Carbon-13 Magnetic Resonance. IX.[1a] The Methylcyclohexanes[1b]

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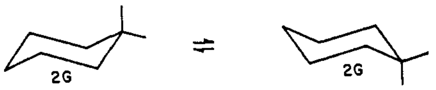
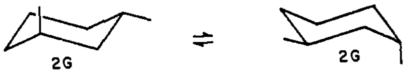
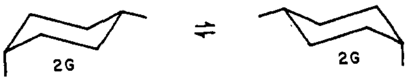
Abstract: Carbon-13 chemical shift data were secured on 15 methylcyclohexanes using the proton-decoupling technique. Spectral assignments are made with the aid of additive parameters derived from compounds in which unequivocal assignments are possible. A factor analysis was carried out to obtain more accurate chemical shift parameters characteristic of detailed geometrical and conformational features found in this class of compounds. These parameters are used to characterize the spectra of three compounds which exist to a significant extent in more than one form, and their conformational energies are estimated. The relationship between chemical shift and the rotation of vicinal methyls to relieve steric strain is briefly considered.

It was suggested[2] early that cyclohexane could exist in chair and boat conformations and that various monosubstitution products were possible for each of these geometrical isomers. Experimental verification[3-10] of these predictions, however, awaited the refinement of crystallographic and spectroscopic techniques. Recent estimates[11] of conformational energies indicate that the *true* boat form should be higher in energy than the chair structure by 6.9 kcal/mole while the similar *skew* or *twist* boat conformation is 5.3 kcal/mole greater than the chair. Thus, at room temperature cyclohexane is predominantly in the chair form, and the boat forms make little contribution to a ground-state description of this molecule.

Pitzer and associates[6,10,12] have discussed the thermodynamics of some of the derivatives of cyclohexane. In the axial (a) conformation of monomethylcyclohexane, a steric repulsion energy of 1.8 kcal/mole is realized from the interaction of one of the methyl protons with the axial protons at C-3 and C-5. The magnitude of the steric energy is approximately twice that in *gauche* butane in keeping with the fact that there are two *gauche* interactions in the axial form of methylcyclohexane. If the methyl is equatorial (e), monomethylcyclohexane is expected to have little more strain energy than the cyclohexane parent, since no unfavorable *gauche* interactions exist. In the aa conformation of compounds having *cis*-1,3-methyl groups an additional repulsion energy results from the steric interaction of the two proximate methyls. This interaction contributes an additional 3.7 kcal/mole of steric strain to such molecular structures.[13]

A barrier of 10.8 kcal/mole for chair–boat–chair interconversions was determined[14] from kinetic data taken on cyclohexane. The rate corresponding to a barrier of this magnitude is sufficiently rapid at room temperatures to average the chemical shift values existing for interconverting conformational isomers whenever both forms have equal or comparable energies. If one conformer predominates the spectrum will not exhibit the effect of kinetic averaging. The 15 methylcyclohexanes available for study in this work can be divided into three characteristic groups. First are those which have two equally favored, but rapidly interconverting, forms. These compounds are given in Table I and include the 1,1-, *cis*-1,2-, *trans*-1,3-, and *cis*-1,4-dimethyl compounds. Both conformations of each of these molecules have one axial and one equatorial methyl group, and therefore are of equal

Table I. Dimethylcyclohexanes with Conformations of Equal Energy

		ΔE, kcal/mole
1,1		0
cis-1,2		0
trans-1,3		0
cis-1,4		0
	$G = 0.9$ kcal/mole	

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[1] (a) Previous paper in this series is B. V. Cheney and D. M. Grant, *J. Am. Chem. Soc.*, **89**, 5319 (1967); (b) taken in part from the Ph.D. dissertation of D. K. Dalling, University of Utah.

[2] H. Saches, *Ber.*, **23**, 1363 (1890); also *Z. Physik. Chem.*, **10**, 203 (1892).

[3] S. B. Hendricks and C. Bilicke, *J. Am. Chem. Soc.*, **48**, 3007 (1926).

[4] R. G. Dickinson and C. Bilicke, *ibid.*, **50**, 764 (1928).

[5] K. W. F. Kohlrausch, A. W. Reitz, and W. Stockmair, *Z. Physik. Chem.*, **B32**, 229 (1936).

[6] C. W. Beckett, K. S. Pitzer, and R. Spitzer, *J. Am. Chem. Soc.*, **69**, 2488 (1947).

[7] D. H. R. Barton, *Experientia*, **6**, 316 (1950).

[8] O. Hassel, *Tidsskr. Kjemi, Bergvesen Met.*, **3**, 32 (1943).

[9] R. S. Rasmussen, *J. Chem. Phys.*, **11**, 249 (1943); also see previous work cited herein.

[10] K. S. Pitzer, *Chem. Rev.*, **27**, 39 (1940).

[11] J. B. Hendrickson, *J. Am. Chem. Soc.*, **83**, 4537 (1961); see also ref 10.

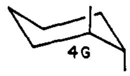
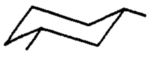
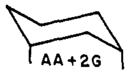
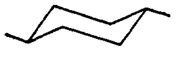
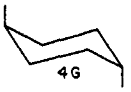
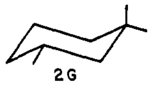
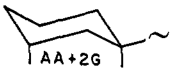
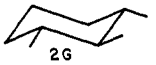
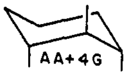
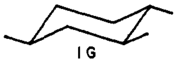
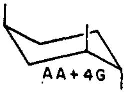
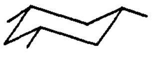
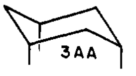
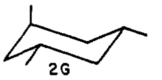
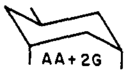
[12] D. H. R. Barton, O. Hassel, K. S. Pitzer, and V. Prelog, *Science*, **119**, 49 (1953).

[13] N. L. Allinger and M. A. Miller, *J. Am. Chem. Soc.*, **83**, 2145 (1961).

[14] F. A. L. Anet and A. J. R. Bourn, *ibid.*, **89**, 760 (1967). This paper contains an extensive compilation of previous references on cyclohexane inversion.

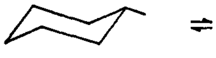
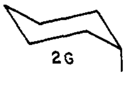
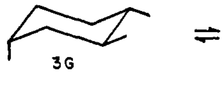
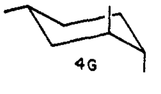
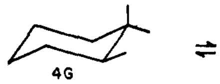
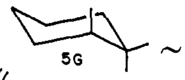
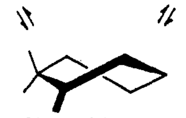
energy. The second group of compounds consists of several dimethylcyclohexanes in which the two methyls occupy either an aa configuration or the more favored ee form. They are presented in Table II together with five similar trimethylcyclohexanes which have a highly favored conformation. The number of *gauche* and axial–axial interactions existing in each conformer is indicated beneath the structure, and the approximate energy difference existing between the conformers is given in the last column. The third group of compounds, presented in Table III, consists of methylcyclohexane and two trimethyl compounds. Based on very simple energy considerations these three molecules are expected to exhibit similar energies for each of the two chair conformations. While each molecule will have a favored form, considerable contribution from the less favored configuration is anticipated. Rapid interconversion between the two forms will still average the chemical shifts of each conformer, but the contribution of each form will be weighted by its statistical population.

