Letters to the Editor

5,6-Dihydropyridines from isothiocyanates and lithiated 1-(alkylthio)propynes

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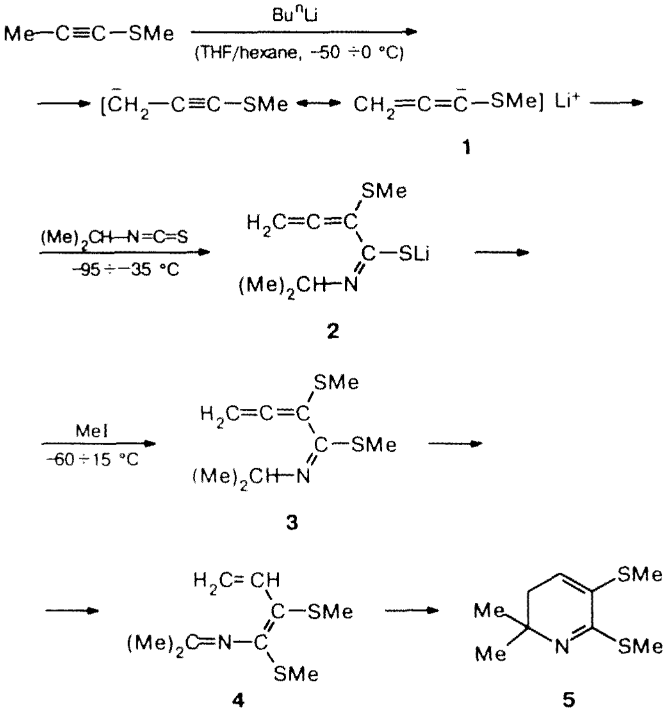
The known reactions of organolithium compounds with isothiocyanates result in the formation of thioamides.[1–4]

We have established that reactions of lithiated 1-(alkylthio)alkynes with isothiocyanates provide a simple way to prepare not easily accessible 5,6-dihydropyridines. For example, the alkylation of thiolate **2**, which is the adduct of lithiated 1-(methylthio)propyne (**1**) and isopropyl isothiocyanate, results in the previously unknown 2,3-bis(methylthio)-6,6-dimethyl-5,6-dihydropyridine (**5**), which was isolated in 70% yield (Scheme 1).

Intermediate azatriene **4** was isolated in 96% yield. The structure of compound **5** was confirmed by the data of elemental analysis and IR, ^1H and ^{13}C NMR spectra.

The corresponding 5,6-dihydropyridines were also synthesized using 1-(ethylthio)propyne and methyl-, ethyl-, and cyclohexyl isothiocyanates.

Scheme 1



Experimental

^1H and ^{13}C spectra were recorded on Varian EM-390 (90 MHz, ~20% solution in CCl_4, $SiMe_4$ as the internal standard) and Bruker AC 300 (^1H: 300 MHz, ^{13}C: 75 MHz, ~20% solution in $CDCl_3$, $SiMe_4$ as the internal standard) spectrometers. IR spectra were recorded on Specord 75-IR and Perkin-Elmer 283 spectrophotometers in a thin layer. GLC analysis was performed on a Varian 3400 gas chromatograph (with a flame-ionization detector, a 15-m capillary column with an inner diameter of 0.53 mm and 1.5-μm DB-5 covering, and nitrogen as the carrier-gas).

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All procedures were carried out in an atmosphere of N_2. 1-(Methylthio)propyne and isopropyl isocyanate were synthesized by the known methods.[5,6] Tetrahydrofuran was purified using mechanically dispersed KOH (~50 g L^{-1}) and by distillation over $LiAlH_4$ in the presence of benzophenone in an N_2 atmosphere. *n*-Butyllithium (1.6 *M* solution in hexane) was presented by Chemetall (Germany).

