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AN AXIAL t-BUTYL GROUP : CRYSTAL STRUCTURE OF 1-PHENYL-c-4-t-BUTYL-r-CYCLOHEXYLPIPERIDINE HYDROCHLORIDE

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SUMMARY : *The structure of 1-Phenyl-c-4-t-butyl-r-cyclohexylpiperidine hydrochloride 1 is shown by X-ray crystallography to have an axial t-butyl group. The conformational deformations are smaller than expected except for the outward bending of the alkyl substituent with a concomittant flattening of the corresponding half part of the chair.*

As the *t*-butyl group on a cyclohexane ring is supposed to avoid the axial position, it is used to obtain fixed chair structures in these cyclohexane series[1]. Compounds with a *t*-butyl group in axial position in a chair system are uncommon and generally such a conformation has been found in some molecule only, e.q. in the dioxane series[2], in the case of vicinal substitution of two *t*-butyl groups[3], or in unsaturated systems[4]. Recently, Eliel and coll.[5] reported the X-ray structure analysis of 8β-*t*-butyl-*trans*-decahydroquinoline picrate with an axial *t*-butyl group and relatively weak distortions of the chair.

We have found such a structure for solid 1-Phenyl-c-4-*t*-butyl-*r*-cyclohexylpiperidine hydrochloride 1. This salt is a derivative of the powerful anesthetic and psychotomimetic agent *phencyclidine*[6,8].

It should be emphasized that in such a case there are no proximity interactions due to the 1,4 position of the gemsubstitution and of the alkyl substitution. The ^{1}H and ^{13}C NMR measurements[7,8] show that 1 HCl in solution has phenyl and *t*-butyl groups equatorial. This result was confirmed by NMR and pK measurements of the free base[8,9]. Surprisingly enough, the X-ray structure determination of solid 1, HCl revealed the phenyl and *t*-butyl groups to be axial (Fig.1).

The crystals are triclinic, space group $P\bar{1}$. The cell parameters are $\underline{a}$ = 8.973 (1), $\underline{b}$ = 11.002 (3), $\underline{c}$ = 11.425 (3)Å, α = 83.75 (2), β = 76.84 (2), γ = 115.60 (1)° ; Z = 2. The diffraction data were collected with a 4-circle automatic diffractometer using a Bragg max angle 2θ(40°) with MoKα radiation. The crystal structure was solved using MULTAN 78 series of programs[10]. The refinement was performed by a least-squares treatment with complete matrix by SHELX-76 programs[11] to a R value of 5.1% with 1150 observed reflexions[12].

The cyclohexyl ring of 1 appears to be in a chair form with equatorial piperidine cycle and both axial *t*-butyl and phenyl groups. The mean endocyclic torsional angle of the cycle is 53.6° corresponding to a flattened chair[13]. The flattening is mostly located in the cyclohexyl moiety adjacent to the alkyl substituent.

In order to minimize severe nonbonded interactions between the axial *t*-butyl group

and the syn-axial hydrogens on $C_{(2)}$ and $C_{(6)}$ the t-butyl substituent deviates from the perfect staggered arrangement relative to the ring[5,13] (twist angle 10.4°).

The relief from steric crowding is accomplished mostly by the outward bending of the t-butyl group (Fig.2). The corresponding effect at the opposite part of the ring is a relative shutting of the exocyclic angles.

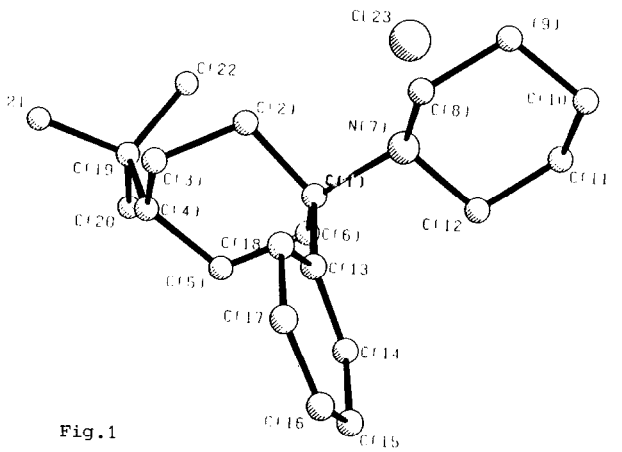

Fig.1

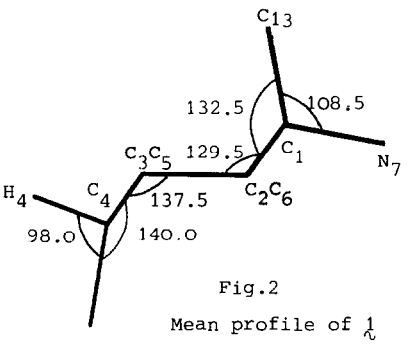

Fig.2
Mean profile of $\underset{\sim}{1}$

The low deformations of the system are closer to those observed in 2-t-butyl alkylidencyclohexane[4] than in the 8β-t-butyl-*trans*-decahydroquinoline[5] with a comparable outward bending of the t-butyl group. The reasons for the structure of $\underset{\sim}{1}$ stand probably in the "gem-effect" allowing serious modifications only at the opposite extremity of the cyclohexane.

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