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Synthesis of 1-Alkyl-5,6-bis(alkylthio)-1,2-dihydropyridines and Their Thermally Induced Conversion into 1-Alkyl-3-alkylthio-2*H*-pyridine-2-thiones

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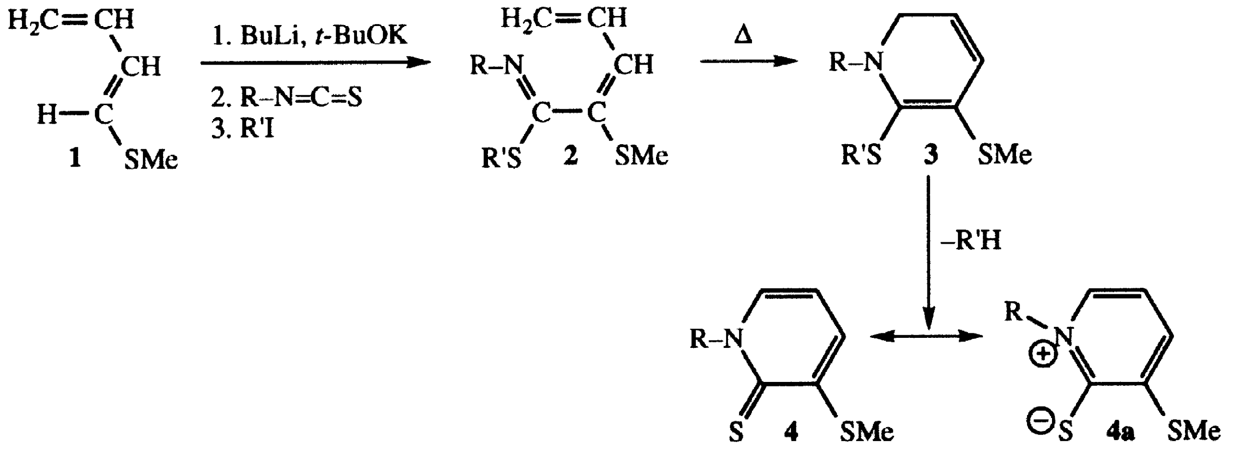
Abstract: Heating of the imidates *E*-**2** (R and R' = alkyl) in refluxing DMF gives derivatives **3** of 1,2-dihydropyridine, which at higher temperatures lose alkane R'H with formation of the cyclic thioamides **4**. © 1998 Elsevier Science Ltd. All rights reserved.

In analogy with previously[1,2] reported electrocyclizations of the two systems C=C–C=C–C(=S)– and C=C–C=C–C(=N)– we considered the possibility of synthesizing the 1,2-dihydropyridines **3** starting from the readily available[3] *E/Z* mixture of **1** (>90% *E*) and alkylisothiocyanates (cf. ref.[4]):



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Heating of **2**, R = R' = CH_3 under N_2 up to ~160 °C resulted in a strongly exothermic reaction. NMR-spectroscopy of the dark product showed the presence of the expected derivative **3**, but the main component was the thioamide **4**. Pure **4** (R = CH_3) was obtained in ~70% yield by flash chromatography on neutral Al_2O_3 using THF as eluent. Heating of **2** with R' = C_2H_5 afforded the same compound, leading to the conclusion that the compounds **3** had lost CH_4 and C_2H_6, respectively. Fairly pure (~8% of Z-**3** present) **3** (R = CH_3, R' = CH_3 or C_2H_5), extremely O_2-sensitive, yellow liquids, were obtained in ~75% yields by heating 1 : 2 mixtures of **2** and DMF for ~10 minutes under reflux in an atmosphere of N_2. The dihydropyridines were isolated by simple distillative separation. As expected, strong heating (200 °C) of **3** (without solvent) under N_2 afforded the thiones **4**, in good yields. Further preliminary experiments showed the possibility of synthesizing other representatives of **3** and **4** (R and R' = alkyl) by using similar conditions.

The driving force for the formation of **4** could be their strongly aromatic character (major contribution of the resonance structure **4a**).

Elemental analysis of compounds **3** and **4** with R = R' = CH_3 gave satisfactory results, while the mass spectra showed the expected parent peaks and degradation patterns.

Compound **3** (R = R' = CH_3) has: ^1H NMR-spectrum (90 MHz, CCl_4): δ = 2.17 (s, 3 H), 2.28 (s, 3 H), 2.78 (s, 3 H), 3.60 (d, 2 H), 5.20 (m, 1 H), 6.00 (dd, 1 H) ppm; ^{13}C NMR-spectrum (75 MHz, $CDCl_3$): δ = 17.24, 19.10, 38.04, 50.63, 112.61, 113.52, 128.16, 147.56 ppm.

Compound **4** (R = CH_3) has: ^1H NMR-spectrum (500 MHz, $CDCl_3$): δ = 2.34 (s, 3 H), 4.00 (s, 3 H), 6.67 (t, 1 H), 7.00 (d, 1 H), 7.55 (d, 1 H) ppm; ^{13}C NMR-spectrum (75 MHz, $CDCl_3$): δ = 16.78, 46.42, 112.42, 125.92, 135.46, 147.01, 175.40 ppm. Mass-spectrum (m/z, I, %): 171 (100, $M^{+\bullet}$), 156 (98, $M^{+\bullet}$ –CH_3), 138 (20, $M^{+\bullet}$ –SH), 124 (12, $M^{+\bullet}$ –SCH_3).

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