Cyclododecane. Force-Field Calculations and ^{1}H NMR Spectra of Deuterated Isotopomers

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Abstract: Iterative force-field calculations have been carried out on cyclododecane (**1**). The (strain energy) barrier for pseudorotation of the lowest energy [3333] conformation of **1** is calculated to be 7.9 kcal/mol, in agreement with the (free energy) barrier obtained from NMR data. In order to simplify the complex low-temperature ^{1}H NMR spectrum, two isotopomers of **1** have been synthesized and their ^{1}H{D} spectra at -143 °C have been analyzed. The chemical shifts of the exo (δ 1.18), corner (δ 1.28), and endo (δ 1.39) hydrogens, and the vicinal couplings of the corner-endo (13.0 $\pm$ 0.5 Hz) and corner-exo (4.6 $\pm$ 0.5 Hz) hydrogens as well as the geminal coupling of the exo–endo (-13.5 ± 0.5 Hz) hydrogens have been determined.

Cyclododecane (**1**) is generally considered as the first member of the large-ring cycloalkanes. It is the most readily available compound of its class, and is the smallest cycloalkane which is crystalline at room temperature. Unfortunately, **1** has a disordered crystal structure and this has caused difficulties in the determination of its conformation by X-ray diffraction methods.[1] Originally, a structure of D_{2d} symmetry was proposed, but this was subsequently changed to a D_2 (nearly D_4) conformation as a result of energy considerations.[1] Because of the crystal disorder and large thermal motions, the structural parameters obtained for **1** are not very accurate.

The conformation of **1** found in the crystalline state can be conveniently described by Dale's nomenclature[2,3] as [3333], and this designation is not limited to D_4 symmetry but also includes more or less distorted structures. The digits in the square brackets refer to the number of C–C bonds between "corner" atoms. Other 12-membered rings related to **1** have ordered crystal structures and X-ray diffraction analyses have revealed the presence of [3333] conformations.[4-7]

The crystals of **1** have been observed by X-ray[1] to undergo a reversible phase transition between -80 and -100 °C; the same effect has also been detected in the NMR of crystalline **1**.[8] Dunitz has suggested that above the transition temperature the molecules undergo rapid inversion; below the transition temperature no molecular motion occurs and the structure is frozen in some order–disorder arrangement.[1]

The infrared and Raman spectra of **1** have been analyzed with the help of force-field calculations in terms of a [3333] conformation of D_2 symmetry and with assumed bond lengths and bond angles.[9] The ^{1}H and ^{13}C NMR spectra of **1** show, at about -110 °C, dynamic NMR effects, which are associated with a conformational barrier of 7.3 kcal/mol.[10] The low-temperature ^{13}C NMR spectrum of **1** is consistent with a [3333] conformation, since it consists of two lines in the ratio of 2:1. The low-temperature ^{1}H NMR spectrum of **1** is too complex for any meaningful analysis and hence the chemical shifts and coupling constants of the different hydrogens in **1** cannot be determined.[10] The ^{13}C NMR spectra of some mono-[11] and disubstituted[12] cyclododecanes and heterocyclic analogues[13,14] have been analyzed in terms of [3333] conformations.

Several force-field calculations have been carried out on **1**, and the lowest energy conformation has always been found to be the [3333].[2,15-18] Dale[2,3] has presented a scheme for site exchange in this conformation and has shown that conformations of higher energies are involved as intermediates. The highly simplified force field used by Dale gives a satisfactory map of these interconversions, but it leads sometimes to poor values of strain energies, especially for transition states of conformational processes.

In this paper we report ^{1}H chemical shifts (including assignments) and coupling constants for the [3333] conformation of **1**, as obtained from the ^{1}H NMR spectra at low temperatures of two specifically deuterated isotopomers of **1**. We also present iterative force-field calculations of the conformational energy surface of **1**.

Results and Discussion

Force-Field Calculations. The strain energies of four conformations (Figure 1) of cyclododecane were determined by iterative force-field calculations[19] and are given in Table I.[20] The lowest energy conformation is the [3333] with D_2 symmetry, as found by other workers.[15,16,18] However, the distortion from D_4 symmetry is actually very slight, and the calculated strain energies of the D_2 and D_4 structures are virtually the same. The next two conformations in order of increasing total strain energies are the [2334] and the [2343], as also found by Dale.[2,3] However, our results show that the [2334] is only 1.6 kcal/mol above the [3333], whereas Dale found a difference of 4.4 kcal/mol. Such a difference is perhaps not surprising because Dale's calculations were based on a very simplified force field.[2,3]

Because of their different symmetries, the [2334] conformation should have a higher entropy[21] than that of the [3333] and may therefore be significantly populated at or above room temperature. Although there is currently no experimental support for the [2334], its presence as a minor conformation of **1** at room temperature cannot be ruled out.

