# Studies in Nuclear Magnetic Resonance—XII

## Complete Analysis of the Proton Spectra of *tert*-Butylcyclohexane-3,3,4,4,5,5-$d_6$ and -3,3,5,5-$d_4$.

**Virginia R. Haddon and L. M. Jackman**

*Chemistry Department, The Pennsylvania State University, University Park, PA* 16802, *USA*

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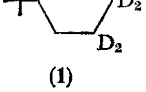
Abstract—Accurate parameters for the two title compounds have been obtained by the aid of a spectral subtraction technique in conjunction with analysis by LAOCN3. It is observed that $J_{1eq,6eq}$ and $J_{1ax,2ax}$ are abnormally large and small, respectively, and the significance of these and other coupling constants are discussed in terms of the probable geometry of *tert*-butylcyclohexane. The *tert*-butyl group affects the chemical shifts of the 4-protons, indicating that *tert*-butylcyclohexyl derivatives are poor models for fixed conformers of monosubstituted cyclohexanes. The deuterium isotope effects on proton chemical shifts appear to be influenced by the same factors as proton-proton coupling constants.

4-*Tert*-BUTYLCYCLOHEXYL derivatives have played an important role in the development of the theory of conformational analysis of cyclohexane systems. A method frequently used[1,2,3] for determining the equilibrium between the two rapidly exchanging chair conformers of simple cyclohexyl derivatives, utilizes chemical shift measurements on such averaged systems, together with values for the analogous protons in the epimeric 4-*tert*-butylcyclohexyl derivatives, it being assumed that the latter are satisfactory models for the fixed conformations. Low temperature NMR studies have, however, indicated that the chemical shifts for the 'pure' conformers are different from those of the model compounds.[4,5,6] The origin of these discrepancies has not been determined, and several factors such as long-range shielding and geometric distortion might be implicated.

There has been no direct determination of the geometry of *tert*-butylcyclohexane, although the electron diffraction study of *cis*- and *trans*-4-*tert*-butyl-1-chlorocyclohexane has been reported[7] and an X-ray diffraction structure determination has been carried out for *cis*-(*p*-bromophenyl)-4-*tert*-butylcyclohexane.[8] Several force field calculations of the structure of *tert*-butylcyclohexane have been published,[9,10] of which that by Altona and Sundaralingam[10] is the most complete.

Recently, Remijnse, Van Bekkum and Wepster deduced all the chemical shifts of *tert*-butylcyclohexane, and four of the ten vicinal coupling constants, from the spectra of three *tert*-butylperdeuterocyclohexanes retaining *cis* vicinal pairs of protons, and from an incomplete analysis of the spectrum of *tert*-butylcyclohexane-3,3,5,5-$d_4$.[11] We now report complete analyses of this compound (2) and of the -3,3,4,4,5,5-$d_6$ derivative (1), which confirm and augment the results of these workers.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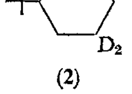

(2)

## EXPERIMENTAL

The mass spectral data were obtained using an AEI-MS 9 mass spectrometer at 70 eV. Vapour phase chromatography (GLC) data were obtained using a Perkin-Elmer 881 Gas Chromatograph.

All solvents used in the experiments described were distilled. Ether for use in lithium aluminum hydride reductions was dried by distillation from calcium hydride and stored over sodium wire.

4-tert-*Butylcyclohexanone*-2,2,6,6-$d_4$. 4-*tert*-Butylcyclohexanone (5 g, Aldrich Chemical Co), dry benzene (5 ml) and a solution of sodium (100 mg) in $D_2O$ (10 ml, Stohler Isotope Chemicals, 99·8% D) were vigorously stirred with a 'vibromix' for 60 hrs at 75°. The $D_2O$ solution was separated and the ketone solution treated as above with two additional amounts of fresh alkaline $D_2O$ solution. Removal of benzene yielded 4-*tert*-butylcyclohexanone-2,2,6,6-$d_4$ (4·9 g, 96%). Mass spectral analysis indicated that the product contained 3·95 D/molecule (98·7% deuteration).

tert-*Butylcyclohexane*-3,3,4,4,5,5-$d_6$ (1). A mixture of mossy zinc (1 g), mercuric chloride (0·3 g), DCl (0·1 ml, 38% in $D_2O$, 99% D, Stohler Isotope Chemicals) and $D_2O$ (1 ml) was shaken for 5 mins. The aqueous solution was decanted, and the amalgamated zinc covered with DCl (1·5 ml) and $D_2O$ (1 ml). 4-*tert*-Butylcyclohexanone-2,2,6,6-$d_4$ (0·5 g) was added to the freshly prepared zinc amalgam, and the mixture was refluxed vigorously for 16 hrs. The mixture was extracted with ether (2 × 15 ml) and the combined extracts washed with water (1 × 10 ml), 5% $Na_2CO_3$ solution (2 × 10 ml) and water (1 × 10 ml). The solution was dried ($MgSO_4$), and after removal of solvent, the product was shown by GLC (SE30, 120°) to consist of deuterated *tert*-butylcyclohexane (91%) and 4-*tert*-butylcyclohexene (9%). The olefin was removed by washing the product with 87·5% $H_2SO_4$ (2 × 10 ml). Distillation using a line-transfer apparatus yielded pure *tert*-butylcyclohexane-3,3,4,4,5,5-$d_6$ (0·110 g, 24%). By mass spectral analysis, the isotopic content of the product was determined to be 5·94 D/molecule (99·0% deuteration).

