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BOROHYDRIDE REDUCTION OF PYRIDINIUM SALTS.III. FORMATION OF A DIELS-ALDER ADDUCT IN THE REDUCTION OF 1-METHYL-4-CYANOPYRIDINIUM IODIDE.

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Although an exhaustive study of the $NaBH_4$ reduction of 1-methyl-3-cyanopyridinium iodide has been reported (1), no analogous investigation on the isomeric 2-and 4-cyanopyridinium salts has been made. This letter reports the borohydride reduction of 1-methyl-4-cyanopyridinium iodide in 1:1 water-methanol solution, giving a single product (b.p.92°C/8 mm), identified by elemental analysis, molecular weight, I.R. and N.M.R. spectra, as 1-methyl-4-cyano-1,2,5,6-tetrahydropyridine (III). The formation of (III) can be easily explained in the light of the wealth of literature on the reduction of pyridinium salts in aqueous alcoholic media: the initial formation of 1,2-dihydropyridine (II) can be postulated, which, due to its enaminic nature and the reduction conditions (1 c,d), is protonated on carbon 3, forming the corresponding immonium cation which is reduced to tetrahydropyridine. If (I) is reduced in 0.8 N $NaOH/CH_3OH$ solution at 0°C, the single product (IV), m.p.175°C, is obtained, having the following spectral data: I.R.(nujol) 2230 and 2215 cm^{-1} (nitrile absorption); 1645 and 1605 cm^{-1} (double bonds); U.V. (EtOH), end-absorption ca. 210 nm; λ_{max} 245 nm (ε =6100), 283 nm (ε = 1900). Elemental analysis and molecular weight measurement (240: from mass spectrum) indicate a dimeric structure for (IV) with respect to (II). The above data and accurate N.M.R. analysis (100 MHz; $CDCl_3$.Table) show that (IV) is endo-4,9-dimethyl-7,11-dicyano-4,9-diazatricyclo-$[6.2.2.0^{2,7}]$-dodeca-5,11-diene. In the N.M.R. spectrum the three olefinic protons, H_Y, H_X and H_P are easily identified at 6.9, 5.92 and 4.32 δ respectively; the coupling of H_X and H_P shows they are on the same double bond. The chemical shifts of these protons are in good agreement with reported values for protons on α and β carbon atoms of enamine double bonds. The assignment of H_X, H_Y and H_P has been confirmed by comparison with the

N.M.R.spectra of both the partially reduced products (V) and (VI) (2) and of the selectively deuterated products (VII) and (VIII) (see later). In the spectrum of (V) the H_{Y*} proton is found at 7.00 δ and has a J_{Y*M*} value identical to that of the corresponding proton in (IV), while in (VI) the δ and J values of H_{X*} and H_{P*} (6.09 δ_{X*}; 4.28 δ_{P*}; J_{X*P*}=8.00 Hz) are almost equal to those of the corresponding protons of (IV).

The single coupling observed for H_M(J_{MY}=5.7 Hz) and the small J_{CD} value (1.9 Hz) corresponding to a dihedral angle of ca.60° between H_C and H_D (seen from the molecular model) are in agreement with the proposed structure.

The large difference between the chemical shifts of the geminal protons α to N_9(H_E and H_N) should be noted. This difference must be related to the fixed boat form of the ring containing N_9 and, in our opinion, to the absence of inversion of the heteroatom (3). Consequently H_N is held in a cis-diaxial position with both the lone-pair of nitrogen and the nitrile on C_7, and is deshielded by the magnetic anisotropy of the lone-pair and of the electric dipole of the CN; while H_E trans-equatorial to the lone-pair, is shielded.The effect of the shielding is reinforced by the fact that H_E is in the positive shielding cones of the C_{11} double bond. In this connection it should be noted that inversion of N_9 would bring the methyl group into a 1,3 diaxial position with respect to the CN on C_7, causing severe steric interaction.

The absence of coupling between H_D and H_E allows the endo configuration to be assigned to (IV): in fact, in the exo configuration the H_D-C_2-C_1-C_{10}-H_E system should have a perfectly coplanar zig-zag pattern and therefore a long range coupling through four bonds should be expected (4). Confirmation of the endo configuration of (IV) is given by U.V. absorption maximum at 283 nm(ε =1900). This maximum, also found in the spectrum of (V) but not in that of (VI),may be attributed only to a long range interaction (5) between the lone-pair of N_4 and the α-β-unsaturated nitrile chromophore. It is obvious that only the endo configuration of (IV) provides the stereo-electronic requirements necessary to establish this interaction.

The formation of (IV) can be satisfactorily explained by postulating that the initial intermediate is always dihydropyridine (II), which in the absence of a protonating species (1 c,d), due to the strongly basic reaction medium, cannot be further reduced to the tetrahydro derivative (III), and therefore undergoes a dimerisation, where two molecules of dihydropyridine react, one acting as the diene the other as the dienophile, to give cyclic adduct (4+2).

