New Reaction of Iminium Ions: Deprotonation at the *sp*²-Hybridized Carbon Atom

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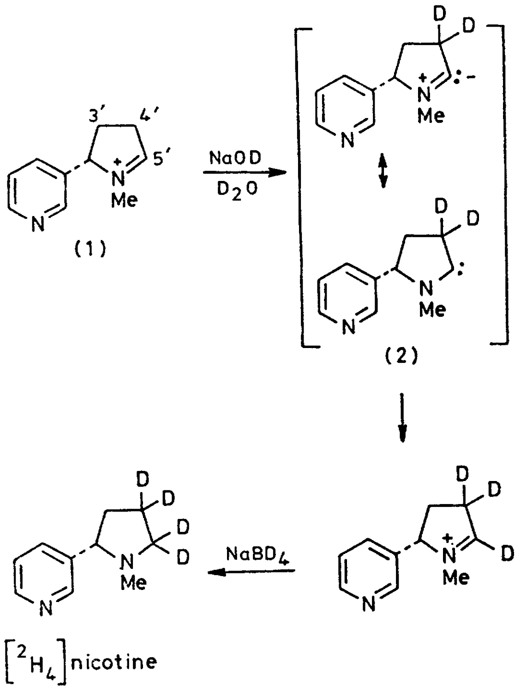
Summary The iminium ion (**1**) slowly exchanges its 5′-hydrogen for deuterium when treated with NaOD–D_2O.

Strongly alkaline solutions of NaOD in D_2O convert the iminium ion (**1**), an intermediary metabolite of nicotine, into equilibrium mixtures in which the corresponding carbinolamine greatly predominates.[1] When such a mixture (pD$_C$ 13·4†) was investigated by ^{1}H n.m.r. spectroscopy at 70 °C, the signal from H-5′ (δ 4·70) was found to integrate for less than one hydrogen. To account for this, a protium–deuterium exchange reaction was assumed to occur *via* the dipole-stabilized carbanion[2] (amino carbene) (**2**) (Scheme). We here present evidence for such a reaction.



SCHEME

That a protium–deuterium exchange takes place at C-5′ was verified in the following way. After being subjected to a strongly alkaline solution (pD$_C$ 14·1, 20—22 °C, 7 days), the iminium ion (0·025 M) was reduced with NaBD$_4$ and the nicotine formed was investigated by ^{1}H n.m.r. (acidic solution in D$_2$O) and mass spectroscopy. In the ^{1}H n.m.r. spectrum, the signals from H-2′, H-5′α, and H-5′β appear completely resolved[3] and it was thus easily confirmed that H-2′ was untouched and that in all only *ca.* 0·4 H occupied the two 5′ positions. The mass spectral analysis consistently showed the presence of a 69:31 mixture of [^{2}H$_4$]- and [^{2}H$_3$]-nicotine. Of these two compounds, only the former originates from iminium molecules which have undergone the exchange reaction at C-5′; incorporation of three deuterium atoms is trivial. The exchange reaction rate at pD$_C$ 13·8 (20—22 °C) was followed as above by mass spectroscopy and the pseudo-first order rate constant was found to be 2×10^{-6} s^{-1}.

No incorporation of deuterium at C-1 could be demonstrated (mass spectroscopy) with certainty after treatment of butanal with NaOD–D$_2$O (0·1 M, 22 °C, 2 days). This indicates that the amino-aldehyde form, which is hypothetically in equilibrium with the iminium ion, does not play an important role in this context.

The exchange reaction is much slower in CD$_3$ONa–CD$_3$OD, not only at C-5′ but also at C-4′. After 4 weeks at 20—22 °C, at most a 5% exchange had occurred at C-5′ and only *ca.* 50% exchange at C-4′. This result is probably due to a lower equilibrium concentration of iminium ion than in the experiments with NaOD–D$_2$O. The variation of extent of exchange at C-5′ with pD$_C$ is shown in the Figure.

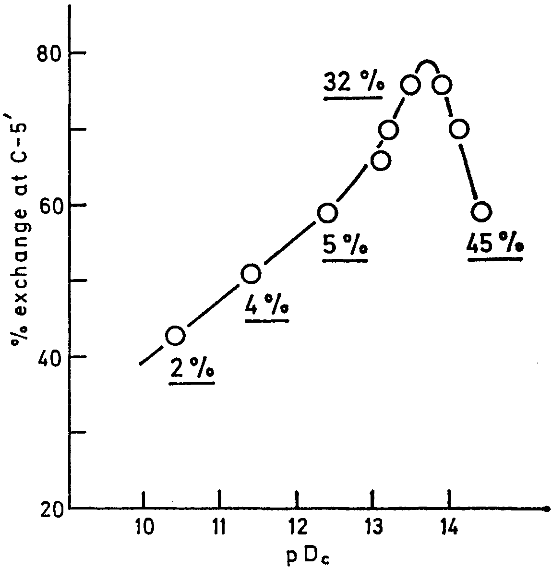


FIGURE. pD$_C$-dependence of the exchange reaction. Solutions of (**1**) (0·025 M) in NaOD–D$_2$O were left at 20—22 °C for 7 days, then reduced with NaBD$_4$ and the nicotine formed investigated by mass spectroscopy. The underlined figures refer to the yields of nicotine.

Coupling constants $^1J_{CH} = 192·5 \pm 1$ and 216 Hz have been recorded for the methine groups at C-5′ of (**1**) and at C-2 of 3,4-dimethylthiazolium ion,[4] respectively. The degrees of *s* character, and hence relative acidities, that can be calculated by means of the Muller–Pritchard relationship[5] are consistent with the much greater ease of exchange displayed[4] by the latter compound and its analogues.[6] Smaller coupling constants (179—188 Hz) have been noted for acyclic iminium ions.[7]

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† pD$_C$ = (pH meter reading) + 0·40 (P. K. Glasoe and F. A. Long, *J. Phys. Chem.*, 1960, **64**, 188). Measurements were performed using a Futura Full-range (pH 0—14) Combination Electrode (Beckman).

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