The [2343] conformation has a relative strain energy of 2.9 kcal/mol and should not be populated except at very high temperatures. There are also a number of other possible conformations of **1**, but Dale[2] has already reported that these conformations have very high strain energies, and therefore we did not consider it worthwhile to carry out iterative force-field calculations on them, except in the case of the [2424] conformation, which is of special interest, since it belongs to the diamond lattice. The [2424] conformation has a relative strain energy of 4.9 kcal/mol, substantially lower than that found by Dale,[2] but still high enough to make it be unimportant.

Dale has considered the interconversion paths available to the four conformations of **1** discussed above, and has shown that four distinct transition states are involved.[2,3] The results of our force-field calculations on these transition states are given in Table II and Figure 2.[20] The best mechanism calculated for pseudorotation, or site exchange, in the [3333] conformation is shown in Figure 3, and is similar to the scheme proposed by Dale.[2,3] The interconversion of the [3333] and [2334] conformations proceeds via the [12333]‡ transition state, while the [2334]–[2343] interconversion requires the
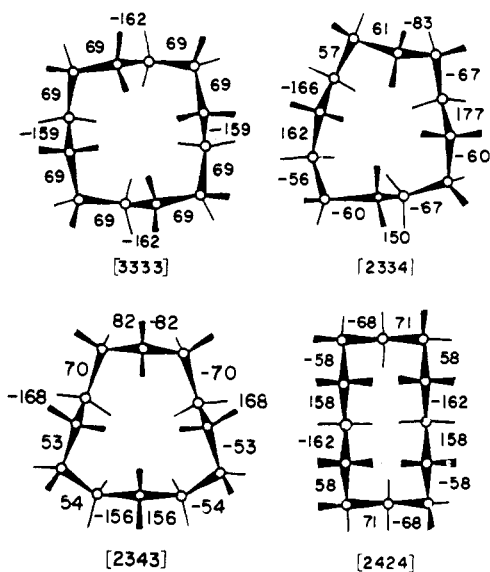
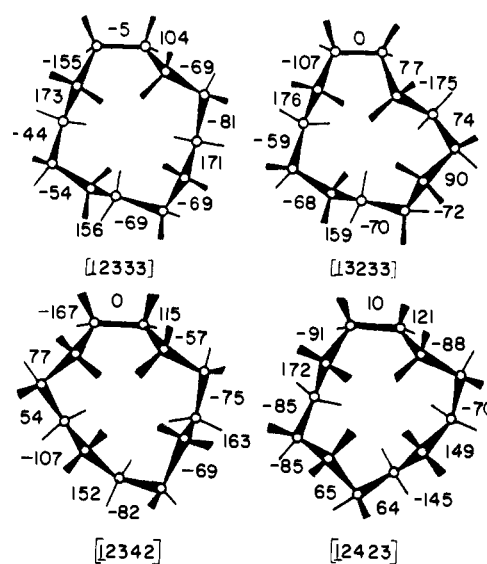Figure 1. Calculated torsional angles in various conformations of cyclododecane.

Figure 2. Calculated torsional angles in various transition states of cyclododecane.

Table I. Calculated Strain Energies[a] (kcal/mol) of Various Energy-Minimum Conformations of Cyclododecane

conformation	symmetry group	E_r	E_θ	E_ϕ	E_{nb}	E_T	E_Δ	E_Δ[b]
[3333]	D_2[c]	0.83	2.24	3.08	5.61	11.8	0	0
[2334]	C_1	0.89	3.73	2.89	5.87	13.4	1.6	4.4
[2343]	C_s	0.91	3.41	4.01	6.40	14.7	2.9	4.4
[2424]	C_2[d]	1.02	6.47	2.79	6.44	16.7	4.9	7.6

[a] The following symbols are used: E_r, bond length strain; E_θ, angle strain; E_ϕ, torsional strain; E_{nb}, nonbonded interaction strain. Total strain energy, $E_T = E_r + E_\theta + E_\phi + E_{nb}$. E_Δ, strain energy relative to that of the [3333] conformation. [b] Relative strain energy calculated by Dale.[13] [c] The symmetry is approximately D_4. [d] The symmetry is approximately C_{2v}.

Table II. Calculated Strain Energies[a] (kcal/mol) of Various Transition States of Cyclododecane

transition state[b]	E_r	E_θ	E_ϕ	E_{nb}	E_T	E_Δ[c]	E_Δ[d]
[12333]‡	0.99	4.15	7.43	7.09	19.7	7.9	14.0
[13233]‡	0.94	5.13	7.25	6.37	19.7	7.9	13.6
[12342]‡	0.96	3.92	9.81	7.01	21.7	9.9	12.1
[12423]‡	0.98	5.23	11.24	7.06	24.5	12.7	16.4

[a] See Table I for meaning of symbols. [b] All transition states have C_1 symmetry. [c] Strain energy of a transition state relative to that of the [3333] conformation. [d] Relative strain energy calculated by Dale.

