

## SYNTHESIS OF POLYHALOID PYRIDINE-CONTAINING PREDIOXINS

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### Introduction

Among the numerous studies of dioxins, the special class of heterocyclic compounds<sup>1)</sup>, there are few considering their chemistry. We believe new compounds possessing useful properties can be discovered amidst some dioxine derivatives, e.g. antidotes of toxic dioxins<sup>2)</sup> or model compounds for studying functions of dioxins in organisms<sup>3)</sup>. This is especially important now due to the danger of contamination of environment by dioxins because of numerous fires in Yugoslavia. Incomplete diaryl ethers, predioxins, are of interest as precursors of dioxins and their probable metabolites. The special attention should be paid to pyridine-containing polyhaloid predioxins as potentially promising compounds.

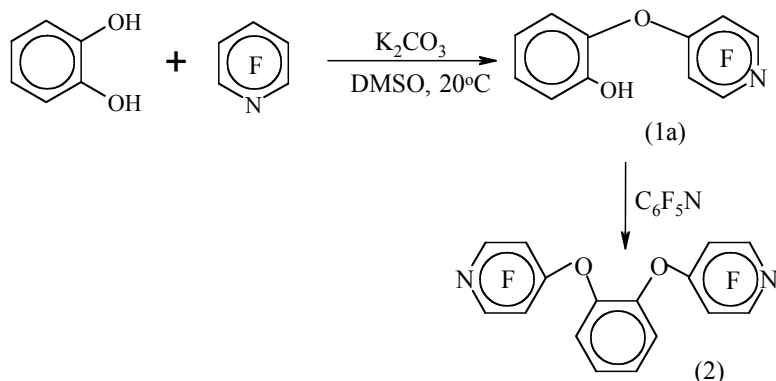
This work continues our earlier investigations<sup>4-6)</sup>.

### Materials and Methods

A mixture of substrate (2 g), nucleophile, and potash (molar ratio, 1:1:1.2) in 10 ml of water was stirred at 50-60°C during 3-5 hours. The reaction mixture was diluted by water; the products were extracted by chloroform and purified by recrystallization from carbon tetrachloride or ethanol or by distillation. The structure of compounds was proved by the element analysis and IR and <sup>1</sup>H, <sup>19</sup>F, and <sup>13</sup>C NMR-spectroscopy.

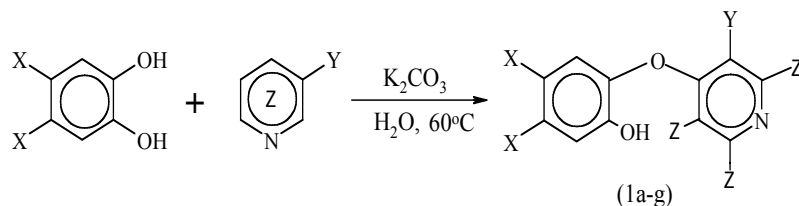
### Results and Discussion

The synthesis of incomplete ether (1a) is accompanied by the formation of an appreciable amount of complete ether (2) even if the excess of pyrocatechin is used.



It can be explained by the competition for the substrate between the more acidic hydroxy group of predioxin and those of pyrocatechin, despite essential steric hindrances exist in the predioxin

molecule due to the presence of the tetrafluoropyridine fragment. The use of a protic solvent, which can solvate anions stronger than aprotic DMSO, would stipulate the creation of additional steric hindrances in predioxins due to formation of solvating shell around the nucleophilic centers. Moreover, solvation of heteroatom would be a barrier to substitution of the most labile fluorine atoms in ortho position to nitrogen in the pyridine cycle. Indeed, the best results have been obtained when water was used as a solvent. The corresponding predioxins are formed with a high yield (65-80%) in the reactions of polyfluorinated pyridines with a small excess of pyrocatechin or its dihaloid derivative under moderate heating in water in the presence of potash.



- |      |         |         |        |
|------|---------|---------|--------|
| (1a) | X = H,  | Y = F,  | Z = F  |
| (1b) | X = H,  | Y = Cl, | Z = F  |
| (1c) | X = H,  | Y = Cl, | Z = Cl |
| (1d) | X = Cl, | Y = F,  | Z = F  |
| (1e) | X = Cl, | Y = Cl, | Z = F  |
| (1f) | X = Cl, | Y = Cl, | Z = Cl |
| (1g) | X = Br, | Y = Cl, | Z = F  |

Diaryl ethers are of interest for screening their numerous derivatives in order to find practically important products. Several easily modified centers in diaryl ethers (three labile fluorine atoms and the nucleophilic hydroxy group reveal inexhaustible possibilities for the selective modification of predioxins using aromatic and aliphatic substitution reactions.

### References

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