Synthesis of Novel 1-(4-Fluorophenyl diazoalkanes) and C,C-Disubstituted-N-(tetrafluoro-4-pyridyl)nitrones

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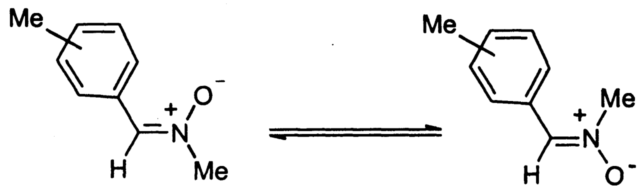
A valuable synthesis of novel dimer of C-(4-fluorophenyl)-C-methyl-N-(tetrafluoro-4-pyridyl)nitrone (**9**) and C,C-diphenyl-N-(tetrafluoro-4-pyridyl)nitrone (**18**) have been reported. The reaction of 2,3,5,6-tetrafluoro-4-nitrosopyridine (**7**) with a novel 1-(4-fluorophenyl diazoethane) (**8a**) in petroleum ether (40–60°C) affords the previous fluorinated nitrone (**9**) in good yield. In a similar fashion to that described, C,C-diphenyl-N-(tetrafluoro-4-pyridyl)nitrone (**18**) was synthesized in high yield (65%). The dipolar cycloaddition of this fluorinated nitrone to mono-substituted ethylene was unsuccessful.

Key Words: Synthesis, Tetrafluoronitrosopyridine, Fluorinated nitrones, Cycloaddition.

INTRODUCTION

Concerning the synthesis of nitrones, there are a surprisingly large number of methods of preparing nitrones and a number of routes have been developed, the most important of which are now listed: (a) from N-substituted hydroxyl amine[1]. (b) from N,N-disubstituted hydroxylamines: This method is only applicable when at least one of the groups bonded to nitrogen has an α-hydrogen. The oxidizing agents usually employed are: yellow mercuric oxide[2], cupric acetate[3], hydrogen peroxide and potassium permanganate[4], potassium ferricyanide[5]. Several nitrones, trisubstituted nitrones were prepared and the nitrones themselves proved to be remarkably stable upon refluxing in toluene or xylene[6], in contrast to other allylic dipoles such as azomethine[7, 8], carbonyl ylides[9] and only slow decomposition was observed after a few days reaction time. (c) From aromatic nitroso compounds[10, 11]. The existence of geometric isomers of asymmetrical nitrones has been reported on several occasions[12, 13]. The interconversion barriers of the E- and Z-isomers **1a** and **1b (Scheme-1)** were obtained using the direct thermal stereomutation technique (NMR) in purified diphenyl ether[4]; at 147°C, $K_f = 5.3 \pm 0.2 \times 10^{-5}\ S^{-1}$, $\Delta G_f^{\ddagger} = 33.1$

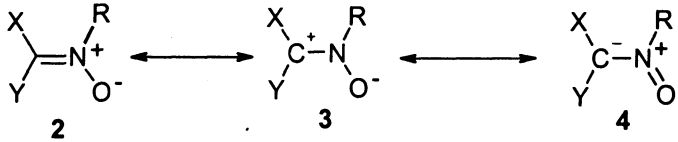


1a **1b**

Scheme-1

kcal mol^{-1}, $K_r = 0.9 \pm 0.2 \times 10^{-5}$ S^{-1} and $\Delta G_r^{+} = 34.6$ kcal mol^{-1}. An estimate of the energy required for the configuration exchange of several nitrones has been made using ^{1}H NMR techniques[14, 15].

Several workers have investigated the chemistry of nitrones, since the nitrone group is a resonance hybrid of the canonical forms **2, 3 and 4 (Scheme-2)**. The canonical form **3** represents the nitrone as 1,3-dipolar reagent and thus explains its ready participation in 1,3-cycloaddition.



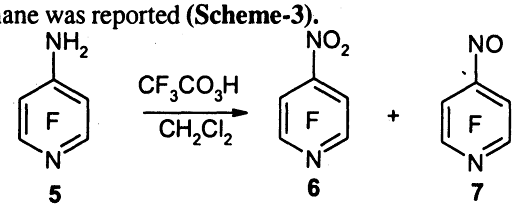
Scheme-2

The cycloaddition reaction of nitrones with unsaturated compounds has been extensively studied in recent years[16]. The nitrones undergo many typical reactions, *i.e.*, 1,3-dipolar cycloaddition of nitrones to flurinated dipolarphiles[17], starting from variously substituted nitrones, allow for construction of N, O-nucleosides[18–20], 1,3-cycloadditions of hetaryl and dialdose derived nitrones[21]. In addition nitrones are useful spin trap reagents[6, 22].

Since the literature concerning the synthesis of fluorinated nitrones contains little or no information on trisubstituted nitrones of the type $Ar_FR'C{=}N^+(O^-)Py_F$, we wish to report the synthesis of the dimer isomers C-(4-fluorophenyl)-C-methyl-N-(tetrafluoro-4-pyridyl)nitrone, C,C-diphenyl-N-(tetrafluoro-4-pyridyl) nitrone in high yields and attempted 1,3-dipolar cycloaddition of this fluorinated nitrone to mono-substituted alkenes.

