Tetrahedron Letters No. 20, pp. 1665-1670, 1971. Pergamon Press. Printed in Great Britain.

INTRAMOLECULAR HYDROGEN BOND IN A SYSTEM WITH UNCOMMON TORSIONAL ANGLES : 4,5-DISUBSTITUTED DERIVATIVES OF TRICYCLO/4,4,0,$0^{3,8}$/DECANE (TWISTANE)

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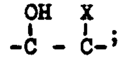
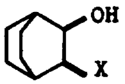
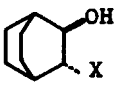
(Received in UK 23 March 1971; accepted in UK for publication 6 April 1971)

The infrared spectroscopic determination of intramolecular hydrogen bonding represents a stereochemical tool of great value[1]. It has been shown that the spectral shift of the bonded hydroxyl band, $\Delta\nu$, depends very strongly on molecular conformation and many attempts are reported[2-6] to correlate the magnitude of $\Delta\nu$ with the torsional angle τ between the C-OH and C-X bonds in compounds of the type  $-\overset{\overset{\text{OH}}{|}}{\text{C}}-\overset{\overset{\text{X}}{|}}{\text{C}}-$; however, all these attempts suffer from a scarcity of suitable models with "guaranteed" fixed values of τ .

The angles 0-10° and 120±10° may be found in the epimeric 2,3-disubstituted bicyclo[2,2,2]octane derivatives I and II. Other, yet more flexible, models are some biased derivatives of cyclohexane in which - assuming a sterically homogeneous chair conformation - the axial-equatorial (cis) and diequatorial (trans) arrangement such as III and IV may represent very approximately the



I



II

III

IV

values $\tau \leqq 60°$ and $\tau \geqq 60°$, respectively. However, no models are known as yet which contain "intermediate" values, i.e. $\tau \sim 30°$, $\tau \sim 90°$, and $\tau \sim 150°$, nor is it known with sufficient accuracy up to which τ the intramolecular hydrogen bond in a given system is capable of existing.

One completely fixed system bearing such angles is the tricyclo/4,4,0,0^{3,8}/decane (twistane) system in which the torsional angles between substituents on C_4 and C_5 are 30°, 90° and 150° (cf. Fig. 1). We synthesised the stereoisomeric 4,5-disubstituted derivatives V-XI (Scheme 1) to obtain for the first time information about the interactions and energetic situation in compounds with these dihedral angles[7].

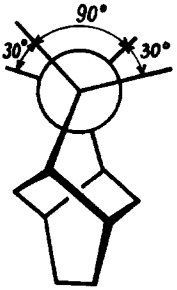
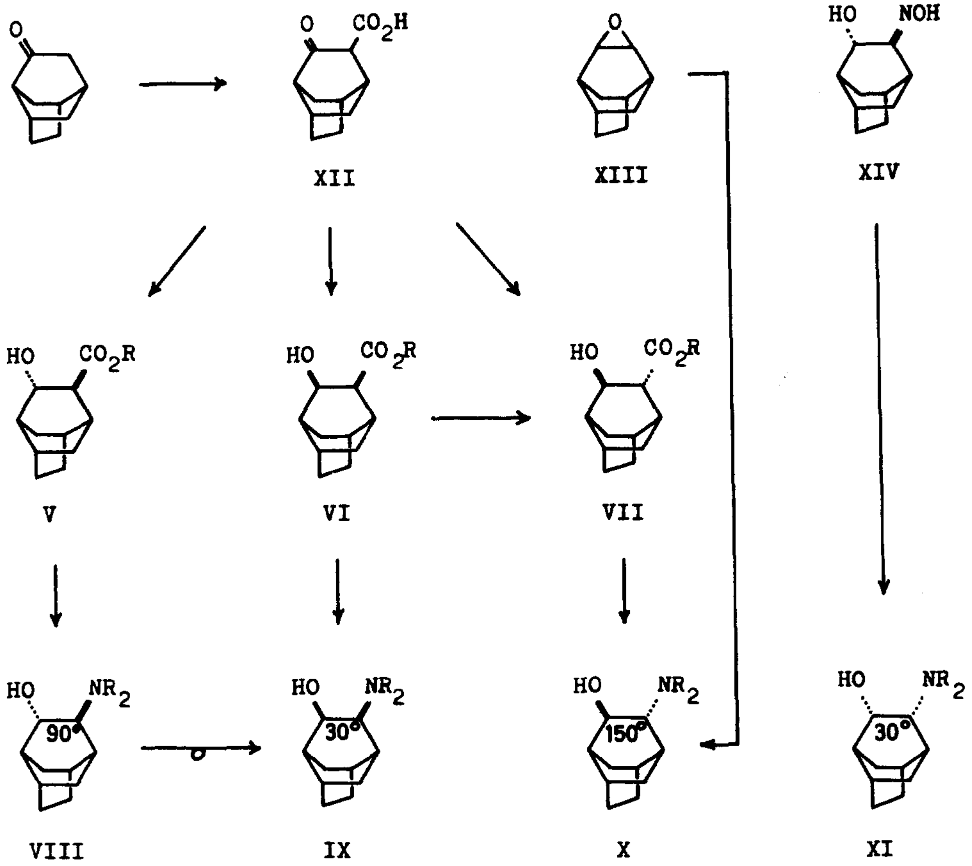


