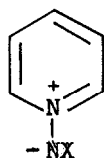FLUOROCARBON DERIVATIVES OF NITROGEN. PART VII [1]. REACTION OF N-IMINOPYRIDINIUM YLIDE WITH PERFLUORO-1-AZACYCLOHEXENE, PERFLUORO-2-AZAPROPENE, AND PERFLUOROACETONITRILE

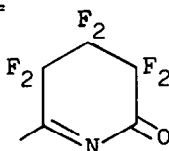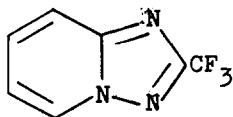RONALD E.BANKS* and STEPHEN M.HITCHEN

Chemistry Department, The University of Manchester Institute of Science and Technology, Manchester M60 1QD (Great Britain)
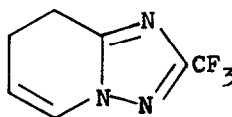
SUMMARY

(I) X = H (NIPY)

(II) X =

(III) X = CF=NCF$_3$

(IV)

(V)

The novel ylides (II) and (III) have been obtained via treatment of perfluoro-1-azacyclohexene and perfluoro-2-aza-propene, respectively, with N-iminopyridinium ylide (I) generated in situ from N-aminopyridinium iodide and anhydrous potassium carbonate in methylene chloride. A mixture of the s-triazolo[1,5-a]pyridine (IV) and a compound thought to be
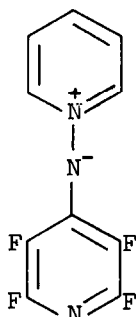
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*To whom enquiries should be addressed.

its dihydro-analogue (V) were isolated following attack on perfluoroacetonitrile by the parent ylide (I); the former product was also prepared by heating 1,2-diamino-pyridinium iodide with trifluoroacetic anhydride.
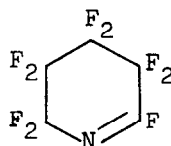
INTRODUCTION
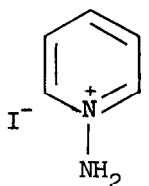
(VI) NAPI

(VII)

(VIII)

