Conformational Isomerism in 1-Substituted Derivatives of 3,3-Dimethylbutane

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Abstract: The difference in energy between *gauche* and *trans* conformers of several 1-substituted 3,3-dimethylbutanes has been determined using nmr spectroscopy. The relative order of "size" of the substituent groups estimated from these energy differences is significantly different from that obtained from previous studies of the equilibria between axial and equatorial conformers of the corresponding substituted cyclohexanes.

The conformational analysis of acyclic organic molecules has been explored less systematically than that of alicyclic compounds, in part because the former isomerism has proved the more difficult to investigate experimentally.[2,3] In consequence, most data dealing with the general problem of the influence of substituents on conformational equilibra, and with the particular problem of the proper relative "sizes" to be assigned to common organic groups, have been obtained by examination of the influence of these groups on the conformations of cyclohexane rings. It is not presently clear to what extent these data are applicable to other types of conformational problems.

Nuclear magnetic resonance spectroscopy provides an attractive alternative to the experimentally difficult infrared spectroscopic techniques which have been commonly employed in acyclic conformational analysis. In favorable cases, it has proved possible to determine the relative populations of rotational conformers in solution directly, by examining the sample at temperatures sufficiently low to slow the rate of conformational interconversion to less than the value required to average the resonances due to the separate conformers.[4] However, even for compounds with which such low-temperature studies are impractical, examination of the magnitudes and temperature dependence of vicinal spin–spin coupling constants may provide an indirect method of examining the populations of rotational conformers in solution.[5,6] The work reported in this paper is concerned with the conformational analysis of derivatives of 3,3-dimethylbutane, using these indirect techniques.

Methods and Results

Derivatives of 3,3-dimethylbutane substituted at the 1 position exist in solution as a rapidly interconverting mixture of one *trans* and two *gauche* conformers around the C_1–C_2 bond (I, II, III). The nmr spectra of the
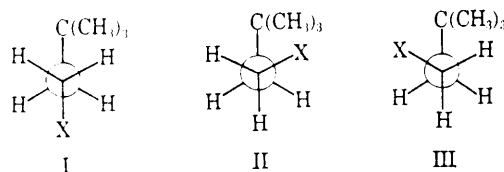
methylene protons in these compounds is not complicated by coupling with the protons of the *t*-butyl group. In the absence of coupling to nuclei in the substituent group X, the methylene protons can be treated as AA'XX' or A_2X_2 spin systems, and their spectra described using a maximum of four coupling constants: two vicinal coupling constants J and J', and two geminal coupling constants J_A and J_X.[7] Examination of the vicinal coupling constants provides a method of investigating the populations of I, II, and III.

The magnitude of J or J' in a 1,2-disubstituted ethane is determined primarily by the corresponding $HCCH$ dihedral angle, and is in consequence dependent on the relative populations of the *trans* and *gauche* conformations.[3] Abraham and Bernstein have shown that if

$$J - J' < [2\Delta\nu_1 (J_A - J_X)]^{1/2} \tag{1}$$

the spectrum of the methylene protons will appear as an A_2X_2 spectrum ($\Delta\nu_1$ is the width at half-height of the component lines).[9] If $J - J'$ is greater than the quantity given in eq 1, the spectrum of the methylene protons will be an AA'XX' spectrum, and analysis of the spectrum may yield values for each of the coupling constants. Unfortunately, the electronegativity and polarizability of substituents, and structural features of the molecule other than the $HCCH$ dihedral angle, influence these coupling constants in a manner which is difficult to predict quantitatively.[3] As a result of this uncertainty, the relative magnitudes of the vicinal coupling constants cannot be relied on in the absence of other information to provide an accurate measure of conformer populations. However, examination

(1) This research was supported by the National Science Foundation through Grant No. GP-2018, and through its undergraduate research participation program. Calculations were carried out in part at the Massachusetts Institute of Technology Computation Center, Cambridge, Mass.

(2) See, for example, S. Mizushima, "Structure of Molecules and Internal Rotation," Academic Press Inc., New York, N. Y., 1954; N. Sheppard, *Advan. Spectry.*, 1, 288 (1959). The extinction coefficients for vibrational absorption bands in infrared studies have proved particularly difficult to determine accurately in solution: A. W. Baker, H. O. Kerlinger, and A. T. Shulgin, *Spectrochim. Acta*, 20, 1467 (1964).

(3) E. L. Eliel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience Publishers, Inc., New York, N. Y., 1965.

(4) R. A. Newmark and C. H. Sederholm, *J. Chem. Phys.*, 43, 602 (1965), provide a careful demonstration of this technique.

(5) H. S. Gutowsky, G. G. Belford, and P. E. McMahon, *ibid.*, 36, 3353 (1962).

(6) N. Sheppard and J. J. Turner, *Proc. Roy. Soc.* (London), A252, 506 (1959).

(7) The nomenclature used is that employed by Pople, *et al.*, and by Roberts: J. A. Pople, W. G. Schneider, and H. J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw-Hill Book Co., Inc., New York, N. Y., 1959, Chapter 6; J. D. Roberts, "An Introduction to the Analysis of Spin-Spin Splitting in High Resolution Nuclear Magnetic Resonance Spectra," W. A. Benjamin, Inc., New York, N. Y., 1962, Chapter 4.

(8) For a recent review, see: M. Barfield and D. M. Grant, *Advan. Magnetic Resonance*, 1, 149 (1965); M. Karplus, *J. Am. Chem. Soc.*, 85, 2870 (1963). For proton–fluorine couplings, the issue is less clear: R. J. Abraham and L. Cavalli, *Mol. Phys.*, 9, 671 (1965).

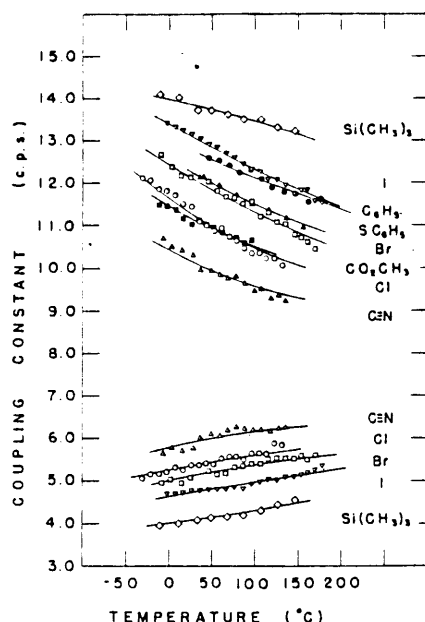(9) R. J. Abraham and H. J. Bernstein, *Can. J. Chem.*, 39, 216 (1961).

Figure 1. Temperature dependence of the vicinal coupling constants of 1-substituted derivatives of 3,3-dimethylbutane. The solid curves are the theoretical temperature dependences, calculated using the parameters in Table I. The upper set of curves represent values for J, the lower set J'.

of the *temperature dependence* of the vicinal coupling constants does provide a direct method of determining the position of rotational conformational equilibria.[5,6]

The coupling constants J and J' are averages over vicinal couplings in each of the rotational conformers I, II, and III. In theory, the *gauche* and *trans* coupling constants in each of these conformers might be different. We will make the approximation that only three different coupling constants are necessary to describe all of the spin–spin interactions in the three conformers: one *trans* coupling constant J_t, which is the same in both *gauche* and *trans* conformers; and two *gauche* coupling constants J_g^g and J_g^t which describe the coupling between *gauche* protons when the substituent X on C_1 is *gauche* or *trans*, respectively, to the proton on C_2 (IV, V). The justification for the use of only

IV   V
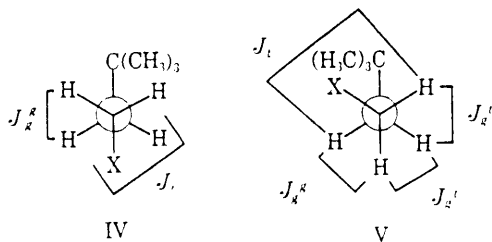
three limiting coupling constants follows from the clear experimental[5,10] and theoretical[8] evidence that the influence of the substituent X on the magnitude of the vicinal proton–proton coupling constant in an *XCHCH* fragment also depends upon the *XCCH* dihedral angle. Since this angle is approximately 60° for both β protons in the *trans* conformer I and for one of the β protons in conformers II and III, but approximately 180° for the remaining β proton in conformers II and III, at least two different limiting *gauche* coupling

(10) K. L. Williamson, *J. Am. Chem. Soc.*, **85**, 516 (1963); K. L. Williamson, C. A. Lanford, and C. R. Nicholson, *ibid.*, **86**, 762 (1964), and references therein.

constants are needed to describe the coupling in the individual conformers. The assumption that two *gauche* and one *trans* coupling constants are sufficient to describe these couplings is equivalent to saying that the *XCCH* dihedral angle is the most important parameter in determining the influence of X on the magnitude of the vicinal coupling constants.