4-tert-*Butylcyclohexanol*-2,2,6,6-$d_4$. 4-*tert*-Butylcyclohexanone-2,2,6,6-$d_4$ (0·938 g) in dry ether (15 ml) was added under nitrogen to a stirred, refluxing solution of lithium aluminum hydride (0·480 g) in dry ether (40 ml). After refluxing for 3 hrs, the mixture was cooled, and water (30 ml) and then dilute $H_2SO_4$ (20 ml) were added cautiously. The ether layer was separated and the aqueous phase extracted with ether (3 × 25 ml). The combined ether solutions were washed with saturated $NaHCO_3$ solution (2 × 25 ml) and dried ($K_2CO_3$). Removal of the solvent yielded pure 4-*tert*-butylcyclohexanol-2,2,6,6-$d_4$ (0·875 g, 92%), shown by GLC (SE30, 150°) to consist of a mixture of isomers (*trans*/*cis* $\approx$ 9). The deuterium content of the product was shown by mass spectral analysis to be the same as that of the starting ketone (3·95 D/molecule).

4-tert-*Butylcyclohexyl p-Toluenesulfonate*-2,2,6,6-$d_4$. A solution of 4-*tert*-butylcyclohexanol-2,2,6,6-$d_4$ (0·788 g) in pyridine (5 ml; dried over NaOH) was cooled to approx. 10°. *p*-Toluenesulfonyl chloride (1·5 g) was added slowly with stirring and the resulting clear solution was kept overnight at approx. 5°.

Water (4 ml) was added, followed by sufficient conc. HCl (approx. 10 ml) to neutralize the pyridine. The product was extracted with ether (3 × 25 ml), and the combined extract washed with dilute HCl (2 × 20 ml), water (20 ml), aq. $Na_2CO_3$ (2 × 20 ml), water (2 × 20 ml), and then dried ($K_2CO_3$). Removal of solvent yielded the mixture of *p*-toluenesulfonates (1·337 g, 87%; 3·95 D/molecule).

tert-*Butylcyclohexane*-3,3,5,5-$d_4$ (2). 4-*tert*-Butylcyclohexyl *p*-Toluenesulfonate-2,2,6,6-$d_4$ (1·34 g) in dry ether (25 ml) was added during 30 mins to a stirred, refluxing solution of lithium aluminum hydride (0·6 g) in ether (50 ml) under a nitrogen atmosphere. Stirring and refluxing were continued for 2 days by which time the ester was shown to be absent by thin layer chromatography. Water (30 ml) and then 20% $H_2SO_4$ (20 ml) were added and the mixture was poured into water (200 ml). The product was extracted with ether (4 × 25 ml) and the combined extracts washed with 5% $Na_2CO_3$ solution (2 × 20 ml) and water (2 × 20 ml). Removal of the solvent afforded a product shown by GLC (SE30, 80°) to consist of deuterated *tert*-butylcyclohexane (87%) and 4-*tert*-butylcyclohexene (13%). After washing with 87·5% $H_2SO_4$, the product was distilled using a line-transfer apparatus to yield pure *tert*-butylcyclohexane-3,3,5,5-$d_4$ (0·220 g, 36%). Mass spectral analysis indicated that the deuterium content of the product was the same as the starting ketone (3·95 D/molecule).

*Nuclear Magnetic Resonance Spectra.* The 100 MHz spectra were obtained using a Varian HA 100 Spectrometer and were calibrated with a frequency counter (±0·1 Hz). Deuterium decoupling was accomplished with an NMR Specialties HD60B decoupler and the temperature of the samples under decoupling conditions was determined to be 67°, with reference to a standard Varian sample of ethylene glycol.

A Varian C1024 spectrum accumulator was used in the spectral subtraction experiment (see below). For the plotting of all calculated spectra, a Calcomp 564 Plotter interfaced with an IBM 1401 computer was used.

## ANALYSIS OF SPECTRA AND RESULTS

The spectra of both **1** and **2** (10% in $CCl_4$) were obtained at 100 MHz at 67°. In both cases deuterium decoupling resulted in considerable sharpening of the spectra.

