REACTION OF HALOGEN WITH METAL SALTS OF PYRIDINECARBOXYLIC ACID —— DECARBOXYLATIVE IPSO-SUBSTITUTION

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Various metal salts (e.g., Hg(II), Tl(I), Tl(III), Na(I), Ag(I), and Pb(IV) salts) of pyridinecarboxylic acids have been prepared in high yields. When these salts were treated with iodine and bromine in nitrobenzene at 120-180°C for 2-17 h, only the Hg(II) and Tl(I) salts afforded monohalogenopyridines, which were formed by attack at the ipso position, without accompanying any of regioisomers and polyhalogenopyridines. For example, 3-iodo- and 3-bromopyridines were obtained from mercury(II) nicotinate in 48% and 27% yields respectively (at 180°C for 2 h) and 3-bromopyridine was formed in 8% yield from thallium(I) nicotinate at 160°C for 1 h.

In accordance with the above results halogenodecarboxylation of nicotinic acid using the free acid, mercury(II) oxide, and halogen was found to occur in nitrobenzene: 3-bromopyridine, 21% yield, at 165°C for 2 h; 3-iodopyridine, 42% yield, at 178°C for 2 h. Of the oxides that were tested as replacements for yellow or red mercury(II) oxide, only thallium(I) oxide showed a slight activity and others were proved to be ineffective: silver, copper, lead, cobalt, cadmium, and iron oxides.

The two conceivable reaction pathways for this decarboxylative ipso-substitution are as follows: (1) the acylhypohalite formation ($PyCO_2X$) and its radical decomposition, (2) the decomposition to pyridylmercury(II) compound followed by electrophilic substitution of mercury by halogen. Although the precise nature of the reaction is not yet known, we have not noticed any sign of a radical reaction (e.g., no product derived from 3-pyridyl radical) and have found that 3-pyridylmercury(II) chloride, prepared separately, reacted smoothly with iodine and bromine in nitrobenzene to give the corresponding 3-halogenopyridine (86% yield at 120-160°C for 2 h).