Addition of activated (in the S_NAr sense) fluoroaromatics to freshly-prepared [from N-aminopyridinium iodide (VI;NAPI) plus KOH aq. or K_2CO_3 in EtOH or DMF] purplish-blue solutions of N-iminopyridinium ylide (I; NIPY) was found previously [2] to lead to the formation of the corresponding N-arylimino-pyridinium ylides [e.g. (I) + $C_5F_5N \longrightarrow$ (VII)]. This prompted us to examine the action of NIPY on perfluoro-1-aza-cyclohexene (VIII), a substrate well known to undergo Ad_N-E reactions with more conventional nucleophiles [3].
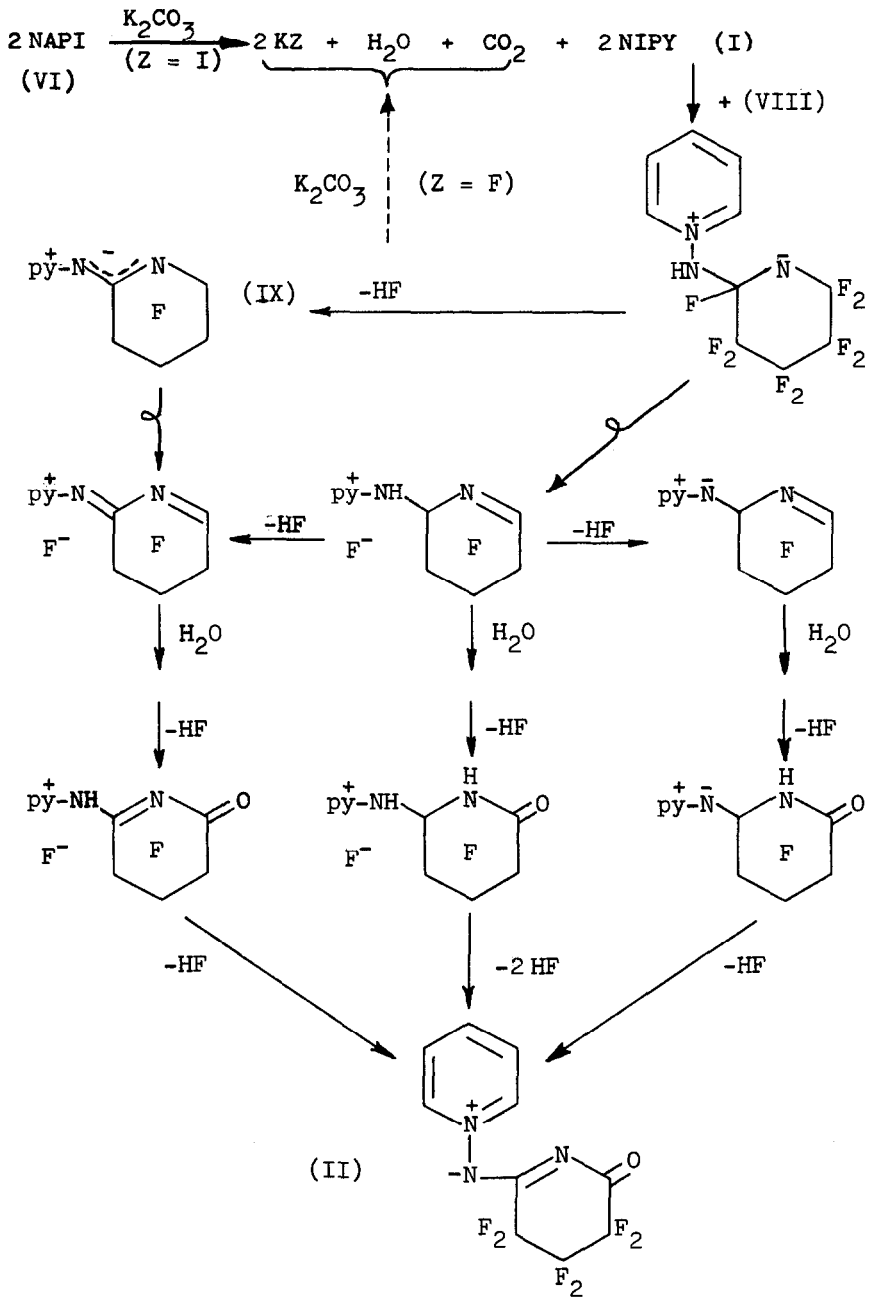
RESULTS AND DISCUSSION

'Flash' chromatographic [4] purification on silica of the crude product isolated after stirring a mixture of NAPI (VI), anhydrous potassium carbonate, perfluoro-1-azacyclohexene [molar ratio(VIII):(VI) = 1:1], and methylene chloride for

