

SYNTHESIS AND SPECTROPOLARIMETRIC BEHAVIOR OF α -PHENYLETHYLAMIDES OF INDOLECARBOXYLIC ACIDS

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Optically active amides of 2- and 3-indolecarboxylic acids are synthesized, and their rotary dispersion plots obtained.

In a previous spectropolarimetric study of the phenylethylamides of pyridine carboxylic acids [1], it was established that the direction of the rotary dispersion curves (RD curve) is a function of the position of the carboxyl group in the pyridine ring. Thus the amide of 2-pyridinecarboxylic acid gives RD plots opposite in direction and sign to that of the starting amine, and unaffected by the solvent. The amide of 4-pyridinecarboxylic acid retains the sign of rotation and direction of the plots of the starting amine, which do not depend on solvent. In the case of the amide of 3-pyridinecarboxylic acid, the direction of the RD plot is the opposite of that of the plot of the starting amine, while in benzene the direction and sign of the rotation are the same as with the starting amine.

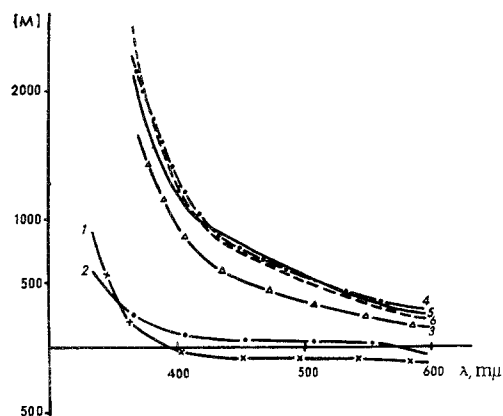
The special behavior of the amide of 2-pyridinecarboxylic acid is evidently connected with chelation due to the free pair of electrons of the pyridine nitrogen. In connection with this, using the same $(-)\alpha$ -phenylethylamine, the amides of 2- and 3-indolecarboxylic acid were synthesized, where the basicity (protonizability) of the heterocyclic nitrogen atom is very low and they both gave RD plots in the positive region which were practically independent of solvent nature (figure). On passing from the α to the β amide the value of the rotation drops, and on methylating the heterocyclic nitrogen atom, it increases somewhat, without the direction of the plot and the sign of rotation being changed.

The similar behavior of all three amides indicates that chelation does not, apparently, occur.

EXPERIMENTAL

Phenylethylamide of 2-indolecarboxylic acid. A mixture of 0.5 g (0.0026 mole) ethyl 2-indolecarboxylate (mp 122° C), 0.62 g (0.0052 mole) $(-)\alpha$ -phenylethylamine ($[\alpha]_D -41^\circ$), and 1 drop conc. H_2SO_4 were refluxed together for 5 hr. After cooling, the viscous mass was repeatedly boiled with heptane. The residual black crystalline mass, still contained amide (determined by chromatography, not extracted even by heptane). Evaporation of the heptane gave 0.24 g (36.3%), mp 164°-165° C, R_f^* 0.57. Found: C 77.21;

76.96; H 6.29; 6.19%. Calculated for $C_{17}H_{16}N_2O$: C 77.20; H 6.10%.



Molecular optical rotation dispersion of $(-)\alpha$ -phenylethylamides. 1) 3-Indolecarboxylic acid in MeOH; 2) 3-indolecarboxylic acid in dioxane; 3) 2-indolecarboxylic acid in $CHCl_3$; 4) 2-indolecarboxylic acid in MeOH; 5) N-methyl-2-indolecarboxylic acid in MeOH; 6) N-methyl-2-indolecarboxylic acid in $CHCl_3$.

Phenylethylamide of 3-indolecarboxylic acid. A mixture of 0.5 g (0.0031 mole) 3-indolecarboxylic acid and 2.1 g (0.0178 mole) $SOCl_2$ in dry benzene was stirred for 18 hr at room temperature, the solvent and excess $SOCl_2$ vacuum-distilled off, the residue dissolved in dry ether, and 0.47 g Et_3N and 0.5 g $(-)\alpha$ -phenylethylamine added. Addition of water gave a white precipitate, which was filtered off, and recrystallized from EtOH. Yield 40%, mp 194°-195° C. R_f 0.25. Found: C 77.09; 77.31; H 6.23; 6.15%. Calculated for $C_{17}H_{16}N_2O$: C 77.20; H 6.10%.

Phenylethylamide of N-methyl-2-indolecarboxylic acid. This was obtained similarly. Yield 0.43 g (55%), mp 202°-203° C (ex MeOH), R_f 0.80. Found: C 77.47; 77.47; H 6.54; 6.72%. Calculated for $C_{18}H_{18}N_2O$: C 77.66; H 6.51%.

The RD curves were plotted from measurements made with a Soviet VNIKIProd mash (Machinery Supply All-Union Scientific Research Experimental Institute) spectropolarimeter. 0.3-0.34% solutions were used for making the measurements.

REFERENCES

1. A. P. Terent'ev, V. M. Dem'yanovich, L. A. Goloveva, and A. N. Kost, DAN, 162, 356, 1965.

*All R_f values relate to thin-layer chromatography, activity II alumina layer not fixed, system: benzene-MeOH 9:1.