

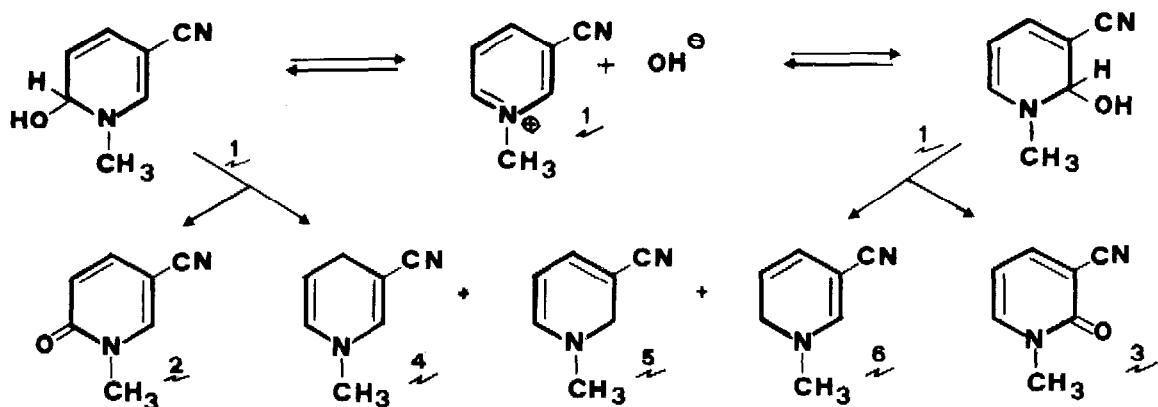
DIHYDROPYRIDINES AND PYRIDONES FROM 3-CYANO-1-METHYLPYRIDINIUM IODIDE IN AQUEOUS NaOH

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Since the work of Hofmann¹ a number of studies was carried out, dealing with the reactivity of pyridinium salts toward hydroxide ions.² Only in a few cases,³ hydroxydihydropyridines were isolated from this reaction, although they are postulated⁴ as unstable intermediates leading to the formation of ring opening products.^{5,4} In connection with our work on the NaBH₄ reduction of cyanosubstituted pyridinium salts,⁶ we have studied the behaviour of 3-cyano-1-methylpyridinium iodide in aqueous NaOH. Previously,⁷ 5-cyano-1-methyl-2-pyridone was isolated from the reaction of 3-cyano-1-methylpyridinium perchlorate in KOH solution. Some what different results were obtained in our experiments. In fact, addition of the pyridinium salt (6.2g, 25mmol) to a solution of NaOH (2.0g, 50mmol) in H₂O (100ml), stirring at room temperature for 2 hr, extraction with CH₂Cl₂ (4x20 ml), and evaporation of the organic layer, gave a residue (1.5g) which was resolved by column chromatography (250g SiO₂; AcOEt/MeOH 9:1 as eluent) into three major fractions: i) a mixture of the known isomeric dihydropyridines 4, 5, and 6 (0.46g); ii) the known 5-cyano-1-methyl-2-pyridone 2 (0.39g); iii) the known 3-cyano-1-methyl-2-pyridone 3 (0.13g). The mixture of dihydropyridines, further analyzed by glpc, contained 4, 5, and 6 in the ratios 11:2:1; minor amounts of other compounds were not investigated. Parallel experiments carried out under N₂ yielded the dihydropyridines 4, 5, and 6 and the pyridones 2, and 3 in the same ratios. The aqueous layer from CH₂Cl₂ extraction, after neutralization with H₂SO₄ and evaporation, yielded a residue, which was extracted with EtOH. By evaporation of the solvent a solid was recovered, whose column chromatography (SiO₂; AcOEt/MeOH 9:1 as eluent) allowed the isolation of the sodium enolate of the glutaconaldehyde 2-cyano derivative, [O=CH=C(CN)=CH=CH=CH=O]⁻Na⁺ 7, unambiguously identified by uv (H₂O) λ_{max} 263, 350nm, ir(nujol) ν̄ 2220 (CN), 1630 cm⁻¹ (enolic unsaturated aldehyde), nmr (D₂O) δ 8.98 (d, 1, H-5, J_{4,5}=9 Hz), 8.70 (s, 1, H-1), 7.80 (d, 1, H-3, J_{3,4}=14 Hz), and 5.82 ppm (dd, 1, H-4). As shown by their close δ values, the aldehyde protons H-1



and H-5 are nearly equivalent, indicating the mesomeric state depicted in structure 7, whereas the large $J_{3,4}$ strongly suggests a transoid conformation of the diene system. The isolation of the 4-cyano-5-methylamino-2,4-pentadienal from the reaction between 3-cyano-1-methylpyridinium perchlorate and aqueous NaOH was described.⁷ We were unable to find this product whose reported spectral data are however surprisingly close to those we observed for compound 7.

As a whole, our results can be rationalized in terms of a reaction pathway analogous to that suggested by Katritzky (path D) for the process leading to ring opening of N-alkoxy pyridinium salts.⁴ In our case, the intermediate 2-hydroxydihydropyridines, in addition to undergoing the normal ring opening reaction, behave as reducing agents toward the pyridinium cation. In fact, the concurrent formation of equimolar amounts of the dihydropyridines 4, 5 and 6, and of the 2-pyridones 2 and 3, can be traced, in our opinion, to a redox process, involving a hydride ion transfer from the intermediate 2-hydroxydihydropyridines to the electron-deficient centers of the pyridinium cation 1. In the authors' knowledge, this work provides the first experimental evidence for such a process among the pyridine derivatives.

References

- 1) A.W.Hofmann, *Ber.*, **14**, 1497 (1881).
- 2) O.R.Rodig in "The Chemistry of Heterocyclic Compounds" Vol.14, "Pyridine and its derivatives" Supp.Part 1, R.A. Abramovitch Ed., J.Wiley & Sons, New York, N.Y., 1974, p. 344.
- 3) K.Wallenfels, and W.Hanstein, *Angew.Chem.Int.Ed.*, **4**, 869 (1965).
- 4) R.Eisenthal, and A.R.Katritzky, *Tetrahedron*, **21**, 2205 (1965); A.R.Katritzky, and E.Lunt, *Tetrahedron*, **25**, 4291 (1969).
- 5) P.Baumgarten, *Ber.*, **57**, 1622 (1924). See also ref.2, pag.370.
- 6) F.Liberatore, A.Casini, V.Carelli, A.Anonc, and R.Mondelli, *J.Org.Chem.*, **40**, 559 (1975), and previous papers in the series.
- 7) E.M.Kosower, and J.W.Patton, *Tetrahedron*, **22**, 2081 (1966).

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