7 days[*] at 20 °C in glass provided N̲-(4,4,5,5,6,6-hexafluoro-3-
oxo-2-azacyclohex-1-enyl)iminopyridinium ylide (II) in 65%
yield; in a similar experiment, carried out for 8 days with no
potassium carbonate present to effect deprotonation of the NAPI
[5], the latter was recovered in > 80% yield and the
unidentified fluorine-containing product neither contained the
substituted ylide (II) nor was converted into that product on
treatment with traces of water. As expected, therefore,
formation of product (II) requires liberation of NIPY (I) which
could trigger off quite a complex set of events (see Scheme 1).
The logical 'initial' product, N̲-(octafluoro-2-azacyclohex-1-
enyl)iminopyridinium ylide (IX), would clearly enjoy ample
opportunity to rearrange then suffer replacement of fluorine by
hydroxyl both during the reaction period and at the work-up stage;
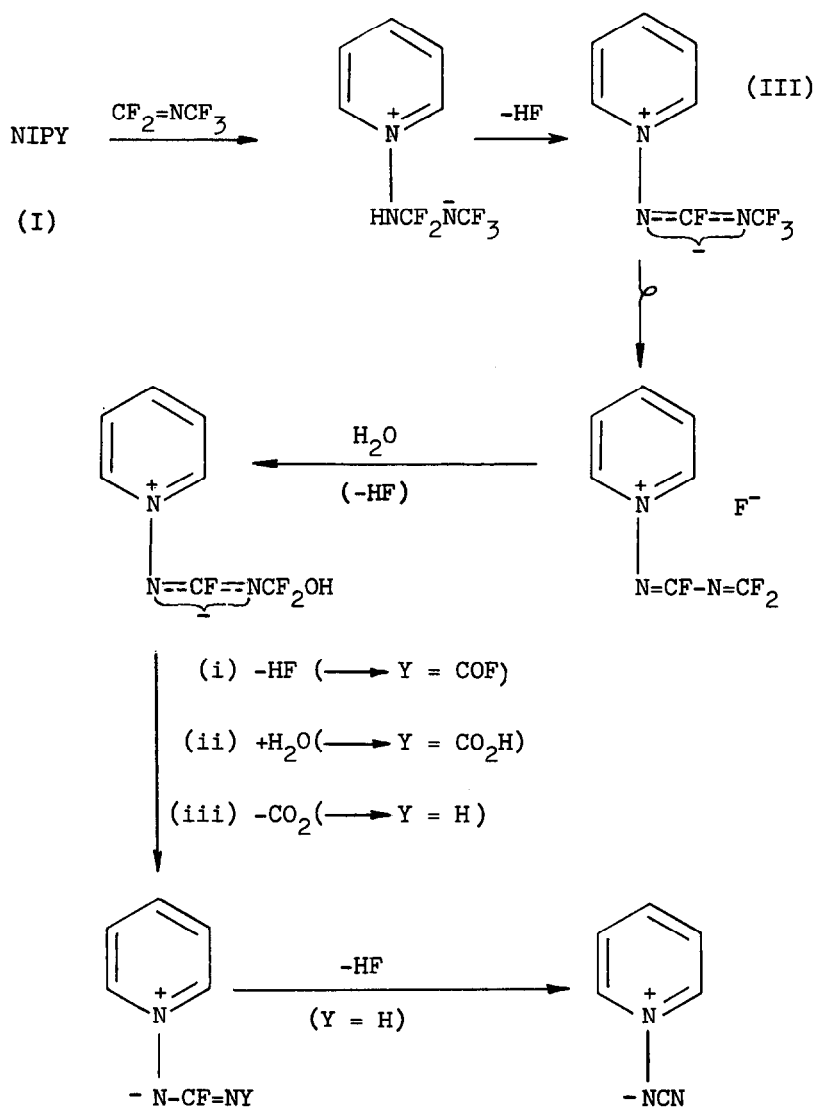the alternative pathways to (II) involve similar chemistry.

     In keeping with these ideas, treatment of perfluoro-2-aza-
propene, an acyclic analogue of (VIII), with NIPY (I) gave
traces of material possessing spectroscopic properties
consistent with N̲-(tetrafluoro-2-azaprop-1-enyl)imino-
pyridinium ylide (III) [≡(IX)] plus the known [6] N̲-cyano-
iminopyridinium ylide (34%). This result can be rationalized
as shown in Scheme 2.

