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Synthesis of 3-(4-Oxo-4*H*-3,1-benzoxazin-2-yl)-1-benzenesulfonyl Chloride and Its Reactivity toward Amines

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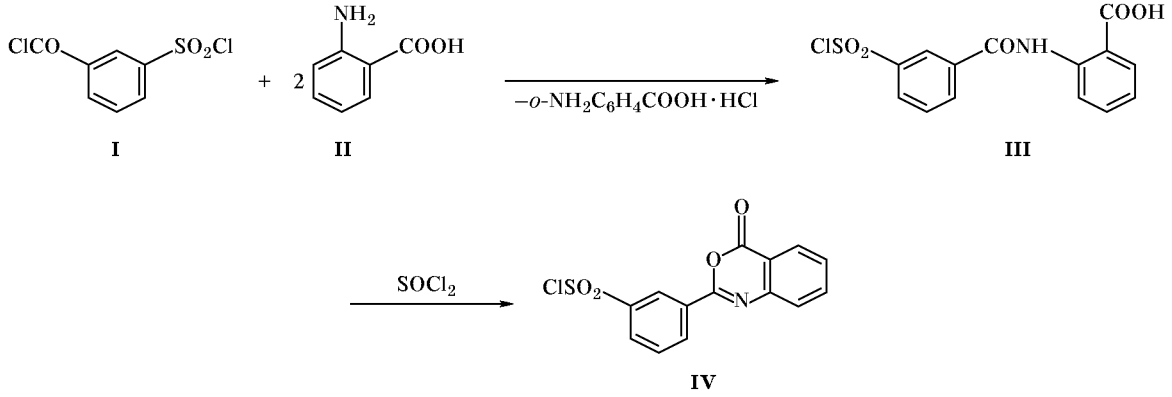
Abstract—3-(4-Oxo-4*H*-3,1-benzoxazin-2-yl)-1-benzenesulfonyl chloride was synthesized, and reactivity of its functional groups was studied. Reactions of the title compound with equimolar amounts of aniline and piperidine gave the corresponding sulfonamides with retention of the benzoxazine moiety. The same reactions with excess amine resulted in opening of the oxazine ring and formation of *o*-(*m*-aminosulfonylbenzoylamino)benzamides.

We previously [1–3] studied the reactivity of 3-chlorosulfonylbenzoyl chloride toward substituted anilines and found that the chloroformyl group is by 2–3 orders of magnitude more active than the chlorosulfonyl group. Therefore, the reaction can be performed selectively at the chloroformyl group, the chlorosulfonyl group remaining unchanged. In continuation of our studies on the relative reactivity of sulfonic and carboxylic acid derivatives in the present work we synthesized 3-(4-oxo-4*H*-3,1-benzoxazin-2-yl)benzenesulfonyl chloride and examined its behavior in reactions with amines.

2-Alkyl- and 2-arylbenzoxazinones are widely used in the synthesis of polymeric materials [4], herbicides, medicines, and optical bleaching agents [5, 6]. Some benzoxazinones possessing sulfonylamino groups are fluorescent dyes [7]. The main procedure for synthesizing such compounds is cyclization of anthranilic acid amides [5]. 2-Alkylbenzoxazinones are very sensitive to water and other nucleophiles. They reacts with amines to give *o*-(acylamino)anthranilamides which can undergo recyclization into quinazolones. 2-Phenylbenzoxazinones are less reactive than their alkyl-substituted analogs [5]; nevertheless, they also react with amines, and such reactions are used, e.g., for preparation of polyquinazolones [4]. Sulfonyl chlorides react with amines to give the corresponding sulfonamides [8]. However, there are no published data on the relative reactivity of benzoxazinone and chlorosulfonyl fragments, especially when these are present in a single molecule. Such information would be useful for proper choice of conditions for synthesis of new compounds with practically important properties.

3-(4-Oxo-4*H*-3,1-benzoxazin-2-yl)benzenesulfonyl chloride (**IV**) was synthesized as shown in Scheme 1.

Scheme 1.



