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PREPARATION AND NUCLEOPHILIC SUBSTITUTION OF HEXAFLUOROQUINAZOLINE.

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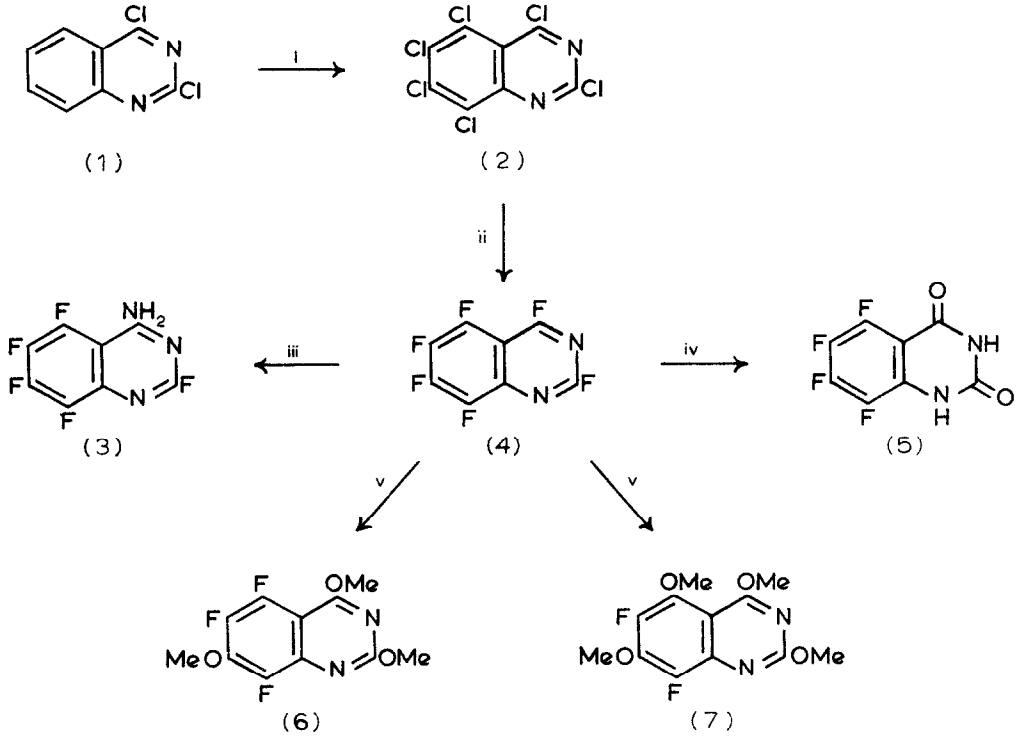
Summary: Reaction between hexachloroquinazoline and potassium fluoride gives hexafluoroquinazoline, which is readily susceptible to nucleophilic attack under either acidic or basic conditions.

Studies of perfluoroaromatic nitrogen heterocyclic compounds have proved interesting in connection with the mechanisms of nucleophilic aromatic substitution[1] and more recently with novel rearrangement reactions[2]; we now report the preliminary results of our extension of this work to the quinazoline system.

The known[3] dichloroquinazoline (1) was chlorinated under autogenous pressure with phosphorus pentachloride at 300° to give hexachloroquinazoline [(2); as primrose yellow prisms m.p. 163-166° (from benzene/cyclohexane), $\lambda_{max.}$ (ethanol) 245 infl, 253·5, 257, 291·5, 301·5, 315 infl, 329·5, 344, and 353 infl nm]. Fluorination of the hexachloro-compound (2) with anhydrous potassium fluoride at 350°, without solvent, gave hexafluoroquinazoline in good yield. Purified by distillation, hexafluoroquinazoline b.p. 84-87°/50 mm. formed colourless rods, m.p. 37-39°, $\lambda_{max.}$ (cyclohexane) 255·5, 263, 309, and 318 nm.

Hexafluoroquinazoline (4) is extremely susceptible to hydrolysis by atmospheric moisture giving the dihydroxy-derivative [(5); m.p. 320-323°, $\lambda_{max.}$ (ethanol) 240 infl, 267, and 311 nm.] whose i.r. and u.v. spectra are most consistent with the dicarbonyl tautomer (5). This dihydroxy-derivative was also obtained when water was added to a solution of hexafluoroquinazoline in sulphuric acid.

Hexafluoroquinazoline is also very readily attacked by nucleophilic reagents under basic conditions; it reacted violently with aqueous ammonia giving the 4-amino-derivative [(3); m.p. 238-240°, $\lambda_{max.}$ (ethanol) 224, 269, 277, 317·5, and 329 infl nm.].



Reagents: i, PCl_5; ii, KF; iii, NH_3aq.-Me_2CO; iv, H_2O-H_2SO_4; v, NaOMe-MeOH.

At 30° excess methanolic sodium methoxide reacted with hexafluoroquinazoline to give a trimethoxy-derivative [m.p. ca. 161°, indistinct owing to crystal structure changes, $\lambda_{max.}$ (ethanol) 236 and 317 nm.] whose ^{19}F n.m.r. spectrum is most consistent with the structure (6). At reflux temperature a fourth fluorine atom was slowly displaced by the same reagent to give a tetramethoxy-derivative [m.p. 144-146·5°, $\lambda_{max.}$ (ethanol) 238 and 321·5 nm.] to which the structure (7) has been assigned on the basis of its ^{19}F n.m.r. spectrum which showed absorption at +150 and +151·5 p.p.m. (from $CFCl_3$) $J_{FF} < 3Hz$.

The ^{19}F n.m.r. spectrum of hexafluoroquinazoline (in benzene) shows complex bands centred at 43·5 (2F), 47·7 (4F), 140·5 (5F), 144·2, 150·5, and 156·7 p.p.m. (upfield from $CFCl_3$). The modulus of the peri-coupling constant between the fluorine atoms at positions 4 and 5 is 50 Hz, similar to that observed in hexafluorophthalazine[4] and other systems related to perfluoronaphthalene.

Both hexachloro- and hexafluoroquinazoline display vivid blue fluorescence in u.v. light.

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