

CHIROPTICAL PROPERTIES OF
 (–)-4-METHYL-4-AZATRICYCLO[4,4,0,0^{3,8}]DECAN-5-ONE —
 A LACTAM WITH A NON-PLANAR TERTIARY *cis*-AMIDE GROUP

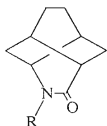
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CD spectra of the title lactam *II* were measured in solvents of various polarity. Parameters of the dichroic bands (negative and positive for the respective $n-\pi^*$ and $\pi-\pi^*$ transition of the (–)-enantiomer) compared with the analogous data of the related non-methylated lactam *I* indicate a probable decrease of the pyramidal character of bonds attached to the nitrogen atom of the tertiary amide group. The methyl group position was optimized by the CNDO/2 method and the found most stable molecular geometry ($\theta_N = 20.1^\circ$; $\phi = 86.7^\circ$) was utilized in the CNDO/S calculation of the optical rotatory strengths of $n-\pi^*$ and $\pi-\pi^*$ transitions. The results obtained exhibit satisfactory agreement with experiment.

In the foregoing communications¹⁻⁴ we reported a relation between CD data and molecular geometry of (–)-(2*S*,5*S*)-4-azatricyclo[4,4,0,0^{3,8}]decan-5-one (*I*). X-Ray analysis of this optically active lactam possessing a rigid twistane skeleton revealed a torsional deformation ($\Delta\omega = -14.49^\circ$ according to notation of Ramachandran⁵) of the amide group. Having optimized the position of the hydrogen atom bonded to the amide nitrogen by the CNDO/2 method we found, that in addition to the above value of $\Delta\omega$ the non-planarity of the amide group in this compound could be described by the angle $\theta_N = 26.4^\circ$ characterizing the pyramidal arrangement of bonds attached to the nitrogen atom. CNDO/S calculation based on this molecular geometry affords



(–) – *I*. R = H

(–) – *II*. R = CH₃

spectral parameters of $n-\pi^*$ and $\pi-\pi^*$ transitions well reproducing the basic features of UV and CD spectra excepting band positions. Calculations demonstrated the

non-planarity of the amide group to be manifest among others by an augmentation of the rotatory strength of the $n-\pi^*$ transition relative to that of the $\pi-\pi^*$ transition.

In the present report we will discuss CD and ORD spectra of (-)-(2*S*,5*S*)-4-methyl-4-azatricyclo[4,4,0,0^{3,8}]decan-5-one (*II*), the N-methyl derivative of the lactam *I*, in order to verify the validity of the above conclusions also for the case of a tertiary amide.

EXPERIMENTAL

Synthesis of the lactam (-)-*II*, $[\alpha]_D^{25} -485^\circ$ (c 0.066, cyclohexane) has been reported². CD spectra were recorded on Roussel-Jouan Dichrographe CD 185/II equipped with cryostat. The solvents as well as the conditions of measurement were identical with those used in the case of lactam³ *I*. ORD measurements were carried out using Jasco ORD/UV-5 spectropolarimeter; the spectra were measured in cyclohexane. CD curves were simulated by the sum of Gaussian bands and the parameters describing them were utilized in the calculation of experimental values of rotatory strength. Simulated curves of both the lactams *I* and *II* related to the measurements performed in cyclohexane were compared with the experimental ORD spectra using the Kronig-Kramers relationship. The integral evaluating subroutine reported by DeTar⁶ was utilized for this purpose. All the above mentioned transformations of experimental data were performed on Hewlett-Packard 9830A calculator.

Molecular geometry was optimized by the standard CNDO/2 method while excitation energies and optical rotatory strengths were computed within the framework of the CNDO/S procedure with the parameters reported by Ellis and coworkers⁷. The excited state wave functions were obtained by the configuration interaction of 36 singly excited electronic configurations. Details of these calculations executed on CDC 3300 computer are reported elsewhere⁴.

RESULTS AND DISCUSSION

CD data of the lactam (-)-*II* are summarized in Table I. Analogously to the case of the secondary amide (-)-*I* a negative Cotton effect in the range of the amide $n-\pi^*$ transition has been detected. The band is bathochromically shifted in less polar solvents (the shift of 18.6 nm for the pair 1,1,1,3,3,3-hexafluoro-2-propanol-cyclohexane). The wavenumbers denoting the maxima exhibit a linear correlation to E_T values characterizing the polarity of the particular solvents⁸ (for this case of four experimental points the correlation coefficient amounts to 0.97). Compared with the data of the non-methylated lactam *I* the positive Cotton effect related to the $\pi-\pi^*$ transition exhibits a shift of about 10 nm to longer wavelengths. The spectrum simulated by Gaussian bands indicates the presence of an additional weakly negative dichroic band at 218 nm (in cyclohexane, Fig. 1). The band in question corresponds to a similar transition found in this spectral range also in the case of lactam *I* and assigned therein to a Rydberg $n-3s$ transition^{3,4}. This Cotton effect is hard to observe in the spectra of lactam *II* since it overlaps with the neighbouring bathochromically shifted $\pi-\pi^*$ transition. The tail of fourth negative band in the short wavelength region has been found in lactam *II* dissolved in cyclohexane and water. Rotatory