Table II. Methylcyclohexanes with a Highly Favored Conformation

	Favored form		Unfavored form	ΔE, kcal/mole
trans-1,2		⇌		~+2.7
cis-1,3		⇌		~+5.5
trans-1,4		⇌		~+3.6
1,1,3		⇌		~+3.7
1-*trans*-2-*cis*-3		⇌		~+5.5
1-*trans*-2-*trans*-4		⇌		~+6.4
1-*cis*-3-*cis*-5		⇌		~+11.1
1-*cis*-3-*trans*-5		⇌		~+3.7

G = 0.9 kcal/mole; AA = 3.7 kcal/mole

Table III. Cyclohexanes with Intermediate Differences in Conformational Energies

	Favored form		Unfavored form	ΔE, kcal/mole
1-Methyl		⇌		~+1.8
1-*trans*-2-*cis*-4		⇌		~+0.9
1,1,2		⇌		~+0.9
	 Skewed boat			

G = 0.9 kcal/mole; AA = 3.7 kcal/mole

The proton nmr spectra of the dimethylcyclohexanes have been investigated,[15–18] and some proton work has been done on the trimethylcyclohexanes.[18] Aside from the cyclohexane parent[19] no carbon-13 magnetic resonance studies have yet been reported on the compounds considered in this paper. However, work on other hydrocarbons such as the simple alkanes,[20] the methylbenzenes,[21] and various alkanes and alkynes[22] has been reported. These studies illustrate the marked dependence of carbon-13 chemical shift data on molecular structural features. Both substituent[1] and conformational[23] effects have been shown to be important in these other hydrocarbons even though interconversion between rotameric forms greatly limited the definitive information which could be obtained. As many of the methylcyclohexanes have well-characterized conformations (see Table I and II), these particular systems present an excellent opportunity for studying the effect of detailed structural features on carbon-13 chemical shift parameters. The carbon-13 chemical shift data reported recently by Buchanan, Ross, and Stothers[24] emphasizes the importance of such conformational effects in related cyclohexanol derivatives.

Experimental Section

A. **Equipment.** The carbon-13 magnetic resonance spectra were obtained with a Varian high-resolution spectrometer operating at 15.1 Mcps. Simultaneous proton decoupling was accomplished with a heteronuclear Varian V-4320 spin decoupler functioning at 60 Mcps. The Varian V-4331 high-resolution probe, modified for dual-frequency irradiation, was equipped with a Wilmad spinner assembly that accepts 12-mm sample tubes. The frequency of both the transmitter and proton decoupler was measured to ±1 cps with a Hewlett-Packard 524C electronic counter equipped with a 525A frequency converter. Proton chemical shifts were determined using a Varian A-60 spectrometer, equipped with a Varian V-6058A homonuclear spin decoupler.

B. **Spectral Techniques.** The general technique is essentially that used by Royden[25a] and Paul and Grant.[25b] The 15.1-Mcps transmitter is monitored only intermittently since it is inherently very stable so long as the ambient temperature does not vary. The proton decoupler is monitored continuously while numerous sweeps, at different frequencies, are made through a given carbon-13 resonance signal. The peak height is plotted against the decoupler frequency to determine the most favorable decoupling conditions. This decoupler frequency, f_i, is then used along with the transmitter frequency, ν_i, and proton shift, δ_H, to calculate the chemical shift. Equation 1[21] presents the relationship between the carbon and pro-

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(15) S. Brownstein and R. Miller, *J. Org. Chem.*, **24**, 1886 (1959).

(16) J. I. Musher, *Spectrochim. Acta*, 16, 835 (1960).

(17) N. Muller and W. G. Tosch, *J. Chem. Phys.*, **37**, 1167 (1962).

(18) A. Segre and J. I. Musher, *J. Am. Chem. Soc.*, **89**, 706 (1967).

(19) J. J. Burke and P. C. Lauterbur, *ibid.*, **86**, 1870 (1964).

(20) D. M. Grant and E. G. Paul, *ibid.*, **86**, 2984 (1964).

(21) W. R. Woolfenden and D. M. Grant, *ibid.*, **88**, 1496 (1966).

(22) R. A. Friedel and H. L. Retcofsky, *ibid.*, **85**, 1300 (1963).

(23) D. M. Grant and B. V. Cheney, *ibid.*, **89**, 5315 (1967).

(24) G. W. Buchanan, D. A. Ross, and J. B. Stothers, *ibid.*, **88**, 4301 (1966).

(25) (a) V. Royden, *Phys. Rev.*, **96**, 543 (1954); (b) E. G. Paul and D. M. Grant, *J. Am. Chem. Soc.*, 86, 2977 (1964).

Table IV. Chemical Shift Data for the Methylcyclohexanes

Compd	Item	Carbon[a]	Γ_i	δ_H (from TMS)[b]	$\delta_{C^{13}}$ (from benzene)	Lit. values of δ_H
Cyclohexane	1	1–6	3.97682978	1.44	101.44	(1.68, 1.20)[c]
Methylcyclohexane	2	2,6	79510	1.43 (1.70,1.16)	92.73	
	3	1	80604	1.48[d]	95.44	
	4	3,5	83175	1.43 (1.70,1.16)	101.95	
	5	4	83234	1.43 (1.70, 1.16)	102.10	
	6	CH_3	84484	0.89	105.78	0.87[e]
1,1-Dimethylcyclohexane	7	2,6	77843	1.30	88.67	
	8	1	81580	0.88[f]	98.49	
	9	CH_3	82049	0.88	99.67	
	10	4	83110	1.39	101.83	
	11	3,5	84738	1.39	105.92	
cis-1,2-Dimethylcyclohexane	12	1,2	80130	1.65[d]	94.07	1.6[e]
	13	3,6	81198	1.42	96.99	
	14	4,5	84366	1.42	104.83	
	15	CH_3	87239	0.86	112.76	0.84[e]
trans-1,2-Dimethylcyclohexane	16	1,2	77842	1.02	88.95	
	17	3,6	79367	1.34 (1.66,1.02)	92.47	
	18	4,5	83019	1.34 (1.66,1.02)	101.65	
	19	CH_3	85479	0.89	108.28	0.89[e]
cis-1,3-Dimethylcyclohexane	20	2	75831	1.1 (1.58,0.52)	83.8	
	21	4,6	79656	1.40 (1.67,1.12)	93.13	
	22	1,3	80583	1.18[d]	95.68	1.3[e]
	23	5	83203	1.40 (1.67,1.12)	102.05	
	24	CH_3	84429	0.84	105.69	0.86[e]
trans-1,3-Dimethylcyclohexane	25	2	77250	1.40	87.08	
	26	4,6	80247	1.40	94.62	
	27	1,3	83024	1.75[d]	101.45	1.8[e]
	28	5	85470	1.40	107.75	
	29	CH_3	85371	0.90	108.00	0.89[e]
cis-1,4-Dimethylcyclohexane	30	2,3,5,6	81445	1.42	97.61	
	31	1,4	81777	1.49[d]	98.37	
	32	CH_3	85555	0.92	108.44	
trans-1,4-Dimethylcyclohexane	33	2,3,5,6	79532	1.35 (1.70–1.00)	92.87	
	34	1,4	80693	1.25[d]	95.89	
	35	CH_3	84504	0.90	105.82	
1,1,2-Trimethylcyclohexane	36	2	77070	1.32	86.71	
	37	6	77289	1.32	87.26	
	38	1	80427	0.83[f]	95.64	
	39	3	81223	1.32	97.15	
	40	CH_3(e)	81362	0.83	97.99	
	41	4	83037	1.32	101.71	
	42	5	84634	1.32	105.73	
	43	CH_3(a)	85894	0.83	109.39	
	44	CH_3(2)	87001	0.83	112.17	
1,1,3-Trimethylcyclohexane	45	2	74097	1.40 (1.49,1.30)	79.15	
	46	6	78008	1.40 (1.49,1.30)	88.99	
	47	4	79519	1.40 (1.49,1.30)	92.79	
	48	CH_3(e)	80129	0.88	94.84	
	49	1	81283	0.88[f]	97.74	
	50	3	82463	1.40 (1.49,1.30)	100.19	
	51	CH_3(a)	83629	0.88	103.64	
	52	CH_3(3)	84292	0.83	105.36	
	53	5	84730	1.40 (1.49,1.30)	105.89	
1-*trans*-2-*cis*-3-Trimethylcyclohexane	54	2	75089	0.77	82.28	
	55	1,3	78059	1.17[d]	89.35	
	56	4,6	79206	1.35 (1.65,1.05)	92.05	
	57	5	83190	1.35 (1.65,1.05)	102.07	
	58	CH_3(1,3)	85278	0.92	107.75	
	59	CH_3(2)	86922	0.90	111.90	
1-*trans*-2-*cis*-4-Trimethylcyclohexane	60	3	77518	1.39	87.77	
	61	1	78174	1.13	89.68	
	62	2	80428	1.55	94.92	
	63	5	81104	1.39	96.68	
	64	6	81999	1.39	99.03	
	65	4	82788	1.88[d]	100.53	
	66	CH_3(1,2)	85441	0.89	108.19	
	67		85554	0.89	108.47	
	68	CH_3(4)	85984	0.97	109.47	

