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Facile synthesis of novel CF_3-substituted ring-fused furo[2,3-*c*]pyrazoles through $Rh_2(OAc)_4$ catalyzed [3+2] cycloaddition of 4-diazo-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one with aromatic alkynes

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ABSTRACT

The $Rh_2(OAc)_4$ catalyzed [3+2] cycloaddition of 4-diazo-1-phenyl-3-(trifluoromethyl)-1*H*-pyrazol-5(4*H*)-one with aromatic alkynes was studied, and this protocol can be efficiently applied to the synthesis of the novel CF_3-substituted ring-fused furo[2,3-*c*]pyrazoles.

1. Introduction

Pyrazoles, one of the most valuable *N*-heterocyclic compounds, attract attentions due to their wide range of pharmacological proprieties.[1] They are present in leading drugs, such as Viagra[1a] and Celebrex,[1b] therefore, are considered very important for pharmaceutical industries. Pyrazolo[3,4-*d*]pyrimidines of type A (Fig. 1) show inhibition properties towards Src in a cell-free assay, as well as antiproliferative activity towards the epidermoid (A431) and breast cancer (BC-8701) cell line.[2] Thieno[2,3-*c*]pyrazoles B (Fig. 1) are an important class of potent kinase inhibitors.[3] Furo[2,3-*c*]pyrazoles C (Fig. 1) are an important structural unit of cyanine dyes[4] and have been screened in vitro for antibacterial and antifungal activities.[5] It is well known that, the introduction of fluorine atoms into a medicinal molecule can often bring some unpredictable influence on its bioactivity.[6] But, how to efficiently and selectively introduce the fluorine-containing group into the ring-fused structure is an often met problem. Therefore, the preparation of pyrazole-fused ring derivatives is very important and challenging from a synthetic point of view.

α-Diazocarbonyl compounds have been extensively studied for their synthetic applications over the last few decades.[7] They are recognized as important precursor in synthetic organic chemistry for highly reactive metal carbenoids, particularly with copper[8] and rhodium.[9]The Rh(II)-catalyzed reactions have been well-established as powerful approaches to generate Rh(II) carbene species, which promote a number of unique transformations including addition,[10] C–H insertion[11] and ylide formation.[12] Despite a number of synthetic methods available for ring-fused pyrazoles,[13] few studies using α-diazocarbonyl compounds in the synthesis of CF_3-substituted ring-fused pyrazoles have also been reported.[14]

Our research group has a long-standing interest in exploring the reaction of CF_3-substituted diazocompounds.[15] Herein, we wish to report a method for the synthesis of CF_3-substituted ring-fused furopyrazoles based on Rh catalyzed [3+2] cycloaddition of CF_3-substituted diazocarbonyl compound with aromatic alkynes (in Scheme 1).

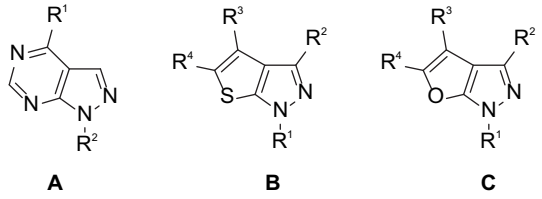

Fig. 1. Ring-fused pyrazoles **A**–**C**.

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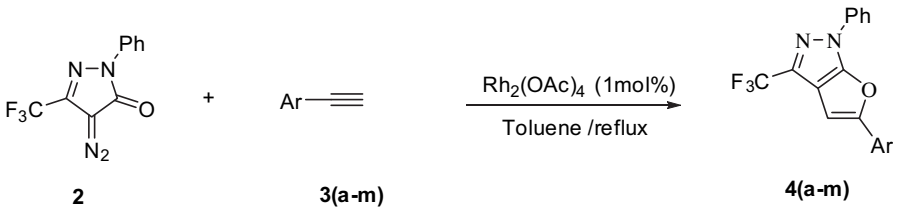


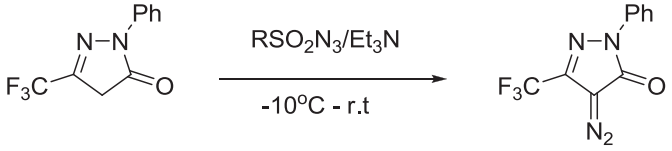
Scheme 1. Rh catalyzed diazocompound with aromatic alkynes.

