Tetrahedron Letters No. 14, pp.13-16, 1959. Pergamon Press Ltd. Printed in Great Britain.

THE CONFORMATION OF 2-FLUOROCYCLOHEXANONE

Andrew S. Kende

Lederle Laboratories Division, American Cyanamid Co., Pearl River, N.Y.

(Received 19 August 1959)

IN connection with studies on the Favorskii rearrangement we have prepared 2-fluorocyclohexanone (I) in 40 per cent yield by reaction of the sodium salt of 2-hydroxymethylenecyclohexanone with perchloryl fluoride in ethanol.[1] Fluorination is accompanied by loss of the formyl group and leads directly to I, b.p. 76-77°/17 mm, n_D^{25} = 1.4390 (Found: C, 61.74; H, 7.81; F, 15.96). The conformation of this simple α-haloketone is of interest since it provides a test for the hypothesis[2] that conformational equilibria in cyclic α-haloketones are controlled largely by (1) electrostatic dipole-dipole repulsions which destabilize equatorial halogen, and (2) steric 1,3-diaxial interactions, of particular importance in the case of large axial ring substituents, which destabilize the axial conformer. Calculation of the electrostatic effect using the mathematical model of Allinger and Allinger[3]

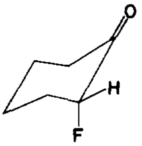
---

[1] Inman, Oesterling and Tyczkowski, J. Amer. Chem. Soc. 80, 6533 (1958). An independent synthesis of I has been achieved by W. S. Johnson and V.J. Bauer, University of Wisconsin (Private communication).

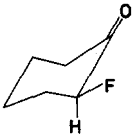
[2] Corey, J. Amer. Chem. Soc. 75, 2301 (1953). Predominance of the "chair" form is assumed cf. [Nace and Turner, Ibid. 75, 4063 (1953)].

[3] Allinger and Allinger, Tetrahedron 2, 64 (1958). The value 1.40 Å for for the C-F bond length and the limits 1.40-1.80 for the C-F bond moment were employed in the present calculations.

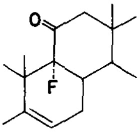
leads to an energy difference favoring Ia over Ie by 2.1 ± 0.3 kcal/mole. Since fluorine is only slightly larger than hydrogen[4] the steric effect in favor of Ie should not exceed 0.5 kcal/mole,[2] so that the net predominance of the axial conformation Ia by a factor of about 10 would be predicted.



Ia



Ie



II

In chloroform solution the fluoroketone I exhibits a single carbonyl peak at 5.78μ (in CCl_4, at 5.74 μ). The ultraviolet spectrum of I has λ_{max}^{EtOH} = 283 mμ, ε = 17.5 (in cyclohexane, λ_{max} = 294 mμ, ε = 17.7). Comparison of these data with the values observed[5] for the axially-fluorinated 9α-fluoro-11-ketosteroid grouping II, $\lambda_{CO}^{CHCl_3}$ = 5.83 μ and $\lambda_{max}^{EtOH-CHCl_3}$ = 310 mμ, (ε = 41), and with the well established conformational correlations in the infrared[6] and ultraviolet[7] spectra of cyclic α-chloro-

---

[4] Pauling, Nature of the Chemical Bond pp. 164, 189-191. Cornell University Press, Ithaca (1948). Van der Waals radii given are: F, 1.35; H, 1.2 Å.

[5] Kende and Allen, unpublished observations.

and α-bromoketones strongly suggests that 2-fluorocyclohexanone exists mainly as Ie. This assignment was supported by a determination of the dipole moment of I in benzene solution at 35°.[8] The experimental value, 3.86 ± 0.10 D, is in reasonable agreement with the calculated[3] value for Ie (4.0 ± 0.2 D) and precludes any substantial percentage of conformer Ia (2.7 ± 0.2 D) under these conditions.

Clearly the published[2,3] semiquantitative treatment of the α-haloketone problem leads to a prediction strikingly at variance with the experimental data in this and in related systems.[9] A further anomaly arises from the observation that spectra of 21-fluoropregnenolone[10] (III) in dioxane or chloroform solutions of varying concentrations possess two distinct carbonyl peaks, near 5.78 and 5.83 μ, the former somewhat more intense. Since such splitting is not observed in solid state spectra of III it may be attributed to the presence of two principal types of rotamers, possibly IIIa and IIIb, of which the former appears to predominate despite increased dipole repulsions.[11]

---

[6] Jones, Ramsay, Herling and Dobriner, *J. Amer. Chem. Soc.* **74**, 2828 (1952).

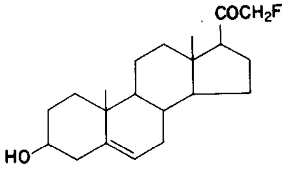
[7] Cookson, *J. Chem. Soc.* 282 (1954); see also ref. 9.

[8] The author is indebted to R. J. Best (Research Division, American Cyanamid Co., Stamford, Conn.) for the dipole moment measurements, which were carried out by the technique of Halverstadt and Kumler, *J. Amer. Chem. Soc.* **64**, 2988 (1942).

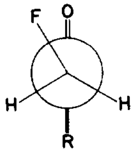
[9] E.g., 2-fluorocholestan-3-one, for which the (equatorial) 2α configuration was inferred by Gabbard and Jensen [*J. Org. Chem.* **23**, 1406 (1958)] and Djerassi, Fornaguera and Mancera [*J. Amer. Chem. Soc.* **81**, 2383 (1959)] on the basis of spectroscopic and rotatory dispersion data.

[10] Tannhauser, Pratt and Jensen, *J. Amer. Chem. Soc.* **78**, 2658 (1956).

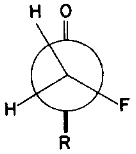
[11] Entirely comparable phenomena have been observed for chloroacetone



III



IIIa



IIIb

The factors contributing to the observed stabilities of electrostatically unfavorable conformers are difficult to evaluate. It is likely that a dipole-solvent interaction of the type studied by Powling and Bernstein[12] effects a substantial decrease in the electrostatic energy term for the more polar isomer. In addition, the possible operation of a stereospecific hyperconjugation effect involving that component of each α C-H sigma bond which is perpendicular to the C-C-O plane could provide optimum stabilization to those conformers (such as Ie and IIIa) having the C-F bond very nearly within the C-C-O plane.[13]

---

and for a number of α-chloroacetophenones by Bellamy, Thomas and Williams, J. Chem. Soc. 3704 (1956); 4294 (1957).

[12] Powling and Bernstein, J. Amer. Chem. Soc. 73, 1815 (1953).

[13] Evidence in favor of hyperconjugative stabilization of carbonyl compounds by α C-H bonds has been presented by Baddeley and Gordon, J. Chem. Soc. 2190 (1952); and by Taft and Kreevoy, J. Amer. Chem. Soc. 79, 4011 (1957).