Fig. 1

Carboxylation of 4-twistanone[9] followed by catalytic reduction of the resulting keto-acid XII in acetic acid gave predominantly the cis-acid VIa, m.p. 166-167.5°C, which was isomerised via the ester to the trans-acid VIIa, m.p. 188-190°C. Sodium borohydride reduction of the keto acid XII afforded a mixture of acids Va, VIa, and VIIa from which the pure acid Va, m.p. 184-186°C, was isolated, together with VIa and VIIa, by chromatographic separation of the esters on silica gel and subsequent saponification. The esters Vb (m.p. 47°C), VIb (m.p. 52°C), and VIIb (oil) were transformed separately by Curtius degradation into aminoalcohols VIIIa, IXa and Xa, melting at 146-148°C, 150.5-151°C and 195-200°C, respectively. The trans-aminoalcohol Xa was also obtained by a stereospecific ammonolysis of the epoxide XIII (m.p. 188-190°C) which in turn was prepared from 4-twistene[10] by treatment with m-chloroperoxybenzoic acid. The remaining cis-aminoalcohol XIa, m.p. 126-128°C was synthesised by stereospecific catalytic reduction of the oxime XIV, m.p. 166-167°C (obtained from the acyloin[10]). Clarke-Eschweiler methylation afforded the corresponding N,N-dimethyl derivatives VIIIb, IXb, Xb and XIb which melted at 70-72°C, 44.5-45.5°C, 102-103°C and 38-39°C, respectively. The configuration of all compounds was unequivocally deduced from their chemical behaviour and/or from their infrared and NMR spectra. Satisfactory analytical and mass spectroscopic data were obtained.

The infrared spectroscopic data on hydrogen bonding in twistane derivatives are summarised in TABLE 1 together with results obtained on systems representing other important dihedral angles. For obvious geometric reasons, the compounds with $\tau \sim 150^\circ$ exhibit no hydrogen bonding, as in the case of



a, R = H

b, R = CH_3

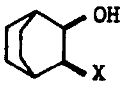
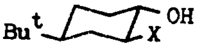
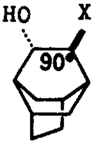
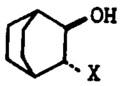
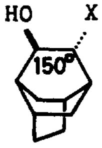
Scheme 1

the already known compounds with $\tau \sim 120^\circ$.

The situation is, however, different with derivatives where $\tau \sim 90^\circ$. Thus, the spectrum of the aminoalcohol VIIIa exhibits, in addition to the free hydroxyl band at 3622 cm^{-1}, a band at 3604 cm^{-1}. The intensity of this band decreases with increasing temperature whereas the intensity of the band at higher wave-number increases. This, together with other reasons which we shall discuss in the full communication, leads us to assume that the band at lower wave-number is due to hydrogen-bonded hydroxyl rather than to another non-bonded rotamer.

