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To the memory of Professor G.I. Koldobskii

Tetrazoles: LVII.* Preparation and Chemical Properties of 1-Substituted 5-Arylsulfonyltetrazoles

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Abstract—Oxidation of 1-substituted 5-arylsulfanyltetrazoles with *m*-chloroperoxybenzoic acid and $NaIO_4$ in the presence of $RuCl_3$ leads to the formation of the 5-arylsulfonyltetrazoles. The microwave activation significantly accelerates the oxidation with sodium periodate. The phenylsulfonyl group in compounds obtained underwent the nucleophilic substitution when treated with ethanol, phenol, or benzimidazole in acetonitrile in the presence of NaOH.

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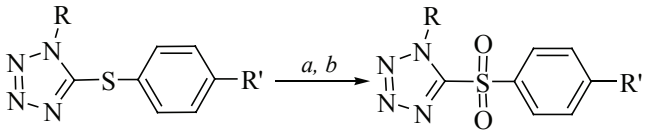
Substituted sulfonyltetrazoles are promising substances in view of their biological activity [1] and the possibility of their application to further functionalization of tetrazoles [2], yet compared to the 1-substituted 5-alkylsulfonyltetrazoles methods of the synthesis and the chemical properties of the corresponding 5-arylsulfonyltetrazoles are poorly understood. Recently certain advances were observed in the development of the method of copper-catalyzed arylation of heterocyclic thiols, in particular, the substituted 5-mercapto-tetrazoles [3]. Therefore the oxidation of the respective 5-arylsulfanyltetrazoles seems to be the simplest procedure for the preparation of 1-substituted 5-arylsulfonyltetrazoles.

We found formerly that 5-(4-toluenesulfinyl)- and 5-tosyl-1-phenyl-1*H*-tetrazoles could be obtained by the oxidation of 5-(4-tolylsulfanyl)-1-phenyl-1*H*-tetrazole with hydrogen peroxide in acetic acid both at convection heating and under microwave activation [4]. However the oxidation of 1-phenyl-5-phenylsulfanyl-1*H*-tetrazole in the same conditions afforded a mixture of the corresponding sulfinyl- and sulfonyltetrazoles, and besides raising the temperature or hydrogen peroxide concentration resulted in the accumulation of 1-phenyltetrazol-5-one.

In continuation of the examination of the preparation procedures for the 5-aryl-sulfonyltetrazoles we studied the oxidation of a series of 1-substituted 5-arylsulfanyltetrazoles with hydrogen peroxide in acetic acid, with hydrogen peroxide in acetone, with hydrogen peroxide in the presence of tungstates, with OXONE oxidant (potassium peroxymonosulfate), with *m*-chloroperoxybenzoic acid, and with $NaIO_4$ in the presence of a catalytic quantity of $RuCl_3$.

Among the oxidants we tested the best results were obtained only at the use of *m*-chloroperoxybenzoic acid and $NaIO_4$ in the presence of $RuCl_3$, in the other cases the oxidation resulted in a mixture of arylsulfinyl- and arylsulfanyltetrazoles or was accompanied with the hydrolysis of the reaction products giving the corresponding tetrazol-5-ones.



Ia–Ie

(*a*) 3-ClC_6H_4COOOH, $CHCl_3$; (*b*) $NaIO_4$, $RuCl_3$, MeCN–H_2O; R = Ph, R' = Me (**a**), MeO (**b**), NO_2 (**c**), H (**d**); R = Me, R' = H (**e**).

*For Communication LVI, see [1].

The oxidation of 1-substituted 5-arylsulfanyltetrazoles proceeds cleanly at the treatment with a triple excess of of *m*-chloroperoxybenzoic acid in chloroform at 40°C within 0.5–5 h (method *a*). In the course of the reaction the formation of intermediate arylsulfinyltetrazoles was observed, but we failed to isolate them for simultaneously a considerable amount of the completely oxidized product was obtained.

Interestingly, the microwave activation did not affect this process. The duration of the oxidation and the yields in the reaction occurring at the dielectric and convection heating practically coincided.