     Not unexpectedly, since it contains no imidoyl fluorine
and its hydrocarbon analogue is known [7] to partake in a 1,3-
dipolar cycloaddition with NIPY [——► (X)], perfluoro-
acetonitrile reacted with NAPI in the presence of potassium
carbonate to yield 2-trifluoromethyl-s̲-triazolo[1,5-a̲]pyridine
(IV). However, this product was accompanied by an inseparable

---

[*]This was an excessive period: the purple colour associated
with NIPY had disappeared by the time the reaction mixture had
reached room temperature from -196 °C, the liquid phase turning
yellow and eventually brown.

$$2\ \text{NAPI} \xrightarrow[\text{(Z = I)}]{K_2CO_3} 2\ \text{KZ} + H_2O + CO_2 + 2\ \text{NIPY} \quad (\text{I})$$

(VI)

$+ (\text{VIII})$

$K_2CO_3 \quad (\text{Z = F})$

$py-N=N$ (IX) $-HF$

HN

F

$py-N=N$ F^- F $-HF$ $py-NH\quad N$ F^- F $-HF$ $py-\bar{N}\quad N$ F

H_2O H_2O H_2O

$-HF$ $-HF$ $-HF$

$py-NH\quad N \quad O$ F^- F

$py-NH\quad \overset{H}{N}\quad O$ F^- F

$py-\bar{N}\quad \overset{H}{N}\quad O$ F

$-HF$ $-2\ HF$ $-HF$

(II) $-N\quad N \quad O$

$F_2 \quad F_2$

F_2

Scheme 1

NIPY $\xrightarrow{\text{CF}_2=\text{NCF}_3}$

(I)

$\text{HNCF}_2\bar{\text{N}}\text{CF}_3$

$\xrightarrow{-\text{HF}}$ (III)

$\text{N}{=\!\!=}\text{CF}{=\!\!=}\text{NCF}_3$

$\text{N}=\text{CF}-\text{N}=\text{CF}_2$ F^-

$\xleftarrow[(-\text{HF})]{\text{H}_2\text{O}}$

$\text{N}{=\!\!=}\text{CF}{=\!\!=}\text{NCF}_2\text{OH}$

(i) $-\text{HF}$ ($\longrightarrow$ Y = COF)

(ii) $+\text{H}_2\text{O}$ ($\longrightarrow$ Y = CO$_2$H)

(iii) $-\text{CO}_2$ ($\longrightarrow$ Y = H)

$-\text{N}-\text{CF}=\text{NY}$

$\xrightarrow[(\text{Y = H})]{-\text{HF}}$

$-\text{NCN}$

Scheme 2

dihydro-derivative which, on the basis of [1]H n.m.r. analysis of
the mixture, is thought to possess either structure (V) or
(XI), with the former preferred. The structure of the major
product (IV) is not in doubt because the same compound was
obtained via treatment of 1,2-diaminopyridinium iodide
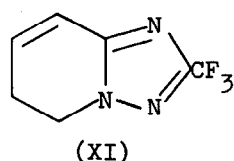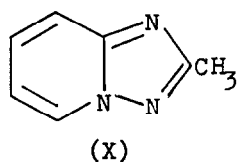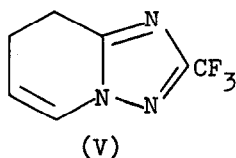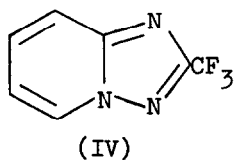with trifluoroacetic anhydride [cf. 7,8].

(IV) (V) (X)

(XI) (XII) (XIII)

