One-pot synthesis of 2-(trifluoromethyl)pyridines from *N*-silyl-1-aza-allyl anions with trifluoroacetylketene diethyl ketal or (*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one

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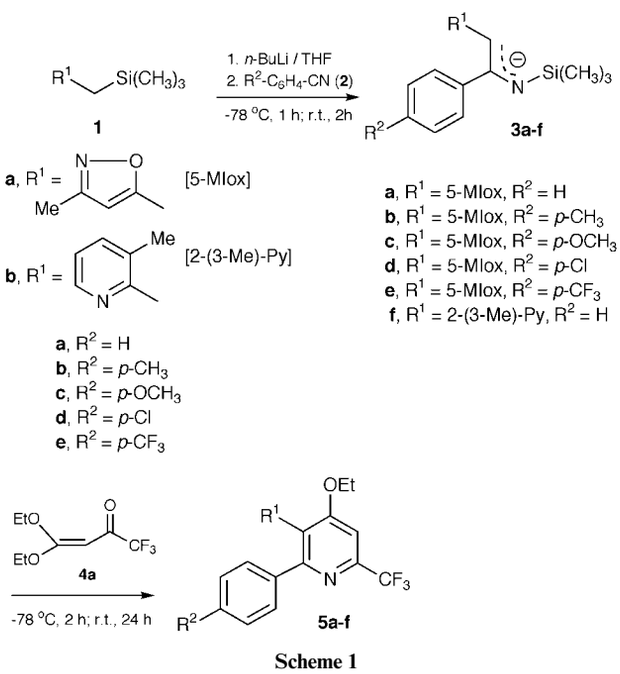
Received (in Cambridge, UK) 8th June 1999, Accepted 19th August 1999

The reaction of *N*-silyl-1-aza-allyl anions with trifluoroacetylketene diethyl ketal and (*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one are described. The anions, which were prepared from an α-silyl carbanion of 3-methyl-5-(trimethylsilylmethyl)isoxazole [or 3-methyl-2-(trimethylsilylmethyl)pyridine] and *para*-substituted benzonitriles (R = H, *p*-Me, *p*-OMe, *p*-Cl, *p*-CF_3), reacted with a slight excess of trifluoroacetylketene diethyl ketal or (*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one in dry tetrahydrofuran to afford the corresponding 2-(trifluoromethyl)pyridine derivatives in 75, 71, 78, 48, 46, 60, 83% yield, respectively.

Introduction

Although much attention has been paid to the chemistry of 1-aza-allyl anions,[1] most of them have been utilized for carbon–carbon bond formation. The utility of anions bearing a trialkylsilyl group on the nitrogen for the synthesis of heterocyclic compounds such as pyridine derivatives is almost completely unexplored. The pyridine nucleus is a major component of a variety of natural products and drugs.[2] On the other hand, trifluoromethylated N-heterocycles are most important compounds and widely applied in the field of medicinal[3] and agricultural[4] chemistry. Recently we have developed an efficient method for the synthesis of 2,3,4,5- or 2,3,4,6-tetra-substituted pyridine derivatives from *N*-silyl-1-aza-allyl anions[5–7] and 2-acetyl-3-methoxyprop-2-enoate[8] or 1,3-diphenylprop-2-en-1-one.[9] The *N*-silyl-1-aza-allyl anions, which are easily generated from the corresponding aromatic nitriles and α-silyl carbanions, show ambident reactivity at the nitrogen and carbon atoms and can be utilized as a versatile building block for the synthesis of N-heterocyclic compounds.[10–13] We now report a one-pot synthesis route of 2-(trifluoromethyl)-pyridine derivatives by the reaction of *N*-silyl-1-aza-allyl anions **3** with trifluoroacetylketene diethyl ketal **4a** or (*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one **4b**.

