REACTION OF N-PHENYLSULFONYLBENZOXAZOLONE WITH SOME AMINES

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The reaction of N-phenylsulfonylbenzoxazolone with amines was investigated in order to study the mechanism of the reaction between aryloxazolones and amines. The sulfonyl group accelerates the reaction considerably. The structure of 2-(phenylsulfamido)phenyl esters of the corresponding N-substituted carbamic acids was assigned to the products on the basis of the IR spectra and alternative synthesis. The reaction with secondary aliphatic amines (dimethyl- and diethylamine) proceeds considerably more slowly and results in the formation of 2-(phenylsulfamido)phenol.

In one of our earlier papers [1] we assumed that the first step in the reaction between aryloxazolones and amines is addition of the base to the double bond of the carbonyl group and that this step determines the reaction rate. In this case, one should expect that substituents that lower the electron density on the carbonyl carbon atom would increase its reactivity in reactions of this type, and vice versa. This assumption is in good agreement with several of our observations during an investigation of the aminolysis of ring- or nitrogen-substituted benzoxazolones [2,3]. In order to further study the effect of substituents with various inductive and mesomeric effects on the rate of this reaction and to ascertain its mechanism, we investigated the reaction of N-phenylsulfonylbenzoxazolone (I) with some amines.

As expected, the presence of a substituent with strong electron-acceptor properties in the vicinity of the reaction center leads to a sharp acceleration in the reaction. Under the conditions at which benzoxazolone is converted to the corresponding N-(2-hydroxyphenyl)-N'-alkylureas (by heating at 60-80°C for 2-3 h with excess amine), compound I gives a sym-disubstituted urea and 2-(phenylsulfamido)phenol (II).

To isolate the intermediates, experiments were carried out with equimolar amounts of the reagents in ethanol at −5 to 0°. Primary amines of the aliphatic series, piperidine, and morpholine gave compounds whose elementary analyses corresponded to structures IIIa-f or IVa-f:

IIIa-f IVa-g

a NRR'=NHCH$_3$; b NRR'=NHC$_2$H$_5$; c NRR'=NHC$_3$H$_7$-*n*; d NRR'=NHC$_4$H$_9$-*n*,
e NRR'=NC$_5$H$_{10}$; f NRR'=N(CH$_2$CH$_2$)$_2$O; g NRR'=NHCH$_2$C$_6$H$_5$

In analogy with the cases that we described previously, structure III should have been assumed [2,3]. However, the absorption band of the carbonyl group is found at 1755 cm^{-1} (IVa-d) and 1725-1720 cm^{-1} (IVe,f) in the IR spectra of the compounds (in chloroform). It is known that the carbonyl group frequency of substituted ureas is ~1660 cm^{-1}. In this case, we are probably dealing with a carbonyl group in a structure of the RNHCOOR' type. According to the literature, a number of urethanes absorb at 1700-1736 cm^{-1} [4]. The absorption frequency of the carbonyl group of the phenyl ester of N-butylcarbamic acid is 1743 cm^{-1}. (We recorded the spectrum of a chloroform solution.) The band of medium intensity at 3370 cm^{-1} is apparently due to the stretching vibrations of the N−H sulfamide bond; the position of this band does not correspond to our data for N-(2-hydroxyphenyl)-N'-alkylureas (3440-3450 cm^{-1}) but turns out to be close

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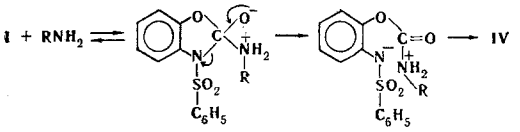
to the absorption of the band of the stretching vibrations of the N–H bond in II (3360 cm^{-1}). Another band is observed in this region at 3450-3460 cm^{-1} in the IR spectrum of compounds obtained from primary amines and is caused by the NH group in urethanes. The presence of an SO_2 group is confirmed by intense absorption bands at 1170 and 1340-1345 cm^{-1}, which are present also in the IR spectrum of II. There are no bands in the hydroxyl group region. The absence of a phenolic hydroxyl group is also confirmed by the fact that these compounds do not give color reactions with $FeCl_3$ solution.

The above facts can be explained by assuming that the reaction proceeds with cleavage of the nitrogen–carbon bond of the carbonyl group in the oxazolone ring and the formation of esters of 2-(phenylsulfamido)phenol and the corresponding N-substituted carbamic acid (IV).

