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Formation and dehydration of a series of 5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazoles

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Abstract

Reaction of five (3-oxo-4,4,4-trifluorobutanoyl)heterocycles with hydrazine hydrate under mild conditions gave the corresponding 3-heterocyclyl-5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazoles. Thermal elimination of water from the 3-(thien-2-yl), 3-(pyridin-2-yl) and 3-(pyridin-4-yl) compounds readily gave the corresponding pyrazoles but acid catalysis was required to form 3-(benzothiazol-2-yl)-5-trifluoromethylpyrazole and 3-(1-methylbenzimidazol-2-yl)-5-trifluoromethylpyrazole. More forcing conditions were required for the analogous dehydration/aromatisations giving 3,5-bis(trifluoromethyl)-1-(4-nitrophenyl)pyrazole and 3,5-bis(trifluoromethyl)-1-pentafluorophenylpyrazole.

Keywords: 5-Hydroxy-5-trifluoromethyl-4,5-dihydropyrazole; 5-Trifluoromethylpyrazole; Dehydration

1. Introduction

We recently reported [1] our studies on the mechanism and regioselectivity of the reaction of hydrazinoquinolines with a range of trifluoromethyl β-diketones, specifically 1,1,1-trifluoropentane-2,4-dione, 1,1,1-trifluoro-4-phenylbutane-2,4-dione and 1,1,1-trifluoro-4-(thien-2-yl)butane-2,4-dione (**2e**). Regioselectivity, but not regiospecificity, was noted in that 2-hydrazino-4-methylquinoline was predominantly added initially at the carbonyl carbon (or the corresponding enol carbon) remote from the CF_3 group, although minor amount of products derived from attack at the trifluoromethyl ketone carbonyl were isolated. Interestingly, the intermediate 5-substituted 3-hydroxy-1-(4-methylquinolin-2-yl)-3-trifluoromethyl-4,5-dihydropyrazoles could not be isolated as water was eliminated rapidly under the reaction conditions (boiling ethanol) to give the minor products, the 5-substituted 1-(4-methylquinolin-2-yl)-3-trifluoromethylpyrazoles. In contrast, the 3-substituted 5-hydroxy-1-(4-methylquinolin-2-yl)-5-trifluoromethyl-4,5-dihydropyrazoles were resistant to elimination of water under these conditions and treatment with sulphuric acid in boiling acetic acid was necessary for conversion to the 3-substituted 1-(4-methylquinolin-2-yl)-5-trifluoromethylpyrazoles. These [1] and other observations [2–5] concerning the reaction of (substituted)hydrazines with trifluoromethyl β-diketones suggest that the final elimination of water from 5-hydroxy-4,5-dihydropyrazoles to form pyrazoles is dependent on the electronic nature of the 5-substituent and of any 1-substituent present. We now report the results of our studies on the conditions required to effect this elimination in seven additional 5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazoles.

2. Results and discussion

We sought to prepare a range of 5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazoles as substrates for investigations of methods and ease of dehydration to the corresponding trifluoromethylpyrazoles. Whereas most of the starting trifluoromethyl β-diketones **2c**–**2f** were commercially available, the benzothiazol-2-yl analogue **2a** and the 1-methylbenzimidazol-2-yl analogue **2b** were prepared by Claisen condensation of ethyl trifluoroacetate with 2-acetylbenzothiazole **1a** and 2-acetyl-1-methylbenzimidazole **1b**, respectively. Treatment of **2a** with hydrazine hydrate in ethanol at ambient temperature gave exclusively the 3-aryl-5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazole **3a**