I **II** **III** **IV**

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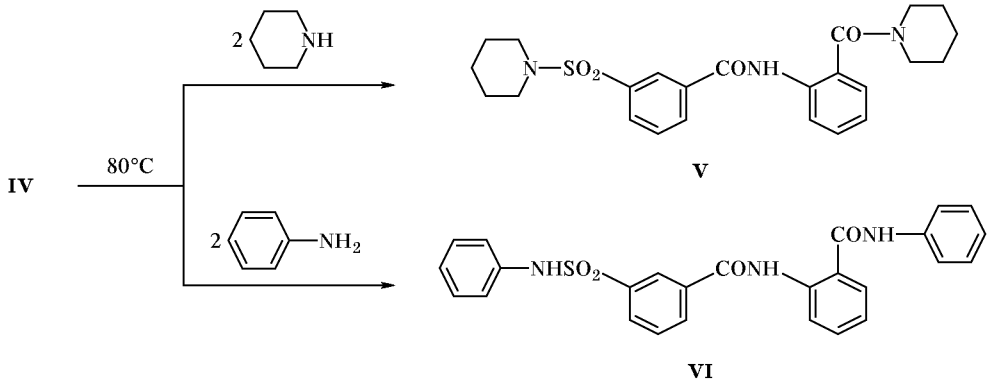
Scheme 2.



Initially, by reaction of 3-chlorosulfonylbenzoyl chloride (**I**) with anthranilic acid (**II**), following the procedure reported in [2], we obtained *N*-(*m*-chlorosulfonylbenzoyl)anthranilamide (**III**). Treatment of compound **III** with thionyl chloride [6] gave the target product **IV**.

In order to compare the reactivities of the chlorosulfonyl group and benzoxazine moiety in compound **IV**, the latter was brought into reactions with excess aniline and piperidine. The reactions were carried out in acetonitrile on heating under reflux for 2 h. As a result, we obtained *N*-(2-piperidinocarbonylphenyl)-3-(piperidinosulfonyl)benzamide (**V**) and *N*-(2-phenylaminocarbonylphenyl)-3-(phenylaminosulfonyl)benzamide (**VI**) in almost quantitative yields. These products were formed via reaction at both fragments. On the other hand, the reactions of **IV** with equimolar amounts of the same amines at 20°C in acetonitrile containing pyridine as HCl acceptor or in pyridine afforded the corresponding aminosulfonyl derivatives, the benzoxazine fragment remaining unchanged (Scheme 3). The products, 2-(3-piperidinosulfonylphenyl)-4*H*-3,1-benzoxazin-4-one (**VII**) and 2-(3-phenylaminosulfonylphenyl)-4*H*-3,1-benzoxazin-4-one (**VIII**), were isolated in ~80% yield. Compound **VIII** reacted with piperidine in boiling acetonitrile to give *N*-(2-piperidinocarbonylphenyl)-3-(phenylaminosulfonyl)benzamide (**IX**) (Scheme 4).

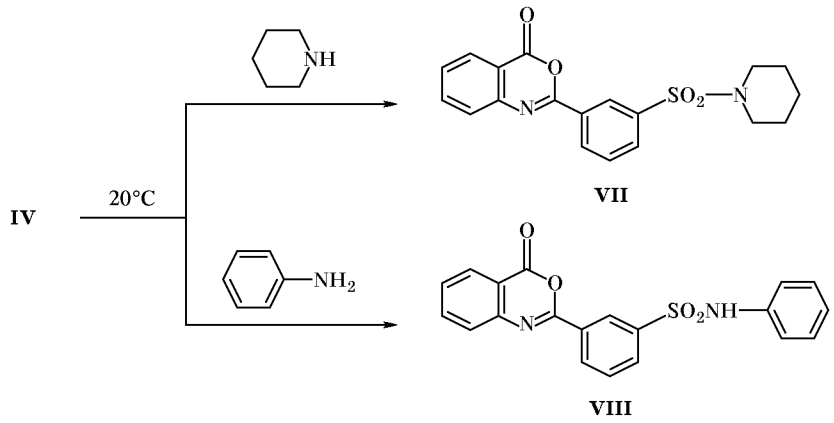
We can conclude that the chlorosulfonyl group in compound **IV** is considerably more reactive than the benzoxazine fragment with respect to amines. This makes it possible to obtain compounds having different amine residues by consecutive reactions of **IV** with different amines.

EXPERIMENTAL

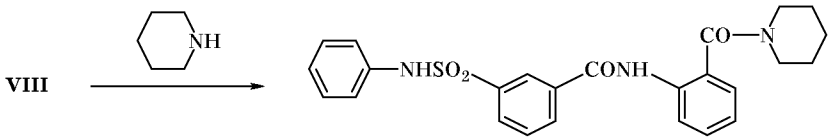
The ^{1}H NMR spectra were recorded on a Bruker AM-300 instrument (300 MHz) in DMSO-d_6. The purity of the products was checked by TLC on Silufol UV-254 plates using hexane–ethyl acetate (1 : 1) as eluent. *N*-(3-Chlorosulfonylbenzoyl)anthranilic acid (**III**) was synthesized as described in [2].