With these approximations, the observed coupling constants J and J' can be expressed in terms of the coupling constants of the individual rotational conformers J_t, J_g^g, and J_g^t.[11]

$$J = (1 - 2n_{II})J_t + n_{II}(J_g^g + J_g^t) \qquad (2)$$

$$J' = (1 - 2n_{II})J_g^g + n_{II}(J_t + J_g^t) \qquad (3)$$

$$n_{II} = \exp(-\Delta E/RT)/[1 + 2\exp(-\Delta E/RT)] \qquad (4)$$

Here n_{II} is the mole fraction of *one* of the *gauche* conformers, and ΔE is the difference in energy between *gauche* and *trans* conformers. Equation 4 assumes that $E_{gauche} > E_{trans}$.

Explicit values for each of the four parameters in these equations can be obtained from the experimentally determined temperature dependence of the vicinal coupling constants by a least-squares procedure. in which the function φ

$$\varphi = \sum_{T_i} (J - J_{calcd})^2 + (J' - J'_{calcd})^2 \qquad (5)$$

is minimized by systematic variation of the parameters ΔE, J_t, J_g^g, and J_g^t. Here, J and J' are respectively the larger and smaller of the observed vicinal coupling constants at each measured temperature T_i, and J_{calcd} and J'_{calcd} are the corresponding values calculated using eq 2, 3, and 4 with trial values for the unknown parameters. Our calculations (carried out using an iterative FORTRAN II program), made the assumptions that measurements at each temperature T_i carried equal weight, and that the errors in the temperatures could be neglected. The values obtained for J_t, J_g^t, and J_g^g by applying this procedure to the temperature dependence of the vicinal coupling constants of nine derivatives of 3,3-dimethylbutane are shown in Table I. For comparison and for future reference, the results of a similar three-parameter analysis in which J_g^g was assumed equal to J_g^t are included in this table; the single *gauche* coupling constant in the three-parameter analysis was called J_g. Equal values were obtained for ΔE using either the three- or the four-parameter procedures; these values are listed in Table IV, together with values obtained by approximate methods described below. Figure 1 shows the agreement obtained between the observed temperature dependence for the vicinal coupling constants for several of these compounds, and that calculated using the values of ΔE and the coupling constants obtained from the four-parameter analysis.

The probable error in the parameters from the least-squares analysis can be estimated using a procedure suggested by Gutowsky.[5] In this procedure, φ is expanded in Taylor series in the neighborhood of the minimum value φ_0 obtained during the least-squares variation on the parameters.

(11) These equations are modifications of similar equations used by Gutowsky and co-workers.[5]

Table I. Coupling Constants (cps) Obtained from Least-Squares Analyses of the Temperature Dependence of the Methylene Proton Spectra of 1-Substituted Derivatives of 3,3-Dimethylbutane

	Three-parameter calculations		Four-parameter calculations			Huggins electronegativity[a]	N[b]
Substituent	J_t	J_g	J_t	$J_g{}^g$	$J_g{}^t$		
1. $Si(CH_3)_3$	14.3	3.9	14.3 ± 0.3	3.9 ± 0.3	4.7 ± 5.6	1.90	9
2. C_6H_5	13.7	4.2	13.7 ± 0.3	4.2 ± 0.3	4.1 ± 2.2	2.60	11
3. I	14.3	4.1	14.5 ± 0.3	4.3 ± 0.3	1.6 ± 2.1	2.65	20
4. SC_6H_5	14.2	3.7	14.2 ± 0.4	3.7 ± 0.4	3.7 ± 1.6	2.60	8
5. Br	13.8	4.2	14.1 ± 0.3	4.5 ± 0.3	1.8 ± 1.4	2.95	18
6. Cl	14.0	4.0	14.5 ± 0.4	4.4 ± 0.4	1.3 ± 1.2	3.15	19
7. CO_2CH_3	13.8	4.2	13.8 ± 0.4	4.2 ± 0.4	4.2 ± 1.3	2.60	13
8. CO_2H	14.1	3.9	14.1 ± 0.4	3.9 ± 0.4	3.9 ± 1.1	2.60	18
9. CN	13.6	4.2	13.9 ± 0.4	4.5 ± 0.4	2.8 ± 0.9	2.60	15
Average	14.0	4.0	14.1	4.2	3.1		

[a] The values given are for the atom bonded directly to the methylene group. M. L. Huggins. *J. Am. Chem. Soc.*, **75**, 4123 (1953). [b] N is the number of temperatures included in the least-squares analysis.

$$\varphi = \varphi_0 + \left(\frac{\partial\varphi}{\partial\Delta E}\right)(\Delta\Delta E) + \left(\frac{\partial\varphi}{\partial J_t}\right)(\Delta J_t) + \ldots +$$
$$\frac{1}{2}\left(\frac{\partial^2\varphi}{\partial\Delta E^2}\right)(\Delta\Delta E)^2 + \frac{1}{2}\left(\frac{\partial^2\varphi}{\partial J_t^2}\right)(\Delta J_t)^2 + \ldots \quad (6)$$

The first derivatives in this equation, evaluated at φ_0, are zero. Neglecting third- and higher order derivatives, and holding all parameters except J_t constant, one obtains eq 7. Analogous equations are obtained

$$\Delta J_t = [2(\varphi - \varphi_0)/(\partial^2\varphi/\partial J_t^2)]^{1/2} \quad (7)$$

for ΔE, $J_g{}^g$, and $J_g{}^t$. An upper limit on the values allowed φ can be estimated from eq 5 and the experimental uncertainties δJ and $\delta J'$ in the values of the observed coupling constants

$$\varphi \leq \sum_{T_i}(\delta J)^2 + (\delta J')^2 \quad (8)$$

In evaluating eq 8 in this work, we estimated somewhat arbitrarily that the experimental uncertainty in each of the observed vicinal coupling constants was 0.2 cps.

Since φ_0 is known, the probable error ΔJ_t in J_t can then be obtained using eq 7. The second derivatives used in estimating the error in each of the parameters in the four-parameter analysis can be obtained by differentiating eq 2–5.

$$\frac{\partial^2\varphi}{\partial J_t^2} = \frac{\partial^2\varphi}{\partial(J_g{}^g)^2} = \sum_{T_i}(2 - 8n_{II} + 10n_{II}{}^2) \quad (9)$$

$$\frac{\partial^2\varphi}{\partial(J_g{}^t)^2} = \sum_{T_i}4n_{II}{}^2 \quad (10)$$

$$\frac{\partial^2\varphi}{\partial\Delta E^2} = \sum_{T_i}\left\{2\frac{\partial^2 n_{II}}{\partial\Delta E^2}[(J_{calcd} - J)(J_g{}^g + J_g{}^t - 2J_t) + \right.$$
$$(J'_{calcd} - J)(J_t + J_g{}^t - 2J_g{}^g)^2] + 2\left(\frac{\partial n_{II}}{\partial\Delta E}\right)^2[(J_g{}^g +$$
$$\left. J_g{}^t - 2J_t)^2 + (J_t + J_g{}^t - 2J_g{}^g)^2]\right\} \quad (11a)$$

where

$$\frac{\partial^2 n_{II}}{\partial\Delta E^2} = \frac{\exp(-\Delta E/RT) - 4\exp(-3\Delta E/RT)}{R^2T^2[1 + 2\exp(-\Delta E/RT)]^4} \quad (11b)$$

$$\left(\frac{\partial n_{II}}{\partial\Delta E}\right)^2 = \frac{\exp(-2\Delta E/RT)}{R^2T^2[1 + 2\exp(-\Delta E/RT)]^4} \quad (11c)$$

The uncertainties in the parameters obtained from the variable-temperature analysis and given in Table I

and Table IV were estimated using this procedure. Errors are listed as, *e.g.*, $J_t \pm \Delta J_t$. It is worthwhile to point out explicitly that this procedure makes no attempt to estimate the magnitudes of *systematic* errors incorporated into the variable-temperature analysis.