2. Results and discussions

Starting material **2** was prepared by diazo-transfer reaction from the corresponding 1-*phenyl*-3-*trifluoromethyl*-2-*pyrazolin*-5-*one* **1**.[16] Initially, We set out to improve the yield by screening several diazo transfer reagents and solvents (Table 1). Whereas arylsulfonyl azides, such as *p*-tuoluenesulfonyl azide and *p*-nitrobenzenesulfonyl azide resulted in poor yields (Table 1, entries 1 and 2) and require longer time, polyfluoroalkanesulfonyl azides gave improved yields and efficiency (Table 1, entries 3, 4 and 5). Also, solvents screening identified that dichloromethane is the best solvent for this transformation.

Secondly, we optimized conditions for the Rh catalyzed [3+2] cycloaddition. Under nitrogen, the reaction of CF_3-substituted diazocompound (**2**) with phenylacetylene (**3a**) was systematically examined under different reaction conditions, which was outlined in Table 2. It was found that 1 mol % $Rh_2(OAc)_4$ was effective to catalyze this reaction. Among several solvents examined, toluene was turned out to be the best one.

Table 1
Optimization of diazo-transfer reaction[a]



1 2

Entry	R	Time	Solvent	Yield[b] (%)
1	*p*-$CH_3C_6H_4$	1.5 h	CH_2Cl_2	47
2	*p*-$NO_2C_6H_4$	1.5 h	CH_2Cl_2	56
3	$I(CF_2)_2O(CF_2)_2$	8 min	CH_2Cl_2	89
4	C_4F_9	8 min	CH_2Cl_2	91
5	$Cl(CF_2)_4$	8 min	CH_2Cl_2	87
6	$I(CF_2)_2O(CF_2)_2$	8 min	Et_2O	83
7	$I(CF_2)_2O(CF_2)_2$	8 min	CH_3CN	86
8	$I(CF_2)_2O(CF_2)_2$	8 min	THF	79

[a] Molar ratio of **1**: diazo transfer reagent: Et_3N=1:1:1.
[b] Isolated yield.

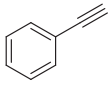
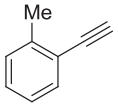
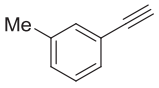
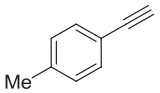
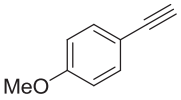
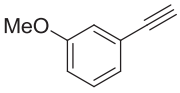
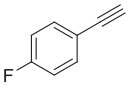
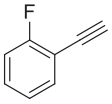
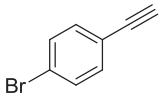
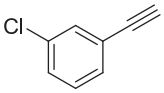
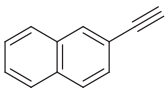
Table 2
Screening the reaction conditions[a]

Entry	Cat. (mol %)	Solvent	Temp	Time (h)	Yield[b] (%)
1	—	Toluene	Reflux	8	—
2	$Rh_2(OAc)_4$ (1)	CH_2Cl_2	Reflux	16	38
3	$Rh_2(OAc)_4$ (1)	Et_2O	Reflux	11	29
4	$Rh_2(OAc)_4$ (1)	Toluene	Reflux	8	82
5	$Rh_2(OAc)_4$ (1)	CH_3CN	Reflux	15	10
6	$Rh_2(OAc)_4$ (1)	THF	Reflux	20	—
7	$Rh_2(OAc)_4$ (1)	1,4-Dioxane	Reflux	20	27
8	$Rh_2(OAc)_4$ (1)	Benzene	Reflux	12	43
9	$Rh_2(OAc)_4$ (1)	$HCCl_3$	Reflux	15	47
10	$Rh_2(OAc)_4$ (1)	$ClCH_2CH_2Cl$	Reflux	10	25
11	$Rh_2(OAc)_4$ (2)	Toluene	Reflux	6	85

[a] Molar ratio of **2**/**3a**=1:1.
[b] Isolated yield.

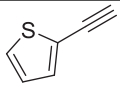
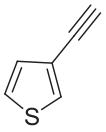
With the optimized reaction condition in hand (Table 2, entry 4), a series of aromatic alkynes (**3a**–**m**) were subjected to diazocompound **2** in the presence of $Rh_2(OAc)_4$ to synthesize the corresponding CF_3-substituted ring-fused furo[2,3-*c*]-pyrazoles (**4a**–**m**) in good yields. All the results are summarized in Table 3. The structure of these novel CF_3-substituted ring-fused heterocycles are fully characterized by spectral methods. For the compound **4j**, it was further confirmed by X-ray diffraction analysis (in Fig. 2).

