Chemistry of Heterocyclic Compounds, Vol. 39, No. 1, 2003

NEW 6-ARYLSULFONYL-1,2-BENZOISOTHIAZOL-3(2H)-ONE 1,1-DIOXIDES DERIVED FROM DIPHENYL SULFONE MONOSULFONYL CHLORIDES

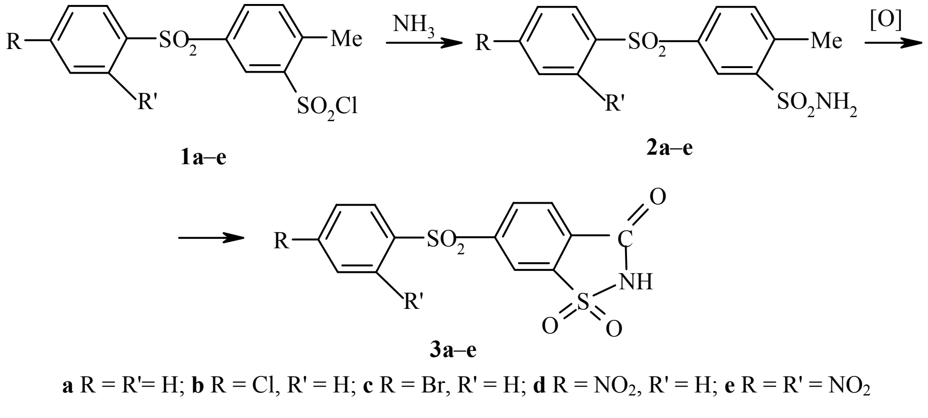
A. V. Tarasov, P. O. Yablonsky, and Yu. A. Moskvichev

Various methods were studied for the oxidation of 2-methyl-5-(phenylsulfonyl)benzenesulfamide and its derivatives. The oxidation by sodium dichromate in sulfuric acid was found most efficient. The effects of temperature, concentration, reagent ratio, and time of the oxidation reaction on the yield of the desired product were investigated. Conditions were proposed for obtaining the desired product in yields up to 95%. A synthesis was developed for a series of new saccharin derivatives.

Keywords: amides of 5-arysulfonyl-2-methylbenzenesulfonic acids, 6-arylsulfonyl-1,2-benzoisothiazol-3(2H)-one 1,1-dioxides, oxidation, saccharins.

Functionally substituted diphenyl sulfones containing sulfonyl chloride, thiol, and amino groups have found common use as monomers [1-3], starting reagents for the preparation of biologically active compounds, and synthones in organic synthesis [4, 5].

In a continuation of work in this area, we have synthesized new monosulfonyl chlorides of various substituted diphenyl sulfones, including derivatives with a methyl group in the position *ortho* to the sulfonyl chloride moiety [6]. These compounds were used in this work for obtaining new 1,2-benzoisothiazol-3(2H)-one 1,1-dioxides substituted at $C_{(6)}$ (saccharin analogs):



1a–e

2a–e

3a–e

a R = R'= H; **b** R = Cl, R' = H; **c** R = Br, R' = H; **d** R = NO_2, R' = H; **e** R = R' = NO_2

Yaroslavl State Technical University, Yaroslavl 150023, Russia; e-mail: abt@polytech.yaroslavl.su. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 126-130, January, 2003. Original article submitted April 20, 2000.

The corresponding amides of 5-arylsulfonyl-2-methylbenzenesulfonic acids **2a-e** were obtained by treating sulfonic acid chlorides **1a-e** or their solutions in dioxane or benzene with 25% aqueous ammonia and subsequent crystallization from acetic acid (Table 1).

Potassium permanganate in aqueous alkaline media and sodium dichromate in sulfuric acid are the most common oxidizing systems for obtaining saccharins [7]. Comparison of the results of the oxidation revealed several disadvantages of using permanganate, namely, yields of the desired product ≤50%, low solubility of both the starting sulfamides and saccharins **3a-e** in the reaction mixture, and difficulty in isolating the saccharins. Thus, the use of sodium dichromate in sulfuric acid was found preferable.

