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PRELIMINARY NOTE

Synthesis of Indolizines from Pyridinium (Trifluoroacetyl)methylide and Fluorinated Dipolarophiles

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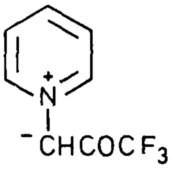
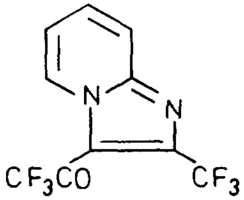
SUMMARY

Some new fluoroindolizines have been synthesised via 1,3-cycloaddition reactions between pyridinium (trifluoroacetyl)methylide (I) and fluorinated dipolarophiles [$CF_3C{\equiv}N \longrightarrow$ (II); $CF_3C{\equiv}CCF_3 \longrightarrow$ (III) (mainly) + (IV) and (V); $CF_3C{\equiv}CH \longrightarrow$ (VI); $CF_3CF{=}CF_2 \longrightarrow$ (VII)] and dimethyl acetylenedicarboxylate [$\longrightarrow$ (VIII)]. Treatment of (III) with base converted it to (IX).



(I)



(II)

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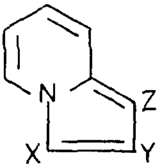
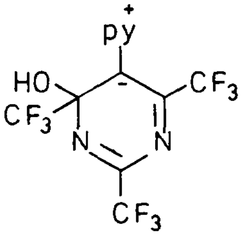


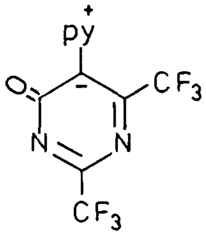
(III) X = $COCF_3$, Y = Z = CF_3
(IV) X = $COCF_3$, Y = CF_3, Z = H
(V) X = $COCHF_2$, Y = Z = CF_3
(VI) X = $COCF_3$, Y = H, Z= CF_3
(VII) X = $COCF_3$, Y = F, Z = CF_3
(VIII) X = $COCF_3$, Y = Z = CO_2Me
(IX) X = H , Y = Z = CF_3

The development recently [1] of a simple, though tedious, route to pyridinium (trifluoroacetyl)methylide (I) has enabled us for the first time to extend our pioneering studies [2,3] on the synthesis of fluorinated indolizines via 1,3-dipolar cycloaddition reactions to a dipole carrying a fluorinated substituent at the methylidic position.

Reactions between the isolable trifluoroacetylmethylide (I) and trifluoroacetonitrile, hexafluorobut-2-yne, 3,3,3-trifluoropropyne, hexafluoropropene and DMAD proceeded at room temperature in DMF to yield complex products from which the expected indolizines (1-azaindolizine in the case of CF_3CN) were isolated chromatographically in low yields [II (10%, m.p. 119-121 °C); III (20%, m.p. 50-52°C); VI (4%, m.p. 64-66°C); VII (10%, m.p.83-85 °C); and VIII (70%, m.p. 124-126°C), respectively].



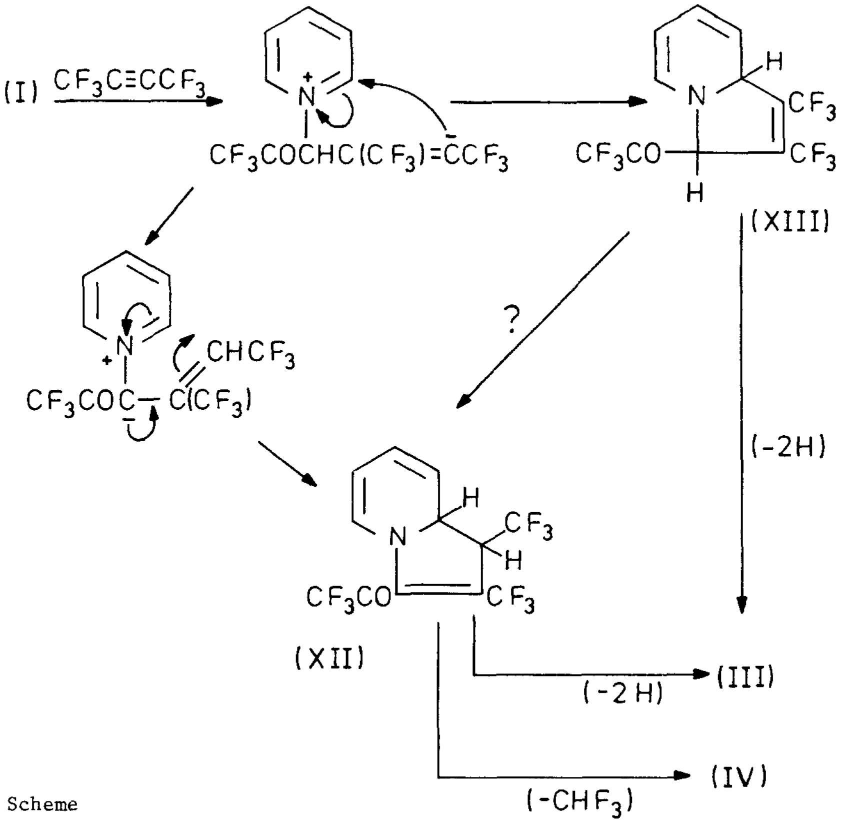
(X)



(XI)

In the case of the reaction involving trifluoroacetonitrile, a product believed to be the pyridinium methylide (X) was also isolated (6% yield, m.p. 183-185°C); this again was not unexpected in view of the production of the analogue (XI) from pyridinium (t-butoxycarbonyl)methylide and CF_3CN [3].

Not anticipated, however, was the formation of by-products (IV; 4%) and (V; 3%) in the cycloaddition involving hexafluorobut-2-yne. The incursion of a 1,5-dipolar cyclization (see the Scheme) is thought to be the source of the former indolizine; discussion of possible routes to the difluoroacetyl compound (V) is deferred to a full paper. Neither the dihydroindolizine (XII) postulated to be involved in the formation of 3-trifluoroacetyl-2-trifluoromethylindolizine (IV), nor any of its analogues (e.*g*. XIII) presumably [cf. 2,4] involved in the 1,3-cycloadditions reported here were isolated.



Scheme

Treatment of the major product (III) from the reaction of pyridinium (trifluoroacetyl)methylide with hexafluorobut-2-yne with hot alcoholic aqueous sodium hydroxide gave 1,2-bis(trifluoromethyl)indolizine (IX; m.p. 44-46 °C) in 58% yield (after recrystallization).

All the new compounds (II-X) claimed here possessed correct elemental compositions (C, H, N) and spectroscopic properties [IR, NMR (^1H, ^{19}F, ^{13}C) and mass] consistent with the structures assigned.

1 H. Wittmann, E. Ziegler, K. Peters, E. M. Peters, and H. G. von Schnering, Monatsh. Chem., 114 (1983) 1097.

2 R. E. Banks and J. Thomson, J. Chem. Res. (S), (1985) 33; *ibid.* (M), 0671-0689.

3 R. E. Banks and J. Thomson, J. Fluorine Chem., 22 (1983) 589; *idem*, J. Chem. Soc., Perkin Trans. I, in the press.

4 R. E. Banks and S. M. Hitchen, J. Fluorine Chem., 20 (1982) 373.