Tetrahedron Letters,Vol.25,No.8,pp 799-802,1984
Printed in Great Britain

0040-4039/84 $3.00 + .00

WHAT IS THE SHAPE OF A *CIS*-FUSED CYCLOHEXANE BEARING A PSEUDOEQUATORIAL *t*-BUTYL GROUP?

Kay D. Onan
Department of Chemistry, Northeastern University
Boston, MA 02115 USA

Friedrich W. Vierhapper
Institut für Organische Chemie, Universität Wien
A-1090 Wien, Austria

Summary: N,2α-Dimethyl-8α-*t*-butyl-*cis*-decahydroquinoline (I) picrate crystallizes as a double chair with an equatorial *t*-butyl group and an axial N-methyl group. N,2α-Dimethyl-8β-*t*-butyl-*cis*-decahydroquinoline (II) picrate crystallizes with the equatorially substituted heterocyclic ring adopting a chair conformation. The strained A ring gives evidence that a distorted twist-boat form may be nearly as favorable as a flattened chair form.

A *tert*-butyl group will generally, due to its steric bulk, adopt an equatorial orientation on a cyclohexane ring.[1,2] Several axially, *t*-butyl substituted cyclohexane derivatives have been reported but they have been, in the main, dioxanes,[3] unsaturated systems[4] or systems with vicinal *t*-butyl groups.[5] Recently two crystallographic studies of structures bearing axial *t*-butyl groups on saturated cyclohexanes have appeared in the literature. The crystallographic study of 1-phenyl-*c*-4-*t*-butyl-*r*-cyclohexylpiperidine hydrochloride (III) shows an axial *t*-butyl group on a ring which adopts a slightly flattened chair conformation.[6] The structure of 8β-*t*-butyl-*trans*-decahydroquinoline picrate (IV) shows this molecule to adopt a minimally distorted double chair form.[7] This latter conformation is due, at least in part, to the relatively rigid *trans*-fused system. We have chosen to study the conformational consequences of *t*-butyl substitution on the more flexible *cis*-decahydroquinoline system. Our initial studies have been on N,2α-dimethyl-8α-*t*-butyl-*cis*-decahydroquinoline (I) and N,2α-dimethyl-8β-*t*-butyl-*cis*-decahydroquinoline (II), compounds biased towards one of the two possible double chair conformations by equatorial substitution at C(2).

^{1}H- and ^{13}C-NMR data from I and II[8] were consonant with double chair conformations bearing equatorial 2-methyl- and equatorial (I) and axial (II) *t*-butyl groups, respectively. No definite conclusion as to the position of the N-CH_3 substituent in I could be drawn. The rather deshielded resonance of H-2 ax indicated axial orientation, but ^{13}C shift parameters for the resulting highly strained conformation were not known. Similarly, a deformation of the cyclohexane ring in II to a twist-boat conformation could not be excluded. The room temperature ^{13}C-NMR spectrum of II showed a number of rather broad lines, indicating a contribution of a second conformer. At -40°C all resonances were sharp, but no signals of a second conformation

could be detected. To obtain additional structural information about these molecules, x-ray crystallographic studies were carried out on the picrate salts of I and II.

Molecule I·HPic (Figure 1) mitigates strain by several means. The methyl group on nitrogen is axial which obviates a *cis*-1,3-diequatorial methyl/*t*-butyl interaction. This, however, involves C(11) in α-side, transannular interactions with the hydrogens on C(5) and C(7) which, in turn, are alleviated by ring flattening. Concomitant with the closing of the endocyclic torsion angles is the opening of the exocyclic C(9)-N(1)-C(11), N(1)-C(9)-C(8) and C(9)-C(8)-C(13) valency angles (118.0, 119.0, and 119.0°, respectively). Also the bonds to C(9) are all slightly long.

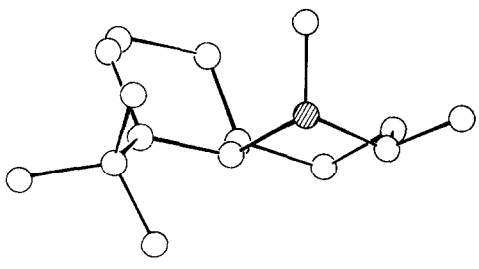

Figure 1.

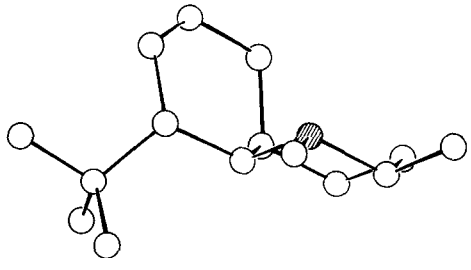

Figure 2.

