Reactions of Zincke´s salts with 2,3-dimethylbenzothiazolium iodide

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Reactions of 1-(2,4-dinitrophenyl)pyridinium chloride and 2-(2,4-dinitrophenyl)isoquinolinium chloride with 2,3-dimethylbenzothiazolium iodide in hot pyridine allows introduction of an aryl residue into the thiazole ring *via* intermolecular transformation of the pyridine ring of Zincke´s salts with participation of the methyl group in position 2 of the benzothiazolium salt.

Key words: Zincke´s salts, benzothiazolium salt, ring transformation, 2-phenylbenzothiazole, 2-(2-naphthyl)benzothiazole, phenothiazine.

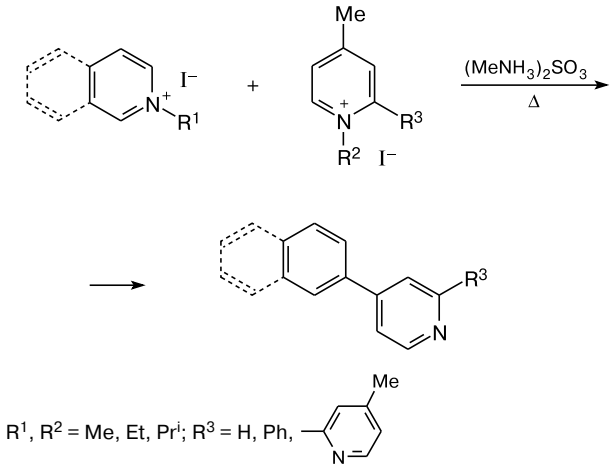
Ring transformation under the action of nucleophilic reagents is the very interesting property of quaternary pyridinium salts.[1—6] The earliest, best understood transformation of this type was the Zincke—König reaction,[2,7] in which 1-(2,4-dinitrophenyl)pyridinium decomposes in the presence of aromatic amines to give glutaconaldehyde dianils. However, transformations of Zincke´s salts under the action of C-nucleophiles that would result in the formation of the benzene ring have not been discovered.[2,8]

Earlier,[9—13] we have found that pyridinium and isoquinolinium salts, as well as pyridine and isoquinoline themselves, react with 4-methylpyridinium salts in the presence of methylammonium sulfite to give, as a result of a new transformation of the pyridine ring, 4-phenylpyridine and 4-(2-naphthyl)pyridine in up to 57 and 62% yields, respectively (Scheme 1).

To reveal the potential scope of this reaction, we studied the possibility of transforming the pyridine ring under the action of quaternary benzothiazolium salt **1**.

However, heating of both 1-methylpyridinium iodide and 2-methylisoquinolinium iodide with benzothiazolium salt **1** and aqueous methylammonium sulfite gave no 2-arylbenzothiazoles. Opening of the pyridine ring in pyridinium and isoquinolinium salts under the action of alkylammonium sulfite occurs in strongly basic media at high temperatures. Apparently, the five-membered ring of benzothiazole is unstable under these conditions, which results in resinification of the reaction mixture. We assumed that the use of 1-(2,4-dinitrophenyl)pyridinium chloride (**2**) and 2-(2,4-dinitrophenyl)isoquinolinium chloride (**3**) would make the pyridine ring more electron-deficient for its opening to occur under milder conditions.

Scheme 1



We found that the pyridine ring undergoes the desired transformation when heating Zincke´s salts **2** and **3** with quaternary benzothiazolium salt **1** in pyridine. The target products 2-phenylbenzothiazole (**4**) and 2-(2-naphthyl)-benzothiazole (**5**) were obtained in 12 and 5% yields, respectively (Scheme 2).

