Conformational Analysis of 5-t-Butylcyclohexa-1,3-diene

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Summary Analysis of variable temperature circular dichroism spectra of (+)-(5R)-t-butylcyclohexa-1,3-diene gave a conformational energy of 1·7 kJ/mol, indicating that where 1,3-diaxial interactions are minimised, the equatorial configuration is only slightly favoured over the axial.

It has long been a goal of conformational analysis to provide an understanding of factors influencing the relative stabilities of axially and equatorially substituted cyclohexanes.[1–5] Conformational free energy differences (ΔG°_{ax-eq}) have been determined for a variety of substituted cyclohexanes[6] for which the equatorial and axial configurations are interconverted by a chair ⇌ chair ring conformational isomerism. For example, ΔG°_{ax-eq} (Me) = 7·1 kJ/mol,[6] and with larger groups the conformational energy becomes greater, *e.g.* ΔG°_{ax-eq} (Bu^t) > 18·4[6] (= 22·6)[3] kJ/mol. The principal destabilising influence on an alkyl group in the axial configuration is usually viewed as a combination of gauche interactions and across-the-ring 1,3-diaxial interactions,[1,2,4,7–9] although it has also been postulated that gauche H–H interactions may explain the observations just as well.[5] Notably, when 1,3-diaxial interactions are reduced, the axial conformation becomes more populated. Thus, $\Delta H^\circ_{ax-eq} = 2·45 \pm 0·11$ and $4·07 \pm 0·35$ kJ/mol for 3-methyl- and 4-methyl-cyclohexene, respectively;[7–9] and $\Delta G^\circ_{ax-eq} = 3·3$—$4·1$ and $5·69$—$6·11$ kJ/mol for 5-methyl- and 5-t-butyl-1,3-dioxan, respectively.[2] Consequently, the larger Bu^t group may be viewed as an especially sensitive probe of conformational energies in sterically less-crowded environments than that provided by cyclohexane. Further examination of this conformational probe required six-membered rings with either no, or minimal, 1,3-diaxial interactions. Because these conditions are suitably met in cyclohexa-1,3-diene, we prepared (+)-(5R)-t-butylcyclohexa-1,3-diene (1) and analysed the pseudo(ψ)-axial ⇌ ψ-equatorial conformational equilibrium using variable temperature circular dichroism (c.d.) measurements (Figure).

(+)-(5R)-t-Butylcyclohexa-1,3-diene was prepared from optically pure (+)-*trans*-(2R)-bromo-(5R)-t-butylcyclohexanone,[10] whose tosylhydrazone could be dehydrobrominated with Et₃N in benzene to give (+)-(5R)-t-butylcyclohex-2-enone tosylhydrazone.† The latter, upon treatment with Bu^{n}Li in tetramethylenediamine at −60 °C, gave (1) stereospecifically. Assuming only the ψ-axial ⇌ ψ-equatorial equilibrium depicted in the Figure, and applying the free energy extrapolation method of Moscowitz, Wellman, and Djerassi,[11] we estimate that equatorial t-butyl is only slightly more stable than axial ($\Delta G^\circ_{ax-eq} = 1·67 \pm 0·21$ kJ/mol), corresponding to *ca.* 35% of the less stable ψ-axial isomer at room temperature. This value is considerably smaller than that determined (> 18·4 kJ/mol)[6] or calculated (22·6 kJ/mol)[3] for t-butylcyclohexane. The large difference underscores the importance of 1,3-diaxial H–Bu^t interactions in destabilising the axial Bu^t configuration.
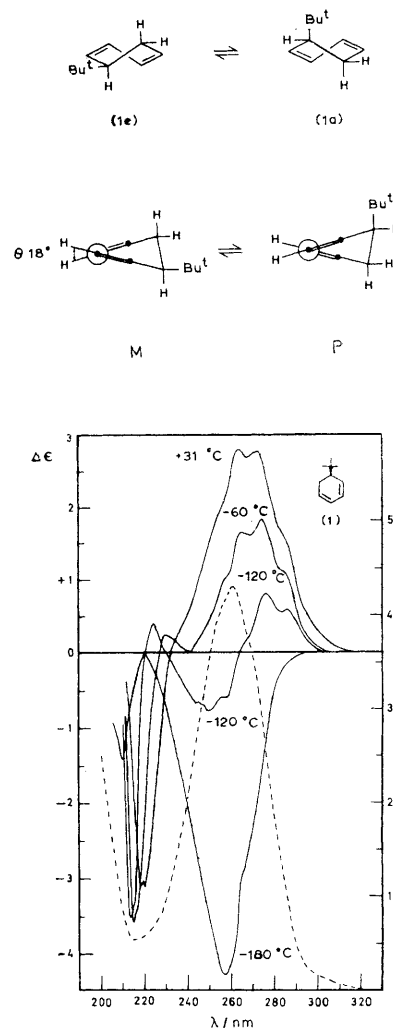

FIGURE. (Upper part) Conformational equilibrium between M-diene helicity and P-diene helicity conformers of (1) having pseudo (ψ)-equatorial (1e) and ψ-axial (1a) Bu^t groups. (Lower part) U.v. (— — — —) spectrum of (1) at 28 °C in methylcyclohexane–isopentane 4:1, v/v; and circular dichroism (————) spectra of (1) measured in 10 mm pathlength cuvettes as 1·8 × 10^{-4} M solutions in the same solvent mixture. Temperatures are indicated on the c.d. curves which were obtained on a JASCO J-40 instrument equipped with photoelastic modulator and run at a sensitivity setting of 5 × 10^{-5} ΔAbs./cm with a 30 s time constant and a 1nm/min scanning speed.

The ΔG°_{ax-eq} value for (1) is also smaller than the value ($\Delta G^\circ_{ax-eq} = 12·47$ kJ/mol) previously determined for 5-t-butylcyclohexa-1,3-diene[12] by a study of the temperature dependence of the product ratios for its photochemical electrocyclic ring opening. However, that study[12] assumed no dynamic effects on the product ratios. That is, the

† All compounds exhibited satisfactory elemental analyses and characteristic spectroscopic properties.

results are based on the assumption that there are no differences in rates of ring opening for each reacting conformer, and also that the conformations of the excited states leading to products are identified with (only two) ground state conformations. We therefore believe that the conformational energy determined from c.d. data is more nearly correct because it is derived from a thermodynamic method (not a kinetic method), a method which is sufficiently sensitive to be used in the determination of conformational energies of deuterium (*vs.* hydrogen).[13]

The c.d. Cotton effect (C.E.) signs of (**1**) are determined[11] to be (+) for the P-conformer (Figure) having a ψ-axial Bu[t] group and (−) for the M-conformer with a ψ-equatorial Bu[t] group. It may be noted that either Burgstahler's allylic axial chirality rule[14] or an earlier diene helicity rule[15] would predict that same associated C.E. signs.

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