

A Novel Cyclisation Process involving Fluorine Displacement

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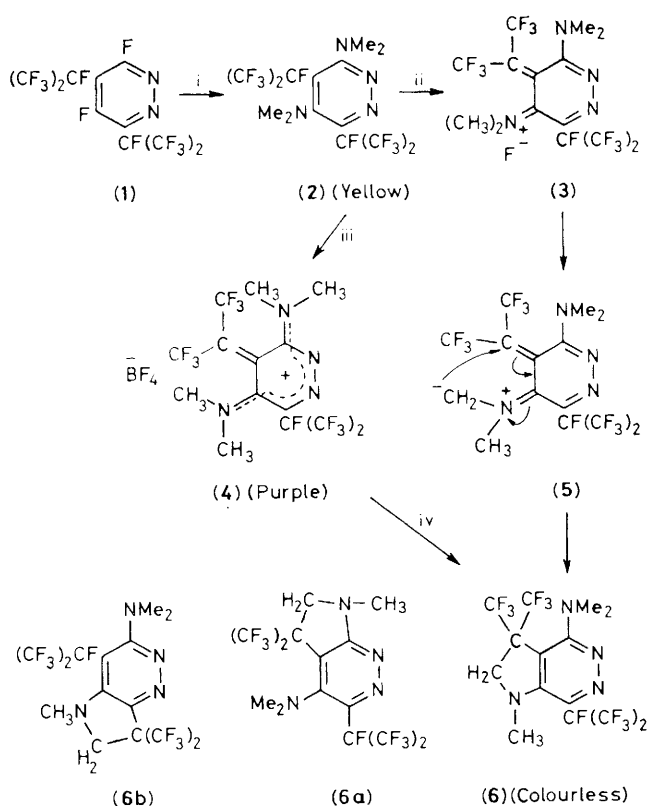
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Reaction of perfluoro-3,5-di-isopropylpyridazine with dimethylamine gives a bis(dimethylamino)-derivative which then undergoes cyclisation by a novel displacement of fluorine from a perfluoroisopropyl group.

In the course of our investigations concerning the chemistry of highly fluorinated pyridazine derivatives^{1,2} we have

observed the formation of an unusual bicyclic compound. 3,5-Bis-heptafluoroisopropyl-4,6-difluoropyridazine (1) was prepared from tetrafluoropyridazine by the method that we have already reported² and then treated with an excess of dimethylamine in dry dimethylformamide (DMF), at room

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Scheme 1. i, Me_2NH , DMF, room temp.; ii, standing, or on addition of H_2O ; iii, $\text{BF}_3 \cdot \text{Et}_2\text{O}$; iv, moist acetone.

temperature, to give yellow crystals of the dimethylamino-derivative (2) in 66% yield. Rather dramatically, the colour of compound (2), when set aside, changed to purple and then became colourless. We later established that this process is accelerated by adding water to the solution of (2) in DMF to give the colourless compound (6) in 90% yield.

The structure of (6) was established by elemental analysis, and mass and n.m.r. spectroscopy. The ^1H and ^{19}F n.m.r. spectra established that the product was one of the three possible cyclic structures (6), (6a), (6b). Furthermore, the existence of $\text{CH}_3\text{-F}$ coupling (J 8 Hz) between the methyl

group attached to the five-membered ring, and the 'tertiary' F atom of the remaining perfluoroisopropyl group, rules out (6a). To distinguish between (6) and (6b), we needed to establish the position of the perfluoroisopropyl group that had taken part in the cyclisation and this was achieved unambiguously by ^{13}C n.m.r. spectroscopy. We have used tetrafluoropyridazine, and perfluoro-4-, -4,5-di-, and -3,5-di-isopropylpyridazines as model compounds for ^{13}C n.m.r. studies and observed that a coupling between ring carbon and 'tertiary' fluorine atoms of 25–32 Hz is quite characteristic. Therefore, having established the assignment of resonances associated with ring-carbon atoms from the spectra of the model compounds loss of fluorine from the perfluoroisopropyl group at the 5-position is clear and this establishes (6) as the correct structure.

The formation of (6) involves a novel cyclisation process and we have outlined a mechanism in Scheme 1. Loss of the 'tertiary' fluorine (2) \rightarrow (3) is assisted by the addition of water and the observed purple stage is attributable to the formation of (3). Indeed, we have isolated a purple solid (87% yield) by adding boron trifluoride-diethyl ether to (2). This solid was identified as the tetrafluoroborate salt (4), by a combination of elemental analysis, mass spectrometry, ^1H and ^{19}F n.m.r. spectroscopy, and the conversion of (4) into the cyclic compound (6), by addition of moist acetone. The ^{19}F n.m.r. spectrum (CD_3COCD_3) indicated fluorine atoms in trifluoromethyl groups in the ratios 6:3:3 and the ^1H spectrum showed four non-equivalent methyl groups. These observations are accounted for by the planar configuration of the groups shown in structure (4) and the isolation of intermediate (4) is good confirmation of the mechanism proposed in the Scheme 1, *i.e.*, removal of a proton from (3), giving the ylide (5). This intermediate will cyclise very readily by nucleophilic attack on unsaturated carbon, which is activated by the two trifluoromethyl groups and also by the presence of positively charged nitrogen in the conjugated system.

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