Apparently, the reaction mechanism involves pyridine-promoted formation of anhydrobase **6** from quaternary salt **1** followed by a nucleophilic attack of the enamine C atom on the electron-deficient α-position of the pyridine

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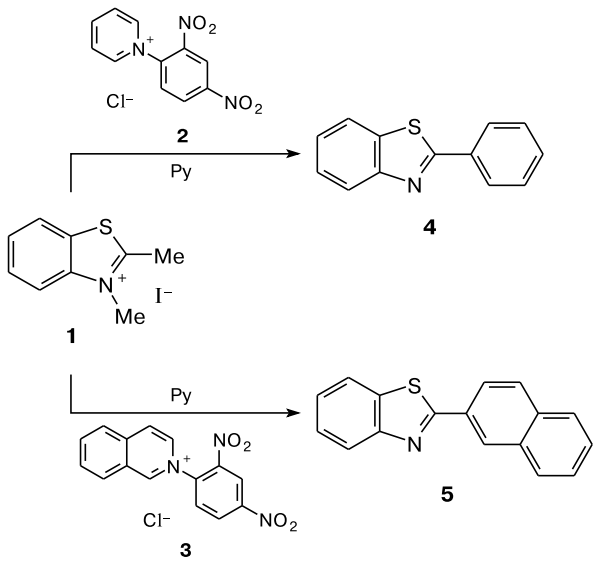
Scheme 2



ring of salts **2** and **3** (Scheme 3). The resulting adduct **7** undergoes electrocyclic ring opening, probably into intermediate **8**. Its subsequent cyclization with elimination of aromatic amine produces quaternary salt **9**. In a final step, base-catalyzed N-dealkylation yields 2-arylbenzothiazoles **4** and **5**.

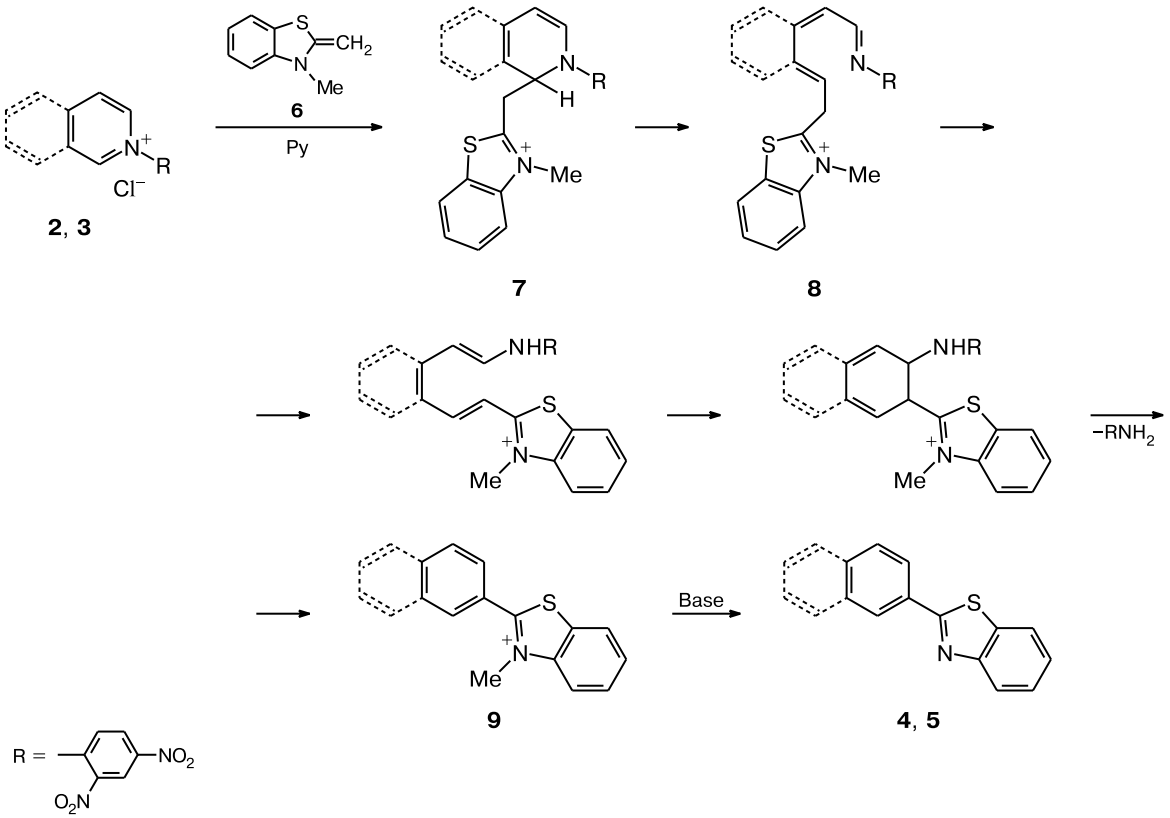
The low yields of compounds **4** and **5** can be attributed to competitive reactions, *e.g.*, N-dealkylation of the starting salts **1**—**3** under the action of pyridine. This was confirmed by the presence of 2-methylbenzothiazole, pyridine, and isoquinoline among reaction products, which are inert to the ring transformation under the conditions of the reaction studied. Use of other bases instead of pyridine did not increase the yields of the target products. Interestingly, the reaction between salts **1** and **3** gives phenothiazine derivative **10** as a by-product (Scheme 4).