The decoupled spectrum of **1** was analyzed as an ABB'XX' system using LAOCN3.[12] Suitable starting parameters, together with 43 assigned lines, yielded, after three iterations, a calculated spectrum whose RMS deviation from the observed spectrum was 0·081 Hz. A program was written by Dr R. C. Haddon to superimpose a Lorentzian line shape on the calculated stick function output. A line-width of 0·7 Hz was assumed and the *tert*-butyl group (not included in the analysis) was added to the data deck before plotting. This was given the observed chemical shift (δ0·84) and its intensity was normalized to equal nine fifths of the total intensity of the calculated data. Because of the broadness of the base of the singlet, all peaks were assigned a base width of 50 times the line-width. The resultant theoretical spectrum was displayed using the Calcomp plotter and is reproduced in Fig. 1, together with the observed spectrum. The NMR parameters yielded by the iterative calculation are presented in Tables 1, 2 and 3, together with those for **2** (see below) and the appropriate values of Remijnse, Van Bekkum and Wepster.[11]

The ring protons of **2** constitute an ABB'CXX'Y system. In the absence of magnetic equivalence, the total analysis of such a seven spin system is a formidable task unless very accurate starting parameters are available. Accurate values for the 1-, 2- and 6-positions were taken from the analysis of **1**. To obtain the chemical shifts of the 4-protons and their geminal coupling constant, a spectral subtraction technique was used.

The 4-protons of **2** were effectively insulated from the spin systems of the rest of the molecule by deuteration in the 3- and 5-positions, and deuterium decoupling further simplified the spectrum. It was then expected that spectral subtraction of the spectrum of **1** from that of **2** would result in cancellation of all resonances, except those of the 4ax and 4eq protons. Accordingly, four scans of the 100 MHz spectrum of **2** with deuterium decoupling were accumulated in digital form (1024 points) in the memory of a small dedicated computer (positive mode). Similarly, four scans of **1** were accumulated in the negative mode and further scans at a much reduced gain were subtracted until cancelling of the *tert*-butyl singlets appeared complete. The difference spectrum was then read out of the memory onto the spectrometer recorder, and is reproduced in Fig. 2, together with the spectrum of *tert*-butylcyclohexane-$d_0$ for comparison. The appearance of the subtracted spectrum is that of an AB quartet and from this the

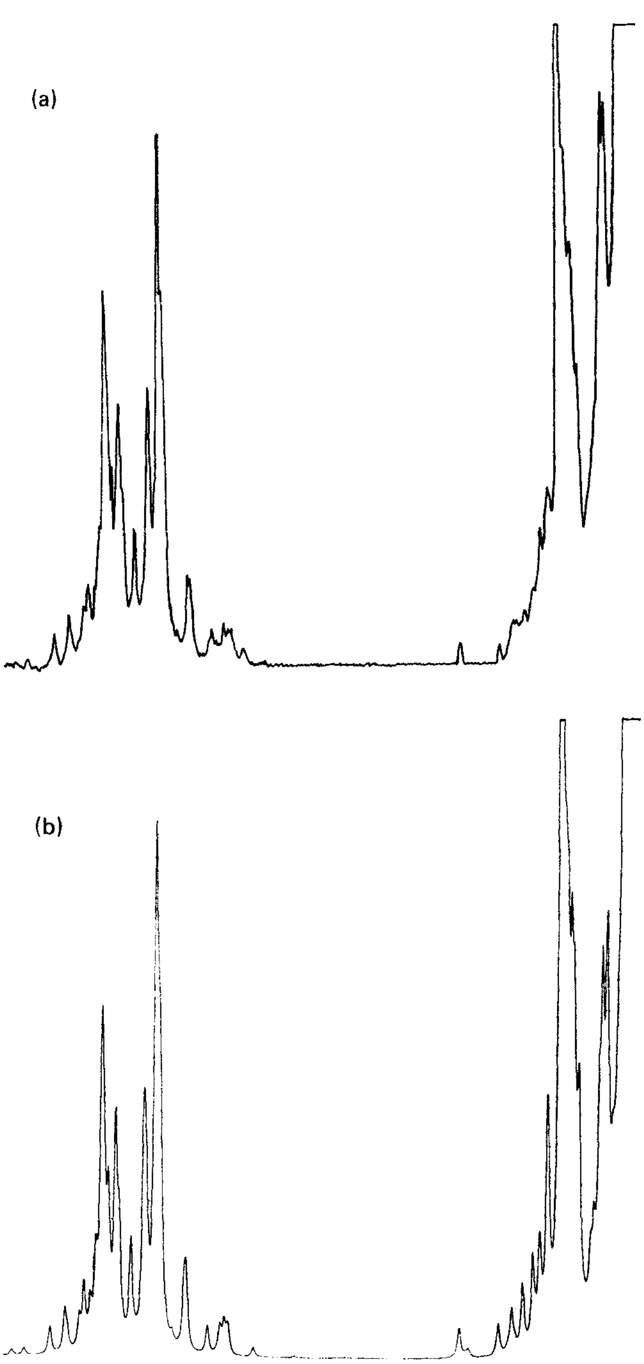


FIG. 1. Observed and calculated deuterium decoupled spectra of *tert*-butylcyclohexane-3,3,4,4,5,5-$d_6$. (a) Observed spectrum, 10% in $CCl_4$ at 67°. (b) Calculated spectrum. Total width of spectrum 115 Hz.