Table IV (*Continued*)

Compd	Item	Carbon[a]	Γ_i	δ_H (from TMS)[b]	$\delta_{C^{13}}$ (from benzene)	Lit. values of δ_H
1-*trans*-2-*trans*-4-Trimethylcyclohexane	69	3	3.976 75742	1.27 (1.65,0.89)	83.42	
	70	1,2	77937	0.90	89.31	
	71		77983	0.90	89.63	
	72	5,6	79382	1.27 (1.65,0.89)	92.57	
	73		79455	1.27 (1.65,0.89)	92.76	
	74	4	80542	1.15[d]	95.61	
	75	CH_3(4)	84480	0.90	105.76	
	76	CH_3(1,2)	85454	0.90	108.21	
	77		85551	0.90	108.45	
1-*cis*-3-*cis*-5-Trimethylcyclohexane	78	2,4,6	76010	1.06 (1.65,0.47)	84.30	(1.64,0.47)[g]
	79	1,3,5	80726	1.40[g]	95.82	1.4,[e] 1.40[g]
	80	CH_3	84443	0.88	105.69	0.86[e] 0.86[g]
1-*cis*-3-*trans*-5-Trimethylcyclohexane	81	2	75664	0.98 (1.48,0.47)	83.51	(1.52 ± 0.10,0.47)[g]
	82	4,6	77401	1.28 (1.58,1.01[g])	87.58	(1.52 ± 0.10,1.01)[g]
	83	5	82587	2.00[d]	99.90	2.0,[e] 2.00[g]
	84	1,3	83230	1.56[d]	102.06	1.52 ± 0.10[g]
	85	CH_3(1,3)	84331	0.83	105.46	0.82,[e] 0.83[g]
	86	CH_3(5)	86041	0.97	109.62	0.96,[e] 0.97[g]

[a] Number or letter in parentheses indicates either the carbon to which a methyl is attached or its spatial orientation, respectively. [b] Indicates position of equatorial and axial bands, respectively, which were averaged to find the value used in eq 1. [c] F. A. L. Anet, M. Ahman, and L. D. Hall, *Proc. Chem. Soc.*, 145 (1964); also F. A. Bovey, F. P. Hood, E. W. Anderson, and R. L. Kornegay, *ibid.*, 146 (1964). [d] Value verified by proton decoupling. [e] The authors thank J. L. Jungnickel, D. O. Schissler, C. A. Reilly, and G. G. Henry for a private communication of these values. [f] The proton chemical shift of adjacent methyls was used for quaternary carbons to obtain agreement with slow sweep data. See Assignment of Proton Chemical Shifts section. [g] Reference 18.

ton chemical shifts and the decoupling parameter, Γ_i, which is the ratio (f_i/ν_i) of decoupler to transmitter frequency.

$$\delta_{C^{13}} = (\Gamma_i - \Gamma_0)/\Gamma_i + \Gamma_0\delta_H/\Gamma_i \cong (\Gamma_i - \Gamma_0)\Gamma_i + \delta_H \qquad (1)$$

C. **Sample Preparation.** All of the compounds examined were neat liquids. They were obtained from standard commercial sources and from the American Petroleum Institute. The samples used for carbon-13 study were sealed in 12-mm o.d. glass tubes under vacuum after having been degassed. The samples used for proton study were treated similarly and sealed in 5-mm o.d. tubes with several drops of tetramethylsilane added as an internal reference.

Spectral Assignments

The experimental values of the decoupling parameters and the proton and carbon-13 chemical shift data are given in Table IV for the methylcyclohexanes used in this study. The assignment of chemical shift values to specific carbon atoms is facilitated by first identifying the spectral peaks which arise from methyl carbons. This is possible as methyl signals are easily recognized from their decoupling characteristics. When the power level of the proton decoupler is held constant, it has been observed that a methyl quartet collapses to give a single peak over a narrower frequency range than is noted for other types of proton-induced multiplets. In this way the methyl carbon peaks are distinguished from the ring carbon signals, and the two groups are assigned independently in the manner indicated in the following sections.

A. **Assignment of the Methyl Carbons.** In methylcyclohexane, in all seven dimethyl compounds, and in 1-*cis*-3-*cis*-5-trimethylcyclohexane, the methyl peaks (items 6, 9, 15, 19, 24, 29, 32, 35, and 80 in Table IV) may be assigned unequivocally as there is only a single methyl peak in the spectrum of each of these compounds. On the basis of intensity arguments, the two different methyl peaks (items 58, 59 and 85, 86) may be specified with certainty in 1-*trans*-2-*cis*-3-trimethylcyclohexane and in 1-*cis*-3-*trans*-5-trimethylcyclohexane, respectively.

While the methyl assignments in the four remaining compounds are somewhat tentative, several reasonable correlations can be made. If one compares items 6, 24, 35, 80, and 85 included in Table V, all of which are assigned above to isolated equatorial methyls not involved in 1,2 methyl–methyl interactions, it is observed that they have an average chemical shift value of 105.65 ± 0.12 ppm. Items 52 and 75, given in

Table V. Carbon-13 Chemical Shifts of Isolated, Equatorial Methyls

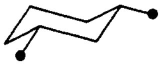
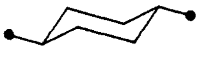
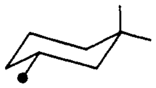
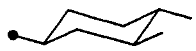
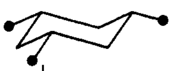
	Item	$\delta_{C^{13}}$, ppm
	6	105.78
	24	105.69
	35	105.82
	52	105.36
	75	105.76
	80	105.69
	85	105.46
	Av	105.65

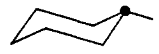
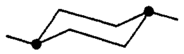
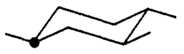
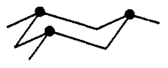
Table V, also have shift values which compare favorably with this average value, and undoubtedly arise from the isolated equatorial methyls in their respective compounds. Having assigned item 52 to the methyl on C-3, one is then left with the characterization of the two methyl peaks associated with C-1 in the 1,1,3-trimethyl compound. The axial methyl is assigned to the upfield signal because of its steric proximity to the two axial hydrogens at C-3 and C-5. Such steric interactions have been shown to lead to upfield shifts in previous work,[21,23] and similar upfield shifts are noted in the ring carbons to be discussed in the next section. Item 68 is assigned to the axial methyl on C-4 of 1-*trans*-2-*cis*-4-trimethylcyclohexane, since its value (109.47 ppm) is similar to that (109.62 ppm) of item 86 which has already been assigned to a methyl in an isolated axial configuration. The upfield methyl signal in the 1,1,2-trimethyl compound is designated as the methyl at C-2, because it is involved in two simultaneous *gauche* interactions while unperturbed by β-methyls. The axial C-1 methyl in this compound is then assigned to the remaining upfield peak and the equatorial methyl to the lower field peak. This tentative assignment rests upon arguments similar to those used in the case of 1,1,3-trimethylcyclohexane. The remaining two sets of unassigned methyl peaks, items 66, 67 and 76, 77, are in both cases separated by less than 0.3 ppm, and, although it is reasonably certain they result from slightly nonequivalent 1,2-diequatorial methyl groups, it is not possible to assign these peaks in these two compounds at this time.