RESULTS AND DISCUSSION

In 1987, the preparation of 2,3,5,6-tetrafluoro-4-nitrosopyridine[23] **(7)**, *via* oxidation of 4-amino-2,3,5,6-tetrafluoropyridine **(5)** with peroxytrifluoro acetic acid in dichloromethane was reported **(Scheme-3)**.

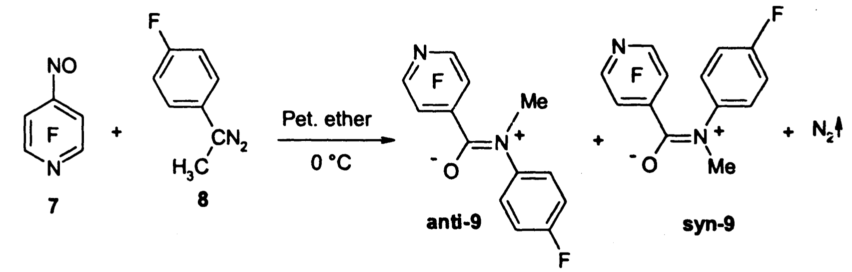


Scheme-3

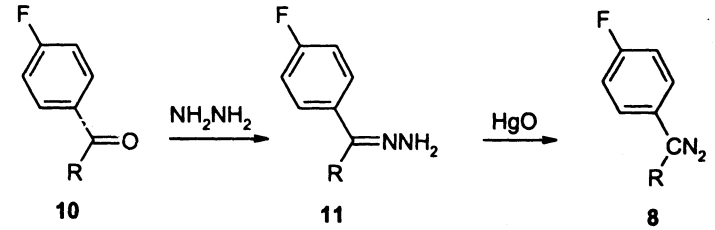
The synthesis of this interesting compound **7** has provided the key to the synthesis of C-(4-fluorophenyl)-C-methyl-N-(tetrafluoro-4-pyridyl)nitrone **(9)** using 1-(4-fluorophenyldiazoethane) **(8)** as shown in **Scheme-4.**

In order to prepare the previous nitrone, the first step involves the preparation of fluorinated diazoalkane **(8)** from 4-fluoroacetophenone **(10)** and hydrazine hydrate to give 1-(4-fluoroacetophenone)hydrazone **(11)**, then followed by addition of yellow mercuric oxide to give the diazoalkane **(8) (Scheme-5).**

The second step was to react the diazoalkane **(8a)** with fluorinated nitroso compound **7** and the reaction can be represented as shown in **Scheme-6.**

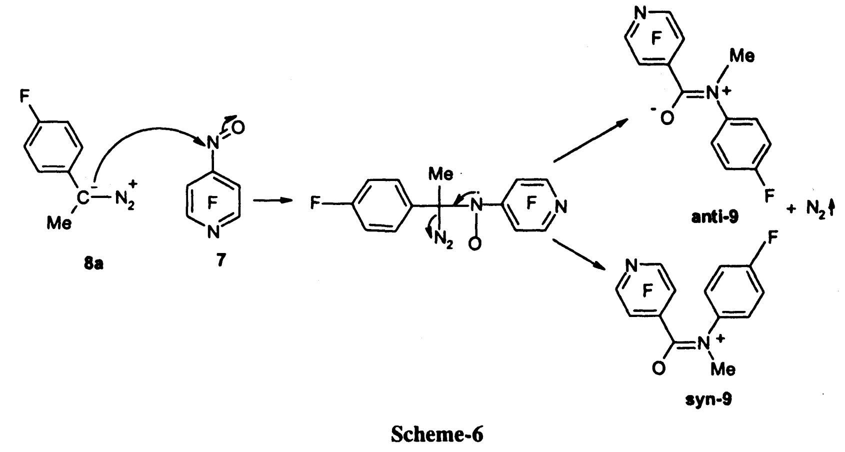


Scheme-4



a) R=CH_3, b) R=CH_3CH_2

Scheme-5

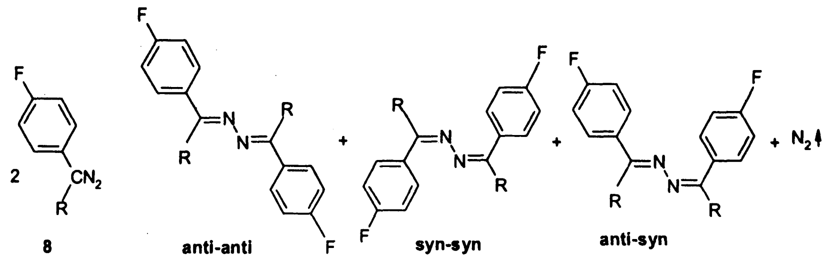


Scheme-6

In addition to the reaction of diazoalkanes with N=O group, it was found recently[24] that the diazoalkanes react also with carbonyl group in polyfluorinated cyclohexadienones not only at C=C bond of non-fluorinated cyclohexadianones.