strengths of both the $n-\pi^*$ and $\pi-\pi^*$ transitions exhibit no correlation to E_T values. The dependence of the CD parameters on temperature (methanolic solution; temperature range within -80° to $+40^\circ\text{C}$) does not exhibit a significant deviation from the data obtained at the same conditions for the lactam *I*. At low temperature a hypsochromic shift accompanied by hyperchromic effect has been observed for Cotton effects of the respective $n-\pi^*$ and $\pi-\pi^*$ transitions. Hence, the basic features of the CD spectra of lactam *II* are identical with those of its non-methylated analogue *I*. Certain minor differences were found which are given as follow: Low values of the rotatory strength of $n-\pi^*$ transition relative to that of $\pi-\pi^*$ transition, bathochromic shift of $\pi-\pi^*$ transition and existence of a further CD band lying below 184 nm.

TABLE I

CD Spectra of Lactam (–)-*II* in Various Solvents

Solvent	Direct readings ^{a,b}		Separated values ^a			
	λ_{\max}	$[\Theta]_{\max} \cdot 10^{-3}$	λ_{\max}	$[\Theta]_{\max} \cdot 10^{-3}$	Δ_{\max}	$R \cdot 10^{39}$
<i>n</i> - π^* transition						
Cyclohexane	231.0	-36.9	230.0	-38.0	16.5	-3.35
Acetonitrile	227.5	-48.7	226.6	-50.0	14.6	-3.97
Methanol	222.0	-31.0	219.5	-33.0	15.9	-2.94
Water	220.0	-36.8	217.0	-41.0	14.0	-3.26
2,2,2-Trifluoroethanol	218.0	-44.1	215.8	-46.0	13.3	-3.49
1,1,1,3,3,3-Hexafluoro-2-propanol	215.5	-33.2	212.0	-39.5	14.4	-3.31
π - π^* transition						
Cyclohexane	204.5	53.0	205.2	56.5	13.0	4.41
Acetonitrile	204.5	60.9	205.6	67.0	9.8	3.93
Methanol	201.5	34.2	203.3	45.5	10.5	2.90
Water	200.0	33.9	202.3	45.5	10.5	2.91
2,2,2-Trifluoroethanol	197.5	44.9	198.9	54.0	10.0	3.34
1,1,1,3,3,3-Hexafluoro-2-propanol	195.5	30.3	198.0	44.0	11.0	3.01
Rydberg <i>n</i> -3 <i>s</i> transition						
Cyclohexane	^c	^c	218.3	-10.0	6.0	-0.34

^a $[\Theta]_{\max}$ molar ellipticity at the CD maximum in $\text{deg cm}^2 \text{ dmol}^{-1}$, Δ_{\max} band halfwidth in nm, R rotatory strength in cgs. ^b These values characterize the apparent band maxima and are directly related to the chart reading. ^c The band is not directly observed.

It is possible that the last mentioned band causes the observed difference between the experimental ORD curve of lactam *II* and the curve computed from the simulated CD data (Fig. 2) with the use of the Kronig-Kramers relationship. In the case of compound *I* this procedure results in a good agreement of the calculated and observed ORD curves.

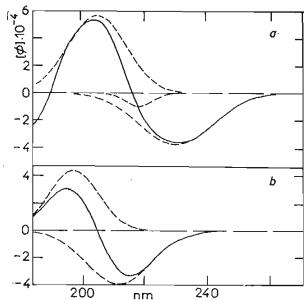


FIG. 1

CD Spectra of Lactam (-)-*II* *a* in Cyclohexane; *b* in 1,1,1,3,3,3-Hexafluoro-2-propanol

(—) Experimental CD spectra;
 (---) Gaussian bands obtained by simulation.

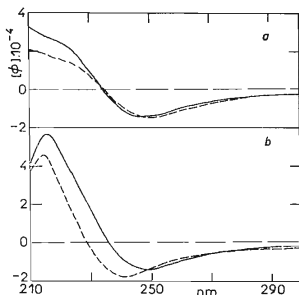


FIG. 2

ORD Spectra of Lactams *a* (-)-*I*; *b* (-)-*II*
 (—) Experimental curves; (---) spectra computed from the simulated CD data via the Kronig-Kramers relationship. Measurements were carried out in cyclohexane.