B. Assignment of the Ring Carbons. In the spectra of the ring carbons, those signals due to quaternary carbons, in which large proton splittings are absent, were easily characterized (items 8, 38, and 49) because they enhance over a wide frequency range and at low decoupler power. Having specified item 8 as a quaternary carbon in 1,1-dimethylcyclohexane one can assign by default the remaining peak (item 10) of unit intensity to C-4. The resonance signals due to ring carbons in *cis*-1,4- and *trans*-1,4-dimethylcyclohexane (items 30, 31 and 33, 34) may be assigned on the basis of the 2:1 intensity patterns.

The rapid passage spectra of most of the compounds in this study consist of complex, overlapping multiplets which are not amenable to simple analysis, and assignments in general cannot be made easily on the basis of multiplet structure. Nevertheless, inspection of the adiabatic, rapid passage spectrum of the highly symmetrical 1-*cis*-3-*cis*-5-trimethylcyclohexane reveals a triplet (item 78) and a doublet (item 79) which can be identified with C-2,4,6 and C-1,3,5, respectively.

By utilizing the trends established by the above compounds, most other assignments can be made with a high degree of confidence. Table VI contains a list of compounds which have ring carbons α to an isolated equatorial methyl substituent. In each of these cases a chemical shift can be specified for the designated carbon which is within ±0.3 ppm of the average value of 95.69 ppm. As there is no ambiguity in the assignment of items 34 and 79, the close agreement in Table VI is taken as a basis for assigning the remaining three items 3, 22, and 74. Furthermore, from the data in Table VI a value for the α_e (α equatorial) substituent parameter of −5.7 ppm is obtained which can be used in unraveling the spectra of more complex molecules. As the existence of remote methyl groups in the γ_e (γ equatorial) and/or δ_e (δ equatorial) positions did not give rise to large variations in the shift values contained in Table VI, it can be concluded that such substituent effects must be small (not greater than ±0.3 ppm). Items 3 and 22 having been assigned on this basis, the assignment of items 5 and 21 proceeds directly, as the peaks from which these shifts are taken are due to the only unassigned carbons of the proper intensity remaining in each of the respective spectra.

Table VI. The Effects of an α_e-Methyl Group

	Item	$\delta_{C^{13}}$, ppm	α_e
	3	95.44	−6.00
	22	95.68	−5.76
	34	95.89	−5.55
	74	95.61	−5.83
	79	95.82	−5.62
	Av	95.69	−5.75

Listed in Table VII are those compounds which have carbons β to one or to two equatorial methyls and otherwise are subject only to the influence of γ_e, δ_e, or δ_a (δ axial) substituents. It is noted that there are resonance signals in all these compounds which lie within 0.61 ppm of the position predicted by a β_e (β equatorial) substituent parameter of −8.7 ppm. These results again suggest that the parameters γ_e and δ_e as well as δ_a are relatively small (less than 1.0 ppm). As items 21, 33, and 78 have already been assigned, confidence is gained in the assignment of the remaining items, 2, 17, 20, 47, 56, 69, and 81. Items 4, 23, 55, and 83 in Table IV may now be assigned by default, as the uncertainty in assigning a set of two peaks of equal intensity has been removed by the above arguments. With item 83 assigned to C-4 in 1-*cis*-3-*trans*-5-trimethylcyclohexane, it is now possible to estimate a value of −2 ppm (the difference between items 83 and 1) for the α_a (α axial) parameter. This approximation depends upon the γ_e parameter being negligible for the methyls at C-1,3. It is not possible at this time to assign the two lines (items 72 and 73) arising from C-5 and C-6 in the 1-*trans*-2-*trans*-4-trimethyl compound, but this creates no serious problem in later discussion of the data, as they are separated by only 0.19 ppm (a value which barely exceeds the experimental error). The assignment of items 69, 72, and 73 leaves items 70 and 71, separated by 0.32 ppm, to be assigned to C-1 and C-2 in 1-*trans*-2-*trans*-4-trimethylcyclohexane, but again it is not possible to decide which of the two possible ways of pairing up the carbons and lines is correct.

In Table VIII are found compounds having carbons sufficiently remote from substituents that they are influenced only by substituent effects which have been shown to be small (*i.e.*, the γ_e, δ_e, δ_a parameters).

Table VII. The Effect of a β_e-Methyl Group

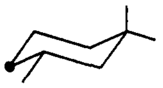
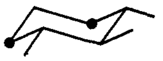
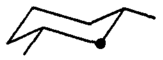
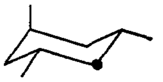
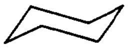
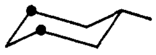
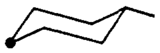
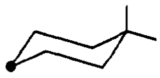
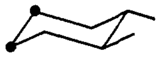
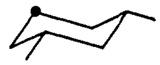
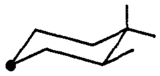
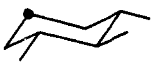
	Item	$\delta_{C^{13}}$, ppm	$2\beta_e$	β_e
	2	92.73	...	−8.71
	17	92.47	...	−8.97
	21	93.13	...	−8.31
	33	92.87	...	−8.57
	47	92.19	...	−8.25
	56	92.05	...	−8.39
	72,73	92.57 92.76	... ...	−8.87 −8.68
	20	83.8	−17.6	−8.8
	69	83.42	−17.93	−8.96
	78	84.30	−17.14	−8.57
	81	83.51	−17.80	−8.90
			Av	−8.66

Table VIII. The Effect of Remote γ_e-, δ_e-, and δ_a-Methyl Groups

	Item	$\delta_{C^{13}}$, ppm	$\delta_{C^{13}}-\delta_{C^{13}(C_6H_{12})}$
	1	101.44	...
	4	101.95	+0.51
	5	102.10	+0.66
	10	101.83	+0.39
	18	101.65	+0.21
	23	102.05	+0.61
	41	101.71	+0.27
	57	102.07	+0.63

In these cases there are peaks in the respective spectra which lie within 0.6 ppm of the chemical shift of cyclohexane. This enables us to assign items 18, 41, and 57, and by default items 16 and 54 are assigned to the otherwise equivalent, and unassigned, peaks remaining in the respective spectra.

