Synthetic Approach to Alkoxy-β-(trifluoromethyl)styrenes and Their Application in the Synthesis of New Trifluoromethylated Heterocycles

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Received 29 December 2008; revised 26 March 2009

Abstract: A new convenient stereoselective pathway to alkoxy-β-(trifluoromethyl)styrenes is described. Reactions of β-chloro- and β-bromo-β-(trifluoromethyl)styrenes with sodium methoxide and potassium *tert*-butoxide led to methoxy- and *tert*-butoxy-β-(trifluoromethyl)styrenes in good to excellent yields. Bromination of *tert*-butoxy-β-(trifluoromethyl)styrenes proceeded with formation of aryl(bromo)methyl trifluoromethyl ketones. The latter compounds were found to be useful starting materials for the synthesis of different heterocyclic compounds bearing a trifluoromethyl group. In this way trifluoromethylated derivatives of imidazopyridine, imidazopyrimidine, imidazobenzimidazole, imidazothiazole, thiazole, and aminothiazole were obtained in moderate to high yield.

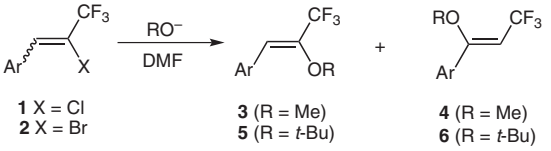
Key words: alkenes, alkynes, ethers, fluorine, heterocycles, nucleophilic substitution

Recent decades have seen remarkable progress in organofluorine chemistry and a variety of applications for fluorinated compounds.[1] Particularly fluorine-containing drugs and pesticides have enjoyed increased interest in bioorganic chemistry, as well as for medicinal and agricultural applications due to the remarkable effect of fluorine substitution on biological activity.[2] Consequently, a broad spectrum of synthetic methods towards such compounds has been developed in recent years.[3]

Earlier, a new catalytic olefination reaction starting from aldehydes or ketones was discovered by our research group.[4] Based on this reaction, we elaborated new methods for the synthesis of various fluorinated alkenes.[5] It was also demonstrated that a halogen atom in β-chloro- and β-bromo-β-(trifluoromethyl)styrenes or β-bromo-β-fluorostyrenes, obtained by these methods, can be easily substituted by different nucleophiles. For example, reactions with copper cyanide, sodium 4-toluenesulfinate, alkanethiolates, and arenethiolates led to α-fluoro- and α-(trifluoromethyl)acrylonitriles,[6] α-fluoro-β-arylvinyl sulfones,[7] or to (trifluoromethyl)vinyl sulfides,[8] respectively.

We supposed that treatment of β-halo-β-(trifluoromethyl)styrenes with alkoxides would lead to β-alkoxy-β-(trifluoromethyl)styrenes. Similar compounds have already been used for the synthesis of epoxy ethers,[9] β-alkyl-β-(trifluoromethyl)styrenes,[10] α-bromostyrenes,[11] or enamines,[12] bearing trifluoromethyl groups.

In continuation of our investigations on the synthesis and application of β-halo-β-(trifluoromethyl)styrenes, we have now found that *Z*/*E*-mixtures of β-chloro- **1** and β-bromo-β-(trifluoromethyl)styrenes **2** (3:1 to 10:1)[5b,e] easily reacted with sodium methoxide in *N*,*N*-dimethylformamide forming methoxy-β-(trifluoromethyl)styrenes **3** and **4** in good to excellent yields (Scheme 1, Table 1).



1 X = Cl
2 X = Br

3 (R = Me)
5 (R = *t*-Bu)

4 (R = Me)
6 (R = *t*-Bu)

Scheme 1 Reactions of β-chloro- **1** and β-bromo-β-(trifluoromethyl)styrenes **2** with alkoxides

Table 1 Synthesis of the Regioisomeric Methoxy-β-(trifluoromethyl)styrenes **3** and **4**

Entry	Styrene[a]	Ar	Yield (%) of **3** + **4**		Ratio[b] **3**/**4**
			From **1**	From **2**	
1	**1a** or **2a**	Ph	73	76	80:20
2	**1b** or **2b**	4-MeC_6H_4	88	85	67:33
3	**1c**	4-ClC_6H_4	94	–[c]	83:17
4	**1d**	4-$O_2NC_6H_4$	91	–[c]	100:0
5	**1e**	3-$O_2NC_6H_4$	97	–[c]	90:10
6	**2f**	2-$MeOC_6H_4$	–[c]	89	100:0

[a] **1** (X = Cl) or **2** (X = Br).
[b] Determined by ^1H NMR spectroscopy.
[c] The reaction was not carried out.