Nitrogen atoms are indicated by cross hatching. Hydrogen atoms have been omitted.

The refinement of II·HPic did not proceed in a straightforward manner. Refinement of carbons 6 and 7 (to R 0.067) with anisotropic thermal parameters resulted in large thermal ellipsoids and unrealistic bond lengths and torsion angles. The electron density corresponding to the C(6),C(7) portion of the ring would not accommodate two sets of half atoms corresponding to separable conformations. Therefore carbon atoms 6 and 7 were placed at the maxima in the electron density and each was given a large isotropic thermal parameter (B = 10.9 and 16.2 $\AA^2$, respectively). These positional and thermal parameters were held constant throughout the remainder of the refinement.

Ring B of II·Hpic, equatorially substituted at both N(1) and C(2), adopts a very nearly ideal chair conformation (Figure 2). The conformation of ring A, as defined above, is seen to be a very flattened chair which helps alleviate β-side, 1,3-diaxial, transannular interactions.

Calculation of the angle between the C(8)-C(13) bond and the C(7),C(8),C(9) plane yields an indication of how far the *t*-butyl group is bent away from the ring. In III[6] and IV[7] the angle is quite large, 140.0 and 141.4°, respectively, but in II·HPic the value is 145.0°, almost identical to that found for I·HPic (145.5°) in which the *t*-butyl group is equatorial.

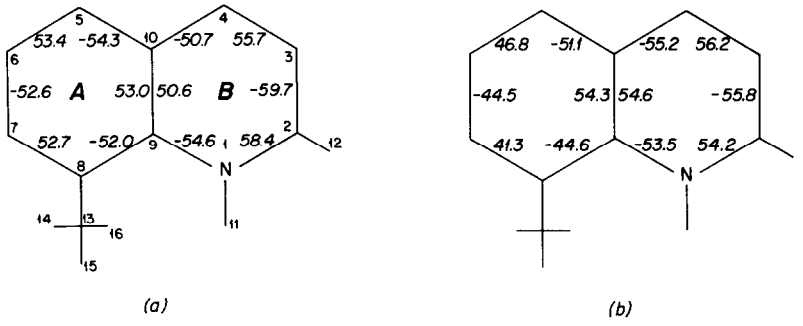

Figure 3. Endocyclic torsion angles for a) I·HPic (σ = 0.2°) and b) II·HPic (σ = 0.6-0.7°)

Examination of the final difference Fourier synthesis for II·HPic showed residual density (at the level of *ca.* 1.5 electrons/atom) in the C(6),C(7) region of the molecule (Table). These peaks define a twist-boat conformation for ring A. In this conformation C(8) is an axis carbon and therefore the *t*-butyl substituent may be described as isoclinal. This seems to indicate that in this strained, flexible system there is only a small energy barrier between a very flattened chair form and a distorted twist-boat form.

TABLE

Ring A parameters for II·HPic as defined by a) placing C(6) and C(7) atoms and b) residual electron density (*ca.* 1.5 electrons/atom)

	a(Å)	b(Å)		a(deg.)	b(deg.)
C(10)-C(5)	1.553(11)		C(10)-C(5)-C(6)-C(7)	46.8(-)	-34.0
C(5)-C(6)	1.557(-)	1.51	C(5)-C(6)-C(7)-C(8)	-44.5(-)	67.6
C(6)-C(7)	1.355(-)	1.67	C(6)-C(7)-C(8)-C(9)	41.3(-)	-43.0
C(7)-C(8)	1.540(-)	1.68	C(7)-C(8)-C(9)-C(10)	-44.6(-)	-17.2
C(8)-C(9)	1.545(9)		C(8)-C(9)-C(10)-C(5)	54.3(6)	54.3
C(9)-C(10)	1.520(9)		C(9)-C(10)-C(5)-C(6)	-51.1(-)	-25.8

Experimental

Synthesis: I and II were synthesized from the parent secondary amines[9] via Eschweiler-Clark synthesis. While methylation to II proceeded smoothly, repeated reaction was necessary to give complete conversion to I, due to the considerable strain engendered by the substituent on the nitrogen.

NMR-Spectra ($CDCl_3$, δ). I, ^1H: H-9, 2.99 (*t*, $w_{1/2}$ = 9.2); H-2a, 2.71 (d, 11, of q, 6.8, of d, 2.4); N-CH_3, 2.39 (s); CH_3-2, 1.02 (d, 6.8); CH_3-butyl, 1.00 (s). ^{13}C (+20°C): 61.0_9 (C-9); 58.6_1 (C-2); 52.7_3 (C-8); 38.2_9 (C-10); 34.3_3 (C-11); 33.1_0 (C-13); 32.4_8 (C-4); 29.0_4 (C-5); 28.9_8 (C-14,15,16); 27.2_7 (C-6); 22.9_2 (C-7); 21.7_3 (C-3); 20.8_6 (C-12).