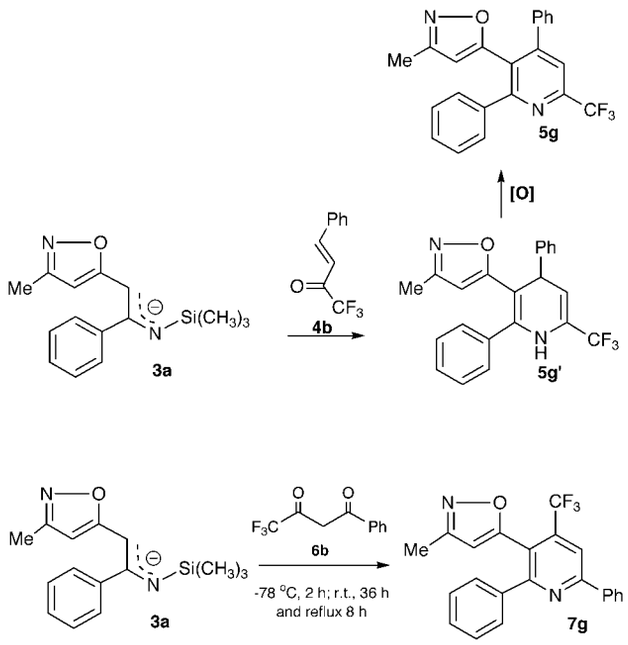


Scheme 1

Results and discussion

3-Methyl-5-(trimethylsilylmethyl)isoxazole **1a** and 3-methyl-2-(trimethylsilylmethyl)pyridine **1b**, each prepared by a previously reported procedure,[6,7] were chosen as starting materials. A solution of 3-(3-methylisoxazol-5-yl)-2-phenyl-*N*-trimethylsilyl-1-aza-allyl anion **3a**, generated from **1a** and benzonitrile **2a** (Scheme 1),[7] was treated with a slight excess of trifluoroacetylketene diethyl ketal **4a**[14] to give 4-ethoxy-3-(3-methylisoxazol-5-yl)-2-phenyl-6-(trifluoromethyl)pyridine **5a** in 75% yield as a single regioisomer under the optimized reaction conditions, as shown in the Experimental section. Similarly, the reaction of anions **3b–e** with **4a** also afforded the corresponding pyridine derivatives **5b–e** in 71, 78, 48 and 46% yield, respectively. The anion **3f**, which was derived from **1b** and **2a**, also reacted with **4a**, to give 4-ethoxy-3-(3-methyl-2-pyridyl)-2-phenyl-6-(trifluoromethyl)pyridine **5f** in 60% yield. Michael addition of **3a** to (*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one **4b**[15] under the same reaction conditions as described above afforded a mixture of 1,4-dihydro-3-(3-methylisoxazol-5-yl)-2,4-diphenyl-6-(trifluoromethyl)pyridine **5g′** and 3-(3-methylisoxazol-5-yl)-2,4-diphenyl-6-(trifluoromethyl)pyridine **5g** in 6 and 83% yield, respectively (Scheme 2). The dihydropyridine **5g′**, initially formed, was dehydrogenated *in situ* to afford **5g**. Subsequent oxidation of the isolated dihydropyridine intermediate **5g′** with cupric [copper(II)] acetate gave the pyridine **5g** in 92% yield.

The structures of products **5** were established by their spectral and elemental analyses. For example, the mass spectrum of **5a** showed *m*/*z* 348 (M^+), and the IR spectrum suggested the presence of an aryl group and a C–F functional group (1400–1130 cm^{-1}), but no carbonyl group. The ^1H NMR spectrum showed the presence of an ethoxy group with resonances at δ 1.42 and 4.2, and three singlets at δ 2.28, 6.01, 7.22 which are assignable to the methyl group, 4-H of the isoxazolyl group and



Scheme 2

5-H of the pyridine nucleus, respectively; and the multiplet signal at δ 7.28–7.40 is assignable to the phenyl group.

The position of the trifluoromethyl group in products **5** is evidenced by ^{13}C and ^{19}F NMR spectral characteristics; in the ^{19}F NMR spectrum, the CF_3 group of 4-(trifluoromethyl)quinoline resonates at a lower field than that of 2-(trifluoromethyl)-quinoline;[16] the CF_3 group of 4-(trifluoromethyl)pyridine also resonates at a lower field than that of 2-(trifluoromethyl)-pyridine.[17,18] In addition, the CF_3-substituted carbon of 4-(trifluoromethyl)pyridine resonates at a higher field than that of 2-(trifluoromethyl)pyridine in the ^{13}C NMR spectrum.[18,19] In order to confirm that compounds **5** are 2(6)-trifluoromethyl isomers, we prepared 3-(3-methylisoxazol-5-yl)-2,6-diphenyl-4-(trifluoromethyl)pyridine **7g** through the reaction of **3a** and 4,4,4-trifluoro-1-phenylbutane-1,3-dione **6b** under the reaction conditions described in the Experimental section. This reaction regioselectively afforded **7g** in 78% yield (Scheme 2), which was confirmed by TLC. Katsuyama and co-workers[18] reported that the reaction of 3-aminocrotononitrile (a primary enamine) with **6b** regioselectively gave the corresponding 4-(trifluoromethyl)-pyridine, and the *N*-silyl-1-aza-allyl anion such as **3a** is the stable equivalent of an unstable primary enamine.[12] Comparing the ^{13}C and ^{19}F NMR spectra of **7g** with those of **5g**, the CF_3-substituted carbon of **7g** resonates at higher field (C-4, 139.38 ppm, q, $J_{C\text{-}F}$ 33.0 Hz) than that of **5g** (C-6, 148.58 ppm, q, $J_{C\text{-}F}$ 35.1) in the ^{13}C NMR spectrum, and the CF_3 group of **7g** resonates at lower field (13.88 ppm, s) than that of **5g** (8.11 ppm, s) in the ^{19}F NMR spectrum.