3-(4-Oxo-4*N*-3,1-benzoxazin-2-yl)benzenesulfonyl chloride (IV). A mixture of 3.39 g of sulfonyl chloride **III** and 11.9 g of thionyl chloride was heated

Scheme 3.



Scheme 4.



IX

for 3 h under reflux. Excess thionyl chloride was distilled off under reduced pressure, and the residue was recrystallized from toluene. Yield 2.8 g (87%), mp 135–137°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.65–8.60 m (8H, H_{arom}). Found, %: C 52.20; H 2.42; Cl 11.37; N 4.42; S 10.17. $C_{14}H_8ClNO_4S$. Calculated, %: C 52.26; H 2.51; Cl 11.02; N 4.35; S 9.96.

Sulfonamides V and VI (*general procedure***).** A mixture of 0.03 mol of piperidine or aniline and 3.22 g of sulfonyl chloride **IV** in 10 ml of acetonitrile was heated for 2 h under reflux. The mixture was poured into water, and the precipitate was filtered off and recrystallized from acetic acid.

***N*-(2-Piperidinocarbonylphenyl)-3-(piperidinosulfonyl)benzamide (V).** Yield 4.2 g (92%), mp 180–182°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.20–8.25 m (8H, H_{arom}), 1.55 m [12H, $(CH_2)_3$], 3.30 m (8H, NCH_2), 10.45 s (CONH). Found, %: C 63.15; H 6.21; N 9.17; S 6.92. $C_{24}H_{29}N_3O_4S$. Calculated, %: C 63.27; H 6.42; N 9.22; S 7.03.

***N*-(2-Phenylaminocarbonylphenyl)-3-(phenylaminosulfonyl)benzamide (VI).** Yield 4.38 g (93%), mp 231–233°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.00–8.60 m (18H, H_{arom}), 10.45 s (1H, CONH), 10.25 s (1H, SO_2NH), 12.10 s (1H, CONH). Found, %: C 66.11; H 4.23; N 8.72; S 6.88. $C_{26}H_{21}N_3O_4S$. Calculated, %: C 66.22; H 4.49; N 8.91; S 6.80.

Benzoxazines VII and VIII (*general procedure***).** Piperidine or aniline, 0.01 mol, was added with stirring to a solution of 3.22 g of sulfonyl chloride **IV** in 10 ml of acetonitrile. Pyridine, 0.01 mol, was then added, and the mixture was kept for 1 h at 20°C and poured into water. The precipitate was dried and recrystallized from toluene.

2-(3-Piperidinosulfonylphenyl)-4*H*-3,1-benzoxazin-4-one (VII). Yield 2.92 g (79%), mp 174–176°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.65–8.50 m (8H, H_{arom}), 1.55 m [6H, $(CH_2)_3$], 3.20 m (4H, NCH_2). Found, %: C 61.72; H 4.82; N 7.61; S 8.77. $C_{19}H_{18}N_2O_4S$. Calculated, %: C 61.61; H 4.90; N 7.56; S 8.65.

2-(3-Phenylaminosulfonylphenyl)-4*H*-3,1-benzoxazin-4-one (VIII). Yield 2.91 g (77%), mp 190–192°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.00–8.65 m (13H, H_{arom}), 10.25 s (1H, SO_2NH). Found, %: C 63.22; H 3.57; N 7.52; S 8.78. $C_{20}H_{14}N_2O_4S$. Calculated, %: C 63.48; H 3.73; N 7.40; S 8.47.

***N*-(2-Piperidinocarbonylphenyl)-3-(phenylaminosulfonyl)benzamide (IX).** A mixture of 3.78 g of benzoxazinone **VIII** and 0.01 mol of piperidine in 10 ml of acetonitrile was heated for 1 h under reflux. It was then poured into water, and the precipitate was filtered off and recrystallized from acetic acid. Yield 4.03 g (87%), mp 147–150°C. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.00–8.35 m (13H, H_{arom}), 1.60 m [6H, $(CH_2)_3$], 3.40 m (4H, NCH_2), 10.45 s (CONH), 10.25 s (1H, SO_2NH). Found, %: C 64.25; H 5.23; N 9.17; S 6.92. $C_{25}H_{25}N_3O_4S$. Calculated, %: C 64.77; H 5.44; N 9.06; S 6.92.

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