

Nuclear Magnetic Resonance Spectroscopy. Conformational Equilibria and Equilibration of 3,3-Difluoro-*trans*-cyclodecene¹

Eric A. Noe,^{2a} Robert C. Wheland,^{2b} Edward S. Glazer, and John D. Roberts*

Contribution No. 4253 from the Gates and Crellin Laboratories of Chemistry, California Institute of Technology, Pasadena, California 91109.

Received May 17, 1971

Abstract: On cooling 3,3-difluoro-*trans*-cyclodecene from room temperature to -152° , three different processes which equilibrate cyclodecene conformations appear to become slow on the nmr time scale. At -152° , at least five out of eight possible conformational classes are present, four of which are separated by 0.8 kcal/mol or less. The free energy of activation for the slowest of the equilibration processes compares well with that for *trans*-cyclodecene itself.

Several approaches have been used to study the conformational behavior of *trans*-cyclodecene. Attempts to follow the racemization of *trans*-cyclodecenes have been the least effective because the half-lives are apparently very short at reasonably accessible temperatures.^{3,4} Even if the half-lives were sufficiently long, the disadvantage remains that the rate of racemization apparently fails to separate the three motions required for racemization, C=C and C-6-C-7 bond rotations through the cyclodecene ring and flipping of the C-4 and C-9 methylene groups.⁵

An X-ray determination of the structure of the *trans*-cyclodecene-silver nitrate complex suggests a ring conformation for the *trans*-cyclodecene moiety resembling that of the twist-boat-chair-chair form (see later) of cyclodecane.⁶ The conformational implications for a *trans*-cyclodecene ring free in solution remain unclear, however, because the CC=CC dihedral angle was 138° and quite different conformations have been observed for more highly substituted *trans*-cyclodecenes.⁷

The most successful approach so far to the dynamic problem presented by the conformations and conformational equilibrations of *trans*-cyclodecene has been a study of the temperature-dependent ¹H nmr spectrum of the 1,2,4,4,9,9-*d*₆ derivative.⁵ The singlet allylic resonance at δ 2.04 of this substance was observed to split into an AB quartet at -74° and the singlet of the C-5-C-6-C-7-C-8 tetramethylene proton resonance at δ 1.37 changed into a broad unsymmetrical multiplet. Further spectral changes at and below -143° suggested the slowing of additional conformational changes. It was argued from the results that the rate-limiting process for racemization was the turning of the double-bond segment through the ring, although there was no proof of this, nor explanation of the spectral changes below -143° .

A study of the ¹⁹F spectra of 3,3-difluoro-*trans*-cyclodecene as a function of temperature was expected

to provide substantially more information because geminal CF₂ resonances normally promise a 10- to 50-fold expansion in chemical shift over geminal CH₂ resonances without substantial alteration in the conformational distribution or the energy barriers between conformations.⁸ With these larger chemical shifts, higher coalescence temperatures and better resolution of the spectra of individual conformers are expected.

Experimental Results

The ¹⁹F nmr spectrum of 3,3-difluoro-*trans*-cyclodecene⁹ dissolved in propene at 14° was an exchange-broadened singlet, 30.0 ppm upfield from internal ethyl chlorodifluoroacetate. On cooling to -30° , the singlet broadened and split into an AB pattern with $J_{FF} = 236$ Hz and an apparent chemical-shift difference of 252 Hz. The separation of the two inner lines decreased by about 8 Hz as the temperature was lowered from -11 to -30° , presumably because of incursion of other rate processes, as will be described below; but in spite of this, the usual kinetic analysis using total line-shape fitting¹⁰ could be carried out between $+17$ and -11° with a chemical-shift difference of 272 Hz. Representative spectra and the Arrhenius plot are shown in Figures 1 and 2. The activation energy and frequency factor determined by least squares are $E_a = 14.9 \pm 0.4$ kcal/mol and $\log A = 14.68 \pm 0.28$. At 2.8° , $\Delta G^\ddagger = 12.4$ kcal/mol and $\Delta S^\ddagger = 6.9$ eu.

Dramatic fmr spectral changes occur on cooling 3,3-difluoro-*trans*-cyclodecene to -148° , as can be seen in Figure 3. Around -150° , equilibration is slowed sufficiently that a number of minor absorptions could be observed after separate time averaging of the lower (Figure 4a) and upper (Figure 4b) halves of the spectrum. In order to clarify the overall placement of the absorptions, the numbering in Figures 4a and 4b is repeated for the major absorptions shown in the single, wider sweep of Figure 4c.