According to the literature, the CF_3-substituted carbon of 3-cyano-2-methyl-6-phenyl-4-(trifluoromethyl)pyridine resonates at higher field (C-4, 141.3 ppm, q, $J_{C\text{-}F}$ 33.9) than that of 3-cyano-2-methyl-4-phenyl-6-(trifluoromethyl)pyridine (C-6, 149.7 ppm, q, $J_{C\text{-}F}$ 35.6) in the ^{13}C NMR spectrum; and the CF_3 group of 3-cyano-2-methyl-6-phenyl-4-(trifluoromethyl)-pyridine resonates at lower field (13.7 ppm, s) than that of 3-cyano-2-methyl-4-phenyl-6-(trifluoromethyl)pyridine (9.2 ppm, s) in the ^{19}F NMR spectrum;[18] the ^{13}C NMR spectra give a characteristic quadruplet at δ_C 134.1 ppm with a coupling to ^{19}F of 31.7 Hz for the C-4 of 2-acylhydrazino-6-methyl-4-(trifluoromethyl)pyridine, while in the regioisomeric 2-acylhydrazino-4-methyl-6-(trifluoromethyl)pyridine the C-6 quadruplet resonates at lower field (δ_C 143.4 ppm, with $J_{C\text{-}F}$ 33.6).[19] These results suggest that **7g** is the 4-trifluoromethyl isomer, and both **5g** and **5a** are the 6-trifluoromethyl isomers.

Experimental

All mps were obtained on a Mitamura Micro-Melting point apparatus and are uncorrected. IR spectra were recorded on a JEOL JIR-5300 spectrophotometer. ^1H and ^{13}C NMR spectra were obtained on a Bruker DPX-300 or JEOL AL-300 spectrometer for samples in $CDCl_3$ solution using tetramethylsilane (Me_4Si) as internal standard, ^{19}F NMR spectra were obtained on the same apparatus using trichlorofluoromethane ($CFCl_3$) or trifluoroacetic acid (TFA) as an internal standard. *J*-Values are given in Hz. Elemental analyses were performed at the Institute of Physical and Chemical Research, Wako, Saitama, Japan. Mass spectra were obtained with a Shimadzu GC/MS-QP2000A mass spectrometer at 70 eV. High-resolution mass spectra were obtained on a JEOL JMS-700 mass spectrometer by FAB ionization mode.

3-Methyl-5-(trimethylsilylmethyl)isoxazole **1a** and 3-methyl-2-(trimethylsilylmethyl)pyridine **1b** were each prepared by a method reported previously.[6,7] Trifluoroacetylketene diethyl ketal **4a**,[14] (*E*)-1,1,1-trifluoro-4-phenylbut-3-en-2-one **4b**[15] and 4,4,4-trifluoro-1-phenylbutane-1,3-dione **6b**[18] were prepared by literature methods. Benzonitrile **2a** and *p*-benzonitriles **2b**–**e** were used after distillation or recrystallization of commercial products, and tetrahydrofuran (THF) was distilled from Na–benzophenone ketyl before use. Ether refers to diethyl ether.

Synthesis of pyridines 5a–g. General procedure

The synthesis of the pyridine **5a** is representative.