Remarkable heat evolution and fast consumption of starting material were observed for the compounds containing a nitro group even at room temperature. In all other cases, heating at 70–80 °C for 1–2 minutes or stirring of the mixture at room temperature for 24 hours were needed to complete the reaction. This reaction is quite general and both methoxy-β-(trifluoromethyl)styrenes bearing elec-

SYNTHESIS 2009, No. 13, pp 2249–2259
Advanced online publication: 12.05.2009
DOI: 10.1055/s-0029-1216697; Art ID: T22808SS

tron-withdrawing as well as electron-donating substituents could be obtained in high yields, independently of the nature of the halogen atom. The total yields and ratios of regioisomers **3** and **4** were almost equal for the reactions of β-chloro- **1** and β-bromo-β-(trifluoromethyl)styrenes **2** bearing the same aryl substituent (Table 1, entries 1 and 2).

As expected, the more bulky *tert*-butoxy-β-(trifluoromethyl)styrenes had even better regioselectivity (Scheme 1, Table 2).[13]

Table 2 Synthesis of the Regioisomeric *tert*-Butoxy-β-(trifluoromethyl)styrenes **5** and **6**

Entry	Styrenes[a]	Ar	Yield (%) of **5**+**6**		Ratio[b] **5**/**6**	Ref
			From **1**	From **2**		
1	**1a** or **2a**	Ph	41	74	90:10	13
2	**1b** or **2b**	4-MeC_6H_4	4	49	83:17	–
3	**1c** or **2c**	4-ClC_6H_4	83	84	86:14	13
4	**1d**	4-$O_2NC_6H_4$	83	–[c]	100:0	13
5	**1e**	3-$O_2NC_6H_4$	70	–[c]	91:9	–
6	**2f**	2-$MeOC_6H_4$	–[c]	97	100:0	13
7	**2g**	3-$MeOC_6H_4$	–[c]	88	92:8	13
8	**2h**	4-$MeOC_6H_4$	–[c]	91	67:33	–
9	**1i** or **2i**	2-BrC_6H_4	65	70	100:0	13
10	**1j** or **2j**	4-$MeO_2CC_6H_4$	62	73	100:0	–
11	**2k**	3,4-$(MeO)_2C_6H_3$	–[c]	98	67:33	–
12	**1l**	2-pyridyl	72	–[c]	100:0	–

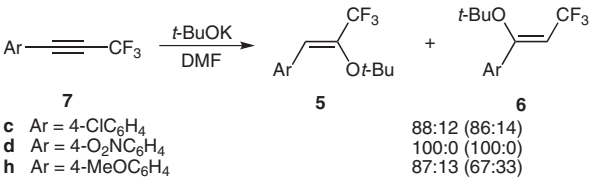
[a] **1** (X = Cl) or **2** (X = Br).
[b] Determined by ^{1}H NMR spectroscopy.
[c] The reaction was not carried out.

Indeed, in the case of styrenes with a phenyl substituent **1a** and **2a** (entry 1) or electron-donating substituents at the aryl group **1b** and **2b** (entry 2), the share of the α-regioisomer **6** drops significantly comparing to the reactions of the same styrenes and sodium methoxide, while, in case of styrenes with electron-withdrawing substituents, a similar effect was not observed. Again, the nature of halogen in the starting styrenes did not affect the ratio and the total yield of products **5** and **6** in case of styrenes with attached electron-withdrawing substituents **1c** and **2c**, **1f** and **2f**, and **1j** and **2j** (entries 3, 6, and 10). However, using the bromostyrenes **2a** and **2b** bearing no or an electron-donating substituent, the yields were higher compared to the chloro compounds **1a** and **1b**. Moreover, the regioselectivity of the reaction with alkoxides was influenced by both electronic and steric properties of the aryl(hetaryl) substituent and the bulkiness of the alkoxide. Caused by negative mesomeric effect of the electron-deficient aryl ring, the excessive positive charge on the carbon atom in β-position of the double bond directed the alkoxide to that position. The opposite polarization of the double bond in the case of electron-donating substituents led to admixtures of the α-regioisomer. Steric hindrance of the aryl(hetaryl) ring played a decisive role on the direction of alkoxide attack, thus, styrenes with *ortho*-substituents in the aryl ring gave the β-regioisomer exclusively, in spite of their electronic properties (entries 6 and 9).

