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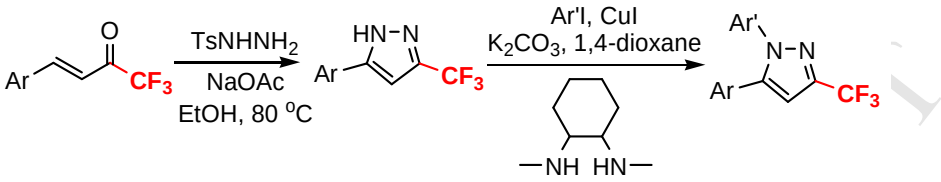


An Efficient Route to 3-Trifluoromethylpyrazole *via* Cyclization/1,5-H Shift and Its Applications in the Synthesis of Bioactive Compounds

Yongdong Wang[a], Jing Han[b], Jie Chen[b], Weiguo Cao*[,a,b,c,d]

[a] *School of Environmental and Chemical Engineering, Shanghai University, Road, Shanghai 200444, P. R. China*

[b] *Department of Chemistry, Innovative Drug Research Center, Shanghai University, Shanghai 200444, P. R. China*

[c] *State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P. R. China*

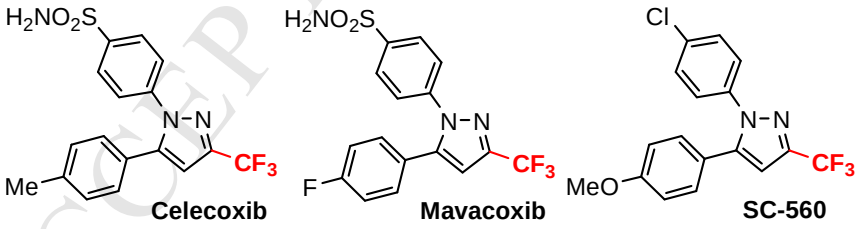
[d] *Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, P. R. China*

Abstract: A methodology for regioselective synthesis of 3-trifluoromethylpyrazole from the reaction of trifluoromethyl alkenone and tosylhydrazone has been developed. The reaction was proposed to proceed through a tandem cyclization and 1,5-H shift reaction, which can be applied to the synthesis of bioactive compounds like Celecoxib, Mavacoxib, and SC-560.

Keywords: Trifluoromethyl; Pyrazole; 1,5-H shift; Cyclization

1. Introduction

The pyrazole moiety is the core structure of many naturally occurring and bioactive molecules.[1] It's well known that the introduction of fluorine atoms into organic molecules allows the simultaneous modulation of electronic, lipophilic, and steric parameters, all of which can profoundly influence both the physical and biological properties due to the unique physical properties of the fluorine atom.[2] Among the fluorinated pyrazoles, 3-trifluoromethylpyrazole is the core unit of many drugs, agrochemicals, and related candidates.[3] For example, as shown in **Scheme 1**, both Celecoxib[4] and Mavacoxib[5] are the most recognized drug that contain a trifluoromethylated pyrazole moiety. Celecoxib is a COX-2 selective nonsteroidal anti-inflammatory drug, while Mavacoxib is a veterinary drug used to treat pain and inflammation in dogs with degenerative joint disease. SC-560 shows antitumor activity.[6]

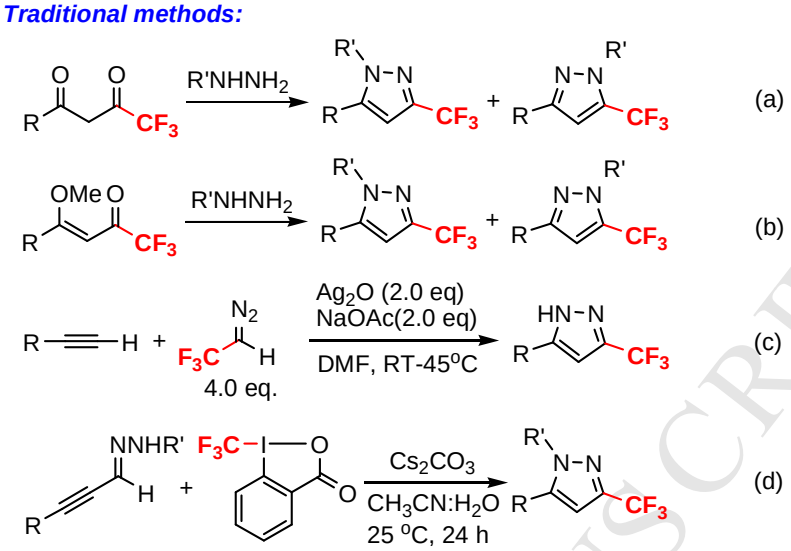


Scheme 1 Bioactive compounds bearing a 3-trifluoromethylpyrazole moiety

Traditionally, 3-trifluoromethylpyrazoles can be accessed by cyclocondensation of hydrazine with the corresponding 1,3-dicarbonyl compounds[7] (**Scheme 2a**) or 4-alkoxy-1,1,1-trifluoro-3-alken-2-one[8] (**Scheme 2b**). However, both methods suffered from the formation of regioisomeric mixtures of 3- and 5-trifluoromethyl pyrazole. In 2013, Ma reported an elegant silver-mediated cycloaddition of alkynes with CF_3CHN_2 to regioselectively synthesize 3-trifluoro-methylpyrazole (**Scheme 2c**).[9] In this method, excess amount of $CF_3CH_2NH_2 \cdot HCl$ (4.0 eq.) and Ag_2O (2.0 eq.) are essential for the efficiency of cycloaddition reaction. Very recently, Wang and coworkers reported an alternative method to synthesize 3-trifluoromethylpyrazoles *via* trifluoromethylation/cyclization of α,β-alkynic