(XIV) (XV) (XVI)
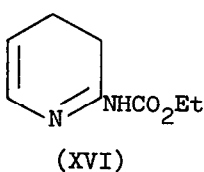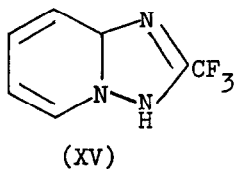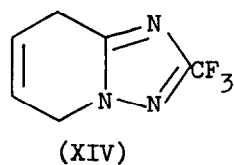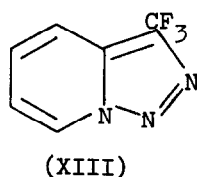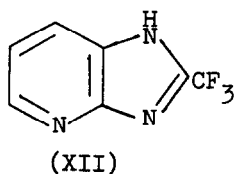
The white crystalline NIPY-CF$_3$CN reaction product
isolated initially by conventional column chromatography was
shown by elemental analysis, mass spectrometry, and [19]F n.m.r.
spectroscopy (the spectrum comprised two singlets at 13.5 and
13.2 p.p.m. to low field of external TFA)to be a 3:1 mixture of
compounds possessing molecular formulae C$_7$H$_4$F$_3$N$_3$ and C$_7$H$_6$F$_3$N$_3$,
respectively. Attempts to effect even partial separation of
these components by fractional sublimation having failed, the
problem was set aside after synthesis of an authentic specimen
of 2-trifluoromethyl-s-triazolo[1,5-a]pyridine (IV) (see
above) had enabled the major component of the mixture to be
identified. The [1]H n.m.r. spectrum of the 3:1 mixture showed
nondescript absorptions in the δ (TMS) region 2.47-7.04 p.p.m.
plus a clear indolizine pattern caused by (IV). As expected,

the [1]H n.m.r. spectrum of the trifluoromethyl compound (IV)
closely resembled that of its methyl analogue (X), a sample of
which was prepared from NIPY and acetonitrile [7] for
comparison purposes.

Subsequently, the advent of 'flash' column chromatography
[4] enabled the 3:1 mixture of (IV) and its dihydro-derivative
(δ_{CF_3} + 13.2 p.p.m.) to be enriched in the latter. The
new mixture (ca. 2:1) gave a much more satisfactory [1]H n.m.r.
spectrum, analysis of which, together with the availability of
an authentic sample of the fluoromidine analogue (XII), finally
dispelled any remaining doubts surrounding the deduction made
from the mass spectral data [the enriched mixture showed
intense peaks corresponding to $\underline{M}^+$ for (IV) and (V) or (XI) of
relative intensities 100 and 41%, respectively] and elemental
analysis that the minor component was a'dihydro-derivative'
and not the regioisomer (XIII) of the major product (IV) or
the other plausible alternative (XII). The n.m.r. spectral
pattern assignable to the minor component comprised 4
absorption systems at 2.47-2.75 (complex multiplet), 3.16
(br.t), 5.79 (dt, $\underline{J}_{CH,CH}$ 8.0 Hz), and 7.04 (dt) p.p.m. of
relative intensities 2:2:1:1, which is consistent with the
presence of a $CH_2CH_2CH=CH$ moiety as in structures (V) and (XI),
thus eliminating the other two possible dihydro-derivatives of
(IV), (XIV) and (XV) (see Scheme 3). Although an absolute
choice between structures (V) and (XI) still cannot be made,
the former is favoured by the [1]H n.m.r. data, which closely
resemble those for other 3,4-dihydropyridine derivatives [9],
e.g. (XVI).

The two possible modes of formation of 2-trifluoromethyl-
s-triazolo[1,5-a]pyridine (IV) from NIPY and perfluoroaceto-
nitrile are outlined in Scheme 3. Nothing concrete can be
said about the mechanism of either the cycloaddition or the
aromatization step. Regarding the latter, previous workers
[7], using hydrocarbon nitriles as dipolarophiles, failed to
isolate dihydro-intermediates of type (XV) and suspected that
a dimer of NIPY acted as a hydrogen acceptor; and in related
studies aimed at the synthesis of indolizines, i.e. pyrrolo-
[1,2-a]pyridines, from pyridinium ylides and acetylenes, the