TABLE 1. CHEMICAL SHIFTS[a] OF DEUTERATED *tert*-BUTYLCYCLOHEXANES

| Position | (1)[b] | (2)[b] | Perdeutero-compounds[c] |
|---|---|---|---|
| $1_{ax}$ | 0·974 | 0·975 | 0·939 |
| $2_{ax}$ | 0·919 | 0·919 | 0·856 |
| $2_{eq}$ | 1·747 | 1·751 | 1·723 |
| $3_{ax}$ | | | 1·156 |
| $3_{eq}$ | | | 1·723 |
| $4_{ax}$ | | 1·072 | 1·056 |
| $4_{eq}$ | | 1·627 | 1·606 |

[a] Chemical shifts are quoted in ppm downfield from TMS.

[b] At 67°, 10% in $CCl_4$.

[c] Derived from the data of Ref. 11. These authors inferred values for undeuterated *tert*-butylcyclohexane by applying a 3 Hz correction for deuterium isotope shifts to the observed parameters of the $d_8$-compounds. We have removed this correction and also applied a temperature correction (0·0002 ppm/deg.),[13] so that the results for the various *deuterated tert*-butylcyclohexanes at 67° may be compared directly.

TABLE 2. VICINAL COUPLING CONSTANTS IN DEUTERATED *tert*-BUTYLCYCLOHEXANES

| $J$ | (1) | (2) | Perdeutero-compounds[a] |
|---|---|---|---|
| $1_{ax}, 2_{ax}$ | 11·94 | 12·00 | |
| $1_{ax}, 2_{eq}$ | 3·08 | 3·13 | 3·03 |
| $2_{eq}, 3_{ax}$ | | | 3·61 |
| $3_{ax}, 4_{eq}$ | | | 3·76 |
| $3_{eq}, 4_{ax}$ | | | 3·77 |

[a] Data from Ref. 11.

following parameters were derived: $\delta H_{4ax} = 1{\cdot}071 \pm 0{\cdot}003$, $\delta H_{4eq} = 1{\cdot}625 \pm 0{\cdot}003$ and $J_{4ax,4eq} = -13{\cdot}3 \pm 0{\cdot}3$ Hz.

It should be noted that adequate cancelling of the sharp nine-proton singlet was achieved and that the resultant AB pattern corresponds to two protons only. Thus, we feel that use of a spectrum accumulator to effect subtraction of two compounds differing only by the replacement of the protons of interest by deuterium, is a generally viable technique, although deuteration in the positions vicinal to the protons of interest is necessary to overcome the problem of virtual coupling of the protons to the remaining spin system. The method may fail, however, in those cases where a long-range coupling exists between the isolated protons and other protons in the system. In the present case, a four bond coupling of the 4eq to the 2eq protons exists (1·49 Hz, see below), but the subtracted spectrum readily yielded the desired chemical shift data. Within these limits and provided the specific deuteration does not present insurmountable synthetic problems, the technique—used in conjunction with deuterium decoupling—could be applied to quite complicated molecules, for instance the steroids.

TABLE 3. GEMINAL AND LONG-RANGE COUPLING CONSTANTS IN DEUTERATED *tert*-BUTYLCYCLOHEXANES

| $J$ | (1) | (2) | Perdeutero-compounds[a] |
|---|---|---|---|
| $2_{ax}, 2_{eq}$ | −12·74 | −12·80 | |
| $4_{ax}, 4_{eq}$ | | −13·32 | |
| $2_{eq}, 6_{eq}$ | 2·35 | 2·46 | |
| $2_{eq}, 4_{eq}$ | | 1·49 | 1·4 |
| $1_{ax}, 4_{eq}$ | | −0·01 | |
| $1_{ax}, 4_{ax}$ | | 0·04 | |
| $2_{ax}, 4_{ax}$ | | −0·32 | |
| $2_{ax}, 4_{eq}$ | | −0·11 | |
| $2_{eq}, 4_{ax}$ | | −0·18 | |
| $2_{ax}, 6_{ax}$ | −0·37 | −0·25 | |
| $2_{ax}, 6_{eq}$ | −0·19 | −0·06 | |

[a] Data from Ref. 11.

The parameters so obtained for the 4-protons, together with those from the analysis of **1**, were used as input parameters for the analysis of **2**, together with reasonable estimates for the remaining (long-range) coupling constants. The program was modified so that *two* sets of up to 300 lines (from the ax and eq regions) would be generated from the calculation. Assignment of 61 lines in the ax region and 65 lines in the eq region yielded, after two iterations, a parameter set having an RMS deviation of 0·049 Hz. The calculated parameters are given in Tables 1, 2 and 3, and the observed and calculated spectra are reproduced in Fig. 3.