II, ^1H: N-CH_3, 2.22 (s); H-9, 2.17 (*t*, $w_{1/2}$ = 5.6); H-2a, 1.97 (d, 11.6, of q, 6.3 of d, 3.5); CH_3-2, 1.11 (d, 6.3); CH_3-butyl, 0.95 (s). ^{13}C (+20°, -70°C): 65.0_3, 64.6_4 (C-2); 60.5_5, 61.7_2

(C-9); 44.3_2, 42.6_4 (C-8); 39.4_8, 38.7_4 (C-11); 33.7_3, 33.6_1 (C-13); 31.3_5, 31.2_4 (C-10); 30.0_8, 30.1_1 (C-3); 29.5_7, 29.2_5 (C-14,15,16); 29.0_4, 29.7_4 (C-4); 25.8_8, 24.2_9 (C-5); 23.1_6, 21.7_6 (C-7); 22.5_3, 22.3_9 (C-12); 21.5_1, 21.0_6 (C-6).

Crystallography: I·HPic $C_{21}H_{32}N_4O_7$, M = 452.5, Triclinic, a = 8.729(2), b = 9.449(2), c = 14.421(4) Å, α = 106.31(2), β = 90.98(2), γ = 95.09(2), U = 1136.0 Å^3, D_c = 1.323 g cm^{-3}, Z = 2, D_m = 1.32 g cm^{-3}. Cu-K radiation (λ = 1.5418 Å). Space group $P\bar{1}$ (C_i^1).
II·HPic $C_{21}H_{32}N_4O_7$, Monoclinic, a = 7.821(3), b = 10.239(2), c = 29.202(5) Å, β = 103.50(2)°, U = 2273.0 Å^3, D_c = 1.322 g cm^{-3}, Z = 4, D_m = 1.31 g cm^{-3}. Cu-K radiation. Space group $P2_1/c$ (C_{2h}^5) from systematic absences.

All unique diffraction maxima with $4 \leq 2\theta \leq 115°$ were collected on a Syntex automated diffractometer using variable $\theta/2\theta$ scans. Of the 3125 data collected for I·HPic, 2653 were judged observed ($I \leq 2.0\sigma(I)$) while for II·HPic 1853 of the 3567 data collected were considered observed. The structures were solved using direct phasing methods and I·HPic was refined (anisotropic O,N,C; isotropic H) to R 0.054.[10] Molecule II·HPic was refined (anisotropic O,N,C except C(6) and C(7), *vide supra*) to R 0.101.[11]

References and Footnotes

1. S. Winstein and H.J. Holness, J. Am. Chem. Soc., 77, 5562 (1955).
2. E.L. Eliel, N.L. Allinger, S.J. Angyal, and G.A. Morrison, Conformational Analysis, Wiley, NY, 1965.
3. E.L. Eliel and M.C. Knoeber, J. Am. Chem. Soc., 88, 5347 (1966); 90, 3444 (1968).
4. F. Johnson, S.W. Zito, R. Sarma, and B.M. McKeever, Tetrahedron Lett., 753 (1978).
5. B. van de Graaf, H. van Bekkum, H. van Konigsveld, A. Sinnema, A. van Veen, B.M. Wepster, and A.M. van Wijk, Rec. Trav. Chim. Pays-Bas, 93, 135 (1974).
6. P. Geneste, J.-M. Kamenka, R. Roques, J.P. Declercq, and G. Germain, Tetrahedron Lett., 949 (1981).
7. a) K.D. Hargrave and E.L. Eliel, Tetrahedron Lett., 1987 (1979); b) Isr. J. Chem., 20, 127 (1980).
8. A detailed discussion of the NMR spectra of a number of strained *cis*-decahydroquinolines will be published elsewhere.
9. F.W. Vierhapper, E.L. Eliel, and G. Zúñiga, J. Org. Chem., 45, 4844 (1980).
10. All crystallographic calculations were carried out on a VAX 11/780 computer. The principal programs used were: FMLS, anisotropic full-matrix least squares refinement, Ganzel, P.K., Sparks, R.A. and Trueblood, K.N., UCLA, modified by McPhail, A.T., Duke University; ORTEP, crystallographic illustration programs, Johnson, C.K., Oak Ridge, ORNL-3794; MULTAN 80, for description see Germain, G., Main, P., Woolfson, M.M., Acta Crystallogr., Sec. B, 1970, B26, 274.
11. Supplementary crystallographic information defining the structures has been deposited with the Cambridge Crystallographic Data Centre.

(Received in USA 6 September 1983)