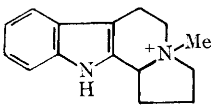
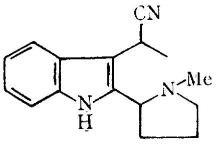
The Reactions of Some Heterocyclic Quaternary Salts with Potassium Cyanide

By G. H. FOSTER and JOHN HARLEY-MASON*
(*University Chemical Laboratory, Lensfield Road, Cambridge*)

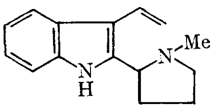
IN an earlier Communication[1] we described the action of potassium cyanide in diethylene glycol on the hexahydroindoloindolizine methiodide (I) and assigned to the major product the structure of an indoloazanonane derivative formed by cleavage of the central carbon–nitrogen bond. We have now found that this assignment is erroneous and that the product has in fact the unexpected isomeric structure (II).



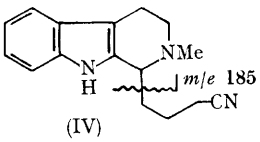
(I)



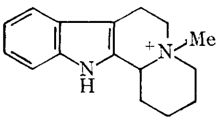
(II)



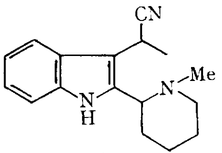
(III)



(IV)



(V)



(VI)

Treatment of the cyano-compound with methanolic hydrogen chloride gave the corresponding methyl ester (II; CO_2Me for CN). Examination of the high-field region of the 100 MHz n.m.r. spectrum of the carefully purified ester in several solvents showed (by duplication of some of the peaks) that it was clearly a mixture of two very closely related compounds, and this was confirmed on t.l.c. when the material gave two spots of about equal intensity running close to each other. The n.m.r. spectrum showed τ 8·46 and 8·47 (2d, *J* 7·5 c./sec., 3 H) and 6·10 (q, *J* 7·5 c./sec., 1 H). On irradiation at τ 6·10 the pair of high-field doublets collapsed to a singlet and on irradiation at τ 8·5 the quartet at τ 6·10 collapsed to a singlet. This indicates the presence of the structural unit MeCH<. Further chemical confirmation of structure (II) was obtained as follows. The methiodide (I) was subjected to Hofmann elimination conditions, when only one basic product was obtained. This contained a vinyl group as shown by its n.m.r. spectrum, and its u.v. spectrum (λ_{max} 225, 258, and 282 mμ) showed clearly that it was a 3-vinylindole[2] with structure (III). When this compound was treated with potassium cyanide it was smoothly converted into (II) which was identical with the material obtained above.

Thus the cyanide-induced cleavage of (I) plainly involves two steps: (i) Hofmann elimination in which the potassium cyanide merely acts as a base and (ii) conjugate addition of cyanide ion to a 3-vinylindole. This second step appears to be a new reaction. This product contains two asymmetric centres and is therefore obtained as a mixture of two racemates.

Two minor products of the reaction of (I) with cyanide were also examined. One was the parent hexahydroindoloindolizine; demethylation of a quaternary salt by potassium cyanide has once previously been recorded.[3] The other was a nitrile isomeric with (II). This exhibited the very simple mass spectrum associated with a tetrahydro-β-carboline[4] showing the molecular ion (*m/e* 253) and a base peak at *m/e* 185 corresponding to the cleavage indicated. The compound was therefore formulated as (IV).

Thus in the simple system (I) no indication was found of cyanide-induced cleavage of the central carbon–nitrogen bond. However, it is interesting to note that in two more complex quaternary salts[5] containing the hexahydroindoloindolizine skeleton that central bond cleavage does occur, albeit in low yield, and accompanied by other products. In these more complex cases there is no doubt of the structures of the products since direct correlation with natural products has been made. Clearly the direction of cleavage depends critically on the precise structure of the compound under study.

The action of potassium cyanide on the octahydroindoloquinolizinium salt (V) was also examined. Two products were isolated; the major one was the nitrile (VI) (the structure was proved as in the comparable case above) and the minor one was the demethylated free-base.

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[3] H. R. Snyder and J. H. Brewster, *J. Amer. Chem. Soc.*, 1949, **71**, 1061.

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[5] (a) J. Harley-Mason and Atta-ur-Rahman, *Chem. Comm.*, 1967, 208; (b) J. P. Kutney, K. K. Chan, A. Failli, J. M. Fromson, C. Gletsos, and V. R. Nelson, *J. Amer. Chem. Soc.*, 1968, **90**, 3891.