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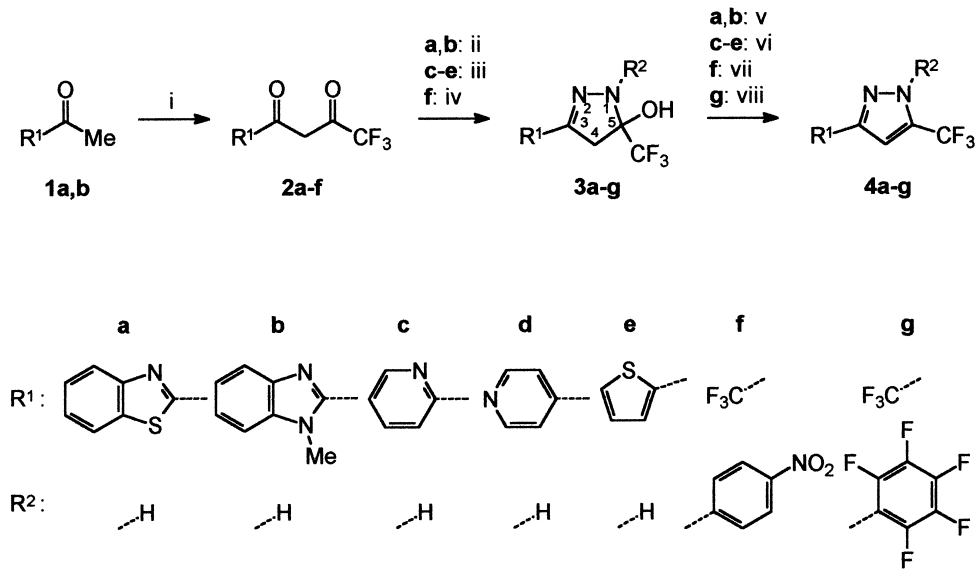
in high yield with no evidence for formation of the other regioisomer formally derived from initial attack at the trifluoromethyl ketone. A similar reaction of **2b** with ethanolic hydrazine hydrate gave exclusively the analogous 3-aryl-5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazole **3b**. Modification of the reaction conditions was necessary to achieve high yields of the 3-aryl-5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazoles **3c–3e** from the trifluoromethyl β-diketones **2c–2e** bearing pyridine or thiophene as substituent. In these cases, small quantities of the corresponding aromatic pyrazoles **4c–4e** were formed when the condensations were conducted in ethanol but replacement of the solvent with diethyl ether allowed clean conversion of **2c–2e** with hydrazine hydrate to the 3-aryl-5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazoles **3c–3e**. In contrast, as we reported previously [5], prolonged treatment of hexafluoropentane-2,4-dione **2f** at elevated temperature was necessary to effect condensation with hydrazines bearing deactivating nitrophenyl and pentafluorophenyl groups giving the 1-aryl-5-hydroxy-3,5-bis(trifluoromethyl)-4,5-dihydropyrazoles **3f** and **3g**. No dehydration to the 1-aryl-3,5-bis(trifluoromethyl)pyrazoles **4f** and **4g** was observed even in boiling ethanol (Scheme 1).

The dihydropyrazoles were identified by ^{1}H and ^{13}C NMR spectroscopy and by other techniques as appropriate. For example, the ^{1}H NMR spectrum of **3a** displayed the dihydropyrazole 4-CH_2 protons as an AB system (doublets at δ_A 3.34 and δ_B 3.51, with the geminal coupling constant $^{2}J = 18.3$ Hz), which corresponds with our previous observations for 1-aryl-5-hydroxy-3,5-bis(trifluoromethyl)-4,5-dihydropyrazoles [5]. Further support for the structure of **3a** was provided by the ^{13}C NMR spectrum which contained signals at δ 40.73 and δ 91.53 for dihydropyrazole 4-C and 5-C, respectively, with the latter showing 2-bond coupling to fluorine ($^{2}J_{C\text{-}F} = 30.9$ Hz). Finally, the ^{19}F spectrum showed a signal at δ −76.03, which is typical for CF_3 attached to an sp^3 carbon [1,5,6].

