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CHEMISTRY

Reaction of Thiocarboxylic Acids with *N*-*tert*-Butyl-2-halo-2-methylpropanimines

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Abstract—Reaction of *N*-*tert*-butyl-2-chloro-2-methylpropanimine with thiocarboxylic acids has proceeded by two routes, one involving nucleophilic substitution of the chlorine atom in the primary iminium salt by acylthio group, and another via reduction of its cation at the C–Cl bond. Thiocarboxylic acids have reacted with 2-bromoaldimines only via reduction of primary salt cation at the C–Br bond. Acylthio-substituted iminium salts, aldehydes, and their acetals have been prepared.

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Reactions of dithiophosphoric acids with *N*-alkyl-2-haloaldimines **I** have been described in the literature [1, 2], but there are no data on the reactions of compounds **I** with thiocarboxylic acids **II**, which can result in formation of new types of organic compounds with useful properties.

The aim of this work is to reveal the routes of reaction between compounds **I** and **II**, determine their contribution to the overall process, and synthesize new types of aldehydes and their derivatives.

We established for the first time (Scheme 1) that the reaction between *N*-*tert*-butyl-2-chloroaldimine **Ia** and acids **II** proceeds by two routes: the nucleophilic substitution (S_N) of chlorine atom in intermediate iminium salt **III** by thioacyl group (a) and the reduction (Red, b) of its cation at the C–Cl bond.

The contribution of each route depended on the structure of acid **II** and reagent ratio. At the 1 : 1 ratio of initial reagents for acids **IIa** and **IIb**, the contributions of routes (a) and (b) were 4 : 1 and 3 : 2, respectively. These ratios were determined from the integrated intensities of resonance signals in the ^{1}H NMR spectra of mixtures of compounds **IV** and **V** isolated from the reaction mixtures after removal of disulfide **VI**. At a twofold excess of chloroimine **I**, the ratio of contributions of routes (a) and (b) for acid **IIb** increased from 3 : 2 to 4 : 1; i.e., the contribution of nucleophilic substitution of chlorine atom in salt **III** by thioacyl group increased with acid strength and chloroimine **I** excess. This seems to be due to the additional shift of equilibrium toward the formation of intermediate salt **III**, i.e., more complete binding of acid **I** that participate in the reduction of the C–Cl bond.

Both acids **II** reacted with bromoimine **Ib** only through one route: the cation of intermediate salts **VII** underwent reduction at the C–Br bond to give the bromide salt of reduced iminium **VIII** and disulfide **VI** (Scheme 2).

With the aim to confirm the structure of iminium salts **IV** and synthesize new types of S-containing organic compounds, we prepared aldehydes **IX** by hydrolysis and converted them into acetals **X** (Scheme 3).

Thus, the reaction between *N*-*tert*-butyl-2-chloro-2-methylpropanimine and thiocarboxylic acids, studied for the first time, proceeds via two routes: nucleophilic substitution of chlorine atom in the intermediate iminium salt by acylthio group and reduction of its cation at the C–Cl bond. The contribution of each route depended on the acid nature and reagent ratio. Enhancement of acidic properties and an excess of 2-chloroaldimine favored nucleophilic substitution because it led to a decrease in the content of the acid involved in the reduction of the C–Cl bond. *N*-*tert*-Butyl-2-bromo-2-methylpropanimine reacted with the thiocarboxylic acids only via one route by the reduction of the cation of the intermediate salt at the C–Br bond to form the bromide salt of reduced iminium and the disulfide. In the course of the work, we prepared new types of iminium salts and aldehydes and their acetals.

