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A simple method for the preparation of 5-alkylsulfinyl-1-aryltetrazoles

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Abstract—A simple method is suggested for the preparation of 5-alkylsulfinyl-1-aryltetrazoles via oxidation of 5-alkylsulfanyltetrazoles with 34% peracetic acid in high yields under mild conditions.

Tetrazoles and their sulfides have recently been an extensively studied group of compounds, their structure being an important moiety of many drugs, for example, sartanes, β-lactam antibiotics, etc. Various modifications to their structure have been undertaken to obtain compounds with different physicochemical properties and, subsequently, with different pharmacodynamic and pharmacokinetic properties.

One type of substance, with different polarity, is the oxidative product of sulfide–sulfoxide. While many methods of oxidation of dialkyl-, diaryl-, and alkylarylsulfides have been described, sulfoxides derived from alkylsulfanyltetrazoles, unlike similar sulfones, are not very common in the literature.

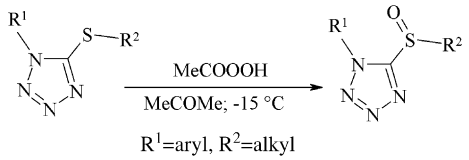
Nevertheless, a few reports on this topic have appeared recently, because both sulfones and sulfoxides are important intermediates of reactions such as eliminations,[1] or olefinations, particularly in modified Julia olefination.[2] Alkylsulfanyltetrazoles are readily oxidized to sulfones. One of the first papers studying oxidation of these compounds described the use of $KMnO_4$ in acetic acid.[3]

Currently, the most widely used reagents for the preparation of alkylsulfonyltetrazoles are *m*-chloroperbenzoic acid (MCPBA) at temperatures from −10 °C[4] to room temperature[5] and ammonium heptamolybdate tetrahydrate in ethanol,[6] a reagent introduced as early as 1963. Such sulfones have also been prepared using 30% H_2O_2 in acetic acid at 70 °C.[7]

Alkylsulfinyltetrazoles can be prepared using practically the same method—MCPBA at 0 °C. The fact that this reaction can lead to both oxidation products was confirmed by the work of Jungheim, who obtained sulfoxides and sulfones at −78 and −10 °C, respectively.

We have developed a simple method for the preparation of 5-alkylsufinyl-1-aryltetrazoles, which consists of oxidizing the relevant sulfanyl derivatives with 34% peracetic acid (Scheme 1).

The reactions proceed at −15 °C for 24–36 h (Table 1). Yields of sulfinyltetrazoles in most cases were high. Several solvents were tested as reaction medium, for example, acetone, chloroform, and peracetic acid itself, acetone was the best choice.



Scheme 1.

Keywords: Oxidation; Sulfoxides; Tetrazoles; Peracetic acid.
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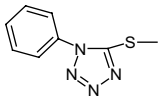
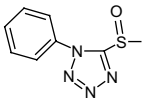
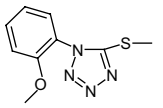
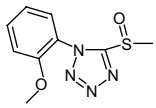
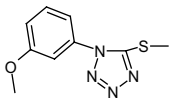
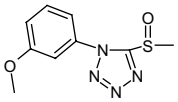
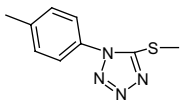
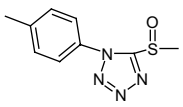
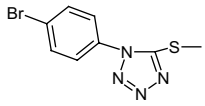
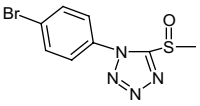
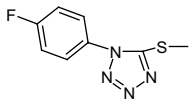
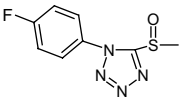
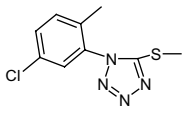
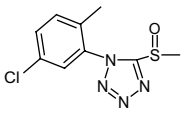
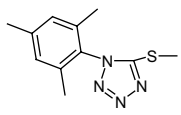
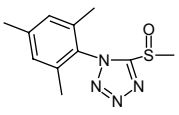
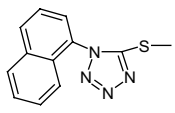
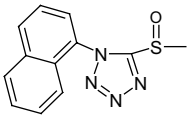
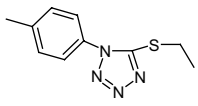
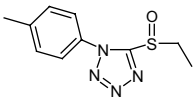
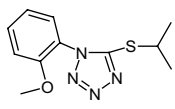
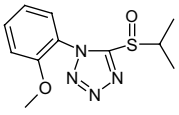
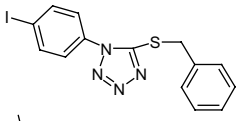
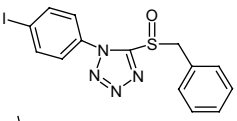
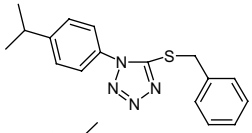
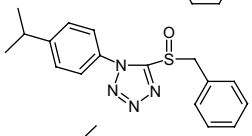
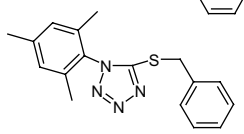
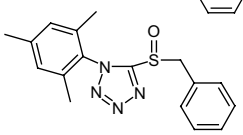
Table 1. Oxidation of 5-alkylsulfanyltetrazoles with 34% peracetic acid at −15 °C