The hydroxydihydropyrazoles **3a–3g** were dehydrated to the corresponding pyrazoles **4a–4g** under a variety of conditions. Water was easily eliminated from **3c–3e** by heating in ethanol as previously reported for **3c** [7]. In contrast, the dehydration of **3a** and **3b** required the presence of acetic acid in the solvent mixture. The 5-hydroxy-3,5-bis(trifluoromethyl)-4,5-dihydropyrazoles **3f** and **3g**, which also carry electron-deficient aryl substituents at nitrogen, required much more vigorous conditions. Prolonged treatment of the *N*-mononitrophenyl compound **3f** with hydrochloric acid in boiling ethanol afforded the pyrazole **4f** in good yield but even these conditions failed to effect elimination of water from the *N*-pentafluorophenyl compound **3g**. In this case, it was necessary the acetylate the OH with acetic anhydride and carry out the one-pot elimination in boiling acetic acid to form **4g**. The ^{1}H NMR spectrum of **4a** exhibits a singlet at δ 7.71 for the aromatic pyrazole 4-H. The aromatic pyrazole is also confirmed by the observation of ^{13}C NMR signals at δ 140.30, δ 104.73 and δ 141.61 for 3-C, 4-C and 5-C, respectively. Assignment of 5-C was possible, since it resonates as a quartet, with $^{2}J_{C\text{-}F}$=38.1 Hz. Furthermore, the ^{19}F NMR spectrum showed a singlet at δ −57.35 for the trifluoromethyl group, a chemical shift consistent with those reported for other 5-trifluoromethylpyrazoles [1,5].

It is evident, when ranking the ease of elimination of water from **3a–3g** to form the pyrazoles **4a–4g** (**3c–3e**> **3a**,**3b**>**3f**>**3g**), that the presence of electron-withdrawing groups at the dihydropyrazole 5-C, the 3-C or the 1-N



Scheme 1. Formation of 3-substituted 5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazoles and different methods for dehydration to 3-substituted 5-trifluoromethylpyrazoles. *Reagents*: i, EtO_2CCF_3, NaOMe, Et_2O; ii, N_2H_4, EtOH; iii, N_2H_4, Et_2O; iv, R^2NHNH_2, EtOH, △; v, AcOH, EtOH, △; vi, conc. H_2SO_4, EtOH, △; vii, HCl, aq. EtOH, △; viii, Ac_2O, AcOH, △.

inhibits this process. The electron-withdrawing CF_3 group at position 5 would destabilise any carbocation character in an *E*1-like mechanism as shown by the much greater ease of elimination from 3-hydroxy-1-(4-methylquinolin-2-yl)-3-trifluoromethyl-4,5-dihydropyrazoles than from 3-substituted 5-hydroxy-1-(4-methylquinolin-2-yl)-5-trifluoromethyl-4,5-dihydropyrazoles [1]. Inhibition of elimination by the lowering of the electron density at 1-N can be rationalised similarly, comparing the formation of **4g** with that of **4f** and that of 3,5-bis(trifluoromethyl)pyrazole [5]. The origin of the observed inhibition of elimination by the bicyclic benzothiazol-2-yl (**3a**→**4a**) and 1-methylbenzimidazol-2-yl (**3b**→**4b**) substituents at position 3 is less clear but may involve the influence of this substituent on the acidity of the pyrazole 4-CH_2 protons.

3. Experimental details

Melting points were measured on samples in open capillaries in a Mel-Temp apparatus and are uncorrected. ^{1}H NMR spectra were obtained at 270, 300 and 400 MHz, ^{13}C spectra at 67.5, 75 and 100 MHz and ^{19}F spectra at 376 MHz using Jeol GX270, Bruker 300 and Jeol EX400 instruments, respectively, using $CDCl_3$ as solvent, unless otherwise noted. The internal standard for the ^{19}F spectra was $CFCl_3$, setting the $CF^{35}Cl_3$ signal as δ 0.00. Solvents were evaporated under reduced pressure. The stationary phase for chromatography was silica gel. High resolution mass spectra were measured on VG 7070 and Kratos MS-50 spectrometers. Elemental analyses were performed at RSIC, Chandigarh, India. 3,5-Bis(trifluoromethyl)-5-hydroxy-1-(4-nitrophenyl)-4,5-dihydropyrazole **3f** and 3,5-bis(trifluoromethyl)-5-hydroxy-1-(pentafluorophenyl)-4,5-dihydropyrazole **3g** were prepared as previously described by us [5].