* Corresponding authors. Fax: +86-21-66134856; E-mail: wgcao@staff.shu.edu.cn

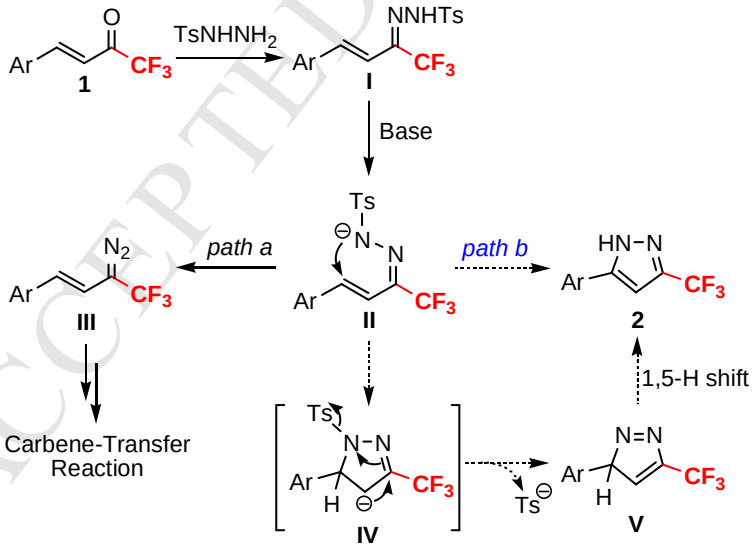
hydrazones using a hypervalent iodine reagent (**Scheme 2d**). However, the expensive hypervalent iodine reagent (Togni reagent) makes this transformation less practical. Therefore, it is still highly desirable to develop new methods for the synthesis of 3-trifluoromethylpyrazoles.



Scheme 2 Traditional methods for the synthesis of 3-CF_3-pyrazoles

2. Results and Discussion

It's well known that tosyl hydrazone salt is the key precusor in the Bamford-Stevenes reaction for the generation of diazo compounds from the carbonyl compound, such as aldehyde or ketone.[11] We conceived that α,β-alkenylic hydrazone salt **II** might serve as both the precursor for the diazo **III** through the Banford-Stevenes process (**Scheme 3**, path a) or the precursor for the 3-trifluoromethylpyrazole **2** through a tandem cyclization/1,5-H Shift reaction (path b).

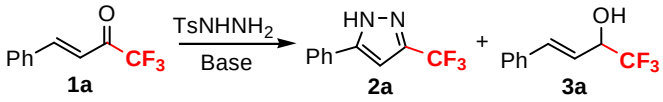


Scheme 3 Two proposed pathways

We initiated our study with trifluoromethyl alkenone **1a** as the model substrate. The reaction was set in one-pot manner. In the presence of 1.1 eq. of $TsNHNH_2$, the reaction was upon treatment with various bases in different solvent. Preliminary examination showed that the desired 3-trifluoromethylpyrazole **2a** could be easily obtained in excellent yield at 80 °C by using NaOAc as base in EtOH (**Table 1**, entry 2). Among three different bases, sodium acetate is the best of choice for this reaction (entry 2). Interestingly, the alcohol **3a** could be also detected when water was used as the solvent. Presumably, the allylic alcohol **3a** was formed through the carbene involved O-H insertion

(the Bamford-Stevenes process). To the best of our knowledge, it is the first example that the solvent may tune the reaction pathway of the hydrazone salt.

Table 1 Optimization of reaction conditions[a]

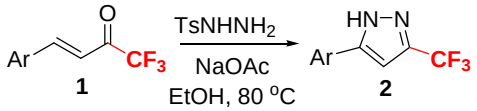


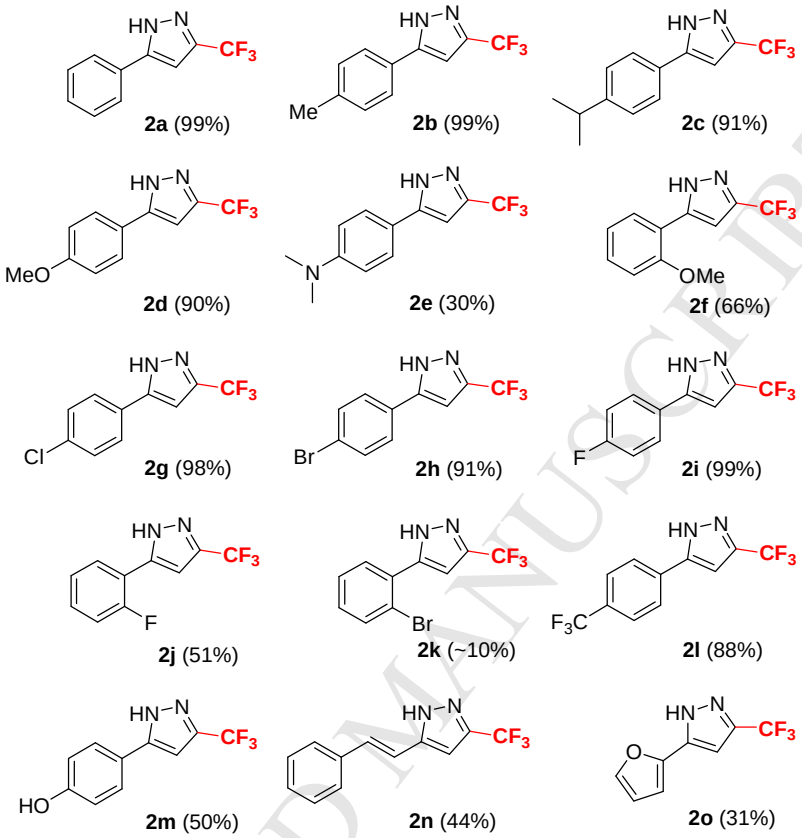
Entry	Base	Solvent	Temp.	Yield (%)[b]	
				2a	**3a**
1	NaOH	EtOH	80	15	-
2	NaOAc	EtOH	80	99	-
3	K_2CO_3	EtOH	80	70	-
4	NaOAc	H_2O	80	13	7
5	NaOAc	EtOH	rt	trace	-

[a] The reaction was set using **1a** (0.25 mmol), $TsNHNH_2$ (0.275 mmol), base (0.275 mmol), solvent (1.0 mL);
[b] NMR yield.

With the optimized conditions in hand (**Table 1**, entry 2), the substrate scope was then examined. As summarized in **Scheme 4**, the base-promoted process could be successfully applied to a variety of trifluoromethyl alkenone **1**. For example, both electron-donating and electron withdrawing groups on the phenyl rings had little effects upon the product yields. The yields of the products are typically higher than 90% (**2a-2d**, **2g-2i**, **2l**). However, 4-N,N-dimethylamino group has an obviously negative effect on this reaction, giving the corresponding product **2e** only in 30% yield. Furthermore, the reaction was very sensitive to the steric hindrance: all substrates with substituents at 2-position of the phenyl ring gave inferior results (**2f**, **2j**, **2k**). The reaction functioned well with the hydroxyl group functional group, although with only moderate yield (**2m**). The trifluoromethyl alkenone with one more C=C can be served as the substrate as well, giving pyrazole **2n** in 44%. Furyl ethenylic ketone was not a good substrate either, with the yield being 31% (**2o**). It was noted that only the regioisomer 3-trifluoromethyl pyrazole **2** was detected in all cases.