It is known[14,15] that base-catalyzed opening of the thiazolium ring of the quaternary benzothiazolium salt gives aniline derivative **11**. Apparently, phenothiazine **10** is formed in a reaction of compound **11** with salt **3**.

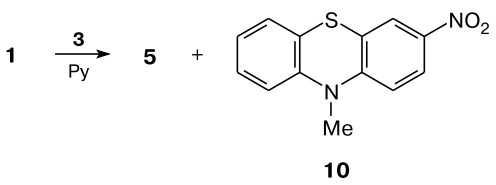
A plausible mechanism involves nucleophilic displacement of the isoquinoline residue and the formation of diphenylamine derivative **12** followed by its heterocyclization into phenothiazine derivative **10** *via* intramolecular nucleophilic *ipso*-substitution (Scheme 5).

Structure **10** was determined by NMR spectroscopy, mass spectrometry, and elemental analysis. However, according to X-ray diffraction data, a single crystal grown

Scheme 3

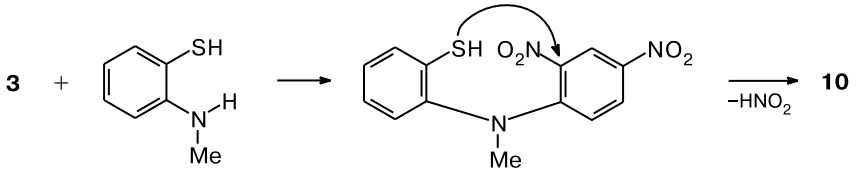


Scheme 4



10

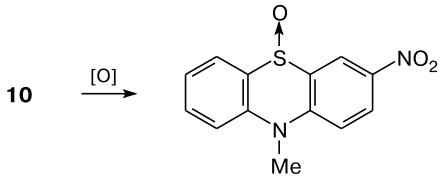
Scheme 5



11 **12**

from a saturated solution in DMSO has the structure of *S*-oxide **13** (Scheme 6).

Scheme 6



13

Apparently, phenothiazine **10** is oxidized into sulfoxide **13** during the formation of single crystals. The general view of structure **13** with atomic numbering is shown in Fig. 1. Its crystallographic parameters and the data collection and refinement statistics are given in Table 1.

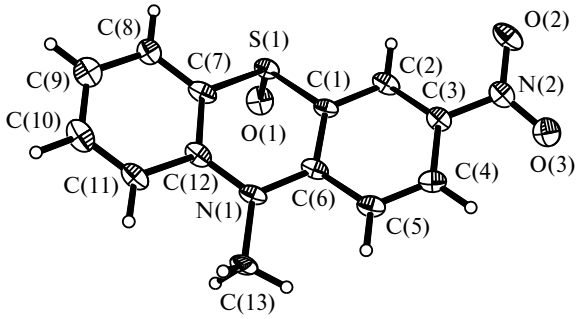


Fig. 1. Structure **13** with atomic thermal displacement ellipsoids (p = 50%). Selected bond lengths: S(1)—O(1), 1.487(4) Å; S(1)—C(1), 1.768(5) Å; S(1)—C(7), 1.749(5) Å; N(1)—C(6), 1.387(6) Å; N(1)—C(12), 1.402(6) Å; N(1)—C(13), 1.474(6) Å. Selected bond angles: C(1)—S(1)—C(7), 97.0(2)°; O(1)—S(1)—C(1), 107.2(2)°; O(1)—S(1)—C(7), 105.3(2)°; C(6)—N(1)—C(12), 121.2(4)°; C(6)—N(1)—C(13), 119.6(4)°; C(12)—N(1)—C(13), 118.3(4)°.