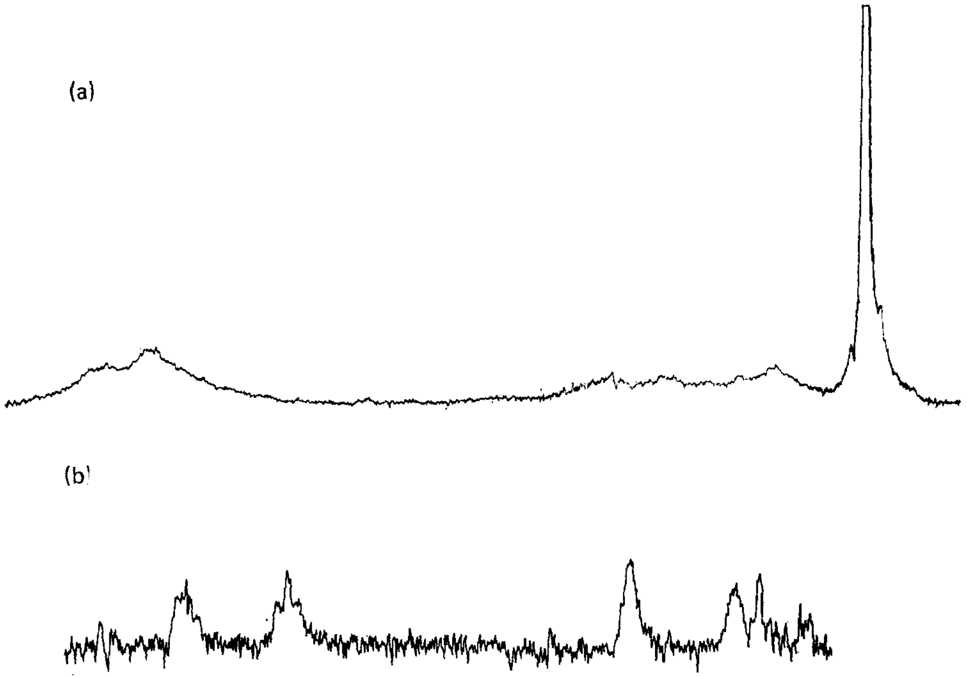


FIG. 2. (a) *tert*-Butylcyclohexane, 10% in $CCl_4$, room temperature, 100 MHz. (b) AB quartet of the 4ax and 4eq protons of *tert*-butylcyclohexane obtained by spectral subtraction [(**2**) − (**1**)].

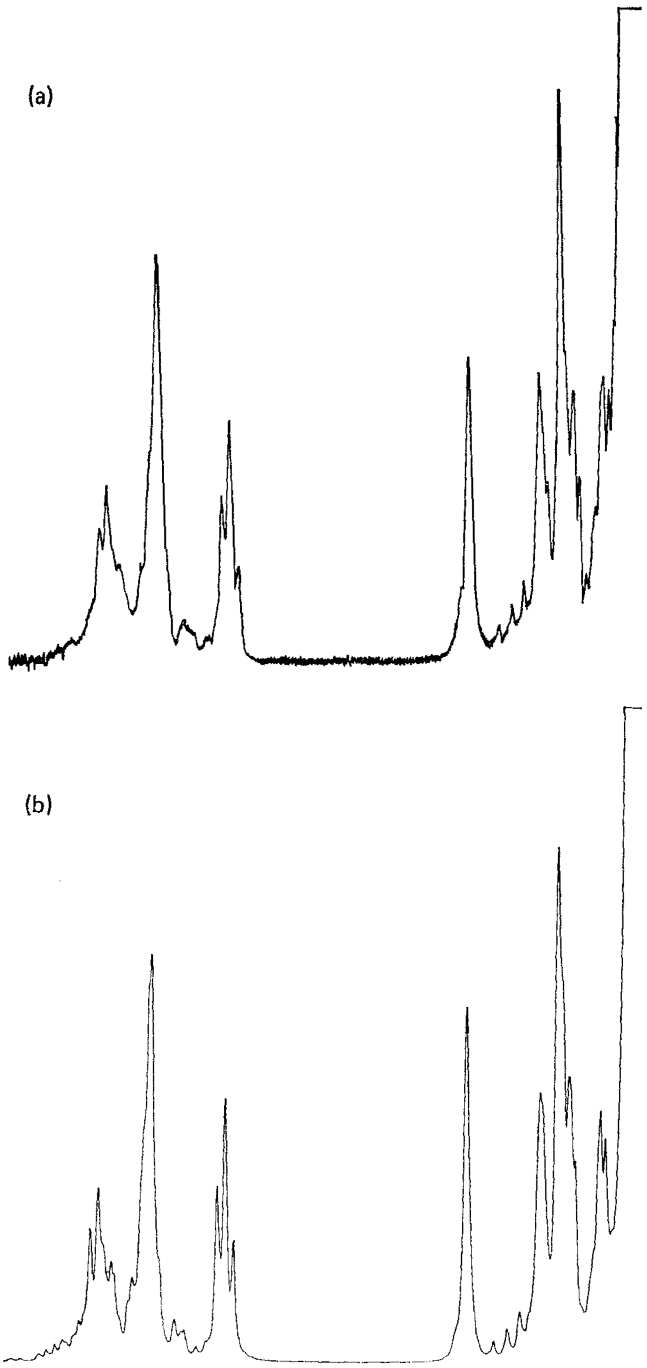


FIG. 3. Observed and calculated deuterium decoupled spectra of *tert*-Butylcyclohexane-3,3,5,5-$d_4$. (a) Observed spectrum, 10% in $CCl_4$ at 67°. (b) Calculated spectrum. Total width of spectrum 115 Hz.