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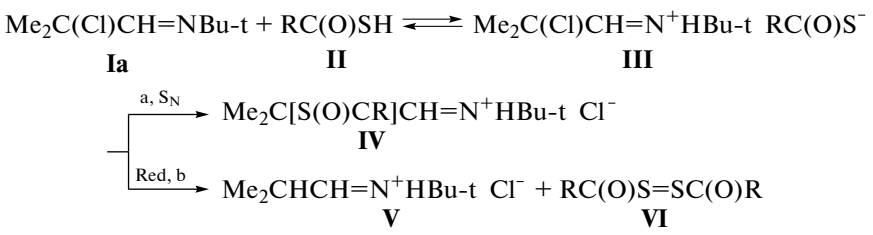
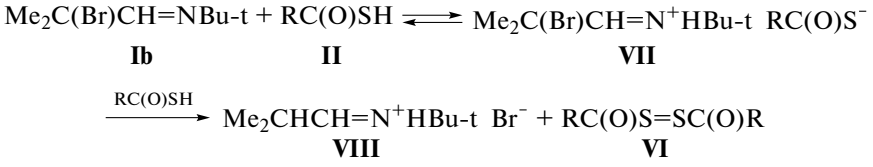


II, **III**, **IV**, **VI**: R=Ph (a), Me (b)

Scheme 1.



II, **VII**, **VI**: R=Ph (a), Me (b)

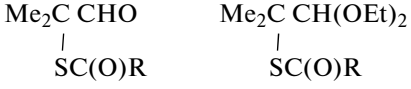
Scheme 2.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Tesla BS 567 A (100 MHz) and a Bruker AVANCE 400WB (400.13 and 100.61 MHz, respectively) spectrometers in $CDCl_3$. Chemical shifts were determined relative to tetramethylsilane using the signals of residual protons and carbon nuclei of the deuterated solvent as references.

Reaction of thiobenzoic acid IIa with imine Ia. A solution of 6.9 g (0.05 mol) of acid **IIa** in 15 mL of CH_2Cl_2 was added dropwise at 5–10°C to a solution of 8.1 g (0.05 mol) of chloroimine **Ia** in 25 mL of CH_2Cl_2. Three days later, the solvent was removed, the residue was treated with methyl-*tert*-butyl ether, and the resultant crystals were separated by filtration and dried to give 9.08 g of a mixture of salts **IVa** and **V** in 4 : 1 ratio.

^{1}H NMR ($CDCl_3$, δ, ppm): salt **IVa**: 1.60 (s, 9H, CMe_3), 1.98 (s, 6H, CMe_2), 7.47 (dd, 2H, m-CH_{Ar}, $^3J_{HH}$ = 7.6 Hz), 7.64 (dd, 1H, *p*-CH_{Ar} $^3J_{HH}$ = 7.6 Hz), 7.87 (dd, 2H, *o*-CH_{Ar} $^3J_{HH}$ = 7.6 Hz), 8.25 (br s, 1H, CH=N$^+$), 15.31 (br s, 1H, N$^+$H); salt **V**: 1.24 (d, 6H, $\underline{MeCH_2}$, $^3J_{HH}$ = 6.8 Hz), 1.52 (s, 9H, CMe_3), 3.75 (sextet, 1H, $Me_2\underline{CH}$, $^3J_{HH}$ = 6.8 Hz), 8.35 (br s, 1H, CH=N$^+$), 15.72 (br s, 1H, N$^+$H). Dibenzoyl disulfide **VIa** (1.55 g) was isolated from the mother liquor, mp 128–129°C (ethanol, mp 128°C, [3]).



IX, **X**: R=Ph (a), Me (b)

Scheme 3.

Reaction of thioacetic acid (IIb) with imine Ia. Ratio 1 : 1. A solution of 4.6 g (0.06 mol) of acid **IIb** in 10 mL of CH_2Cl_2 was added dropwise to a solution of 9.70 g (0.06 mol) of chloroimine **Ia** in 35 mL of CH_2Cl_2 at 5–10°C. Four days later, the solvent was removed and the residue was treated with ether. The resultant oil became crystalline when stored for 2 days in a refrigerator. The crystals were separated by filtration and dried in a vacuum to give 6.68 g of a mixture of salts **IVb** and **V** in 3 : 2 ratio.

Diacetyl disulfide **VIb** (1.5 g), bp 49–50°C (0.1 mmHg) and 72–74°C (2 mmHg, [3]) was isolated from the mother liquor.