Table 2 Scope of the synthesis of 3-trifluoromethyl pyrazoles **2**[a]

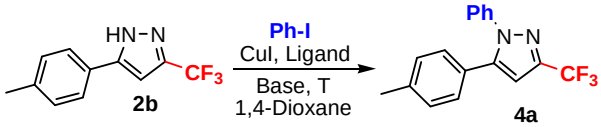




[a] The reaction was set using **1a** (0.25 mmol), $TsNHNH_2$ (0.275 mmol), base (0.275 mmol), EtOH (1.0 mL); isolated yield; the reactions were monitored by TLC.

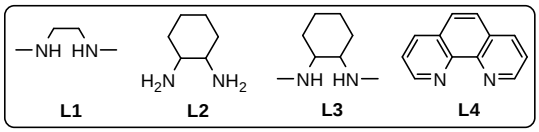
To futher synthesize the bioactive molecules, such as Celecoxib, Mavacoxib, and SC-560, we then proceeded to couple 3-trifluoromethyl-1*H*-pyrazoles **2** with aryl halide. Followed the similar reported process,[9] the reaction was set by using **2b** and iodobenzene as the model substrates and CuI as the catalyst. Four different ligands **L1**-**L4** were initially tested for this reaction. As shown in **Scheme 4**, pyrazole **4a** was obtained in 35% yield when **L1** was used. However, ligands **L2** and **L4** only gave trace desired product **4a**. The pyrazole **4a** could be obtained 43% yield when **L3** was used. The yield could be further improved to 80% when the temperature was enhanced to 150 °C.

Table 3 Optimization reaction conditions[a]



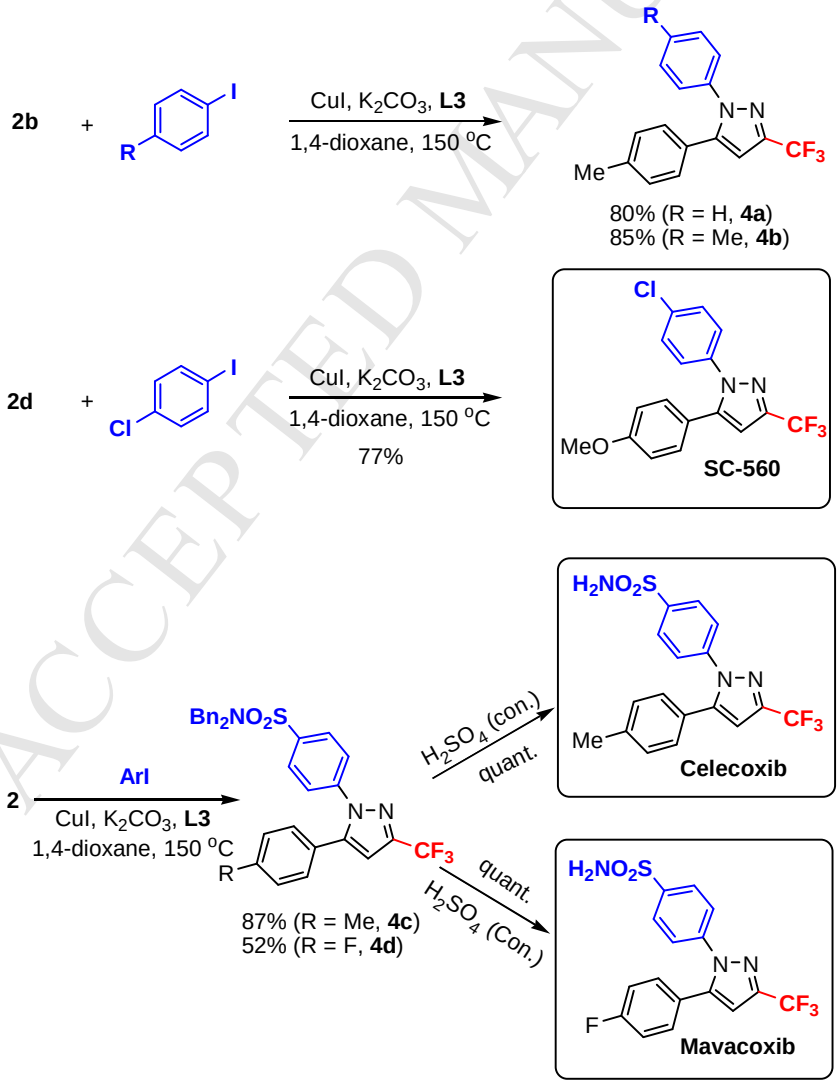
Entry	Ligand	Base	Temp.	Time	Yield[b]
1	**L1**	K_2CO_3	120 °C	48 h	35%
2	**L2**	K_2CO_3	120 °C	48 h	trace
3	**L3**	K_2CO_3	120 °C	48 h	43%

4	**L4**	K_2CO_3	120 °C	48 h	trace
5	**L3**	**K_2CO_3**	**150 °C**	**48 h**	**80%**



[a] The reaction was set using **2b** (0.25 mmol), PhI (1.25 mmol), base (0.53 mmol), solvent (1.0 mL); [b] Isolated yields.

Having established the cyclocondensation reaction and Cu-catalyzed N-arylation reaction as a reliable and efficient synthetic process, we then set out to synthesize the bioactive molecules as shown in Scheme 1. With the optimized reaction conditions (**Table 3**, entry 5), 3-trifluoromethyl-1*H*-pyrazoles **2b** could couple with both iodobenzene and 4-iodotoluene, giving the desired pyrazoles **4a** and **4b** in excellent yields (**Scheme 4**). When pyrazole 2**d** and 1-chloro-4-iodobenzene was applied as the substrate, SC-560 was obtained in 77%. Similarly, the precursors of Celecoxib and Mavacoxib (**4c** and **4d**) were prepared in 87% and 52% yields when N,N-dibenzyl-4-iodobenzenesulfonamide was severed. Subsequently, both Celecoxib and Mavacoxib could be obtained in quantitative yields by simply treating with concentrated H_2SO_4 (**Scheme 4**).