4-Ethoxy-3-(3-methylisoxazol-5-yl)-2-phenyl-6-(trifluoromethyl)pyridine 5a. To a stirred solution of **1a** (0.85 g, 5 mmol) in THF (30 cm^3) was added a solution of *n*-butyllithium (2.14 g of 15% hexane solution, 5 mmol) at −80 °C, and the mixture was stirred under nitrogen for 1 h. To this solution was added **2a** (0.52 g, 5 mmol) slowly and the reaction mixture was stirred for an additional 1 h at −80 °C and then for 2 h at room temperature to give **3a**. After recooling of the solution to −80 °C, a THF solution of **4a** (1.27 g, 6 mmol) was added dropwise to the solution of **3a**, and the mixture was stirred for 2 h at −80 °C and then for 24 h at room temperature. The mixture was cooled to −5–0 °C and quenched with saturated aq. ammonium chloride (30 cm^3), then extracted with ether. The combined extract was dried with anhydrous Na_2SO_4 overnight and concentrated under reduced pressure, then was purified by column chromatography on silica gel using chloroform as eluent to give **5a** (1.31 g, 75%) as *colorless needles* after recrystallization from ether–hexane, mp 124.5–125.9 °C (Found: C, 61.97; H, 4.32; N, 8.08. $C_{18}H_{15}N_2O_2F_3$ requires C, 62.07; H, 4.34; N, 8.04%); ν_{max}(KBr)/cm^{-1} 3070, 1610, 1575, 1500, 1360, 1280, 1140, 760; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.42 (3H, t, *J* 7.0, CH_3CH_2O), 2.28 (3H, s, isoxazolyl-CH_3), 4.20 (2H, q, *J* 7.0, CH_3CH_2O), 6.01 (1H, s, isoxazolyl-H), 7.22 (1H, s, Py-H), 7.28–7.40 (5H, m, Ph); δ_C(75.45 MHz; $CDCl_3$ Me_4Si) 11.47, 14.18, 102.59, 106.85, 114.58, 119.32, 122.96, 128.14, 128.90, 129.02, 138.40, 150.10, 150.54, 159.62, 160.42, 163.73, 164.82; δ_F(282.38 MHz; $CDCl_3$; $CFCl_3$) −68.81 (s, CF_3); *m*/*z* 348 (M^+, 80%) and 279 (100).

4-Ethoxy-3-(3-methylisoxazol-5-yl)-2-(*p*-tolyl)-6-(trifluoromethyl)pyridine 5b. Yield 1.29 g (71%), mp 144.0–144.9 °C (from hexane) (Found: C, 62.96; H, 4.68; N, 7.70%. $C_{19}H_{17}N_2O_2F_3$ requires C, 62.98; N, 4.73; N, 7.73%); ν_{max}(KBr)/cm^{-1} 3080, 1600, 1580, 1500, 1360, 1280, 1140, 760; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.35 (3H, t, *J* 7.0, CH_3CH_2O), 2.29 (3H, s, isoxazolyl-CH_3), 2.33 (3H, s, CH_3), 4.19 (2H, q, *J* 7.0, CH_3CH_2O), 6.03 (1H, s, isoxazolyl-H), 7.19 (1H, s, Py-H), 7.09–7.30 (4H, m, ArH); δ_C(75.45 MHz; $CDCl_3$; Me_4Si) 11.51, 14.19, 21.25, 65.26, 102.26, 106.74, 114.27, 119.35, 122.99, 128.85, 128.87, 135.54, 139.08, 150.06, 150.49, 159.64, 160.40, 163.93,

164.79; δ_F(282.38 MHz; $CDCl_3$; $CFCl_3$) −68.62 (s, CF_3); *m*/*z* 363 (M + 1, 24%), 362 (M^+, 100) and 293 (77).

4-Ethoxy-2-(*p*-methoxyphenyl)-3-(3-methylisoxazol-5-yl)-6-(trifluoromethyl)pyridine 5c. Yield 1.48 g (78%), mp 132.7–133.8 °C (from hexane) (Found: C, 60.39; H, 4.48; N, 7.35. $C_{19}H_{17}N_2O_3F_3$ requires C, 60.32; H, 4.53; N, 7.40%); ν_{max}(KBr)/cm^{-1} 3080, 1600, 1580, 1500, 1360, 1280, 1140, 760; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.38 (3H, t, *J* 7.0, CH_3CH$_2$O), 2.28 (3H, s, isoxazolyl-CH_3), 3.77 (3H, s, CH_3O), 4.15 (2H, q, *J* 7.0, CH_3CH_2O), 6.00 (1H, s, isoxazolyl-H), 6.78–6.81 (2H, m, ArH), 7.14 (1H, s, Py-H), 7.30–7.34 (2H, m, ArH); δ_C(75.45 MHz; $CDCl_3$; Me_4Si) 11.49, 14.15, 55.19, 65.23, 102.01, 106.60, 113.57, 113.92, 119.48, 130.41, 130.80, 149.97, 150.43, 159.68, 159.93, 160.32, 164.07, 164.86; δ_F(282.38 MHz; $CDCl_3$; $CFCl_3$) −68.87 (s, CF_3); *m*/*z* 378 (M^+, 100%) and 309 (38).