It is of interest that both J_t and $J_g{}^g$ in Table I appear to be insensitive to the character of the substituent. The total variation observed in these constants is 0.8 cps, and is of the same order of magnitude as their uncertainty. Moreover, the deviations from their average values bear no obvious relation to any property of the substituent. In contrast, $J_g{}^t$ appears to be moderately sensitive to substituent electronegativity, although the probable error in this constant is appreciably larger that that in $J_g{}^g$ or J_t. The total variation in the magnitude of $J_g{}^t$ is comparable with that observed for a corresponding range of substituents in substituted bicyclo[2.2.1]heptenes,[10] although less than that observed for substituted ethylenes.[12]

Approximate Methods. The least-squares analysis of the temperature dependence of the vicinal coupling constants is the most accurate method presently available for obtaining the magnetic and thermodynamic parameters describing the rotational conformers of 1,2-disubstituted ethanes from nmr data. Unfortunately, collection and analysis of accurate variable-temperature data is time consuming. Consequently, two more approximate methods requiring only ambient temperature spectra have been used to obtain approximate values for ΔE for other common organic substituent groups.

The first of these methods was proposed by Snyder and is based on the assumption that the magnitude of a vicinal coupling constant can be related approximately to the corresponding $HCCH$ dihedral angle ϕ by eq 12.[13]

$$J_{vic} = A + B\cos^2\phi \quad (12)$$

The form of this equation is that originally obtained by Karplus,[14] with the additional assumption that only one value of the constant A is required over the range of dihedral angles encountered. With this assumption

(12) C. N. Banwell and N. Sheppard, *Mol. Phys.*, **3**, 351 (1960); *Discussions Faraday Soc.*, **34**, 115 (1962); T. Schaefer, *Can. J. Chem.*, **40**, 1 (1962).
(13) E. I. Snyder, *J. Am. Chem. Soc.*, **88**, 1165 (1966). We wish to thank Dr. Snyder for sending us a copy of this paper prior to its publication.
(14) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

Table II. Chemical Shifts (cps) and Coupling Constants (cps) Obtained from the Ethylene Proton Spectra of 3,3-Dimethylbutyl Derivatives at 60.0 Mc/sec and 32°

	Substitutent	J'	J'^a	$J_A{}^a$	$J_B{}^a$	$\Delta\nu^b$	Solvent	Solvent concn. %
1.	AlR$_2$·n(Et$_2$O)^c	14.2	3.9	13.4	13.4	−87.0	(CH$_3$CH$_2$)$_2$O	1
2.	MgR·n(Et$_2$O)^c	14.2	4.2	13.4	12.5	−124	(CH$_3$CH$_2$)$_2$O	1–6
3.	Si(CH$_3$)$_3$	13.9	4.0	13.9	13.9	−44.7	CCl$_4$	20
4.	ZnR·n(Et$_2$O)^c	13.3	4.7	13.6	12.4	80.2	(CH$_3$CH$_2$)$_2$O	1
5.	I	13.0	4.8	13.6	9.2	72.2	CCl$_4$	20
6.	P(C$_6$H$_5$)$_2$	13.0	4.3	13.3	13.3	40.9	C$_6$H$_6$	20
7.	C$_6$H$_5$	12.9	4.7	13.6	13.3	62.0	CCl$_4$	20
8.	NH(CH$_3$)$_2$$^+SO_3H^-$	12.9	4.7	(13.7	13.7)^d	88.5	D$_2$O	20
9.	NH$_3$$^+SO_3H^-$	12.7	4.8	(13.3	13.3)^d	82.1	D$_2$O	20
10.	CD$_2$OH	12.3	4.6	14.0	14.0	15.5	CCl$_4$	20
11.	SCH$_3$	12.3	4.8	13.6	12.4	54.6	CCl$_4$	20
12.	SCN	12.2	4.7	13.4	12.2	67.2	CCl$_4$	20
13.	SC$_6$H$_5$	12.1	4.7	13.4	12.3	76.0	CCl$_4$	20
14.	Br	12.1	5.1	14.0	9.9	86.7	CCl$_4$	20
15.	CONH$_2$	11.9	5.1	13.6	14.6	38.6	CDCl$_3$	10
16.	HgR^c	11.8	5.1	13.6	12.5	34.2	(CH$_3$CH$_2$)$_2$O	5–15
17.	Phthalimide	11.6	5.2	13.4	13.3	122.1	CDCl$_3$	10
18.	HgCl	11.6	5.3	(12.8	10.4)^d	17.6	CDCl$_3$	10
19.	CO$_2$$^-K^+$	11.6	5.3	13.9	13.9	39.7	D$_2$O	20
20.	Cl	11.3	5.4	13.6	10.5	104.1	CCl$_4$	20
21.	CO$_2$H	11.2	5.4	13.8	15.6	42.4	CCl$_4$	20
22.	NH$_2$	11.1	5.1	13.1	11.7	78.7	C$_6$H$_6$	20
23.	COCH$_3$	11.1	5.2	13.9	16.4	55.0	CCl$_4$	20
24.	CO$_2$CH$_3$	11.0	5.6	13.7	15.2	40.3	CCl$_4$	20
25.	COCl	10.9	5.4	13.7	16.5	70.5	CCl$_4$	20
26.	NHCHO	10.8	5.4	(12.6	12.6)^d	103.5	CCl$_4$	20
27.	N(CH$_3$)$_2$	10.7	5.0	(13.0	11.6)^d	90.7	C$_6$H$_6$	20
28.	CN	10.2	5.8	13.8	17.0	40.1	CCl$_4$	20
29.	OH	9.5	5.8	13.5	10.3	128.7	CCl$_4$	20
30.	OC$_6$H$_5$	7.2	7.2	e	e	134	CCl$_4$	20
31.	F	6.5	6.5	e	e	172	CCl$_4$	20

^{a} The geminal and vicinal coupling constants were assumed to have opposite signs. The uncertainty in the vicinal coupling is estimated to be no larger than ±0.2 cps; the uncertainty in the geminal coupling constants is larger. ^{b} A positive sign for $\Delta\nu$ implies that the (CH$_3$)$_3$-CCH$_2$ resonance occurred at higher field than the CH$_2$X resonance. ^{c} M. Witanowsky and J. D. Roberts, *J. Am. Chem. Soc.*, **88**, 737 (1966). R is 3,3-dimethylbutyl. ^{d} Obtained using assumptions described in the Experimental Section. $J_A - J_B$ is meaningful for these; the absolute magnitudes are only approximate. ^{e} Geminal coupling constants cannot be obtained by direct analysis of A$_2$X$_2$ spectra.

it is easily shown that[13]

$$\Delta E = RT \ln 2n_{\mathrm{I}}/(1 - n_{\mathrm{I}}) \qquad (13)$$

where

$$n_{\mathrm{I}} = \frac{0.5r[\cos^2(120 - \phi) + \cos^2(120 + \phi) - \cos^2\phi]}{1 - \cos^2\phi - r\{0.25 - 0.5[\cos^2(120 - \phi) + \cos^2(120 + \phi)]\}} +$$

$$\frac{A(r - 1)}{B(1 - \cos^2\phi - r\{0.25 - 0.5[\cos^2(120 - \phi) + \cos^2(120 + \phi)]\})} \qquad (14)$$

and $r = J/J'$. Here ϕ is defined as the dihedral angle between the *t*-butyl group and the substituent in a *gauche* conformation, and n_{I} is the mole fraction of the *trans* conformer I.

The value of A/B used in eq 14 in this work was 0.05, and was estimated by inserting the average values of J_t and J_g obtained from the three-parameter least-squares data in Table I into eq 12, with appropriate values for the dihedral angle.

$$J_t = A + B \cos^2 180 = 14.0$$

$$J_g = A + B \cos^2 60° = 4.0$$

The value for r was obtained for each substituent by analysis of the ambient-temperature spectra using conventional methods; chemical shifts and coupling constants for the derivatives of 3,3-dimethylbutane examined are listed in Table II. The spectra of most of

these compounds were of the AA'XX' type, and analysis yielded all four coupling constants. These coupling constants appear to be relatively insensitive to solvent and concentration. For example, the results of analysis of the spectrum of 3,3-dimethylbutyl iodide in several solvents are given in Table III. The variation in the coupling constants reported in this table is typical of that observed for other of the compounds in Table II on changing solvent and concentration, and serves to indicate the reproducibility of the spectra. In all of these spectra, the geminal coupling constant J_A is assigned to the methylene group directly bonded to the *t*-butyl group, since its magnitude is essentially independent of the substituent.

The values obtained for ΔE by setting ϕ in eq 14 equal to 65° and using the coupling constants in Table II are listed in Table IV.[15] The agreement between the values of ΔE obtained by this approximate method and the values obtained by the least-squares analyses is good.