The probable errors in all parameters determined by LAOCN3 are less than 0·03 Hz. In the determination of coupling constants, however, the error associated with interpolation of calibration frequencies is estimated at 0·3% and is therefore the major source of uncertainty for those parameters with values in excess of 10 Hz. The absolute values of the chemical shifts are subject to rounding errors in the frequency measurements, i.e. ± 0·001 ppm.

## DISCUSSION

### Vicinal Coupling Constants

The total analyses of the $d_4$ and $d_6$ derivatives yield values of $J_{1ax,2eq}$ which are in substantial agreement (Table 2) with the value determined directly from *tert*-butylcyclohexane-2,3,3,4,4,5,5,6,6-$d_9$.[11] The minor differences may be due to random errors or possibly a small isotope effect. In addition, the more detailed analysis has yielded the value of $J_{1ax,2ax}$ (Table 2).

The vicinal coupling constants are particularly important since, in conjunction with the Karplus relation [Eqn. (1)], they provide information about the geometry

$$J_{vic} = A(\cos^2 \varphi_{vic} - n \cos \varphi_{vic}) \qquad (1)$$

of the ring of *tert*-butylcyclohexane. The overall geometry of a cyclohexane ring is best defined by the average ($\varphi_{av}$) of the ring torsion angles $\varphi$, (Fig. 4) the value of which serves as an index of the extent of flattening (<60°) or puckering (>60°) of the ring. The external dihedral angles can be related to $\varphi$ by the relationships given in Eqn. (2), *but only if the assumption of trigonal projection symmetry is valid for the system under study.* Trigonal projection symmetry requires that both carbons in the $CH_2$—$CH_2$ fragment of interest have perfect tetrahedral valence angles (109·5°).

$$\varphi_{ax,eq} = \varphi; \; \varphi_{eq,eq} = 120 - \varphi, \; \varphi_{ax,ax} = 120 + \varphi \qquad (2)$$

This is least likely to be true in those cases where an axial substituent or a bulky equatorial group could relieve steric interactions by the deforming of valence angles, although these are often the very cases where geometric information is sought. For *tert*-butylcyclohexane, it is therefore not possible to estimate $\varphi$ from the vicinal coupling constants without a knowledge of the H—C—H bond angles, which only become available from the type of measurements which yield $\varphi$ directly (e.g. electron diffraction studies). We must be content, then, to evaluate $\varphi_{ax,eq}$ and $\varphi_{ax,ax}$ and compare them with the calculated values.

Table 4 summarizes electron diffraction data for cyclohexane and methylcyclohexane[14,15] in terms of the ring torsion angles $\varphi$, together with the calculated (full relaxation molecular mechanics approach) $\varphi$ and $\varphi_{ax,eq}$ values for these two compounds and for *tert*-butylcyclohexane and (hypothetical) ax-methylcyclohexane.[10] The $\varphi_{1ax,2eq}$ values as calculated from the measured $J_{1ax,2eq}$ values using Eqn. (1) are also listed. For the Karplus parameters $A$ and $n$, values of 12·95 and −0·02, respectively, were used.[16] It can be seen that although $J_{1ax,2eq}$ for cyclohexane and methylcyclohexane are very similar (3·65, 3·56 Hz), the observed *tert*-butylcyclohexane value (3·1 Hz) is much smaller and reflects a significant increase in the dihedral angle between the

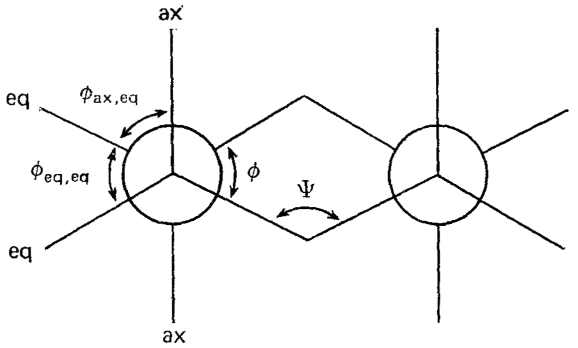
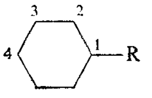


FIG. 4. Newman projection of cyclohexane.