[13233]‡ transition state. Whereas Dale obtained a strain energy barrier of 14 kcal/mol for the process shown in Figure 3, our calculations give a value of 7.9 kcal/mol,[22] which is in good agreement with the observed free-energy barrier of 7.3 kcal/mol.[10]

Alternative mechanisms for pseudorotation of the [3333] conformation were investigated, but were found to have barriers substantially higher than 7.9 kcal/mol. For example, the [2334]-[2343] interconversion discussed above can also proceed via the [12342]‡ transition state, which has a relative strain energy of 9.9 kcal/mol (Table II) and is therefore unimportant. A pseudorotation path involving the diamond-lattice [2424] conformation, namely, [3333] → [2334] → [2424] → [2334] → [3333], can be excluded since the [12423]‡ transition state which links the [2334] and [2424] conformations has a relative strain energy of 12.7 kcal/mol (Table II).

We have found that it is generally easier to determine the lowest energy path between two conformations of different strain energies by starting from the higher energy site. For example, in the [3333] to [2334] process, which proceeds to a higher energy conformation, it is necessary to "drive"[23] more

than one torsional angle, whereas in the reverse process only one torsional angle needs to be driven.

Cyclododecane Isotopomers. The strain energy calculations presented in the preceding section, and the low-temperature ^{13}C NMR spectrum of **1**,[10] indicate that only the [3333] conformation is appreciably populated at low temperatures. In this conformation, as shown below, there are three different

C = corner
I = endo (inner)
O = exo (outer)

[3333]
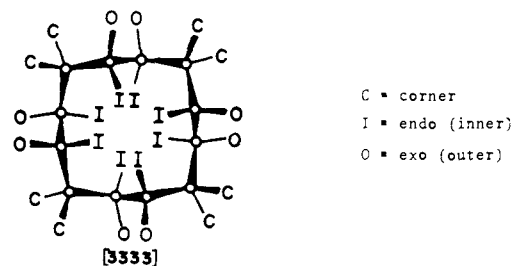
kinds of hydrogens, namely, corner, exo (outer), and endo (inner).

At high temperatures (>−60 °C) ring pseudorotation is fast and the ^1H NMR spectrum is simply a single line.[10] At low temperatures (<−130 °C) the spectrum is in the slow ex-
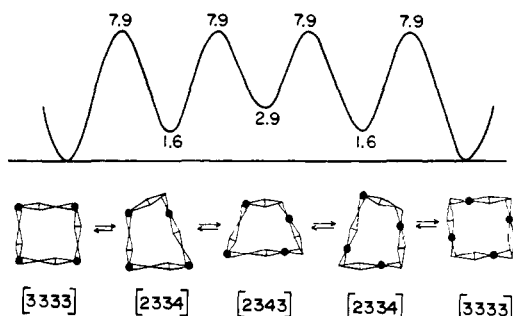
Figure 3. Pseudorotation itinerary for the [3333] conformation of cyclo-dodecane. Intermediate conformations, but not transition states, are shown. Black circles are carbon labels.

Figure 4. The D_3 and C_2 isotopic isomers of cyclododecane-d_{18}-*trans*-*1,2-trans-5,6-trans-9,10-h₆*. Black circles are CD_2 groups.

change region and has to be described in terms of a 24-spin system with three chemical shifts, as well as two geminal and seven vicinal proton–proton coupling constants. As a result of this, the low-temperature ^1H spectrum of **1** is not expected to exhibit resolved lines, in agreement with the reported spectrum.[10] It is essentially impossible to analyze such a spectrum for chemical shifts and coupling constants.

Simplification of the low-temperature ^1H spectrum of **1** can be achieved by replacing most of the hydrogens by deuterons and observing the spectrum with the deuterons decoupled. The simplest spectrum would be given by cyclododecane-d_{23}, which has only one hydrogen. Although this compound would be ideal for the determination of chemical shifts, it would not be possible to determine which chemical shift belongs to which proton in the [3333] conformation. Furthermore, a molecule with a single hydrogen cannot give information about proton–proton coupling constants. Cyclododecane molecules with two hydrogens in geminal, cis vicinal, or trans vicinal arrangements should also be suitable for low-temperature NMR observations because the spectra are expected to be relatively simple. On the other hand, cyclododecane molecules with more than two hydrogens on adjacent carbons would probably give very complex spectra at low temperatures.

