Novel Synthesis of a [10](2,6)Pyridinophane, a Structural Isomer of Muscopyridine

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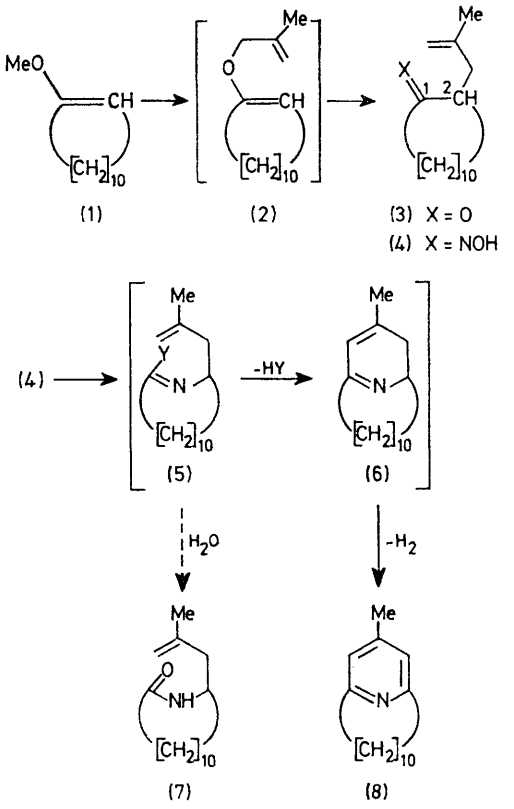
Summary The [10](2,6)pyridinophane (**8**) is readily prepared in three steps from 1-methoxycyclododecene (**1**); the activated intermediate (**5**), formed by Beckmann rearrangement of the oxime (**4**), is intercepted by the intramolecular C=C bond.

WHILE investigating structure–odour relationships in a series of compounds with molecular characteristics resembling those of muscopyridine we required an efficient synthesis of the [10](2,6)pyridinophane (**8**). A convenient synthesis of this[1] and similar[2] pyridinophanes has not been described, although compounds of this type have been investigated extensively.[3] We now report a simple synthesis of (**8**) by a route involving a novel intramolecular cyclisation of the cyclododecanone oxime derivative (**4**).

1-Methoxycyclododecene (**1**) (mixture of 17% *Z*- and 83% *E*-isomers),[4] obtained in almost quantitative yield from cyclododecanone,[5] was converted into (**3**) (b.p. 93—95 °C, at 0·025 mmHg; 90% yield), presumably *via* a Claisen–Cope rearrangement of the unstable intermediate (**2**), by heating with an excess of 2-methylpropen-2-ol in the presence of catalytic amounts of mercury(II) acetate. Treatment of (**3**) with hydroxylamine hydrochloride in refluxing pyridine gave (**4**) (80% yield), which was shown by ^{13}C-n.m.r. spectroscopy[6] to be a mixture of *E*- (75%) [m.p. 70·5—72 °C (from n-hexane—ether, 4:1)], and *Z*-oximes (25%) [m.p. 92—93·5 °C (from n-hexane–ether, 4:1)]. Both isomers are separable by silica gel chromatography (n-hexane–ether, 20:1). The *Z*-stereochemistry was assigned to the first compound eluted.

Beckmann rearrangement of the mixture of isomers (**4**) ($POCl_3$, pyridine; 80 °C; under argon) directly afforded the [10](2,6)pyridinophane (**8**) [b.p. 113—114 °C at 0·04 mmHg; 25% yield from (**4**)], whose spectral characteristics were identical with those reported by Georgi and Rétey.[1b] The lactam (**7**) [m.p. 125—127 °C (from $CHCl_3$–Et_2O); 20% yield from (**4**)] was the main by-product in this last step.

These results can reasonably be rationalized assuming intermediate formation of an activated imino-derivative of type (**5**) (Y = leaving group), which could undergo reaction to form (**7**) on work-up, or further reaction to a transient dihydropyridine (**6**), which should easily be dehydrogenated to (**8**).†



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† All new compounds gave satisfactory elemental analyses and mass spectral data.

[1] For previous syntheses of the pyridinophane (**8**), *cf.* (a) A. T. Balaban, M. Gavăt, and C. D. Nenitzescu, *Tetrahedron*, 1962, **18**, 1079; (b) U. K. Georgi and J. Rétey, *Chem. Comm.*, 1971, 32.

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