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OPTICALLY ACTIVE 4-AZATRICYCLO/4,4,0,0^{3,8}/DECAN-5-ONE: MODEL OF A NON-PLANAR AMIDE BOND

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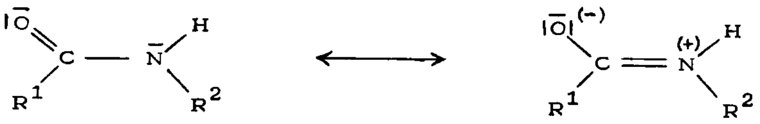
The generally accepted concept of the amide group as a resonance hybrid of the canonical forms A and B leads to the assumption of a planar arrangement of all the atoms of the group. However, recent X-ray[1,2] and spectroscopic[3] investigations indicate that in a number of amides and peptides the geometry of the amide group to some extent deviates from planarity. This deviation can be due either to rotation of the R^1-C=O and H-N-R^2 planes around the $C_{(O)}$-N bond, or to a pyramidal arrangement at the nitrogen[1].



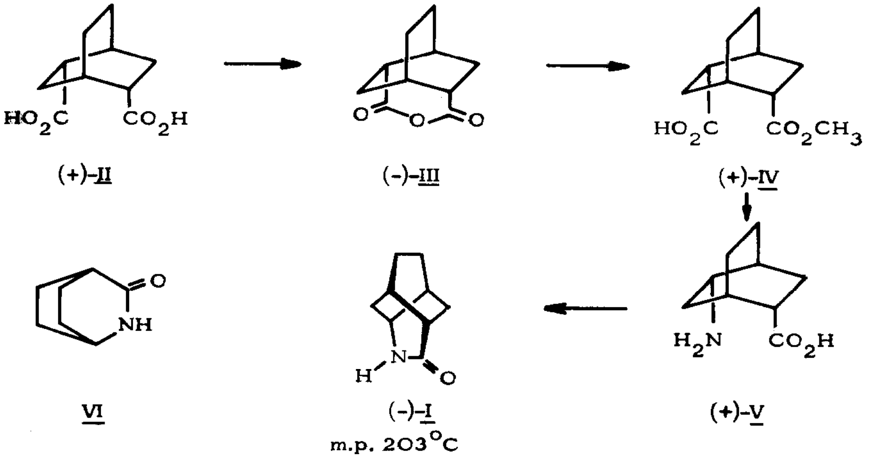
A B

A method of detection of a non-planar amide group in solution would evidently be of great importance. Spectral, particularly chiroptical, methods seem to be suitable for this purpose. It follows from quantum chemical calculations that in a non-planar amide group the energy of both electron transitions ($n-\pi^*$ and $\pi-\pi^*$) is lowered[4] and consequently a bathochromic shift of the corresponding CD-bands should be observed.

We have now prepared the optically active 4-azatricyclo/4,4,0,0^{3,8}/decan-5-one, (-)-I, of known absolute configuration (P helicity). It was synthesized starting from (2S,5S)-endo-bicyclo/2,2,2/octane-2,5-dicarboxylic acid, (+)-II, which was obtained by resolution of its dehydroabietylamine salt (for the preparation of (-)-II, its correlation with (+)-twistane and revision of absolute configuration of twistane see[5,6,7]). The reaction sequence is outlined in Scheme 1.

The torsion angle between the $R^1-C_{(O)}$ and R^2-N bonds in (-)-I is about 30°. Since this system is rigid we may anticipate that solvent-induced conformational changes will be negligible. The non-planar arrangement of the amide group should favour the canonical structure A and thus bring the spectral parameters close to that found for ketones and amines. The IR-spectrum of the unassociated lactam I (in CCl_4) was compared with the spectrum of 2-azabicyclo/2,2,2/octan-3-one (VI), compound with planar amide group and approximately the same bond angles. The wavenumber of the N-H stretching vibration band is lowered by 18 cm^{-1}, that of the C=O stretching vibration band is increased by 12 cm^{-1}, and the cis-amide-II band (contributed by the $C_{(O)}-N$ stretching vibration) is shifted by 20 cm^{-1} to lower wavenumbers relative to the values found for VI (Table 1). Similar differences were also found in chloroform solutions. These differences can be rationalised - in agreement with the above considerations - as a consequence of a pronounced non-planarity of the amide group in I.

Scheme 1



The CD-curves show that the n-π* transition band exhibits a substantial bathochromic shift in less polar solvents, while the π-π* transition is only very little changed (Table 2). The CD-curve of (-)-I in cyclohexane exhibits, in addition to both well-separated extrema, a shoulder at 215 nm of an unclear origin. Since in I the only chromophore capable of absorption in this region is the amide group, this shoulder might be tentatively ascribed to n-σ* transition, the existence of which has already been suggested several times (see e.g.[8]). The bathochromic shift of n-π* and π-π* bands due to the non-planarity

TABLE 1

Wavenumbers (cm^{-1}) of Selected IR-Bands of Lactams I and VI

Compound	Solvent	ν (N-H)	ν (C=O)	cis-Amide-II
I	CCl_4 (6×10^{-4} M)	3421.8[a]	1710[a,b]	1405[a]
I	$CHCl_3$ (3×10^{-2} M)	3416[c]	1679, 1690[c]	1418[c]
VI	CCl_4 (6×10^{-4} M)	3439.8[a]	1698.2[a]	1425
VI	$CHCl_3$ (4×10^{-2} M)	3422[c]	1670sh, 1678[c]	1438[c]

[a] Measured on a Perkin Elmer 621 instrument. [b] Value corrected for Fermi resonance, see[9]; experimental values: 1702.0 and 1716.8 cm^{-1}. [c] Measured on a UR-10 Zeiss Jena spectrometer.

TABLE 2

Wavelengths (nm) and Molar Ellipticities ($\theta \times 10^{-3}$) of CD-Bands of Lactam (-)-I in Various Solvents[a]

Solvent	$n-\pi^*$	$\pi-\pi^*$
Cyclohexane	231.5 (-26.3)	197 (+29.1)
Dioxan	230.5 (-34.0)	b
Acetonitrile	227.5 (-34.0)	b
Methanol[c]	219.5 (-42.8)	196.5 (+22.6)
CF_3CH_2OH	215.5 (-14.7)	194 (+ 8.8)
$CF_3CHOHCF_3$	212 (-28.7)	191 (+15.7)
$CF_3COCF_3.3H_2O$	210.5 (-15.4)	196 (-1.0)

[a] Measured on a Jouan CD-185/II instrument, concentration about 25 mg/100 ml. [b] Out of the measured region. [c] $[\alpha]_D^{20}$ -324.3° (c 0.5).

of the amide group does not seem to be pronounced. Unfortunately, no reference compound of a similar structure with a planar amide group is available. Contrary to the situation generally found in amides, the intensity of the $n-\pi^*$ dichroic band is higher than the intensity of the $\pi-\pi^*$ band. According to the quantum chemical calculations of Scheraga and collaborators[4], the oscillator strength of the $\pi-\pi^*$ transition decreases as the amide bond is twisted showing a minimum at 90°, whereas the dependence of the oscillator strength of the $n-\pi^*$ transition on the torsion angle is more complicated, having two maxima (at 30° and at 150°) and one minimum (at 90°). If we accept these calculations, we could interpret the high intensity of the $n-\pi^*$ band as a consequence of non-planarity of the amide group in the lactam I.

Studies on other conformationally fixed amides are in progress and the results will be published in the Collection of Czechoslovak Chemical Communications.

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