3-Halo-2,6-dimethyl-4-nitropyridine 1-oxides react with sodium methanethiolate giving 3-halo-2,6-dimethyl-4-methylthiopyridine 1-oxides which are oxidized into respective methylsulfonyl derivatives and reduced to 3-halo-2,6-dimethyl-4-methylthiopyridines.

Sulfur-containing derivatives of 1-oxides of heteroaromatic amines, especially of pyridine, are known to possess antifungal and antibacterial properties [1—4]. It has been reported recently that sulfonyl derivatives of pyridine 1-oxides have found wide applications as herbicides and plant growth regulators and as phase-transfer catalysts of $S_N$2 reactions [5—8]. In addition, chloropyridylsulfone 1-oxide was used as toxicant of Escherichia coli in agar [9].

For many years investigations have been carried out in our laboratory on the reactivities of 1-oxides of halonitropyridines [10—13]. Particular attention has been paid to the nucleophilic exchange reactions of substituents at positions 2 and 4 as these positions are very strongly activated towards this substitution through mesomerism by the $N$-oxide group. Among the reactions of this type the preparation of 3-halo-2,6-dimethyl-4-ethylthiopyridine 1-oxides was described [12]. This paper is a continuation of our studies on the syntheses of sulfur-containing pyridine derivatives and their 1-oxides via easy replacement of the nitro group in position 4 of pyridine 1-oxides.

The 3-halo-2,6-dimethyl-4-nitropyridine 1-oxides were prepared by oxidation of the respective 3-substituted 2,6-dimethylpyridines and by subsequent nitration of the resulting 1-oxides [14, 15]. Starting from these 1-oxides (Ia, Ib) in the first step, through the reaction with sodium methanethiolate exclusively the corresponding methylthio derivatives (IIa, IIb) were prepared in good yields; the presence of the halogen atom at a vicinal position to the nitro group seems to additionally facilitate this type of exchange of this group (Scheme 1). It is worth noting that in contrast to the 3-methylthio derivatives [16], the sulfur atom in IIa, IIb is very susceptible to oxidation. As it is shown in Scheme 2, only methylsulfonyl derivatives IIIa, IIIb were obtained from the above-mentioned reactions.

When compounds IIa, IIb were treated with phosphorus tribromide the corresponding 4-methylthiopyridines were obtained (IVA, IVb) in which the nitrogen atom of the ring showed also susceptibility to the oxidation in contrast to the nitrogen atom in 2,6-dimethyl-3-methylthiopyridine [16]. Consequently, there is an additional pathway to IIIa, IIIb through the oxidation of
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**Scheme 2**

\[ \text{IIIa, IIIb} \]

\[ \text{H}_2 \text{O}_2 \quad (\text{CF}_3 \text{CO})_2 \text{O} \]

\[ \text{IIa, IIb} \]

**EXPERIMENTAL**

Melting points were determined in open capillary tubes on a Büchi apparatus and are uncorrected. The infrared spectra were taken on a Specord IR 75 (Zeiss, Jena) spectrophotometer. \(^1\)H NMR spectra were recorded on a Tesla BS-598 A spectrometer (100 MHz) using CDCl\(_3\) as solvent and TMS as the internal standard. Chemical shifts are expressed as \(\delta\).

3-Chloro-2,6-dimethyl-4-methylthiopyridine 1-oxide (\(\text{IIa}\)) and 3-bromo-2,6-dimethyl-4-methylthiopyridine 1-oxide (\(\text{IIb}\)) were prepared from \(\text{Ia}\) and \(\text{Ib}\) as described in [12].

\(\text{IIa}\): Colourless crystals (67%), m.p. = 169–170 °C (from H\(_2\)O). For C\(_8\)H\(_{10}\)ClNOS (\(M = 203.69\)) w(calc.): 47.17 % C, 4.94 % H, 6.87 % N; w(found): 46.66 % C, 4.92 % H, 6.64 % N.

IR spectrum (KBr), \(\tilde{\nu}/\text{cm}^{-1}\): 2983, 2920 \(\tilde{\nu}(\text{CH})_3\), 1593 (ring), 1441, 1422, 1370, 1355 \(\delta(\text{CH})_3\), 1234 \(\tilde{\nu}(\text{NO})\), 1018 \(\nu(C-CI)\), 790, 647, 542 \(\tilde{\nu}(\text{CS})\). \(^1\)H NMR spectrum, \(\gamma\): 6.93 (s, 1H), 2.60 (3H, C-2—CH\(_3\)), 2.45 (s, 3H, C-6—CH\(_3\)), 2.98 (s, 3H, S—CH\(_3\)).