*2-(3-Oxo-4,4,4-trifluorobutanoyl)benzothiazole (***2a**). Ethyl trifluoroacetate (3.22 ml, 27 mmol) was added dropwise to a stirred suspension of sodium methoxide (1.60 g, 30 mmol) in dry diethyl ether. 2-Acetylbenzothiazole **1a** (4.80 g, 27 mmol) was added and the mixture was stirred for 16 h. The solvent was evaporated and the residue in water (30 ml) was acidified with sulphuric acid (10% aq.). The mixture was extracted thrice with chloroform. The combined extracts were dried (Na_2SO_4) and the solvent was evaporated to give **2a** (3.7 g, 50%) as a white solid, m.p. 86–88°C. MS (EI) *m/z*: 273.0072 (M) ($C_{11}H_6F_3NO_2S$ requires 273.0072), 204 (M – CF_3), 162 (M – CH_2COCF_3), 134 (M – $COCH_2COCF_3$).

*2-(3-Oxo-4,4,4-trifluorobutanoyl)-1-methylbenzimidazole (***2b**). 1-Methylbenzimidazole **1b** was treated with ethyl trifluoroacetate and sodium methoxide, as for the synthesis of **2a**, to give **2b** (34%) as a white solid, m.p. 118–120°C. MS (EI) *m/z*: 270.0611 (M) ($C_{12}H_9F_3N_2O_2$ requires 270.0617), 201 (M – CF_3), 159 (M – CH_2COCF_3), 132 (M – $COCH_2COCF_3$).

*3-(Benzothiazol-2-yl)-5-hydroxy-5-trifluoromethyl-4,5-dihydropyrazole (***3a**). Compound **2a** (819 mg, 3 mmol) was added dropwise to hydrazine hydrate (170 μl, 3.5 mmol) in ethanol (10 ml) and the mixture was stirred for 2 h. The solvent was evaporated and the solid was washed with water and dried to give **3a** (650 mg, 76%) as a white solid, m.p. 188°C. ^{1}H NMR ($(CD_3)_2SO$) δ: 3.34 (d, 1H, J=18.3 Hz, pyrazole 4-H), 3.51 (d, 1H, J=18.3 Hz, pyrazole 4-H), 7.43 (t, 1H, J=8.3 Hz, benzothiazole 6-H), 7.49 (t, 1H, J=8.3 Hz, benzothiazole 5-H), 7.64 (s, 1H, NH), 8.00 (d, 1H, J=7.6 Hz, benzothiazole 7-H), 8.08 (d, 1H, J=7.6 Hz, benzothiazole 7-H), 8.99 (s, 1H, OH) ppm. ^{13}C NMR ($(CD_3)_2SO$) δ: 40.73 (pyrazole 4-C), 91.53 (q, J_{C-F} =30.9 Hz, pyrazole 5-C), 122.25 (benzothiazole 7-C), 122.80 (benzothiazole 4-C), 123.76 (q, J_{C-F}=283.4 Hz, CF_3), 125.95 (benzothiazole 6-C), 126.51 (benzothiazole 5-C), 133.95 (benzothiazole 7a-C), 143.27 (pyrazole 3-C), 152.99 (benzothiazole 3a-C), 161.03 (benzothiazole 2-C) ppm. ^{19}F NMR ($(CD_3)_2SO$) δ: −76.03 (CF_3) ppm. Analysis: Found: N, 14.40%. $C_{11}H_8F_3N_3OS$ requires: N, 14.63%.