The PMR spectrum of the substance obtained from I and n-butylamine is in agreement with the proposed structure. A group of peaks at 0.7-1.6 ppm (7 H) that is extremely characteristic for a long hydrocarbon chain is displayed in it. A multiplet appears at weaker field (3.25 ppm) and may be due to the methylene group bonded to the nitrogen atom. A complex multiplet appears in the aromatic proton region at 6.9-7.85 ppm (9.6 H). A broad signal at 5.40 ppm may be due to the proton of the CONH group. The other imine proton ($NHSO_2$) apparently gives a signal in the region that is overlapped by aromatic proton signals.

In this case, one can apparently assume that the reaction commences with nucleophilic addition of the amine to the carbonyl group. In the next step, however, the carbon–nitrogen bond rather than the carbon–oxygen bond is cleaved:



This sort of trend of the reaction must be expected also from theoretical considerations. The electron-acceptor SO_2 grouping directly bonded to the nitrogen atom induces a considerable decrease in the nitrogen carbonyl-carbon bond order and thereby decreases its energy as compared with these parameters in unsubstituted benzoxazolone or its N-alkyl derivatives and leads to its easier cleavage.

The structures of the compounds obtained were also confirmed by alternative synthesis. A substance that was identical to the product of the reactions between I and n-butylamine was obtained by prolonged heating of a mixture of equimolecular amounts of II and butyl isocyanate in dry toluene. The band at 3370 cm^{-1} caused by the stretching vibrations of the NH bond in II is retained in the IR spectrum of IVd obtained in this way, and the band at 3600 cm^{-1} caused by the stretching vibrations of the OH group vanishes. In contrast to II, IVd does not give a color reaction with $FeCl_3$ solution. These facts confirm that the OH group has reacted with butyl isocyanate.

When benzylamine and secondary aliphatic amines (dimethyl- and diethylamine) are used, the reaction is distinguished by several peculiarities. The reaction of I and benzylamine in a molar ratio of 1:1 at low temperatures results in the formation of a mixture of 2-(phenylsulfamido)phenyl ester of benzylcarbamic acid (IVg), II, and N,N'-dibenzylurea. We were unable to find conditions under which the major product would be IVg. Its rate of formation and cleavage are apparently commensurable:

$$I + C_6H_5CH_2NH_2 \longrightarrow IVg \xrightarrow{C_6H_5CH_2NH_2} II + (C_6H_5CH_2NH)_2CO$$

Only II and dibenzylurea were isolated when excess benzylamine was used at temperatures above 0-5°. The reaction of I with dimethyl- and diethylamine at temperatures below 0° proceeds very slowly. At higher temperatures (heating at 40-45° for 30 min), the chief product is II. The reason for the reduced reactivity of secondary aliphatic amines is probably the sterically hindered attack of the reaction center.

EXPERIMENTAL

The IR spectra of chloroform solutions were recorded with a UR-10 spectrophotometer. The PMR spectra were obtained with a JEOL-C-60-S spectrometer. The chemical shifts are given in the δ scale with respect to tetramethylsilane as the internal standard. Thin-layer chromatography was performed on silica gel G in a benzene–chloroform–ethyl acetate system (20:20:3).

TABLE 1, 2-(Phenylsulfamido)phenyl Alkylcarbamates (IVa-g)

Comp.	Mp, °C	IR spect., cm^{-1}			Empirical formula	Found, %			Calc., %			Yield, %
		$\nu C=O$	$\nu N-H$	νSO_2		C	H	N	C	H	N	
IV a	116—117	1755	3370 3460	1170 1340	$C_{14}H_{14}N_2O_4S$	54,9	4,6	9,4	54,9	4,6	9,2	98
IV b	118	1755	3370 3460	1170 1340	$C_{15}H_{16}N_2O_4S$	56,3	5,2	8,8	56,2	5,0	8,8	87
IV c	130—131,5	1755	3375 3460	1175 1345	$C_{16}H_{18}N_2O_4S$	57,4	5,9	8,3	57,5	5,3	8,4	90
IV d	135—136	1755	3370 3460	1170 1340	$C_{17}H_{20}N_2O_4S$	58,9	5,9	8,1	58,6	5,7	8,0	94
IV e	128—130	1720	3370	1170 1345	$C_{18}H_{20}N_2O_4S$	59,8	5,5	7,9	60,0	5,5	7,8	70
IV f	180—181,5	1725	3370	1170 1340	$C_{17}H_{18}N_2O_5S$	56,3	5,0	8,0	56,6	5,1	8,1	82
IV g	124—125,5	1755	3370 3455	1175 1340	$C_{20}H_{18}N_2O_4S$	62,8	4,8	7,4	62,8	4,7	7,3	25

