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SHORT COMMUNICATIONS

Synthesis and Chemical Properties of 5-Alkylsulfonyl-1-(4-nitrophenyl)tetrazoles

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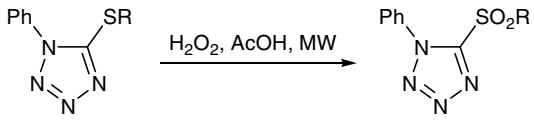
While performing studies in the field of synthesis and properties of 5-alkylsulfonyl-1-aryltetrazoles, we have developed a simple and efficient procedure for the preparation of these compounds. The procedure includes oxidation of the corresponding 5-alkylsulfanyl-1-phenyltetrazoles with hydrogen peroxide under conditions of microwave activation (MW) and subsequent nitration of the sulfones thus formed.

5-Alkylsulfonyl-1-aryltetrazoles were synthesized previously by oxidation of 5-alkylsulfanyl-1-aryltetrazoles with potassium permanganate in the two-phase system methylene chloride–aqueous acetic acid using tetrabutylammonium bromide as phase-transfer catalyst [1]. However, this procedure requires subsequent utilization of manganese dioxide, and the reaction time is considerably long. The use of hydrogen peroxide as oxidant under microwave irradiation is free from the above disadvantages. The reaction time shortens from 10–12 to 2–7 h, and there is no need of utilizing by-products, while the target 5-alkylsulfonyltetrazoles **Ia**–**Ic** are formed in 76–90% yield (Scheme 1).

Scheme 1.



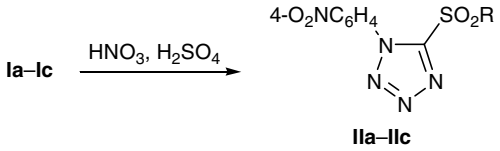
Ia–Ic

R = Me (**a**), Et (**b**), Pr (**c**).

By treatment of compounds **Ia**–**Ic** with a mixture of nitric and sulfuric acids we obtained 5-alkylsulfonyl-1-(4-nitrophenyl)tetrazoles **IIa**–**IIc** (Scheme 2).

We previously showed [1–3] that 1-aryl-5-(methylsulfonyl)tetrazoles are highly reactive toward various C-, N-, and O-centered nucleophiles. Moreover, nucleophilic replacement of the methylsulfonyl group in such substrates may be regarded as a very promising method for functionalization of tetrazoles [4]. While studying chemical properties of 1-aryl-5-(methylsulfonyl)tetrazoles, we recently revealed that 5-methylsulfonyl-1-(4-nitrophenyl)tetrazole reacts with formaldehyde in the presence of triethylamine under microwave activation to give 5-methylsulfonylmethoxy-1-(4-nitrophenyl)tetrazole [5]. We now report that this reaction is general, and other 5-alkylsulfonyl-1-(4-nitrophenyl) tetrazoles give rise to the corresponding alkylsulfonylmethoxy derivatives as well (Scheme 3).

Scheme 2.

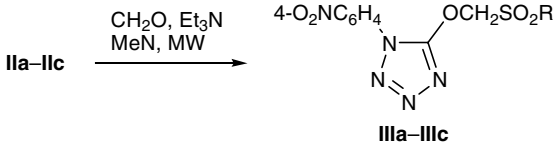


IIa–IIc

R = Me (**a**), Et (**b**), Pr (**c**).

We cannot still propose a rigorous mechanism of the process. Presumably, compounds **IIIa**–**IIIc** are formed via addition of formaldehyde molecule to the tetrazole carbon atom to give a dipolar intermediate and subsequent migration of the alkylsulfonyl group to the positively charged center of that dipole. It should

Scheme 3.



IIIa–IIIc

R = Me (**a**), Et (**b**), Pr (**c**).

be noted that such transformations in the tetrazole series were not described previously.

The structure of tetrazoles **IIIa**–**IIIc** was proved by the analytical data, IR and NMR spectra, and X-ray analysis [5].

5-Methylsulfonyl-1-phenyltetrazole (Ia). A Pyrex reactor was charged with a solution of 15 g (78 mmol) of 5-methylsulfanyl-1-phenyltetrazole in 150 ml of glacial acetic acid, 30 ml of 35% hydrogen peroxide was added at 20°C, and the mixture was stirred for 2 h under microwave irradiation (30 W, 70°C). The mixture was cooled to 18°C and diluted with 100 ml of ice water, and the precipitate was filtered off, washed with water (3×20 ml), and dried in air. Yield 15.7 g (90%), mp 83–84°C (from ethanol) [1]. IR spectrum, ν, cm^{-1}: 981, 1017, 1054, 1074, 1108, 1154, 1157, 1173, 1233, 1270, 1295, 1322, 1335, 1350, 1403, 1428, 1458, 1593, 2929, 3015. ^{1}H NMR spectrum, δ, ppm: 3.67 s (3H, CH_3), 7.62–7.76 m (5H, H_{arom}). Found, %: C 42.84; H 3.40; N 24.97; S 14.46. $C_8H_8N_4O_2S$. Calculated, %: C 42.86; H 3.57; N 25.00; S 14.29.