Table 1. Crystallographic parameters and the data collection and refinement statistics for structure **13**

Parameter	Value
Molecular formula	$C_{13}H_{10}N_2O_3S$
Molecular mass	274.29
Crystal color and shape	Yellowish prism
Crystal size/mm	0.28×0.26×0.24
Crystal system	Monoclinic
Space group	$P2_1/n$
a/Å	10.003(5)
b/Å	11.638(6)
c/Å	10.003(5)
α/deg	90
β/deg	93.957(18)
γ/deg	90
V/Å^3	1161.7(10)
Z	4
d_{calc}/mg m^{-3}	1.568
μ(Mo-Kα)/mm^{-1}	0.284
F(000)	568
Scan range θ/deg	$1.75 \le \theta \le 27.00$
Ranges of h, k, l indices	$-8 \le h \le 12$, $-14 \le k \le 14$, $-12 \le l \le 12$
Number of measured reflections	7225
Number of independent reflections	2526 (R_{int} = 0.1534)
Number of parameters refined	173
GOOF on F^2	1.061
R Factors for $I > 2\sigma(I)$	0.0960, 0.2403
R Factors for all reflections	0.1394, 0.2721
Residual electron density (max/min)/e Å^{-3}	0.871/−0.790

To sum up, we discovered that the pyridine ring in Zincke´s salts can be transformed into the benzene ring under the action of C-nucleophiles, which is of theoretical interest for the chemistry of pyridine.

Experimental

^{1}H NMR spectra were recorded on a Bruker DRX-500 spectrometer (500.13 MHz) in $CDCl_3$ and DMSO-d_6 with residual signals of the solvent as the internal standards (δ 7.27 and 2.50, respectively). ^{13}C NMR spectra were recorded on a Bruker DRX-500 spectrometer (125.76 MHz) in DMSO-d_6 with its signal as the internal standard (δ 128.02). Chemical shifts and coupling constants were measured to within 0.01 ppm and 0.1 Hz, respectively. The signals for the protons and carbon atoms were assigned using homonuclear (^{1}H—^{1}H COSY, NOESY) and heteronuclear techniques (^{1}H—^{13}C COSY, HSQC, HMBC).

Mass spectra were recorded on a Varian MAT-311A mass spectrometer (ionizing energy 70 eV, direct inlet probe).

Elemental analysis was carried out at the Microanalysis Laboratory of the A. N. Nesmeyanov Institute of Organoelement Compounds (Russian Academy of Sciences).

Melting points were determined in capillaries on a MEL-Temp II instrument.

The course of the reactions was monitored by TLC on DC-Alufolien Kieselgel 60 F_{254} plates (Merck). Column chromatography was carried out on Kieselgel 60 (0.063—0.100 mm, Merck).

2,3-Dimethylbenzothiazolium iodide (**1**), 1-(2,4-dinitrophenyl)pyridinium chloride (**2**), and 2-(2,4-dinitrophenyl)-isoquinolinium chloride (**3**) were prepared according to known procedures.[16,17]

2-Phenylbenzothiazole (4). A mixture of 1-(2,4-dinitrophenyl)pyridinium chloride (**2**) (0.282 g, 1 mmol) and 2,3-dimethylbenzothiazolium iodide (**1**) (0.582 g, 2 mmol) was heated in dry pyridine (5 mL) in a sealed metal-jacketed tube on a Wood´s alloy bath at 180 °C for 40 h. The tube was opened and the reaction mixture was evaporated to dryness. The residue was purified by column chromatography on SiO_2 with benzene or pentane—ethyl acetate (20 : 1) as an eluent. The yield of compound **4** was 25 mg (12%), m.p. 113 °C (*cf.* Ref. 18: m.p. 112—113 °C). ^{1}H NMR ($CDCl_3$), δ: 7.41 (m, 1 H, H(5) of benzothiazole); 7.51 (m, 4 H, H(2), H(3), H(5), H(6) of phenyl); 7.93 (d, 1 H, H(4) of benzothiazole, J = 8.1 Hz); 8.09—8.12 (m, 3 H, H(6), H(7) of benzothiazole, H(4) of phenyl). MS, m/z (I_{rel} (%)): 211 [M^+] (100), 210 (18), 184 (6), 108 (40), 81 (11), 76 (6), 69 (38), 63 (6), 58 (15), 51 (16).