2-(*p*-Chlorophenyl)-4-ethoxy-3-(3-methylisoxazol-5-yl)-6-(trifluoromethyl)pyridine 5d. Yield 0.92 g (48%), mp 98.8–99.4 °C (from hexane) (Found: C, 56.70; H, 3.99; N, 7.00. $C_{18}H_{14}N_2O_2F_3Cl$ requires C, 56.48; H, 3.69; N, 7.32%); ν_{max}(KBr)/cm^{-1} 3080, 1600, 1580, 1500, 1360, 1280, 1140, 760; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.25 (3H, t, *J* 7.0, CH_3CH$_2$O), 2.31 (3H, s, isoxazolyl-CH_3), 4.20 (2H, q, *J* 7.0, CH_3CH_2O), 6.10 (1H, s, isoxazolyl-H), 7.22 (1H, s, Py-H), 7.28–7.34 (4H, m, ArH); δ_C(75.45 MHz; $CDCl_3$; Me_4Si) 11.52, 14.19, 65.46, 102.76, 107.04, 119.39, 122.92, 128.44, 130.31, 150.68, 151.08, 159.77, 163.04, 164.88; δ_F(282.38 MHz; $CDCl_3$; $CFCl_3$) −68.72 (s, CF_3); *m*/*z* 382 (M^+, 88%), 313 (72) and 277 (100).

4-Ethoxy-3-(3-methylisoxazol-5-yl)-4-ethoxy-6-trifluoromethyl-2-(*p*-trifluoromethylphenyl)pyridine 5e. Yield 0.95 g (46%), mp 117.1–118.0 °C (from hexane) (Found: C, 54.91; H, 3.43; N, 7.01. $C_{19}H_{14}N_2O_2F_6$ requires C, 54.82; H, 3.39; N, 6.73%); ν_{max}(KBr)/cm^{-1} 3080, 2980, 1616, 1570, 1419, 1386, 1323, 1274, 1140, 1088, 977, 727; δ_H(300 MHz; $CDCl_3$; Me_3Si) 1.44 (3H, t, *J* 7.0, CH_3CH$_2$O), 2.31 (3H, s, isoxazolyl-CH_3), 4.23 (2H, q, *J* 7.0, CH_3CH_2O), 6.13 (1H, s, isoxazolyl-H), 7.40 (1H, s, Py-H), 7.50–7.60 (4H, m, ArH); δ_C(75.45 MHz; $CDCl_3$; Me_4Si) 11.47, 14.15, 65.58, 103.18, 107.34, 114.78, 119.19, 122.15, 122.82, 125.12, 125.16, 125.74, 129.31, 130.65, 131.08, 141.98, 150.24, 150.71, 158.70, 159.79, 162.84, 164.78; δ_F(282.38 MHz; $CDCl_3$; $CFCl_3$) −68.64 (s, CF_3, Py) and −63.01 (s, CF_3, Ar); *m*/*z* 416 (M^+, 74%) and 347 (100).

4-Ethoxy-3-(3-methyl-2-pyridyl)-2-phenyl-6-(trifluoromethyl)-pyridine 5f. Yield 1.08 g (60%), mp 162.0–162.9 °C (from hexane) (Found: C, 66.74; H, 4.93; N, 7.53. $C_{20}H_{17}N_2OF_3$ requires C, 67.03; H, 4.78; N, 7.82%); ν_{max}(KBr)/cm^{-1} 3000, 1590, 1580, 1450, 1420, 1390, 1360, 1260, 1120, 785, 700; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.20 (3H, t, *J* 7.0, CH_3CH$_2$O), 1.91 (3H, s, 3-CH_3-Py), 4.12 (2H, q, *J* 7.0, CH_3CH_2O), 7.15 (1H, s, Py-H), 7.11–8.45 (3H, m, Py-H), 7.17–7.31 (5H, m, Ph); δ_C(75.45 MHz; $CDCl_3$; Me_4Si) 14.14, 18.45, 64.73, 102.78, 122.73, 126.26, 127.75, 128.26, 129.28, 132.78, 137.55, 138.80, 146.80, 148.88, 149.36, 153.56, 158.98, 164.16; δ_F(282.38 MHz; $CDCl_3$; $CFCl_3$) −68.54 (s, CF_3); *m*/*z* 358 (M^+, 88%) and 343 (100).

