TRANSCYCLIZATION OF BENZOXAZOLES

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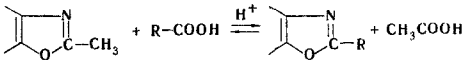
UDC 547.787.3

The reaction of benzoxazoles with aromatic and aliphatic acids, which gives transcyclization products – 2-substituted benzoxazoles – was studied. The reaction of 2-hydroxyacetanilide with aliphatic acids gives a mixture of 2-substituted benzoxazoles. Under similar conditions, 2-methylbenzothiazole, 2-alkyl-Δ^2-oxazolines, and 2-alkyl-Δ^2-thiazolines do not undergo transcyclization, but ring opening is observed in the latter two cases.

It is known that benzoxazoles readily undergo ring opening during acid hydrolysis [1,2]. Moreover, the reverse cyclization reaction also occurs relatively readily on heating o-aminophenol with acids [3]. A comparison of these factors made it possible to hope that opening of the oxazole ring would also be possible in the reaction of benzoxazoles with organic acids and that subsequent transformation would lead to cyclization with another acid.



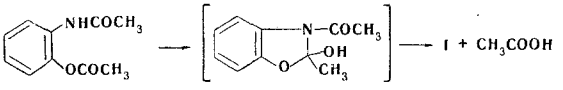
I IIa-f IIIa-f

a R = C_2H_5; b R = n-C_3H_7; c R = n-C_4H_9; d R = C_6H_5; e R = p-ClC_6H_4; f R = o-ClC_6H_4

The data in Tables 1 and 2 are evidence that transcyclization really does occur when 2-methylbenzoxazole (I) is heated with both aromatic and aliphatic acids. The low yield of 2-arylbenzoxazoles IIId-f form the reaction of I with aromatic acids IId-f is apparently explained by decarboxylation of the latter [6,7] under the experimental conditions.

The reaction mass obtained during the transcyclization of I with acids IIa-c was analyzed by gas-liquid chromatography (GLC) (Table 2). The character of the acid determines the ratio of 2-alkylbenzoxazoles. The transcyclization is reversible; this is proved by the fact that, under similar conditions, we accomplished the transcyclization of 2-ethylbenzoxazole with acetic acid, as a result of which we obtained I (8%). Since the percentage of IIIa-c increases as compared with the percentage of I when the amount of acid and the reaction time are increased (Table 2), it can be concluded that equilibrium is not reached in the reaction. When IIId was heated with IIb (at 210° for 17 h in a ratio of 1 : 8 with sulfuric acid as the catalyst), IIIb was identified in the reaction products by GLC. A similar result was obtained in the reaction of 2-hydroxybenzanilide with IIb.

We simultaneously studied the reaction of 2-hydroxyacetanilide with aromatic acids IIa-c. The data in Table 2 attest to the fact that benzoxazoles IIIa-c are formed along with a small amount of I in the reaction of 2-hydroxyacetanilide with acids. Since the reaction of 2-hydroxyacetanilide with I was carried out under identical conditions, the results can be compared. One's attention is directed to the fact that the percentage of IIIa-c is considerably greater in the reaction carried out with 2-hydroxyacetanilide. In agreement with [8,9], the diacyl derivative of o-aminophenol readily forms I via the scheme



Siberian Technological Institute, Krasnoyarsk. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 11, pp. 1480-1482, November, 1972. Original article submitted October 20, 1971.

TABLE 1. 2-Arylbenzoxazoles (IIId-f)

Comp.	R	mp, °C	Empirical formula	N, % found	N, % calc.	Yield, %
IIId	C_6H_5	101—103 (102—103[4])	$C_{13}H_9NO$	7,1	7,2	50
IIIe	p-C_6H_4Cl	149—150 (151[5])	$C_{13}H_8ClNO$	6,2	6,5	23
IIIf	o-C_6H_4Cl	60—62	$C_{13}H_8ClNO$	6,1	6,5	25

TABLE 2. Composition of 2-Alkylbenzoxazoles (mass %)

Acid	τ=17 h				τ=25 h
	1 : 1	1 : 2	1 : 3	1 : 3*	1 : 3
Propionic	9	11	17	84	21
Butyric	7	19	30—37 †	86	46
Valeric	2—5†	7	15	81	19

*The reaction was carried out with 2-hydroxyacetanilide; 2-methylbenzoxazole was used in the remaining cases.
† The experiment was repeated.

One can explain the lower percentage of IIIa-f in the case of transcyclization with I by assuming that the transcyclization of I with IIa-f proceeds with prior opening of the ring.

We also attempted to transcyclize 2-methylbenzothiazole, 2-methyl- and 2-ethyl-Δ^2-thiazolines, and 2-methyl- and 2-ethyl-Δ^2-oxazolines with propionic and acetic acids. The starting material was isolated in the case of 2-methylbenzothiazole, while ring opening was observed in the remaining cases.

EXPERIMENTAL

Transcyclization of 2-Methylbenzoxazole (I) with Aromatic Acids IId-f. A 0.03-mole sample of I was refluxed with 0.09 mole of the appropriate acid in the presence of 0.2 ml of concentrated sulfuric acid in a flask equipped with a reflux condenser. The reaction time for IId, IIe, and IIf was 25 h, 12 h, and 16 h, respectively. The reaction mass was poured into 200 ml of concentrated hydrochloric acid, and the mixture was heated with clarifying charcoal. The filtrate was diluted with water, and the resulting 2-arylbenzoxazole was removed by filtration. The solid on the filter was repeatedly extracted with four 200-ml portions of hot concentrated hydrochloric acid. The product was crystallized two to three times from aqueous ethanol. The properties of the compounds and the results of analysis are presented in Table 1.

Transcyclization of I with Aliphatic Acids IIa-c. A mixture of 0.03 mole of I, 0.09 mole of the appropriate acid, and 0.2 ml of concentrated sulfuric acid was heated in sealed ampule at 210°, after which the reaction mass was chromatographed (see Table 2). The reactions of 2-ethylbenzoxazole (with acetic acid), and of 2-alkyl-Δ^2-oxazolines and 2-alkyl-Δ^2-thiazolines with aliphatic acids were accomplished with equimolar amounts of the components. The reaction time was 17 h. 2-Methylbenzothiazole was heated for 25 h with a threefold excess of aliphatic acid. It should be noted that in the preparation of 2-methyl- and 2-ethyl-Δ^2-thiazolines via the method in [8], the indicated compounds contain the corresponding oxazolines as impurities.

The chromatograms were interpreted by means of test substances, for which the corresponding 2-substituted benzoxazoles, oxazolines, and thiazolines were synthesized. The areas of the peaks were determined from the product of the peak height and the retention time. The logarithm of the relative retention volumes of 2-alkylbenzoxazoles was a linear function of the number of CH_2 groups in the alkyl residue. The composition of the 2-alkylbenzoxazoles (Table 2) was determined from calculation in such a way that their overall content was 100 mass %. The analytical conditions were as follows: a UKh-2 chromatograph with a 4-m long column 6 mm in diameter was used; the temperature was 250°, the stationary phase was Apiezon L, the solid support was Chromosorb P, the stationary phase was 23% of the solid support, and the carrier gas was hydrogen.

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