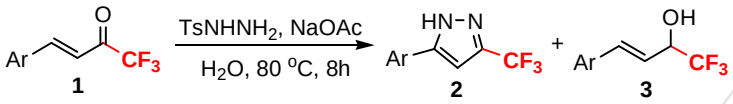


[a] **2** (0.2 mmol), halides (1.0 eq.), CuI (5 mol%), **L3** (20 mol%); K_2CO_3 (2.1 eq.). Isolated yields.

Scheme 4 Copper-catalyzed *N*-arylation[a]

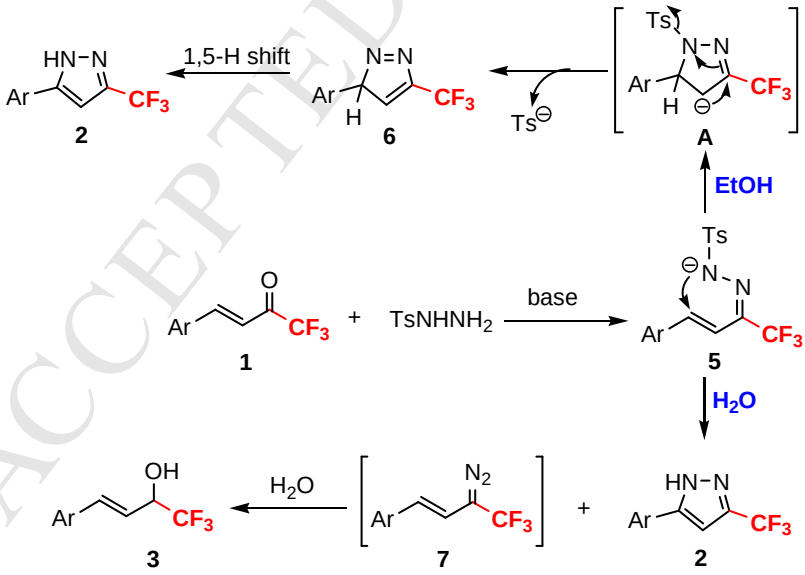
In **Table 1**, the formation of the allylic alcohol **3** in water was perfectly consistent with our mechanism speculation, although the yield was only 7%. We are wondering that whether similar allylic alcohols would be formed for other substrates. For this purpose, we then further investigated two more examples. As shown in **Table 4**, when 4-bromo- or 4-hydroxyphenyl alkenones were treated with $TsNHNH_2$ and NaOAc in water, the starting materials were consumed completely in 8 h. Both pyrazole **2** and allylic alcohol **3** could be isolated, with the yields of **3** are up to 60% (**3h**).

Table 4 The reaction results in water



Entry	Ar	Yield	
		Yield (**2**)	Yield (**3**)
1	C_6H_5-	13% (**2a**)	7% (**3a**)
2	4-Br-C_6H_4-	40% (**2h**)	60% (**3h**)
3	4-HO-C_6H_4-	54% (**2m**)	46% (**3m**)

A tentative reaction mechanism for the base-promoted cyclocondensation reaction was then proposed in **Scheme 5**. The tosyl hydrazone salt **5** was formed from the reaction of the ketone **1** and $TsNHNH_2$ in the presence of base. The reaction of hydrazone salt **5** was then a solvent-dependent process. When EtOH was used as the solvent, a tandem nucleophlic-cyclization and 1,5-H Shift occured to afford the desired pyrazole **2**. Besides the pyrazole **2**, the Bamford-Stevenes reaction product (diazo **7**) was formed simultaneously. A carbene-involved O-H insertion reaction occured to give the allylic alcohol **3**.



Scheme 5 Proposed reaction mechanism

3. Conclusions

In conclusion, we have developed an convenient and practical method to regioselectively synthesize 3-trifluoromethylpyrazoles. The reaction was proposed to proceed through a tandem cyclization and 1,5-H Shift reaction, which can be applied in the synthesis of the bioactive compounds such as Celecoxib, Mavacoxib, and SC-560.

4. Experimental

4.1 General information

Unless otherwise noted, all commercial reagents and solvents were used as received from commercial sources without further purification. Silica gel plates (GF254) were used for TLC monitoring and silica gel (300 - 400 mesh) was used for flash column chromatography. ^{1}H, ^{13}C, ^{19}F NMR spectra were recorded on a Bruker AVANCE 400 spectrometer (400 MHz for ^{1}H; 100 MHz for ^{13}C; 376 MHz for ^{19}F), ^{1}H NMR and ^{13}C NMR chemical shifts were determined relative to internal standard TMS at δ 0.0 as an external standard. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Infrared (IR) spectra were recorded on a Nicolet 210 spectrophotometer. High-resolutionmass spectra were obtained using a Thermo Fisher Scientific LTQ FT Ultra in positive direct analysis in real time (DART) ionization method.

*4.2 General procedure for the preparation of ketones (**1**)* [12-13]

To a stirred solution of aldehydes (5 mmol), acetic acid (0.45g, 7.5 mmol), and piperidine (0.45g, 5 mmol) in dry benzene (5 mL) at 0^{o}C was added dropwise a solution of trifluoroacetone (2.25g, 20 mmol) in dry benzene (5 mL). The mixture was stirred for 2 h at this temperature and then 24 h at room temperature. The reaction was quenched with a saturated aqueous solution of ammonium chloride and was extracted with EtOAc (15 mL×3). The organic layer was washed with brine, and then dried over anhydrous sodium sulfate. After removal of the solvent, the residue was purified by column chromatography on silica gel with *n*-pentane to give the ketones. The yields of the ketones were 30% ~60%. The analytical data are in accordance with the literatures.[13-27]

(E)-1,1,1-trifluoro-4-phenylbut-3-en-2-one (1a)[15]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 16.0 Hz, 1H), 7.57-7.55 (m, 2H), 7.42-7.35 (m, 3H), 6.94 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 150.2, 133.4, 132.3, 129.2, 116.7, 116.4 (q, $^{1}J_{C\text{-}F}$ = 284.1 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.61.

(E)-1,1,1-trifluoro-4-(p-tolyl)but-3-en-2-one (1b)[15]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 15.9 Hz, 1H), 7.53 (d, *J* = 7.6 Hz, 2H), 7.25 (d, *J* = 7.6 Hz, 2H), 6.97 (d, *J* = 15.9 Hz, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 150.2, 143.4, 130.7, 130.0, 129.3, 116.5 (q, $^{1}J_{C\text{-}F}$ = 289.0 Hz), 115.6, 21.7. ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.55.