The oxidation of sulfamides **2a-e** was carried out by adding 98% sulfuric acid to a solution of sodium dichromate and the sulfamide in 70% sulfuric acid over 20 min at a given temperature with subsequent stirring of the reaction mixture at the given temperature for 1 h.

The effect of various factors on the yield of saccharins **3a-e** was studied for the case of the oxidation of the amide of 2-methyl-5-(phenylsulfonyl)benzenesulfonic acid **2a** (Fig. 1). Maintaining the reaction mixture above 55°C and using an initial sulfuric acid concentration above 70 mass % diminish the yield of saccharin **3a**, probably due to hydrolysis of both the starting sulfamide and desired saccharin.

The best conditions are as follows: initial concentration 70 mass % sulfuric acid, 50-55°C reaction temperature, 80 min reaction time, reagent ratio 2 mmol sodium dichromate per mmole sulfamide. The yield is 95% in this case. Saccharins **3b-e** were obtained analogously (Table 1).

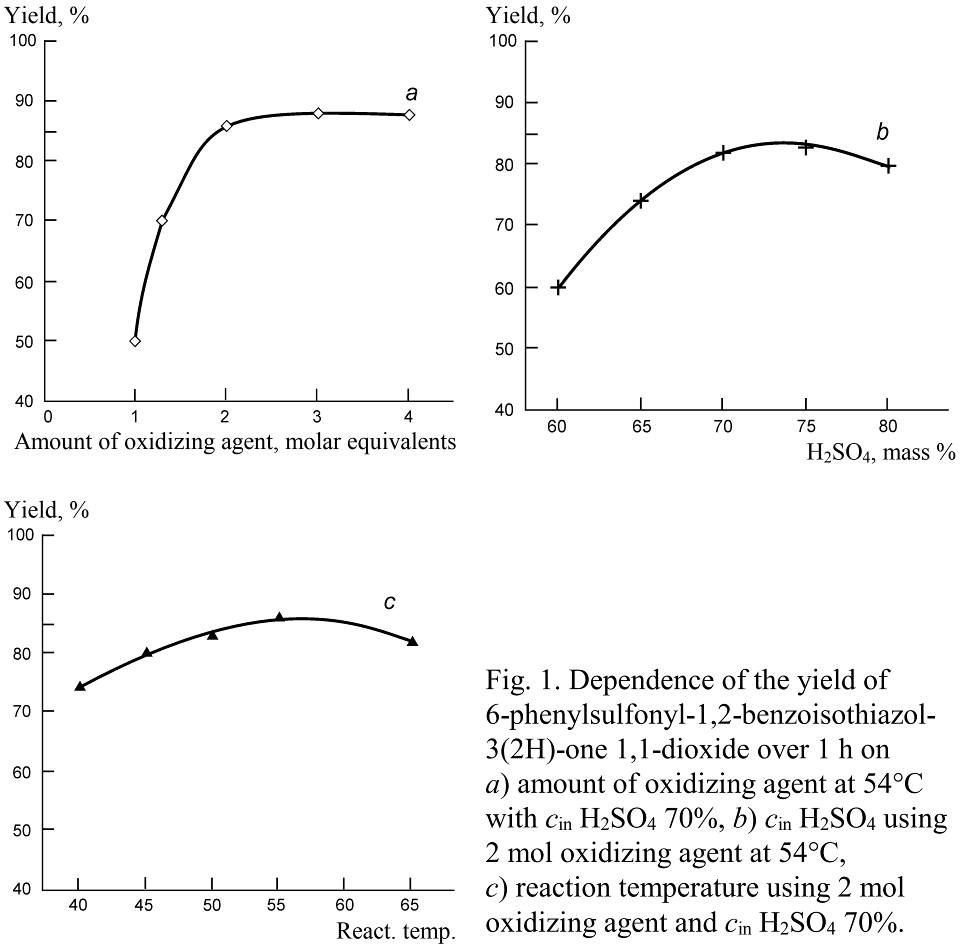


Fig. 1. Dependence of the yield of 6-phenylsulfonyl-1,2-benzoisothiazol-3(2H)-one 1,1-dioxide over 1 h on *a*) amount of oxidizing agent at 54°C with c_{in} H_2SO_4 70%, *b*) c_{in} H_2SO_4 using 2 mol oxidizing agent at 54°C, *c*) reaction temperature using 2 mol oxidizing agent and c_{in} H_2SO_4 70%.