The chemical shifts corresponding to the major resonance lines in Figure 3 are quite sensitive to the temperature. Table I shows the way in which they vary relative to the fluorine resonances of internal ethyl chlorodifluoroacetate. The apparent difference in shifts

(1) Supported by the National Science Foundation.
 (2) (a) National Science Foundation Summer Fellow, 1966 and 1968; National Defense Education Act Trainee, 1968-1969; (b) National Science Foundation Postdoctoral Fellow, 1970-1971.
 (3) A. C. Cope, K. Banholzer, H. Keller, B. A. Pawson, J. J. Whang, and H. J. S. Winkler, *J. Amer. Chem. Soc.*, **87**, 3644 (1965).
 (4) H. H. Westen, *Helv. Chim. Acta*, **47**, 575 (1964).
 (5) G. Binsch and J. D. Roberts, *J. Amer. Chem. Soc.*, **87**, 5157 (1965).
 (6) P. Ganis and J. D. Dunitz, *Helv. Chim. Acta*, **50**, 2379 (1967).
 (7) R. J. McClure, G. A. Sim, P. Coggon, and A. T. McPhail, *Chem. Commun.*, 128 (1970).

(8) J. D. Roberts, *Chem. Brit.*, **2**, 529 (1966), and later papers, especially R. D. Stolow, T. W. Giants, and J. D. Roberts, *Tetrahedron Lett.*, **55**, 5777 (1968).
 (9) E. A. Noe and J. D. Roberts, *J. Amer. Chem. Soc.*, **94**, 2020 (1972).
 (10) J. T. Gerig and J. D. Roberts, *ibid.*, **88**, 2791 (1966).

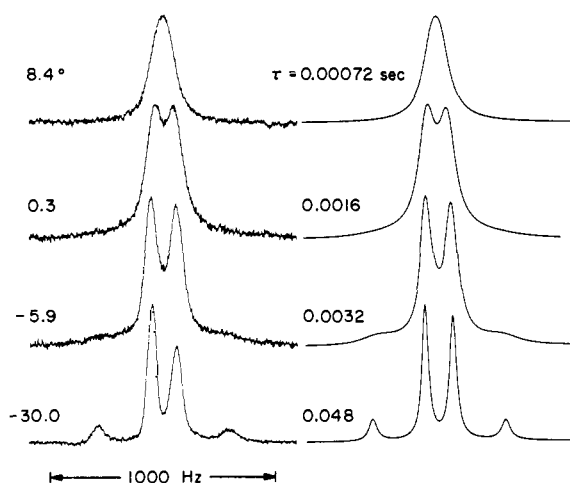


Figure 1. Experimental (left) and calculated (right) ^{19}F nmr spectra of 3,3-difluoro-*trans*-cyclodecene in propene as a function of temperature.

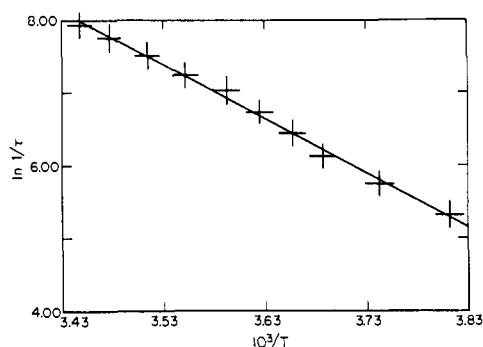


Figure 2. Arrhenius plot for 3,3-difluoro-*trans*-cyclodecene.

between -152 and -148° is largely the result of differences in experimental procedure needed to detect the minor absorptions in the -152° spectra. In any

Table I. Temperature Dependence of Fmr Shifts for 3,3-Difluoro-*trans*-cyclodecene^a

	Temp, $^\circ\text{C}$				
	-152	-148	-134	-127	-116
Shift A_1	1249	1271	1285	1285	1232
Shift B_1	1619	1610	1628	1654	1717
Shift A_2	1339	1351	1355	1349	1352
Shift B_2	2187	2181	2208	2233	2347
Shift A_3	514				
Shift B_3	2730				
Shift A_4	(1350) ^b				
Shift B_4	(3110) ^c				
Population A_1B_1	0.78				
Population A_2B_2	0.14				
Population A_3B_3	0.05				
Population A_4B_4	0.03				
$J_{A_1B_1}$		237			
$J_{A_2B_2}$		227			
$J_{A_3B_3}$	230				
$J_{A_4B_4}$	230				

