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PREPARATION AND NUCLEOPHILIC SUBSTITUTION OF HEXAFLUOROPHTHALAZINE

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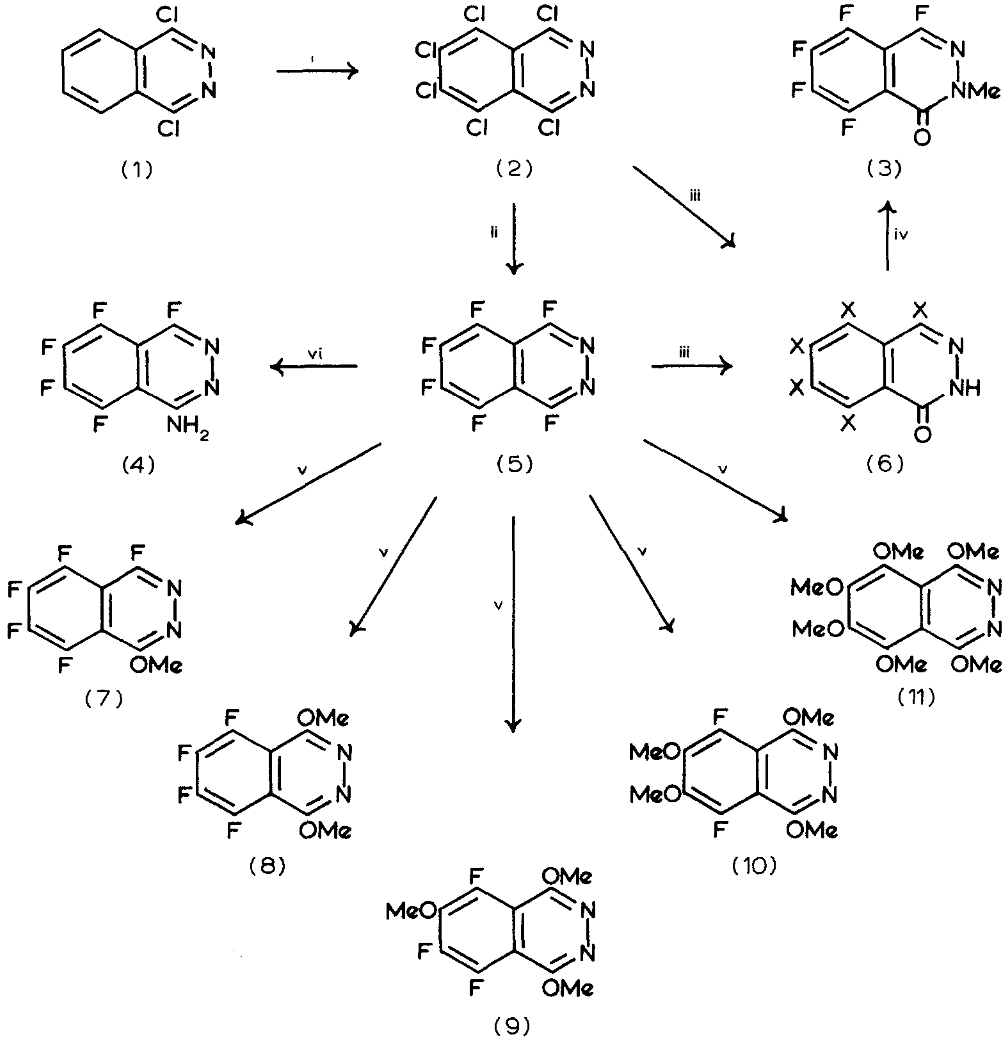
Summary: Hexafluorophthalazine, prepared by reaction between hexachlorophthalazine and potassium fluoride, is susceptible to nucleophilic attack under acidic or basic conditions, and all six fluorine atoms can be displaced by methoxide ion.

Current interest in perfluoro-aromatic heterocyclic compounds and the interesting properties of the tetrafluoro-1,2-diazine system[1,2] prompt us to report our preparation and preliminary studies of hexafluorophthalazine (5).