The undesired yellow crystalline compound of 1-(4-fluorophenyl)acetophenone azines (**12**) which resulted from decomposition of diazoalkanes (**8**) is outlined in **Scheme-7**.

The isomers of fluorinated azines (**12**), *i.e.*, anti-anti, syn-syn, or anti-syn isomers are possible, but the ^{1}H and ^{19}F NMR spectra showed (R=CH_3 or CH_3CH_2) and 4-FC_6H_4 absorptions for only one isomer, which could be revealed to the most stable anti-anti isomer. The greater stability (lower free energy) of this isomer is attributed to steric strain in the syn-syn and anti-syn isomers due to the van der Waals repulsion forces of large groups 4-FC_6H_4 on the same side of each double bond.

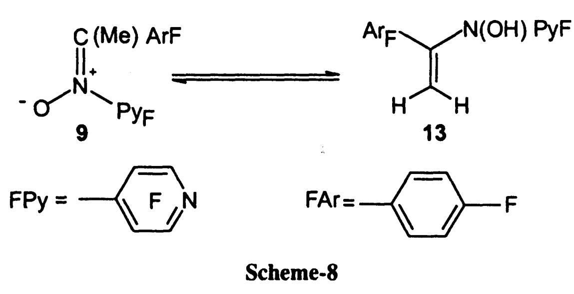


12 a) R= CH_3, b) CH_3CH_2

Scheme-7

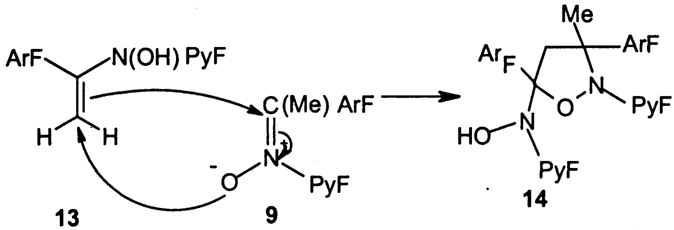
The white solid was identified by elemental analysis and spectral data as a dimer of C-(4-fluorophenyl)-C-methyl-N-(tetrafluoro-4-pyridyl)nitrone **(9)**. The dimer can be thermally cracked to give the desired nitrone **9** and it is frequently more desired to work with this nitrone in solution, where dimerization can be controlled. The IR spectrum showed absorption at 1650 cm^{-1} which could be assigned to ν(—C═N(O^-))stretch or ν(C═N) stretch in the pyridine ring. The mass spectrum showed the molecular ion of nitrone **9** at m/z 302 (6.8%), a base peak at m/z 123 ($C_7H_4FO^+$) and prominent peaks at m/z 271 (56.99%, $C_{13}H_4N_2F_5^+$), 166 (26.0%, $C_5H_2N_2F_4^+$) and 95 (53.4%, $C_6H_4F^+$). The ^{19}F NMR spectrum absorptions at δ_F ($CDCl_3$): –10.45 (AA′ part of AA′XX′ system, 4F, F-2 and F-6), –11.10 (AA′ part of AA′XX′ system, 4F, F-2 and F-6), –29.65 (tt, 1F, 4-$\underline{F}C_6H_4$), –29.68 (tt, 1F, 4-$\underline{F}C_6H_4$), –32.80 (tt, 1F, 4-$\underline{F}C_6H_4$), –35.75 (tt, 1F, 4-$\underline{F}C_6H_4$), –56.75 (AA′ part of AA′XX′ system, 4F, F-3 and F-5), –60.15 (AA′ part of AA′XX′ system, 4F, F-3 and F-5) ppm. The ^1H NMR spectrum exhibited absorption of intensity 3.0 : 3.0 : 3.0 : 3.0 : 16 at δ_H ($CDCl_3$): 1.75 (CH_3, s), 2.27 (CH_3, s), 2.38 (CH_3, s), (CH_3, s), 2.46 (CH_3, s) and 6.80–7.70 (complex) ppm. The isomers of nitrone **9**, *i.e.*, syn and anti, are possible, but the ^1H and ^{19}F spectra showed more CH_3 and 4-$\underline{F}C_6H_4$ absorptions than are possible for these two isomers.

The nitrone **9** could also have the form **13 (Scheme-8)**.



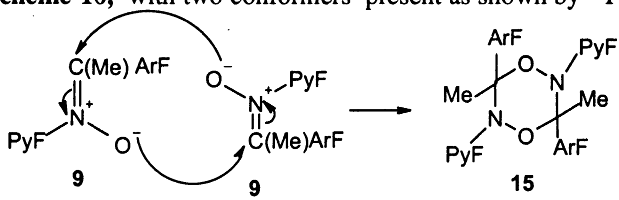
Scheme-8

The structure **14 (Scheme-9)** is possible, but the absence of absorption due to OH in both the IR and ^1H NMR spectra and the absence of an AB system for the CH_2 group in the ^1H NMR spectrum is strong evidence that the dimer does not have structure **14**.