*5-Hydroxy-3-(1-methylbenzimidazol-2-yl)-5-trifluoromethyl-4,5-dihydropyrazole (***3b**). Compound **2b** was treated with hydrazine, as for the synthesis of **3a**, to give **3b** (74%) as a white solid, m.p. 194°C. ^{1}H NMR ($CDCl_3$+$(CD_3)_2SO$) δ: 3.36 (d, 1H, J=18.2 Hz, pyrazole 4-H), 3.54 (d, 1H, J=18.0 Hz, pyrazole 4-H), 4.09 (s, 3H, Me), 7.21–7.28 (m, 2H, benzimidazole 5,6-H_2), 7.41 (dd, 1H, J=7.2 and 2.3 Hz, benzimidazole 4-H), 7.61 (dd, 1H, J=7.4 and 2.3 Hz, benzimidazole 7-H), 8.05 (s, 1H, NH) ppm. ^{13}C NMR ($CDCl_3$+$(CD_3)_2SO$) δ: 31.73 (Me), 42.42 (pyrazole 4-C), 91.05 (q, J_{C-F}=31.1 Hz, pyrazole 5-C), 109.34 (benzimidazole 7-C), 119.04 (benzimidazole 4-C), 121.91 (benzimidazole 5-C), 123.07 (benzimidazole 6-C), 125.37 (q, J_{C-F} =272.5 Hz, CF_3), 136.23 (benzimidazole 7a-C), 141.83 (pyrazole 3-C), 144.93 (benzimidazole 3a-C), 149.313 (benzimidazole 2-C) ppm. ^{19}F NMR ($(CD_3)_2SO$) δ: −78.20 (CF_3) ppm. Analysis: Found: N, 19.42%. $C_{12}H_{11}F_3N_4O$ requires: N, 19.71%.

*5-Hydroxy-3-(pyridin-2-yl)-5-trifluoromethyl-4,5-dihydropyrazole (***3c**). Hydrazine hydrate (130 mg, 2.7 mmol) was added dropwise to **2c** [6] (500 mg, 2.3 mmol) in diethyl ether (40 ml) and the mixture was stirred at ambient temperature for 3.5 h. The solvent was evaporated and the residue was treated with water. Filtration and drying gave **3c** (415 mg, 78%) as a white solid, m.p. 152°C. ^{1}H NMR ($CDCl_3$+$(CD_3)_2SO$) δ: 3.40 (br s, 2H, pyrazole 4-H_2), 7.25 (m, 1H, pyridine 5-H), 7.70 (m, 1H, pyridine 3-H), 7.94 (d, 1H, J=8.0 Hz, pyridine 4-H), 8.55 (d, 1H, J=7.2 Hz, pyridine 6-H) ppm. ^{13}C NMR ($CDCl_3$+$(CD_3)_2SO$) δ: 40.86 (pyrazole 4-C), 91.22 (q, J_{C-F}=31.2 Hz, pyrazole 5-C), 119.77 (pyridine 3-C), 120.80 (q, J_{C-F}=269.7 Hz, CF_3), 122.86 (pyridine 5-C), 135.73 (pyridine 4-C), 148.56 (pyridine 6-C), 149.92 (pyridine 2-C), 150.85 (pyrazole 3-C) ppm. ^{19}F NMR ($CDCl_3$+$(CD_3)_2SO$) δ: −76.7 (s) ppm. Analysis: Found: N, 18.32%. $C_9H_8F_3N_3O$ requires: N, 18.18%.

*5-Hydroxy-3-(pyridin-4-yl)-5-trifluoromethyl-4,5-dihydropyrazole (***3d**). Compound **2d** [6] was treated with hydrazine, as for the synthesis of **3c**, to give **3d** (72%) as a white solid, m.p. 172°C. ^{1}H NMR ($CDCl_3$+$(CD_3)_2SO$) δ: 3.24 (d, 1H, J=17.8 Hz, pyrazole 4-H), 3.28 (d, 1H, J=18.0 Hz, pyrazole 4-H), 7.51 (d, 2H, J=8.2 Hz, pyridine 3,5-H_2), 8.56 (d, 2H, J=8.1 Hz, pyridine 2,6-H_2) ppm. ^{19}F NMR ($CDCl_3$+$(CD_3)_2SO$) δ: −76.9 (s) ppm. Analysis: Found: N, 17.92%. $C_9H_8F_3N_3O$ requires: N, 18.18%.