(E)-1,1,1-trifluoro-4-(4-isopropylphenyl)but-3-en-2-one (1c): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 15.9 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.30 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 15.9 Hz, 1H), 2.99-2.92 (m, 1H), 1.27 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 154.1, 150.2, 131.1, 129.5, 127.4, 117.9, 116.5 (q, $^{1}J_{C\text{-}F}$= 289.0 Hz), 115.1, 34.3, 23.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.54. IR (KBr) ν 2966, 1717, 1600, 1565, 1512, 1421, 1265, 1202, 1147, 1055, 986, 827, 687. GC-MS (EI) calcd. For $C_{13}H_{13}F_3O$ $[M]^+$: 242.1, found: *m/z* 242.0.

(E)-1,1,1-trifluoro-4-(4-methoxyphenyl)but-3-en-2-one (1d)[15]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 (d, *J* = 15.8 Hz, 1H), 7.51 (d, *J* = 8.3 Hz, 2H), 6.86 (d, *J* = 8.3 Hz, 2H), 6.80 (d, *J* = 15.8 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.9 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 162.2, 148.9, 130.3, 125.1, 116.8 (q, $^{1}J_{C\text{-}F}$ = 289.1 Hz), 114.1, 113.7, 113.1, 54.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.50.

(E)-4-(4-(dimethylamino)phenyl)-1,1,1-trifluorobut-3-en-2-one (1e)[20]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 15.5 Hz, 1H), 7.53 (d, *J* = 8.5 Hz, 2H), 6.77 (d, *J* = 15.5 Hz, 1H), 6.67 (d, *J* = 8.5 Hz, 2H), 3.08 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.4 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 153.2, 150.9, 131.8, 121.2, 117.0 (q, $^{1}J_{C\text{-}F}$ = 289.0 Hz), 111.7, 110.4, 40.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.14.

(E)-1,1,1-trifluoro-4-(2-methoxyphenyl)but-3-en-2-one (1f)[21]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 16.1 Hz, 1H), 7.49 (d, *J* = 7.7 Hz, 1H), 7.38-7.34 (m, 1H), 7.04 (d, *J* = 16.1 Hz, 1H), 6.92-6.89 (m, 1H), 6.86 (d, *J* = 8.4 Hz, 1H), 3.83 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.5 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 159.6, 145.8, 133.8, 130.2, 122.3, 120.9, 117.0, 116.6 (q, $^{1}J_{C\text{-}F}$ = 289.0 Hz), 111.4, 55.6. ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.56.

(E)-4-(4-chlorophenyl)-1,1,1-trifluorobut-3-en-2-one (1g)[13]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 16.0 Hz, 1H), 7.57 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 6.98 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.9 (q, $^{2}J_{C\text{-}F}$ = 36.0 Hz), 148.5, 138.5, 131.8, 130.3, 129.6, 117.1, 116.3 (q, $^{1}J_{C\text{-}F}$= 289.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.67.

(E)-4-(4-bromophenyl)-1,1,1-trifluorobut-3-en-2-one(1h)[13]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 15.9 Hz, 1H), 7.60 (d, *J* = 8.3 Hz, 2H), 7.50 (d, *J* = 8.3 Hz, 2H), 7.00 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 148.6, 132.6, 132.2, 130.5, 127.0, 117.1, 116.3 (q, $^{1}J_{C\text{-}F}$ = 289.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.65.

(E)-1,1,1-trifluoro-4-(4-fluorophenyl)but-3-en-2-one (1i)[15]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 15.9 Hz, 1H), 7.74 – 7.58 (m, 2H), 7.17-7.13 (m, 2H), 6.94 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 165.7 (q, $^{1}J_{C\text{-}F}$ = 253.0 Hz), 148.7, 131.4,129.7, 116.6 (q, $^{2}J_{C\text{-}F}$ = 22.0 Hz), 116.0 (q, $J_{C\text{-}F}$ = 3.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.66, -105.61.

(E)-1,1,1-trifluoro-4-(2-fluorophenyl)but-3-en-2-one (1j)[15]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 16.2 Hz, 1H), 7.56 (t, *J* = 7.4 Hz, 1H), 7.41 (dd, *J* = 13.2, 6.5 Hz, 1H), 7.19 – 7.09 (m, 2H), 7.06 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.3 163.5, 142.7, 133.8, 130.1, 124.8, 121.7, 119.0, 116.7, 116.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.83, -112.02.

(E)-4-(2-bromophenyl)-1,1,1-trifluorobut-3-en-2-one (1k)[22]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 15.9 Hz, 1H), 7.73-7.66 (m, 2H), 7.41-7.33 (m, 2H), 6.96 (d, *J* = 15.9 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 182.1 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 160.9, 148.23, 133.9, 133.3, 133.0, 128.2, 127.9, 126.9, 123.5, 119.1 (q, $^{1}J_{C\text{-}F}$ = 289.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.49.

(E)-1,1,1-trifluoro-4-(4-(trifluoromethyl)phenyl)but-3-en-2-one (1l)[23]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J* = 16.0 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.00 (d, *J* = 16.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ179.8 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 147.9, 136.5, 133.5 (q, $^{2}J_{C\text{-}F}$ = 33.0 Hz), 129.3, 126.4, 123.5 (q, $^{1}J_{C\text{-}F}$ = 271.0 Hz), 118.9, 116.2 (q, $^{1}J_{C\text{-}F}$ = 289.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.14, -77.74.

(E)-1,1,1-trifluoro-4-(4-hydroxyphenyl)but-3-en-2-one (1m) : ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 (d, *J* = 16.0 Hz, 1H), 7.57 (d, *J* = 8.4 Hz, 2H), 6.91-6.86 (m, 2H), 6.88 (d, *J* = 16.0 Hz, 1H), 5.67 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.4 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 159.9, 150.5, 131.8, 126.2, 116.6 (q, $^{1}J_{C\text{-}F}$= 289.0 Hz), 116.4, 113.9. ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.49. IR (KBr) ν 2923, 1705, 1576, 1514, 1444, 1273, 1200, 1168, 1062, 831, 708. GC-MS (EI) calcd. for $C_{10}H_7F_3O_2$ $[M]^+$: 216.0, found: *m/z* 216.0.