We chose to synthesize two specifically deuterated cyclo-dodecanes.[24] The first is a cyclododecane-d_{20} (**2**) where the four protons reside in two methylene groups 1,3 to each other. The second is a cyclododecane-d_{18} (**3**) where the six hydrogens are distributed as isolated pairs of vicinal trans hydrogens. As shown in Figure 4, **3** is actually a mixture of two isotopic isomers of unequal populations; the major isomer (C_2 symmetry) has three times the probability of being formed as compared to the minor isomer (D_3 symmetry).

As will be shown later, the two compounds **2** and **3** allow the determination and assignments of the three chemical shifts of the [3333] conformation, as well as the determination of several proton–proton coupling constants, including the important geminal coupling between the exo and endo protons.

The synthetic scheme employed in the synthesis of **2** involves the trimerization of 1,3-butadiene-d_6 on "naked" Ni^0 as the initial step.[25,26] The resulting mixture of isomeric 1,5,9-cy-clododecatriene-d_{18} was reduced by $D_2/Rh(CO)_2(PPh_3)_2Cl_2$ to cyclododecene-d_{22},[27] which in turn was converted to cy-clododecanone-d_{21}-2-h_1 by hydroboration and oxidation.[28] Exchange of the α deuterons in H_2O/Na_2CO_3 followed successively by reduction with $LiAlD_4$, tosylation of the resulting alcohol, and finally a second $LiAlD_4$ reduction yielded **2**. The preparation of **3** was achieved by the reduction of *trans*,-*trans,trans*-1,5,9-cyclododecatriene-d_{18} with diimide generated from tosylhydrazine.

Since reduction by diimide proceeds by a cis mechanism,[29] and any double bond in the triene is trans, the two added hydrogens will be configurationally trans on the 12-membered ring. Although the relationship between any two pairs of trans

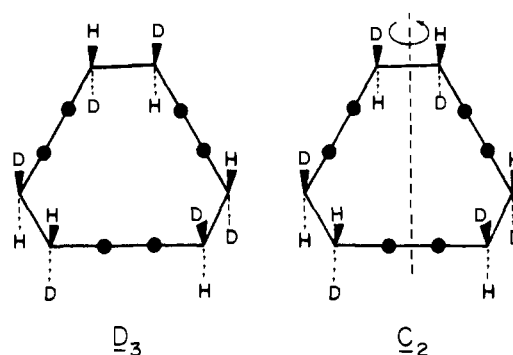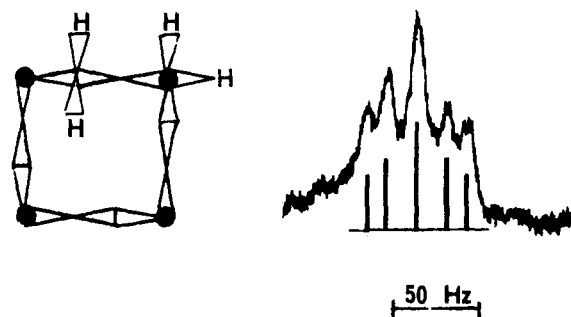Figure 5. The 251-MHz $^1H\{D\}$ NMR spectrum of cyclododecane-d_{20}-*1,1,3,3-h₄* (**2**) in $CHCl_2F$ at −142 °C. A theoretical spectrum based on the [3333] conformation of **2** is also shown.

hydrogens in **3** is random, this does not cause any problem because such pairs are not spin–spin coupled, being separated by two CD_2 groups.

NMR Data. The 251-MHz ^1H NMR spectrum of **2** changes from a single line at −10 °C to the pattern shown in Figure 5 at −142 °C. The low-temperature spectrum of **2** can be analyzed in terms of a [3333] conformation (Figure 5). One of the two CH_2 groups in **2** must occupy a corner position in the [3333] conformation. Because of symmetry, the two hydrogens have the same chemical shift and should give rise to a single line (A_2 system). The second CH_2 group must be at a side (noncorner) position of the [3333] conformation and in this case one hydrogen is endo and the other is exo. This CH_2 group should give rise to an AB quartet. The central absorption (δ 1.28) in Figure 5 is thus assigned to the A_2 spectrum of the corner hydrogens and the remaining four lines are ascribed to the AB system ($|J| = 13.5 \pm 0.5$ Hz) of the exo and endo hydrogens. Since the AB spectrum is symmetrical it is not possible to distinguish the chemical shift of the endo proton from that of the exo proton.

The proton lines in the spectrum of **2** at −142 °C are fairly broad. This is probably due to dipole–dipole relaxation within each CH_2 group, since the protons in such a group are close together, and a molecule as large as cyclododecane will have a relatively small tumbling rate at low temperatures. The low signal to noise ratio of the spectrum is a result of the broadness of the lines, the comparatively small number of protons in **2**, and the very low solubility of cyclododecane at temperatures below −130 °C.