At the oxidation of substituted 5-arylsulfanyltetrazoles with excess $NaIO_4$ in the presence of a catalytic quantity of $RuCl_3$ (method *b*) notwithstanding the ratio substrate–$NaIO_4$ only the corresponding sulfonyltetrazoles were obtained. The reaction time depends on the amount of $RuCl_3$ and on the temperature. At the molar ratio $RuCl_3$–(**Id**) equal ~1 : 10000 the reaction goes to the completion within 48 h at the room temperature, at 70°C under convection heating, within 2–2.5 h, and at the microwave activation at this temperature, in 3 min. The yields were 91, 92, and 96% respectively. The quantity of $RuCl_3$ may be reduced to ~1 : 1000000 without essential decrease in the yield and increase in the reaction duration (see the table).

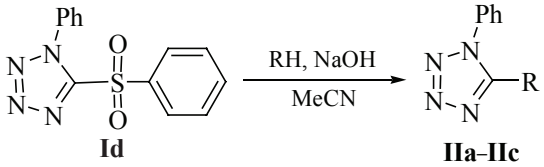
Oxidation of 1-substituted 5-arylsulfanyltetrazoles at the convection heating

Comnd. no.	Method *a*		Method *b*	
	reaction time, h	yield, %	reaction time, h	yield, %
Ia	0.5	93	1.5	95
Ib	0.5	89	6	70
Ic	5	67	6	85
Id	2	96	2.5	88
Ie	1	63	–	–

Aplying the mentioned oxidants we synthesized a series of 1-substituted 5-arylsulfanyltetrazoles.

One method of tetrazoles functionalization consists in the substitution of leaving groups at the carbon atom of the heterocycle. First of all the nucleophilic substitution in the series of 1-R-5-halotetrazoles [5] and electrophilic substitution of the hydrogen in the 1-substituted tetrazoles [6] should be mentioned. However the substituted 5-halotetrazoles are difficultly available compounds, and the hydrogen substitution requires severe conditions and can be used only with the limited range of substrates. It was shown before [2] that 1-substituted 5-methylsulfonyltetrazoles possess sufficiently high reactivity with respect to C-, N-, and O-nucleophiles of various structures. Besides in [7] the nucleophilic substitution of the tolylsulfonyl group with aliphatic and aromatic thiols was used for subsequent functionalization of tetrazoles.

By an example of compound **Id** we investigated the nucleophilic substitution with C-, N-, O-nucleophiles by procedure [2] in acetonitrile in the presence of NaOH. 1-Phenyl-5-phenylsulfonyltetrazole (**Id**) reacted with ethanol in acetonitrile at room temperature. Good yields with phenol and benzimidazole we succeeded to obtain only in DMF medium, and the attempts to carry out the reactions with piperidine and malonodinitrile under the above conditions were unsuccessful. At heating in all events 1-phenyl-tetrazole-5-one was obtained.



Id **IIa–IIc**

R = EtO (**a**), PhO (**b**), benzimidazolyl (**c**).

Thus the developed methods of oxidation of 1-substituted 5-arylsulfanyltetrazoles made it possible to obtain 1-substituted 5-arylsulfonyltetrazoles in good yields. It was shown that the microwave activation significantly accelerated the oxidation of 1-substituted 5-arylsulfanyltetrazoles with sodium periodate and did not affect their oxidation with *m*-chloroperoxybenzoic acid.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Shimadzu FTIR-8400S from pellets with KBr. ^{1}H NMR spectra were registered on a spectrometer Bruker WM-400 (400 MHz) from solutions in DMSO-d_6. Elemental analysis was carried out on an analyzer LECO CHNS-932. The reactions under microwave activation were performed in a reactor Milestone MicroSynth. The monitoring of the reaction progress and checking of the purity and homogeneity of compounds obtained was carried out by TLC on Silufol UV-254 plates. 1-Substituted 5-arylsulfanyl-tetrazoles were prepared by the method [3].