Ratio 1 : 2. Similarly, 24.3 g (0.15 mol) of chloroimine **IIa** and 5.7 g (0.075 mol) of acid **IIb** in 50 mL of CH_2Cl_2 were reacted to give 11.2 g of a mixture of salts **IVb** and **V** in 4 : 1 ratio. Disulfide **VIb** (1.3 g) was obtained from the mother liquor.

Reaction of thiobenzoic acid (IIa) with imine Ib. Acid **IIa** (2.76 g, 0.02 mol) was added dropwise to a solution of 2.06 g (0.01 mol) of imine **Ib** in 15 mL of CCl_4 at 0–5°C. The reaction mixture was stirred at ambient temperature for 3 h and allowed to stand overnight. The resultant crystals were separated by filtration, washed with CCl_4, and dried to give 1.72 g (83%) of salt **VIII**, mp 103–104°C.

^{1}H NMR ($CDCl_3$, δ, ppm): 1.31 (d, 6H, $\underline{Me_2}CH$, $^3J_{HH}$ = 6.8 Hz), 1.61 (s, 9H, CMe_3), 3.80 (d

septets, 1H, $Me_2\underline{CH}$, $^3J_{HH}$ = 6.8 Hz, $^3J_{HH}$ = 9.0 Hz), 8.41 (dd, 1H, CH=N, $^3J_{HH}$ = 9.0 Hz, $^3J_{HH}$ = 6.8 Hz), 14.81 (br s, 1H, N^+H).

For $C_8H_{18}NBr$ anal. calcd. (%): C, 46.17; H, 8.72; N, 6.73.

Found (%): C, 45.91; H, 8.93; N, 6.58.

Dibenzoyl disulfide **VIa** (2.08 g, 76%), mp 130–131°C (ethanol), was isolated from the mother liquor. ^1H NMR ($CDCl_3$, δ, ppm): 7.52 (dd, 4H, *m*-CH_{Ar}, $^3J_{HH}$ = $^3J_{HH}$ = 8.0 Hz), 7.65 (dd, 2H, *p*-CH_{Ar}, $^3J_{HH}$ = $^3J_{HH}$ = 8.0 Hz), 8.07 (d, 4H, *o*-CH_{Ar}, $^3J_{HH}$ = 8.0 Hz).

Reaction of thioacetic acid (IIb) with imine Ib. Similarly to the previous experiment, the reaction of 4.09 g (0.0199 mol) of imine **Ib**, 1.51 g (0.0199 mol) of acid **IIb** in 20 mL of CCl_4 resulted in 1.89 g (91%) of salt **VIII**, mp 103–104°C. Disulfide **VIb** (1.17 g, 78.5%), bp 50–51°C (0.1 mmHg), was obtained from the mother liquor. ^1H NMR ($CDCl_3$, δ, ppm): 2.44 (s, 6H, Me).

For $C_4H_6O_2S_2$ anal. calcd. (%): C, 31.98; H, 4.02; S, 42.69.

Found (%): C, 31.78; H, 3.91; S, 42.50.

1,1-Dimethyl-2-oxoethyl thiobenzoate IXa. A solution of 4.15 g (0.03 mol) of acid **IIa** in 10 mL of CH_2Cl_2 was added dropwise to a solution of 7.3 g (0.045 mol) of chloroimine **Ia** in 30 mL of CH_2Cl_2 at 5–10°C. Forty eight hours later, the solvent and the excess chloroimine were removed in a vacuum. The residue was dissolved in 40 mL of CH_2Cl_2 and 10 mL of water was added at 10–15°C. After 40 min, the organic layer was separated and dried with magnesium sulfate. The solvent was removed and the residue was distilled in a vacuum to give 4.4 g (71%) of aldehyde **IXa**, bp 86–87°C (0.03 mmHg). ^1H NMR ($CDCl_3$, δ, ppm): 1.47 (s, 6H, CMe_2), 7.38 (dd, 2H, *m*-CH_{Ar}, $^3J_{HH}$ = $^3J_{HH}$ = 7.6 Hz), 7.52 (dd, 1H, *p*-CH_{Ar}, $^3J_{HH}$ = $^3J_{HH}$ = 7.6 Hz), 7.85 (dd, 2H, *o*-CH_{Ar}, $^3J_{HH}$ = 7.6 Hz), 9.44 (s, 1H, CHO).