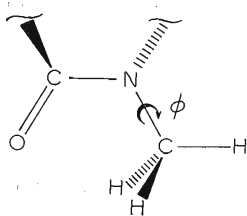


FIG. 3

Starting Orientation of the Methyl Group in Lactam (-)-*II* ($\phi = 0^\circ$)

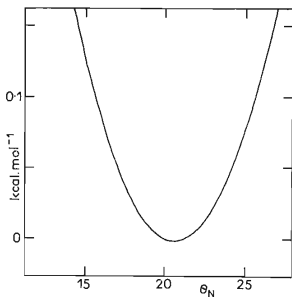


FIG. 4

Dependence of the CNDO/2 Energy of Lactam (-)-*II* on θ_N

Comparing the CD data of lactams *I* and *II* with the calculated relation⁴ of the optical rotatory strength of lactam *I* and the magnitude of angle Θ_N we may suggest the cause of the observed decrease of $n-\pi^*$ rotatory strength to consist in the diminished pyramidity of bonds attached to the amide nitrogen atom of compound *II*. We attempted to verify this hypothesis using semiempirical calculations. Due to the fact, that X-ray geometry of the non-crystalline compound *II* is not known, we started the calculation with the optimized geometry of lactam *I* ($\Delta\omega = -14.5^\circ$; $\Theta_N = 26.4^\circ$, ref.⁴). The N—H group was replaced by the N—CH₃ one. The necessary additional geometric parameters were chosen in the following way: bond lengths C—N 0.147 nm, C—H 0.109 nm; bond angles N—C—H, H—C—H 109.47°. Conformation of the methyl group was described by the angular parameter Φ according to Yan and coworkers⁹ ($\Phi = 0^\circ$ assuming one C—H bond of the methyl group to be antiperiplanar to the C—N bond in the planar arrangement of the amide group. Positive values are related to a clockwise rotation around the CH₃—N bond, cf. Fig. 3). In the first step, the value of Θ_N was optimized by the CNDO/2 method (Fig. 4), while Φ was kept at 60° (in this conformation the C—H bond eclipses the C=O one). Using the optimized value of $\Theta_N = 20.1^\circ$ the second energy minimization was performed with respect to the angle Φ (Fig. 5). The most stable molecular conformation ($\Phi = 86.7^\circ$, Fig. 6) agrees with the situation found by Yan and coworkers⁹ when calculating the molecular geometries of amides methylated on the

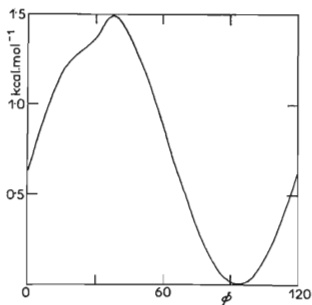


FIG. 5

Alterations of the CNDO/2 Energy of Lactam (—)-*II* Related to Rotation around the N—CH₃ Bond ($\Theta_N = 20.1^\circ$)

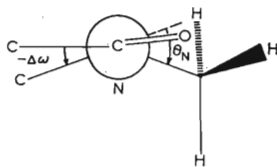


FIG. 6

Optimized Geometry of the Amide Group in Lactam (—)-*II* Projected Along the C—N Bond ($\Delta\omega = -14.5^\circ$; $\Theta_N = 20.1^\circ$; $\Phi = 86.7^\circ$).

For clarity the angles were slightly enlarged.

nitrogen atom. (In the framework of the CNDO/2 method the methyl group tends to direct one C—H bond towards the amide oxygen atom.) However, this conformation differs from the most stable arrangement localized by PCILO¹⁰ and *ab initio*¹¹ methods at $\Phi = 0^\circ$.

In accord with the above idea the calculation has shown a decrease of the pyramidal character of bonds attached to the nitrogen atom. The computed pyramid is not regular in the sense of the Ramachandran's relation⁸ of $\Theta_N = -2\Delta\omega$. However, the deviation found may be influenced by the fact that we do not know the actual geometry of the skeleton of lactam *II*. CNDO/S calculation of the rotatory strength of $n-\pi^*$ and $\pi-\pi^*$ transitions of lactam (-)-*II* was performed for the optimized molecular geometry reported above. In the qualitative sense, the results obtained (Table II) reproduce correctly the experimental CD data as well as the characteristic differences between the chiroptical parameters of lactams *I* and *II* (bathochromic shift of $\pi-\pi^*$ transition and the diminished ratio of $n-\pi^*$ and $\pi-\pi^*$ rotatory strengths in the lactam *II*). The worse overall agreement of the computed numerical values of optical rotatory strength with the experiment exhibited in the case of lactam *II*, may be explained by a less accurate molecular geometry used in the calculation.

TABLE II

Spectral Parameters of $n-\pi^*$ and $\pi-\pi^*$ Transitions of Lactams (-)-*I* and (-)-*II*

Calculations are based on the optimized molecular geometries. Experimental data are related to the measurements performed in the cyclohexane solutions.

Value	<i>I</i>		<i>II</i>	
	exp.	calc.	exp.	calc.
$n-\pi^*$ transition				
λ_{\max} , nm	232	289	230	289
f	0.0056	0.0082		0.0069
$R \cdot 10^{39}$ cgs	-2.51	-2.51	-3.35	-0.81
$\pi-\pi^*$ transition				
λ_{\max} , nm	197	164	205	172
f	0.0345	0.1316		0.1433
$R \cdot 10^{39}$ cgs	2.07	1.21	4.41	2.80

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