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POLYCYCLIC DILACTAMS WITH INHERENTLY CHIRAL AMIDE CHROMOPHORES

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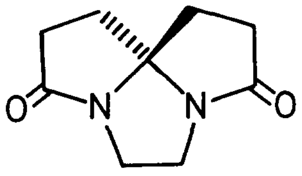
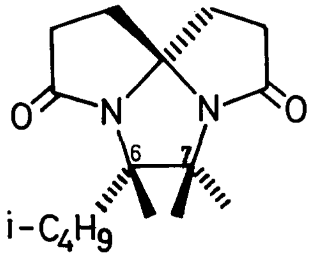
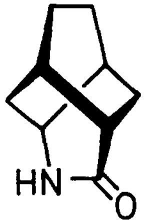
The properties of non-planar amide groups may be directly investigated using polycyclic lactams as models[1,2]. The similar class of dilactams affords an opportunity to study the interactions between amide groups fixed in the rigid polycyclic skeleton[3]. We have previously reported[3] the synthesis and infrared spectral data of the series of racemic dilactams of the type I. These structures belonging to the C_2 symmetry group[4] possess axial chirality and consequently exist in two enantiomeric forms.



(-)-I



(+)-II



(-)-III

Resolution of racemic 5,8-diazatricyclo[6,3,0,0^{1,5}]undecane-4,9-dione (I) on an acetylcellulose column (water) afforded optically active material ($[\theta]_{204}$ = -16400 deg cm^{2}dmol^{-1} in the first fraction. A portion enriched in the (+)-enantiomer (the maximum reached $[\theta]_{205}$ = + 7200 deg cm^{2}dmol^{-1}) was obtained from the last fractions. These portions exhibit CD curves of enantiomeric shape.

The absolute configuration of the resolved dilactam I was determined by an indirect procedure with the use of reference compound II. The dilactam II was prepared by the condensation of diethyl 4-oxoheptanedioate with (S)-1,2-diamino-

-4-methylpentane obtained upon reducing (S)-leucinamide with diborane. Whereas the condensation leading to I occurred already at room temperature, the formation of II took place only at considerable higher temperature (200 °C, sealed tube). In principle, the reaction can afford two stereoisomers differing in chirality of the tricyclic moiety, while the configuration at $C_{(6)}$ must in both cases conform to the starting (S)-leucine. However, only one isomer, melting at 92-94 °C (ether), was isolated and the treatment of the reaction mixture did not show any detectable amount of the other diastereoisomer. The compound conforms to the proposed structure by its elemental analysis and mass spectral data. Neither gas chromatography nor ^{1}H-NMR spectra indicated the presence of two diastereoisomers as well.

We may derive the relation of the configuration at $C_{(6)}$ to the spatial arrangement of II using ^{1}H-NMR spectra[5]. The parameters which are decisive for the solution of the given task are related to protons attached to $C_{(6)}$ and $C_{(7)}$. Considering the racemic dilactam I, the corresponding signals manifest as an isolated $AA'BB'$ system with $\delta_A = 4.04$ ppm and $\delta_B = 2.87$ ppm (the pairs of <u>trans</u>-vicinal protons are symmetry equivalent). The signals related to the three protons at $C_{(6)}$ and $C_{(7)}$ in the compound II are located at a sufficient distance from those of the isobutyl group; nonetheless, the isobutyl group at $C_{(6)}$ enlarges the spin system by further protons. The use of NMDR experiments enabled us to assign these signals and to obtain the related ^{1}H-NMR parameters ($C_{(6)}H$: $\delta = 4.28$ m, $J_{6,7} = 6.0$ and $\leqslant 0.5$ Hz; $C_{(7)}H_2$: $\delta = 3.81$ d, $J_{7,7} = 11.5$ and $J_{7,6} \leqslant 0.5$ Hz, $\delta = 3.02$ dd, $J_{7,7} = 11.5$ and $J_{7,6} = 6.0$ Hz). We may state, comparing the found values of $J_{6,7}$ with dihedral angles derived from the analysis of molecular models and respecting progeny to the starting leucine, that the isomer formed by condensation has the depicted structure II with dihedral angles between protons at $C_{(6)}$ and $C_{(7)}$ approximately 90° and 30°, and not the alternative diastereoisomeric structure with dihedral angles approximately 30° and 150°.

