Dimerization of methyl isothiocyanate to the 2-mercapto-1-methylimidazole-5(4*H*)-thione anion under the action of a superbase

L. Brandsma,[a] N. A. Nedolya,[b] and B. A. Trofimov[b]*

[a]*Department of Preparative Organic Chemistry, Debye Institute, University of Utrecht, Padualaan 8, 3584 CH Utrecht, The Netherlands. E-mail: brandsma@chem.ruu.nl*

[b]*Irkutsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 1 ul. Favorskogo, 664033 Irkutsk, Russian Federation. Fax: +7 (395 2) 35 6046. E-mail: admin@irioch.irk.ru*

Dimerization of methyl isothiocyanate under the action of potassium diisopropylamide followed by alkylation of the intermediate dithiolate gives 2,5-bis(alkylthio)-1-methylimidazoles in 71—74% yields.

Key words: methyl isothiocyanate, reaction with potassium diisopropylamide, deprotonation, heterocyclization, alkylation; imidazoles.

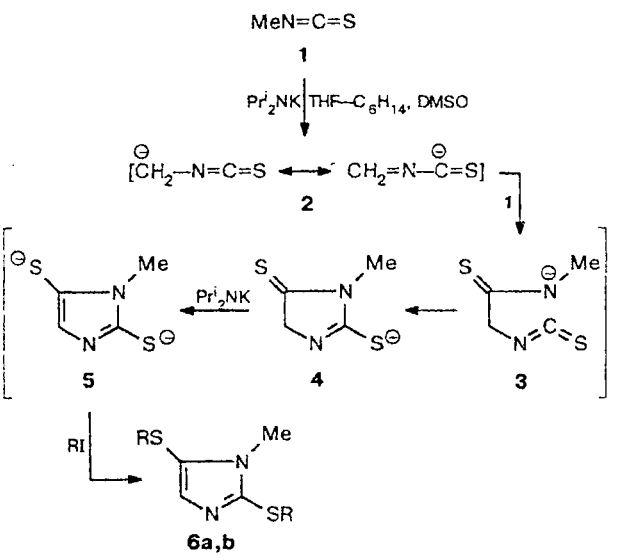
Direct deprotonation of methyl isothiocyanate (**1**) by lithium 2,2,6,6-tetramethylpiperidide in a THF—hexane mixture (−70 °C, 1 h) affords (after alkylation of the intermediate with benzyl bromide) 4-benzylthio-1-[(benzylthio)(methylimino)methyl]-3-methyl-4-imidazoline-2-thione (yield 38%).[1] The attempt to carry out deprotonation of isothiocyanate **1** by potassium *tert*-butoxide was unsuccessful.[1]

Recently[2] we have described the reaction of isothiocyanatomethanide anion (**2**), generated *in situ* by deprotonation of compound **1** by lithium diisopropylamide, with chlorotrimethylsilane as a simple and original pathway to mono-, bis-, and tris(trimethylsilyl)methyl isothiocyanates.

In this communication, we present new data concerning the deprotonation of isothiocyanate **1** by superbases and the possibility of using the resulting carbanion for synthetic purposes. For example, we found that the reactivity of the anion derived from methyl isothiocyanate depends crucially on the counterion and on the composition of the solvent. If deprotonation is carried out by potassium diisopropylamide, isothiocyanate **1** spontaneously dimerizes to give thiolate anion **4** (Scheme 1). This opens up an unexpectedly simple route to imidazole derivatives **6**, which are difficult to prepare by other methods. In this case, they are formed in high yields in one preparative step.

Cycloaddition of carbanion **2** to a second molecule of isothiocyanate **1** occurs at ~40—45 °C in the presence of DMSO. Deprotonation of imidazolylthiolate anion **4** by a second Pr^i_2NK molecule gives dithiolate **5**, which can be easily converted by alkylation into 2,5-bis(organylthio)-1-methylimidazoles **6a,b**.

Scheme 1



6: R = Me (**a**), Et (**b**)

The structures of imidazoles **6a,b** were confirmed by ^{1}H NMR and IR spectroscopy and by elemental analysis.

Experimental

IR spectra were recorded on a Specord 75-IR spectrophotometer in thin films. NMR spectra were measured on a Varian EM-390 spectrometer (90 MHz, ~20% solutions in CCl_4, $SiMe_4$ as the internal standard). GLC analysis was

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 1, pp. 186—187, January, 1998.

1066-5285/98/4701-0187$20.00

carried out on a Varian 3400 gas chromatograph (flame ionization detector, a 15000×0.53 mm capillary column, 1.5 mm DB-5, nitrogen as the carrier gas).

All operations were carried out under nitrogen. THF was purified by dispersed KOH (~50 g L^{-1}) and then distilled over $LiAlH_4$ in the presence of benzophenone in a nitrogen atmosphere. Butyllithium (a 1.6 *M* solution in hexane) and other reagents and solvents used in this study were commercial products.