The ^1H NMR spectra of **3** at various temperatures are given in Figure 6. It is convenient to carry out an analysis of the spectrum at −143 °C by considering only one pair of trans vicinal hydrogens in **3**. As shown in Figure 7, two trans vicinal hydrogens can be arranged in four different ways in the [3333] conformation. In **7A** both of the hydrogens are endo, whereas in **7B** they are both exo. Hence the spectrum of **7A** and that of
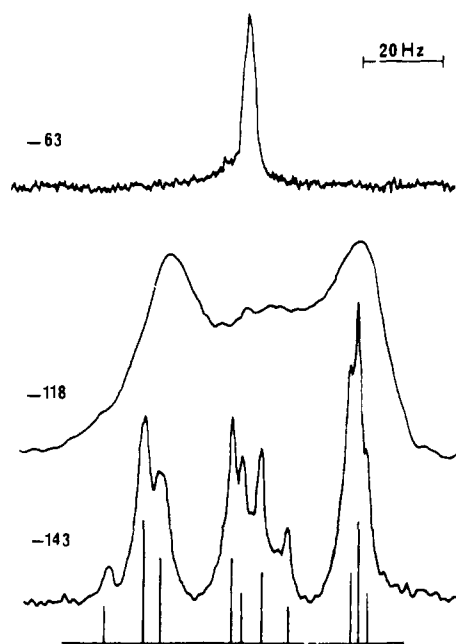
Figure 6. The 251-MHz $^1H\{D\}$ NMR of cyclododecane-d_{18}-*trans-1,2-trans-5,6-trans-9,10-h_6* (3) in CCl_2F_2 at various temperatures, together with a theoretical spectrum (see Figure 7) corresponding to the observed spectrum at -143 °C.

Figure 7. Analysis of the ^1H NMR spectrum of 3 at -143 °C (see Figure 6) in terms of all possible orientations (ignoring mirror images) of two trans vicinal hydrogens in the [3333] conformation of cyclododecane. The two hydrogens are both endo, both exo, endo corner, and exo corner in A, B, C, and D, respectively. The top spectrum is the sum of the spectra of A, B, C, and D.

7B must be single lines (A_2 systems). In **7C** one hydrogen is corner and the other is endo, whereas in **7D** one hydrogen is corner and the other is exo. Hence **7C** and **7D** must each give an AB quartet. Since the torsional angle (HCCH) of the endo and corner hydrogens in **7C** is calculated to be about 170° and thus represents an anti arrangement, the proton-proton coupling constant should be large (12-13 Hz).[30] On the other hand, the torsional angle of the exo and corner hydrogens in **7D** is about 50° (gauche) and the proton-proton coupling should be small (ca. 5 Hz).[30] This predicted difference in the magnitude of the proton-proton couplings in the AB systems of **7C** and **7D** allows an assignment of the exo and endo chemical shifts of the [3333] conformation to be made, since the observed coupling constants are 4.6 ± 0.5 and 13.0 ± 0.5 Hz. This assignment shows that ^1H chemical shifts are as follows: δ 1.18 (exo), 1.28 (corner), 1.39 (endo). Thus the most deshielded protons in cyclododecane are endo.

The deshielding effect is probably associated with the gauche butane 1,4-repulsive interactions of the endo hydrogens in the [3333] conformation. "Steric" deshielding of protons is known to occur in a variety of compounds.[31,32] Whereas the equatorial protons in cyclohexane are strongly deshielded (δ 1.62), the equatorial-like exo protons in the [3333] conformation have a chemical shift similar to that of the cyclohexane axial protons (δ 1.14). Unfortunately, present theories of proton chemical shifts, even when restricted to saturated hydrocarbons, agree only moderately well with experimental facts.[32] The availability of chemical shifts for the [3333] conformation of cyclododecane provides additional experimental data for testing proton chemical shift theories as applied to chemically closely related compounds, i.e., the cycloalkanes.