Interestingly, the reactions proceeded with complete stereoselectivity and the *Z*-isomers of the alkenes **3**–**6** were obtained exclusively, although the initial styrenes **1** and **2** were used as mixtures of *Z*/*E* isomers (see refs[5b,e]). Similar selectivity was previously observed for reactions with copper cyanide and thioles.[6,8]

To assign the configuration of the double bond in the alkoxy-β-(trifluoromethyl)styrenes **3** and **5**, the spin-spin coupling constants $^3J_{C,H}$ of the carbon of the trifluoromethyl group and the vinylic proton were determined. The observed values of 3–4 Hz correspond to *Z*-isomers.[14]

Substitution of vinylic halogen atoms (or other leaving groups in the general case) was found to proceed as an addition–elimination process in most cases.[15] However, the elimination–addition sequence is also possible and cannot be ignored. To clarify this point, we synthesized the acetylenes **7c**, **7d**, and **7h** by elimination of HCl from compounds **1c**, **1d**, and **1h** and reacted them with potassium *tert*-butoxide under the same reaction conditions as the styrenes **1** or **2** (Scheme 2).



Scheme 2 Reactions of acetylenes **7** with potassium *tert*-butoxide, values in parenthesis represent the product ratio for the reactions of compounds **2**

We observed the same distribution of regioisomers in case of the reactions of the acetylenes **7c** and **7d** bearing electron-withdrawing groups, which actually is not conclusive concerning the reaction mechanism, since the ratio of regioisomers could be equal by chance. However, for the electron-rich acetylene **7h** the share of regioisomer **6h** dropped significantly compared to the reaction of styrene **2h**. This noticeable difference suggests that the reaction of styrenes **2** with potassium *tert*-butoxide occurs via an addition–elimination process, at least in case of styrenes with electron-donating substituents.

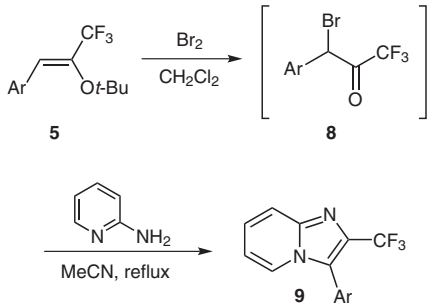
For more than a century it has been known that bromination of enol ethers leads to the corresponding α-bromo ketones.[16] However, in the case of bromination of 1-(trifluoromethyl)enol ethers the nature of the product strongly depends on the substituent at the oxygen atom. If the substituent at the oxygen atom can be eliminated as a stable cation, the aryl(bromo)methyl trifluoromethyl ketone is formed (from silyloxy enol ethers).[17] Otherwise

bromination leads to saturated vicinal dibromides (from alkyl enol ethers).[18]

Since the *tert*-butyl cation belongs to the most stable alkyl cations, we expected that bromination of *tert*-butoxy-β-(trifluoromethyl)styrenes **5c**/**6c** would lead to aryl(bromo)methyl trifluoromethyl ketones. Consequently, we reacted a mixture of the *tert*-butoxy-β-(trifluoromethyl)styrenes **5c**/**6c** with bromine in dichloromethane at room temperature. In the ^{1}H NMR spectrum of the product mixture we no longer found the signal of a vinylic proton or the protons of the *tert*-butyl group. Instead the signal of one benzylic proton appeared at δ = 5.77. The ^{13}C NMR spectrum, among others, exhibited the quadruplet of the trifluoroacetyl carbon at δ = 183.0 (J = 35.9 Hz). Also the signal of the benzylic carbon was observed at δ = 44.6. Thus, the obtained compound is the desired bromo ketone **8c**, which was isolated as a crude product in approximately 85% yield. Due to the instability of such ketones[9] all following reactions were performed in one pot without isolation of bromo ketones **8**.

