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PRELIMINARY NOTE

Reactions of Pyridinium t-Butoxycarbonylmethylide with Perfluoropropene and Some Fluoroaromatics

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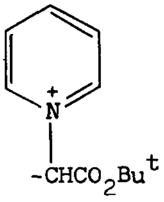
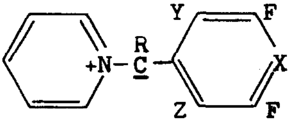
SUMMARY



(I)



R = CO_2Bu^t

(II) X = CCF_3, Y = Z = F

(III) X = N, Y = Z = F

(IV) X = N, Y = Cl, Z = F

(V) X = N, Y = Z = Cl

Perfluorotoluene, pentafluoropyridine, 3-chlorotetrafluoropyridine, and 3,5-dichlorotrifluoropyridine react with pyridinium t-butoxycarbonylmethylide (I) in acetonitrile at 0 — 20 °C to yield, <u>via</u> nucleophilic displacement of a 4-F substituent in each case, the new pyridinium methylides (II)-(V), respectively. Treatment of perfluoropropene with (I) gives 1-(t-butoxycarbonyl)-2-fluoro-3-(trifluoromethyl)-pyrrolo[1,2-<u>a</u>]pyridine (VI) and 1,3-bis(t-butoxycarbonyl)-2-(1,2,2,2-tetrafluoroethyl)pyrrolo[1,2-<u>a</u>]pyridine (VII),

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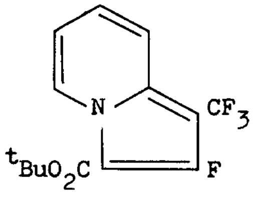
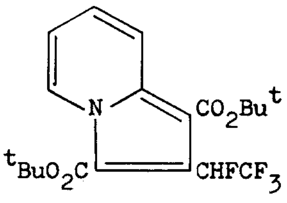
formation of the latter (minor) product providing evidence that the former arises *via* a stepwise dipolar cycloaddition.


(VI)


(VII)

Our long-standing curiosity about possible synthetic applications of reactions between potential dipolarophiles of the fluorocarbon class and heteroaromatic *N*-oxides, *N*-imines and *N*-ylides is currently being satisfied as far as the last type of 1,3-dipole is concerned[**] through studies involving pyridinium t-butoxycarbonylmethylide (I). This ylide was chosen rather than pyridinium methylide itself because it is relatively easy to generate{*via* addition of sodium hydride to *N*–t -butoxycarbonylmethylpyridinium perchlorate [from C_5H_5N + $CH_2ClCO_2Bu^t \longrightarrow C_5H_5\overset{+}{N}CH_2CO_2Bu^t\ Cl^- \longrightarrow$ (with $NaClO_4$) $C_5H_5\overset{+}{N}CH_2CO_2Bu^t\ ClO_4^-$] in acetonitrile under strictly anhydrous conditions [3]} , successful replacement of t-butoxycarbonyl groups by hydrogen in products afforded by trapping reactions can be envisaged {through pyrolysis or protonolysis–pyrolysis [RCO_2Bu^t + Δ or $H^+ \longrightarrow CH_2{=}CMe_2$ + $RCO_2H \longrightarrow$ (with Δ) RH + CO_2]} , and - like *N*-iminopyridinium ylide [2] - it is powerful enough as a nucleophile to displace fluorine from pentafluoropyridine and related substrates under mild conditions (see the Summary). At the

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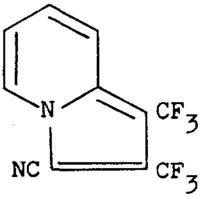
[**] See references 1 and 2 for information about our work with pyridine *N*-oxides and *N*-iminopyridinium ylide,respectively.

outset, no reports on reactions between N-heteroaromatic methylides and fluorocarbon substrates could be found in the open literature except for a claim [4]† that pyridinium dicyanomethylide in acetonitrile attacks perfluorobut-2-yne at room temperature to yield the indolizine (VIII).



(VIII)

Flash-chromatographic [7] work-up of the product procured by treating at room temperature an excess of perfluoropropene (25 mmol) with pre-formed pyridinium t-butoxycarbonylmethylide (I) [from $C_5H_5\overset{+}{N}CH_2CO_2Bu^t$ ClO_4^- (20 mmol) + NaH (20 mmol) in MeCN (100 cm^3 at 5 °C)] in acetonitrile containing anhydrous potassium carbonate [40 mmol as a 'sink' for HF (see Scheme 1)], provided*** the new indolizines 1-(t-butoxycarbonyl)-2-fluoro-3-(trifluoromethyl)pyrrolo[1,2-*a*]pyridine (VI) and 1,3-bis(t-butoxycarbonyl)-2-(1,2,2,2-tetrafluoroethyl)pyrrolo[1,2-*a*]-pyridine (VII) in 37 (after sublimation at *ca.* 60 °C *in vacuo*) and 2% yield (after recrystallization from aqueous ethanol), respectively. This result is noteworthy on two counts: (i) it should stimulate work on the synthesis and applications of fluorinated indolizines; and (ii) it provides