3-(3-Methylisoxazol-5-yl)-2,4-diphenyl-6-(trifluoromethyl)-pyridine 5g. Yield 1.58 g (83%), mp 150.2–151.0 °C (from hexane) (Found: C, 69.63; H, 3.95; N, 7.38. $C_{22}H_{15}N_2OF_3$ requires C, 69.47; H, 3.97; N, 7.36%); ν_{max}(KBr)/cm^{-1} 3050, 1605, 1540, 1400, 1280, 1140, 760; δ_H(300 MHz; $CDCl_3$; Me_4Si) 2.12 (3H, s, isoxazolyl-CH_3), 5.65 (1H, s, isoxazolyl-H), 7.22–7.45 (10H, m, Ph and Py-H), 7.72 (1H, s, Ph); δ_C(75.45 MHz; $CDCl_3$; Me_4Si) 11.31, 107.08, 119.82, 124.28, 128.24, 128.56, 128.94, 129.03, 129.09, 137.08, 138.29, 148.58, 149.07, 153.43, 159.54, 160.17, 165.81; δ_F(282.38 MHz; $CDCl_3$; $CFCl_3$) −68.54 (s, CF_3); δ_F(282.38 MHz; $CDCl_3$; TFA) 8.11 (s, CF_3); *m*/*z* 380 (M^+, 81%) and 338 (100).

1,4-Dihydro-3-(3-methylisoxazol-5-yl)-2,4-diphenyl-6-(trifluoromethyl)pyridine 5g′. Yield 0.12 g (6%), mp 128.2–128.8 °C (from hexane) (HRMS Found: M^+, 382.3848. $C_{22}H_{17}N_2OF_3$ requires *M*, 382.3841); ν_{max}(KBr)/cm^{-1} 3270, 3121, 1624, 1574, 1512, 1419, 1311, 1238, 1180, 1079, 764, 698; δ_H(300 MHz; $CDCl_3$; Me_4Si) 1.98 (3H, s, isoxazolyl-CH_3), 4.75 (1H, d, *J* 4.4, 4-H), 4.93 (1H, s, NH), 5.50 (1H, d, *J* 4.4, 3-H), 5.57 (1H, s, isoxazolyl-H), 7.31–7.42 (10H, m, Ph); δ_C(75.45 MHz; $CDCl_3$; Me_4Si) 11.65, 41.76, 98.63, 102.10, 106.89, 127.53, 127.98, 129.02, 129.28, 129.60, 130.27, 136.33, 139.62, 146.26, 159.47, 169.54; δ_F(282.38 MHz; $CDCl_3$; $CFCl_3$) −70.07 (s, CF_3); *m*/*z* 383 (M + 1, 48%), 382 (M^+, 23) and 305 (100).

The oxidation of 5g′ to 5g

To a solution of cupric acetate (0.157 g, 0.78 mmol) in acetic acid (5 cm^3) was added **5g′** (0.120 g, 0.31 mmol). The mixture was heated and stirred under reflux for 2 h, then was cooled to 0 °C, neutralized by $NaHCO_3$, and extracted with ether. The combined extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure, followed by column chromatography on silica gel with ether–hexane elution to give **5g** (0.109 g, 92%).

Synthesis of 3-(3-methylisoxazol-5-yl)-2,6-diphenyl-4-(trifluoromethyl)pyridine 7g

