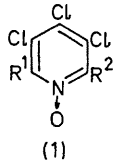
Grignard Reactions on Pentachloropyridine 1-Oxide

By FALMAI BINNS and H. SUSCHITZKY*
(*Department of Chemistry, University of Salford, Salford* M5 4WT)

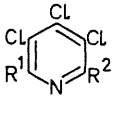
Summary Methylmagnesium iodide reacts readily with pentachloropyridine 1-oxide to give the corresponding 2- and 2,6-alkylated derivatives.

WHILE pentachloropyridine is not susceptible to attack by MeMgBr,[1] we find that its 1-oxide[2] readily reacts with MeMgI to afford a convenient route to the stable 2-methyl and 2,6-dimethylpolychloro 1-oxides. Since deoxygenation of these derivatives occurs easily with PCl_3, the 2- and 2,6-methylated-polychloropyridines become readily available. The tetrachloro-α-picoline has been made previously by Roedig from a polychlorocyclopentenone, using a three-step reaction sequence.[3]



(1)

a; $R^1 = R^2 = Cl$
b; $R^1 = Cl, R^2 = Me$
c; $R^1 = R^2 = Me$



(2)

a; $R^1 = Cl, R^2 = Me$
b; $R^1 = R^2 = Me$

For instance, treatment of pentachloropyridine 1-oxide (**1a**) in ether at room temperature with a 1 : 1 molar ratio of MeMgI gave 2-methyltetrachloropyridine 1-oxide (**1b**, *ca.* 40%) which was readily separable from the starting material. With an excess of Grignard reagent (2M) we obtain a mixture of 2,6-dimethyltrichloropyridine 1-oxide (**1c**, 29%), and the monomethyl derivative (**1b**, 37%). In both reactions very little (< 2%) deoxygenation of either the starting material or the product occurs. When the reactions were carried out in boiling ether, deoxygenation of the starting material became the main reaction and methylated 1-oxides comprised less than 10% of the overall product.

The methylpolychloropyridine 1-oxides were separated by column chromatography on silica (50 : 50 benzene : chloroform as eluant), and purified by sublimation *in vacuo*. 2-Methyltetrachloropyridine 1-oxide (**1b**) was characterized by its i.r. spectrum (a band at 1160 cm^{-1}; N → O), and n.m.r. spectrum [a sharp singlet at τ 7·25 (CH_3)]. In the mass spectrum, a low intensity parent ion at *m/e* 247 (4Cl) broke down readily to give a strong $(M - 16)^+$ ion, due to loss of oxygen, which is characteristic of an *N*-oxide system.[4] Deoxygenation by refluxing with PCl_3 in $CHCl_3$ solution gave 2-methyltetrachloropyridine (**2a**), m.p. 91—92° (*cf.* lit.[3] 93—94°). Its n.m.r. spectrum differed from that of the 4-isomer,[5] as it showed a sharp methyl singlet at τ 7·35, whereas the methyl signal from the 4-isomer appears upfield at τ 7·39. Both give parent ions at *m/e* 231 ($C_6H_3Cl_4N$) but the 2-Me isomer had peaks at *m/e* 195 and 196 due to loss of HCl ($M - 36$) and Cl ($M - 35$) respectively, in proportion approximately 1 : 2, whereas for the 4-methyl isomer the ($M - 35$) and ($M - 36$) peaks had equal intensity. We attribute the difference in the fragmentation pattern to the availability of the two adjacent chlorine atoms (3,5) to eliminate HCl with the 4-methyl group.

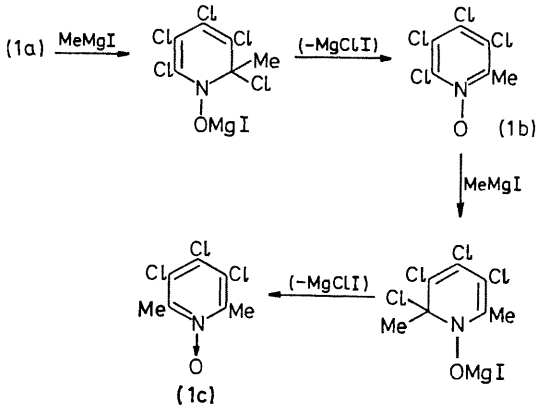
Structural assignment of the dimethyl derivative (**1c**) followed from its n.m.r. spectrum a singlet at τ 7·30 (CH_3). M.s. measurements showed a parent ion of low intensity

at *m/e* 227 (3Cl) losing oxygen to give an intense band at *m/e* 216. Deoxygenation gave 2,6-dimethyltrichloropyridine (**2b**) which gave a sharp methyl signal coincident with that of (**2a**) and a breakdown pattern in the m.s. in which the (M − 36) and (M − 35) peaks appeared in the ratio 1 : 4 respectively. These data are consistent with the 2,6-dimethyl structure, but would not be expected with the isomeric 2,4-dimethyl compound. Analyses for compounds (**1b** → **2b**) were satisfactory.

We rationalize the reaction with the Grignard reagent as shown in the Scheme. 1,3-Attack on the 1-oxide (**1a**) takes place with co-ordination of the Mg atom with the O atom, accompanied by nucleophilic attack of the methyl group at the electron-deficient 2-position.[2] Loss of MgClI gives the methyl compound (**1b**), which with an excess of Grignard reagent can undergo further methylation at the 6-position. The low yields in the dimethylation step may arise from deactivation towards further substitution by the presence of one methyl group.[6]

Grignard reactions for non-polychlorinated quinoline and pyridine 1-oxides have been interpreted similarly by Kato and his co-workers,[7] but the reactions we cite are the first involving replacement of chlorine rather than hydrogen in the 2-position.

We find that the reactions of the title compound with ethyl- and phenyl-magnesium bromide follow a similar pattern, about which we shall report later. Attempts to make the 1-oxide (**1a**) react with lithium-alkyls (Bu^{n}Li, MeLi, PhLi) under various conditions failed. Only starting material or intractable tars were isolated.[8]



SCHEME

We thank S.R.C. for a fellowship (F.B.) and Dr. B. J. Wakefield for valuable advice and discussion.

(*Received, May 4th*, 1970; *Com.* 661.)

[1] S. S. Dua and H. Gilman, *J. Organometallic Chem.*, 1968, **12**, 299.
[2] S. M. Roberts and H. Suschitzky, *Chem. Comm.*, 1967, 893.
[3] A. Roedig, K. Grohe, D. Klatt, and H. G. Kleppe, *Chem. Ber.*, 1966, **99**, 2813.
[4] T. A. Bryce and J. R. Maxwell, *Chem. Comm.*, 1965, 206.
[5] J. D. Cook and B. J. Wakefield, *J. Chem. Soc.* (*C*), 1969, 1973.
[6] T. Kato, H. Hayashi, and T. Anzai, *Chem. and Pharm. Bull.* (*Japan*), 1967, **15**, 1343.
[7] T. Kato and H. Yamanaka, *J. Org. Chem.*, 1965, **30**, 910; T. Kato, H. Yamanaka, and H. Hikichi, *Yakugaku Zasshi*, 1965, **85**, 33.
[8] D. J. Berry and B. J. Wakefield, personal communication.