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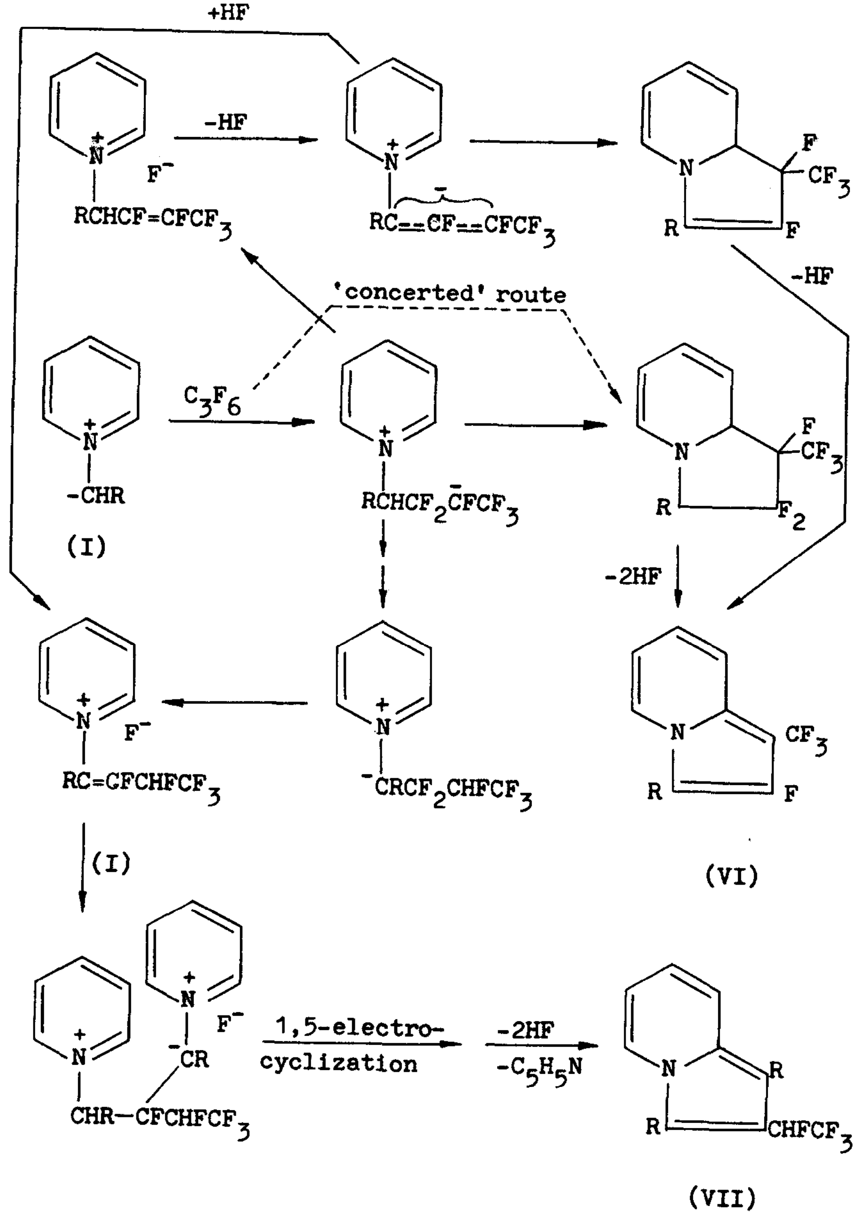
† Since this was mentioned in neither the relevant abstract [Chem. Abs., 77 (1972) 139776r] nor a recent review [5] devoted to construction of the indolizine nucleus, we remained unaware of it until J.T. [6] carried out a detailed literature search.

*** Several other (at least 2 by t.l.c.) minor products (coloured) and a red residue have not yet been identified owing to separation problems.



Scheme 1 ($R=CO_2Bu^t$)

evidence for the occurrence of a stepwise mechanism (see Scheme **1**). Regarding the latter point, even if the minor product (VII) had not been found, several factors (notably the nucleophilicity of pyridinium t-butoxycarbonylmethylide, the susceptibility of perfluoropropene towards anionic attack, the polarity of acetonitrile, and some results achieved using hydrocarbon coupling partners for methylides [8]) would have tempted us to favour a stepwise vis-à-vis a concerted 1,3-cycloaddition (Scheme **1**) for construction of the indolizine skeleton present in 1-(t-butoxycarbonyl)-2-fluoro-3-(trifluoromethyl)pyrrolo[1,2-_a_]pyridine (VI).

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1 R.E. Banks, R.N. Haszeldine, and J.M. Robinson, J. Chem. Soc., Perkin Trans. I, (1976) 1226; J.M. Robinson, Ph.D. Thesis, University of Manchester, 1974.

2 (a) R.E. Banks and S.M. Hitchen, J. Fluorine Chem., _12_ (1978) 159; (b) _idem_, _ibid_., _15_ (1980) 179; (c) S.M. Hitchen, Ph.D. Thesis, University of Manchester, 1980.

3 J.B. Bapat, J. Epsztajn, A.R. Katritzky, and B. Plau, J. Chem. Soc., Perkin Trans I,(1977) 1692.

4 T.Kutsuma, K. Fujiyama, Y. Sekine, and Y. Kobayashi, Chem. Pharm. Bull., _20_ (1972) 1558.

5 T. Uchida and K. Matsumoto, Synthesis (1976) 209 {the earlier review on indolizines by N.S. Prostakov and O.B. Baktibaev [Russ. Chem. Rev., _44_ (1975) 748] does not mention the work either} .

6 J. Thomson, M.Sc. Qualifying Report, UMIST, July 1981.

7 W.C. Still, M. Kahn, and A. Mitra, J. Org.Chem., _43_ (1978) 2923.

8 See, for example, I. Zugrăvescu and M. Petrovanu, '_N_-Ylid Chemistry', McGraw-Hill : New York, 1976; and Y. Tamura, Y. Sumida, S. Haruki, and M. Ikeda, J. Chem. Soc., Perkin Trans. I, (1975) 575.