Table 3
Rh catalyzed [3+2] cycloaddition of **2** with **3**

Entry	3	Time (h)	4	Yield[a] (%)
1	 **3a**	8	**4a**	82
2	 **3b**	8	**4b**	56
3	 **3c**	8	**4c**	75
4	 **3d**	8	**4d**	97
5	 **3e**	8	**4e**	50
6	 **3f**	8	**4f**	72
7	 **3g**	8	**4g**	61
8	 **3h**	8	**4h**	57
9	 **3i**	8	**4i**	69
10	 **3j**	8	**4j**	72
11	 **3k**	8	**4k**	66

(*continued on next page*)

Table 3 (*continued*)

Entry	3	Time (h)	4	Yield[a] (%)
12	 3l	8	**4l**	89
13	 3m	8	**4m**	57

[a] Isolated yield.

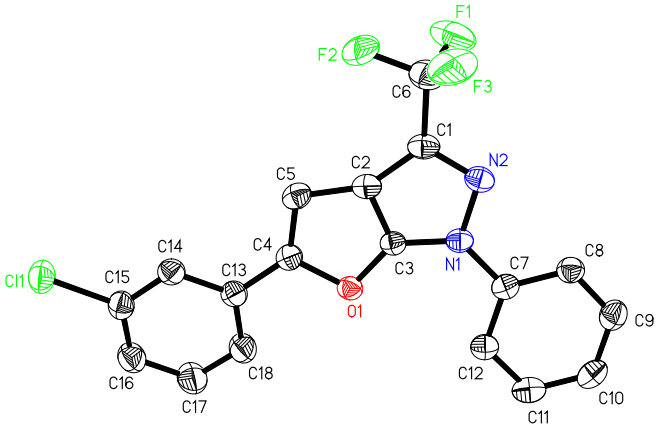


Fig. 2. X-ray crystal structure of **4j**.

3. Conclusions

In summary, we developed a convenient method for preparation of novel CF_3-substituted ring-fused furo[2,3-*c*]pyrazoles through $Rh_2(OAc)_4$ catalyzed [3+2] cycloaddition of diazocarbonyl compounds with aromatic alkynes. They are important structural units in pigments and dyes with remarkable biological activities and useful building blocks in organic synthesis. Therefore, applications in medicinal chemistry call for other studies, which will be reported in due course.

4. Experimental section

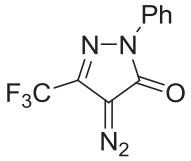
4.1. General remarks and methods

Melting points were measured in Temp-Melt apparatus and uncorrected, ^1H and ^{19}F NMR spectra were recorded in $CDCl_3$ on Bruker AM-300 or AM-400 instruments with Me_4Si and $CFCl_3$ (with upfield negative) as the internal and external standards, respectively. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Lower resolution mass spectra or high-resolution mass spectra (HRMS) were obtained on a FinniganMAT-8430 instrument using the electron impact ionization technique (70 eV). X-ray diffraction crystal structure analysis was obtained on Bruker P4 instrument. All reaction as well as column chromatography were monitored routinely with the aid of TLC or ^{19}F NMR spectroscopy.

4.2. General procedure for the synthesis of compounds 2

Et_3N (1.0 equiv) was added by a syringe pump dropwise to the solution of 1-phenyl-3-trifluoromethyl-2-pyrazolin-5-one **1** (1.0 equiv) and $I(CF_2)_2O(CF_2)_2SO_2N_3$ (1.0 equiv) in CH_2Cl_2 at −10 °C. The resulting deep red-coloured solution was stirred for 8 min at −10 °C and then slowly brought to room temperature. The solvent was then removed under reduced pressure and the crude material was purified by flash chromatography.