Two additional assignments may be made by considering Figure 1. The methyl, C-1, and C-4 peaks of 1,1-dimethylcyclohexane have already been assigned, leaving only C-2,6 and C-3,5 to be specified. One of these two peaks of double intensity is found at a lower field relative to cyclohexane while the other is at a higher field. The lower field peak (item 7) is assigned to C-2,6 as these carbons are affected by β-methyls which thus far have resulted in downfield shifts.[1] This leaves item 11 to be assigned to the C-3,5 carbons which are influenced by γ_e- and γ_a-methyls. Since the first term, γ_e, has already been shown to be small, the γ_a parameter for an axial methyl must have a relatively large magnitude[23] (approximately +5 ppm), and unlike the α- and β-substituent parameters, it carries the positive sign. This upfield shift can be explained by the steric interaction of one of the axial-methyl hydrogens with the axial hydrogens at C-3,5. These hydrogens would have the same spatial orientation as proximate hydrogens in the completely staggered structure of *gauche* butane, and the sign and magnitude of this effect have been discussed elsewhere.[23]

The two peaks (items 82 and 84) which have not been assigned in 1-*cis*-3-*trans*-5-trimethylcyclohexane can be characterized using the +5-ppm value for γ_a. Here it is observed that the peak at +102.06 ppm is upfield a little more than 5 ppm from the chemical shift value noted for carbons (see Table VI) perturbed only by an α_e-methyl. This would be expected for the shift of C-1,3. The other unassigned peak appearing at 87.58 ppm could not be assigned to C-1,3 and still conform to established parametrical values. Thus, items 82 and 84 are assigned to C-4,6 and C-1,3, respectively. Assuming the δ_e parameter to be negligible and the β_e to be −9.0 ppm, one calculates from item 82 the approximate value of −5.0 ppm for β_a.

Using the approximate substituent parameters determined from the above discussion ($\alpha_e \approx -6$ ppm, $\alpha_a \approx -2$ ppm, $\beta_e \approx -9$ ppm, $\beta_a \approx -5$ ppm, $\gamma_a \approx +5$ ppm, $\gamma_e \approx \delta_e \approx \delta_a \approx 0$), some of the remaining unassigned peaks are assigned to specific carbons with reasonable assurance of being properly designated. In *cis*-1,2-dimethylcyclohexane we calculate the ring shifts averaged over the two conformations (see Table II) to be 90 ppm for C-1,2, 97 ppm for C-3,6, and 104 ppm for C-4,5. These predicted values compare reasonably well with the respective values of 94.07, 96.99, and 104.83 ppm noted for items 12, 13, and 14, and on this basis the assignments in this compound were made. In a similar manner the shift values in the *trans*-1,3-dimethyl compound (items 25 and 28), along with the predicted values given in parentheses, are respectively 87.08 (87), 94.62 (94), 101.45 (100), and 107.75 (106) (all values given in ppm). Items 45, 46, 50, and 53 are assigned to C-2, C-6, C-3, and C-5, respectively, in 1,1,3-trimethylcyclohexane on the basis of the following comparison of experimental and predicted values: 79.15 (78), 88.99 (85), 100.19 (100), and 105.89 ppm (106 ppm). In highly branched systems[20] considerable deviations are noted between the experimental and predicted values. The simple additive

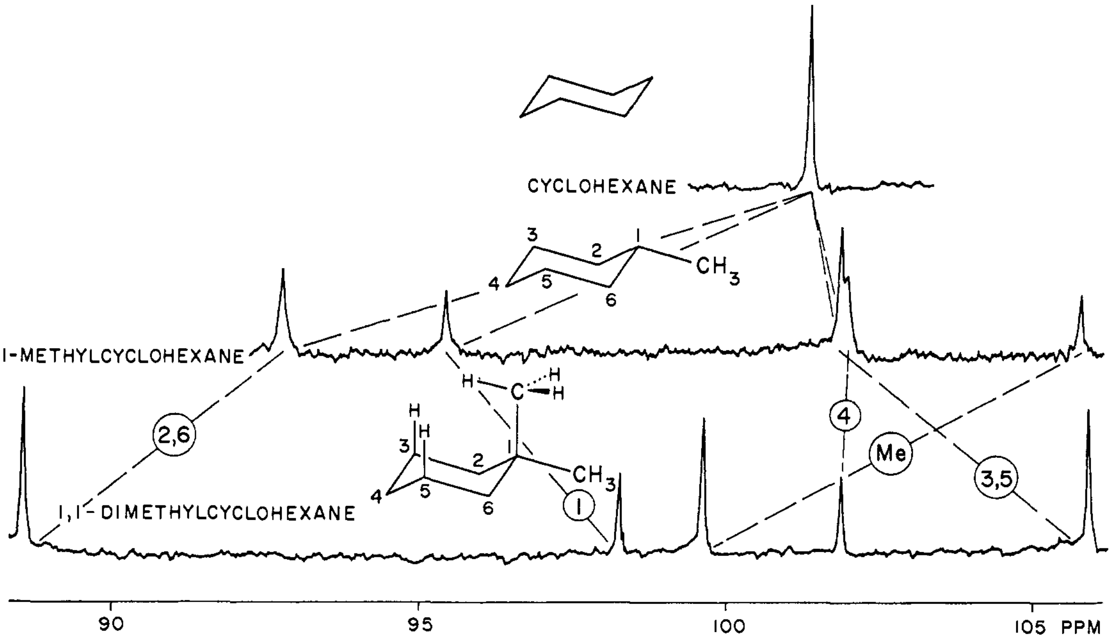


Figure 1. The slow sweep carbon-13 spectra of cyclohexane, methylcyclohexane, and 1,1-dimethylcyclohexane with proton decoupling. The encircled numbers indicate the spectral assignments of the peaks.

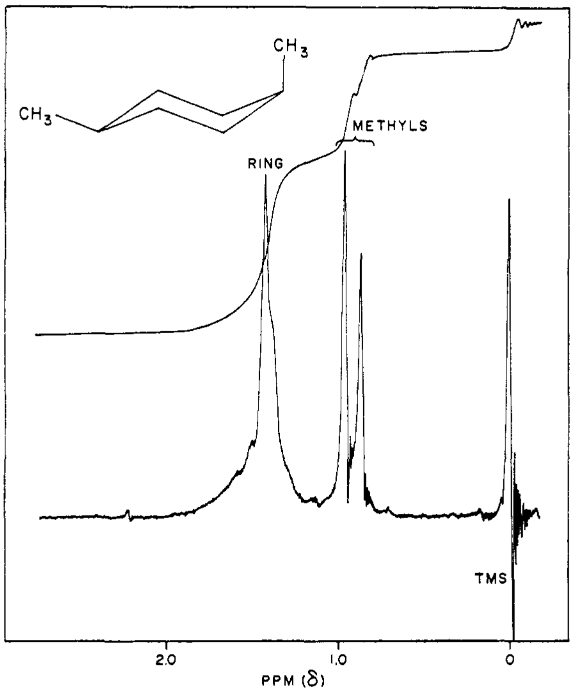


Figure 2. Proton spectrum of *cis*-1,4-dimethylcyclohexane. The narrow band due to ring protons is characteristic of those compounds having equally favored forms which are rapidly interconverting.

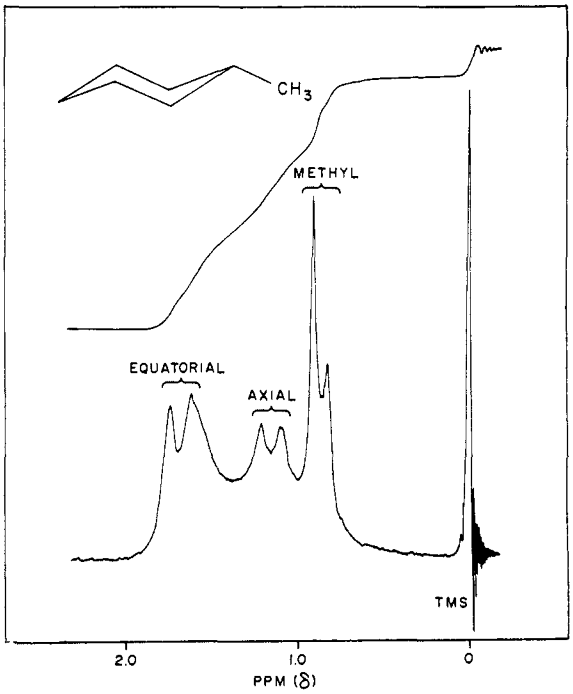


Figure 3. Proton spectrum of methylcyclohexane. The ring proton signals of compounds having a highly favored form are broad and are separated into two bands corresponding to the axial and equatorial protons.

parameters fail to predict the chemical shifts in these systems for carbons near the centers of the branching.