(3E,5E)-1,1,1-trifluoro-6-phenylhexa-3,5-dien-2-one (1n)[27]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (dd, *J* = 14.8, 11.4 Hz, 1H), 7.50 (d, *J* = 6.0 Hz, 2H), 7.38 -7.37(m, 3H), 7.11 (d, *J* = 15.5 Hz, 1H), 6.95 (dd, *J* = 15.2, 11.4 Hz, 1H), 6.53 (d, *J* = 15.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 150.0, 146.2, 135.3, 130.4, 129.1, 127.9, 125.9, 119.8, 116.5 (q, $^{1}J_{C\text{-}F}$ = 289.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.41.

(E)-1,1,1-trifluoro-4-(furan-2-yl)but-3-en-2-one (1o)[15]: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 15.5 Hz, 1H), 7.61 (s, 1H), 6.90 (s, 1H), 6.87 (d, *J* = 15.5 Hz, 1H), 6.58 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.8 (q, $^{2}J_{C\text{-}F}$ = 35.0 Hz), 150.6, 147.0, 134.8, 119.9, 116.4 (q, $^{1}J_{C\text{-}F}$= 288.0 Hz), 113.9, 113.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -77.70.

*4.3 General procedure for the preparation of pyrazoles (**2**)*

To a 25 mL Schlenk were added ketone (0.25 mmol), *p*-toluenesulfonylhydrazide (0.275 mmol, 1.1 eq), sodium acetate(0.275 mmol, 1.1 eq) and EtOH (2 mL). The mixture was stirred at 80^{o}C for 12 h and allowed to cool down to room temperature. After removal of the solvent, the residue was purified by column chromatography on silica gel (hexane/EtOAc) or crystallization to afford the pyrazoles **2**. The analytical data are in accordance with the literatures.[16-26]

5-Phenyl-3-(trifluoromethyl)-1*H*-pyrazole (2a)[16]: Yield 99%. solid, mp: 110-114 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.90 (s, 1H), 7.51-7.50 (m,2H), 7.38-7.36 (m, 3H), 6.68 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 144.0 (q, $^{2}J_{C\text{-}F}$ = 37.7 Hz), 129.4, 129.3, 128.0, 125.7, 122.5 (q, $^{1}J_{C\text{-}F}$ = 267.0 Hz), 101.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.28.

5-(*p*-Tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (2b)[16]: Yield 99%. solid, mp: 103-106 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 7.8 Hz, 2H), 7.28 (d, *J* = 7.8 Hz, 2H), 6.75 (s, 1H), 2.41 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.1, 142.2 (q, $^{2}J_{C\text{-}F}$ = 35.9 Hz), 139.6, 130.0, 125.6, 120.6 (q, $^{1}J_{C\text{-}F}$ = 266.6 Hz), 100.8, 21.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.31.

5-(4-Isopropylphenyl)-3-(trifluoromethyl)-1*H*-pyrazole (2c): Yield 91%. solid, mp: 103-106 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ11.05 (s, 1H),7.50 (d, *J* = 8.0 Hz, 2H), 7.32 (d, *J* = 8.0 Hz, 2H), 6.73 (s, 1H), 2.99 – 2.91 (m, 1H), 1.28 (d, *J* = 6.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 144.9 (q, $^{2}J_{C\text{-}F}$ = 38.2 Hz), 128.9, 127.4, 126.3, 125.7, 125.5, 119.8 (q, $^{1}J_{C\text{-}F}$ = 267.1 Hz), 100.8, 34.0, 23.8. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.21. IR (KBr) ν 2965, 1618, 1498, 1461, 1430, 1250, 1164, 985, 805 cm^{-1}. HRMS (ESI) calcd. for $C_{13}H_{13}F_3N_2$ $[M+H]^+$: 255.1031, found: *m/z* 255.1102.

5-(4-Methoxyphenyl)-3-(trifluoromethyl)-1*H*-pyrazole (2d)[16]: Yield 90%. solid, mp: 135-138 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.08 (s, 1H), 7.50 (d, *J* = 8.4 Hz, 2H), 6.97 (d, *J* = 8.4 Hz, 2H), 6.67 (s, 1H), 3.85 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.5, 144.9, 144.5 (q, $^{2}J_{C\text{-}F}$ = 37.7 Hz), 127.1, 121.1 (q, $^{1}J_{C\text{-}F}$= 267.0 Hz), 120.7, 114.7, 100.4, 55.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.22.

***N*,*N*-Dimethyl-4-(3-(trifluoromethyl)-1*H*-pyrazol-5-yl)aniline (2e):** Yield 30%. solid, mp: 120-122^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.39 (s, 1H),7.36-7.34 (m, 2H),6.68 (s, 3H), 6.57 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.0, 145.4, 126.6,120.0 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 115.7, 112.4, 99.6, 40.3.^{19}F NMR (376 MHz, $CDCl_3$) δ -62.36. IR (KBr) ν 2919, 2850, 1618, 1438, 1363, 1256, 1129, 980, 799 cm^{-1}. HRMS (ESI) calcd. for $C_{12}H_{12}F_3N_3$ $[M+H]^+$: 256.0983, found: *m/z* 256.1055.

5-(2-Methoxyphenyl)-3-(trifluoromethyl)-1*H*-pyrazole (2f)[16]: Yield 66%. solid, mp: 80-82 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.64 (s, 1H), 7.65 (d, *J* = 7.8 Hz, 1H), 7.39-7.35 (m, 1H), 7.10-7.05 (m, 2H), 6.87 (s, 1H), 4.03 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.0, 143.0 (q, $^{2}J_{C\text{-}F}$ = 38.2 Hz), 142.1, 130.2, 128.0, 121.7, 121.5 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 116.3, 111.8, 100.9, 56.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.17.

5-(4-Chlorophenyl)-3-(trifluoromethyl)-1*H*-pyrazole (2g)[16]: Yield 98%. solid, mp: 150-153 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.21 (s, 1H), 7.50 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 8.0 Hz, 2H), 6.73 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 144.3 (q, $^{2}J_{C\text{-}F}$ = 38.6 Hz), 135.5, 129.5, 126.9, 126.4, 122.3, 119.6 (q, $^{1}J_{C\text{-}F}$= 266.6 Hz), 101.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.16.

5-(4-Bromophenyl)-3-(trifluoromethyl)-1*H*-pyrazole (2h)[16]: Yield 91%. solid, mp: 150-153 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.84 (s, 1H), 7.60 (d, *J* = 8.0 Hz, 2H), 7.45 (d, *J* = 8.0 Hz, 2H), 6.77 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 143.6 (q, $^{2}J_{C\text{-}F}$ = 38.2 Hz), 132.6, 127.2, 127.0, 123.7, 120.9 (q, $^{1}J_{C\text{-}F}$= 267.1 Hz), 101.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.19.