3-Chloro-2,6-dimethyl-4-methylsulfonylpyridine 1-Oxide (\(\text{IIIA}\))

To a mixture of \(\text{IIA}\) (2 g; 9.8 mmol) and 30 % H\(_2\)O\(_2\) (8 cm\(^3\)) (CF\(_3\)CO)\(_2\)O (8 cm\(^3\)) was added dropwise under vigorous stirring with external cooling. The resulting mixture was subsequently heated at 90 °C for 10 min and left to stand at room temperature. Afterwards a small quantity of H\(_2\)O was added and it was neutralized with K\(_2\)CO\(_3\), evaporated under reduced pressure to dryness and extracted several times with CHCl\(_3\). After distilling off the solvent the crude product was recrystallized from CH\(_3\)COCH\(_3\) yielding 2 g (87 %) of colourless crystals, m.p. = 193–195 °C. For C\(_8\)H\(_{10}\)ClNOS (\(M = 235.69\)) w(calc.): 40.76 % C, 4.27 % H, 5.94 % N; w(found): 40.71 % C, 4.08 % H, 5.73 % N.

IR spectrum (KBr), \(\tilde{\nu}/\text{cm}^{-1}\): 3004, 2927 \(\tilde{\nu}(\text{CH})_3\), 1593 (ring), 1450, 1400 \(\delta(\text{CH})_3\), 1309 \(\tilde{\nu}(\text{SO}_2)\), 1272 \(\tilde{\nu}(\text{NO})\), 1136 \(\nu(\text{SO}_2)\), 1015 \(\nu(C-Cl)\), 786, 658, 550 \(\nu(C-S)\), 510 \(\gamma(\text{SO}_2)\). \(^1\)H NMR spectrum, \(\gamma\): 7.68 (s, 1H), 2.67 (s, 3H, C-2—CH\(_3\)), 2.50 (s, 3H, C-6—CH\(_3\)), 3.28 (s, 3H, S—CH\(_3\)).

3-Chloro-2,6-dimethyl-4-methylthiopyridine (\(\text{IIIA}\))

To a solution of compound \(\text{IIA}\) (9 g; 44 mmol) in CHCl\(_3\) (95 cm\(^3\)) PB\(_3\) (7 cm\(^3\)) was added carefully. The
mixture was boiled for 1 h and then additional portion of PBr₃ (7 cm³) was added and heated for additional 30 min. After distilling off CHCl₃ and the excess of PBr₃ under reduced pressure, a small quantity of H₂O-ice was added, neutralized with NaHCO₃ to alkaline reaction and steam distilled. The distillate was extracted with (C₂H₅)₂O. The solution was dried over MgSO₄. After evaporating of solvent the crude product was twice recrystallized from benzine to afford 4.9 g of IVa (60%), m.p. = 96—97 °C.

For C₈H₁₀CINS (Mr = 187.69) w(calc): 51.19 % C, 5.37 % H, 7.46 % N; w(found): 51.31 % C, 5.59 % H, 7.33 % N.

IR spectrum (KBr), v/cm⁻¹: 2980, 2917 v(CH₃), 1550 (ring), 1432, 1420, 1376 8(CH₃), 1043 v(C—Cl), 637, 568 v(C—S).

1H NMR spectrum, δ: 7.03 (s, 1H), 2.77 (s, 3H, C-2—CH₃), 2.56 (s, 3H, C-6—CH₃), 2.86 (s, 3H, S—CH₃).

3-Bromo-2,6-dimethyl-4-methylthiopyridine (IVb)

Compound IIb (10.4 g; 44 mmol) was subjected to the same procedure as described above for the preparation of IVa to afford 7.44 g of IVb (73%), m.p. = 87—90 °C.

For C₈H₁₀BrSN (Mr = 232.15) w(calc): 41.39 % C, 4.34 % H, 6.03 % N; w(found): 41.44 % C, 4.49 % H, 5.91 % N.

IR spectrum (KBr), v/cm⁻¹: 2980, 2930 v(CH₃), 1553 (ring), 1433, 1378 8(CH₃), 1020 v(C—Br), 607, 565 v(C—S).

REFERENCES