2-(Phenylsulfamido)phenyl Butylcarbamate (IVd). A) A solution of 1 ml (0.01 mole) of n-butylamine in 10 ml of ethanol was added dropwise with vigorous stirring at −5° to a suspension of 2.75 g (0.01 mole) of I in 12 ml of ethanol. The mixture was stirred for another 2 h at the same temperature and worked up to give 3.3 g (94%) of crystals with mp 129-131°. Two recrystallizations from ethanol gave a product with mp 135-136° and R_f 0.26. The colorless needles were quite soluble in chloroform, ethyl acetate, ethanol, and dilute alkali and insoluble in CCl_4, petroleum ether, and water.

Compounds IVa-c,e (see Table 1) were similarly synthesized. In the preparation of IVf, the reagents were mixed at 0°, and the reaction mixture was stirred for 2 h at room temperature.

B) A mixture of 1 g of II and 0.4 g of butyl isocyanate in 3 ml of dry toluene was heated in a sealed tube at 140° for 16 h. Cooling produced 0.45 g of colorless crystals. These were recrystallized from ethanol to give 0.3 g (27%) of a product with mp 138-139° and R_f 0.73. This sample did not depress the melting point of I. Processing of the filtrate from the recrystallization yielded 0.12 g (8.6%) of a substance with mp 134-136° and R_f 0.26. The IR spectrum was identical to the IR spectrum of IVd. This product did not depress the melting point of that obtained by method A.

Reaction of I with Benzylamine. A) A mixture of 2.75 g of I and 1.1 g of benzylamine was stirred for 2 h at −5 to 0°. The solid material (1.92 g) was dissolved in 15 ml of chloroform, and the solution was extracted three times with 4% aqueous sodium hydroxide. Neutralization of the aqueous alkali extracts yielded 0.85 g (34%) of II with mp 128-130° (mp 138° [5]) and R_f 0.16. Workup of the chloroform solution yielded 0.6 g (21%) of I.

Workup of the filtrate after removal of the first precipitate yielded 0.95 g (25%) of colorless crystals of IVg with mp 123-125°. They were recrystallized from 50% alcohol to give a product with mp 124-125.5°. The analytical data and IR spectral data for IVg are presented in Table 1.

B) A mixture of 2.75 g of I and 1.1 g of benzylamine in 15 ml of ethanol was stirred at 50° for 30 min. The resulting precipitate was removed by filtration, washed with ethanol, and dried at 100° to give 83% of a product with mp 166-168° (from ethanol). This product did not depress the melting point of N,N-dibenzylurea [6]. The filtrate was neutralized and evaporated to dryness, and the residue was dissolved in chloroform. The chloroform solution was extracted with 4% sodium hydroxide solution. Neutralization yielded 55% of II with mp 130-132°.

C) The yield of N,N'-dibenzylurea from heating I and a threefold excess of benzylamine at 80° for 2 h was 92%.

Reaction of I with Diethylamine. A) A solution of 0.8 g (0.011 mole) of diethylamine in 10 ml of ethanol was added dropwise in the course of 30 min with stirring and ice-water cooling to 2.75 g (0.01 mole) of I in 20 ml of ethanol. After 30 min, the temperature was increased to 45°, and the mixture was heated at this temperature for another 30 min. The solution was neutralized with dilute hydrochloric acid, and the solvent was removed by vacuum distillation. The residue was dissolved in 20 ml of chloroform, and the chloroform solution was extracted three times with 4% aqueous sodium hydroxide. The aqueous alkali extract was neutralized with dilute hydrochloric acid (1 : 1) to give 2.4 g (96%) of II with mp 127-130°. Crystal-

lization from 20% ethanol gave a product with mp 133-135°. Compounds I and II were detected in chloroform solution by means of thin-layer chromatography.

B) A solution of diethylamine in alcohol was added to a suspension of I in ethanol in the course of an hour at −5 to 0°. After 1 h, the temperature was raised to room temperature, and the mixture was held at this temperature for 2 h. The precipitate still contained 50% of the starting material. Only I and II were detected in the filtrate by thin-layer chromatography.

The reaction of I with dimethylamine proceeded similarly.

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