^a In Hertz relative to ethyl chlorodifluoroacetate. ^b Estimated indirectly, see text. ^c Taken as center of this upfield wing.

event, whether these differences are significant or not, the shifts for the spectra taken between -148 and -116° were determined in a single and consistent

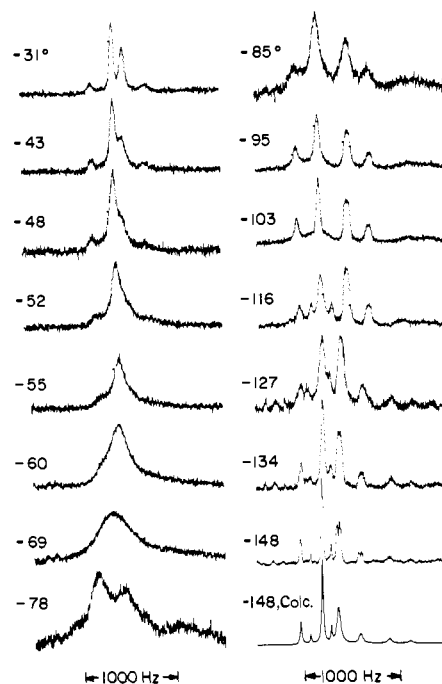


Figure 3. Low-temperature ^{19}F nmr spectra of 3,3-difluoro-*trans*-cyclodecene in propene.

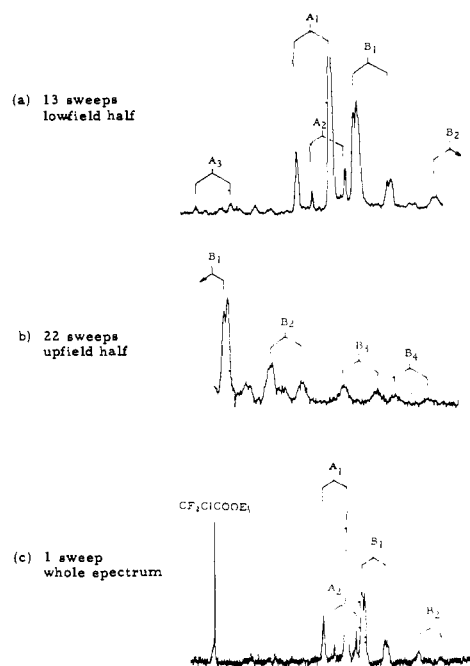


Figure 4. Fluorine-19 nmr spectra of 3,3-difluoro-*trans*-cyclodecene at -152° in propene.

manner, so that the trends are unquestionably real. Between -148 and -116° , the procedure was to accumulate a single spectrum on the CAT with 500-Hz sidebands on internal $\text{CF}_2\text{CICOOEt}$ and then, a second time, with 2900-Hz sidebands on internal $\text{CF}_2\text{CICOOEt}$. The final readout of the summed spectrum then included two sidebands, one from each sweep, for calibration. For the -152° spectrum, several 5000-Hz single-sweep spectra were taken with roughly 1600-Hz sidebands for calibration. These sidebands allowed determination of the shifts of the

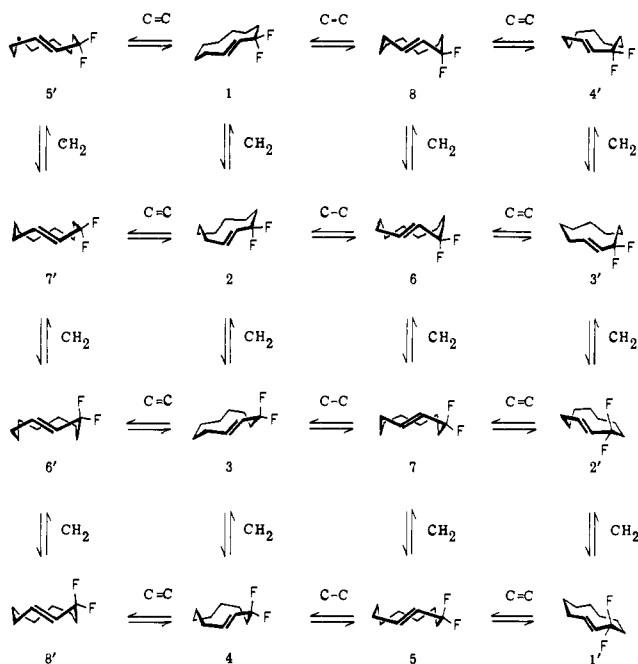


Figure 5. Interconversion of 3,3-difluoro-*trans*-cyclodecene conformations.

major absorptions, and from these shifts, those of the minor absorptions in Figures 4a and 4b were estimated.