Scheme-9

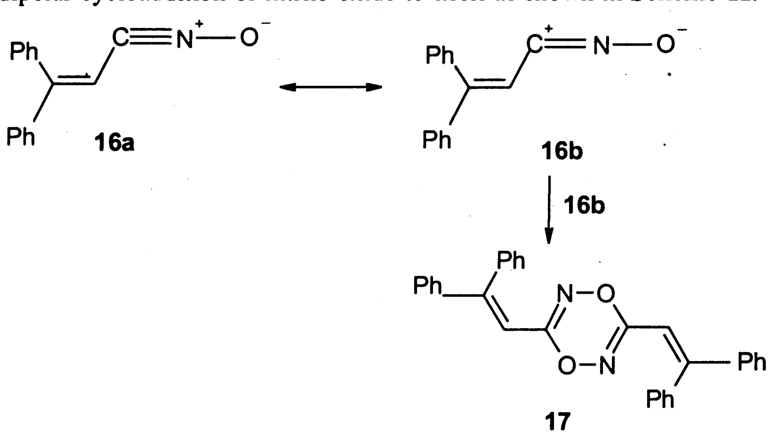
It is, therefore, considered that the product is a nitrone dimer which could have the structure **14** (formed by 1,3-dipolarcy cloaddition of nitrone **9** to itself) as shown in **Scheme-10,** with two conformers present as shown by ^{19}F NMR from



Scheme-10

the absorptions for fluorine in the 4-$\underline{F}C_6H_4$ group. The four ^{1}H NMR absorptions of methyl groups (relative intensity 3 : 3 : 3 : 3) would agree with the ^{19}F NMR spectrum in indicating also that two conformers are present.

This reaction is analogous to the reaction reported recently[6], which involved 1,3-dipolar cycloaddition of nitrile oxide to itself as shown in **Scheme-11.**

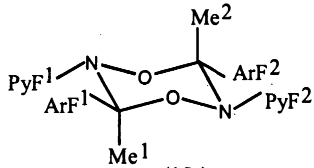
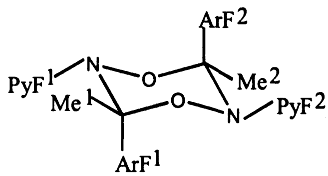
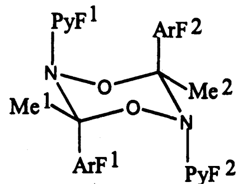
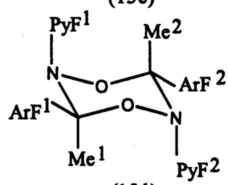
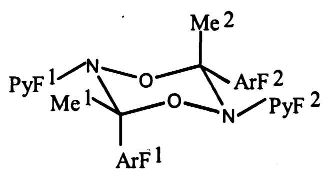
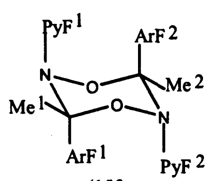


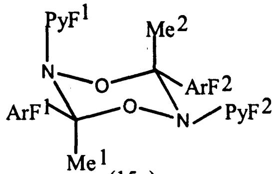
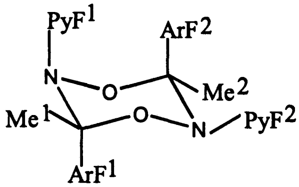
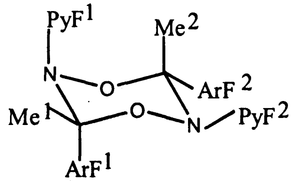
Scheme-11

There are theoretically nine possible dimer conformations in which the aryl, methyl and pyridyl groups can be axial or equatorial and in certain of these only one absorption would be expected for either the $\underline{F}$-C_6H_4 or CH_3 groups since the two $\underline{F}$-C_6H_4 groups would be in one identical environment and the two CH_3 groups would be in a second identical environment. The possible conformations and the number of absorptions expected are as in Table-1:

TABLE-1

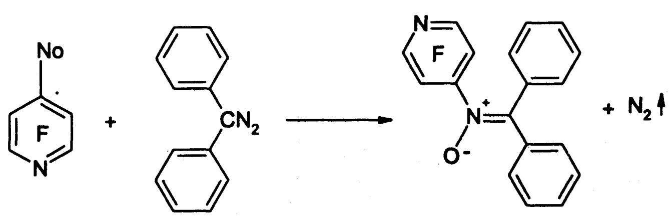
THE N° OF Me OR Ar_F AND Py_F ABSORPTIONS IN ^{1}H AND ^{19}F NMR SPECTRA

Ar^1	Ar^2	Me^1	Me^2	PyF^1	PyF^2	The conformers of dimer 15	N° of FC_6H_4 or Me abs.	N° of PyF absorp.
e	e	a	a	e	e	 (15a)	1	2
a	a	e	e	e	e	 (15b)	1	2
a	a	e	e	a	a	 (15c)	1	2
e	e	a	a	a	a	 (15d)	1	2
a	e	e	a	e	e	 (15e)	2	4
a	e	e	a	a	a	 (15f)	2	4

Ar^1	Ar^2	Me^1	Me^2	PyF^1	PyF^2	The conformers of dimer 15	N° of $\underline{F}C_6H_4$ or Me abs.	N° of PyF absorp.
e	e	a	a	a	e	 (15g)	2	4
a	a	e	e	a	e	 (15h)	2	4
a	e	e	a	a	e	 (15i)	2	4

On the present evidence, the conformers **15a–d** are not possible, since the ^1H and ^{19}F spectra showed more CH_3 and 4-$\underline{F}C_6H_6$ absorptions than are possible for each pair of these conformers. Each pair of the remaining 5 conformers are possible since methyl and 4-$\underline{F}C_6H_4$ groups would agree with the ^1H and ^{19}F spectra, by considering that the two PyF groups would be in one identical environment and the other two PyF groups would be in a second identical environment and further work is necessary including an X-ray structural determination.