5-Alkylsulfonyl-1-phenyltetrazoles **Ib** and **Ic** were synthesized in a similar way.

5-Ethylsulfonyl-1-phenyltetrazole (Ib). Yield 86%, mp 69–71°C (from ethanol). IR spectrum, ν, cm^{-1}: 981, 1017, 1040, 1058, 1075, 1113, 1151, 1241, 1267, 1285, 1328, 1341, 1386, 1395, 1411, 1422, 1458, 1497, 1593, 2890, 2928, 2974, 3063, 3078, 3105. ^{1}H NMR spectrum, δ, ppm: 1.27–1.31 t (3H, CH_3), 3.73–3.78 m (2H, CH_2), 7.62–7.75 m (5H, H_{arom}). Found, %: C 45.29; H 4.21; N 23.57; S 13.68. $C_9H_{10}N_4O_2S$. Calculated, %: C 45.37; H 4.20; N 23.53; S 13.45.

1-Phenyl 5-propylsulfonyltetrazole (Ic). Yield 76%, mp 48–49°C (from ethanol). IR spectrum, ν, cm^{-1}: 920, 1015, 1050, 1077, 1085, 1103, 1155, 1176, 1210, 1249, 1299, 1338, 1401, 1454, 1458, 1465, 1470, 1497, 1594, 2876, 2904, 2940, 2971, 2978, 3062. ^{1}H NMR spectrum, δ, ppm: 0.94–0.98 t (3H, CH_3), 1.71–1.81 m (2H, CH_2), 3.71–3.75 m (2H, CH_2), 7.62–7.74 m (5H, H_{arom}). Found, %: C 47.68; H 4.81; N 22.22; S 12.64. $C_{10}H_{12}N_4O_2S$. Calculated, %: C 47.62; H 4.76; N 22.22; S 12.70.

5-Methylsulfonyl-1-(4-nitrophenyl)tetrazole (IIa). A solution of 2.25 g (10 mmol) of 5-methylsulfonyl-1-phenyltetrazole in 10 ml of 94% sulfuric acid was cooled to 5°C, and 3 ml of 98% nitric acid was added dropwise under stirring, maintaining the temperature below 10°C. An additional 5 ml of 94% sulfuric acid was added, and the mixture was allowed to slowly warm up to 18–20°C, stirred for 2 h, and poured onto 200 g of finely crushed ice. The precipitate was filtered off, washed with water (3×50 ml), and dried in air. Yield 2.4 g (89%), mp 155–156°C (from acetonitrile) [2]. IR spectrum, ν, cm^{-1}: 954, 1010, 1060, 1103, 1118, 1164, 1231, 1270, 1299, 1313, 1326, 1339, 1380, 1416, 1499, 1527, 1539, 1596, 1618, 2300, 2870, 2931, 3009, 3046, 3081, 3122. ^{1}H NMR spectrum, δ, ppm: 3.70 s (3H, CH_3), 8.04–8.68 d (2H, H_{arom}), 8.47–8.52 d (2H, H_{arom}). Found, %: C 35.71; H 2.47; N 26.20; S 11.96. $C_8H_7N_5O_4S$. Calculated, %: C 35.69; H 2.60; N 26.02; S 11.90.

5-Alkylsulfonyl-1-(4-nitrophenyl)tetrazoles **IIb** and **IIc** were synthesized in a similar way.

5-Ethylsulfonyl-1-(4-nitrophenyl)tetrazole (IIb). Yield 86%, mp 135–136°C (from DMF–propan-2-ol, 1:3). IR spectrum, ν, cm^{-1}: 974, 980, 1009, 1033, 1039, 1056, 1113, 1155, 1159, 1177, 1235, 1254, 1268, 1282, 1299, 1314, 1326, 1344, 1379, 1399, 1428, 1447, 1498, 1530, 1596, 1612, 1709, 1821, 1954, 2793, 2866, 2939, 2949, 2974, 3002, 3016, 3060, 3082, 3114. ^{1}H NMR spectrum, δ, ppm: 1.29–1.33 t (3H, CH_3), 3.76–3.81 m (2H, CH_2), 8.07–8.09 d (2H, H_{arom}), 8.47–8.49 d (2H, H_{arom}). Found, %: C 38.24; H 3.14; N 24.75; S 11.25. $C_9H_9N_5O_4S$. Calculated, %: C 38.16; H 3.18; N 24.73; S 11.31.