dipolarophiles have been observed to act as hydrogen acceptors [10]. We made no attempt to determine if the excess of perfluoroacetonitrile used in the reaction with NIPY had acted as a dehydrogenating agent. Starting from the initial NIPY-CF$_3$CN cycloadduct (XV), plausible mechanisms can be written [11] to account for the formation of each of the dihydro-derivatives (V) and (XI) [and, incidentally, of a product possessing structure (XII)].
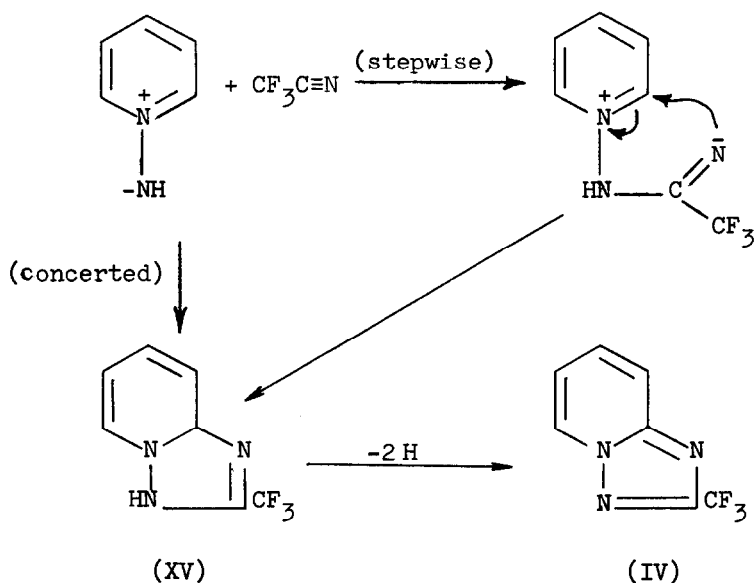
Scheme 3

EXPERIMENTAL

Spectroscopic Analysis

I.r. and mass spectra were obtained with Perkin-Elmer 197 or 720 spectrophotometers and AEI MS902 or Kratos MS45 spectrometers (electron beam energies 70 eV), respectively. N.m.r. analyses were carried on with Perkin-Elmer (R32; ^{1}H at 90, ^{19}F at 84.6 MHz) and Bruker (WP80; ^{13}C at 20.1 MHz) instruments; unless stated otherwise, p-C$_6$H$_4$Cl$_2$ (ext., ^{1}H),

CF_3CO_2H (ext., ^{19}F), and $(CD_3)_2CO$ {int.(solvent and 'lock'), ^{13}C; shifts computed relative to Me_4Si by addition of 29.2 p.p.m. [$(^{13}CD)_3CO$]} were employed as references.

Starting Materials

These were prepared by procedures described in the references quoted in the text.

Reactions of N-Iminopyridinium Ylide (NIPY) (I)

(a) With perfluoro-1-azacyclohexene (VIII)

Perfluoro-1-azacyclohexene (4.9 g, 20 mmol) [12] was condensed, in vacuo, into a cold (-196 °C) Pyrex tube (450 cm^3) equipped with a Rotaflo PTFE-glass valve and containing a PTFE-coated magnetic stirrer follower plus a degassed mixture of dichloromethane (100 cm^3), anhydrous powdered potassium carbonate (8 g), and N-aminopyridinium iodide (NAPI) (4.44g, 20.0 mmol) [13]. After the tube had been sealed and allowed to warm to room temperature, the stirrer was activated and kept so for 7 days. The product was filtered and the precipitate was washed with dichloromethane (3 x 25 cm^3). The brown residue obtained by evaporation of the filtrate plus washings under reduced pressure was dissolved in acetone and 'flash' [4] chromatographed [silica (30 x 6 cm.); Me_2CO] to provide a cream solid (4.3 g) which was recrystallized from ethanol-water (1:2 v/v) to give N-(4,4,5,5,6,6-hexafluoro-3-oxo-2-azacyclo-hex-1-enyl)iminopyridinium ylide (II) (nc) (3.9 g, 13 mmol, 65%) [Found: C, 40.7; H, 1.5; F, 38.9; N, 14.3%; M (mass spec.), 297. $C_{10}H_5N_3F_6O$ requires C, 40.4; H, 1.7; F, 38.4; N, 14.1%; M, 297], white needles, m.p. 182-183 °C, $\lambda_{max.}$ (mull) 5.97s(br., C=O and C=N str.) μm, m/e 297 ($M^{\dagger}$, top mass peak; 1%), 79 ($C_5H_5N^{\dagger}$, 100%), δ_H [30% soln. in $(CD_3)_2CO$] + 1.02 (2-,6-H, br. m), + 0.69 [4-H, tt (7.5, 1.5 Hz)], + 0.32 (3-,5-H, m) p.p.m. (rel. int. 2:1:2), δ_F (same soln.) -42.8 (4-,4- or 6-,6-F, m), -43.9 (6-,6- or 4-,4-F, m), and -59.2 (5-,5-F,9 Hz quintet) p.p.m. (rel. int. 1:1:1), and δ_C [40% soln in $(CD_3)_2CO$] + 163.2 (C-1' or C-3', t; $^2J_{CF}$ 22 Hz), + 161.05 (C-3' or C-1', t; $^2J_{CF}$ 18 Hz), + 143.1 (C-4,s),