TABLE 1

Frequencies (cm^{-1}) and $\Delta\nu$ Values (in parentheses) of Selected Model Systems with Given Torsional Angles τ between the C-OH and C-X Bonds

τ	System	X			
		NH_2	$N(CH_3)_2$	OH	CO_2CH_3
0-10°		- 3370 (237)[b]	- 3342 (275)[c]	3633 3548 (85)[d]	?[e]
30° [a]		- 3375 (248)	- 3350 (269)	3624 3546 (78)[f]	3615
≦60°		3631 3501 (130)[c]	- 3480 (150)[c]	3626 3587 (39)[g]	3620 3540 (75)[h]
≧60°		3630 3535 (95)[i]	- 3480 (150)[i]	3634 3602 (32)[g]	3620 3595 (75)[h]
90°		3622 3604 (18)	3618 - (0)	?[e]	3624 3609 (15)
120±10°		3617 - (0)[b]	3617 - (0)[b]	3633 - (0)[j]	?[e]
150°		3623 - (0)	3619 - (0)	?[e]	3626 - (0)

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[a] Only cis-isomers of the configuration VI were used as models; [b] ref.11; [c] ref.12; [d] ref.3,11; [e] not measured; [f] ref.10; [g] values for the epimeric cyclohexane-1,2-diols[2]; [h] ref.13; [i] ref.14; [j] ref.15.

As estimated from temperature dependence measurements, the enthalpy of the equilibrium $OH_{free} \rightleftharpoons OH_{bonded}$ amounts to $\sim$ -1.5 kcal/mol, which is comparable with ΔH = -2 kcal/mol found[14] in the diequatorial compound IV ($X = NH_2$) ($\tau \geqq 60^\circ$). It must be born in mind, however, that the ΔH values obtained in this way reflect not only the energy of the hydrogen bond as such but also the energetic demands of the rotamers around the C-O and C-N bonds. Therefore the actual net enthalpy of the hydrogen bond is likely to be different from(presumably smaller than) the value found. The spectrum of the corresponding N,N-dimethylaminoalcohol VIIIb exhibits no bonded hydroxyl band. This fact, though surprising on first sight, may be explained by an energetically unfavourable hydrogen-bonded conformation: here both N-methyl groups are pressed heavily against the hydrogens at C_2 and C_3 thus causing a strain of prohibitive magnitude.

The spectrum of the hydroxy-ester Vb also exhibits a hydrogen bond; this is to be expected because in this case the system forming the chelate ring has one more degree of freedom (six-membered ring) as compared with the aminoalcohol VIIIa (five-membered ring)[16].

It is generally known that the $\Delta\nu$ value increases with decreasing torsional angle. However, going from $\tau \sim 30^\circ$ to $\tau \sim 0 - 10^\circ$ one finds practically no further increase in $\Delta\nu$. This fact cannot be due to inherent geometrical differences between the systems used as models (slightly different valence angle deformations in twistane and bicyclo/2,2,2/octane systems) because this should result in an opposite effect. One possible explanation may be that the geometrically optimal planar chelate ring (with the shortest distance between the hydroxyl hydrogen and the acceptor atom) in a system with $\tau \sim 0^\circ$ is not the optimal conformation in terms of energy. In order to minimise eclipsing strain, the functional groups may tend either to increase the angle τ and/or to rotate around the C-O and C-N bonds, thus increasing the distance between the bonded atoms. It can be shown by simple geometric consideration that in a system with $\tau = 0^\circ$ even a relatively small rotation around the C-O and C-N bonds can affect very unfavourably the geometry of the chelate ring.

We are pursuing the problem of reactivity and mutual interactions between vicinal substituents on the twistane system further and the results of our studies will be published shortly.

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