5-(4-Fluorophenyl)-3-(trifluoromethyl)-1*H*-pyrazole (2i)[16]: Yield 99%. solid, mp: 99-100 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.71 (s, 1H), 7.58-7.55 (m, 2H), 7.18-7.14 (m, 2H), 6.73 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, $^{1}J_{C\text{-}F}$ = 248.5 Hz), 144.5, 143.4 (q, $^{2}J_{C\text{-}F}$ = 38.6 Hz), 127.6, 124.3, 119.6 (q, $^{1}J_{C\text{-}F}$= 267.1 Hz), 116.5 (q, $^{2}J_{C\text{-}F}$ = 22.0 Hz), 101.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.24, -110.91.

5-(2-Fluorophenyl)-3-(trifluoromethyl)-1*H*-pyrazole (2j): Yield 51%. solid, mp: 88-92 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.59 (s, 1H), 7.65 (d, *J* = 6.8 Hz, 1H), 7.39 (d, *J* = 5.5 Hz, 1H), 7.27-7.22 (m, 2H), 6.90 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3 (d, $^{1}J_{C\text{-}F}$= 247.0 Hz), 139.4, 130.9, 130.8, 127.9, 125.2, 119.7, 116.6 (q, $^{2}J_{C\text{-}F}$ = 23.0 Hz), 115.8, 102.5, 100.0. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.30, -115.34. HRMS (ESI) calcd. for $C_{10}H_6F_4N_2$ $[M+H]^+$: 231.0467, found: *m/z* 231.0538.

5-(2-Bromophenyl)-3-(trifluoromethyl)-1*H*-pyrazole (2k): Yield 10%. solid, mp: 160-163 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.85 (s, 1H), 7.72 (d, *J* = 8.0 Hz, 1H), 7.51 (d, *J* = 7.6 Hz, 1H), 7.44-7.41 (m, 1H), 7.32-7.29 (m, 1H), 6.84 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9 (q, $^{2}J_{C\text{-}F}$ = 38.2 Hz), 134.1, 130.9, 130.8, 129.1, 128.0, 127.0, 121.4, 119.2 (q, $^{1}J_{C\text{-}F}$ = 266.7 Hz), 104.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.19.IR (KBr) ν 3153, 2926, 1711, 1600, 1566, 1503, 1471, 1250, 1125, 983, 820 cm^{-1}. HRMS (ESI) calcd. for $C_{10}H_6BrF_3N_2$ $[M+H]^+$: 290.9666, found: *m/z* 290.9737.

3-(Trifluoromethyl)-5-(4-(trifluoromethyl)phenyl)-1*H*-pyrazole (2l)[16]: Yield 88%. solid, mp: 110-115°C. ^{1}H NMR (400 MHz, $CDCl_3$)δ7.70 (s, 4H), 6.84 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.2, 131.4, 126.3, 126.3, 126.0, 125.1, 121.0 (q, $J_{C\text{-}F}$= 289.0 Hz), 102.2. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.20, -62.86. IR (KBr) ν 3223, 2947, 1582, 1493, 1328, 1253, 1065, 981, 842, 816 cm^{-1}.

4-(3-(Trifluoromethyl)-1*H*-pyrazol-5-yl)phenol (2m)[24]: Yield 50%. solid, mp: 144-147 °C. ^{1}H NMR (400 MHz, DMSO) δ 13.82 (s, 1H), 9.84 (s, 1H), 7.64 (d, *J* = 8.0 Hz, 2H), 6.86 (d, *J* = 8.0 Hz, 3H), 6.99 (s, 1H). ^{13}C NMR (100 MHz, DMSO) δ 158.1, 144.3, 141.6 (q, $J_{C\text{-}F}$ = 73 Hz), 127.1, 119.1, 115.8, 99.5. ^{19}F NMR (376 MHz, DMSO) δ -60.41. IR (KBr) ν 3565, 2254, 2127, 1667, 1057, 993, 825 cm^{-1}. HRMS (ESI) calcd. for $C_{10}H_7F_3N_2O$ $[M+H]^+$: 229.0510, found: *m/z* 229.0582.

5-Styryl-3-(trifluoromethyl)-1*H*-pyrazole (2n)[16]: Yield 44%. solid, mp: 89-91 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.48 (s, 1H), 7.49-6.93 (m, 7H), 6.70 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ143.5,143.3(q, $^{2}J_{C\text{-}F}$ = 38.4 Hz), 135.6, 133.1, 128.9, 128.8, 126.8, 121.7 (q, $^{1}J_{C\text{-}F}$ = 266.6 Hz), 113.7, 101.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.14.

5-(Furan-2-yl)-3-(trifluoromethyl)-1*H*-pyrazole (2o)[16]: Yield 31%. solid, mp: 41-43 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.56 (s, 1H), 7.48 (s, 1H), 6.71-6.68 (m, 2H), 6.51 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 143.1 (q, $^{2}J_{C\text{-}F}$ = 38.4 Hz), 136.3, 120.1 (q, $^{1}J_{C\text{-}F}$ = 266.6 Hz), 111.8, 108.1, 100.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.40. IR (KBr) ν 2850, 1712, 1507, 1372, 1263, 1144, 975, 806, 742 cm^{-1}. HRMS (ESI) calcd. for $C_8H_5F_3N_2O$ $[M+H]^+$:203.0354, found: *m/z* 203.0425.

(E)-1,1,1-trifluoro-4-phenylbut-3-en-2-ol (3a)[25]: Yield 7%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43-7.33 (m, 2H), 6.87-6.83 (m, 3H), 6.23-6.17 (m, 1H), 4.63 (s, 1H), 2.45 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 136.3, 135.4, 128.7, 126.9, 125.7, 120.7, 100.0, 71.6 (q,$J_{C\text{-}F}$ = 32.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.05.

(E)-4-(4-bromophenyl)-1,1,1-trifluorobut-3-en-2-ol (3h)[26]: Yield 60%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d,*J* = 8.0,2H), 7.27 (d,*J* = 8.0,2H), 6.81 (d, *J* = 16.0 Hz, 2H), 6.20 (dd, *J* = 16.0, 4.0 Hz, 1H), 4.64 (d, *J* = 4.0 Hz, 1H), 2.35 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 135.0, 134.3, 131.9, 128.4, 122.7, 121.4, 100.0, 71.4 (q, $J_{C\text{-}F}$ = 32.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -79.05.