*5-Hydroxy-3-(thien-2-yl)-5-trifluoromethyl-4,5-dihydropyrazole (***3e**). 2-(3-Oxo-4,4,4-trifluorobutanoyl)thiophene (**2e**) was treated with hydrazine, as for the synthesis of **3c**, to give **3e** (84%) as a white solid, m.p. 148°C. ^{1}H NMR ($CDCl_3$+$(CD_3)_2SO$) δ: 3.19 (d, 1H, J=17.3 Hz, pyrazole 4-H), 3.40 (d, 1H, J=17.3 Hz, pyrazole 4-H), 7.02 (dd, 1H, J=3.2 and 1.2 Hz, thiophene 3-H), 7.15 (dd, 1H, J=5.0 and 3.6 Hz, thiophene 4-H), 7.31 (dd, 1H, J=5.0 and 1.0 Hz, thiophene 5-H). ^{13}C NMR ($CDCl_3$+$(CD_3)_2SO$) δ: 42.18 (pyrazole 4-C), 91.51 (q, J_{C-F}=31.2 Hz, pyrazole 5-C), 122.50 (q, J_{C-F}=268.2 Hz, CF_3), 126.87 (thiophene 4,5-C_2), 127.30 (thiophene 3-C), 135.43 (thiophene 2-C), 145.68 (pyrazole 3-C). ^{19}F NMR ($CDCl_3$+$(CD_3)_2SO$) δ: −77.5 (s) ppm. Analysis: Found: N, 11.43%. $C_8H_7F_3N_2OS$ requires: N, 11.86%.

*3-(Benzothiazol-2-yl)-5-trifluoromethylpyrazole (***4a**). Compound **3a** (500 mg, 1.7 mmol) was boiled under reflux in ethanol (40 ml) and acetic acid (10 ml) for 5 h. The ethanol was evaporated. The residue was neutralised with sodium hydrogen carbonate and was extracted with chloroform (3×20 ml). Evaporation and chromatography (ethyl acetate/hexane 1:4) gave **4a** (350 mg, 74%) as a white solid, m.p. 188°C. ^{1}H NMR ($CDCl_3$+$(CD_3)_2SO$+CF_3CO_2H) δ: 7.17 (s, 1H, pyrazole 4-H), 7.40 (t, 1H, J=7.3 Hz, benzothiazole 6-H), 7.48 (t, 1H, J=7.1 Hz, benzothiazole 5-H), 7.98 (d, 1H, J=7.8 Hz, benzothiazole 7-H), 7.99 (d, 1H, J=7.6 Hz, benzothiazole 4-H), 14.66 (s, 1H, NH) ppm. ^{13}C NMR ($CDCl_3$+$(CD_3)_2SO$+CF_3CO_2H) δ: 104.73 (pyrazole 4-C), 121.50 (q, J_{C-F}=267.7 Hz, CF_3), 122.51 (benzothiazole 7-C), 123.48 (benzothiazole 4-C), 126.39 (benzothiazole 6-C), 127.19 (benzothiazole 5-C), 139.09 (benzothiazole 7a-C), 140.30 (pyrazole 3-C), 141.61 (q, J_{C-F}=38.1 Hz, pyrazole 5-C), 153.73 (benzothiazole 3a-C), 157.04 (benzothiazole 2-C) ppm. ^{19}F NMR ($CDCl_3$+$(CD_3)_2SO$+CF_3CO_2H) δ: −57.35 (s, CF_3) ppm. Analysis: Found: N, 15.10%. $C_{11}H_6F_3N_3S$ requires: N, 15.61%.

*3-(1-Methylbenzimidazol-2-yl)-5-trifluoromethylpyrazole (***4b**). Compound **3b** was boiled under reflux in ethanol and acetic acid, as for the synthesis of **4b**, to give **4b** (80%) as a white solid, m.p. 215°C. ^{1}H NMR (($CD_3)_2SO$) δ: 4.02 (s, 3H, Me), 7.34 (m, 2H, benzimidazole 5,6-H_2), 7.47 (s, 1H, pyrazole-H), 7.72 (m, 2H, benzimidazole 4,7-H_2) ppm. ^{19}F NMR (($CD_3)_2SO$) δ: −60.33 (s, CF_3) ppm. Analysis: Found: N, 20.62%. $C_{12}H_9F_3N_4$ requires: N, 20.03%.