All peaks have now been paired up with a given carbon atom except for those in the 1,1,2-trimethyl and 1-*trans*-2-*cis*-4-trimethyl compounds. These molecules can be expected to exist to a considerable extent (see Table III) in more than one conformation with population factors which are not specified by the symmetry of the molecules. Without the populational factors, it is not possible to weight the contribution of the various substituent parameters, and the assignment of the peaks in these two spectra depends in a large part on the factor analysis given in a later section.

C. Assignment of Proton Chemical Shifts. Some aspects of proton spectra of methylcyclohexanes have been treated in the literature.[15–18,26,27] Spectra similar to that of *cis*-1,4-dimethylcyclohexane given in Figure 2 are exhibited by those compounds in which the resonance peaks of axial and equatorial protons are averaged by rapid conformational conversions (compounds

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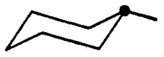
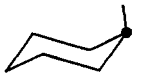
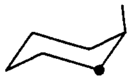
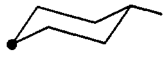
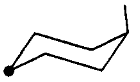
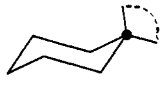
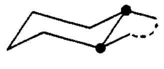
(26) N. F. Chamberlain, *Anal. Chem.*, 31, 56 (1959).

(27) F. A. L. Anet, *Can. J. Chem.*, 39, 2262 (1961).

Table IX. Methyl Substituent Parameters from Factor Analysis[a]

Parameter		Value	No. of occurrences	Parameter		Value	No. of occurrences
α_e		-5.64 ± 0.21	15	α_a		-1.08 ± 0.41	5
β_e		-8.90 ± 0.11	23	β_a		-5.17 ± 0.32	8
γ_e		0.00 ± 0.55	23	γ_a		$+5.39 \pm 0.22$	8
δ_e		$+0.28 \pm 0.16$	15	δ_a		$+0.14 \pm 0.29$	5
G_α		$+3.44 \pm 0.57$	2	G_β		$+1.15 \pm 0.42$	3
V_{ee}		$+2.28 \pm 0.26$	5	$V_{(ea)}$[b]		$+3.07 \pm 0.57$	1

[a] In parts per million. Standard error of fit 0.51 ppm; multiple correlation coefficient 0.9990. [b] $V_{(ea)}$ is an average of V_{ea} and V_{ae}. As only one chemical shift value was obtained which exhibits the effect of these two parameters, it was only possible to obtain the average value. Additional data are needed before the difference in V_{ea} and V_{ae} can be characterized.

in Table I) of the cyclohexane ring. In these cases the average proton shifts to be used in eq 1 are easily determined. Less precise proton shifts are obtained from spectra of the type given in Figure 3 which are characteristic of those compounds having a highly favored form (Table II). The proton resonance spectra under these conditions broaden into bands as a result of the large amount of spin–spin splittings between nonequivalent protons. These same features are observed in the spectra of cyclohexane[28] and of compounds contained in Table I[17] when the temperature is lowered below the coalescence value where kinetic averaging no longer collapses the spectral peaks. In the decoupling experiment both axial and equatorial protons must be decoupled to observe a singlet for the methylene carbons. As the directly bonded C–H couplings should be about the same for both equatorial and axial protons, the most effective setting of the decoupling frequency is the mean position between the two respective chemical shift values. When both the axial and equatorial shift positions could be approximated they have been included in Table IV in parentheses after the mean value which specified the position of decoupler power.

The chemical shifts of protons on tertiary carbons varied considerably and were often difficult to identify because the peaks were small and usually obscured by larger signals. This problem was circumvented in several cases (see Table IV) by utilization of homonuclear spin decoupling to decouple the tertiary proton from the protons on the geminal methyl. The frequency of the homonuclear decoupler indicated the chemical shift difference between the methyl and the tertiary proton when the easily identified methyl signal collapsed from a doublet to a singlet. This method was not useful in many cases, however, because there is a substantial loss of resolution associated with proton decoupling, complicated by the existence of very small splittings in many methyl signals, which made it difficult to accurately determine the exact frequency at which decoupling occurred. In the cases where decoupling data were not available the best approximate shifts were selected, and the values confirmed with slow sweep data in the manner described by Alger, *et al.*[29] Indeed, if carbon-13 sweep data had not been used along with eq 1 it would not have been possible to make some of the proton assignments given in Table IV. The error in proton shifts for the most part is considerably less than 0.1 ppm, but in those few cases where some difficulty was encountered in establishing the center of the spectral bands the error may be in the 0.1–0.2-ppm range.

Results and Discussion

A. Factor Analysis of Carbon-13 Shifts of Ring Atoms. While the approximate substituent parameters were sufficiently accurate to make the assignments given above, a least-squares analysis of factors important in the chemical shifts of compounds given in Tables I and II was undertaken to obtain more precise parameters. Table IX contains a summary of the parameters found to be important in the factor analysis. In addition to the five significant and three negligible positional parameters, four additional terms had to be added to achieve a reasonable fit of the data. These additional parameters specify the effect upon the chemical shifts of proximate methyls in either the geminal or *gauche*-vicinal configurations. The statistical information (multiple correlation coefficient and standard deviations) of the analysis is given also in Table IX, and it is observed that these data indicate a satisfactory fit. The success of the fit is visualized in Figure 4 where the predicted values are plotted *vs.* the experimental ones. The agreement is in many instances well within the experimental error in the measurement.

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(28) F. R. Jensen, D. S. Noyce, C. H. Cederholm, and A. J. Berlin, *J. Am. Chem. Soc.*, **82**, 1256 (1960).

(29) T. D. Alger, D. M. Grant, and E. G. Paul, *ibid.*, **88**, 5397 (1966).

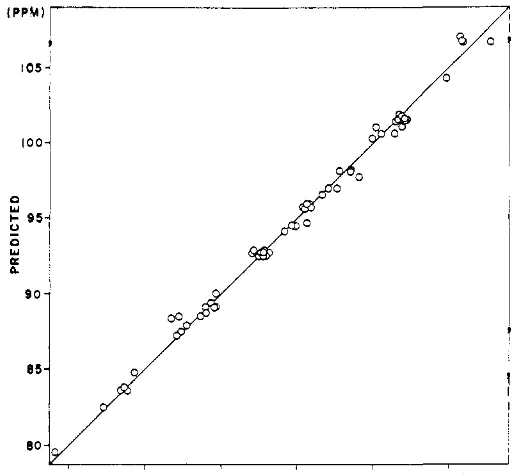

Figure 4. Plot of predicted *vs.* experimental carbon-13 chemical shifts for the ring carbons of the methylcyclohexanes studied.

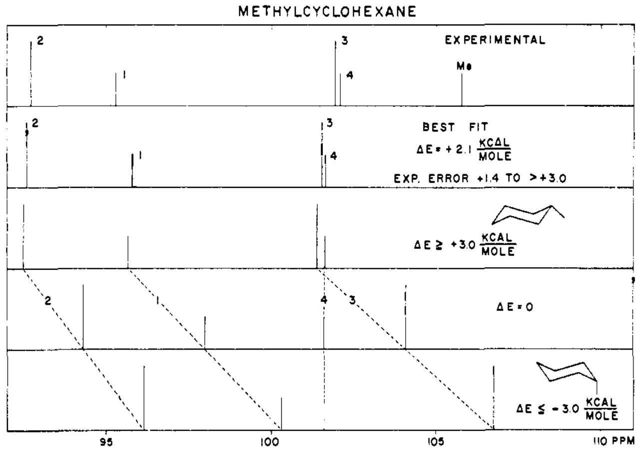

Figure 5. Analysis of the proton-decoupled, carbon-13 spectrum of methylcyclohexane. The substituent parameters were used to predict the spectra of the compound in its extreme conformational forms and for intermediate values of the difference in conformational energies. Statistical methods were used to obtain the spectrum which best fit the experimental data.