The probable errors in the parameters obtained using this method have been discussed in detail by Snyder.[13]

(15) The dihedral angle, ϕ, in conformers II and III should probably be greater than 60°, since nonbonded repulsions between the *t*-butyl group and the substituent in the *gauche* conformations should distort this conformation from a perfect staggered geometry. However, the proper value for ϕ should almost certainly vary with the bulk of the substituent. The value $\phi = 65°$ was chosen somewhat arbitrarily since it seemed to give values for ΔE in good agreement with those obtained from the temperature-dependence studies. See also ref 13 for a discussion of this point.

For $r \sim 2.0$ and $\phi \sim 60°$, ΔE is estimated to change by 0.01 kcal per degree of change in ϕ. Similarly, for $\phi \sim 65°$ and $r \sim 2.5$, a change in r of 0.05 (corresponding approximately to a variation of J' by 0.1 cps) changes the estimated magnitude of ΔE by 0.03 kcal/mole.

hese estimates suggest that the magnitude of the uncertainty in the values of ΔE obtained using eq 13 and 14 (Table IV) is approximately 20%.

Despite the agreement between the values of ΔE derived from the least-squares analysis and those obtained from eq 13 and 14, it seemed advisable to have an alternative method of estimating ΔE from the room temperature coupling constants, which avoided some of the assumptions made by the latter procedure.[16] The approach used was an empirical one which took advantage of the previously demonstrated insensitivity of J_t, J_g^s, and J_g^t to the nature of the substituent. The assumption was made that the *average* values of these limiting coupling constants (Table I) would provide satisfactory approximations to the coupling constants in individual rotamers for all of the substituents listed in Table II. This assumption is certainly reasonable for J_t and J_g^s, both of which seem to be essentially independent of the substituent; a small error (estimated below) is probably introduced into ΔE by making this assumption for J_g^t. With this assumption, a curve relating ΔE to J and J' could be calculated easily using eq 2–4 (Figure 2, curve B). Estimates of ΔE could then be obtained for each of the compounds in Table II by comparing the observed values of J and J' separately with this curve. Usually the value of ΔE estimated from J differed from that estimated from J' by 0.1) 0.5 kcal/mole; each value of ΔE listed in the second .olumn of Table IV is an average of the estimates from the individual coupling constants. These estimates agree well with those obtained using the two methods described previously.

In order to estimate the influence of J_g^t on the value of ΔE determined using Figure 2, curves similar to that calculated for the *average* values of J_t, J_g^s, and J_g^t were calculated using the *extreme* values obtained for J_g^t from the least-squares analysis (Figure 2, curves A and C). These curves indicate that for values of ΔE ranging from approximately 0.7 kcal/mole to 2.0 kcal/mole, a change of 3.4 cps in the value of J_g^t used in constructing curve B would change the values of ΔE estimated using this procedure by approximately 0.2 kcal/mole.

Discussion

Observation of an AA'XX' type spectrum for the methylene protons of the substituted 3,3-dimethylbutanes listed in Table II establishes immediately that their most stable conformation is the one having the *t*-butyl group and the substituent *trans*. A favored *gauche* conformation would necessarily result either in an A_2X_2 spectrum (if conformational interconversion were rapid on the nmr time scale) or a more complicated ABXY spectrum (if interconversion were slow).

A number of factors have significant bearing on the accuracy of the energy differences between the *trans* and *gauche* conformations estimated using the methods

(16) In particular, eq 12 is probably inferior to $J_{vic} = A \cos \phi + B \cos^2 \phi$ as the functional relation between J and ϕ. See M. Barfield, *J. Chem. Phys.*, **44**, 1836 (1966), and ref 8.
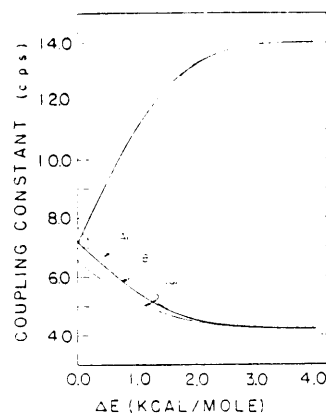

Figure 2. The dependence of J (upper curves) and J' (lower curves) on ΔE, calculated using eq 2–4. The values used for J_t and J_g^s were 14.1 and 4.2 cps, respectively. The values for J_g^t were curve A, 4.7 cps; curve B, 3.1 cps; curve C, 1.3 cps.

discussed above. Of these methods, analysis of the temperature dependence of the vicinal coupling constants is undoubtedly the most accurate. This method requires no important assumptions concerning the effect of substituent electronegativity on coupling constants, or concerning the form of the function relating the coupling constants in the individual rotational conformers to the observed averaged coupling constants. However, it does assume that the contributions of temperature-dependent amplitudes of vibration to the observed temperature dependence of the vicinal coupling constants can be neglected, and that the bond angles and bond lengths in the individual conformers do not change significantly with temperature. Further, it depends upon the accurate measurement of small changes in the observed coupling constants. In order to estimate the reliability of this method, it is important to consider the magnitudes of some of the other effects which might contribute to the temperature dependence of the vicinal coupling constants.

Gutowsky and co-workers have estimated theoretically the magnitudes to be expected from temperature-dependent vibrational contributions to both vicinal[17] and geminal[18] proton–proton coupling constants. With several assumptions concerning the form of the torsional potential function $V(\phi)$, these workers concluded that the vicinal coupling constant J_t in an aliphatic molecule would increase by approximately 0.3 cps on increasing the temperature from 200 to 400°K as a result of increasing amplitude of the torsional motion, and that J_g would decrease over this temperature range by a corresponding amount. These contributions to the *observed* coupling constants are expected to cancel exactly when $V(\phi)$ has threefold symmetry, and experimental measurements of torsional contributions to proton–proton coupling constants in several substituted ethanes have confirmed this expectation.[17,19] In the less symmetrical molecules discussed

(17) J. C. Schug, P. E. McMahon, and H. S. Gutowsky, *J. Chem. Phys.*, **33**, 843 (1960). The HCCH dihedral angle dependence of J was assumed to follow eq 12.
(18) H. S. Gutowsky, V. D. Mochel, and B. G. Somers, *ibid.*, **36**, 1153 (1962).
(19) J. G. Powles and J. H. Strange, *Discussions Faraday Soc.*, **34**, 30 (1962). A small torsional temperature dependence has been observed for fluorine–fluorine couplings. W. S. Brey, Jr., and K. C. Ramey, *J. Chem. Phys.*, **39**, 844 (1963). See also J. Jonas and H. S. Gutowsky, *ibid.*, **42**, 140 (1965).

in this paper, cancellation of the torsional contributions to J_t and J_g is expected to be incomplete. Nonetheless, the calculated dependence of J_t and J_g on temperature is sufficiently small that torsional contributions to the temperature dependence of the vicinal coupling constants can probably be ignored.

It is difficult to estimate the importance of changes with temperature of mean bond lengths or angles other than the torsional angle ϕ. However, it is interesting to note in this connection that for each of the compounds listed in Table II, the magnitude of the observed geminal coupling constants increased by 0.0 to 0.4 cps on increasing the temperature 100°. A temperature dependence of this magnitude is larger that that predicted from estimates of the corresponding increase in the amplitude of the H–C–H bending vibrations,[18] and might reflect changes in molecular geometry which would also influence the vicinal coupling constants. However, the observed variation may also be connected with a difference in the effect of the substituents on the geminal coupling constants in the *gauche* and *trans* conformers,[20] or with temperature-dependent changes in bulk properties of the solution. The data in Table III suggest a similar and probably real sensitivity of J_A to changes in the solvent;[21] the solvent variation of this coupling constant is not accompanied by similar variation in J_B, J, or J'.

Table III. Solvent Dependence of the Coupling Constants (cps) and Chemical Shift (cps) for 3,3-Dimethylbutyl Iodide[a]

	Solvent	J[b]	J'[b]	J_A[b]	J_B[b]	$\Delta\nu$
1.	Cyclohexane	13.0₀	4.7₆	13.6₃	9.1₅	76.6
2.	Carbon tetra-chloride	12.9₉	4.8₀	13.6₀	9.1₇	72.2
3.	3,3-Dimethylbutyl iodide	13.0₅	4.7₉	13.5₅	9.1₂	73
4.	Carbon disulfide	12.9₅	4.7₉	13.5₂	9.1₄	72.4
5.	Chloroform	13.0₃	4.7₉	13.5₀	9.1₇	74.2
6.	Benzene	13.0₁	4.7₄	13.5₀	9.1₇	49.4
7.	Acetic acid	12.9₂	4.8₀	13.4₇	9.1₅	76.3
8.	Acetone	12.9₉	4.8₁	13.4₃	9.2₀	78.8
9.	Nitrobenzene	12.9₃	4.7₃	13.3₆	9.1₄	76.4

[a] All solutions were approximately 10% 3,3-dimethylbutyl iodide by volume. [b] Geminal and vicinal coupling constants are assumed to have opposite sign.