To a stirred solution of **3a**, generated from **1a** (0.68 g, 4 mmol) and **2a** (0.41 g, 4 mmol) in THF (20 cm^3), was added a THF solution of **6b** (0.95 g, 4.4 mmol) dropwise at −80 °C. The mixture was stirred for 2 h at −80 °C and then for 36 h at room temperature. After refluxing for 8 h, the mixture was cooled to −5–0 °C and quenched with saturated aq. ammonium chloride (30 cm^3), then extracted with ether. The combined extract was dried with anhydrous Na_2SO_4 overnight and concentrated under reduced pressure, then was purified by column chromatography on silica gel using CH_2Cl_2–hexane (1 : 5) as eluent to give **7g** (1.19 g, 78%), mp 130.2–130.9 °C (from hexane) (HRMS Found: M^+, 380.3712. $C_{22}H_{15}N_2OF_3$ requires *M*, 380.3709); ν_{max}(KBr)/cm^{-1} 3108, 1616, 1438, 1408, 1365, 1261, 1138, 756, 694; δ_H(300 MHz; $CDCl_3$; Me_4Si) 2.21 (3H, s, isoxazolyl-CH_3), 5.95 (1H, s, isoxazolyl-H), 7.28–8.11 (11H, m, Ph and Py-H); δ_C(75.45 MHz; $CDCl_3$; Me_4Si) 11.42, 107.45, 114.71, 117.86, 120.69, 124.38, 127.31, 128.12, 129.01, 130.50, 137.23, 138.80, 138.94, 139.38, 139.79, 159.24, 159.69, 160.75, 164.34; δ_F(282.38 MHz; $CDCl_3$; $CFCl_3$) −61.17 (s, CF_3); δ_F(282.38 MHz; $CDCl_3$; TFA) 13.88 (s, CF_3); *m*/*z* (FAB$^+$) 381 (M + 1, 100%) 380 (M^+, 28) and 305 (68).

References

1 J. K. Whitesell and M. A. Whitesell, *Synthesis*, 1983, 517; for earlier work, see: D. A. Evans, *J. Am. Chem. Soc.*, 1970, **92**, 7593; G. Wittig, R. Roderer and S. Fischer, *Tetrahedron Lett.*, 1973, 3517.
2 R. T. Courts and A. F. Casy, in *Pyridine and its Derivatives*, Supplement IV, ed. R. A. Abramovitch, Wiley, New York, 1975, p. 445.
3 *Organofluorine Compounds in Medical Applications*, ed. R. Filler, Y. Kobayashi and L. M. Yagupoloskii, Elsevier, Amsterdam, 1993.
4 H. Yoshioka, C. Takayama and N. Matsuo, *J. Synth. Org. Chem. Jpn.*, 1984, **42**, 809.
5 T. Konakahara and K. Sato, *Bull. Chem. Soc. Jpn.*, 1983, **56**, 1241.
6 T. Konakahara and Y. Takagi, *Heterocycles*, 1980, **14**, 393.
7 T. Konakahara and Y. Kurosaki, *J. Chem. Res.*, 1989, (*S*) 130; (*M*) 1068.
8 T. Konakahara, N. Sugama and K. Sato, *Heterocycles*, 1992, **33**, 157.
9 T. Konakahara, M. Hojahmat and K. Sujimoto, *Heterocycles*, 1997, **45**, 271.
10 T. Konakahara, A. Watanabe and K. Sato, *Heterocycles*, 1985, **23**, 383.

11 T. Konakahara, A. Watanabe, K. Maehara, M. Nagata and M. Hojahmat, *Heterocycles*, 1993, **35**, 1171.
12 T. Konakahara, M. Sato, T. Haruyama and K. Sato, *Nippon Kagaku Kaishi*, 1990, 466.
13 O. Tsuge, K. Matsuda and S. Kanemasa, *Heterocycles*, 1983, **20**, 593.
14 M. Hojo, R. Masuda and E. Okada, *Synthesis*, 1986, 1013.
15 D. Mead, R. Loh, A. E. Asato and R. S. H. Liu, *Tetrahedron Lett.*, 1985, **26**, 2873.
16 I. I. Gerus, A. V. Kropachev, M. G. Gorbonova, A. Ya. Ilchenko and V. P. Kukhar, *Ukr. Khim. Zh.* (*Russ. Ed.*), 1993, **59**, 408; *Ukr. Chem. J.* (*Engl. Ed.*), 1993, **59**, 76.
17 W. F. Goure, *J. Heterocycl. Chem.*, 1993, **30**, 71.
18 I. Katsuyama, S. Ogawa, Y. Yamaguchi, K. Funabiki, M. Matsui, H. Muramatsu and K. Shibata, *Synthesis*, 1997, 1321.
19 M. T. Cocco, C. Congiu, V. Onnis, A. M. Bernard and P. P. Piras, *J. Heterocycl. Chem.*, 1997, **34**, 1283.

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