The lines in the ^1H NMR spectrum of 3 at low temperatures are much sharper than those of 2, presumably because the vicinal protons in 3 are much further apart than are the geminal protons in 2, and thus intramolecular dipole-dipole relaxation is rather inefficient in 3.[33] The resonances of the low-field proton (i.e., endo) of 3 are slightly broader and less high than those of the other two protons, but the reason for this effect is not clear.[33]
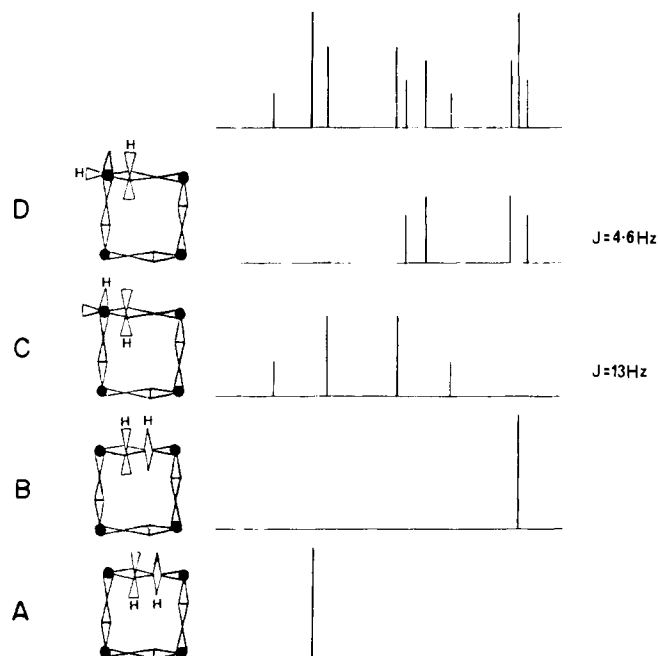
Experimental Section

General. Reactions where hydrogen-deuterium exchange is undesirable where carried out in flame-dried glassware under an atmosphere of dry nitrogen or argon. Reagents and solvents used in these cases were dried by standard procedures. The isotopic purity of all compounds was determined by mass spectrometry recorded on an MS-9 spectrometer, and by ^1H NMR spectrometry at 251 MHz.[34] VPC analyses were carried out using a Varian Aerograph Model A-90-P3. For unsaturated 12-membered ring compounds a 10 ft × 0.25 in. column packed with 35% of a suspension of silver nitrate (40%) in polyethylene glycol (60%) supported on Chromosorb P (80-100 mesh) was used; the column oven was operated at 120-140 °C. Product ratios are based on relative peak areas. Infrared spectra were obtained on a Perkin-Elmer Model 521 spectrophotometer. Model experiments on unlabeled substrates showed that the schemes described below gave the desired products as judged from melting points, infrared, and ^1H and ^{13}C NMR spectra.

***trans,trans,trans*-1,5,9-Cyclododecatriene-d_{18}.** 1,3-Butadiene-d_6 was prepared by the procedure of Craig and Fowler.[25] Trimerization of 1,3-butadiene-d_6 was conducted on "nacked" nickel (generated by the reaction of anhydrous, freshly sublimed nickel acetylacetonate with triethylaluminum in toluene) under experimental conditions favoring the formation of the trans,trans,trans isomer.[26] VPC analysis of the resulting 1,5,9-cyclododecatriene-d_{18} revealed the presence of three isomers: *all-trans-* (90%), *trans,trans,cis-* (4%), and *trans,-cis,cis-* (6%). The all-trans triene was separated from the other two isomers by pressing the crystals obtained from the trimerization reaction between hardened filter papers at 5-10 °C. The remaining two isomers, along with a small amount of the all-trans triene, were subsequently extracted from the filter paper by pentane.

Cyclododecene-d_{22}.[27] Into a sealed 150-mL round-bottom flask fitted with a pressure gauge, a deuterium line, and a dip tube through which the flask could be charged and aliquots of solution withdrawn were added an isomeric mixture of 1,5,9-cyclododecatriene (2 g) in N,N-dimethylformamide (25 mL) and *cis*-dichloro(dicarbonyl)bis-(triphenylphosphine)ruthenium(II) (0.4 g) (prepared by the method of Stephenson and Wilkinson).[35] A heating mantle was wired around the reaction flask, and the temperature was measured by means of a thermocouple inserted in a reentrant tube extending to the bottom of the flask. The system was shaken under 1 atm of deuterium and the reaction was initiated by increasing the temperature. When deuterium

uptake started (as detected by the change of the pressure in the system) the temperature was raised to 130–140 °C. Each time the pressure dropped the system was recharged with deuterium, and the progress of the reaction was followed by analyzing sample aliquots by VPC on a silver nitrate impregnated column. The reaction was stopped when the percentage of deuterated cyclododecene reached a maximum. The solution was treated with water and extracted with pentane, and the pentane extracts were subsequently washed with water, dried over anhydrous $MgSO_4$, and evaporated. Analysis of the resulting liquid (2 g, 95%) by VPC revealed the presence of deuterated cyclododecene (92%) and deuterated cyclododecane (8%).

