The Reduction of Pentachloropyridine with Lithium Aluminium Hydride

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Summary The formation of 2,3,6-trichloropyridine, the main product obtained by reduction of the title compound with lithium aluminium hydride is rationalized on the basis of deuteriation studies and isolation of a stable 3,4-dihydropyridine.

IT has been reported that on treatment with lithium aluminium hydride pentafluoropyridine gives 2,3,5,6-tetrafluoropyridine and that further reduction occurs at the 2-position as expected from a hydride attack.[1] By contrast, we observed that pentachloropyridine (I), on stirring with $LiAlH_4$ at room temperature for 16 hr. in ether gives 2,3,6-trichloropyridine (II) (90%), together with small amounts of the known 2,3,5,6-, 2,3,4,6-, and 2,3,4,5-tetrachloropyridines.[2-5] 2,3,6-Trichloropyridine (isolated by preparative g.l.c.) showed two doublets in the n.m.r. at τ 2·77 (3-H, *J* 8·5 c./sec.) and at τ 2·27 (4-H).

In an effort to elucidate the nature of the reduction at the 3-position we treated the reaction mixture with D_2O, which gave a product (III), identical (i.r., m.p.) to (II), but giving a much simplified n.m.r. spectrum with the high-field doublet (*cf.* above) absent and the low-field signals collapsed to a broad singlet (τ 2·27). Compound (III) was, therefore, 3-deuterio-2,5,6-trichloropyridine. Conversely, reduction of (I) with $LiAlD_4$, followed by hydrolysis gave 4-deuterio-2,3,6-trichloropyridine (IV), as inferred from its n.m.r. spectrum.

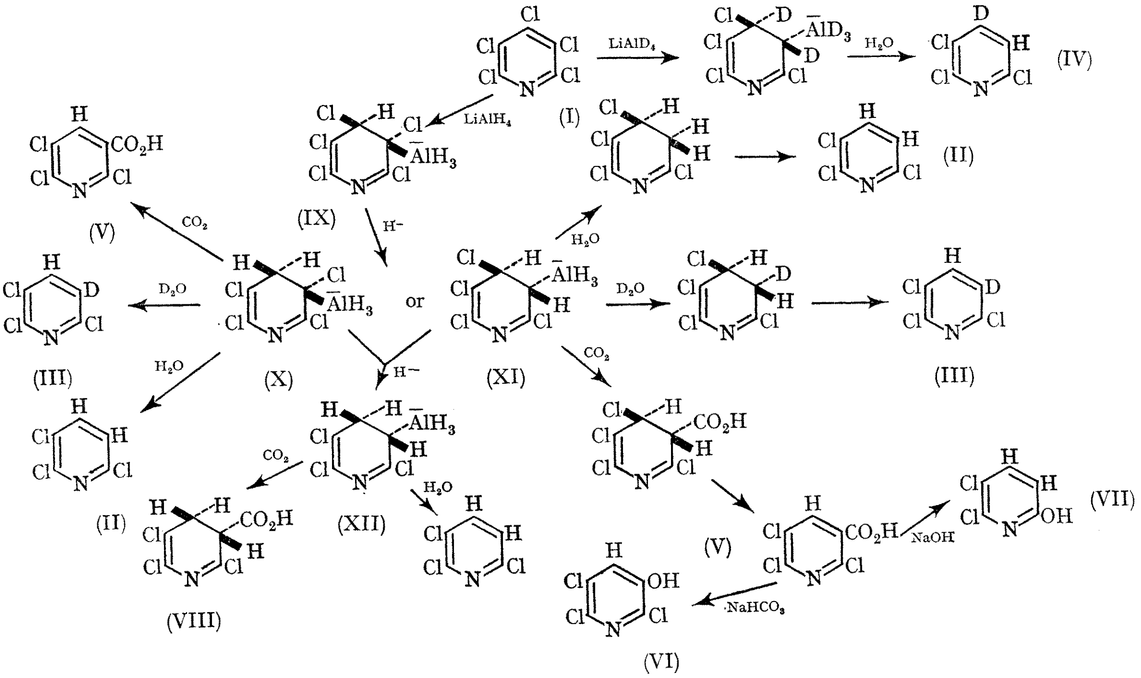
Similar reductions of 2,3,5,6-tetrachloropyridine or 4-deuterio-2,3,5,6-tetrachloropyridine, with $LiAlH_4$ led to a mixture of the 2,3,6- (75%) and the 2,3,5-trichloro-pyridine (25%) or the respective 4-deuterio-compound. Again, deuteriation studies confirmed that replacement of the 3-chlorine atom was not occurring *via* conventional hydride attack.