+ 142.9 (C-2, -6,s), + 128.2 (C-3, -5,s), + 109.6 (C-5', t of
quintets; $^1\underline{J}_{CF}$ 263, $^2\underline{J}_{CF}$ 25.7 Hz), + 108.3 (C-4' or C-6', tt;
$^1\underline{J}_{CF}$ 269, $^2\underline{J}_{CF}$ 25.0 Hz), + 105.2 (C-6' or C-4', tt; $^1\underline{J}_{CF}$ 266,
$^2\underline{J}_{CF}$ 25.0 Hz) p.p.m. Gaseous material recovered from the
reaction vessel proved (i.r.) to be carbon dioxide.

(b) With perfluoro-2-azapropene

Evaporation under reduced pressure of dichloromethane
from the liquid product obtained by substituting perfluoro-2-
azapropene (3.33 g, 25.0 mmol) [14] for perfluoro-1-azacyclo-
hexene in experiment (a) (but with a 5-day reaction period)
above left a dark red tar in which were embedded pale yellow
crystals. Spectroscopic examination of a small sample of the
crystalline material indicated that it was N-(tetrafluoro-2-
azaprop-1-enyl)iminopyridinium ylide (III) (nc) {m/e 207
$[C_7H_5F_4N_3^{+}$ ($\underline{M}^{+}$), 8%], 188 ($\underline{M}^{+}$ -F·, 6%), 90 ($C_2F_2N_2^{+}$, 26.5%),
79 ($C_5H_5N^{+}$, 100%); δ_F (20% soln. in $CDCl_3$) + 33.5 (CF_3, br. d;
$\underline{J}_{CF_3, CF}$ 12 Hz) and + 25.8 (CF, br. q) p.p.m. (rel. int. 3:1);
δ_H (same soln.; int. Me_4Si) + 8.56 [2-,6-H, br. d (6 Hz)],
+ 7.86 [4-H, br. t (7 Hz)], and + 7.60 (3-,5-H, m) p.p.m. (rel.
int. 2:1:2)}; the remainder was lost when the bulk of the
residue was subjected to 'flash' chromatography [silica
(15 x 6 cm); CH_2Cl_2-Me_2CO (75:25 v/v)], the only product
isolated being impure N-cyanoiminopyridinium ylide (0.81 g,
6.8 mmol, 34%) (Found: C, 61.1; H, 4.3; N, 34.5. Calc. for
$C_6H_5N_3$: C, 60.5; H, 4.2; N, 35.3%), m.p. 116-118.5 °C (lit.
[6], 119-120 °C), m/e 119 ($\underline{M}^{+}$, 51.5%), 79 ($C_5H_5N^{+}$, 100%), and
40 (CN_2^{+}, 9%), $\lambda_{max.}$ (mull) 4.67 μm (C≡N str.; lit. [6],
4.69 μm), and δ_H (soln. in $CDCl_3$) + 1.5 (2-,6-H, br. m) and
+ 0.6 (3-,4-,5-H, br. m) p.p.m. (rel. int. 2:3). The gaseous
material recovered from the reaction vessel was shown by i.r.
spectroscopy to be carbon dioxide.