Cyclododecanone-d_{18}-2,2,12,12-h_4.[28] A 50-mL flask fitted with a stirrer, condenser, addition funnel, and thermometer was charged with cyclododecene-d_{22} (2.1 g) and lithium borohydride (0.11 g) in ether (20 mL). To this mixture was added a solution of freshly distilled boron trifluoride etherate (0.2 mL) in ether (2 mL) over a period of 10 min at 25 °C. After 2 h water (3 mL) was added followed by a solution of sodium dichromate dihydrate (2.5 g) in 96% sulfuric acid (1.8 mL) and water (9 mL). The resulting solution was refluxed for 2 h, the upper layer separated, and the aqueous layer extracted with ether. The organic layers were combined, dried over anhydrous $MgSO_4$, filtered, and evaporated. The solid residue was dissolved in dioxane (15 mL) and refluxed with sodium carbonate (1.3 g) and water (2.5 mL) for 4 h. The solution was cooled and worked up with water and ether, the ether extracts were dried over anhydrous $MgSO_4$ and filtered and the resulting crystals were sublimed to give 1.5 g (70%) of the deuterated ketone.

Cyclododecane-d_{20}-1,1,3,3-h_4 (2). A solution of cyclododecanone-d_{18}-2,2,12,12-h_4 (1 g) in ether (10 mL) was added dropwide to a stirred suspension of lithium aluminum deuteride (0.2 g) in ether (20 mL). The reaction mixture was refluxed under an atmosphere of nitrogen for 10 h. Excess lithium aluminum deuteride was destroyed with small portions of water, then 10% HCl solution was added to dissolve the precipitate. The layers were separated and the aqueous solution was extracted with ether. The combined ether layers were back extracted with a little saturated salt solution, dried over anhydrous $MgSO_4$, and filtered and solvent was evaporated. To a stirred solution of the crude alcohol in pyridine (15 mL) at 0 °C was added tosyl chloride (1.7 g). The resulting mixture was allowed to sit at 0–5 °C for 2 days, and was subsequently poured into ice–water and extracted with ether. The ether was washed six times with cold 10% hydrochloric acid solutions, twice with 10% sodium bicarbonate solution, and once with saturated salt solution, then dried over anhydrous $MgSO_4$, filtered, and evaporated. The crude product was dissolved in ether (15 mL) and was added dropwise to a stirred suspension of lithium aluminum deuteride (0.2 g) in ether (20 mL). The reaction mixture was refluxed under an atmosphere of nitrogen for 15 h, then worked up as described in the previous lithium aluminum deuteride reduction. The crystalline product was sublimed to give 0.6 g (60%) of **2**.

Cyclododecane-d_{18}-trans-1,2-trans-5,6-trans-9,10-h_6 (3). trans,-trans,trans-1,5,9-Cyclododecatriene-d_{18} (0.25 g) in 2-ethoxyethanol (6 mL) was heated with tosylhydrazine (1.0 g) and sodium carbonate (1.0 g) at 95–100 °C for 15 h. The resulting solution was worked up with water and ether, and the latter was dried over anhydrous $MgSO_4$, filtered, and evaporated. The crystalline product was sublimed to give 0.2 g (85%) of **3**.

NMR Spectra. ¹H NMR spectra were obtained on a superconducting solenoid operating at 59 kG.[34] The frequency for deuterium decoupling was obtained from a General Radio frequency synthesizer and amplified by a Hewlett-Packard type 230B amplifier. A power of ca. 2 W was applied to the deuterium coil which was situated on the outside of the Dewar vessel containing the sample.

The ¹H{D} spectra of **3** are Fourier transforms of 100 accumulated free induction decays and were obtained in 2-mm (thick walled) sample tubes under the following conditions: 40° pulse angle, 2K data points, and 2048-Hz spectrum width. The ¹H{D} spectra of **2** were obtained with standard 5-mm tubes in a frequency-sweep mode. $CHCl_2F$ and CCl_2F_2 were used as solvents for **2** and **3**, respectively, and the magnetic field was locked on a ¹⁹F peak of the solvent. Small quantities of Me_4Si were added to all samples which were then degassed and sealed.

All the temperatures were measured with a copper–constantan thermocouple situated in the probe a few centimeters below the sample and connected to a Newport Laboratories digital thermometer reading to 0.1 °C and accurate to 0.2 °C.

Force-Field Calculations. Force-field calculations were carried out with Boyd's iterative computer program MOLBUILD,[19] which was modified to allow conformational changes to occur by "driving" the appropriate torsional angles.[23] Approximate coordinates of the [3333] conformation were obtained by means of the program COORD.[36] Pseudorotation paths were explored by inducing 5–10° changes in one torsional angle which should be adjacent to a corner position.[37]

Force-field calculations were carried out on an IBM-360/91 computer at the Campus Computer Network of UCLA.