α-Halo ketones are very reactive compounds that have been widely used in the synthesis of heterocycles.[19] Although the above-mentioned aryl(bromo)methyl trifluoromethyl ketones were previously described,[20] only a few reactions of these compounds have been investigated. For example, the reaction with sodium alkoxides leads to substitution of bromine giving alkylbenzylic alcohols,[20] other examples are the reactions with thiourea and its N-substituted derivatives giving aminothiazoles[21] and reactions with alcohols to give oxiranes.[22]

Table 3 Synthesis of Imidazopyridines **9** from Aryl(bromo)methyl Trifluoromethyl Ketones and 2-Aminopyridine



Entry	Styrenes	Ar	Product	Yield (%)
1	**5a**/**6a**	Ph	**9a**	46
2	**5c**/**6c**	4-ClC_6H_4	**9c**	52
3	**5d**	4-$O_2N$$C_6H_4$	**9d**	53
4	**5e**/**6e**	3-$O_2N$$C_6H_4$	**9e**	42
5	**5f**	2-MeOC_6H_4	**9f**	31
6	**5g**/**6g**	3-MeOC_6H_4	**9g**	51
7	**5h**/**6h**	4-MeOC_6H_4	**9h**	27
8	**5i**	2-BrC_6H_4	**9i**	51

The reaction of α-bromo ketones with 2-aminopyridines is the most general approach to the synthesis of imidazopyridines.[23] The imidazopyridine moiety is the pharmacophore of several drugs, such as Zolpidem, Alpidem, Saripidem, and Necopidem, which are used for the short-term treatment of insomnia, as well as against particular brain disorders.[24,25] Having this interesting biological activity in mind, we refluxed the crude bromo ketones **8** with 2-aminopyridine in acetonitrile and obtained the corresponding imidazopyridines **9** in moderate yields (Table 3).

It should be noted, that even when mixtures of styrenes **5** and **6** were applied, only the regioisomeric imidazopyridines **9** were obtained (entries 1, 2, 4, 6, and 7). No starting material and no other products could be isolated. This seems to be due to the instability of the α-bromo ketones and/or intermediates formed from it. In particular, the low yields of the methoxy compounds **9f** and **9h** support this hypothesis.

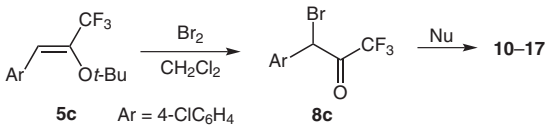
To estimate the synthetic scope of aryl(bromo)methyl trifluoromethyl ketones **8** for the preparation of other heterocycles, we treated the model ketone **8c** with several other binucleophiles. Derivatives of imidazopyridine, imidazopyrimidine, imidazobenzimidazole, imidazothiazole, aminothiazole, and methylthiazole, bearing a trifluoromethyl group were obtained in moderate to high yields (Table 4).

The best yields were obtained for trifluoromethylated thiazole derivatives (entries 5–8). Obviously, the high nucleophilicity of sulfur leads to rapid formation of the isothiouronic salt preventing side reactions.

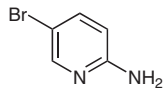
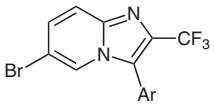
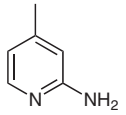
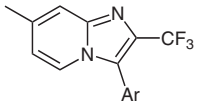
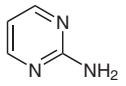
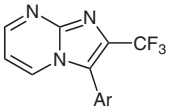
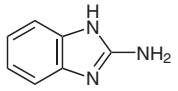
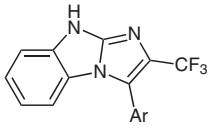
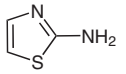
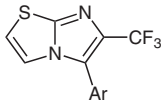
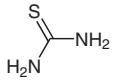
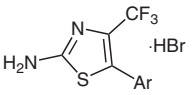
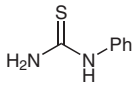
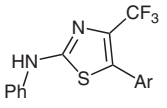
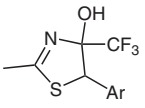
In conclusion, the nucleophilic substitution of one halogen atom of β-chloro- and β-bromo-β-(trifluoromethyl)styrenes **1** and **2** by methoxide and *tert*-butoxide proceeds with complete stereoselectivity and high regioselectivity to give the alkoxy-β-(trifluoromethyl)styrenes **3**–**6** in good to excellent yields. The isomers with *Z*-configuration of the double bond were formed exclusively. It was shown that the *tert*-butoxystyrenes **5** react with bromine to form unstable aryl(bromo)methyl trifluoromethyl ketones **8**. From these building blocks a series of trifluoromethyl-containing heterocycles **9**–**17**, was synthesized in moderate to high yields.