Two observations concerning the magnitudes of J_t, $J_g{}^g$, and $J_g{}^t$ obtained from the least-squares procedure indicate that the geometry and bonding in the derivatives of 3,3-dimethylbutane examined in this study is unexceptional, and consequently that coupling constants and conformational energies obtained in these compounds can legitimately be compared with those obtained in other substituted ethanes. First, the values obtained for J_t and $J_g{}^g$ appear to be approximately the same for each of the compounds examined (Table I). Moreover, empirical functions describing the relation between the magnitude of a vicinal coupling constant and its corresponding dihedral angle, in molecules of

known geometry, predict values for J_t and J_g in good agreement with those observed.[22] These observations suggest that the geometry of the carbon framework of 3,3-dimethylbutane is not appreciably distorted by the introduction of large substituent groups such as phenyl and trimethylsilyl at C_1. Second, the relation observed between $J_g{}^t$ and the electronegativity of the substituent is in qualitative accord with that which has been thoroughly established in molecules of known geometry.[3,12,24,25] If changing the substituent attached to the 3,3-dimethylbutyl grouping resulted in important changes in the molecular geometry of the individual *gauche* and *trans* conformers, these changes might have been expected to produce more pronounced deviations in the relation between $J_g{}^t$ and electronegativity than those observed.

On the basis of these considerations, it seems reasonable to accept the values of ΔE obtained using the least-squares analyses as meaningful estimates of the energy difference between *trans* and *gauche* conformations of substituted 3,3-dimethylbutanes. Moreover, both the similarity between the values of J_t and $J_g{}^g$ obtained with different substituents, and the recognizable dependence of $J_g{}^t$ on electronegativity, indicate that the four-parameter analysis provides an accurate estimate of the coupling constants in the *gauche* and *trans* conformations of these molecules. The remarkable insensitivity of these coupling constants to substituent effects lends support to the usefulness of the two approximate procedures used to obtain estimates of ΔE for those compounds whose spectral temperature dependence was not explicitly examined, since important assumptions in both of these procedures required the neglect of substituent effects of this type. The agreement between these approximate values of ΔE and those from the least-squares analysis further supports the reliability of the approximate values.

It is of some importance to the study of conformational analysis in acyclic molecules that the order of "size" of the groups established by these methods shows significant differences from that determined by examination of their relative order of preference for the equatorial position on a cyclohexane ring. Figure 3 indi-

(20) J. A. Pople and A. A. Bothner-By, *J. Chem. Phys.*, **42**, 1339 (1965), provide a general discussion of substituent effects on geminal coupling constants.

(21) Geminal coupling constants have been observed to vary with solvent even in molecules of rigid geometry. See, for example, V. S. Watts, G. S. Reddy, and J. H. Goldstein, *J. Mol. Spectry.*, **11**, 325 (1963); K. A. McLauchlan, L. W. Reeves, and T. Schaefer, *Can. J. Chem.*, **44**, 1473 (1966).

(22) For example, Bothner-By has suggested the equation J_{vic} (cps) $= 7 - \cos\phi + 5\cos 2\phi$ as describing the angular dependence of vicinal coupling constants.[23] This equation predicts $J_t = 13$ ($\phi = 180°$) and $J_g = 4$ cps ($\phi = 60°$), in reasonable agreement with the average values observed in Table I.

(23) A. A. Bothner-By in ref 8a.

(24) In this series of compounds as well as others,[4,12] it appears that the electronegativity of the atom bonded directly to the ethylenic group is most important in determing the magnitude of J_{vic}. See, for example, R. J. Abraham and K. G. R. Pachler, *Mol. Phys.*, **7**, 165 (1964).

(25) Although several different electronegativity scales have been used in discussing substituent effects on vicinal coupling constants, the most generally useful are those of Huggins and Cavanaugh and Dailey.[26] These scales both differ in some respects from other well-known measures of inductive substituent effects such as σ^*[27] or σ_I.[28] Although the relation between these scales is presently uncertain,[29] it seems clear that vicinal coupling constants in a variety of molecules show qualitatively similar sensitivity to substituent effects.

(26) J. R. Cavanaugh and B. P. Dailey, *J. Chem. Phys.*, **34**, 1099 (1961).

(27) R. W. Taft, Jr., in "Steric Effects in Organic Chemistry," M. Newman, Ed., John Wiley and Sons, Inc., New York, N. Y., 1956, Chapter 13.

(28) R. W. Taft, Jr., and I. C. Lewis, *J. Am. Chem. Soc.*, **80**, 2436 (1958).

(29) For discussions of the general problem of electronegativity, see J. Hinze, M. A. Whitehead, and H. H. Jaffé, *ibid.*, **85**, 148 (1963); H. A. Bent, *Chem. Rev.*, **61**, 275 (1961).

Table IV. Energy Difference ΔE (kcal/mole) between *gauche* and *trans* Conformers of 1-Substituted-3,3-Dimethylbutanes

	Substituent	ΔE^a	ΔE^b	ΔE^c
1.	$AlR_2 \cdot n(Et_2O)^d$	$(2.4)^e$	...	
2.	$MgR \cdot n(Et_2O)^d$	$(2.2)^e$	...	
3.	$Si(CH_3)_3$	$(3.7)^e$	...	2.33 ± 0.88
4.	$ZnR \cdot n(Et_2O)^d$	1.7	1.8	
5.	I	1.6_1	1.6	1.60 ± 0.07
6.	$P(C_6H_5)_2$	1.9_9	...	
7.	C_6H_5	1.6_5	1.7	1.70 ± 0.09
8.	$NH(CH_3)_2^+-$ SO_3H^-	1.6_5	1.7	
9.	$NH_3^+SO_3H^-$	1.5_5	1.6	
10.	CD_2OH	1.5_7	1.6	
11.	SCH_3	1.4_7	1.5	
12.	SCN	1.5_0	1.5	
13.	SC_6H_5	1.4_8	1.5	1.30 ± 0.08
14.	Br	1.3_1	1.3	1.30 ± 0.07
15.	$CONH_2$	1.2_8	1.2	
16.	HgR^d	1.2_6	1.2	
17.	Phthalimide	1.1_9	1.2	
18.	$HgCl$	1.1_6	1.1	
19.	$CO_2^-K^-$	1.1_6	1.1	
20.	Cl	1.0_8	1.0	0.99 ± 0.06
21.	NH_2	1.1_5	1.1	
22.	CO_2H	1.0_7	1.0	0.99 ± 0.08
23.	$COCH_3$	1.1_1	1.1	
24.	CO_2CH_3	0.9_8	0.9	0.99 ± 0.07
25.	$COCl$	1.0_3	1.0	
26.	$NHCHO$	1.0_1	1.0	
27.	$N(CH_3)_2$	1.1_2	1.1	
28.	CN	0.8_3	0.8	0.75 ± 0.07
29.	OH	0.7_3	0.6	
30.	OC_6H_5	<0.6		
31.	$OSO_2C_6H_4$-p-Br	<0.6		
32.	F	<0.6		
33.	H	0.0^f		

a From eq 13 and the coupling constants in Table II. *b* From Figure 2 and Table II. *c* From variable-temperature studies. Probable errors were estimated using eq 7. *d* R is 3,3-dimethylbutyl. *e* Equation 8 did not give a solution in these cases. The values reported are from a value of n_t obtained by truncating eq 14 following the first term, and are very approximate (see ref 13). *f* This value was assumed.
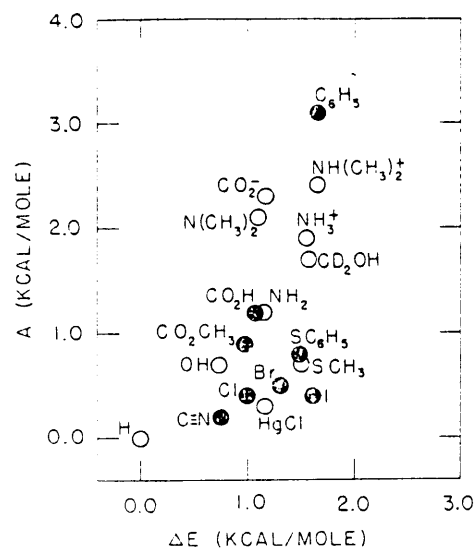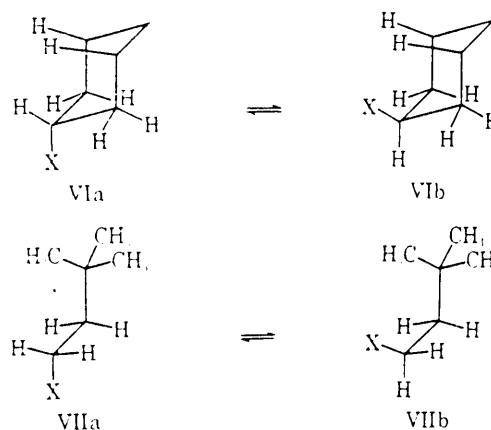