(E)-4-(4,4,4-trifluoro-3-hydroxybut-1-en-1-yl)phenol (3m): Yield 46%. ^{1}H NMR (400 MHz, DMSO) δ 9.62 (s, 1H), 7.32-7.31 (m, 2H), 6.76-6.72 (m, 3H), 6.44-6.42 (m, 1H),6.04-5.98 (m, 1H), 4.64-4.63 (m, 1H). ^{13}C NMR (100 MHz,

DMSO) δ 157.7, 134.5, 128.1, 126.6, 123.8, 119.0, 115.5, 69.9 (q, J_{C-F} = 30.2 Hz). ^{19}F NMR (376 MHz, DMSO) δ -77.28. IR (KBr) ν 3423, 2253, 2127, 1656, 1027, 825, 764, 629 cm^{-1}. GC-MS (EI) calcd. for $C_{10}H_9F_3O_2$ [M]$^+$: 218.0, found: *m/z* 217.9.

4.4 General procedure for the preparation of Celebrex and other compounds

To a 25 mL Schlenk were added pyrazole (1.0 eq, 0.25 mmol), CuI (5 mol%), K_2CO_3 (2.1 eq), *N,N'*-dimethylcyclohexanediamine (20 mol%), iodobenzenederivative (5.0 eq), 1,4-dioxane (1 mL) and a stirring bar under argon. The mixture was stirred at 150 °C for 36h before cooling down to room temperature. The reaction mixture was passed through a plug of silica gel, and washed with EtOAc. After removal of the solvent, the residue was purified by column chromatography on silica gel (hexane/EtOAc) to afford the coupling product **4** or SC-560. The analytical data are in accordance with literatures.[14-28]

1-Phenyl-5-(*p*-tolyl)-3-(trifluoromethyl)-1*H*-pyrazole (4a)[14]: Yield 80%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35–7.32 (m, 4H), 7.11 (s, 4H), 6.72 (s, 1H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 142.9 (q, $^2J_{C-F}$ = 38.2 Hz), 139.4, 139.1, 129.4, 129.1, 128.6, 128.4, 126.3, 125.5, 121.2 (q, $^1J_{C-F}$ = 266.7 Hz), 105.3, 21.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.13.

1,5-Di-*p*-tolyl-3-(trifluoromethyl)-1*H*-pyrazole (4b)[14]: Yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20-7.11 (m, 8H), 6.70 (s, 1H), 2.36 (s, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 143.1 (q, J_{C-F} = 38.2 Hz), 138.9, 138.4, 136.9, 129.6, 129.3, 128.6, 126.4, 125.3, 105.1, 21.3, 21.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.19.

***N,N*-Dibenzyl-4-(5-(p-tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (4c)[16]:** Yield 87%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 8.3 Hz, 2H), 7.24-7.07 (m, 14H), 6.75 (s, 1H), 4.32 (s, 4H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 143.9 (q, $^2J_{C-F}$ = 38.2 Hz), 140.2, 139.8, 135.2, 129.8, 128.7, 128.6, 128.2, 127.9, 125.8, 125.5, 120.6 (q, $^1J_{C-F}$ = 266.7 Hz), 106.4, 50.6, 21.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.41.

***N,N*-Dibenzyl-4-(5-(4-fluorophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (4d)[18]:** Yield 52%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (d, *J* = 7.8 Hz, 2H), 7.43 (d, *J* = 7.8 Hz, 2H), 7.23 (s, 8H), 7.06 (s, 6H), 6.77 (s, 1H), 4.33 (s, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 163.3 (d, $^1J_{C-F}$ = 249.9 Hz), 144.1, 142.0, 140.6, 135.2, 130.9, 128.6, 128.3, 127.9, 125.5, 124.8, 119.7, 116.4 (1, $^2J_{C-F}$ = 21.9 Hz), 106.6, 50.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.47, -110.17.

1-(4-Chlorophenyl)-5-(4-methoxyphenyl)-3-(trifluoromethyl)-1*H*-pyrazole (SC-560)[28]: Yield 77%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 7.13 (d, *J* = 8.0 Hz, 2H), 6.87 (d, *J* = 8.0 Hz, 2H), 6.68 (s, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.3, 144.7, 143.4 (q, $^2J_{C-F}$ = 38.0 Hz), 137.9, 134.2, 130.2, 129.3, 126.6, 121.3 (q, $^1J_{C-F}$ = 264.0 Hz), 121.2, 114.3, 105.4, 55.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.33.

To a 5 mL round bottom flask were added **4c** or **4d**(0.1mmol), concentrated H_2SO_4 (1 mL). The reaction was stirred at room temperature for 8h, and then was added to water (10 mL) carefully. The mixture was extracted with Et_2O. The organic layer was dried over Na_2SO_4, filtered, and then concentrated in vacuo. The residue was purified by column chromatography on silica gel (DCM/EtOAc = 10/1) to afford Celecoxib or Mavacoxib (99% yield) as a white solid. The analytical data are in accordance with literatures.[16-18]

4-(5-(*p*-Tolyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (Celecoxib)[16]: Yield 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.3 Hz, 2H), 7.47 (d, *J* = 8.3 Hz, 2H), 7.18 (d, *J* = 7.4 Hz, 2H), 7.11 (d, *J* = 7.7 Hz, 2H), 6.74 (s, 1H), 4.97 (s, 2H), 2.38 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 142.6, 141.3 (q, J_{C-F} = 38.0 Hz), 139.8, 138.4, 129.8, 128.7, 127.9, 127.5, 125.7, 125.5, 106.4, 21.3. ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.46.

4-(5-(4-Fluorophenyl)-3-(trifluoromethyl)-1*H*-pyrazol-1-yl)benzenesulfonamide (Mavacoxib)[18]: Yield 99%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, *J* = 7.6 Hz, 2H), 7.45 (d, *J* = 7.5 Hz, 2H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.08 (t, *J* = 7.5 Hz, 2H), 6.76 (s, 1H), 5.18 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (d, $^{1}J_{C\text{-}F}$ = 249.7 Hz), 144.4, 144.2(q, $^{2}J_{C\text{-}F}$ = 38.5 Hz), 144.0, 142.2, 141.7, 130.9, 130.8, 127.6, 125.5, 124.8, 120.9 (q, $^{1}J_{C\text{-}F}$ = 267.8 Hz), 116.5, 116.3, 106.7.^{19}F NMR (376 MHz, $CDCl_3$) δ -62.52, -110.15.

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