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Short Communications

Ring–Chain Tautomerism of Myosmine

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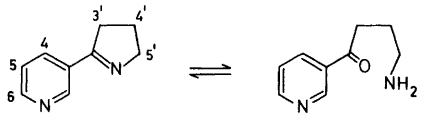
Myosmine (*1a*) is a minor tobacco alkaloid.[1] It is also formed by pyrolysis of nicotine [2] and has been detected in tobacco smoke.[3] On treatment with aqueous hydroxylamine or phenylhydrazine, it reacts as a carbonyl compound and it has therefore been assumed that aqueous solutions of myosmine contain equilibrium mixtures of *1a* and the amino ketone from *1b*, which has been called poikiline.[4–6]



1a *1b*

In connection with studies of the ring–chain tautomerism of nicotine metabolites,[7,8] we recorded ^1H and ^{13}C NMR spectra of aqueous solutions of myosmine and we here report the results. Signals from both *1a* and *1b* were seen in the spectra of acidic solutions and integrations of the signals ascribed to H-5'* gave the percentage of *1a* as a function of the acidity of the D_2O solution as shown in Fig. 1; similar values were obtained from the ^{13}C NMR spectra. There was no NMR evidence for the carbinolamine which reasonably should be an intermediate in the reactions *1a*⇄*1b*. Five ^{13}C NMR spectra of solutions of *1a* in H_2O demonstrate a marked, mixed origin, isotope effect on the equilibrium between *1a* and *1b* (Fig. 1). These latter spectra indicate that the content of *1b* in H_2O should be less than 1 % at physiological pH.

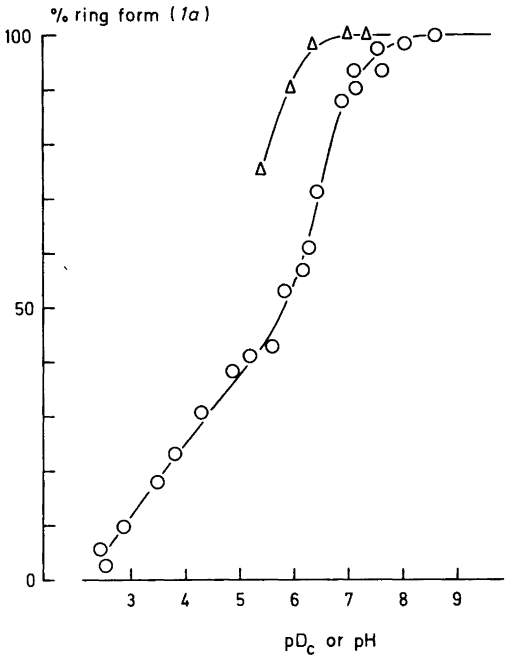


Fig. 1. Ring–chain tautomerism *1a*⇄*1b* as found by ^1H NMR spectroscopy of solutions of myosmine in D_2O (circles) and by ^{13}C NMR spectroscopy of solutions in H_2O (triangles).

As in a similar tautomeric system,[8] the nature of the aromatic ring has a decisive effect on the ring–chain tautomerism. Thus, the phenyl analogue [9] of myosmine is, as found by ^1H NMR, a *ca.* 15:85 mixture of the amino ketone and imino forms between pD_c 1.2 and 6.0 (pD_c=pH meter reading+0.40 [10]).

Experimental. The synthesis of myosmine [11] and the NMR investigation [8] were performed as described.

NMR spectra of 1a. ^1H NMR (D_2O, pD_c 8.6 to 13.9): δ 8.66 (dd, H-2), 8.46 (dd, H-6), 8.00 (m, H-4), 7.40 (ddd, H-5), 3.92 (m, H-5'), 2.92 (m, H-3'), 2.00 (quintet, H-4'). ^{13}C NMR (D_2O, pD_c

* The numbering of nicotine has been used throughout.

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10.2): 172.9 (C-2′), 151.0 (C-6)**, 148.1 (C-2)**, 136.4 (C-4), 129.2 (C-3), 125.0 (C-5), 61.3 (C-5′), 35.3 (C-3′), 22.2 ppm (C-4′). ^{1}H NMR (D_2O, pD_c 3.4): δ9.00 (broad s, H-2), 8.38 (m, H-4), 7.69 (ddd, H-5), 4.25 (m, H-5′), 3.63 (m, H-3′), 2.44 (quintet, H-4′). ^{13}C NMR (D_2O, pD_c 3.2): 155.2 (C-6)**, 150.1 (C-2)**, 139.8 (C-4), C-3 not observed, 126.1 (C-5), 55.4 (C-5′), C-3′ not observed, 20.5 ppm(C-4′).

NMR spectra of 1b. ^{1}H NMR (D_2O, pD_c 1.3): δ 9.28 (dd, H-2), 9.06 (m, H-4) 8.94 (dd, H-6), 8.18 (ddd, H-5), 3.38 (t, H-3′), 3.14 (t, H-5′), 2.12 (quintet, H-4′). ^{13}C NMR (D_2O, pD_c 0.9): 197.6 (C-2′), 146.6 (C-6),** 145.1 (C-2)**, 142.4 (C-4), 135.6 (C-3), 128.8 (C-5), 39.7 (C-5′), 36.8 (C-3′), 36.5 (t, monodeuterated C-3′), 21.5 ppm (C-4′).

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** Tentative assignment.