SYDNONES FROM PHENYLALANINE

I. S. Slyusarenko and V. G. Yashunskii

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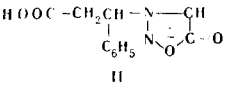
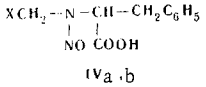
In a continuation of our research on the chemistry of sydnonecarboxylic acids [1], we have accomplished the synthesis of sydnonyl derivatives of phenylalanine.

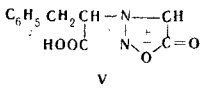
The condensation of d,*l*-β-phenyl-β-alanine with the bisulfite derivative of formaldehyde and potassium cyanide in alkali gave its N-cyanomethyl derivative, which was converted to N-nitroso-N-carboxymethyl-d,*l*-β-phenyl-β-alanine (I) by saponification and subsequent nitrosation. Compound I was cyclized to 3-(2-carboxy-1-phenylethyl)sydnone (II) by the action of acetic anhydride for 3 days in the dark at ~20°. N-Cyanomethyl- (IIIa) and N-carboxymethyl-d,*l*-β-phenyl-α-alanine (IIIb) were synthesized similarly from d,*l*-β-phenyl-α-alanine. Their N-nitroso derivatives (IVa,b) were oily substances.



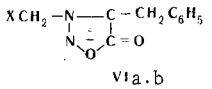
II



IVa,b



V



VIa,b

a X=CN b X COOH

Two sydnones (V and VIb) might have been expected in the cyclization of IVb due to the participation of different carboxyl groups of the molecule in the formation of the mesoionic ring. Since the use of acetic anhydride for closing the ring did not lead to a crystalline product, IVb was treated with trifluoroacetic anhydride at 0° for 10 min. As a result, only one sydnone was isolated and, on the basis of the presence in the PMR spectrum (C_2D_5OD) of a signal at δ 6.81 ppm (as in II) characteristic for a proton attached to the C_4 atom of the sydnone ring [2], was assigned structure V.

The participation of the carboxyl group of phenylalanine in the cyclization is apparently hindered to a considerable degree by the presence of a benzyl group in the vicinity. However, we observed that the carboxyl group of phenylalanine can still participate in the closing of the ring to form a sydnone of the VI type when the second carboxyl group is replaced by a nitrile group. Sydnone VIa was isolated in low yield by the action of trifluoroacetic anhydride on N-nitroso derivative IVa at 2-3° for 20 min. The IR spectra of the sydnones are characterized by the presence of $\nu_{C=O}$ at 1730-1752 cm^{-1} and $\nu_{C=O}$ (COOH) for II and V at 1694 and 1712 cm^{-1} (in mineral oil). The characteristics of the sydnones and the intermediates in their synthesis are presented in Table 1.

TABLE 1. Properties of the Compounds Obtained

Compound	mp, °C	Empirical formula	Found, %			Calc., %			Yield, %
			C	H	N	C	H	N	
I	154—154,5	$C_{11}H_{12}N_2O_5$	52,1	4,8	11,1	52,4	4,8	11,1	20
II	147—149[a]	$C_{11}H_{10}N_2O_4$	56,1	4,3	12,0	56,4	4,3	12,0	23
III	179—180[b]	$C_{11}H_{12}N_2O_3$	64,5	6,0	14,0	64,7	6,0	13,7	44
IIIb	236—237[c]	$C_{11}H_{13}NO_4$	59,3	6,0	6,1	59,2	5,9	6,3	67
V	167—168[c]	$C_{11}H_{10}N_2O_4$	56,4	4,4	12,2	56,4	4,3	12,0	26
VIa	71—72[c]	$C_{11}H_9N_3O_2$	61,3	4,3	19,0	61,4	4,3	19,5	17

[a]From ethyl acetate–hexane. [b]From aqueous alcohol. [c]From water.

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LITERATURE CITED

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2. V. G. Yashunskii, Doctoral Dissertation, "Investigation of sydnones and sydnonimines" [in Russian], Moscow (1963).