TABLE 4. RING TORSION ANGLES, $\varphi$, AND EXTERNAL DIHEDRAL ANGLES, $\varphi_{ax,eq}$, FOR SOME MONOSUBSTITUTED CYCLOHEXANES

| <br>R | $\varphi$ (°)<br>Obs.[a] | <br>Calc. (FRMM)[b] | $J_{1ax,2eq}$<br>(Hz) | Calc. $\varphi_{1ax,2eq}$<br>From $J_{1ax,2eq}$[c] | <br>From FRMM[b] |
|---|---|---|---|---|---|
| H | 55·9 | 56·1 | 3·65[d] | 57 | 58·6 |
| eq-$CH_3$ | av 55·3 | $C_1$ 55·7<br>av 55·9<br>$C_4$ 56·3 | 3·56[e] | 58 | 61 |
| ax-$CH_3$ |  | $C_1$ 52·8<br>av 54·5<br>$C_4$ 55·9 | 4·7[f] | 53[f] | 50 |
| (eq)-*tert*-butyl |  | $C_1$ 53·8<br>av 55·4<br>$C_4$ 56·3 | 3·1[g] | 60<br>59·5[h] | 63 |

[a] Electron Diffraction Studies, Refs. 14, 15.

[b] Values from Computer Calculated Structures using Full Relaxation Molecular Mechanics Approach, Ref. 10.

[c] Calculated from $J_{vic}$ using Eqn. (1) with $A = 12{\cdot}95$, $n = -0{\cdot}02$. (Ref. 16).

[d] Ref. 16.

[e] Ref. 24.

[f] $\varphi_{1eq,2ax}$ from $J_{4ax,5eq} = 4{\cdot}7$ Hz in *cis,trans*-1,3,5-trimethylcyclohexane.[17]

[g] This work.

[h] From Eqn. (1) with A = 11·9.

1ax and 2eq protons. This increase was predicted by the force field calculations and arises from two factors: (1) the 1ax proton is bent towards the center of the ring (by 5° according to the calculations); (2) the *tert*-butyl group is pushed outwards (concomitant with an increase in the $C_2$—$C_1$—$C_7$ angle) to relieve non-bonded interaction between the *tert*-butyl methyls and the adjacent methylene groups.[10] Such a distortion of the external bond angles is in agreement with a recent X-ray diffraction study on *cis*-1-*p*-bromophenyl-4-*tert*-butylcyclohexane.[8]

The calculated $\varphi_{av}$ for *tert*-butylcyclohexane (55·4°) suggests an overall flattening of the ring, primarily associated with flattening in the $C_1$ region and the predicted $\varphi$ value in the region of the 4-protons (56·3°) is very close to that of cyclohexane itself (56·1°).[10] A greater overall flattening was predicted for ax-methylcyclohexane and the bending outwards of the ax-methyl group was expected to result in an abnormally small value for $\varphi_{1eq,2ax}$. From the large value of $J_{4ax,5eq}$ for *cis,trans*-1,3,5-trimethylcyclohexane, reported without comment to be 4·7 Hz,[17] a $\varphi_{1eq,2ax}$ value of 53° was derived from Eqn. (1), in good agreement with predictions.

The dihedral angle $\varphi_{ax,ax}$ predicted from the observed value of $J_{1ax,2ax}$ (Table 2) using Eqn. (1) deviates by approximately 15° from that predicted for the FRMM model.[10] Furthermore we note that this model predicts $\varphi_{ax,ax} = 170$ to 175° for cyclohexane compared with 181° for $\varphi_{1ax,2ax}$ in the *tert*-butyl derivative, whereas the corresponding coupling constants (13·1 and 11·9, respectively) require $\varphi_{ax,ax}$ for cyclohexane to be the larger. In view of the very large deviation (15°), it is probable that the fault lies with the parameterization of the Karplus equation and that the actual parameters are sensitive to all bond angles in the ethane-like fragment. The Altona and Sundaralingam model is, however, to some extent inconsistent, in that using Karplus parameters based on $\varphi_{1ax,2ax} = 181°$ and $J_{1ax,2ax} = 11{\cdot}9$, one obtains $\varphi_{1ax,2eq} = 59°$, compared with 63° from the model.

### Long-range and Geminal Coupling Constants

A somewhat more definitive, although qualitative, picture of the distortions in the *tert*-butylcyclohexane ring is provided by a consideration of long-range coupling constants. The long-range couplings occurring over four bonds ($^4J$) as given in Table 3 represent the first such data for an unstrained cycloalkane. The $^4J_{eq,eq}$ values are significantly larger than the $^4J_{eq,ax}$ and $^4J_{ax,ax}$ coupling, in keeping with well documented experimental[18,19] and theoretical[20] considerations, which have shown that the coupling is a maximum for a perfect planar 'W' path arrangement.