The known 1,4-dichlorophthalazine (1), readily available[3,4] from phthalic anhydride, was treated with chlorine in the presence of aluminium chloride at 200°, to give hexachlorophthalazine [(2); m.p. 194-195·5°, $\lambda_{max.}$ (cyclohexane) 253·5, 306, 315, 337 infl., and 349 infl. nm.]. Fluorination of hexachlorophthalazine (2) with potassium fluoride,[5] without a solvent, at 290° gave hexafluorophthalazine (5) in 60% yield; accurate temperature control of the nickel-lined autoclave was essential to avoid under-fluorination or extensive decomposition. Purified by vacuum sublimation, hexafluorophthalazine formed colourless plates, m.p. 91-93°, $\lambda_{max.}$ (cyclohexane) 249 infl., 259, 267 infl., 288 infl., 299·5, and 313 nm.

Hexafluorophthalazine (5) is rapidly hydrolysed by atmospheric moisture, or by adding water to its solution in sulphuric acid, to the 1-hydroxy-derivative. This derivative was shown to exist as the lactam tautomer [(6; X = F); m.p. 244-246°, $\lambda_{max.}$ (ethanol) 225, 257, 297, and 309 nm.], since its infrared and ultraviolet spectra are very similar to those of the N-methyl derivative [(3); m.p. 150-152°, $\lambda_{max.}$ (ethanol) 225·5, 259, 302 infl., and 313 nm.] which was the only product when the hydroxy-compound (6; X = F) was treated with ethereal diazomethane. The spectra of the corresponding O-methyl derivative (7), described below, differ markedly from those of the phthalazinones (3) and (6; X = F). Hexachlorophthalazine (2) is similarly susceptible to hydrolysis giving the corresponding pentachlorophthalazinone (6; X = Cl).



Reagents: i, Cl_2-$AlCl_3$; ii, KF; iii, H_2O-H_2SO_4; iv, CH_2N_2-Et_2O; v, NaOMe-MeOH; vi, NH_3 aq.-Me_2CO.

Nucleophilic attack on hexafluorophthalazine also occurred readily under basic conditions. Reaction with ammonia, at 0°, gave 1-amino-4,5,6,7,8-pentafluorophthalazine [(4); m.p. 159-165° (decomp.)], while methanolic sodium methoxide progressively replaced all six fluorine atoms, positions 1 and 4 being the most reactive and 5 and 8 the least. At -15° reaction with an appropriate molecular proportion of methanolic sodium methoxide gave the monomethoxy-derivative [(7); m.p. 67·5 - 69·5°, $\lambda_{max.}$ (ethanol) 270, 288·5 infl., 302·5 and 316 nm.], or the dimethoxy-derivative [(8); m.p. 155·5-157°]. At 0° the trimethoxy-derivative [(9); m.p. 142-143°] was obtained, while at 45° the tetramethoxy-compound [(10); m.p. 137-139°] resulted. Treatment with excess of the reagent, in a sealed tube at 85°, gave hexamethoxyphthalazine [(11); m.p. 104-106°].

The high reactivity of the fluorine atoms of the carbocyclic ring of hexafluorophthalazine provides an interesting contrast with hexafluoroquinoxaline,[6] where the carbocyclic fluorines are not replaced by methoxide below 65°.

The ^{19}F n.m.r. spectrum of hexafluorophthalazine (in acetone) shows complex bands centred at 81·5 p.p.m. (1,4-F), 140·7 p.p.m. (5,8-F), and 145·6 p.p.m. (6,7-F) upfield from external trichlorofluoromethane; the modulus of the peri-coupling constant, $|J_{1,8}|$, is 57 Hz, close to that observed in octafluoronaphthalene[7] and related heterocyclic compounds.[8] The structures of the four fluoro-methoxyphthalazines, like those of the hydroxy- and amino-derivatives, have been deduced from their ^{19}F n.m.r. spectra and each is supported by appropriate analytical and mass-spectroscopic data, which have also been obtained for hexafluoro-, hexachloro-, and hexamethoxy-phthalazine.

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