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5,6-DIHYDROPYRIDINE : SYNTHESIS AND CHARACTERIZATION

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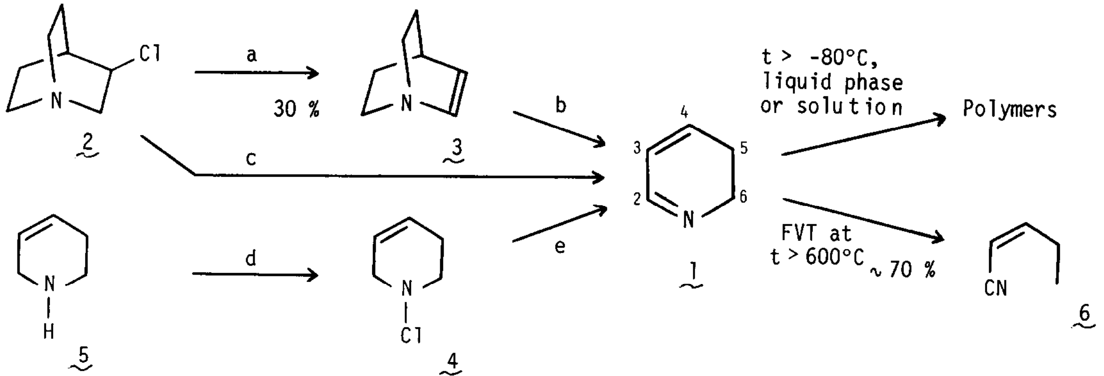
Abstract : 5,6-dihydropyridine 1 is synthesized either by flash vacuum thermolysis of 1-azabicyclo[2.2.2] oct-2-ene 3 or by dehydrochlorination over solid bases of N-chloro-1,2,5,6-tetrahydropyridine 4 and characterized at low temperature by its ^{1}H and ^{13}C nmr and ir spectra.

Although dihydropyridines are of utmost importance in biological systems and have been postulated as intermediates in the biosynthesis of alkaloids[1,2], little is known of the chemistry of the simplest members of the series. Calculations predicted that 5,6-dihydropyridine 1 is the most unstable of the five unsubstituted monocyclic dihydropyridines [3,4] (only the relatively stable 1,4-dihydropyridine has been well characterized [5]). Some alkylated [1,6,7] and fluorinated [8,9] 5,6-dihydropyridines have been prepared and tetrahydropyridine derivatives have been used as equivalents of the 5,6-dihydropyridine system [10].

Flash vacuum thermolysis of Diels-Alder precursors and dehydrochlorination of N-chloramines over solid bases have successfully allowed the obtention of reactive unsaturated nitrogen compounds such as methanimine [11] and ketenimine [12]. We describe here a new application of these reactions to short syntheses of 5,6-dihydropyridine 1 from commercial amines 2 and 5.



a : KO^{t}Bu, DMSO, 60°C, 24 h ; b : 520°C, 5.10^{-7} torr ; c : solid K_2CO_3, 450°C, 10^{-3} torr ; d : solid N-chlorosuccinimide, 25°C, 10^{-3} torr; e : solid K_2CO_3, 300°C, 10^{-3} torr or solid KO^{t}Bu, 50°C, 10^{-3} torr.

Thermolysis at 520°C of isolated 1-azabicyclo [2.2.2]oct-2-ene **3** (scheme, a[13] and b) as well as direct gas phase dehydrochlorination-cycloreversion sequence starting from **2** (scheme, c) yields, besides ethylene and starting material (∿ 70 %), an unstable substance polymerizing above -80°C which was identified as 5,6-dihydropyridine **1** by its nmr[14] and ir spectra [δ ^{1}H (CD_2Cl_2, TMS, -95°C) : 3.23-3.82 (2H), 5.93-6.20 (2H), 7.88 (1H) ; δ ^{13}C (CD_2Cl_2, TMS, -95°C) : 45.5 (C^6), 121.5 (C^3), 136.8 (C^4), 157.8 (C^2) ; ν (solid, -196°C) : 1580, 1645 cm^{-1} (C=N, C=C)] in good agreement with those of 5,6-dihydropyridines [1,6,7] .

Dihydropyridine **1** is also formed, beside a small amount of pyridine and another yet uncharacterized reactive compound, when N-chloro-1,2,5,6-tetrahydropyridine **4** [15] is dehydrochlorinated over solid bases (scheme, e).

At higher temperature of thermolysis (t > 600°C), the presence of **1**, no more observable, is replaced by that of (Z) pent-2-enenitrile **6** (65-70 %) accompanied by much less abundant (E) pent-2-enenitrile and pyridine, identified by comparison with authentical samples [16] . The selective formation of the (Z) isomer **6** could result from a cleavage of dihydropyridine **1** under the conditions of thermolysis, as already observed for pyridyne which yields upon gas thermolysis (or photolysis) β-ethynylacrylonitrile [17].

Further work concerning the syntheses and characterization of other unsubstituted dihydropyridines is in progress.

References and notes.

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13. **3** : mp= 52°C ;[δ ^{1}H ($CDCl_3$, TMS) : 1.22-1.92 (4H), 2.25-3.22 (5H), 6.40-6.58 (2H) ; ir ($CDCl_3$) 1605 cm^{-1} (C=C)]; C.A. Grob, A. Kaiser and E. Renk, *Helv.Chim.Acta*, 40, 2170 (1957).
14. The C^5H_2 chemical shifts could not be assigned without ambiguity.
15. Substance **4** [^{1}H ($CDCl_3$, TMS) : 2.23-2.50 (2H), 3.20-3.40 (2H), 3.60-3.75 (2H), 5.45-5.90 (2H) ; ir ($CDCl_3$) : 1658 cm^{-1} (C=C)] can be isolated or generated in situ from 1,2,5,6-tetrahydropyridine **5** (scheme, d).
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