The major overlapping quartets, A_1B_1 and A_2B_2 , can readily be computer simulated, using the parameters for -148° in Table I. The theoretical spectrum so obtained is shown at the bottom of Figure 3. However, as the temperature is raised, the line positions and general shape of the spectrum become very difficult to reproduce by any averaging scheme including only A_1B_1 and A_2B_2 . The best of these rather poor fits to the major resonance peaks are with the chemical shifts shown in Table I from -134 to -116° and involve axial-axial fluorine exchanges. Similar results were obtained with axial-equatorial exchanges. Because A_1 shifts downfield and B_2 upfield with increasing temperature, these resonances must be averaging with additional absorptions downfield of A_1 and upfield of B_2 .

Consideration of the minor absorptions detected by extended time averaging accounts qualitatively for the observed shifts. The shift assignments of these absorptions are not certain but the argument would not be basically changed by different assignments. For example, B_2 is observed to shift 166 Hz upfield between -148 and -116° . The upfield AB wing of the minor peak detected at -152° , B_4 , is roughly 0.21 the integrated area of B_2 and should shift B_2 about 200 Hz upfield on complete B_2, B_4 averaging. The AB quartet wing A_4 that must be associated with B_4 should average with A_2 . Since A_2 does not shift significantly, A_4 is presumed to be under A_2 and is assigned the same shift as A_2 . In fact, the apparent base line is rather high in this area. Similarly, averaging of B_3 with B_1 is calculated to shift B_1 roughly 70 Hz upfield, and averaging of A_3 with A_1 is calculated to shift A_1 roughly 50 Hz downfield. For B_1 and A_1 the observed shifts are 107 Hz upfield and 49 Hz downfield, respectively. Considering the difficulty of integrating and finding the shifts for these minor absorptions, the agreement is

reasonable. Better results might be obtained if the other minor resonances could be more clearly identified and taken into account. The proportions of the various species at -152° , as judged from their fmr spectra, suggests that the energy difference between them is 0.8 kcal/mol or less.

In the consideration of the effects of the minor absorptions, it is important to see how they check out with the single average chemical shift at higher temperatures. At a temperature of 14° , the center of the 3,3-difluoro-*trans*-cyclodecene fmr resonance appears 30.0 ppm upfield from ethyl chlorodifluoroacetate. At -148° , the average shift of A_1B_1 and A_2B_2 is 24.2 ppm, but including A_3B_3 and A_4B_4 , the spectrum is centered at 26.8 ppm, a shift in the right direction. As the temperature is raised, these minor conformers would be expected to be increasingly important in contributing to the equilibrium of conformations and would thus tend to shift the center of gravity of the spectrum toward 30.0 ppm.

In the low-temperature spectrum, we have evidence that equilibration of four conformations, corresponding to A_1B_1 – A_4B_4 , is slow on the nmr time scale. Moreover, the room-temperature spectrum is very clean and, unless there are impurities which give fluorine resonances identical in chemical shift with that of 3,3-difluoro-*trans*-cyclodecene, it seems likely that some additional minor absorptions appearing at low temperature represent still further conformations. We conclude that there are at least five conformers frozen out at -152° .

No attempt was made to calculate line shapes between -30 and -148° because the changes in the lines for the minor AB quartets were too indistinct.

Discussion

Molecular models indicate that three types of motions—rotation of the carbon-carbon double bond through the cyclodecene ring (designated C=C), rotation of the C-6–C-7 bond through the cyclodecene ring (designated C-C), and flipping of the methylenes at C-4 and C-9 (designated CH_2)⁵—are capable of interconverting the eight possible conformational classes of 3,3-difluoro-*trans*-cyclodecene (Figure 5).¹¹

