INDOLE-CONTAINING AMIDINE SYSTEMS

IV. REACTIONS OF SOME IMINOESTERS WITH TAURINE*

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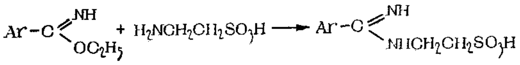
UDC 547.436'298.5

The ability of the easily accessible iminoesters of carboxylic acids to condense with amino acids and peptides provides a means of introducing various biologically active molecular fragments into an amino acid. It should be mentioned that the amino acids thus formed preserve their clearly defined bipolar structure and in aqueous solution exist as zwitterions. Because of this, amidinoacids are soluble both in acids and in alkalis. In the present work, the possibility of acylating taurine (β-aminoethanesulfonic acid, II) with iminoesters of indolecarboxylic and benzoic acids (I) was studied.

The acylating agents were iminoesters of indolylacetic acid (heteroauxin), indolyl-3-carboxylic, benzoic, anisic, veratric, and trimethylgallic acids. The reactions were carried out in a medium of boiling 80% methanol and proceeded according to the equation

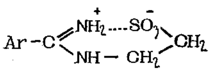


$$\mathrm{Ar{-}C}\begin{matrix}\nearrow \mathrm{NH}\\ \searrow \mathrm{OC_2H_5}\end{matrix} + \mathrm{H_2NCH_2CH_2SO_3H} \longrightarrow \mathrm{Ar{-}C}\begin{matrix}\nearrow \mathrm{NH}\\ \searrow \mathrm{NHCH_2CH_2SO_3H}\end{matrix}$$

I II III-VIII

The compounds prepared (III-VIII, see Table 1) are colorless crystalline high-melting substances with good solubility in water. They separate from alkaline solution as sodium salts possessing a strong alkaline reaction.

Compounds III-VIII are unable to form salts with acids owing to the formation of strong intramolecular bonds leading, apparently, to a separation of the charges in accordance with the formula



$$\mathrm{Ar{-}C}\begin{matrix}\nearrow \overset{+}{\mathrm{N}}\mathrm{H_2}\cdots\overset{-}{\mathrm{SO_3}}\searrow\\ \searrow \mathrm{NH-CH_2}\nearrow\end{matrix}\mathrm{CH_2}$$

Our attempts to cyclize compounds III-VIII to thiadiazine failed. The IR spectra of all these compounds contain an intense absorption in the region 1050 $\mathrm{cm^{-1}}$, corresponding to an ionized sulfo group. Intense peaks with maximum 1650-1700 $\mathrm{cm^{-1}}$ are characteristic of an imino group, being the nitrogen analog of a carbonyl.

The method for preparing the amidino-acids has been published [2].

Pharmacological study of N-(α-imino-3,4,5-trimethoxybenzyl)-β-aminoethanesulfonic acid revealed acute toxicity and an effect on arterial pressure. The experiments were carried out in acute tests on cats anaesthetized with ether-urethane. Arterial blood pressure was recorded by the conventional method. The compound being tested was introduced intravenously as a 1% solution. The LD_{50} of this compound is 750 mg/kg. Administration of the compound at a level of 10 mg/kg caused a persistent reduction in blood pressure (by 20%).

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*For Communication III, see [1].

Leningrad Pharmaceutical Chemistry Institute. Translated from Khimiko-Farmatsevticheskii Zhurnal, Vol. 5, No. 6, pp. 21-22, June, 1971.

TABLE 1. β-Amidinoethanesulfonic Acids

Compound	Ar	Yield, %	mp, °C	Found (in %)		Empirical formula	Calculated (in %)		$C\genfrac{}{}{0pt}{}{\lessdot NH_2^+}{\lessdot NH^-}$ (cm^{-1})	$\nu_{SO_3^-}$ (cm^{-1})
				N	S		N	S		
III	Phenyl	78	285 (from 80% methanol solution)	12.05	14.05	$C_9H_{12}N_2O_3S$	12.15	14.14	1650 1700	1050
IV	p-Methoxyphenyl	67	308 (from water)	11.13	11.60	$C_{10}H_{14}N_2O_4S$	10.75	12.03	1642 1703	1044
V	3,4-Dimethoxyphenyl	70	328 (from 90% ethanol solution)	9.69	11.70	$C_{11}H_{16}N_2O_5S$	9.70	11.38	1630 1697	1051
VI	3,4,5-Trimethoxyphenyl	68	180	8.40	10.5	$C_{12}H_{18}N_2O_6S$	8.54	10.05	1639 1696	1053
VII	N-Formylindolyl-3	50	300	12.88	10.90	$C_{12}H_{13}N_3O_4S$	13.20	10.70	1654 1687	1049
VIII	Indol-3-methyl	75	300	13.80	10.80	$C_{12}H_{15}N_3O_3S$	14.10	10.80	1633 1679	1045

EXPERIMENTAL

N-(α-Imino-3,4-dimethoxybenzyl)-β-aminoethanesulfonic Acid (V). A mixture of 0.19 g (1.5 mole) of taurine, 0.32 g (1.5 mole) of 3,4-dimethoxybenzimino ester, and 15 ml of 80% methanol was boiled with vigorous agitation for 45 min. Then the transparent solution was evaporated to dryness in vacuo. The oily residue was treated with 15 ml of methanol, the insoluble portion was filtered off, and from the mother liquor a white crystalline product was precipitated by the addition of anhydrous ethyl ester. There was obtained 0.3 g of compound V.

The rest of the β-amidinoalkanesulfonic acids, the characteristics of which are shown in Table 1, were prepared by the method described above, except that products III and IV were isolated by way of cooling the reaction mass and filtering the precipitated products.

LITERATURE CITED

1. N. A. Kogan, I. M. Nurova, and I. Kh. Fel'dman, Khim.-Farm. Zh., 5, No. 2, 12 (1969).
2. USSR Patent No. 223,815, Byull. Izobret., 1968, No. 25, p. 25.