretical justifications for this phenomenon have been given.<sup>23</sup> Since the rotational barriers for these  $\text{sp}^3$ - $\text{sp}^2$  bonds tend to be somewhat lower than in the case of  $\text{sp}^3$ - $\text{sp}^3$  bonds, it is interesting that our results for *cis*-crotonaldehyde show that the molecule relieves methyl proton-aldehyde proton steric strain by opening up bond angles rather than by twisting the methyl group.

## Appendix

The fundamental quantity in the NOE equations is  $\rho_{ij}$ , a "rate constant" which is identical with the factor  $1/T_1^{11}$  used by Abragam<sup>24</sup> to characterize the longitudinal relaxation of spins  $I_i$  which are coupled *via* a dipolar interaction through space with spins  $I_j$ . In this appendix we outline the derivation of an equation for  $\rho_{ij}$  for the case that one spin is rigidly attached to a molecular frame and the other spin is in a methyl group rotating about the bond by which it is attached to the frame (eq 11 and 12 in the text).

The Hamiltonian expressing the interaction is

$$H_1(t) = \frac{\gamma_i \gamma_j \hbar}{r_{ij}^3} \{ \vec{I}_i \cdot \vec{I}_j - 3(\vec{I}_i \cdot \hat{r}_{ij})(\vec{I}_j \cdot \hat{r}_{ij}) \} \quad (\text{A1})$$

where  $\hat{r}_{ij}$  is the unit vector  $\mathbf{r}_{ij}/r_{ij}$ . Following Abragam, this Hamiltonian may be decomposed into a sum

$$H_1(t) = \sum_{h=-2}^{+2} F_h(t) A_h \quad (\text{A2})$$

where the factors  $A_h$  depend only on the spin operators and the factors  $F_h(t)$  depend only on  $\mathbf{r}_{ij}(t)$  and may be expressed in terms of spherical harmonics or direction cosines of  $\hat{r}_{ij}$  in the laboratory coordinate system.

The equation of motion of  $\sigma_i(t)$ , the density operator for spin  $i$ , may be solved in the presence of the perturbation  $H_1(t)$  and formally averaged over the possible motions of  $\mathbf{r}_{ij}(t)$  to yield an ensemble-averaged density operator which characterizes the evolution of all observable properties of spins  $i$  in a macroscopic sample of interacting  $i, j$  systems. In particular, Abragam

(23) R. A. Scott and H. A. Scheraga, *J. Chem. Phys.*, **42**, 2209 (1965).

(24) A. Abragam, "The Principles of Nuclear Magnetism," Oxford University Press, London, 1961, Chapter 8.

(22) K. F. Kuhlmann, D. M. Grant, and R. K. Harris, *J. Chem. Phys.*, **52**, 3439 (1970).

derives the result (written here for spins  $1/2$  and with small modifications of notation)

$$\frac{dI_{iz}}{dt} = -\frac{1}{T_1 I_i I_i} (I_{iz} - I_{i0}) - \frac{1}{T_1 I_i I_j} (I_{jz} - I_{j0}) \quad (\text{A3})$$

where

$I_{iz}$  = the expected value of the  $z$  component of spin  $i$  (ensemble averaged)

$I_{i0}$  = the equilibrium value of  $I_{iz}$

$$\frac{1}{T_1 I_i I_i} \equiv \rho_{ij} = \frac{3}{4} \gamma_i^2 \gamma_j^2 \hbar^2 \times$$

$$\left\{ \frac{1}{12} J_0(\omega_i - \omega_j) + \frac{3}{2} J_1(\omega_i) + \frac{3}{4} J_2(\omega_i + \omega_j) \right\} \quad (\text{A4})$$

$\omega_i$  = the Larmor frequency of spin  $i$

The spectral densities  $J_h(\omega)$  are given by<sup>9,10,24</sup>

$$J_h(\omega) = \int_{-\infty}^{\infty} \langle F_h^*(t + \tau) F_h(t) \rangle \exp(i\omega\tau) d\tau \quad (\text{A5})$$

where the angular brackets indicate an ensemble averaging over possible orientations of the vectors  $\mathbf{r}_{ij}$  in the laboratory frame. The factors  $F_h$  may be written explicitly as

$$\begin{aligned} F_0(t) &= (1 - 3n^2)r_{ij}^{-3} \\ F_1(t) &= n(l + im)r_{ij}^{-3} \\ F_2(t) &= (l + im)^2 r_{ij}^{-3} \end{aligned} \quad (\text{A6})$$

where

$$\begin{aligned} l &= \hat{X} \cdot \hat{\mathbf{r}}_{ij}(t) \\ m &= \hat{Y} \cdot \hat{\mathbf{r}}_{ij}(t) \\ n &= \hat{Z} \cdot \hat{\mathbf{r}}_{ij}(t) \end{aligned} \quad (\text{A7})$$

are direction cosines of  $\mathbf{r}_{ij}$  at time  $t$  in the laboratory coordinate system.