*4.2.1. 4-Diazo-1-phenyl-3-(trifluoromethyl)-1H-pyrazol-5(4H)-one (**2**).*

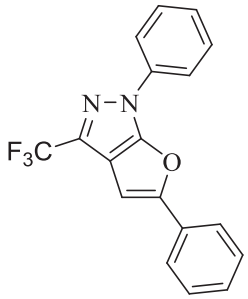


Orange solid; Mp: 98–99 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=7.86 (d, J=8.4 Hz, 2H), 7.45 (t, J=7.8 Hz, 2H), 7.26–7.32 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ=−63.76 (s, CF_3). ^{13}C NMR (100 MHz, CDCl3): δ=161.7, 137.5, 132.3 (q, $^2J_{CF3}$=40.8 Hz), 129.0, 126.6, 119.8, 118.6 (q, $^1J_{CF3}$=266.9 Hz). IR (KBr): ν=2146, 1702, 1594, 1540, 1480, 1364, 1299, 1196, 1147, 988, 913, 823, 758, 723, 690. MS: m/z(%)=254 (M^+, 76), 228 (10), 105 (17), 77 (100), 51 (17). HRMS (EI) calcd for $C_{10}H_5F_3N_4O$: 254.0415; found: 254.0415.

4.3. General procedure for the synthesis of compounds 3

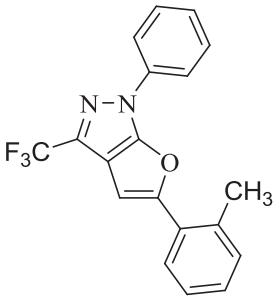
Under nitrogen atmosphere, to a dry Schlenk tube containing $Rh_2(OAc)_4$ (4 mg, 1 mol %), phenylacetylenes **1** (1.2 equiv) and toluene (5 mL), a solution of CF_3-substituted diazocompound **2** (254 mg, 1 mmol) in 2 mL toluene was added by a syringe pump. After addition, the reaction mixture was stirred at reflux temperature for about 8 h, until the starting material of CF_3-substituted diazocompound disappeared while monitoring by TLC. The solvent was removed in vacuum and the residue was purified on silica gel using petroleum ether/ethyl acetate (20:1) as eluent to afford the corresponding products.

*4.3.1. 1,5-Diphenyl-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4a**).*



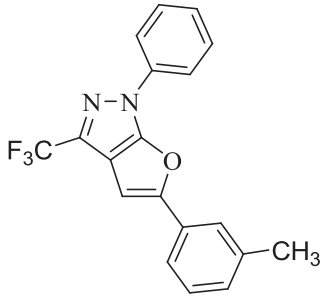
White solid; Mp: 157–158 °C. ^1H NMR (300 MHz, $CDCl_3$): δ=8.00 (d, J=8.1 Hz, 2H), 7.76 (d, J=7.8 Hz, 2H), 7.56 (t, J=7.1 Hz, 2H), 7.47 (t, J=7.1 Hz, 2H), 7.36–7.40 (m, 2H), 6.90 (s, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−61.84 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=159.0, 154.6, 137.3, 131.8 (q, $^2J_{CF3}$=40.1 Hz), 129.9, 129.6, 128.9, 128.7, 127.0, 124.1, 121.0 (q, $^1J_{CF3}$=266.9 Hz), 118.2, 112.0 (m, $^3J_{CF3}$=2.2), 97.6. IR (KBr): ν=1603, 1577, 1508, 1485, 1456, 1442, 1417, 1195, 1120, 1070, 735, 686. MS: m/z(%)=328 (M^+, 100), 259 (35), 231 (32), 180 (24), 128 (33), 102 (19), 77 (73). HRMS (EI) calcd for $C_{18}H_{11}F_3N_2O$: 328.0823; found: 328.0828.

*4.3.2. 1-Phenyl-5-o-tolyl-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4b**).*



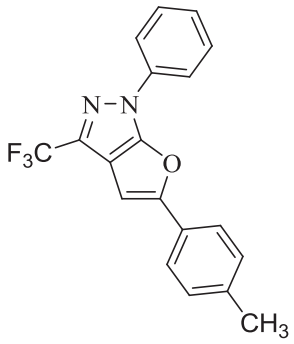
White solid; Mp: 144–145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.98 (d, J=8.1 Hz, 2H), 7.70–7.73 (m, 1H), 7.52 (t, J=7.8 Hz, 2H), 7.31–7.36 (m, 4H), 6.73 (s, 1H), 2.56 (s, 3H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−62.24 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=158.8, 154.4, 137.4, 135.6, 131.7 (q, $^2J_{CF3}$=40.1 Hz), 131.4, 129.6, 129.3, 129.0, 127.9, 126.9, 126.3, 121.1 (q, $^1J_{CF3}$=267.1 Hz), 118.1, 112.1 (m, $^3J_{CF3}$=1.5), 101.3, 21.8. IR (KBr): ν=1598, 1576, 1507, 1487, 1416, 1193, 1176, 1070, 1508, 754, 734. MS: m/z(%)=342 (M^+, 100), 343 (21), 273 (43), 194 (29), 128 (32), 116 (19), 91 (18), 77 (69). HRMS (EI) calcd for $C_{19}H_{13}F_3N_2O$: 342.0980; found: 342.0981.