For $C_{11}H_{12}O_2S_2$ anal. calcd. (%): C, 63.34; H, 5.81; S, 15.40.

Found (%): C, 63.27; H, 5.68; S, 15.22.

1,1-Dimethyl-2-oxoethyl thioacetate IXb. Similarly to the previous preparation, 16.1 g (0.1 mol) of chloroimine **Ia** was reacted with 3.8 g (0.05 mol) of acid **IIb** using 60 mL of CH_2Cl_2 and 10 mL of water to give 5.1 g (70%) of aldehyde **IXb**, bp 80–81°C (10 mmHg). ^1H NMR ($CDCl_3$, δ, ppm): 1.31 (s, 6H, CMe_2), 2.21 (s, 3H, CH_3CO), 9.28 (s, 1H, CHO).

For $C_6H_{10}O_2S_2$ anal. calcd. (%): C, 49.29; H, 6.89; S, 21.93.

Found (%): C, 49.03; H, 7.01; S, 21.79.

1,1-Dimethyl-2,2-diethoxyethyl thiobenzoate Xa. Two drops of sulfuric acid was added to a solution of 5.2 g (0.025 mol) of aldehyde **IXa** and 7.4 g (0.05 mol) of triethyl orthoformate in 15mL of benzene. A slight heating was observed. Twenty four hours later, the solvent and the excess ortho ester were removed and the residue was distilled in a vacuum to give 6.2 g (88%) of acetal **Xa**, bp 98–99°C (0.04 mmHg). ^1H NMR ($CDCl_3$, δ, ppm, *J*, Hz): 1.19 (t, 6H, $CH_2\underline{Me}$, $^3J_{HH}$ = 7.0), 1.50 (s, 6H, CMe_2), 3.56 and 3.77 (both dq, 4H, OCH_2, $^3J_{HH}$ = 7.0, $^2J_{HH}$ = 9.0), 4.91 (s, 1H, CH), 7.35 (t, 2H, *m*-CH_{Ar}, $^3J_{HH}$ = 7.5), 7.46 (t, 1H, *p*-CH_{Ar}, $^3J_{HH}$ = 7.5), 7.87 (d, 2H, *o*-CH_{Ar}, $^3J_{HH}$ = 7.5). ^{13}C NMR ($CDCl_3$, δ, ppm): 15.40 (s, $CH_2\underline{Me}$), 22.55 (s, $C\underline{Me_2}$), 55.20 (s, S–C), 66.10 (s, OCH_2), 105.46 (s, CH), 126.95 (s, *m*-CH_{Ar}), 128.34 (s, *p*-CH_{Ar}), 132.81 (s, *o*-CHAr), 138.06 (s, $\underline{C_{Ar}}$-CO), 192.34 (s, C=O).

For $C_{15}H_{22}O_3S$ anal. calcd. (%): C, 63.80; H, 7.85; S, 11.35.

Found (%): C, 63.58; H, 7.68; S, 11.43.

1,1-Dimethyl-2,2-diethoxyethyl thioacetate Xb. Similarly to the previous preparation, 5.8 g (0.04 mol) of aldehyde **IXb** and 8.9 g (0.06 mol) are of triethyl orthoformate were reacted in 15 mL of benzene to give 7.1 g (81%) of acetal **Xb**, bp 61–62°C (0.08 mmHg). ^1H NMR ($CDCl_3$, δ, ppm): 1.12 (t, 6H, $CH_2\underline{Me}$, $^3J_{HH}$ = 7.0 Hz), 1.33 (s, 6H, CMe_2), 2.13 (s, 3H, MeCO), 3.49 (q, 4H, $\underline{CH_2}Me$, $^3J_{HH}$ = 7.0 Hz), 4.61 (s, 1H, CH).

For $C_{10}H_{20}O_3S$ anal. calcd. (%): C, 54.51; H, 9.15; S, 14.55.

Found (%): C, 54.70; H, 9.09; S, 14.41.

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