The essential step for the present application is the ensemble averaging of the quantities  $F_h^*(t + \tau)F_h(t)$ . If we assume that methyl group rotation does not significantly affect the overall tumbling of the molecule, the averaging may be done in two steps.<sup>9,10</sup> First, we average over the overall tumbling of the molecule, holding the internal conformation fixed, to obtain the intermediate average  $\langle F_h^*(t + \tau)F_h(t) \rangle_1$ . Then we average  $\langle F_h^*(t + \tau)F_h(t) \rangle_1$  over the possible internal motions to obtain the quantity appearing in the integrand of eq A5.

The first averaging has been carried out by Woessner, who uses anisotropic small-step diffusion as a model for the overall tumbling. For the special case of isotropic tumbling, assumed here, his result is

$$\langle F_h^*(t + \tau)F_h(t) \rangle_1 = \frac{1}{2} K_h \exp\left(-\frac{|\tau|}{\tau_c}\right) \times [3(l'l'' + m'm'' + n'n'')^2 - 1] r_{ij}'^{-3} r_{ij}''^{-3} \quad (\text{A8})$$

where  $\tau_c$  is the correlation time for this motion, the direction cosines of  $\mathbf{r}_{ij}$  are given in the principal axis system of the diffusion tensor, and single-primed

quantities refer to  $\mathbf{r}_{ij}(t)$  while double-primed quantities refer to  $\mathbf{r}_{ij}(t + \tau)$ . The  $K_h$  are numerical constants.

To include the effects of the internal motion, we average the quantity

$$Q(\mu, \nu) = [3(l'l'' + m'm'' + n'n'')^2 - 1] r_{ij}'^{-3} r_{ij}''^{-3} \quad (\text{A9})$$

over the  $\mathbf{r}_{ij}$  allowed (relative to molecule-fixed axes) by the particular model chosen for this motion. The indices  $\mu$  and  $\nu$  identify these allowed  $\mathbf{r}_{ij}$ . We use a  $\pm 120^\circ$  jumping model for the motion of the methyl group:  $2/3\tau_j$  jumps per second in random directions among the three minima of the assumed torsional potential. For a given methyl proton at site A at time  $t$ , the conditional probabilities to be at sites A, B, and C at time  $t + \tau$  are

$$p_A^A(\tau) = \frac{1}{3} + \frac{2}{3} \exp(-\tau/\tau_j) \quad (\text{A10})$$

$$p_B^A(\tau) = p_C^A(\tau) = \frac{1}{3} - \frac{1}{3} \exp(-\tau/\tau_j)$$

and we obtain

$$\langle Q(\mu, \nu) \rangle = \sum_{\mu', \nu'=1}^3 \frac{1}{3} p_{\nu', \mu'}(\tau) Q(\mu', \nu') \quad (\text{A11})$$

where  $1/3$  = the *a priori* probability that a given methyl proton will be at the particular site corresponding to the allowed  $\mathbf{r}_{ij}$  indicated by  $\mu'$ . Evaluation of the  $Q(\mu, \nu)$  is simplified by the assumption of isotropic tumbling, since we are free to choose the orientation of the diffusion tensor axes. Choosing the  $z$  axis of this system parallel to the axis of rotation of the methyl group and the  $y$  axis to lie in the molecular plane as illustrated in the text, we easily obtain  $\langle F_h^*(t + \tau)F_h(t) \rangle = \frac{1}{2} K_h \exp(-|\tau|/\tau_c) \langle Q(\mu, \nu) \rangle$  for any particular molecular geometry.

This model is flexible and could be applied to tumbling molecules with other kinds of internal motions by using an appropriate model of the internal motion in the second averaging of the correlation functions. Alternatively, it could be applied to anisotropically tumbling molecules with internal motions if the principal axes of the overall diffusion tensor are determined by dipole-dipole or quadrupole relaxation measurements.<sup>25</sup>

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