5-Tosyl-1-phenyl-1*H*-tetrazole (Ia). *a*. To a solution

of 0.42 g (1.56 mmol) of 5-(4-tolylsulfanyl)-1-phenyl-1*H*-tetrazole in 12 ml of $CHCl_3$ was added 1.34 g (4.68 mmol) of 60% 3-chloroperoxybenzoic acid, and the mixture was stirred for 30 min at 40°C, cooled to room temperature, and diluted with 12 ml of chloroform. The mixture was washed in succession with 5% water solution of $NaHCO_3$ (3 × 25 ml), water (2 × 25 ml), and brine (25 ml). The organic layer was separated, dried with Na_2SO_4, and evaporated. Yield 0.43 g (92%), mp 129°C (2-propanol).

Compounds **Ib–Ie** were synthesized analogously by the method *a*, the reaction time and yields were given in the table.

*b***.** To a solution of 0.42 g (1.56 mmol) of 5-(4-tolylsulfanyl)-1-phenyl-1*H*-tetrazole in 40 ml of acetonitrile was added a solution of $NaIO_4$ in 20 ml of water and 40 μl of freshly prepared solution of $RuCl_3 \cdot 3H_2O$ (10 mg l^{-1} $RuCl_3$) in a mixture MeCN–H_2O, 2:1. The reaction mixture was stirred for 1.5 h at 70°C and then it was diluted with 75 ml of water. The separated precipitate was filtered off. Yield 0.43 g (95%), colorless crystals, mp 129–130°C [4] (2-propanol). IR spectrum, ν, cm^{-1}: 3061, 3040, 3025, 2924 (C–H), 1593 (C=N), 1500 (C=C), 1490, 1454, 1418, 1393, 1367 (C–H bend.), 1289, 1269, 1229, 1167, 1101 (SO_2), 1089, 1063, 1042, 1014, 968, 922, 811, 763, 722, 689, 620. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 2.49 s (3H, CH_3), 7.51–7.52 d (2H_{arom}, *J* 4 Hz), 7.68–7.72 m (5H_{arom}), 7.74–7.75 d (2H_{arom}, *J* 4 Hz).

Syntheses of compounds **Ia–Id** by the method *b* under the microwave heating were similarly performed. The reaction time and yields under convection heating were given in the table.

5-[(4-Methoxyphenyl)sulfonyl]-1-phenyl-1*H*-tetrazole (Ib). Colorless crystals, mp 135–136°C (AcOH–H_2O, 3:1). IR spectrum, ν, cm^{-1}: 3100, 3080, 2971, 2845, 1597 (C=N), 1578, 1498, 1459, 1419, 1340, 1319, 1272, 1186, 1157, 1088, 1023, 1015, 843, 807, 763, 678, 601. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 3.39 s (3H, CH_3), 7.04–7.07 d (2H_{arom}, *J* 12 Hz), 7.62–7.65 m (5H_{arom}), 7.87–7.90 d (2H_{arom}, *J* 12 Hz). Found, %: C 52.99; H 4.09; N 17.63; S 10.19. $C_{14}H_{12}N_4O_3S$. Calculated , %: C 53.16; H 3.82; N 17.71; S 10.14.

5-[(4-Nitrophenyl)sulfonyl]-1-phenyl-1*H*-tetrazole (Ic). Colorless crystals, mp 176–177°C (2-propanol–DMF, 5:1). IR spectrum, ν, cm^{-1}: 3114 (C–H), 3066 (C–H), 1609 (C=N), 1545 (NO_2), 1534, 1497, 1457, 1405, 1370 (NO_2), 1347, 1317, 1310, 1291, 1227, 1171 (SO_2), 1110, 1084, 1012, 856, 761, 751, 743, 691, 679, 627. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 7.67–7.73 m (5H_{arom}), 8.22–8.25 d (2H_{arom}, *J* 12 Hz), 8.47–8.50 d (2H_{arom}, *J* 12 Hz). Found, %: C 47.01; H 2.70; N 20.97; S 9.80. $C_{13}H_9N_5O_4S$. Calculated , %: C 47.13; H 2.74; N 21.14; S 9.68.