2-(2-Naphthyl)benzothiazole (5) and **10-methyl-3-nitro-10*H*-phenothiazine (10).** A mixture of 2-(2,4-dinitrophenyl)-isoquinolinium chloride (**3**) (0.332 g, 1 mmol) and 2,3-dimethylbenzothiazolium iodide (**1**) (0.582 g, 2 mmol) was heated in dry pyridine (5 mL) in a sealed metal-jacketed tube on a silicone oil bath at 120 °C for 40 h. The tube was opened, reaction products were extracted with hot hexane, and the extract was concentrated. The residue was purified by column chromatography on SiO_2 with benzene—hexane (1 : 1 and 2 : 1) as an eluent. The yields of compounds **5** and **10** were 13 mg (5%) and 10 mg (4%), respectively.

2-(2-Naphthyl)benzothiazole (**5**), m.p. 123—125 °C (from hexane) (*cf.* Ref. 19: m.p. 124—126 °C). ^{1}H NMR ($CDCl_3$), δ: 7.42 (m, 1 H, H(5) of benzothiazole); 7.53 (m, 1 H, H(6) of benzothiazole); 7.57 (m, 2 H, H(6), H(7) of naphthyl); 7.90 (m, 1 H, H(8) of naphthyl); 7.97 (m, 3 H, H(5) of naphthyl, H(4), H(7) of benzothiazole); 8.14 (d, 1 H, H(4) of naphthyl, J = 8.6 Hz); 8.23 (dd, 1 H, H(3) of naphthyl, J = 8.6 Hz, J = 1.8 Hz); 8.59 (s, 1 H, H(1) of naphthyl). MS, m/z (I_{rel} (%)): 261 [M^+] (100), 260 (66), 131 (11), 130 (13), 108 (25), 81 (11), 69 (26), 59 (25), 57 (14), 55 (11).

10-Methyl-3-nitro-10*H*-phenothiazine (**10**), m.p. 155 °C (from hexane) (*cf.* Ref. 20: m.p. 144—145 °C). ^{1}H NMR (DMSO-d_6), δ: 3.36 (br.s, 3 H, MeN); 6.97—7.04 (m, 3 H, H(1), H(6), H(8)); 7.14 (d, 1 H, H(9), J = 7.4 Hz); 7.24 (m, 1 H, H(7)); 7.85 (s, 1 H, H(4)); 8.00 (dd, 1 H, H(2), J = 8.9 Hz, J = 2.1 Hz). ^{13}C NMR (DMSO-d_6), δ: 35.76 (s, MeN); 113.95 (C(8)); 115.60 (C(6)); 120.49 (C(4a)); 121.53 (C(4)); 122.52 (C(9a)); 123.97, 124.01 (C(2), C(1)); 126.87 (C(9)); 128.22 (C(7)); 141.72 (C(3)); 143.04 (C(5a)); 150.93 (C(10a)). MS, m/z (I_{rel} (%)): 258 [M^+] (100), 243 (25), 228 (24), 213 (52), 212 (70), 197 (33), 196 (30), 185 (22), 69 (33), 57 (26). Found (%): C, 60.32; H, 3.51; N, 10.98. $C_{13}H_{10}N_2O_2S$. Calculated (%): C, 60.45; H, 3.90; N, 10.85.

X-ray diffraction experiment. Crystals of compound **13** were obtained by slow evaporation of its solution in DMSO at room temperature. Reflection intensities from a single crystal were measured on a Bruker SMART-CCD diffractometer under cooled (T = 120.0(2) K) nitrogen (Mo-Kα radiation, λ = 0.71073 Å, graphite monochromator, ω scan mode). The structure was solved by direct methods and refined in the full-matrix anisotropic approximation on F^2 for non-hydrogen atoms. The hydrogen atoms were located geometrically and refined using a riding model. All calculations were performed with the SHELXTL-Plus program package.[21] Crystallographic parameters and the data collection and refinement statistics are summarized in Table 1. Atomic coordinates and other experimental data have been deposited with the Cambridge Crystallographic Data Center* (CCDC No. 748 021).

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