INDOLE DERIVATIVES

VIII.* REACTION OF INDOLE WITH DIISOPROPYL AMINOFUMARATE

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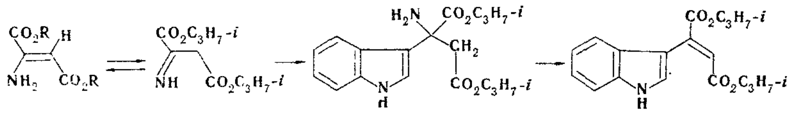
The reaction of indole with diisopropyl aminofumarate gives diisopropyl 2-(3-indolyl)-2-aminosuccinate.

A mixture of diethyl aziridine-2,3-dicarboxylate and diethyl aminofumarate (I) is formed in the reaction of ammonia with diethyl dibromosuccinate [2].

We have found that treatment of a solution of diisopropyl erythrodibromosuccinate in isopropyl alcohol with ammonia gives only one substance. The IR spectrum of this compound contains bands at 1630, 1675, 1725, 3360, and 3490 cm^{-1}, which we assigned, respectively, to a double bond, two ester groups, and a primary amino group. In addition to signals of isopropyl protons, the PMR spectrum contained only one one-proton singlet at 5.30 ppm. On the basis of these data, we proposed structure II for the compound obtained.



I, II III IV V

I $R=C_2H_5$; II $R=i\text{-}C_3H_7$

This enamine reacted with indole (apparently in tautomeric form III) under the influence of p-toluenesulfonic acid to give diisopropyl ester IV. In addition to signals of isopropyl and indole protons, the PMR spectrum of IV contains a two-proton quartet centered at 3.17 ppm with the parameters of an AB system. Considering the chemical shift and the spin–spin coupling constant (J_{AB} = 16 Hz), we assigned this signal to protons of the CH_2 group in IV, which are unequivalent as a result of inhibited internal rotation.

The fact that the substance readily loses ammonia on heating to give a high yield of indolylfumaric ester (V) is also in agreement with structure IV. The trans configuration of this ester follows from the identical character of the UV spectra of V and the known dimethyl ester, its yellow coloration [3], and the inability of the corresponding acid or its salt to give an inner anhydride under various standard conditions.

EXPERIMENTAL

The melting points were determined with a Koffler block and were not corrected. The IR spectra of mineral-oil suspensions of the compounds were recorded with a UR-10 spectrometer. The UV spectrum of an alcohol solution of the ester was measured with a Specord UV-vis spectrophotometer. The PMR spectra of carbon tetrachloride solutions were obtained with an RS-60 spectrometer.

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* See [1] for communication VII.

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Diisopropyl Aminofumarate (II). Dry ammonia was bubbled through 183 ml of anhydrous isopropyl alcohol, and 18.3 g of diisopropyl erythro-dibromosuccinate was added in small portions at 8-10°. After 3 h, most of the solvent was vacuum evaporated, and the residue was shaken with water and extracted with ether. According to the results of thin-layer chromatography (TLC) (aluminum oxide, benzene), the extract contained only one substance. Removal of the ether and vacuum distillation gave 9.06 g of II (83%) as a yellowish liquid with bp 93° (0.2 mm) n_D^{18} 1.4820, and n_D^{20} 1.4807. Found, %: C 55.9; H 7.9; N 6.7. $C_{10}H_{17}NO_4$. Calculated, %: C 55.8; H 8.0; N 6.5.

Diisopropyl 2-(3-Indolyl)-2-aminosuccinate (IV). A 3.73-g (31.9 mmole) sample of indole was added to 6.84 g (31.8 mmole) of II in 35 ml of anhydrous isopropyl alcohol, the mixture was cooled to 10°, and 6.84 g (36.0 mmole) of p-toluenesulfonic acid was added in small portions in the course of 15 min. After 2.5 h, the solution was poured into water, and the aqueous mixture was made alkaline with potassium carbonate and extracted with ether. The extract was dried, and the solvent was removed by distillation to give an oil that crystallized slowly. Recrystallization from carbon tetrachloride gave 6 g (60%) of colorless crystals with mp 77-78°. IR spectrum: 1740 (COOPr), 3320, and 3380 (NH_2, NH) cm^{-1}. Found, %: C 64.8; H 7.3; N 8.4. $C_{18}H_{24}O_4N_2$. Calculated %: C 65.0; H 7.3; N 8.4. The picrate had mp 180° (from propanol). IR spectrum: 1740 (COOPr) and 3390 cm^{-1} (indole NH). Found %: C 51.2; H 5.0; N 12.8. $C_{24}H_{27}N_5O_4$. Calculated %: C 51.3; H 4.9; N 12.5.

Diisopropyl (3-Indolyl)fumarate (V). A 1-g sample of ester IV was heated in vacuo (1 mm) at 150°. After cooling, the solidified mass was crystallized from cyclohexane–hexane to give 0.77 g (81%) of yellow crystals with mp 126°. IR spectrum: 1600 (C=C), 1695 (CO_2Pr), and 3360 cm^{-1} (NH). UV spectrum, λ_{max} (log ε): 219 (4.366), 274 (3.982), and 357 nm (4.327).

LITERATURE CITED

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