4-Nitrosotetrafluoropyridine reacts also with diphenyldiazomethane **(17)** [obtained from benzophenone Ph_2CO **(16)**, using autoclave] **(Scheme-12)** as described earlier for the synthesis of C-(4-fluorophenyl)-N-(tetrafluoro-4-pyridyl)-nitrone. The fluorinated nitrone **18 (Scheme-12)** was obtained in high yield



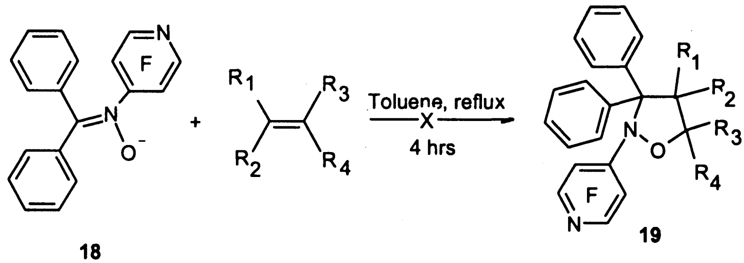
7 17 18

Scheme-12

(*ca.*70% yield) and no secondary products resulted in this reaction such as 2-(tetrafluoro-4-pyridyl)-3,3-diphenyloxaziridine.

The literature concerning 1,3-dipolar cycloaddition of nitrones contains little or no information on trisubstituted nitrones of the type $RR'C{=}CN^{+}(O^{-})Ar$.

It was, therefore, decided to investigate whether nitrones of this type would undergo 1,3-dipolar cycloaddition and so the reaction of C,C-diphenyl-N-(tetrafluoro-4-pyridyl)nitrone **(18)** with styrene $R_1R_2C{=}CR_3R_4$ (R_1 = Ph and $R_2 = R_3 = R_4$ = H) was carried out. The unchanged nitrone **18** was recovered (90% recovered) after removal of solvent and unreacted styrene. The reaction was repeated on the same scale using 2,3,4,5,6-pentafluorostyrene $R_1R_2C{=}CR_3R_4$ (R_1 = pentafluorophenyl and $R_2 = R_3 = R_4$ = H) and again the nitrone **18** (96%) was recovered unchanged and there was no isoxazolidine **19** formed **(Scheme-13).**



Scheme-13

It is considered probable that the reaction did not take place because of steric effect involving the bulky aryl and pyridyl groups. It is possible that reactions of this type may take place under extreme conditions.

EXPERIMENTAL

Nuclear magnetic resonance (NMR) spectra were normally recorded at 35°C using a Perkin-Elmer R10 or R12 or a Perkin-Elmer Hitachi R20A spectrometer operating at 60 MHz for ^{1}H NMR spectra and 54.6 MHz for ^{19}F NMR spectra. Tetramethylsilane (TMS) was used as a reference for ^{1}H NMR spectra; and for ^{19}F NMR spectra, chemical shifts were measured (in ppm) relative to trifluoroacetic acid (TFA) as an external interchange reference unless otherwise stated. Mass spectra were recorded on A.E.I. MS902 double focusing mass spectrometer at 70 eV (ionization beam energy). The intensities of the peaks are given in terms of relative abundance, with the most intense peak (the base peak) taken as 100%. Ultraviolet spectra were measured using a Cary 118 instrument. Samples were examined as dilute solution in methanol. Melting points were determined on a Gallenhamp melting point apparatus and were uncorrected. Nitrogen was determined by the Pregl-Dumas method and fluorine colorimetrically (using the alizarin fluorine blue complex which changes it colour from red to blue in the presence of F^{-} ions) and chlorine by potentiometric titration (with silver nitrate), following decomposition of samples by the Schoniger oxygen-flask method.

1-(4-Fluoroacetophenone)hydrazone (11a): 4-Fluoroacetophenone (15.18 g, 0.11 mol) butan-1-ol (75 cm^3) and hydrazine hydrate (100%, 13.00 g, 0.26 mol) were heated under reflux for 5 h and butan-1-ol was then removed under reduced pressure. The oily residue was dissolved in diethyl ether (50 cm^3) and dried