*3-(Pyridin-2-yl)-5-trifluoromethylpyrazole (***4c**). Compound **3c** (300 mg, 1.3 mmol) was boiled under reflux in ethanol (30 ml) in the presence of conc. sulphuric acid (100 μl) for 30 min. Evaporation and chromatography (ethyl acetate/hexane 1:5) gave **4c** (200 mg, 72%) as a white solid, m.p. 132°C (lit. [6] m.p. 137–138°C).

*3-(Pyridin-2-yl)-5-trifluoromethylpyrazole (***4d**). Compound **3d** was boiled with conc. sulphuric acid in ethanol, as for the synthesis of **4c**, to give **4d** (72%) as a white solid, m.p. 190°C (lit. [6] m.p. 190°C).

*3-(Thien-2-yl)-5-trifluoromethylpyrazole (***4e**). Compound **3e** was boiled with conc. sulphuric acid in ethanol, as for the synthesis of **4c**, to give **4e** (88%) as a white solid, m.p. 116–117°C (lit. [8] m.p. 118–120°C).

*3,5-Bis(trifluoromethyl)-1-(4-nitrophenyl)pyrazole (***4f**). 3,5-Bis(trifluoromethyl)-4,5-dihydro-5-hydroxy-1-(4-nitrophenyl)pyrazole (**3f**) [5] (100 mg, 290 μmol) was boiled under reflux with conc. aq. hydrochloric acid (0.5 ml) in ethanol (10 ml) for 3 d. The solvent was evaporated. The residue, in dichloromethane, was dried ($MgSO_4$+$NaHCO_3$). Evaporation of the solvent gave **4f** (90 mg, 96%) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ: 7.18 (s, 1H, pyrazole-H), 7.77 (d, 2H, J=8.9 Hz, Ar 2,6-H_2), 8.42 (d, 2H, J=8.9 Hz, Ar 3,5-H_2) ppm. ^{13}C NMR ($CDCl_3$) δ: 108.40 (pyrazole 4-C), 118.74 (q, J_{C-F}=270 Hz, CF_3), 120.04 (q, J_{C-F}=270 Hz, CF_3), 124.84 (Ar 2,6-C_2), 126.32 (Ar 3,5-C_2), 134.50 (q, J_{C-F}=40 Hz, C-CF_3), 142.73 (Ar 4-C), 144.04 (q, J_{C-F}=40 Hz, C-CF_3), 148.36 (Ar 1-C) ppm. ^{19}F NMR ($CDCl_3$) δ: −63.18 (s, 3F, CF_3), −58.07 (s, 3F, CF_3) ppm. MS (EI) *m/z*: 325.0288 (M) (100) ($C_{11}H_5N_3F_6O_2$ requires 325.0286).

*3,5-Bis(trifluoromethyl)-1-(pentafluorophenyl)pyrazole (***4g**). 3,5-Bis(trifluoromethyl)-4,5-dihydro-5-hydroxy-1-(pentafluorophenyl)pyrazole (**3g**) [5] (850 mg, 2.2 mmol) was boiled under reflux in acetic anhydride (20 ml) and acetic acid (15 ml) for 16 h. The solvents were evaporated. The residue in dichloromethane (50 ml) was stirred with saturated aqueous sodium hydrogen carbonate (50 ml) for 1 h. The organic phase was separated and dried ($MgSO_4$). Evaporation of the solvent gave **4g** (230 mg, 28%) as a yellow oil. ^{1}H NMR ($CDCl_3$) δ: 7.17 (s) ppm. ^{19}F NMR ($CDCl_3$) δ: −159.84 (m, 2F, Ar 3,5-F_2), −147.30 (m, 1F, Ar 4-F), −144.45 (m, 2F, Ar 2,6-F_2), −63.49 (s, 3F, CF_3), −61.71 (s, 3F, CF_3) ppm. MS (EI) *m/z*: 369.9957 (M) (100) ($C_{11}HF_{11}N_2$ requires 369.9964).

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