(c) With perfluoroacetonitrile

When Experiment (a) above was repeated (except that a
reaction period of 4 d was employed) with a two-fold excess of
trifluoroacetonitrile (3.8 g, 40 mmol) [15] in place of
perfluoro-1-azacyclohexene, the product, isolated

chromatographically [alumina (30 x 3.5 cm); CH_2Cl_2] (1.52 g
was recovered) and finally purified by vacuum sublimation (bath
temp. 60 °C)], was a 3:1 mixture (1.48 g, 7.9 mmol, 39%) of
2-(trifluoromethyl)-s-triazolo[1,5-a]pyridine (IV) and either
its 4,5- or 6,7-dihydro-derivative [(V) or (XI)] (Found:
C, 44.8; H, 2.3; F, 30.5; N, 22.6. Calc. for a 3:1 mixture of
$C_7H_4F_3N_3$ and $C_7H_6F_3N_3$: C, 44.8; H, 2.4; F, 30.4; N, 22.4%).

Unambiguous Synthesis of 2-(Trifluoromethyl)-s-triazolo[1,5-a]-pyridine

A mixture of 1,2-diaminopyridinium iodide (2.37 g,
10.0 mmol) and trifluoroacetic anhydride (10 cm^3) was heated
under reflux (6 h) then, after storage at room temperature
overnight, evaporated at reduced pressure; the oily residue was
poured into 10% aqueous sodium hydroxide solution (200 cm^3).
Isolation of the product by standard techniques {ether
extraction followed by column chromatography ['flash' on silica
(15 x 4 cm); CH_2Cl_2] then vacuum sublimation (70 °C)} afforded
2-(trifluoromethyl)-s-triazolo[1,5-a]pyridine (IV) (nc)
(0.93 g, 5.0 mmol, 50%) (Found: C, 44.9; H, 2.2; F, 31.0;
N, 22.2. $C_7H_4F_3N_3$ requires C, 44.9; H, 2.1; F, 30.5; N, 22.5%),
white needles, m.p. 102.5-104 °C (sealed tube), δ_H (25% soln.
in $CDCl_3$) + 1.45 (7-H, dt), + 0.64 (4-H, dt), + 0.43 (5-H, ddd)
and -0.01 (6-H; td) p.p.m. (rel. int 1:1:1:1) ($J_{4H,5H}$ 9,
$J_{5H,7H}$ 1.5, $J_{5H,6H}$ 7, $J_{6H,7H}$ 7, $J_{4H,6H} \approx J_{4H,7H} \approx 1.5$ Hz), δ_F
(same soln.) + 13.5 (s) p.p.m., δ_C (50% soln. in $CDCl_3$) + 155.3
(C-2, q; $^2J_{CF}$ 39.1 Hz) + 151.0 (C-3a, s), + 130.9 (C-7, s),
+ 128.8 [C-6 (or 4), s], + 119.3 (CF_3, q; $^1J_{CF}$ 271 Hz), + 117.3
[C-4 (or 6), s], and + 115.5 (C-5, s) p.p.m., and m/e 187
(M^+, 100%), 168 (M^+ -F·, 14%), 78 ($C_5H_4N^+$, 52%), 69 (CF_3^+, 11%).

compound (XII), and to Dr. Michael G.Barlow (UMIST) for useful discussions about the n.m.r. data for the dihydro-derivative of the NIPY-CF$_3$CN adduct (IV).

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