1-Phenyl-5-(phenylsulfonyl)-1*H*-tetrazole (Id). Colorless crystals, mp 135–136°C (2-propanol). IR spectrum, ν, cm^{-1}: 3083 (C–H), 3070, 3019, 1595, 1581 (C=N), 1499, 1478, 1451, 1427, 1406, 1338, 1327, 1319, 1292, 1274, 1238, 1176, 1167, 1161 (SO_2), 1106, 1084, 1073, 1051, 1015, 997, 977, 918, 763, 728, 695, 687, 615. ^{1}H NMR spectrum (acetone-d_6), δ, ppm: 7.68–7.76 m (7H_{arom}), 7.87–7.93 m (3H_{arom}). Found, %: C 54.65; H 3.43; N 19.44; S 11.38. $C_{13}H_{10}N_4O_2S$. Calculated , %: C 54.54; H 3.52; N 19.57; S 11.20.

1-Methyl-5-(phenylsulfonyl)-1*H*-tetrazole (Ie). Colorless crystals, mp 92–93°C (2-propanol). IR spectrum, ν, cm^{-1}: 3096 (C–H), 3070, 1584 (C=N), 1464, 1447, 1400, 1350, 1336, 1311, 1284, 1208, 1188, 1155, 1091 (SO_2), 1079, 1068, 758, 741, 718, 689, 679, 610. ^{1}H NMR spectrum, δ, ppm ($CDCl_3$): 4.42 s (3H, CH_3), 7.67–7.71 m (1H_{arom}), 7.81–7.84 m (1H_{arom}), 8.13–8.14 d (2H_{arom}, *J* 4 Hz). Found, %: C 42.78; H 3.68; N 24.91; S 14.19. $C_8H_8N_4O_2S$. Calculated , %: C 42.85; H 3.60; N 24.99; S 14.30.

1-Phenyl-5-ethoxy-1*H*-tetrazole (IIa). To a solution of 0.2 g (0.69 mmol) of compound **Id** in 10 ml of acetonitrile was added 1 ml of ethanol and 0.03 g (0.75 mmol) of NaOH. The mixture was stirred for 30 min and poured into 50 ml of water, the formed precipitate was filtered off. Yield 0.08 g (62%), colorless crystals, mp 70°C (EtOH) [2]. IR spectrum, ν, cm^{-1}: 3074, 2988, 2941, 2904, 2867, 1711, 1595, 1572, 1506, 1476, 1457, 1442, 1388, 1362, 1320, 1302, 1138, 1115, 1071, 1030, 990, 902, 816, 764, 733, 688, 683. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.36–1.38 t (3H, Me, *J* 4 Hz), 4.53–4.63 q (2H, CH_2), 7.29–7.51 m (5H_{arom}).

1-Phenyl-5-phenoxy-1*H*-tetrazole (IIb). To a solution of 0.2 g (0.69 mmol) of compound **Id** in 10 ml of DMF was added 0.065 g (0.70 mmol) of phenol and 0.03 g (0.75 mmol) of NaOH. The mixture was stirred for 1.5 h and poured into 50 ml of water, the formed precipitate was filtered off. Yield 0.16 g (96%), colorless crystals, mp 124–125°C (EtOH) [2]. IR spectrum, ν, cm^{-1}: 3067, 2961, 1597, 1539, 1508, 1480, 1454, 1324, 1297, 1286, 1179, 1157, 1121, 1103, 1074, 1048, 1018, 848, 803, 768, 737, 691. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.24–7.34 m (5H_{arom}), 7.45–7.67 m (5H_{arom}).

5-(Benzimidazol-1-yl)-1-phenyl-1*H*-tetrazole (IIc) was obtained similarly. Yield 55%, colorless crystals, mp 189°C (EtOH) [2]. IR spectrum, ν, cm^{-1}: 3129, 3075, 1711, 1595, 1557, 1498, 1442, 1350, 1303, 1281, 1249, 1172, 1118, 1095, 990, 969, 883, 781, 770, 763, 742, 690, 618. ^1H NMR spectrum (DMSO-d_6), δ, ppm: 7.16–7.34 m ($2H_{arom}$), 7.46–7.74 m ($2H_{arom}$), 7.54 m *(5H*$_{arom}$), 7.92 s ($1H_{arom}$).

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