($MgSO_4$). Evaporation of the ether gave a yellow liquid identified by ^1H, ^{19}F NMR and IR spectroscopy and mass spectrometry as 1-(fluoroacetophenone)hydrazone (14.5 g, 95.35 mmol, 87%). IR (KBr, cm^{-1}): 3500–3300 ν(NH), 3100–2800 ν(CH_3), 1650 ν(C=N) and 1480–1190 ν(Ar-F); UV λ_{max} (ε) EtOH: 259 (12214.29); λ_{min} (ε): 277 (6182.54); ^1H ($CDCl_3$): δ 2.00 (3H, s, CH_3), 5.50 (2H, br s, —NH_2), 7.00 (2H, m, H-2 and H-6), 7.65 (2H, m, H-3 and H-5); ^{19}F ($CDCl_3$): δ-35.8 (1F, tt, J = 9.0, 6.6 Hz, F-4); m/z (FAB): 152 (M^+, 100); 137 (M-CH_3^+, 41.0), 121 ($C_7H_4NF^+$, 12), 95 ($C_6H_4F^+$, 41.2); Anal., Calcd. for $C_8H_9N_2F$: C, 63.2; H, 5.9; F, 12.5; N, 18.4; Found: C, 62.9; H, 6.2; F, 12.5; N, 18.7%.

1-(4-Fluorophenyldiazoethane) (8a): In magnetically-stirred autoclave (500 cm^3) were placed 1-(4′-fluoroacetophenone)hydrazone (12.16 g, 0.08 mol), mixture of yellow mercuric oxide (40.00 g, 0.185 mol), anhydrous sodium sulphate (16.00 g), saturated ethanolic potassium hydroxide (6 cm^3) and diethyl ether (200 cm^3). After 5 h at room temperature, the mixture was filtered, the inorganic residue washed (ether) and the combined filtrate and washings evaporated under reduced pressure to give a deep magenta coloured oil identified by ^{19}F NMR, IR spectroscopy as 1-(4-fluorophenyldiazoethane) (11.52 g, 76.8 mmol, 96%). The novel product was dissolved immediately in a 50 : 50 mixture of petroleum ether (b.p. 40–60°C) and diethyl ether (75 cm^3) and then used immediately. IR (KBr, cm^{-1}): 2800 ν(CH_3), 2000 ν(—N≡N—) and 1480–1190 ν(Ar-F); ^1H ($CDCl_3$): δ 2.00 (3H, s, —CH_3), 7.15 (Ar—H); ^{19}F ($CDCl_3$): δ -42.00 (1F, tt, J = 9.0, 6.0 Hz, F-4).

1-(4-Fluoropropiophenone)hydrazone (11b): Synthesis was in analogous manner to **11a,** using 4-fluoropropiophenone (12.5 g, 82.14 mmol), butan-1-ol (75 cm^3) and hydrazine hydrate (100%, 10.0 g, 200 mmol). The oily residue was vacuum distilled to give a pale yellow liquid identified as 1-(fluoropropiophenone)hydrazone (10.7 g, 64.4 mmol, 78%). b.p. 86°C at 3 mm Hg; IR (KBr, cm^{-1}): 3500–3300 ν(NH), 3200–2850 ν(CH_3CH_2), 1650 ν(C=N) and 1450–1190 ν(Ar-F); UV λ_{max} (ε) EtOH: 263 (9005.23); λ_{min} (ε): 230 (4882.35); ^1H ($CDCl_3$): δ 1.06 (3H, t, J = 8.5 Hz, CH_3), 2.50 (2H, q, J = 8.5 Hz, CH_2), 5.10 (2H, br s, —NH_2), 6.65 (2H, m, H-2 and H-6), 7.05 (2H, m, H-3 and H-5); ^{19}F ($CDCl_3$): δ -36.0 (1F, tt, J = 9.0, 6.0 Hz, F-4); m/z (FAB): 166 (M^+, 31.3); 137 (M-$CH_3CH_2^+$, 20.0), 121 ($C_7H_4NF^+$, 30.9), 95 ($C_6H_4F^+$, 100); Anal., Calcd. for $C_9H_{11}N_2F$: C, 65.1; H, 6.6; F, 11.4; N, 16.9; Found: C, 63.9; H, 7.4; F, 9.2; N, 15.3%.

1-(4-Fluorophenyldiazopropane) (8b): Prepared as for **8a,** using 1-(4-fluoropropiophenone)hydrazone (5.35 g, 32.2 mmol), mixture of yellow mercuric oxide (16.10 g, 0.075 mol), anhydrous sodium sulphate (6.5 g), saturated ethanolic potassium hydroxide (5 cm^3) and diethyl ether (100 cm^3). After 5 hours at room temperature, the mixture was filtered, the inorganic residue washed (ether) and the combined filtrate and washings evaporated under reduced pressure to give a deep magenta coloured oil (95%) identified by IR spectroscopy as 1-(4-fluorophenyldiazo-propane). IR (KBr, cm^{-1}): 2800 ν(CH-), 2000 ν(—N≡N—) and 1480–1190 ν(Ar-F). This fluorinated azo-compound was dissolved immediately in a 50 : 50 mixture of petroleum ether and diethyl ether and then kept in the fridge for further reaction. Unfortunately, this compound was not used for further reaction, since it was completely decomposed to the corresponding azine after a few hours. The residue was recrystallized from ethanol to give a yellow crystalline solid which was identified as fluoropropiophenone)azine **(12b).** IR (KBr, cm^{-1}): ν 3100–2800 (CH-), 1670 (C=N) and 1450–1190 (Ar—F); ^1H ($CDCl_3$): δ 1.10 (3H, t, J = 9.0 Hz, CH_3), 2.88 (2H, q, J = 9.0 Hz, CH_2), 7.10 (2H, m, aromatic-H), 7.85 (2H, m, aromatic-H); ^{19}F ($CDCl_3$): δ –33.0 (1F, tt, J = 9.0, 6.0 Hz, F-4); m/z (FAB): 301(MH^+, 100) 300 (M^+, 96.5), 178 ($C_{11}H_{13}NF^+$, 76.1), 122 ($C_7H_5NF^+$, 96.2), 95 ($C_6H_4NF^+$, 45.6), 55 ($C_2H_3N_2^+$, 41.1); Anal., Calcd. for $C_9H_{11}N_2F$: C, 72.0; H, 6.0; F, 12.7; N, 9.3; Found: C, 72.0; H, 5.8; F, 12.5; N, 9.3%.

