SYNTHESIS OF 2-ALKYL-3-(2-BENZOXAZOLON-3-YL)INDOLES

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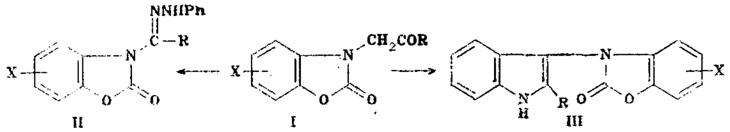
It was shown that 3-(2-oxoalkyl)-2-benzoxazolones with phenylhydrazine in the presence of polyphosphoric acid form the corresponding 2-alkyl-3-(2-benzoxazolon-3-yl)-indoles.

The present work is part of our investigations of the reactions of 3-(2-oxoalkyl)-2-benzoxazolones (I) with nucleophilic agents. Earlier it was established that under mild conditions reactions with hydroxylamine and hydrazine stop at the first stage – the formation of oximes, azines, and hydrazones. Under more rigorous conditions, the carbonyl group of the oxazolone ring also reacts, which leads to the production of such heterocyclic systems as imidazolinones and nonsymmetrical triazinones [1-4].

For a further elucidation of the preparative possibilities of nucleophilic reactions of compounds I we made an investigation of their interaction with phenylhydrazine.



In the selection of the optimum conditions of synthesis of phenylhydrazones II (see Table 1), it was found that phenylhydrazones IIa, b (X = H and 5-Cl) can be produced rather easily and with high yields with wide variation of the reaction conditions, whereas phenylhydrazones IIc, d (X = 5- and 6-SO_2NH_2) can be obtained in low yields only by boiling in phenylhydrazine. Under all other reaction conditions, the starting materials remained unchanged. Preservation of the carbonyl group of the benzoxazolone ring in phenylhydrazones II is evidence for the appearance of strong absorption bands in their IR spectra in the region of 1770-1750 cm^{-1}.

Preliminary isolation of the phenylhydrazones is not necessary for the conversion of compounds I to the corresponding indoles III. The action of the catalyst on a mixture of compound I with phenylhydrazine was sufficient; moreover, of a whole series of investigated catalysts, polyphosphoric acid proved the most suitable [5].

TABLE 1. Phenylhydrazones of 3-(2-Hydroxyalkyl)-2-benzoxazolones

Compound	X	Conditions of reaction			mp, °C	Found, N, %	Empirical formula	Calculated N, %	Yield, %
		solvent	T, °C	time, h					
IIa	H	Ethanol	100	2	152—153 [2]		$C_{16}H_{15}N_3O_2$		96
		Ethanol	25	2					82
		Ethanol	−3	2					71
		AcOH	100	2					70
IIb	5-Cl	Ethanol	100	2	169—170	13,3	$C_{16}H_{14}ClN_3O_2$	13,3	95
		Ethanol	25	2					93
		AcOH	100	2					76
IIc	5-SO_2NH_2	$PhNHNH_2$	100	2	215—216	15,5	$C_{16}H_{16}N_4O_4S$	15,6	51
		Ethanol	100	6					—
		AcOH	100	6					—
IId	6-SO_2NH_2	$PhNHNH_2$	100	2	225—226	15,6	$C_{16}H_{16}N_4O_4S$	15,6	59
		Ethanol	100	6					—
		AcOH	100	6					—

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TABLE 2. 2-Alkyl-3-(2-benzoxazolon-3-yl)indoles

Compound	X	R	mp, °C	Found, N, %	Empirical formula	Calculated, N, %	Yield, %
IIIa	H	CH_3	240—241	10,6	$C_{16}H_{12}N_2O_2$	10,6	75
IIIb	5-Cl	CH_3	237—238	9,3	$C_{16}H_{11}ClN_2O_2$	9,4	70
IIIc	5-SO_2NH_2	CH_3	207—208	12,0	$C_{16}H_{13}N_3O_4S$	12,2	37
IIId	6-SO_2NH_2	CH_3	264—265	12,2	$C_{16}H_{13}N_3O_4S$	12,2	43
IIIe	6-Cl	CH_3	213—214	9,6	$C_{16}H_{11}ClN_2O_2$	9,4	60
IIIf	6-Br	CH_3	217—218	8,1	$C_{16}H_{11}BrN_2O_2$	8,2	62
IIIg	6-Br	C_2H_5	194—195	8,1	$C_{16}H_{13}BrN_2O_2$	8,1	67
IIIh	5-Cl—6-Br	CH_3	244—245	7,6	$C_{16}H_{10}BrClN_2O_2$	7,4	61

In the IR spectra of compounds III, two intense absorption bands are observed: The band in the region of 1790-1750 cm^{-1} is associated with the stretching vibrations of the carbonyl group of the oxazolone, while the band at 3400-3300 cm^{-1} is due to the stretching vibrations of the NH group of indole.

EXPERIMENTAL

The IR spectra were recorded on an UR-10 instrument in chloroform solution. The melting points were determined by a capillary method and were not corrected.

2-Alkyl-3-(2-benzoxazolon-3-yl)indoles (IIIa-h). To a mixture of 0.05 mole of compound I and 0.055 mole phenylhydrazine we added 20 g of pyrophosphoric acid. The mixture was heated slowly up to a sharp temperature rise caused by the beginning of the reaction, after which a temperature of 170-190°C was maintained. At the end of the reaction the cooled reaction mixture was diluted with 50 ml of cold water. The precipitate was filtered off, washed with water, and recrystallized from ethanol. For data on compounds III, see Table 2.

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