NMR spectra were recorded on Bruker ARX 300 and Bruker AMX 400 in $CDCl_3$, DMSO-d_6, or acetone-d_6 with TMS as internal standard. IR spectra were obtained as films. Mass spectra (ESI-MS) were measured on a MicroTof Bruker Daltonics. Column and TLC chromatography were performed using silica gel Merck 60 or Merck 60F_{254} plates, respectively. The β-chloro- **1** and β-bromo-β-(trifluoromethyl)styrenes **2** were synthesized according to our previously reported procedure.[5b,e] All solvents were distilled before using. ^{1}H NMR spectra of compounds **7c**, **7d**, and **7h** are in agreement with published data.[25]

Table 4 Synthesis of Various Trifluoromethylated Heterocycles **10–17** from **5c**/**6c**



5c Ar = 4-ClC$_6$H$_4$ **8c**

Entry	Nucleophile	Product[a]	Yield (%)
1		 **10**	44
2		 **11**	47
3		 **12**	52
4		 **13**	37
5		 **14**	60
6		 **15**·HBr	72
7		 **16**	80
8		 **17**	54

[(1*Z*)-3,3,3-Trifluoro-2-methoxyprop-1-enyl]benzenes 3 and [(1*Z*)-3,3,3-Trifluoro-1-methoxyprop-1-enyl]benzenes 4; General Procedure

A one-neck, 25-mL round-bottomed flask was charged with anhyd DMF (2 mL), the corresponding styrene **1** or **2** (2 mmol) and a soln of NaOMe (0.108 g, 2 mmol) in anhyd DMF (2 mL) were added dropwise with stirring. The mixture was heated at 70–80 °C for 1–2 min then cooled to r.t. (no heating is necessary for compound **1d**) and poured into H_2O (100 mL). The products were extracted with CH_2Cl_2 (3 × 20 mL) and the combined extracts were washed with H_2O (2 × 50 mL) and brine (50 mL) and dried (Na_2SO_4). CH_2Cl_2 was evaporated in vacuo and the residue was filtered through a short silica gel pad (hexane or appropriate mixtures of hexane–CH_2Cl_2). The regioisomers **3** and **4** could not be separated by column chromatography.

[(1*Z*)-3,3,3-Trifluoro-2-methoxyprop-1-enyl]benzene (3a) and [(1*Z*)-3,3,3-Trifluoro-1-methoxyprop-1-enyl]benzene (4a)

From styrenes **1a** (415 mg, 2 mmol) or **2a** (502 mg, 2 mmol) as a colorless oil; yield (**3** + **4**): 294 mg (73%, from **1a**), 307 mg (76%, from **2a**); ratio **3a**/**4a** 80:20.

Anal. Calcd for $C_{10}H_9F_3O$: C, 59.41; H, 4.49. Found: C, 59.52; H, 4.63.

Regioisomer 3a

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 6.53 (s, 1 H, CH=CCF_3), 7.37–7.55 (m, 3 H, Ar), 7.72 (d, *J* = 7.3 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 60.0 (OCH_3), 117.2 (q, *J* = 4.4 Hz, *C*H=CCF_3), 121.4 (q, *J* = 275.9 Hz, CF_3), 128.7 (Ar), 128.9 (Ar), 129.6 (Ar), 132.2 (Ar), 143.5 (q, *J* = 32.2 Hz, *C*-CF_3).