*4.3.3. 1-Phenyl-5-m-tolyl-3-(trifluoromethyl)-1H-furo[2,3-c] pyrazole (**4c**).*



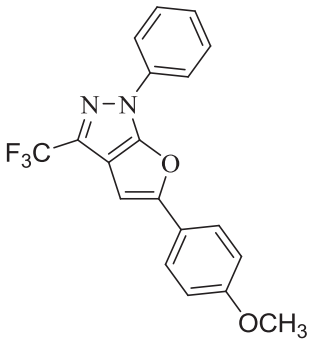
White solid; Mp: 109–110 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.91 (d, J=7.8 Hz, 2H), 7.45–7.51 (m, 4H), 7.25–7.32 (m, 2H), 7.08–7.11 (m, 1H), 6.75 (s, 1H), 2.37 (s, 3H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−62.57 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=159.2, 154.5, 138.7, 137.3, 131.7 (q, $^2J_{CF3}$=40.1 Hz), 129.8, 129.6, 128.8, 126.9, 124.6, 121.3, 121.1 (q, $^1J_{CF3}$=267.6 Hz), 118.2, 112.0 (m, $^3J_{CF3}$=2.2), 97.4, 21.5. IR (KBr): ν=1600, 1578, 1508, 1455, 1413, 1195, 1117, 1070, 748, 686. MS: m/z(%)=342 (M^+, 60), 273 (35), 243 (25), 187 (100), 186 (36), 132 (37), 128 (30), 77 (76). HRMS (EI) calcd for $C_{19}H_{13}F_3N_2O$: 342.0980; found: 342.0985.

*4.3.4. 1-Phenyl-5-p-tolyl-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4d**).*



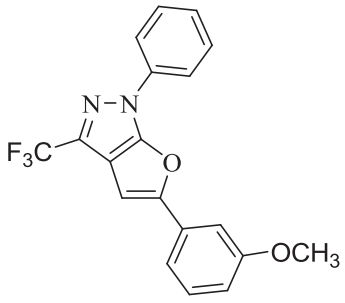
White solid; Mp: 166–167 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.96 (d, J=8.1 Hz, 2H), 7.59 (d, J=7.8 Hz, 2H), 7.52 (t, J=8.1 Hz, 2H), 7.33 (t, J=7.5 Hz, 1H), 7.22 (d, J=8.1 Hz, 2H), 6.77 (s, 1H), 2.37 (s, 3H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−61.79 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=159.3, 154.5, 138.8, 137.4, 131.7 (q, $^2J_{CF3}$=40.1 Hz), 129.6, 129.5, 127.2, 127.0, 124.0, 121.1 (q, $^1J_{CF3}$=267.1 Hz), 118.2, 112.0 (m, $^3J_{CF3}$=1.5), 96.8, 21.3. IR (KBr): ν=1602, 1569, 1454, 1416, 1366, 1331, 1044, 910, 778, 753. MS: m/z(%)=342 (M^+, 100), 343 (19), 273 (47), 245 (28), 194 (21), 128 (27), 119 (18), 77 (54). HRMS (EI) calcd for $C_{19}H_{13}F_3N_2O$: 342.0980; found: 342.0978.

*4.3.5. 5-(4-Methoxyphenyl)-1-phenyl-3-(trifluoromethyl)-1H-furo [2,3-c]pyrazole (**4e**).*



