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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 available³ E/Z mixture of 1 (>90% E) and alkylisothiocyanates (cf. ref.⁴):



0040-4039/98/\$19.00 © 1998 Elsevier Science Ltd. All rights reserved. PII: S0040-4039(98)00114-2 Heating of 2, $R = R' = CH_3$ under N₂ up to ~160 °C resulted in a strongly exothermic reaction. NMRspectroscopy 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 Al₂O₃ using THF as eluent. Heating of 2 with R' = C₂H₅ afforded the same compound, leading to the conclusion that the compounds 3 had lost CH₄ and C₂H₆, respectively. Fairly pure (-8% of Z-3 present) 3 ($R = CH_3$, R'= CH₃ or C₂H₅), extremely O₂-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 N₂. The dihydropyridines were isolated by simple distillative separation. As expected, strong heating (200 °C) of 3 (without solvent) under N₂ 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' = CH₃) has: ¹H NMR-spectrum (90 MHz, CCl₄): 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; ¹³C NMR-spectrum (75 MHz, CDCl₃): δ = 17.24, 19.10, 38.04, 50.63, 112.61, 113.52, 128.16, 147.56 ppm.

Compound 4 (R = CH₃) has: ¹H NMR-spectrum (500 MHz, CDCl₃): 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; ¹³C NMR-spectrum (75 MHz, CDCl₃): δ = 16.78, 46.42, 112.42, 125.92, 135.46, 147.01, 175.40 ppm. Mass-spectrum (m/z, I, %): 171 (100, M⁺⁺), 156 (98, M⁺⁺ -CH₃), 138 (20, M⁺⁺ -SH), 124 (12, M⁺⁺ -SCH₃).

REFERENCES

- 1. Brandsma, L.; Schuijl-Laros, D. Recl. Trav. Chim. Pays-Bas 1970, 89, 110-113.
- Brandsma, L.; Nedolya, N.A.; Verkruijsse, H.D.; Owen, N.L.; Li, D.; Trofimov, B.A. Tetrahedron Lett. 1997, 38, 6905-6908.
- Everhardus, R.H.; Peterse, A.; Vermeer, P.; Brandsma, L.; Arens, J.F. Recl. Trav. Chim. Pays-Bas 1974, 93, 90-91.
- 4. Everhardus, R.H.; Gräfing, R.; Brandsma, L. Recl. Trav. Chim. Pays-Bas 1978, 97, 69-72.