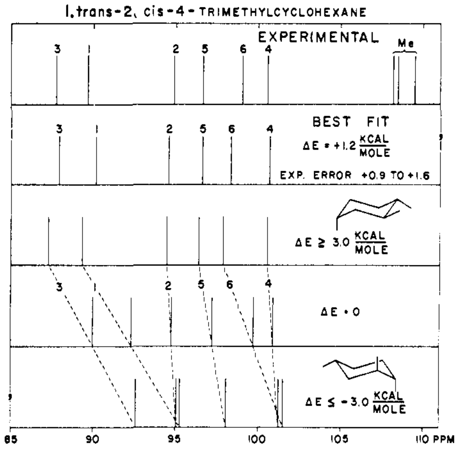

Figure 6. Analysis of the carbon-13, proton-decoupled spectrum of 1-*trans*-2-*cis*-4-trimethylcyclohexane. The format is the same as Figure 5.

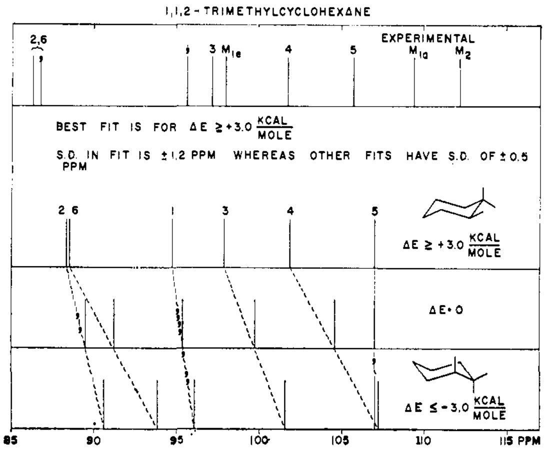

Figure 7. Analysis of the carbon-13, proton-decoupled spectrum of 1,1,2-trimethylcyclohexane. The format is the same as Figure 5. The chemical shift parameters failed to give a satisfactory fit for the spectrum of this molecule, indicating that the molecule may exist in other conformational structures not considered in the predicted spectra.

The substituent values given in Table IX are admittedly empirical and in all probability do not completely characterize the structural features important in the chemical shift parameter. Nevertheless the contents of Table IX should prove useful in identification work and several appropriate generalizations can be made. First, methyls in the γ_e, δ_e, and δ_a positions have a negligible effect on the carbon-13 chemical shift of the designating carbon atom. As these groups are remote both in terms of the number of intermediate chemical bonds and in terms of a spatial orientation of the two interacting molecular segments, these data constitute evidence that long-range effects are relatively unimportant in carbon-13 chemical shift studies. Second, the fairly sizeable γ_a parameter clearly indicates that spatial proximity of otherwise separated molecular moieties can lead to a considerable effect upon the carbon-13 chemical shift. As this effect has been discussed in detail elsewhere,[23] we shall not consider it further in this work. Third, the α and β parameters, along with those associated with the geminal, G_α and G_β, and vicinal, V_{ea} and V_{ee} effects, reflect trends which were observed in the flexible hydrocarbon series. The α and β substituents shift the resonance to lower fields, whereas the geminal and vicinal branching effects lead to higher field resonances. While present theoretical approaches[1] rationalize some of the gross effects, it is not profitable to attempt an extensive discussion of the details of these substituent shifts at the present time.

B. Conformational Energies Obtained from Carbon-13 Shift Data. Using the parameters given in Table IX the predicted spectra were calculated for 1-methyl-, the 1-*trans*-2-*cis*-4-trimethyl-, and the 1,1,2-trimethylcyclohexanes for conformational energies differing by $>+3.0$ kcal/mole, 0 kcal/mole, and <-3.0 kcal/mole, and these spectra are shown, respectively, in Figures 5, 6, and 7. As indicated in Figure 5, the experimental spectrum of methylcyclohexane is fit best for a $\Delta E = +2.1$ but a statistical analysis of the fit indicates that the experimental error in ΔE ranges from +1.4 to over +3.0 kcal/mole. Clearly, this method at the present time does not give the precision in conformational energies as found for methylcyclohexane by other methods.

A conformational energy of +1.2 kcal/mole with an error range of 0.9–1.6 kcal/mole was found for *1-trans*-2-*cis*-4-trimethylcyclohexane indicating that the conformation with two equatorial methyls is favored. The approximate populational factors found for this fit, given in Figure 6, are $p_{eea} \simeq 0.88$ and $p_{aae} \simeq 0.12$. It is interesting to note that the approximate method used in Tables I–III for estimating the difference in energy is substantiated by the data on 1-*trans*-2-*cis*-4-trimethylcyclohexane.

In many respects, the data on 1,1,2-trimethylcyclohexane lends itself to the most interesting interpretations. If this compound exists only in the two chair conformations then the spectral analysis given in Figure 7 would indicate that the compound is essentially all in the conformation with two equatorial methyls. Two observations argue against this possibility. First, there is a rather sizeable deviation in the fit of the experimental spectrum with the eae chair conformation of this compound. The second reason is found in the spectrum of the ring protons given in Figure 8 which exhibits a single band for this compound. For all compounds (see Table II) in which a single conformation exists, both axial and equatorial proton bands are observed in the pmr spectra as indicated in Figure 3, whereas single bands are observed for those compounds in which rapid averaging between the two chair forms exists (see Figure 2). Taken together, the relatively poor fit of the carbon-13 spectra and the single proton band support the possible contribution of additional conformational structures as anticipated in Table III with the skew-boat form. The steric repulsive energy (4*G*) for the aee chair conformation is higher than that of the lower energy form of any of the other compounds considered in this study. It, therefore, is not unreasonable to propose that the skew boat makes a considerable contribution in the description of this molecule. This would prevent a successful analysis of the carbon-13 shift data with parameters obtained from molecules in the chair conformation and remove the apparent incompatibility between the proton and carbon-13 spectral data.

As noted in Assignment of the Ring Carbons, the assignment of peaks in the 1,1,2- and 1-*trans*-2-*cis*-4-trimethylcyclohexanes rests upon the agreement between the experimental spectra and predicted spectra obtained by using the difference in conformational energy as a variable to achieve the best fit. In the 1-*trans*-2-*cis*-4-trimethyl compound there is no ambiguity. Numerical ordering of lines is the same for essentially all energies with only the extreme aae conformation in disagreement. Thus, the assignment of items 60–65 in Table IV is made with a high degree of confidence. The assignment of lines in the spectrum of 1,1,2-trimethylcyclohexane must be considered at best to be tentative until the problem of the conformational analysis has been completely resolved. As the chair conformations undoubtedly will make a significant contribution to a description of the 1,1,2 compound, the peak assignment given in Figure 6 which assumes chair structures is not without some support.