Tetrafluoro-4-nitrosopyridine (7): This compound was prepared by similar procedure to that reported[23]. The product was identified by comparison to its spectroscopic data with that of an authentic sample. IR spectroscopy as tetra-4-nitrosopyridine **(7)** (8.5 g, 47.4 mmol, 33%). m.p. 63–65°C {Lit. [23] 63.5–65 °C}; IR (KBr, cm^{-1}): 1650 (C=N), 1480–1190 ν(Ar-F) and strong absorption at 1350 ν(NO); ^{19}F ($CDCl_3$): δ –6.65 (2F, AA'XX', F-2 and F-6), –82.80 (2F, AA'XX', F-3 and F-5); m/z (FAB): 180 (M^+, 100); Anal., Calcd. for $C_5N_2OF_4$: C, 33.3; N, 15.6; F, 4.2; Found: C, 33.3; N, 15.6; F, 42.2%.

Dimer of C-1-(4-fluorophenyl)-C-methyl-N-(tetrafluoro-4-pyridyl)nitrone (9): Tetrafluoro-4-nitrosopyridine (1.70 g, 9.40 mmol) was dissolved in petroleum ether (20 cm^3, b.p. 40–60°C) and a solution of 1-(4-fluorophenyldiazoethane) (1.54 g, 10.27 mmol in 50/50 diethyl ether/petroleum ether (20 cm^3, b.p. 40–60°C) was added dropwise at 0°C; a slow evolution of nitrogen took place and it was several seconds after the addition of each further drop of diazo solution before the deep red color of the diazo compound was discharged. The addition was continued until no further reaction took place, at which stage the colour of the solution had changed from blue-green to brown, and it was determined that 1-(4-fluorophenyldiazoethane) (1.35 g, 9.40 mmol) had been added after storing the resulting solution in the fridge for two days; the precipitated white solid was separated by filtration, washed with petroleum ether (b.p. 40–60°C), dried *in vacuo* to afford a white solid (0.35 g). The combined filtrate and washing were evaporated (rotavapor) to give a brown oil, which when subjected to dry column flash chromatography gave a second crop as a white solid (0.52 g). The combined white solid was identified as two dimer isomers (50/50) of C-1-(4-fluorophenyl)-C-methyl-N-(tetrafluoro-4-pyridyl) nitrone (0.87 g, 2.88 mmol, 31%). m.p. 131.5–132°C; ^1H ($CDCl_3$): δ 1.75 (3H, s, —CH_3), 2.27 (3H, s, —CH_3), 2.38 (3H, s, —CH_3), 2.46 (3H, s, —CH_3), 6.80–7.70 (16H, m, Ar-H); ^{19}F ($CDCl_3$): δ –10.45 (4F, AA'XX', F-2 and F-6), –11.10 (4F, AA'XX', F-2 and F-6), –29.65 (1F, tt, J = 9.0, 6.3, 4-F.C_6H_4), –29.68 (1F, tt, J = 9.0, 6.3, 4-$\underline{F}C_6H_4$), –32.80 (1F, tt, J = 9.0, 6.3, 4-$\underline{F}C_6H_4$), –35.75 (1F, tt, J = 9.0, 6.3, 4-$\underline{F}C_6H_4$), –56.75 (2F, AA'XX', F-3 and F-5), –60.15 (2F, AA'XX', F-3 and F-5). The $(CD_3)_2CO$ was used and similar spectrum was obtained ^{19}F ($(CD_3)_2CO$): δ –12.75 (4F, AA'XX', F-2 and F-6), –13.56 (4F, AA'XX', F-2 and F-6), –31.31 (1F, tt, J = 9.0, 6.3, 4-$\underline{F}C_6H_3$) –31.43 (1F, tt, J = 9.0, 6.3, 4-$\underline{F}C_6H_4$), –33.46 (1F, tt, J = 9.0, 6.3, 4-$\underline{F}C_6H_4$), –36.42 (1F, tt, J = 9.0, 6.3, 4-$\underline{F}C_6H_4$), –56.66 (2F, AA'XX', F-3 and F-5), –60.29 (2F, AA'XX', F-3 and F-5); IR (KBr, cm^{-1}): 1650 ν[(—C=N(O^-)] or ν(C=N) in the pyridine ring, 300–2700 ν(CH_3) and 1480–1190 ν(Ar-F); UV λ_{max} (ε) EtOH: 271(6801.80); λ_{min} (ε): 240 (2040.54); m/z (FAB): 302 (M^+, 6.8), 123 ($C_{13}H_{14}FO^+$, 100), 271 ($C_{13}H_4N_2F_5^+$, 56.9), 166 ($C_5H_2N_2F_4^+$, 26.0) and 95 $C_6H_4F^+$, 53.4); Anal. ,Calcd. for $C_{13}H_7N_2OF_5$: C, 51.7; H, 2.3; N, 9.3; F, 31.5; Found: C, 51.5; H, 2.0; N, 8.9; F, 32.0%.