Reaction of lithiated 1-(methylthio)propyne with isopropyl isocyanate and methyl iodide. 1-(Methylthio)propyne (9.1 g, 0.10 mol) was added to a solution of Bu^nLi (0.10 mol) in anhydrous THF (80 mL) and hexane (65 mL) cooled to −60 °C. When the temperature increased to 0 °C, it was decreased to −95 °C, then isopropyl isothiocyanate (10.97 g, 0.11 mmol) was rapidly added. The reaction mixture, whose temperature had increased again to −35 °C, was again cooled to −60 °C, and methyl iodide (22 g, 0.15 mol) was added. The mixture was stirred for 10—15 min at 10—15 °C and diluted with cold water (~60 mL) with intense stirring. The organic layer was separated, the aqueous layer was extracted with pentane (three times) and ether, and the combined organic fractions were dried over K_2CO_3. After the solvent was evaporated on a rotary evaporator, 2-methyl-4,5-di(methylthio)-3-azahepta-2,4,6-triene (**4**) was obtained (19.34 g, 96.2%) (^1H NMR, δ: 6.10 (d d, 1 H, CH); 5.40 and 4.85 (dd, 2 H, CH_2); 2.27 (s, 3 H, SMe); 2.17 (s, 3 H, SMe); 2.03 (s, 3 H, Me); 1.85 (s, 3 H, Me)) with a minor admixture of azatriene **3** (^1H NMR: 5.14 (s, CH_2)).

After short heating of compound **4**, the exothermic reaction of heterocyclization began (the temperature of self-warming was ~200 °C). 2,3-Bis(methylthio)-6,6-dimethyl-5,6-dihydropyridine (**5**) (14.1 g, 70.1%) with 96.4% purity (GLC) (b.p. 143—145 °C (15 Torr), n_D^{20} 1.5682) was isolated by distillation *in vacuo*. IR, ν/cm^{-1}: 600, 670, 800, 810, 870, 880 sh, 940, 950 sh, 990, 1010, 1080, 1130, 1170, 1220, 1250, 1280, 1300, 1350, 1360, 1410, 1440 sh, 1460 sh, 1550, 1590, 2800, 2860, 2910, 2950, 3050, 3100. ^1H NMR (300 MHz, $CDCl_3$), δ: 5.92 (t, 1 H, H-4); 2.13 (d, 2 H, H-5); 2.14 (s, 3 H, SMe); 2.19 (s, 3 H, SMe); 1.10 (s, 6 H, 2 Me). ^{13}C NMR (75 MHz, $CDCl_3$), δ: 158.52 (C-2); 129.02 (C-3); 128.75 (C-4), 35.80 (C-5); 54.09 (C-6); 16.34 (3-SMe); 12.41 (2-SMe); 28.01 (Me). Found (%): C, 53.63; H, 7.99; N, 6.95; S, 31.52. $C_9H_{15}NS_2$. Calculated (%): C, 53.73; H, 7.46; 6.96; S, 31.84.

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Nickel acetate-promoted reaction of benzoylcyanamide with 1-aryl-3-methyl-2-pyrazolin-5-ones

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It has been found previously[1,2] that nickel salts and complexes promote the addition of methylene-active β-diketones and esters of β-oxocarboxylic acids to cyanamides. However, similar transformations involving monocarbonyl compounds were unknown. We have established that 3-methyl-2-pyrazolin-5-ones (**1a,b**), which have a phenyl group with electron-withdrawing substituents at position 1, are also capable of adding to the C≡N bond of cyanamides. For example, the corresponding adducts **3a,b**, which are new representatives of ketene aminals of the heterocyclic series, were obtained from compounds **1a,b** and benzoylcyanamide (**2**).

The reaction does not occur in the absence of $Ni(OAc)_2$. Probably, the nickel enolates, forming from compounds **1a,b** as intermediates, participate in the formation of ketene aminals **3a,b**.

4-(*N*-Benzoyl)diaminomethylene-3-methyl-1-(4-nitrophenyl)pyrazolin-5-one (3a). A mixture of pyrazolinone **1a** (0.219 g, 1 mmol), cyanamide **2** (0.160 g, 1.1 mmol), and $Ni(OAc)_2$ (0.089 g, 0.5 mmol) in DMF (3 mL) was refluxed

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