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# THE BASE-CATALYZED DEUTERATION OF N-METHYL-4-PYRIDONE

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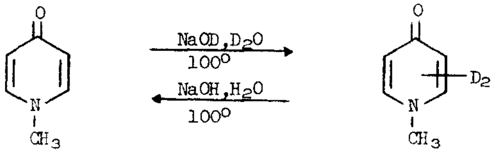
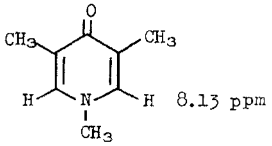
The chemistry of those heterocyclic ylides which can be generated in protic solvents is of considerable current chemical and biochemical interest (1,2,3,4,5,6). A principal line of evidence supporting the intermediacy of an ylide has been the base-catalyzed deuterium exchange of a proton bonded to a formally $sp^2$ carbon atom and adjacent to a positively charged hetero atom. With the exception of the exchanges observed for pyrazolium (4) and pyridinium (5,6) ions the positions of exchange have also been adjacent to a second hetero atom. Recently formally neutral molecules similarly containing two hetero atoms flanking a formally $sp^2$ carbon atom bearing a proton have been reported to exchange that proton on heating in deuterium oxide (7,8). We wish to report that a formally neutral molecule of the pyridine series, N-methyl-4-pyridone (I), undergoes base-catalyzed deuteration at the unsaturated carbon atoms adjacent to the nitrogen atom.

Treatment of N-methyl-4-pyridone, m.p. 91-93°, with a 0.2N solution of sodium deuteroxide oxide at 100° for forty hours followed by isolation gave a 52% yield of a product, m.p. 80-92°, which was shown by ultraviolet and infrared spectral criteria to have retained the chromophore and functional groups of the starting material. Mass spectral analysis showed this product to be 61% $C_5H_5D_2NO$, 32% $C_5H_6DNO$, and 8% $C_5H_7NO$. Treatment of the deuterated product with 1.0N sodium hydroxide in water for nine hours at 100° gave N-methyl-4-pyridone in 60% yield. Deuteration could not be affected by similar treatment under neutral or acidic conditions.

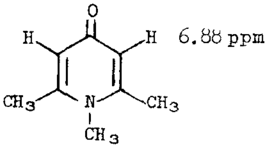


I II

The location of the deuterium atoms on the carbon atoms adjacent to nitrogen in the major deuterated product follows from the chemical shifts[†] and integral areas of the ring protons of the deuterated material. A comparison of the chemical shifts of the ring protons in 3,5-dimethyl-N-methyl-4-pyridone (III)[‡], 2,6-dimethyl-N-methyl-4-pyridone (IV) (9) confirm that the assignments in N-methyl-4-pyridone (10) are correct. Since the n.m.r. spectrum of the deuterated material has the resonance at 8.28 p.p.m. reduced to one-fourth the area of the resonance at 7.01 p.p.m. the product is clearly deuterated at the 2 and 6 positions and is predominately 2,6-$\underline{d}_2$-N-methyl-4-pyridone (II).



III



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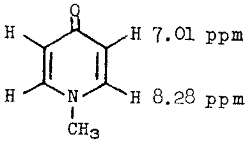

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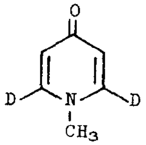

II

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[†] The chemical shifts are at infinite dilution relative to external tetramethylsilane for deuterium oxide solutions and are in δ p.p.m.

[‡] Satisfactory analytical and spectral data were obtained for this compound; m.p. 131-132°.

The reaction is approximately first-order in base over a base concentration range of 0.1 to 0.5N. The course of the reaction is consistent with previous exchanges of pyridinium (5,6) compounds and with a present observation that 4-methoxy-N-methylpyridinium fluoborate rapidly exchanges at the 2 and 6 positions in 1.0N sodium methoxide in deuteromethanol at room temperature while N-methyl pyrrole does not exchange in the same median even on heating at 60° for forty hours.

The difference between these results and the exchange observed at the 3 and 5 positions observed for 4-pyrone in acidic or neutral deuterium oxide (11) is striking. The structural features which determine the position of the exchange and the scope of this reaction are under further investigation.

The N-methyl-4-pyridone used in this work was prepared in 84% yield by heating 4-methoxypyridine with a one-tenth molar amount of methyl iodide for fourteen hours at 130°. 4-Methoxypyridine is stable under these conditions in the absence of methyl iodide. This process is believed to be an *insitu* generation of 4-methoxy-N-methyl-pyridinium iodide which can act as a catalyst for the conversion of 4-methoxy pyridine to N-methyl-4-pyridone in accordance with the considerations previously outlined (12).

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