CHART 1

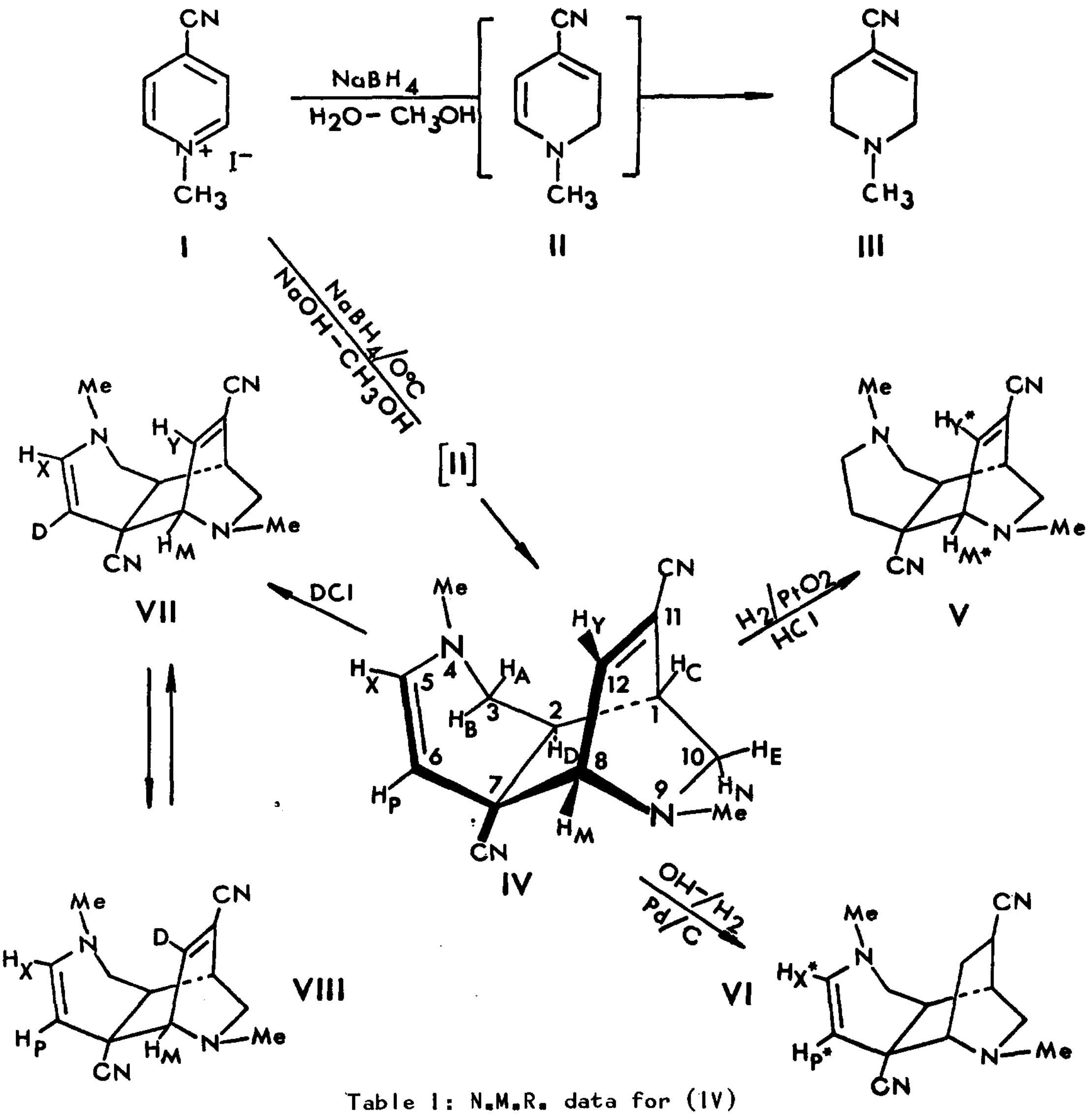

Table I: N.M.R. data for (IV)

H	A or B	B or A	C	D	E	M	N	P	X	Y	Me
ppm	2.93	2.82	2.63	2.54	1.90	3.54	3.40	4.32	5.92	6.90	2.32,2.69
J	AB	AD(orBD)	BD(orAD)	CD	CE	CN	CY	EN	MY	PD	PX
Hz	12.0	4.0	2.0	1.9	2.0	2.7	1.8	9.5	5.7	1.0	7.8

Owing to the enaminic C_5 double bond it is possible to obtain the selectively deuterated product (VII) by treatment of (IV) with DCl and subsequent basification with NaOD. The N.M.R. spectrum of (VII) is the same as that of (IV) except for an almost total absence of H_P and a corresponding decoupling of H_X. It is interesting to note that slight warming (e.g. crystallisation from boiling benzene) causes the equilibration of (VII) with the isomer (VIII) in which H_Y is substituted by deuterium. In fact the N.M.R. spectrum of the crystallised product shows that it is composed of an equimolar mixture of (VII) and (VIII) because the areas relative to H_P and H_Y are halved and the signals corresponding to H_X and H_M result from the superposition of a doublet and a singlet. This equilibration involves a [3,3]sigmatropic shift and shows a close similarity with intramolecular rearrangements observed in some Diels-Alder adducts where both the components, as in the present case, have dienic character. On the basis of the work of Woodward and Katz (6) these rearrangements can be interpreted as concerted processes, sterically possible only when the compounds are in the endo configuration (7).

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2) (V):m.p.=148°C; I.R. (nujol), 2220, 2210 cm^{-1} (nitrile bands),1610 cm^{-1}(double bond); U.V. (EtOH), end-absorption ca.210 nm, λ_{max} 290 nm (ε =1430). (VI): m.p.=171°C; I.R.(nujol), 2220 cm^{-1} (nitrile),1645 cm^{-1} (double bond); U.V.(EtOH) λ_{max} 245 nm (ε =7450).

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