Regioisomer 4a

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.70 (s, 3 H, OCH_3), 5.37 (q, *J* = 7.6, 1 H, $CHCF_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.0 (OCH_3), 100.6 (q, *J* = 34.4 Hz, C=*C*HCF_3), 123.6 (q, *J* = 269.3 Hz, CF_3), 127.5 (Ar), 128.8 (Ar), 133.1 (Ar); the other signals are identical to those of the regioisomer **3a**.

1-Methyl-4-[(1*Z*)-3,3,3-trifluoro-2-methoxyprop-1-enyl]benzene (3b) and 1-Methyl-4-[(1*Z*)-3,3,3-trifluoro-1-methoxyprop-1-enyl]benzene (4b)

From styrenes **1b** (440 mg, 2 mmol) or **2b** (530 mg, 2 mmol) as a colorless oil; yield (**3** + **4**): 380 mg (88%, from **1b**), 367 mg (85%, from **2b**); ratio **3b**/**4b** 67:33.

Anal. Calcd for $C_{11}H_{11}F_3O$: C, 61.11; H, 5.13. Found: C, 61.40; H, 4.94.

Regioisomer 3b

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.45 (s, 3 H, CH_3), 3.84 (s, 3 H, OCH_3), 6.49 (s, 1 H, CH=CCF_3), 7.27 (d, *J* = 8.0 Hz, 2 H, Ar), 7.61 (d, *J* = 8.0 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (CH_3), 60.0 (OCH_3), 117.3 (q, *J* = 4.4 Hz, *C*H=CCF_3), 121.6 (q, *J* = 275.9 Hz, CF_3), 127.5 (Ar), 129.4 (Ar), 129.5 (Ar), 139.0 (Ar), 143.8 (q, *J* = 32.2 Hz, *C*-CF_3).

Regioisomer 4b

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.48 (s, 3 H, CH_3), 3.70 (s, 3 H, OCH_3), 5.33 (q, *J* = 7.8 Hz, 1 H, $CHCF_3$), 7.32 (d, *J* = 8.0 Hz, 2 H, Ar), 7.43 (d, *J* = 8.0 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 58.9 (OCH_3), 100.2 (q, *J* = 33.7 Hz, C=*C*HCF_3), 123.6 (q, *J* = 268.6 Hz, CF_3), 127.5 (Ar), 140.7 (Ar), the other signals are identical to those of the regioisomer **3b**.

1-Chloro-4-[(1*Z*)-3,3,3-trifluoro-2-methoxyprop-1-enyl]benzene (3c) and 1-Chloro-4-[(1*Z*)-3,3,3-trifluoro-1-methoxyprop-1-enyl]benzene (4c)

From styrene **2c** (482 mg, 2 mmol) as a colorless oil; yield (**3** + **4**): 444 mg (94%); ratio **3c**/**4c** 83:17.

Anal. Calcd for $C_{10}H_8ClF_3O$: C, 50.76; H, 3.41. Found: C, 50.52; H, 3.53.

Regioisomer 3c

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 6.41 (s, 1 H, CH=CCF_3), 7.38 (d, *J* = 8.4 Hz, 2 H, Ar), 7.60 (d, *J* = 8.4 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.9 (OCH_3), 115.8 (q, *J* = 4.4 Hz, *C*H=CCF$_3$), 121.2 (q, *J* = 275.9 Hz, CF_3), 128.9 (Ar), 130.8 (Ar), 134.5 (Ar), 143.8 (q, *J* = 32.2 Hz, *C*-CF_3).

Regioisomer 4c

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.66 (s, 3 H, OCH_3), 5.34 (q, *J* = 7.6 Hz, 1 H, $CHCF_3$), 7.19 (d, *J* = 8.1 Hz, 2 H, Ar), 7.32 (d, *J* = 8.1 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.1 (OCH_3), 101.3 (q, *J* = 34.4 Hz, C=*C*HCF$_3$), 123.3 (q, *J* = 268.6 Hz, CF_3), 128.3 (Ar), 129.1 (Ar), 136.5 (Ar).