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Intramolecular Excimer Study of Rates of Conformational Transitions. Dependence on Molecular Structure and the Viscosity of the Medium[1]

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Abstract: Fluorescence spectra for compounds of the type $ArCH_2XCH_2Ar$ where Ar is phenyl, 1-naphthyl, or 4-biphenyl and X is $-CH_2-$, $-O-$, $-NH_2^+-$, $-N(CH_3)_2^+-$, or $-N(COCH_3)-$ were recorded as a function of temperature in heptane, ethanol, and ethylene glycol. All the compounds studied with the exception of dibenzyldimethylammonium chloride exhibited intramolecular excimer formation. The temperature dependence of the ratio of emission intensities of the excimer and the monomer (I_d/I_m) in the temperature range −70 to −40 °C was interpreted in terms of the activation energy for the conformational transition required for excimer formation. Measurements of (I_d/I_m) in ethanol–ethylene glycol mixtures at 0 °C were supplemented with excited lifetime determinations of the compounds forming intramolecular excimers and their analogues containing a single chromophore. The viscosity dependence of the rate of conformational transition derived from these data was interpreted in terms of Kramers' diffusion model of chemical reactions. Plots of the reciprocal rate constant against the viscosity of the medium exhibited the initial upward curvature predicted by Kramers and had limiting slopes increasing sharply with an increasing bulk of the chromophore. The temperature dependence of I_d/I_m of two of the model compounds was compared in ethanol and ethylene glycol solutions above 0 °C. The difference in the apparent activation energies, E_a, for conformational transition in the two media derived from these data are not in accord with Kramers' theory which predicts E_a in very viscous solvents to be the sum of the barrier height and the activation energy for viscous flow $\Delta E_\eta^{\ddagger}$. The results agree with analyses by Christiansen, by Marcus, and by Noyes, which predict that E_a should approach $\Delta E_\eta^{\ddagger}$ in media of high viscosity.

Until recently, ultrasonic absorption provided the only experimental method for the study of rates of conformational transitions of small molecules with low energy barriers in the liquid phase. Typical of such an investigation is the study of butane and its homologues by Piercey and Rao[2] which led to an estimate of the potential energy barriers for hindered rotation around the C–C bonds in the range of 3–4 kcal/mol. A number of other techniques (e.g., dielectric dispersion, depolarization of fluorescence, NMR relaxation) have been employed for the study of the conformational mobility of polymers,[3] but they all depend on the fact that the rotational diffusion of the macromolecule is slow compared to the rate of conformational transitions—they are, therefore, not applicable to the study of small molecules.

The discovery of intramolecular excimer fluorescence[4] has provided a new, powerful tool for the study of conformational changes with relaxation times in the range of 10^{-9}–10^{-7} s. This is so since the conformation required for the sandwich complex between two aromatic chromophores which is responsible for excimer emission would have a prohibitive energy requirement in the absence of electronic excitation. We must assume, therefore, that a conformational transition has to take place during the lifetime of the excited state of one of the chromophores to bring it into proper juxtaposition with the second chromophore for excimer formation. Since this process is exothermic,[5] the dissociation of the excimer is negligible at low temperatures and the relative emission intensity of excimer and normal fluorescence yields information on the ratio of the rate constants for excimer formation and monomer emission. This principle was first used by Klöpffer[6] to estimate the rates of excimer formation from excited 1,3-diphenylpropane and 1,3-dicarbazolylpropane. Later work used time-resolved fluorescence decay techniques to determine rate constants for both excimer formation and dissociation.[7-9]

The use of intramolecular excimer fluorescence as a measure of conformational mobility is particularly valuable in allowing us to study the rates of conformational transitions as a function of the nature of the solvent medium. This was first attempted by Klöpffer and Liptay;[10] Avouris et al.[7] tried later to find a correlation between such rates and the viscosity of the medium, but Johnson found in a detailed study on 1,3-dicarbazolylpropane that such correlations hold only within homologous series of solvents.[9]

In the present investigation we have used a series of compounds of the type $ArCH_2XCH_2Ar$ where Ar is phenyl, 1-naphthyl, or 4-biphenyl and X may be $-CH_2-$, $-O-$, $-NH_2^+-$, or $-N(COCH_3)-$. Excimer fluorescence was determined as a function of temperature in heptane, ethanol, and ethylene glycol and in ethanol–glycol mixtures at 0 °C. In addition, fluorescent lifetimes were measured by the phase shift and the demodulation method. We attempted to define the dependence of the rate of conformational change on the nature of the bond around which hindered rotation takes place and on the bulk of the chromophore which experiences a frictional resistance to its motion through the solvent. The experimental data were discussed in terms of two alternative theoretical approaches, the first suggested by Kramers,[11] the second formulated by Christiansen,[39] Marcus,[12] and Noyes,[13] for rates of chemical processes in viscous media.

Results and Discussion

Temperature Dependence of Fluorescence Behavior in Low-Viscosity Media. The temperature dependence of the fluorescence spectra of $ArCH_2OCH_2Ar$ with Ar = phenyl,