Figure 3. Plot of A vs. ΔE. Filled circles indicate that ΔE was obtained from temperature-dependence studies.

cantly relieved for substituents with long C–X bonds in 1-substituted derivatives of 3,3-dimethylbutane.

cates the low correlation observed between the values of ΔE in Table IV and the corresponding A values.[30]

Two features of this plot suggest possible reasons for the difference in the relative sizes of groups in the environments provided by the 3,3-dimethylbutyl and cyclohexyl moieties. First, iodine, bromine, and mercury-(II) atoms appear anomalously small when attached to cyclohexane; their apparent relative sizes when attached to a 3,3-dimethylbutyl group are more nearly commensurate with their large van der Waals radii. The former observation is believed to be a consequence of the fact that these groups form bonds to carbon of sufficient length that the 1,3-diaxial interactions, which are normally responsible for producing a preference for the equatorial conformation, are less than those encountered with groups forming shorter bonds.[3] The *t*-butyl group in derivatives of 3,3-dimethylbutane extends appreciably further parallel to the direction of a *gauche* C–X bond (VIIb) then does the 3-axial C–H bond in the axial conformation of the substituted cyclohexane (VIb); in consequence, the interaction between the substituent X and the *t*-butyl group is not signifi-

A second point of interest in comparing the values of ΔE from Table IV with the corresponding A values is that for most substituents the values of ΔE are smaller than might have been anticipated from examination of the relative geometry of 3,3-dimethylbutyl and cyclohexyl groups. If one assumes as a first approximation that the bond lengths and bond angles in the acyclic molecule VII are the same as those for the corresponding part of the cyclohexane ring VI, the most important interactions in determining the magnitudes of ΔE and A are respectively the repulsion between the substituent and the closest methyl groups of the *t*-butyl group of VIIb and the 1,3-diaxial interactions in VIb.[31] The van der Waals radius of a methyl group is approximately 2.0 A; that of a hydrogen atom is 1.2 A.[32a]

(31) A better standard of comparison for values of ΔE in Table IV would be provided by the 1,3-diaxial interaction of a methyl group and the substituent on a cyclohexane ring. Unfortunately, too few of these interactions have been investigated to make comparison worthwhile. See ref 3, p 52.

(32) (a) A. Bondi, *J. Phys. Chem.*, **68**, 441 (1964). The radii of CD_2-OH, NH_3^-, and $NH(CH_3)_2^-$ are undoubtedly anisotropic; in Figure 4 all are assumed to have a *minimum* radius equal to that of a methylene group. The organometallic compounds listed in Table IV are not included in this plot, because their apparent sizes are probably due to one or more tightly bound solvent molecules, or to aggregation. (b) This difference is partially compensated for by the fact that there are two 1,3-diaxial interactions in VIIIb and only one methyl-substituent interaction in VIIb.
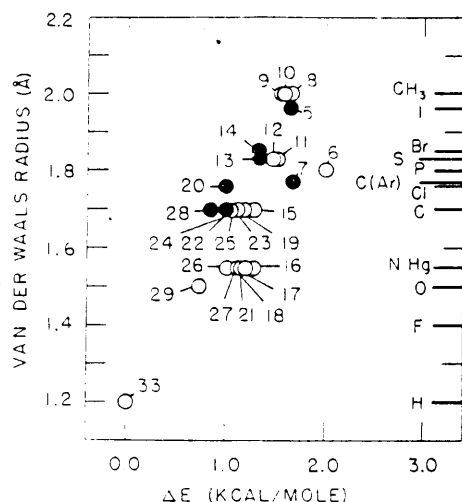
(30) For the sake of comparison with the corresponding A values, ΔE is assumed equal for CD_2OH and CH_3 groups, and for $HgCl$ and $HgBr$ groups. Other values are the "recommended" values given by Eliel, *et al.*, ref 3, pp 44 and 436ff.

Figure 4. Plot of ΔE vs. the van der Waals radius of the atom in the substituent which is directly bonded to the 3,3-dimethylbutyl group. C(Ar) is the van der Waals radius of a carbon atom in an aromatic ring. The numbers refer to Table IV. Filled circles indicate that ΔE was obtained from temperature-dependence studies.

Since the repulsive part of the van der Waals curve rises very steeply for short distances between atoms, the *gauche* conformer VIIb with its short methyl-substituent distance might have been expected to have higher energy relative to the *trans* conformer VIIa than the corresponding axial conformer VIb relative of the equatorial form VIa.[2b] It is clear from Figure 3 that this situation does not hold. In fact, large substituents (*e.g.*, phenyl, trimethylsilyl, dimethylammonium) appear to be relatively smaller attached to a 3,3-dimethylbutyl group than to a cyclohexyl group. It seems possible to rationalize this observation qualitatively by assuming that the alkane represents a less rigid environment than the cyclohexane ring, and that certain distortions of bond angles are possible in VIIb which are not possible in VIb. In particular, the acyclic molecules can relieve nonbonded interactions by rotation around carbon–carbon bonds; corresponding torsional motions in the cyclohexane are of relatively higher energy. Partial rotation around the C_1-C_2 bond of VIIb would relieve a part of the interaction between substituent and the *t*-butyl group; similarly it might be possible to decrease this interaction further by adjusting the torsional angle around the C_2-C_3 bond. Corresponding motions in cyclohexane can be accomplished only at the expense of major deformation of the molecular geometry.[33]

The idea that the acyclic compounds are sufficiently flexible to minimize the interaction between the *t*-butyl group and the substituent by low-energy deformations from the staggered ethane geometry, without having these distortions produce more important strains in other parts of the molecule, is supported by Figure 4. This Figure is a plot of ΔE vs. the van der Waals radius[12] for the substituent atom bonded directly to the 3,3-dimethylbutyl group. It is of interest here that the size of each group appears to be determined almost entirely by this directly bonded atom; atoms further removed seem to have little influence on

the size of the group. For example, amine, dimethylamine, and phthalimide substituents all appear to be approximately the same size. These observations suggest that the *smallest* dimension of the substituent in these molecules determines the magnitude of its interaction with the *t*-butyl group. A similar but less conspicuous effect has been observed in conformational analysis of substituted cyclohexane rings, where, for example, the *A* value for a dimethylamine group is approximately 0.9 kcal/mole greater than that for amine group.

Experimental Section

Spectra were taken at 60 Mc/sec on a Varian A-60 spectrometer, equipped with a V-6040 variable-temperature probe and controller. Sweep widths were calibrated for each spectrum using a Krohn-Hite Model 450 push-button oscillator. The frequency output of this oscillator was checked periodically using a Hewlett-Packard Model 524 electronic counter. Deuterium decoupling experiments were carried out using an NMR Specialties Model HD-60A decoupler. Calibration of the temperature controller was accomplished using a methanol or ethylene glycol thermometer. These calibrations were checked occasionally using a copper–constantan thermocouple inserted directly into a solution in an nmr tube correctly positioned in the probe; temperatures measured using either technique differed by a maximum of $\pm 3^\circ$ at the extremes of temperature employed.

Melting points and boiling points are uncorrected. Infrared spectra were obtained with Perkin-Elmer Model 237 or 337 grating spectrophotometers. Microanalyses were performed by Dr. S. M. Nagy and associates or by the Midwest Microlab, Inc.

Analyses of spectra to obtain coupling constants and chemical shifts were carried out using the iterative program MARIP,[1] following initial analysis using approximate procedures.[35] Line frequencies used for analysis were normally those obtained by averaging corresponding frequencies from three upfield and three downfield sweeps. No effort was made to correct for the effect of overlap on the apparent separation of peaks close to one another. Occasionally, the intensity of the weak inner lines of the symmetric quartets of the AA'XX' spectra examined were of such low intensity that these lines could not be detected. In these cases, analyses were carried out either by the approximate procedure described by Servis and Roberts,[36] or by a procedure which consisted of measuring the quantity $J_A - J_B$ directly from the spectrum,[35] assuming that $J_A = 13.5$ cps, and *assigning* calculated frequencies to the $2S_{-1} \rightarrow 3S_0'$ and $3S_0' \rightarrow 2S_1$ transitions. MARIP was then used to obtain values for all the coupling constants. In general, the values of J and J' were not very sensitive to the values assumed for J_A and J_B. Values of J_A and J_B obtained using either of these approximate procedures are enclosed in parentheses in Table II.