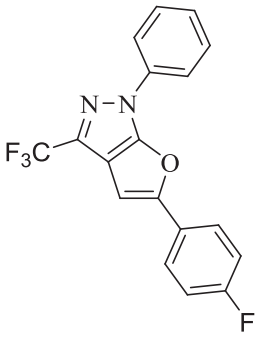
White solid; Mp: 128–129 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.98 (d, J=8.1 Hz, 2H), 7.67 (d, J=8.4 Hz, 2H), 7.53 (t, J=7.7 Hz, 2H), 7.34 (m, 1H), 6.97 (d, J=7.8 Hz, 2H), 6.72 (s, 1H), 3.86 (s, 3H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−61.72 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=160.1, 159.2, 154.4, 137.4, 131.6 (q, $^2J_{CF3}$=40.1 Hz), 129.6, 126.9, 125.7, 122.7, 121.1 (q, $^1J_{CF3}$=266.9 Hz), 118.2, 114.4, 112.1 (m, $^3J_{CF3}$=2.2), 96.0, 55.4. IR (KBr): ν=1599, 1559, 1546, 1483, 1456, 1306, 1197, 1119, 1071, 829, 752. MS: m/z(%)=358 (M^+, 60), 290 (15), 289 (67), 210 (26), 135 (35), 128 (20), 77 (100), 51 (25). HRMS (EI) calcd for $C_{19}H_{13}F_3N_2O_2$: 358.0929; found: 358.0926.

*4.3.6. 5-(3-Methoxyphenyl)-1-phenyl-3-(trifluoromethyl)-1H-furo [2,3-c]pyrazole (**4f**).*



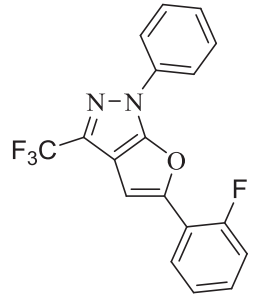
White solid; Mp: 118–119 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.97 (d, J=8.1 Hz, 2H), 7.54 (t, J=7.1 Hz, 2H), 7.31–7.37 (m, 3H), 7.26 (s, 1H), 6.86–6.91 (m, 2H), 3.88 (s, 3H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−61.71 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=156.0, 158.8, 154.5, 137.3, 131.7 (q, $^2J_{CF3}$=40.1 Hz), 131.1, 130.0, 129.6, 126.9, 121.0 (q, $^1J_{CF3}$=266.9 Hz), 118.1, 116.6, 113.9, 112.0 (m, $^3J_{CF3}$=1.5), 109.9, 97.8, 55.3. IR (KBr): ν=3017, 1578, 1546, 1508, 1457, 1328, 1315, 1286, 1179, 1157, 1071, 1040. MS: m/z(%)=358 (M^+, 100), 359 (22), 289 (34), 210 (12), 132 (16), 128 (21), 77 (47), 51 (11). HRMS (EI) calcd for $C_{19}H_{13}F_3N_2O_2$: 358.0929; found: 358.0923.

*4.3.7. 5-(4-Fluorophenyl)-1-phenyl-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4g**).*



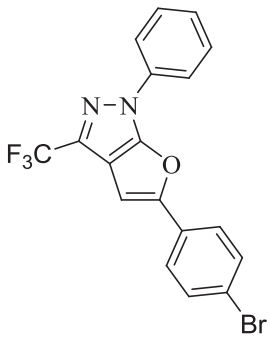
White solid; Mp: 182–183 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.96 (d, J=7.8 Hz, 2H), 7.69–7.74 (m, 2H), 7.54 (t, J=7.8 Hz, 2H), 7.33–7.38 (m, 1H), 7.15 (t, J=8.7 Hz, 2H), 6.81 (s, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−61.78 (s, 3F), −111.44 (s, 1F). ^{13}C NMR (100 MHz, CDCl3) δ=162.9 (d, ^1J_F=247.9 Hz), 158.1, 154.6, 137.3, 131.8 (q, $^2J_{CF3}$=40.1 Hz), 129.7, 127.1, 126.3 (d, ^4J_F=3.7 Hz), 126.1 (d, ^3J_F=8.1 Hz), 121.0 (q, $^1J_{CF3}$=267.1 Hz), 118.3, 116.2 (d, ^2J_F=21.9 Hz), 112.0 (m, $^3J_{CF3}$=2.2), 97.4 ppm. IR (KBr): ν=1599, 1580, 1496, 1484, 1253, 1121, 1101, 847, 816. MS: m/z(%)=346 (M^+, 78), 277 (42), 249 (25), 198 (43), 128 (57), 123 (23), 77 (100), 51 (35). HRMS (EI) calcd for $C_{18}H_{10}F_4N_2O$: 346.0729; found: 346.0727.