1-Methyl-2,5-bis(methylthio)imidazole (6a). A solution of Bu^nLi (0.059 mol) in 37 mL of hexane was added to a solution of Bu^tOK (6.5 g, 0.058 mol) and Pr^i_2NH (6.5 g, 0.064 mol) in 70 mL of THF maintained at −50 °C. The mixture was cooled to −100 °C, and a solution of isothiocyanate **1** (3.8 g, 0.052 mol) in 20 mL of THF was added portionwise (over a period of ~1 min). Then the temperature of the reaction mixture was increased to −20 °C, 30 mL of DMSO was added, and the mixture was heated to 40 °C and stirred at this temperature for 15—20 min. After that, the mixture was cooled to −10 °C, and MeI (22 g, 0.153 mol) was added. The mixture was stirred for 15 min at 40 °C and diluted with 100 mL of water. The organic layer was thoroughly washed with water, the aqueous layer was extracted with pentane and with ether, and the combined extracts were dried with K_2CO_3. The solvents were evaporated under reduced pressure, and the residue was distilled *in vacuo* to give 3.1 g (71%) of imidazole **6a** of a 95.2% purity (GLC), b.p. 100—110 °C (0.8 Torr), n_D^{20} 1.5949. Found (%): C, 41.78; H, 6.07; N, 15.58; S, 37.01. $C_6H_{10}N_2S_2$. Calculated (%): C, 41.38; H, 5.75; N, 16.09; S, 36.78. IR, ν/cm^{-1}: 565, 635, 680, 700, 830, 935, 970, 1035, 1080, 1130, 1160, 1250, 1310, 1370, 1390, 1440, 1500, 1600, 2850, 2910, 2980, 3100. ^1H NMR, δ: 2.20 (s, 3 H, SMe); 2.57 (s, 3 H, SMe); 3.50 (s, 3 H, NMe); 7.05 (s, 1 H, CH=).

2,5-Bis(ethylthio)-1-methylimidazole (6b). A solution of Bu^nLi (0.120 mol) in 75 mL of hexane was added to a solution of Bu^tOK (12.57 g, 0.112 mol) and Pr^i_2NH (12.60 g, 0.125 mol) in 90 mL of THF maintained at −60 °C. The mixture was cooled to −100 °C, and a solution of isothiocyanate **1** (7.6 g, 0.104 mol) in 20 mL of THF was introduced with a syringe. The temperature of the reaction mixture was increased to −10 °C, and 55 mL of DMSO was added. Then the mixture was heated to 40 °C, stirred at 40—45 °C for 15 min, and cooled to 0 °C. After that, EtI (25 g, 0.158 mol) was added, and the reaction mixture was stirred at 40—45 °C for 15 min and diluted with 100 mL of water. The organic layer was washed with water, and the aqueous layer was extracted with ether and pentane. The combined extracts were dried with K_2CO_3, the solvents were evaporated, and the residue was distilled *in vacuo* to give 7.5 g (74.3%) of imidazole **6b** of a 96.6% purity (GLC), b.p. 155 °C (15 Torr), n_D^{20} 1.5645. Found (%): C, 47.86; H, 6.78; N, 13.79; S, 31.87. $C_8H_{14}N_2S_2$. Calculated (%): C, 47.52; H, 6.93; N, 13.86; S, 31.68. ^1H NMR, δ: 1.20 (t, 3 H, Me); 1.40 (t, 3 H, Me); 2.53 (q, 2 H, SCH_2); 3.17 (q, 2 H, SCH_2); 3.50 (s, 3 H, NMe); 7.07 (s, 1 H, CH=).

References

1. D. Hoppe and R. Follmann, *Chem. Ber.*, 1976, **109**, 3047.
2. L. Brandsma, N. A. Nedolya, H. D. Verkruijsse, and B. A. Trofimov, *Synthesis*, 1997, 423.

Received July 24, 1997

Claisen aromatic amino rearrangement in the series of fluorinated anilines

A. G. Mustafin, A. R. Gimadieva, I. N. Khalilov, L. V. Spirikhin, A. A. Fatykhov, R. A. Nurushev, I. B. Abdrakhmanov, and G. A. Tolstikov*

Institute of Organic Chemistry, Ufa Research Center of the Russian Academy of Sciences, 71 prosp. Oktyabrya, 450054 Ufa, Russian Federation. Fax: +7 (347 2) 35 6066

The effect of *meta*-substituents in the aromatic ring on the route of Claisen rearrangement of *N*-(pent-3-en-2-yl)-3-fluoro(or 3-trifluoromethyl, 3,4-difluoro)anilines induced by $ZnCl_2$ was investigated. The formation of two possible *ortho*-alkenylated reaction products was observed. The ratio of these isomers depends on the nature of the acid catalyst.

Key words: *N*-(pent-3-en-2-yl)-3-fluoroaniline, *N*-(pent-3-en-2-yl)-3,4-difluoroaniline, *N*-(pent-3-en-2-yl)-3-trifluoromethylaniline, Claisen amino rearrangement; 4-(pent-3-en-2-yl)-3-trifluoromethylaniline.

Substituents in the aromatic ring have a substantial effect on the Claisen rearrangement pathway.[1,2] It is known that, depending on the nature of the substituents in positions 2 and 5, *ortho—para* migrations of the allylic fragment can occur.[3,4] However, when a substituent is present in the *meta*-position, the two possible reaction sites become nonequivalent, and the migration of the alkenyl radical affords two *ortho*-isomers.[5] The ratio of

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 1, pp. 188—190, January, 1998.

1066-5285/98/4701-0188$20.00