3,3-Dimethylbutyltrimethylsilane. Trimethylchlorosilane (10.8 g, 0.1 mole) was heated with a solution of 3,3-dimethylbutylmagnesium chloride (prepared from 12 g of 3,3-dimethylbutyl chloride and 2.4 g of magnesium in 50 ml of freshly distilled tetrahydrofuran) in a sealed tube at 80° for 12 hr. The tube was cooled, opened, and the contents were poured onto ice. The resulting mixture was extracted twice with 100-ml portions of pentane. The combined organic layer was washed once with 20 ml of concentrated sulfuric acid, once with water, dried (MgSO$_4$), concentrated, and distilled, giving 9 g (55%) of product, bp 140–145°; infrared absorption (film) at 825 and 855 cm^{-1} [Si(CH$_3$)$_3$].

Anal. Calcd for C$_9$H$_{22}$Si: C, 68.26; H, 14.00. Found: C, 68.10; H, 14.05.

3,3-Dimethylbutylmercuric chloride was prepared by reaction between 60 g (0.22 mole) of mercuric chloride and 0.2 mole of 3,3-dimethylbutylmagnesium chloride in 250 ml of ether. After 3 hr at reflux, the solution was cooled and the ether removed under reduced pressure. The residual solid was triturated with water to remove magnesium salts, and the residue recrystallized from ethanol, yielding 47.3 g (68%) of product, mp 132.0–132.4°(lit.[37] mp 133–133.5°).

(33) The torsional flexibility of acyclic molecules has been suggested previously to offer an explanation for the relative energies of *gauche* and *trans* conformations in several simple aliphatic halides. See ref 3, p 17, and ref 13 for examples.

(34) J. D. Swalen and C. A. Reilly, *J. Chem. Phys.*, **37**, 21 (1962).
(35) B. Dischler and G. Englert, *Z. Naturforsch.*, **16a**, 1180 (1961); B. Dischler and W. Maier, *ibid.*, **16a**, 318 (1961); R. C. Hirst and D. M. Grant, *J. Chem. Phys.*, **40**, 1909 (1964).
(36) K. L. Servis and J. D. Roberts, *J. Phys. Chem.*, **67**, 2885 (1963).

3.3-Dimethylbutyl Bromide. A vigorously stirred suspension of 32.1 g (0.1 mole) of 3.3-dimethylbutylmercuric chloride in 100 ml of water was treated at room temperature with a solution of 17 g of bromine and 25 g of potassium bromide in 100 ml of water. After 2 hr of stirring, the suspended solid had been replaced by a heavy oil. This oil was separated from inorganic salts by steam distillation and redistilled, yielding 12.3 g (74%) of product, bp 60–61° (51.8 mm) [lit.[38] bp 58.5–59.0° (51 mm)]; infrared absorption (film) 650 cm⁻¹(C–Br).

3.3-Dimethylbutyl iodide was prepared using an analogous procedure, from a suspension of 15.1 g of 3.3-dimethylbutylmercuric chloride in 100 ml of water and a solution of 13.5 g of iodine and 20.0 g of potassium iodide in 50 ml of water. Before steam distillation, excess iodine was reduced by addition of sodium thiosulfate. Redistillation of the oil collected on steam distillation yielded 5.5 g (55%) of product, bp 71° (38 mm); infrared absorption (film) at 605 cm⁻¹(C–I).

Anal. Calcd for $C_6H_{13}I$: C, 33.98; H, 6.18. Found: C, 34.21; H, 6.05.

3.3-Dimethylbutyl phenyl ether was prepared by refluxing 25 g of 85% aqueous phenol, 16 g of sodium hydroxide, and 21.6 g of 3.3-dimethylbutyl chloride for 40 hr. The reaction mixture was cooled, the organic layer separated, and the aqueous layer extracted twice with diethyl ether. The combined organic layers were washed consecutively with 100-ml portions of water, 5% aqueous ferrous sulfate solution, and water, and then dried (CaSO₄), concentrated, and distilled two times, yielding 10.6 g (33%) of product, bp 125–133° (34.6 mm). The nmr spectrum of the product was consistent with the assigned structure.

3.3-Dimethylbutyl methyl sulfide was prepared by refluxing ~35 g of potassium hydroxide, 25 g of methyl mercaptan, and 35 g of 3.3-dimethylbutyl chloride in 200 ml of 10% aqueous ethanol for 4 days. The reaction mixture was poured into water and extracted three times with pentane. The combined organic layers were dried (MgSO₄) and concentrated, and the product was isolated by distillation. The yield was approximately 25 g, bp 156–158°.

3.3-Dimethylbutyl phenyl sulfide was prepared by an analogous procedure, starting with 50 g (0.5 mole) of thiophenol, 36 g (0.3 mole) of 3.3-dimethylbutyl chloride, and 35 g (0.5 mole) of potassium hydroxide in 300 ml of 10% aqueous ethanol. The product was obtained in approximately 80% yield and had bp 95–96° (1.5 mm).

Anal. Calcd for $C_{12}H_{18}S$: C, 74.17; H, 9.34. Found: C, 73.83; H, 9.50.

3.3-Dimethylbutyl thiocyanate was prepared using the "Organic Syntheses" procedure for isopropyl thiocyanate.[39] The product had bp 76° (8.0 mm), with infrared absorption (film) at 2155 cm⁻¹ (RSC≡N).[40]

Anal. Calcd for $C_7H_{13}NS$: C, 58.70; H, 9.15; N, 9.77. Found: C, 58.93; H, 9.37; N, 9.97.

3.3-Dimethylbutyldiphenylphosphine. Lithium diphenylphosphide was prepared under helium by stirring triphenylphosphine (26 g, 0.1 mole) and lithium (1.4 g, 0.2 g-atom) in 200 ml of anhydrous tetrahydrofuran until the lithium had dissolved.[41] To the resulting dark red solution was added 12 g (0.1 mole) of 3.3-dimethylbutyl chloride. The reaction mixture was refluxed for 4 hr, then hydrolyzed by cautious addition of 50 ml of water. Organic solvents were removed under reduced pressure; the residue was taken up in ether, dried (MgSO₄), concentrated, and distilled, yielding ~10 g of product, bp 110° (0.3 mm).

Anal. Calcd for $C_{18}H_{23}P$: C, 79.97; H, 8.58. Found: C, 79.80; H, 8.30.

4.4-Dimethylpentanoic acid was prepared by pouring approximately 1 mole of 3.3-dimethylbutylmagnesium chloride in ether onto a slurry of 200 ml of ether and 700 g of crushed Dry Ice. Conventional work-up yielded 102 g (78%) of acid: bp 205–211° (lit.[42] bp 211–214°); infrared absorption (CCl₄) at 2500–3500 (O–H) and 1705 cm⁻¹(C=O).

4.4-Dimethylpentanoyl chloride was prepared from 26 g (0.2 mole) of the corresponding acid by slow addition of 65 g of thionyl chloride with stirring, using 0.5 ml of pyridine as catalyst. The reaction mixture was refluxed for 2 hr. excess thionyl chloride removed by distillation, and the residue distilled, yielding 18 g (60%) of product, bp 40–51° (37 ± 5 mm). The sample was not purified further, but was used directly in the following reaction.

4.4-Dimethylpentanamide was prepared by slow addition of 18.30 g (0.122 mole) of 4.4-dimethylpentanoyl chloride to 125 ml of concentrated (29%) ammonia at 0° with stirring, in three-necked, round-bottomed. 500-ml flask equipped with a mechanical stirrer and a dropping funnel. Following completion of the addition, the reaction mixture was stirred for 10 min, and the resulting precipitate isolated by filtration with suction. The precipitate was dried at 80° for 2 hr, then triturated with 400 ml of boiling ethyl acetate. The ethyl acetate solution yielded the amide as white crystals on cooling. Recrystallization (ethyl acetate) gave 10.6 g (67%) of product, mp 140–143° (lit.[42] mp 140–141°); infrared absorption (CH₂Cl₂) at 3500, 3400, 3170 (N–H), and 1670 cm⁻¹ (C=O).

Anal. Calcd for $C_7H_{15}NO$: C, 65.07; H, 11.70; N, 10.84. Found: C, 65.09; H, 11.83; N, 10.62.