Two major principles stand out in analyzing the various spectral possibilities. First, any conformer considered individually as a rigid species would be sufficiently asymmetric to give a fmr AB quartet. Second, rapid interconversion of any conformer with its enantiomer would average equatorial and axial fluorines, giving an fmr singlet for the enantiomeric pair. The types of fmr spectra expected to be observed for 3,3-difluoro-*trans*-cyclodecene as a function of the number and kinds of slow conformational equilibrations corresponding to those in Figure 5 follow: (1) all fast \rightarrow singlet; (2) one slow (A) CH_2 slow \rightarrow 1 or 2 AB quartets, (B) C-C slow \rightarrow 1 AB quartet, (C) C=C slow \rightarrow 1 AB quartet; (3) two slow (A) CH_2 and C=C slow \rightarrow 1 to 4 AB quartets, (B) CH_2 and C-C slow \rightarrow 1 to 4 AB

(11) P. Fanta of the Illinois Institute of Technology has suggested to us an alternative to rotation of the C-6–C-7 bond through the ring for interconversion of *trans*-cyclodecene conformations which have the C-6–C-7 bond crossed and parallel with respect to the C-1–C-2 bond.⁵ This process involves a 360° rotation around the C-6–C-7 bond axis and an unfavorable eclipsed conformation, but does not require passage of a methylene group through the ring.

quartets, (C) C—C and C=C slow \rightarrow 1 or 2 AB quartets; (4) all slow \rightarrow 1 to 8 AB quartets.

As an example of how the types of spectra were deduced, consider the case in which both CH₂ and C—C motions are slow on the nmr time scale. This means that there are eight sets of interconverting conformers: $1 \rightleftharpoons 5'$; $1' \rightleftharpoons 5$; $2 \rightleftharpoons 7'$; $2' \rightleftharpoons 7$; $3 \rightleftharpoons 6'$; $3' \rightleftharpoons 6$; $4 \rightleftharpoons 8'$; $4' \rightleftharpoons 8$. Sets such as $1 \rightleftharpoons 5'$ and $1' \rightleftharpoons 5$ are enantiomeric and therefore nmr equivalent. But because sets such as $1 \rightleftharpoons 5'$ and $1' \rightleftharpoons 5$ do not interconvert, there is no exchange which allows equatorial and axial fluorines to become equivalent. Thus, $1 \rightleftharpoons 5'$ and $1' \rightleftharpoons 5$ will give a single, common AB quartet much as would also $2 \rightleftharpoons 7'$ plus $2' \rightleftharpoons 7$, $3 \rightleftharpoons 6'$ plus $3' \rightleftharpoons 6$, and $4 \rightleftharpoons 8'$ plus $4' \rightleftharpoons 8$. In total there would thus be four AB quartets. Of course, to the extent that any of these conformers overlap or are not significantly populated, the number of AB quartets observed would be diminished.

What firm conclusions can be drawn from the spectra? The singlet at room temperature corresponds to all motions, CH₂, C—C, and C=C, being rapid. Lowering the temperature to -30° gives an AB quartet. Keeping in mind that at least five conformations are present, and assuming no overlap of lines, it follows that either C—C or C=C rotation must be the slow equilibration responsible for the quartet. At the lowest temperature, there are at least five AB quartets, which corresponds to all three motions being frozen out. The complex changes in the spectra between -30 and -148° must reflect a change from one equilibrium being slowed to three being slowed.

In general, 3,3-difluoro-*trans*-cyclodecene behaves remarkably like the parent hydrocarbon⁵ and we have no evidence which would contradict the idea that the twist-boat-chair-chair conformation **8**, found for the silver nitrate complex of *trans*-cyclodecene⁶ itself, is not the predominant isomer in solution. The values of ΔG^\ddagger and ΔS^\ddagger for *trans*-cyclodecene-1,2,4,4,9,9-*d*₆ at 2.8° , as calculated from reported⁵ E_a and A values, are 12.0 kcal/mol and -6.8 eu, respectively. The free energy of activation differs from that of the difluoro compound by only 0.4 kcal/mol while the difference in activation energies (4.2 kcal/mol) is considerably larger. The values of ΔG^\ddagger obtained by the nmr method are generally more accurate and reproducible than the corresponding activation energies.¹² For this reason, the close agreement of the free energies of activation may be an indication that some or all of the differences in activation energies may be the result of systematic errors. Molecular models suggest that a substantial part of the barrier to rotation of the double bond through the ring arises from additional out-of-plane bending at the two sp² centers, reducing the interaction of the alkenic hydrogen with the CH₂ groups across the ring; if this is so, there is no very obvious reason for a large increase in activation energy on replacement of two of the α hydrogens by fluorine.

