# An Interesting Stable Twist-boat Fused Cyclohexane Derivative

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THE syntheses and unambiguous proof of stereo-chemistry of cyanomalonates (I) and (II) and of 4-t-butyl-1-cyano-1-ethoxycarbonylcyclohex-2-yl-acetic acid (III) have been given.[1] Hydrogenation of (I) at 115° and 1400 p.s.i. gave (IVa), m.p. 92—93°, as expected, which was hydrolysed to (IVb), m.p. 133—135°; this lost CO_2 readily to give (IVc), m.p. 163—164°. Reduction of (IVc) with lithium
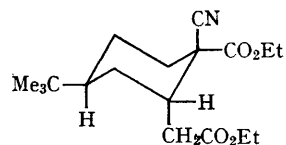
transition state having a twist–boat conformation in which the t-butyl, acetate, and cyano-groups are pseudo-equatorial. The cyclohexane ring in (VIa) must be a twisted boat. This is confirmed by an analysis of the n.m.r. spectra of (VIa) and its N-deuterated derivative, and estimation of the approximate dihedral angles between $C–H_a$ and $N–H_c$, $C–H_b$ and $N–H_c$, $C–H_d$ and $C–H_f$, and
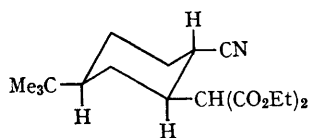
(I)
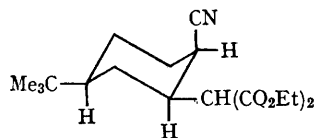
(II)

(III)

aluminium hydride gave *trans*-6-t-butyldecahydro-isoquinoline (picrate, m.p. 197—198°). Compound (II) similarly gave (Va), m.p. 138—140°, which in turn gave (Vb), m.p. 178°, (Vc), m.p. 187—188·5°, and *cis*-6-t-butyldecahydroisoquinoline (picrate, m.p. 220—221°).

Surprisingly at first, reduction of (III) proceeded smoothly to give an 89% yield of 6-t-butyl-9-ethoxycarbonyl-3-oxodecahydroisoquinoline (VIa), m.p. 99—100·5° [ν_{max} 3200 (NH), 1732 (CO_2Et), 1658 cm.$^{-1}$ (amide C=O)], which gave the stable acid (VIb), m.p. > 300°, with 3% KOH. Since chair–chair interconversion of (III) is highly unlikely, reductive cyclisation must involve a

$C–H_e$ and $C–H_f$ using a modified Karplus curve.[2] The results are summarised in the Table. Conformation (VII) is the one that gives the closest fit with the desired dihedral angles.[3] A similar analysis of the n.m.r. spectra of (IVa), (IVa-N-d), and (IVa-4, N-d_2) confirms the expected chair–half chair conformation for the alicyclic and heterocyclic rings, respectively.

The facile cyclisation of hydrogenated (III) through the twist–boat form can be explained by assuming that the effective size of C≡N is greatly increased by adsorption at the catalyst surface. This, coupled with the presence of an axial CH_2CO_2H, gives rise to repulsions which will seek

relief in the stretched boat conformation. In addition, once the cyanide has been reduced to aminomethyl the combined diaxial interactions of this and of CH_2CO_2H (> 3.4 kcal./mole) would be large enough to reduce appreciably the magnitude

two possible isomers of a simple *cis*-decalin type of compound in conformationally pure states. Unfortunately, all attempts to effect the decarboxylation of (VIb) either failed or gave intractable tars.

TABLE

| H_a and H_b	H_c	H_d and H_e
AB quartet at τ 6·43 and 6·59 ($J_{ab} = 12.5$ c./sec.)	Doublet at τ 1·86 ($J_{ac} = 3$ c./sec.); disappears on addition of D_2O	AB quartet at τ 7·51 and 8·18 ($J_{de} = 17.0$ c./sec.).[4]
A side: each peak a doublet ($J_{ac} = 3$ c./sec.)		A side: each peak a doublet ($J_{df} = 6.5$ c./sec.)
B side: not further coupled ($J_{bc} = 0$ c./sec.)		B side: not further coupled ($J_{ef} = 0$ c./sec.)
CCl_4 solution + 1 drop D_2O: A side no longer further coupled, each peak a singlet		
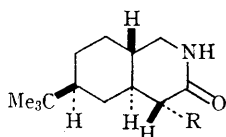
(IV) a; R = CO₂Et
b; R = CO₂H
c; R = H
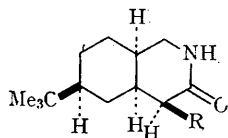
(V) a; R = CO₂Et
b; R = CO₂H
c; R = H
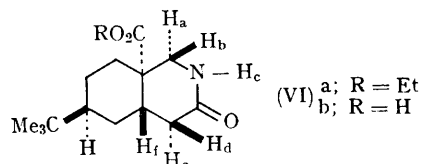
(VI) a; R = Et
b; R = H
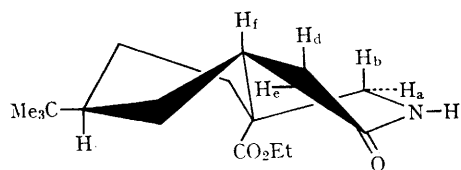
(VII)

of $\Delta G^{\ddagger}$ between the chair and the twist boat forms in equilibrium with each other. Cyclisation *via* the latter form would then result in further chair → twist-boat interconversion to restore the equilibrium.

The availability of (VIb) leads to the very interesting possibility (*via* decarboxylation and reduction) of obtaining the second frozen conformation of *cis*-6-t-butyldecahydroisoquinoline. This would be the first example of the preparation of the

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[1] R. A. Abramovitch and D. L. Struble, *Tetrahedron Letters*, 1966, 289.

[2] R. J. Abraham and J. S. E. Holker, *J. Chem. Soc.*, 1963, 806; K. Kuriyama, E. Kondo, and K. Tori, *Tetrahedron Letters*, 1963, 1485.

[3] For a better fit, the curve will probably have to be modified to take into account the influence of the electronegative substituents upon the magnitudes of the coupling constants (H. Booth, *Tetrahedron Letters*, 1965, 411).

[4] T. Takahashi (*Tetrahedron Letters*, 1964, 565) reports $J = 16.5$ c./sec. for methylene groups adjacent to an amide function.