Methyl 4.4-dimethylpentanoate was prepared by refluxing a mixture of 13.02 g (0.1 mole) of the corresponding acid, 10 g of methanol, ten drops of concentrated sulfuric acid, and 30 ml of methylene chloride for 50 hr. The yield of ester was 12.9 g (89%) having bp 77–84° (40 mm). The product had infrared absorption (CCl₄) at 1740 cm⁻¹, and was characterized by its nmr spectrum.

3.3-Dimethylbutyl Alcohol. A rapid stream of dry air was passed through a solution of 0.5 mole of 3.3-dimethylbutylmagnesium chloride in 500 ml of ether for 2 hr. The resulting viscous paste was hydrolyzed at 0 with 200 ml of saturated aqueous ammonium chloride solution followed by 600 ml of water containing sufficient sulfuric acid to bring the reaction mixture to pH 5. The organic layer was separated, and the aqueous phase was extracted with two 150-ml portions of ether. The combined organic phase was washed twice with saturated salt solution, dried (Na₂SO₄), and distilled. The product (36 g, 70%) had bp 140–145 (lit.[43] bp 141–143°).

4.4-Dimethylpentanol-1,1-d_2 was prepared by reduction of methyl 4.4-dimethylpentanoate (7.2 g) with LiAlD₄ (1.1 g) in ether. Conventional work-up and distillation gave 4 g of product, bp 157–160° [lit.[44] bp 158° (for 4.4-dimethylpentanol)]. The nmr spectrum of the alcohol indicated that its isotopic purity was greater than 95%.

1-Phenyl-3.3-dimethylbutane. Benzyl bromide (70 g, 0.4 mole) was added dropwise to a refluxing solution of 2.2-dimethylpropylmagnesium chloride, prepared from 10.7 g (0.1 mole) of 2.2-dimethylpropyl chloride and 2.4 g of magnesium turnings in 150 ml of ether. After the reaction mixture had been refluxed for 2 hr, excess benzyl bromide was converted to bibenzyl by addition of 5 g of magnesium turnings, the solution was hydrolyzed with aqueous ammonium chloride solution, and the organic layer was separated and dried (MgSO₄). Ether was removed from the organic layer under vacuum, and bibenzyl separated by crystallization from the resulting oil by cooling to 0. Distillation of the residue from this precipitation yielded 3.1 g of 1-phenyl-3.3-dimethylbutane, bp 211° (lit.[45] bp 211.6–212°).

3.3-Dimethylbutyl *p*-bromobenzenesulfonate was prepared by slow addition of 31.6 g of pyridine to a slurry of 51.1 g of *p*-bromobenzenesulfonyl chloride in 20.4 g (0.2 mole) of 3.3-dimethylbutyl alcohol at 0°, followed by addition of 50 ml of concentrated hydrochloric acid and 50 ml of water. The resulting slurry was extracted with three 200-ml portions of ether. The ether layers were combined, washed with 150 ml of saturated aqueous sodium chloride solution, dried (Na₂SO₄), and concentrated to a volume of approximately 75 ml. On cooling to –10°, the product precipitated as white crystals. Recrystallization yielded 49.4 g (77%) of product, mp 54–55°. The product had infrared absorption (CCl₄) at 1375 and 1185 cm⁻¹ (SO₂–O); its nmr spectrum was consistent with the assigned structure.

N-(3.3-Dimethylbutyl)phthalimide was prepared by refluxing a mixture of 24.1 g (0.2 mole) of 3.3-dimethylbutyl chloride, 41.2 g of potassium phthalimide, and 100 ml of dimethylformamide for 50

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(38) L. Schmerling, *ibid.*, **67**, 1153 (1945).

(39) R. L. Shriner, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p 366.

(40) E. Lieber, C. N. R. Rao, and J. Ramachandran, *Spectrochim. Acta*, **13**, 296 (1958). The infrared absorption of 3,3-dimethylbutyl isothiocyanate which was present as an impurity occurred at 2095 and 2180 cm⁻¹.

(41) J. Chatt and F. A. Hart, *J. Chem. Soc.*, 1378 (1960); G. P. Schiemenz, *Ber.*, **99**, 514 (1966).

(42) C. Moureu and R. Delange, *Bull. Soc. Chim. France*, (3) 29 665 (1903).

(43) R. C. Huston and A. H. Agett, *J. Org. Chem.*, **6**, 123 (1941).

(44) F. C. Whitmore and A. H. Homeyer, *J. Am. Chem. Soc.*, **55**, 4555 (1933).

(45) E. Berliner and F. Berliner, *ibid.*, **72**, 223 (1950).

hr. The mixture was filtered while hot and all components boiling below 160° were removed by distillation. Upon cooling, the residue formed a solid which was recrystallized from ethanol to mp 37–38°. The yield of product was 30.5 g (66%).

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.77; H, 7.12.

3,3-Dimethylbutylamine was prepared by dissolving 84 g (0.36 mole) of N-(3,3-dimethylbutyl)phthalimide in 400 ml of hot ethanol and cooling the solution rapidly with stirring to form a fine suspension. To this suspension, 21 g (0.42 mole) of hydrazine hydrate and 200 ml of ethanol were added slowly. The addition of 300 ml of 6 N hydrochloric acid to the resulting slurry produced first a clear solution and then a granular precipitate. The precipitate was removed by filtration, and ethanol removed from the filtrate by distillation. The aqueous residue was adjusted to pH 12 with concentrated potassium hydroxide solution and extracted with two 400-ml portions of ether. The combined ether extracts were dried and distilled, yielding 10 g (22%) of amine, bp 115–116°.

Anal. Calcd for $C_6H_{15}N$: C, 71.22; H, 14.94; N, 13.84. Found: C, 71.25; H, 14.58; N, 13.89.

N-(3,3-Dimethylbutyl)formamide. A mixture of ethyl formate (7.8 g, 0.11 mole) and 3,3-dimethylbutylamine (9.5 g, 0.095 mole) was refluxed under a nitrogen atmosphere for 3 hr. The product, isolated as a viscous liquid in 80% yield by distillation directly from the reaction mixture, had bp 76–78° (0.4 mm) and was used without further purification.

3,3-Dimethylbutyldimethylamine. A mixture of 8.5 ml of 37% aqueous formaldehyde, 8.4 g of formic acid, and 3.8 g of 3,3-dimethylbutylamine was refluxed for 48 hr. The reaction mixture was cooled, treated with 14 ml of 4 N HCl, and evaporated to dryness under reduced pressure. The residue was dissolved in 30 ml of water, extracted once with ether, made strongly basic, and extracted twice with ether. The ether extracts from the basic solution were dried (KOH), concentrated, and distilled yielding ~1 g of product, bp 123–124°.

Anal. Calcd for $C_8H_{19}N$: C, 74.35; H, 14.82; N, 10.84. Found: C, 74.02; H, 14.53; N, 10.48.

3,3-Dimethylbutyl cyanide was prepared by refluxing a solution of 21.6 g of 3,3-dimethylbutyl chloride and 35.2 g of potassium cyanide in 400 ml of ethanol for 1 week. The reaction mixture was cooled, poured into 1 l. of water, and extracted with 500 ml of diethyl ether. The ether layer was extracted with three 500-ml portions of water, dried (MgSO₄), concentrated, and distilled, yielding 5.8 g (30%) of nitrile as a colorless liquid, bp 165–170°; infrared absorption (CCl₄) at 2250 cm⁻¹ (C≡N).

Anal. Calcd for $C_7H_{13}N$: C, 75.62; H, 11.78; N, 12.60. Found: C, 75.76; H, 12.00; N, 12.80.

3,3-Dimethylbutyl fluoride was prepared by heating a mixture of 30.1 g of 3,3-dimethylbutyl chloride, 100 g of anhydrous potassium fluoride, and 150 ml of ethylene glycol at 100° in a hood.[46] After 6 days, the components of the reaction mixture boiling below 100 were separated by distillation, dried (CaSO₄), and redistilled. The product (bp 75–77°, lit.[47] bp 75–77°) obtained using this procedure was 70% pure as estimated from its nmr spectrum; however, the spectra of the impurities did not interfere with the spectrum of the fluoride, and no further purification was attempted.

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(46) See F. L. M. Pattison and J. J. Norman, *J. Am. Chem. Soc.*, 79, 231 (1957), for a discussion of the toxicity of monofluoroalkanes.

(47) C. B. Linn and L. Schmerling, U. S. Patent 2,451,843 (1948); *Chem. Abstr.*, 43, 2623 (1949).