

Naod Kebede and James W. Pavlik*

Department of Chemistry and Biochemistry, Worcester Polytechnic Institute,
Worcester, MA 01609

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Dimethylpyridines undergo deuterium-hydrogen exchange when heated in deuterium oxide containing potassium carbonate at ring positions 2 and 6 when these positions are unsubstituted and at methyl groups located at ring positions 2, 4, and 6 exclusively.

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As part of our program to study the photochemistry of hetero-aromatic compounds, we required samples of dimethylpyridines highly deuterated at specific positions. A review of the literature revealed that deuterium-hydrogen exchange in pyridine and its methyl and dimethyl derivatives has been the subject of both mechanistic [1-3] and synthetic investigations [4-11] and has been the topic of several reviews [12,13]. Synthetic methods have been developed for the partial deuteration of methyl groups in pyridines [4,5] and for the exchange at ring positions and/or at methyl substituents. The conditions employed range from reactions in neutral deuterium oxide [7] to the use of acid, base or metal catalyzed reactions [8-11]. Most of these studies have focused on the deuterium exchange reactions of pyridine and its monomethyl derivatives. No systematic report including the reactions of all six isomeric dimethylpyridines has appeared.

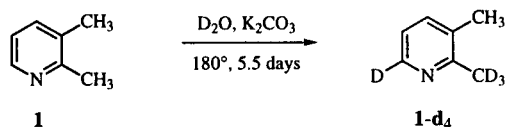
The method that we now describe involves heating a solution of dimethylpyridine in deuterium oxide containing anhydrous potassium carbonate at 180° for 5.5 days. The yields of the isolated deuterated dimethylpyridines

ranged from 65-93% with more than 95% deuterium incorporation and are summarized in Table 1. Hydrogen-deuterium exchange was found to occur at ring positions 2 and 6 when these positions were unsubstituted and at methyl groups located at ring positions 2, 4 and 6 exclusively.

When a sample of 2,3-dimethylpyridine (**1**) was treated under these conditions, the mass spectrum of the product showed a parent peak at *m/e* 111 indicating the incorporation of four deuterium atoms in the structure. In addition, the ¹H nmr spectrum showed a three proton singlet at δ 2.24 where the C-3 methyl group is known to absorb, but only very small signal at δ 2.47 due to residual protons on the C-2 methyl group. Furthermore, while the one proton doublet (*J* = 5.0 Hz) at δ 8.31 due to the C-6 proton in undeuterated **1** was absent in the spectrum of the deuterated sample, the C-4 and C-5 protons, which appear as a doublet (*J* = 7.5 Hz) and as a doublet of doublets (*J* = 7.5 Hz, 5.0 Hz) respectively in the spectrum of the undeuterated sample, were observed as a pair of doublets (*J* = 7.5 Hz) at δ 7.38 and 7.00 after deuteration. These data con-

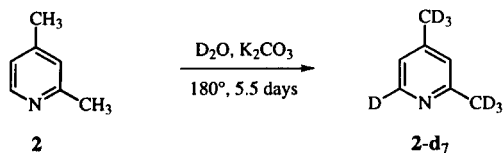
Table 1
Reactants, products, yields and spectral data.

Dimethylpyridine	Product	yield (%)	δ (ppm), <i>J</i> (Hz)	Mol. ion <i>m/e</i>
2,3- 1	6-deuterio-3-methyl-2-trideuteriomethylpyridine (1-d₄)	82	2.24 (s, 3H), 7.00 (d, 7.5, 1H), 7.38 (d, 7.5, 1H)	111
2,4- 2	6-deuterio-2,4-bis(trideuteriomethyl)pyridine (2-d₇)	78	6.88 (s, 1H), 6.94 (s, 1H)	114
2,5- 3	6-deuterio-5-methyl-2-trideuteriomethylpyridine (3-d₄)	93	2.15 (s, 3H), 6.90 (d, 7.9, 1H), 7.30 (d, 7.9, 1H)	111
2,6- 4	2,6-bis(trideuteriomethyl)pyridine (4-d₆)	86	6.91 (d, 7.5, 2H), 7.41 (dd, 7.5, 1H)	113
3,4- 5	2,6-dideuterio-3-methyl-4-trideuteriomethylpyridine (5-d₅)	65	2.18 (s, 3H), 6.99 (s, 1H)	112
3,5- 6	2,6-dideuterio-3,5-dimethylpyridine (6-d₂)	89	7.30 (s, 1H), 2.30 (s, 6H)	109



firm that 2,3-dimethylpyridine (**1**) was converted to 6-deuterio-3-methyl-2-trideuteriomethylpyridine (**1-d₄**).

In contrast, the mass spectrum of the product obtained from deuteration of 2,4-dimethylpyridine (**2**) exhibited a parent peak at *m/e* 114 consistent with incorporation of seven deuterium atoms per molecule. Moreover the ¹H nmr spectrum showed only a pair of one proton singlets for C-3 and C-5 protons at δ 6.88 and 6.94 confirming that deuterium exchange has occurred at both methyl groups and at the C-6 ring position to yield 6-deuterio-2,4-bis(trideuteriomethyl)pyridine (**2-d₇**). A summary of the mass spectral and ¹H nmr data of all deuterated products is given in Table 1.



EXPERIMENTAL

The ¹H nmr spectra were recorded at 200 MHz on a Bruker FT-nmr relative to internal chloroform. Mass spectral data were generated on a Hewlett Packard HP5890/5970B GCMS system. 2,6-Dimethylpyridine was purchased from Lancaster Chemical Co. while all other dimethylpyridines were purchased from Aldrich Chemical Co. Reactions were carried out in a stainless steel reaction chamber (3.8 cm internal diameter, 14.2 cm depth and 1.2 cm wall thickness) with a glass liner sleeve.

General Method.

The dimethylpyridine (2.0 g, 18.8 mmoles) was placed in a solution of deuterium oxide (25.0 ml) containing anhydrous potassium carbonate (0.6 g, 434.1 mmoles). The pH of the mixture was measured using pHDrion paper and was in the range 8.5-9.5.

The mixture was placed in the reaction chamber, sealed tight and left in an oven at 180° for 5.5 days. At the end of the reaction period, the reaction mixture was recovered and extracted with dichloromethane (7 x 50 ml) and the extract dried over anhydrous sodium sulfate. Most of the solvent was removed using fractional distillation at atmospheric pressure. The remaining solvent was removed by spinning band distillation using a Hickman apparatus and the final product was purified further using Kugelrohr distillation (18 mm Hg, 75-80° oven temperature).

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- * To whom correspondence should be addressed.
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