Whereas only the trichloropyridine (II) is obtained from pentachloropyridine (I) with $LiAlH_4$,the formation of both the 2,3,6- (II) and the 2,3,5-trichloro-pyridine from 2,3,5,6-tetrachloropyridine under the same conditions suggests that the reduction of (I) proceeds by a concerted attack on the 3- and the 4-positions rather than by two independent steps. Moreover, the absence of deuterium scrambling in these reactions precludes a pyridyne mechanism. Also an insertion–elimination scheme, such as that suggested by Burton and Mettille[6] to rationalize the $LiAlH_4$ reduction of various fluoro-olefins is accompanied by hydrogen evolution, unlike our reactions.

On the basis of our deuteriation experiments we suggested[5] an organometallic intermediate which would be expected to react with carbon dioxide. In fact, when the reaction mixture was poured on to solid CO_2, the crude product contained only a little trichloropyridine (II), but showed two strong resonances in the n.m.r. ($CDCl_3$), at τ 1·00 (extinguished by D_2O addition) and at τ 2·09, and a strong peak at 1700 cm.$^{-1}$ in the i.r. spectrum providing evidence for the presence of 2,3,6-trichloronicotinic acid (V). However, attempts to isolate the acid (V) by extraction with sodium hydrogen carbonate led to 2,3,6-trichloro-5-hydroxypyridine (VI) or to 2,3-dichloro-6-hydroxypyridine (VII) with 2N-sodium hydroxide. Similar results in the hydrolysis of polychloropyridine carboxylic acids have been noted previously.[7]

Another product which separated from the ether extract from the carbonation experiment on standing showed typical ABX splitting [$(CD_3)_2CO$] with no aromatic signals. Two complex bands, a quartet of lines at τ 4·75, 4·85, 4·94, 5·04, and a multiplet (τ 6·73—7·68) led us to assign the structure (VIII), confirmed by analysis. This compound is a rare example of a 3,4-dihydropyridine, which is presumably stabilized by the electron deficiency of the polychloro-ring. It is obviously formed by $LiAlH_4$ addition across the 3–4 bond. Only a few examples of $LiAlH_4$ addition across unconjugated olefins have been reported,[8] but many additions of substituted aluminium hydrides across both double and triple bonds yielding organo-aluminium intermediates have been observed.[9] Pyridine itself undergoes $LiAlH_4$ reduction to give 1,2-dihydro- or 1,4-dihydro-pyridine[10] and various pyridines with electron-withdrawing groups are similarly reduced,[11] but in all cases the products readily aromatize.

We consider that an organo-aluminium intermediate is involved in the reduction of (I) containing an AlH_3 group of which examples have been cited[12]—rather than a lithio-derivative of polychloropyridine which requires low temperature for its formation.[13] Thus on the basis of the described experimental evidence the reduction of pentachloropyridine (I) can be rationalized as set out (Scheme): *trans*-addition across the 3–4 bond which no doubt possesses a degree of olefinic character gives the aluminium-containing intermediate (IX) which at room temperature for 16 hr. suffers reduction of either the 'allylic' 4-, or 3-chlorine atom to give (X) or (XI) with inversion. Further reduction to give (XII) can also occur. Addition of H_2O, D_2O, or CO_2 causes replacement of the metal group as shown. This is followed by an unusual *cis*-elimination which aromatises the intermediate diene to yield the observed products (II) and (III). In support of our thesis an analogous case of *cis*-elimination observed by Tatlow and his co-workers in a polyfluorohexane is particularly relevant.[14]



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Moreover, various 4-substituted tetrachloropyridines ($4\text{-X-}C_5Cl_4N$; X = NHEt, $C_5H_{10}N$, OMe) were attacked by $LiAlH_4$ at the 3- or under more drastic conditions, the 3- and 4-positions. These results are equally well accommodated by analogy with the reaction scheme and will be reported in detail with others still under investigation. We also observed exclusive formation of 2,3,4,5-tetrachloropyridine by $LiAlH_4$ reduction of pentachloropyridine *N*-oxide[15] presumably by 1,2-addition.

We thank the S.R.C. for a studentship (S.M.R.) and a fellowship (F.B.).

(*Received, July 28th*, 1969; *Com.* 1143.)

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