TABLE 1. Characteristics of Prepared Sulfamides **2a-e** and Saccharins **3a-e, 4,** and **5**

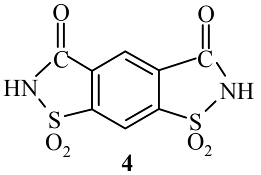
Compound	Empirical formula	Found, % Calculated, %				mp, °C	Yield, %
		C	H	N	S		
2a	$C_{13}H_{13}NO_4S_2$	50.09 50.15	4.22 4.21	4.00 4.05	20.49 20.60	137-140	83
2b	$C_{13}H_{12}ClNO_4S_2$	45.18 45.15	3.58 3.50	3.99 4.05	18.51 18.54	154-156	79
2c	$C_{13}H_{12}BrNO_4S_2$	39.79 40.01	3.11 3.10	3.60 3.59	16.40 16.43	188-190	81
2d	$C_{13}H_{12}N_2O_6S_2$	45.84 43.94	3.12 3.12	7.85 7.88	17.93 18.05	249-252	74
2e	$C_{13}H_{11}N_3O_8S_2$	38.97 38.90	2.75 2.76	10.41 10.47	16.01 15.98	206-209	77
3a	$C_{13}H_9NO_5S_2$	48.39 48.29	2.79 2.81	4.32 4.33	19.71 19.83	211-214	95
3b	$C_{13}H_8ClNO_5S_2$	43.97 43.64	2.24 2.25	3.88 3.91	17.84 17.92	250-253	73
3c	$C_{13}H_8BrNO_5S_2$	38.83 38.82	2.04 2.00	3.45 3.48	15.95 15.94	275-276	78
3d	$C_{13}H_8N_2O_7S_2$	42.31 42.39	2.20 2.19	7.60 7.61	17.45 17.41	259-260	72
3e	$C_{13}H_7N_3O_9S_2$	37.84 37.78	1.73 1.71	10.23 10.17	15.48 15.52	278-280	75
4*	$C_8H_4N_2O_6S_2$	33.36 33.33	1.37 1.40	9.66 9.72	22.35 22.25	405	95
5*[2]	$C_{14}H_8N_2O_8S_3$	39.31 39.25	1.91 1.88	6.51 6.54	22.63 22.45	326-328	90

---

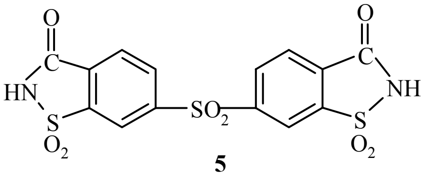
* Acoording to the data [2]: mp 405°C, yield 89%.

*[2] Acoording to the data [2]: mp 329-330°C, yield 84%.

Known bisaccharins **4** and **5** were also obtained under these conditions with better yields (Table 1) than previously obtained [2]:



4



5

In light of the strong heat evolution in this reaction, especially for loads greater than 10 g sulfamide, efficient heat removal is required to maintain the given temperature. In some cases, uncontrolled heating of the reaction mixture up to 120°C occurred with decomposition of the reaction products. In order to optimize the reaction, we studied the effect of the reagent load in the reactor. The reaction proceeds in a more controlled manner when the sulfamide is added in portions to the solution of sodium dichromate in 87% sulfuric acid, while the rate of the reaction is controlled by the amount of added sulfamide. However, this procedure led to a drop in the saccharin yield by 5-15%.

The most convenient method for purifying the saccharins is reprecipitation from aqueous $NaHCO_3$. A water-soluble sodium salt of the saccharin is formed upon adding the reaction mixture to aqueous $NaHCO_3$. Possible impurities and unreacted sulfamide remain undissolved and are removed by filtration. The desired saccharin precipitates with purity up to 99% upon acidification of the mother liquor by adding hydrochloric acid to pH 4.

The structures of the compounds synthesized were supported by ^1H NMR and IR spectroscopy.