There is no compelling evidence as to whether the C=C equilibration or the C—C equilibration is the slowest one. Inspection of models suggests that C=C rotation is likely to be slower but, irrespective of which is, there is a rather surprising implication which can be

drawn from the four spectra of 3,3-difluoro-*trans*-cyclodecene at the intermediate temperatures. Normally, in cyclic systems, the axial fluorine in a geminal CF₂ group tends to be upfield of and broader than the equatorial fluorine.^{8,10,13} The extra broadness of the axial lines is a consequence of the fact that vicinal hydrogen-fluorine couplings follow a Karplus-type relation,¹⁴ which makes the transoid axial fluorine-axial hydrogen couplings particularly strong. Models show that in *trans*-cyclodecenes such axial fluorine-axial hydrogen couplings should also be substantial. Consistent with this is the observation that the upfield wings of A₁B₁, A₂B₂, A₃B₃, and perhaps A₄B₄ are markedly broader than their corresponding downfield wings, which implies that B₁, B₂, B₃, and B₄ are all axial fluorines. On this basis, the exchanges (B₁ \rightleftharpoons B₃ and B₂ \rightleftharpoons B₄) proposed earlier, slowed at the lowest temperatures, represent axial-axial fluorine exchanges rather than axial-equatorial fluorine exchanges which result only from CH₂ flipping ($6' \rightleftharpoons 7'$, $2 \rightleftharpoons 3$, $6 \rightleftharpoons 7$, and $3' \rightleftharpoons 2'$ in Figure 5). Thus it would seem that at least these CH₂ flippings ($6' \rightleftharpoons 7'$, $2 \rightleftharpoons 3$, $6 \rightleftharpoons 7$, $8' \rightleftharpoons 2'$ in Figure 5) and perhaps by extension all CH₂ flippings are not the last type of equilibration to be frozen out. If indeed this is the case, then CH₂ flipping is the second process frozen out because we have already argued that it cannot be the first process frozen out. A corollary of rapid C—C bond rotation and the number of observed conformations is that there must be significant amounts of conformations both with the double bond parallel and crossed with respect to the C-6-C-7 bond, as proposed earlier.⁵ However, if the C—C equilibration is very fast compared to the C=C equilibration, then the isolation of stable forms corresponding to these different classes of conformations in smaller *trans*-cycloalkenes may well be difficult.

Experimental Section

The fluorine nmr spectra were obtained with a Varian A-56/60A spectrometer. The spectra were calibrated by the side-band technique using a Lenkurt Model 6200 DS audiooscillator and a Hewlett-Packard Model 5216A counter. The signal-to-noise ratio of the low-temperature fluorine spectra was enhanced as necessary with a time-averaging computer, Varian Model C-1024; the number of scans required varied between 1 and 22. The Varian Model V-6040 variable temperature accessory was used to control the temperature. Temperatures were measured by replacement of the sample tube with an open tube containing a suitable solvent and a copper-constantan thermocouple.

The theoretical spectra of Figure 1 were generated by an IBM 360/75 computer using the Gerig program¹⁰ based on the equations of Alexander.¹⁵ The parameters used in calculation of the spectra included a chemical shift, a mean lifetime, τ , and an effective relaxation time, T_2 , for each nucleus in the system. The effective relaxation times were used to adjust for the effects of hydrogen-fluorine coupling. The values of τ were then determined by comparison of the calculated and experimental spectra.

Ethyl chlorodifluoroacetate was used as an internal standard for the low-temperature fmr spectra. The concentration of 3,3-difluoro-*trans*-cyclodecene was 43% by volume in propene for the spectra above -30° , 23% by volume in propene for the spectra below -30° .

(13) (a) K. Nagarajan and J. D. Roberts, unpublished. See J. D. Roberts, *Angew. Chem., Int. Ed., Engl.*, **2**, 52 (1963); (b) S. L. Spassov, D. L. Griffith, E. S. Glazer, K. Nagarajan, and J. D. Roberts, *J. Amer. Chem. Soc.*, **89**, 88 (1967).

(14) K. L. Williamson, Y.-F. L. Hsu, F. H. Hall, S. Swager, and M. S. Coulter, *ibid.*, **90**, 6717 (1968).

(15) S. Alexander, *J. Chem. Phys.*, **37**, 974 (1962).

(12) A. Allerhand, H. S. Gutowsky, J. Jonas, and R. A. Meinzer, *J. Amer. Chem. Soc.*, **88**, 3185 (1966).