Of greater importance is the fact that the value of $J_{2eq,6eq}$ (2·4 Hz) is the largest four bond coupling reported for an unstrained, saturated cyclohexane ring, $^4J_{eq,eq}$ generally being in the range 1 to 2 Hz[19] (*cf.* $J_{2eq,4eq} = 1{\cdot}49$ Hz). In strained systems much larger four bond couplings have been observed,[19] the largest known value being a coupling of 18 Hz between the bridgehead protons of bicyclo[1.1.1]pentane.[21] Although the presence of multiple coupling paths enhances the coupling in such systems, it has been suggested[22] that the increase in coupling results from a decreased separation between the small posterior lobes of the C—H molecular orbitals for the coupled protons. Indeed, an X-ray study[23] of a derivative of bicyclo[1.1.1]pentane indicated that the distance between the non-bonded bridgehead carbons was extremely short (1·89 Å) and the C—C—C angle correspondingly small (75°). Recent calculations[20] have also demonstrated that $^4J_{eq,eq}$-like coupling is decreased when the C—C—C bond angle ($\Psi$, Fig. 4) is increased from 109·5° to 120°. It thus seems likely that the large $J_{2eq,6eq}$ value in *tert*-butylcyclohexane is a response to a closing of the ring angle at the carbon bearing the *tert*-butyl substituent. This is consistent with the calculated structure,[10] whose bond angles were $C_6$—$C_1$—$C_2$ = 108·8° (*cf.* the experimentally determined ring bond angle of cyclohexane, 111·6[15]). Should future data in unstrained saturated hydrocarbons obey this trend, the four bond W couplings may be established as efficient probes for small changes in the carbon bond angles.

The $^4J_{ax,ax}$ values in Table 3 of approximately −0·3 Hz are not atypical of cyclohexanes.[19] The $^4J_{ax,eq}$ values are smaller in magnitude than the normal range (0·4 to 0·8 Hz),[19] although their negative signs are consistent with theoretical considerations.[20] Although these small couplings are probably not greatly sensitive to changes in the C—C—C angle,[20] the effect of changes in substituents or dihedral angles may well be relatively significant.

The observed difference between the geminal coupling constant at the 2-position (−12·8 Hz) and the 4-position (−13·3 Hz) is evidence for a change of hybridization, presumably associated with a change in the H—C—H angle. The factors which affect geminal coupling constants in saturated hydrocarbons are still not fully understood.

## Chemical Shifts and Their Isotope Effects

In discussing the effect of the *tert*-butyl group on the chemical shifts of the ring protons of cyclohexane, it is first necessary to correct the observed values for temperature and isotope effects. The former was assumed to be the same ($2 \times 10^{-4}$ ppm/deg) as established for cyclohexane itself[13] and the latter are discussed in detail below. The adjusted chemical shifts, relative to the axial or equatorial protons of cyclohexane itself are recorded in Table 5, which also includes the analogous values for the protons of the equatorial conformer of methylcyclohexane.[24]

TABLE 5. SUBSTITUENT EFFECTS FOR EQUATORIAL METHYL AND *tert*-BUTYL GROUPS

| Proton | Substituent effect[a] eq-Methyl[b] | eq-*tert*-Butyl |
|---|---|---|
| $1_{ax}$ | −0·12 | 0·23 |
| $2_{ax}$ | 0·33 | 0·27 |
| $2_{eq}$ | 0·00 | −0·08 |
| $3_{ax}$ | 0·00 | |
| $3_{eq}$ | −0·04 | |
| $4_{ax}$ | 0·10 | 0·11 |
| $4_{eq}$ | 0·01 | 0·04 |

[a] In ppm. A negative sign represents a downfield shift relative to the standard cyclohexane resonances.
[b] From the data of Ref. 24.

The most important result is for the 4-protons, which differ significantly from their cyclohexane counterparts. Thus it is clear[11] that *tert*-butylcyclohexyl derivatives should not be used as fixed conformer models, a conclusion which has also been reached from low temperature studies of some monosubstituted cyclohexanes.[4,5,6] It is also striking that the *tert*-butyl group causes increased shielding of the proton attached to the same carbon atom, a reversal of the usual 'alkylation shift.'[25]

The magnitude of deuterium isotope effects on proton chemical shifts in cyclohexane and *tert*-butylcyclohexane are definitely dependent on the disposition of the deuterium atom. Using our data and that of Remijnse, Van Bekkum and Wepster[11] for *tert*-butylcyclohexane, together with selected values for cyclohexane[26] and some of its deuterated analogues,[13,16] we have set up twelve equations in the following five isotope effects: geminal ($\delta_g$), vicinal equatorial D on axial H ($\delta_{eq,ax}$), vicinal equatorial D on equatorial H ($\delta_{eq,eq}$), vicinal axial D on axial H ($\delta_{ax,ax}$) and a long range effect ($\delta_{l.r.}$) associated with deuterium four bonds removed. The data have been subjected to regression analysis which established a multiple correlation coefficient of 0·996 and the values of the parameters given in Table 6. It is interesting that the magnitudes of the isotope effects appear to parallel the coupling constants between analogously oriented protons. It is known that chemical shift isotope effects are also dependent on the same factors that affect the geminal coupling constants.[27]

TABLE 6. DEUTERIUM ISOTOPE EFFECTS[a] ON PROTON CHEMICAL SHIFTS

| | |
|---|---|
| $\delta_g$ | 0·019 ± 0·002 |
| $\delta_{eq,ax}$ | 0·007 ± 0·002 |
| $\delta_{eq,eq}$ | 0·007 ± 0·002 |
| $\delta_{ax,ax}$ | 0·014 ± 0·001 |
| $\delta_{l.r.}$ | 0·0035 ± 0·001 |

[a] In ppm. The presence of the deuterium causes deshielding.

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