*4.3.8. 5-(2-Fluorophenyl)-1-phenyl-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4h**).*



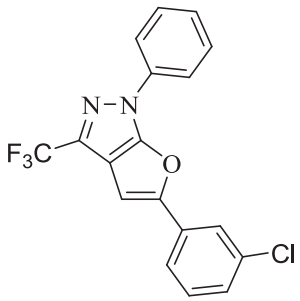
White solid; Mp: 161–162 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.95–7.97 (m, 2H), 7.49–7.57 (m, 3H), 7.32–7.44 (m, 3H), 7.02–7.07 (m, 1H), 6.89 (s, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−61.89 (s, 3F), −111.82 (s, 1F). ^{13}C NMR (100 MHz, $CDCl_3$): δ=163.2 (d, ^1J_F=245.0 Hz), 157.6 (d, ^4J_F=2.9 Hz),154.6, 137.2, 132.0 (q, $^2J_{CF3}$=40.1 Hz), 131.9 (d, ^3J_F=8.0 Hz), 130.7 (d, ^3J_F=8.7 Hz), 129.7, 127.2, 120.9 (q, $^1J_{CF3}$=266.9 Hz), 119.7 (d, ^4J_F=2.9 Hz), 118.3, 115.6 (d, ^2J_F=21.1 Hz), 111.9 (m, $^3J_{CF3}$=1.5), 111.1 (d, ^2J_F=23.3 Hz), 98.8 ppm; IR (KBr): ν=1615, 1599, 1582, 1488, 1456, 1416, 1137, 1117, 1045, 985, 956. MS: m/z(%)=346 (M^+, 100), 347 (21), 334 (32), 277 (35), 249 (32), 198 (23), 128 (56), 77 (97). HRMS (EI) calcd for $C_{18}H_{10}F_4N_2O$: 346.0729; found: 346.0732.

*4.3.9. 5-(4-Bromophenyl)-1-phenyl-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4i**).*



White solid; Mp: 167–168 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.97 (d, J=7.8 Hz, 2H), 7.52–7.59 (m, 6H), 7.34–7.39 (m, 1H), 6.89 (s, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−61.82 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=157.8, 154.5, 137.2, 132.2, 131.8 (q, $^2J_{CF3}$=40.8 Hz), 129.6, 128.8, 127.1, 125.4, 122.7, 120.9 (q, $^1J_{CF3}$=266.8 Hz), 118.1, 112.1 (m, $^3J_{CF3}$=2.2), 98.2. IR (KBr): ν=1601, 1581, 1479, 1453, 1412, 1188, 1120, 1070, 1043, 998, 871. MS: m/z(%)=406 (M^+, 89), 407 (26) 408 (86), 337 (32), 339 (29), 258 (33), 128 (66), 77 (100). HRMS (EI) calcd for $C_{18}H_{10}BrF_3N_2O$: 405.9929; found: 405.9932.

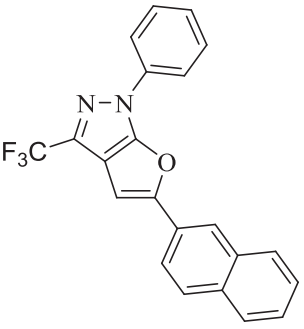
*4.3.10. 5-(3-Chlorophenyl)-1-phenyl-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4j**).*



White solid; Mp: 131–132 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.96 (d, J=7.8 Hz, 2H), 7.70 (s, 1H), 7.52–7.61 (m, 3H), 7.30–7.39 (m, 3H), 6.89 (s, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−61.77 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=157.3, 154.5, 137.1, 135.1, 131.9 (q, $^2J_{CF3}$=40.1 Hz), 131.5, 130.2, 129.6, 128.6, 127.1, 123.9, 122.0, 120.8 (q, $^1J_{CF3}$=267.6 Hz), 118.1, 111.8 (m, $^3J_{CF3}$=1.5), 98.7. IR (KBr): ν=1601, 1574, 1507, 1484, 1339, 1119, 1070, 1044, 901, 785, 757. MS: m/z(%)=362 (M^+), 342 (90), 273 (44), 245 (28), 194 (30), 128 (49), 91 (28), 77 (100). HRMS (EI) calcd for $C_{18}H_{10}ClF_3N_2O$: 362.0434; found: 362.0435.