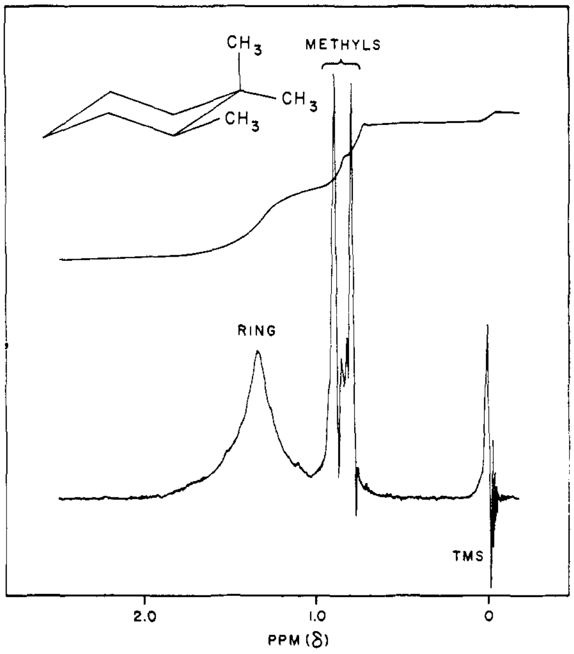

Figure 8. Proton spectrum of 1,1,2-trimethylcyclohexane. The unsplit band due to ring protons indicates that this molecule does not have a locked structure with characteristic axial and equatorial protons.

C. Carbon-13 Chemical Shifts and Rotational Conformations of Methyl Groups. All attempts to find a relatively simple set of linear, additive parameters which correlate the chemical shifts of the methyl carbons were unsuccessful. Nevertheless, several observations may be made. As indicated in Table V, isolated equatorial methyl carbons exhibit a characteristic chemical shift of 105.7 ppm. The relative constancy of this value in different compounds having remote groups again indicates that long-range shielding effects are small when compared with the over-all carbon-13 chemical shift range. An isolated axial methyl (*e.g.*, item 86) is shifted upfield by +3.9 ppm from the position occupied by an equatorial methyl peak. Steric interaction of the axial-methyl protons with 3,5-axial protons is proposed as a partial explanation for this upfield shift, but the nonreciprocal relationship existing between the +3.9-ppm value and the +5.4-ppm value for the γ_a (see Table IX), however, poses a difficult problem. As the two *gauche* interactions should have shifted the resonance upfield by approximately +10.5 ppm, it can only be concluded that the axial and equatorial positions differ in some manner other than can be explained solely on the basis of a steric interaction between axial groups. The discrepancy between +3.9 and +10.5 ppm is too large to explain by considering only deviations from the idealized staggered conformation, and some basic difference in the electronic structure of axial and equatorial methyls probably exists which prevents one from characterizing the additional steric effects by directly comparing the shifts of isolated axial and equatorial methyl groups. An upfield shift in axial methyl groups is also observed for certain interconverting conformers, such as the *trans*-1,3-dimethyl and the *cis*-1,4-dimethyl compounds. In both of these cases the methyl peak appears about midway between the shift values of an axial and an equatorial methyl as expected for rapidly interconverting conformers.

The *gauche* interaction of 1,2-dimethyl groups in the ee conformation also results in an upfield shift in the resonance relative to that observed for isolated

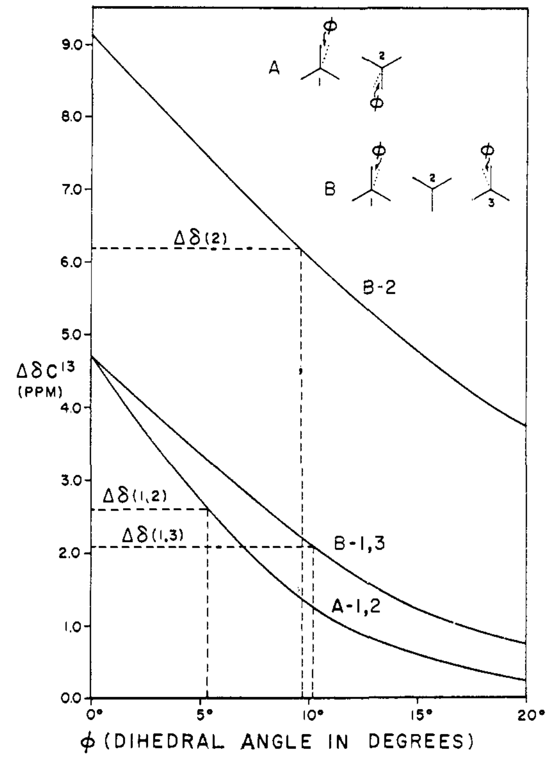

Figure 9. Plot of chemical shift *vs.* dihedral angle as calculated by eq 2 for the methyls of *trans*-1,2-dimethylcyclohexane and 1-*trans*-2-*cis*-3-trimethylcyclohexane.

equatorial methyls. In such molecules a direct comparison of the sterically perturbed equatorial methyl with a corresponding isolated equatorial methyl may be expected to reflect only the effect of steric interactions. Four compounds, *trans*-1,2-dimethylcyclohexane, 1-*trans*-2-*cis*-4-, 1-*trans*-2-*trans*-4-, and 1-*trans*-2-*cis*-3-trimethylcyclohexane, exhibit adjacent ee dimethyl interactions. In the first three compounds the 1,2-methyls might be expected to rotate equally about the bonds between the methyl carbons and ring carbons to relieve any steric strain between the two proximate hydrogens found in the *gauche* methyls. Relief of strain through distortion in the vicinal dihedral angles between adjacent ee methyls in 1-*trans*-2-*cis*-3-trimethylcyclohexane, however, must be limited to rotation of the 1,3-methyl groups as symmetry would prevent the central 2-methyl from rotating with respect to the plane of the cyclohexane ring.

Equation 2 (see eq 7 of ref 23) was used to study the effect upon the carbon-13 chemical shift of rotating equatorial methyls in the *trans*-1,2 and 1-*trans*-2-*cis*-3 compounds

$$\delta_{C^{13}}\,(\text{ppm}) = +1680 \cos\theta \exp(-2.671r) \qquad (2)$$

where θ is the H···H–C angle and r is the hydrogen–hydrogen distance. Only rotations affecting the dihedral angles about the carbon–carbon bonds were considered important as a means for relaxing the steric strain, and all other angles are assumed to be those found in normal tetrahedral bonding. Within the limits of these approximations, curves showing the angular dependence of the chemical shift are obtained for each of the three chemically different methyls found in the compounds under consideration. The results are presented in Figure 9. In the *trans*-1,2 molecules, the ee methyls were found on the average at +2.7 ppm upfield from the average value given for an isolated methyl resonance in Table V. This value corresponds to a distortion (see Figure 9) of 5° 20′ in the methyl dihedral angle. The distance between proximate protons is calculated to be 2.03 A. If there were no distortions in the angle the distance would be 1.89 A. Conclusions regarding 1-*trans*-2-*cis*-3-trimethylcyclohexane are perhaps more convincing, as this molecule has two different methyl shifts and only one rotational parameter to adjust. The 2.1-ppm steric shift in the 1,3-methyls corresponds to a rotation through an angle of 10° 10′ while the 6.2-ppm steric shift in the 2-methyl carbon predicts a rotation of the outer methyl groups of 9° 40′. These two values are within the experimental error of one another. The distance between the proximate hydrogens is calculated as 2.03 A, which is the same as in the *trans*-1,2 case. The fact that these distances are found to be the same corroborates the validity of the analysis. Apparently spatial separation is the variable which affects most significantly the amount of interaction energy between nonbonded atoms, since in the 1-*trans*-2-*cis*-3 molecule the outer methyls were found to rotate twice as far as those in the *trans*-1,2 case in order to relieve the steric strain. The chemical shifts of the methyl carbons, however, involves both the separation of nonbonded hydrogens and the HHC angle in accordance with eq 2.

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