Further elution afforded a yellow crystalline solid which was recrystallized from ethanol and identified as 1-(4-fluorphenyl)acetophenone azine **(12a)** (0.32 g, 1.18 mmol, 25%). m.p. 130–132°C; IR (KBr, cm^{-1}): 3100–2800 ν(CH_3), 1650 ν(C=N); UV λ_{max} (ε) EtOH: 267 (21030.93); λ_{min} (ε): 234 (7711.34); ^1H ($CDCl_3$): δ 2.3 (3H, s, CH_3), 7.1 (2H, m, H-2 and H-6), 7.9 (2H, m, H-3 and H-5); ^{19}F ($CDCl_3$): δ –32.6 (2F, tt, J = 8.8, 5.7 Hz, F-4); m/z (FAB): 272 (M^+, 100); 257 (M-CH_3^+, 76.7), 136 ($C_8H_6NF^+$, 54.7), 121 (41.1); Anal., Calcd. for $C_{16}H_{14}N_2F_2$: C, 70.6; H, 5.1; N, 10.3; F, 14.0; Found: C, 70.5, H, 5.1;N, 10.1; F, 14.1%.

C,C-Diphenyl-N-(tetrafluoro-4-pyridyl)nitrone (18): The compound was prepared in a similar fashion to that described above for C-1-(4-fluorophenyl)-C-methyl-N-(tetrafluoro-4-pyridyl)nitrone. m.p. 152–154°C; IR (KBr, cm^{-1}): 1650 ν(—C=N); UV λ_{max} (ε) EtOH: 232 (14045.10), 352 (13153.35); λ_{min} (ε): 220 (13376.26), 280 (9809.28); ^1H ($CDCl_3$): δ 7.4–8.2 (10H, m, Ar-H); ^{19}F ($CDCl_3$): δ –7.5 (2F, AA′XX′, F-2 and F-6), –68.3 (2F, AA′XX′, F-3 and F-5); m/z (FAB): 346 (M^+, 11.3); 105 ($C_4F_3^+$, 97.8), 78 [(B + 1, 17.3)], 77 [($C_6H_5^+$ (B), 100)]; Anal., Calcd. for $C_{18}H_{10}N_2OF_4$: C, 62.4; H, 2.9; N, 8.1; F, 22.0; Found: C, 62.7; H, 2.9; N, 8.1; F, 22.0%.

Attempted 1,3-dipolar cycloaddition of C,C-diphenyl-N-(tetrafluoro-4-pyridyl)nitrone (18) to styrene: A round-bottomed flask (50 cm^3) fitted with a reflux condenser, magnetic stirrer and nitrogen inlet was charged with C,C-diphenyl-N-(tetrafluoro-4-pyridyl)nitrone (0.75 g, 2.17 mmol), dry toluene (30 cm^3) and styrene (0.23 g, 2.17 mmol). After heating under reflux (4 h) reaction had not taken place as shown by TLC and evaporation of the mixture under reduced pressure gave a brown oil when subjected to dry column flash chromatography afforded a bright yellow solid which was identified as unchanged C,C-diphenyl-N-(tetrafluoro-4-pyridyl)nitrone (0.68 g, 1.96 mmol, 96%, recovered).

Attempted 1,3-dipolar cycloaddition of C,C-diphenyl-N-(tetrafluoro-4-pyridyl)nitrone (18) to 2,3,4,5,6-pentafluorostyrene: The reaction was repeated on the same scale using 2,3,4,5,6-pentafluorostyrene and the C,C-diphenyl-N-(tetrafluoro-4-pyridyl)nitrone (0.72 g, 2.08 mmol, 96%) was recovered unchanged.

Conclusions

In conclusion, a new fluorinated trisubstiututed nitrone of the type ArFRC = NP_yF *i.e.,* the synthesis of the C-(4-fluorophenyl)-N-(tetrafluoro-4-pyridyl)nitrone and C,C-diphenyl-N-(tetrafluoro-4-pyridyl)nitrone is generated. The synthesis of this novel fluorinated nitrone will provide the key to 1,3-dipolar cyclocycloaddition of fluorinated nitrones to dipolarphiles instead of 1,3-cycloaddition of non-fluorinated nitrones to the fluorinated dipolarphiles as found in many cases in literature.

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