Entry	Substrates	Time (h)	Products	Yield (%)[a]	Mp (°C)
1		24		64	77–80
2		28		94	101–103
3		28		56	73–74
4		24		71	101–102
5		28		77	135–137
6		28		92	99–100
7		28		62	100–101
8		24		89	113–114
9		36		85	124–126
10		32		95	109–111
11		32		85	72–73
12		36		61	135–136
13		36		91	88–90
14		36		98	102–103

[a] Yields refer to isolated yields. The compounds were purified by recrystallization or chromatographically and characterized by ^{13}C, ^{1}H NMR, and IR spectroscopy and elemental analyses.

The advantages of this method are the following: very low cost of the oxidizing agent, convenient preparation (the reagent can be added all at once into the cooled reaction mixture), and it affords a unique product—alkylsulfinyltetrazole—in very good yields even when there is steric hindrance of the sulfur atom by a bulky isopropyl group.

Typical procedure: (a) 5-Methylsulfinyl-1-phenyltetrazole. 5-Methylsulfanyl-1-phenyltetrazole (0.38 g, 2.0 mmol) was dissolved in acetone (10 mL), cooled to −15 °C, and 34% peracetic acid (10 mL) was added. The reaction mixture was kept for 24 h at this temperature, 15 mL of chloroform were added, and the mixture was stirred for 0.5 h at 18 °C, the chloroform layer was separated, washed with 10% NaOH (3 × 15 mL) and water (2 × 20 mL), after which it was dried over anhydrous $MgSO_4$, filtered, and the solvent was removed under reduced pressure. Yield 0.27 g (64%), mp 77–80 °C. ^{13}C NMR (75 MHz, $CDCl_3$): δ 38.9, 124.8, 130.0, 131.3, 132.9, 156.5; ^1H NMR (300 MHz, $CDCl_3$): δ 3.35 (s, 3H, CH_3), 7.71–7.61 (m, 5H, Ph); IR (KBr): 3432, 3074, 3030, 2932, 1620, 1595, 1501, 1463, 1417, 1339, 1298, 1226, 1160, 1112, 1075, 1047, 1038, 1016, 991 cm^{-1}. Anal. calcd for $C_8H_8N_4OS$: C, 46.14; H, 3.85; N, 26.90. Found: C, 46.38; H, 4.02; N, 27.00. (b) 5-Benzylsulfinyl-1-(4-iodophenyl)-tetrazole. Yield 0.13 g (61%), mp 135–136 °C; ^{13}C NMR (75 MHz, $CDCl_3$): δ 60.4, 97.1, 126.5, 127.1, 127.2, 129.1, 129.4, 130.6, 132.3, 138.6, 155.8; ^1H NMR (300 MHz, $CDCl_3$): δ 4.66–4.70 (d, 1H, J = 12.9 Hz, CH_2) 4.83–4.87 (d, 1H, J = 12.9 Hz, CH_2), 6.72–6.85 (m, 2H, Ar), 7.11–7.15 (m, 2H, Ar), 7.26–7.39 (m, 3H, Ar), 7.74–7.79 (m, 2H, Ar); IR (KBr): 3443, 3065, 2924, 1623, 1489, 1455, 1402, 1224, 1192, 1077, 1066, 1029, 1004, 983 cm^{-1}. Anal. Calcd for $C_{14}H_{11}IN_4OS$: C, 40.98; H, 2.68; N, 13.66. Found: C, 41.28; H, 2.65; N, 13.48.

Acknowledgements

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References and notes

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