The IR spectra of suspensions of **3-5** in the carbonyl group region show, as a rule, bands at 1740-1725 and 1715-1690 cm^{-1}, which may be ascribed to the free carbonyl group and carbonyl groups involved in hydrogen bonding. On the other hand, only one carbonyl group band is always found in DMSO solutions at 1740-1730 cm^{-1}. This finding suggests that there is no hydrogen bonding in DMSO and amide–DMSO associated species (=NH···O=S–) are formed, which are more stable species. The carbonyl groups remain free in this case. The existence of associated species in DMSO solutions was also shown by ^{1}H NMR spectroscopy. The signal for the NH group proton is shifted upfield with increasing temperature.

EXPERIMENTAL

The IR spectra were taken on a Shimadzu IR-435 spectrometer at 4000-400 cm^{-1} for suspensions in vaseline. The IR spectra of solutions in DMSO were taken in KBr cells with layer thickness 0.035 and 0.058 mm (the reference cell was filled with pure DMSO). The reaction course and the purity of the products were monitored by thin-layer chromatography using Sorbton diol UV-254 with 1:3 ethyl acetate–heptane as the eluent. The acid chloride derivatives of 5-arylsulfonyl-2-methylbenzenesulfonic acids were obtained as described in our previous work [6].

Amide of 2-Methyl-5-(phenylsulfonyl)benzenesulfonic Acid (2a). A solution of sulfonyl chloride **1a** (5 g, 15 mmol) in dioxane (10 ml) was placed into a three-necked flask equipped with a stirrer, thermometer, and reflux condenser and then, 25% aqueous NH_3 (2 ml, 30 mmol) was added rapidly with stirring at 20°C. The reaction mixture was maintained at 40-60°C for 1 h. At the end of the reaction, the mixture was poured into water. The precipitate formed was filtered off, washed with water, dried, and recrystallized from acetic acid.

Products 2b-e were obtained analogously.

Oxidation of Sulfamide 2a to 6-Phenylsulfonyl-1,2-benzoisothiazol-3(2H)-one 1,1-Dioxide (3a). A sample of water (0.42 g, 23 mmol), 98% sulfuric acid (1.1 g, 15 mmol), and $Na_2Cr_2O_7$ (1.68 g, 6.4 mmol) were placed into a four-necked flask equipped with a stirrer, thermometer, dropping funnel, and reflux condenser and heated to 55°C. Then, sulfamide **2a** (1 g, 3.2 mmol) was added in portions at this temperature with stirring. 98% Sulfuric acid (1 g, 10 mmol) was added slowly with vigorous stirring, maintaining the temperature in the flask at 55°C. The color of the solution turned from red-brown to green. The mixture was stirred for 1 h and then poured onto ice (50 g). The precipitate formed was filtered off and washed with water. The product was reprecipitated from 20% aqueous $NaHCO_3$. Yield of **3a** 0.99 g (95%).

Products **3b-e**, **4**, and **5** were obtained analogously. The loads of the starting sulfamides prepared according to our previous procedure [2] were half compared to the procedure described for **3a**.

REFERENCES

1. S. K. Kramerova, Yu. A. Moskvichev, G. S. Mironov, and E. M. Alov, in: *Fundamental Organic Synthesis and Petrochemistry* [in Russian], issue 2, Yaroslavl Polytechnical Institute, Yaroslavl (1975), p. 119.
2. E. B. Gatsa, Yu. A. Moskvichev, G. G. Kryukova, G. S. Mironov, and M. I. Farberov, *Zh. Org. Khim.*, **10**, 1693 (1974).
3. V. V. Korshak (editor), *Advances in the Synthesis of Heteroorganic Polymers* [in Russian], Nauka, Moscow (1988), p. 320.
4. M. D. Mashkovskii, *Drugs* [in Russian], Vols. 1-2, Meditsina, Moscow (1986)
5. N. N. Mel'nikov, *Pesticide Chemistry and Technology* [in Russian], Khimiya, Moscow (1974), 766 p.
6. P. O. Yablonskii, A. V. Tarasov, and Yu. A. Moskvichev, *Zh. Org. Khim.*, **36**, 68 (2000).