1-(4-Nitrophenyl)-5-propylsulfonyltetrazole (IIc). Yield 98%, mp 95–96°C (from ethyl acetate). IR spectrum, ν, cm^{-1}: 1009, 1052, 1086, 1107, 1148, 1260, 1292, 1298, 1312, 1342, 1378, 1401, 1458, 1494, 1529, 1533, 1595, 1614, 2884, 2924, 2976, 3063, 3077. ^{1}H NMR spectrum, δ, ppm: 0.98–1.00 t (3H, CH_3), 1.78–1.80 m (2H, CH_2), 3.71–3.79 m (2H, CH_2), 8.06–8.08 d (2H, H_{arom}), 8.47–8.49 d (2H, H_{arom}). Found, %: C 40.23; H 3.78; N 23.39; S 10.79. $C_{10}H_{11}N_5O_4S$. Calculated, %: C 40.40; H 3.70; N 23.57; S 10.77.

5-Methylsulfonylmethoxy-1-(4-nitrophenyl)-tetrazole (IIIa). 5-Methylsulfonyl-1-(4-nitrophenyl)-tetrazole (**IIa**), 2.0 g (7 mmol), was dissolved in 25 ml of acetonitrile, 1 ml of a 37.4% formaldehyde solution and 1.06 g (10.5 mmol) of triethylamine were added, and the mixture was stirred for 1.5 h under microwave irradiation (25 W, 40°C). The mixture was then diluted with 50 ml of ethanol, and the precipitate was filtered off and dried in air. Yield 1.98 g (89%), mp 149–150°C (from acetonitrile). IR spectrum, ν, cm^{-1}: 943, 975, 1097, 1109, 1133, 1151, 1297, 1312, 1323, 1340, 1352, 1368, 1404, 1416, 1445, 1460, 1507, 1522, 1560, 1599, 1619, 2925, 2946, 3019, 3110, 3132, 3450. ^{1}H NMR spectrum, δ, ppm: 3.19 s (3H, CH_3), 5.79 s (2H, CH_2),

8.03–8.06 d (2H, H_{arom}), 8.48–8.50 d (2H, H_{arom}). Found, %: C 36.10; H 2.79; N 23.38; S 10.68. $C_9H_9N_5O_5S$. Calculated, %: C 36.12; H 3.01; N 23.41; S 10.70.

5-Alkylsulfonylmethoxy-1-(4-nitrophenyl)tetrazoles **IIIb** and **IIIc** were synthesized in a similar way.

5-Ethylsulfonylmethoxy-1-(4-nitrophenyl)tetrazole (IIIb). Yield 95%, mp 131–132°C (from ethyl acetate). IR spectrum, ν, cm^{-1}: 944, 1024, 1047, 1091, 1099, 1110, 1129, 1138, 1275, 1299, 1310, 1326, 1342, 1351, 1417, 1454, 1463, 1507, 1527, 1562, 1597, 1614, 2926, 2964, 3027, 3104. ^{1}H NMR spectrum, δ, ppm: 1.88–1.92 t (3H, CH_3), 3.76–3.81 m (2H, CH_2), 6.16 s (2H, CH_2), 8.55–8.57 d (2H, H_{arom}), 8.99–9.01 d (2H, H_{arom}). Found, %: C 38.50; H 3.39; N 22.60; S 10.56. $C_{10}H_{11}N_5O_5S$. Calculated, %: C 38.34; H 3.51; N 22.36; S 10.22.

1-(4-Nitrophenyl)-5-propylsulfonylmethoxytetrazole (IIIc). Yield 94%, mp 100–102°C (from ethanol–acetonitrile, 5:1). IR spectrum, ν, cm^{-1}: 955, 978, 1009, 1024, 1044, 1092, 1100, 1110, 1124, 1138, 1181, 1215, 1243, 1257, 1293, 1307, 1314, 1343, 1350, 1369, 1384, 1418, 1458, 1504, 1523, 1532, 1558, 1599, 1617, 1727, 1753, 2880, 2936, 2954, 2974, 3024, 3105, 3126. ^{1}H NMR spectrum, δ, ppm: 1.56–1.60 t (3H, CH_3), 2.37–2.42 m (2H, CH_2), 3.73–3.77 m (2H, CH_2), 6.14 c (2H, CH_2), 8.54–8.57 d (2H, H_{arom}), 8.98–9.01 d (2H, H_{arom}). Found, %: C 40.42; H 3.80; N 21.64; S 10.05. $C_{11}H_{13}N_5O_5S$. Calculated, %: C 40.37; H 3.98; N 21.40; S 9.78.

The IR spectra were measured on a Shimadzu FTIR-8400S spectrometer from samples prepared as KBr pellets. The ^{1}H NMR spectra were recorded on a Bruker AC-400 instrument from solutions in DMSO-d_6. The elemental compositions were determined on a LECO CHNS(O)-932 analyzer. Microwave-assisted reactions were performed in a Milestone P/N 44072 reactor. The purity of the products was checked by TLC on Silufol plates using ethyl acetate–carbon tetrachloride (2:3) as eluent.

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