CD spectrum of the compound IIa (water) reveals the presence of three dichroic bands. The first positive, shown as a shoulder at 219 nm, was assigned to an $n-\pi^*$ transition because of the bathochromic shift to 223.5 nm in acetonitrile. The second positive band with maximum at 204.5 nm is considered to be a long wavelength branch of the $\pi-\pi^*$ couplet the short wavelength branch of which is indicated by the negative dichroic absorption below 200 nm. It may be inferred that the overall chirality of the tricyclic moiety in this case contributes decisively to the optical activity owing to the spatial fixation of inherently chiral non-planar amide groups. The contribution due to the simultaneously operating isobutyl group at $C_{(16)}$ is probably of minor importance. In accord with this hypothesis, we find a significant similarity in CD parameters (including the solvent dependence) of the lactams (+)-II and (-)-I, cf. Fig. I. Comparison of the CD spectra of these dilactams may then be used for determination of the absolute configuration of the resolved dilactam (-)-I in which the permolecular chirality of the tricyclic moiety represents the only source of optical activity. The actually measured dilactams (+)-II and (-)-I exhibit mirror-shaped CD curves and consequently their respective absolute configurations should be opposite, as shown by formulae II and I.

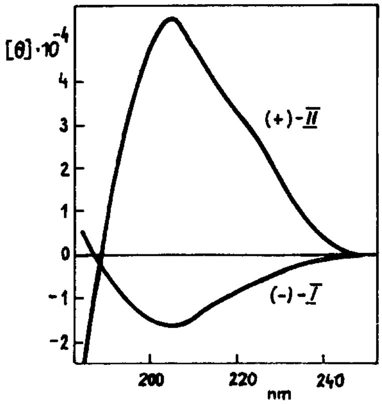


Fig. I

CD-Curves of the Dilactams (-)-I and (+)-II in Water

CD spectra of both dilactams are characterized by large ellipticity values of dichroic bands. The large rotational strengths of the $n-\pi^*$ transitions conform to the presence of inherently chiral non-planar amide chromophores. The spatial arrangement of the chromophore groups is known[6] with sufficient precision from the X-ray analysis of the racemic compound I. We may state that the given chirality of the amide grouping in the compound (-)-I (Fig. 2) is related to the negative CD band of the $n-\pi^*$ transition, similarly to the case of the monolactam (3S)-4-azatricyclo$[4,4,0,0^{3,8}]$decan-5-one[1,7] (III). On the contrary, the signs of the $\pi-\pi^*$ bands in (-)-I are opposite to those of the monolactam III, probably due to the interaction of the two amide groups in dilactams of the type I.

We have performed CNDO/S calculation of the CD parameters related to the dilactam (-)-I using the experimentally found molecular geometry[6]. The computed rotatory strengths ($R_{n-\pi^*} = -6.3 \cdot 10^{-40}$ esu^{2}cm^2, $R_{\pi-\pi^*_1} = -4.9 \cdot 10^{-40}$ esu^{2}cm^2, $R_{\pi-\pi^*_2} = +3.8 \cdot 10^{-40}$ esu^{2}cm^2) agree qualitatively with the experimental CD data.

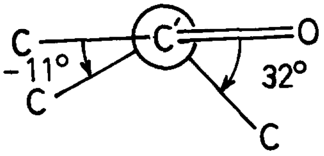


Fig. 2

Geometry of the Amide Grouping, Viewed along the C′-N Bond

The full paper will be published in Collection of Czechoslovak Chemical Communications.

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