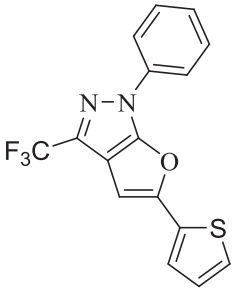
Crystal data of **4j**. $C_{18}H_{10}ClF_3N_2O$: M_w=362.73, CCDC reference number is no. 816716, orthorhombic, space group $P2(1)2(1)2(1)$, a=4.7199(4), b=15.3676(14), c=21.928(2) Å, α=90, β=90, γ=90, V=1590.5(2) Å^3, Z=4, Dc=1.515 mg/m^3, F(000)=736, radiation, Mo Kα (λ=0.7107 Å), 4.556≤2θ≤48.261, intensity data were collected at 296 K with a Bruker axis D8 diffractometer, and employing $\omega/2\theta$ scanning technique, in the range of −5≤h≤5, −18≤k≤18, −22≤l≤27.

*4.3.11. 5-(Naphthalen-2-yl)-1-phenyl-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4k**).*



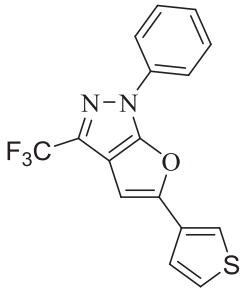
White solid; Mp: 152–153 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=8.16 (s, 1H), 8.00 (d, J=8.1 Hz, 2H), 7.79–7.89 (m, 3H), 7.73 (d, J=8.7 Hz, 1H), 7.46–7.58 (m, 4H), 7.33–7.38 (m, 1H), 6.93 (s, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−61.75 (s, 3F). IR (KBr): ν=1602, 1574, 1553, 1484, 1411, 1187, 1153, 1132, 1120, 961, 904. MS: m/z(%)=378 (M^+, 100), 379 (24), 309 (38), 281 (24), 155 (13), 128 (15), 127 (22), 77 (31). HRMS (EI) calcd for $C_{22}H_{13}F_3N_2O$: 378.0980; found: 378.0981.

*4.3.12. 1-Phenyl-5-(thiophen-2-yl)-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4l**).*



Yellow solid; Mp: 144–145 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.85 (d, J=8.4 Hz, 2H), 7.43 (t, J=7.8 Hz, 2H), 7.22–7.30 (m, 3H), 6.97–7.00 (m, J=1H), 6.60 (s, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−62.01 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=154.2, 137.2, 132.1, 131.7 (q, $^2J_{CF3}$=40.1 Hz), 129.6, 127.9, 127.1, 125.8, 124.4, 121.0 (q, $^1J_{CF3}$=266.9 Hz), 118.2, 112.0 (m, $^3J_{CF3}$=1.4), 97.6. IR (KBr): ν=1601, 1568, 1455, 1417, 1232, 1117, 1070, 906, 735, 698. MS: m/z(%)=334 (M^+, 73), 265 (44), 237 (30), 186 (21), 128 (33), 108 (16), 77 (100), 51 (37). HRMS (EI) calcd for $C_{16}H_9F_3N_2O_2S$: 334.0388; found: 334.0392.

*4.3.13. 1-Phenyl-5-(thiophen-3-yl)-3-(trifluoromethyl)-1H-furo[2,3-c]pyrazole (**4m**).*



Yellow solid; Mp: 143–144 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ=7.94 (d, J=7.8 Hz, 2H), 7.61 (s, 1H), 7.51 (t, J=7.8 Hz, 2H), 7.30–7.35 (m, 3H), 6.66 (s, 1H). ^{19}F NMR ($CDCl_3$, 282 MHz): δ=−62.63 (s, 3F). ^{13}C NMR (100 MHz, CDCl3): δ=155.9, 154.3, 137.3, 132.2 (q, $^2J_{CF3}$=40.1 Hz), 131.6, 129.6, 127.0, 124.4, 121.0 (q, $^1J_{CF3}$=267.6 Hz), 120.8, 118.3, 118.2, 111.8 (m, $^3J_{CF3}$=1.5), 97.3. IR (KBr): ν=1602, 1569, 1454, 1366, 1230, 1214, 1117, 1070, 910, 882, 820, 687. MS: m/z(%)=334 (M^+, 100), 335 (20), 265 (35), 237 (33), 128 (47), 111 (22), 77 (93), 51 (32). HRMS (EI) calcd for $C_{16}H_9F_3N_2O_2S$: 334.0388; found: 334.0392.

Acknowledgements

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2011.09.007. These data include MOL files and InChIKeys of the most important compounds described in this article.

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