1-Nitro-4-[(1*Z*)-3,3,3-trifluoro-2-methoxyprop-1-enyl]benzene (3d)

From styrene **1d** (502 mg, 2 mmol) as a yellow oil; yield: 450 mg (91%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.85 (s, 3 H, OCH_3), 6.44 (s, 1 H, CH=CCF$_3$), 7.79 (d, *J* = 8.6 Hz, 2 H, Ar), 8.21 (d, *J* = 8.6 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.2 (OCH_3), 113.8 (q, *J* = 4.4 Hz, *C*H=CCF$_3$), 120.0 (q, *J* = 275.9 Hz, CF_3), 123.5 (Ar), 130.1 (Ar), 138.5 (Ar), 145.8 (q, *J* = 31.5 Hz, *C*-CF_3), 147.2 (Ar).

Anal. Calcd for $C_{10}H_8F_3NO_3$: C, 48.59; H, 3.26. Found: C, 48.79; H, 3.43.

1-Nitro-3-[(1*Z*)-3,3,3-trifluoro-2-methoxyprop-1-enyl]benzene (3e) and 1-Nitro-3-[(1*Z*)-3,3,3-trifluoro-1-methoxyprop-1-enyl]benzene (4e)

From styrene **1e** (502 mg, 2 mmol) as a yellow oil; yield (**3** + **4**): 479 mg (97%); ratio **3e**/**4e** 90:10.

Anal. Calcd for $C_{10}H_8F_3NO_3$: C, 48.59; H, 3.26. Found: C, 48.73; H, 3.41.

Regioisomer 3e

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.84 (s, 3 H, OCH_3), 6.43 (s, 1 H, CH=CCF$_3$), 7.55 (t, *J* = 8.0 Hz, 1 H, Ar), 7.91 (d, *J* = 8.0 Hz, 1 H, Ar), 8.10–8.15 (m, 1 H, Ar), 8.48 (br s, 1 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 59.8 (OCH_3), 113.9 (q, *J* = 4.4 Hz, *C*H=CCF$_3$), 120.6 (q, *J* = 276.6 Hz, CF_3), 123.1 (Ar), 123.9 (Ar), 129.5 (Ar), 133.8 (Ar), 135.1 (Ar), 145.0 (q, *J* = 32.2 Hz, *C*-CF_3), 148.3 (Ar).

Regioisomer 4e

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.68 (s, 3 H, OCH_3), 5.45 (q, *J* = 7.8 Hz, 1 H, $CHCF_3$), 7.65 (t, *J* = 7.9 Hz, 1 H, Ar), 7.83 (d, *J* = 7.9 Hz, 1 H, Ar), 8.27–8.33 (m, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 56.1 (OCH_3), 102.7 (q, *J* = 34.4 Hz, C=*C*HCF$_3$), 123.6 (Ar), 124.9 (Ar), 130.0 (Ar), 132.9 (Ar), 134.1 (Ar), 148.4 (Ar), the other signals are identical to those of the regioisomer **3d**.

1-Methoxy-2-[(1*Z*)-3,3,3-trifluoro-2-methoxyprop-1-enyl]benzene (3f)

From styrene **2f** (562 mg, 2 mmol) as a colorless oil; yield: 415 mg (89%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.78 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 6.93 (s, 1 H, CH=CCF$_3$), 6.97 (d, *J* = 7.9 Hz, 1 H, Ar), 7.06 (t, *J* = 7.9 Hz, 1 H, Ar), 7.38 (td, *J* = 7.9, 1.4 Hz, 1 H, Ar), 7.98 (dd, *J* = 7.9, 1.4 Hz, 1 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4, 60.1 (both OCH_3), 110.9 (q, *J* = 3.7 Hz, *C*H=CCF$_3$), 110.5 (Ar), 120.7 (Ar), 120.9 (Ar), 121.5 (q, *J* = 275.2 Hz, CF_3), 130.0 (Ar), 130.1 (Ar), 143.4 (q, *J* = 32.2 Hz, *C*-CF_3), 157.1 (Ar).

Anal. Calcd for $C_{11}H_{11}F_3O_2$: C, 56.90; H, 4.77. Found: C, 57.03; H, 4.93.

[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]benzenes 5 and [(1*Z*)-1-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]benzenes 6; General Procedures

According to the given protocol using potassium *tert*-butoxide,[13] the following *tert*-butyl enol ethers were prepared. The ^{1}H NMR data of compounds **5a**, **5c**, **5d**, **5f**, and **5i** agree with published data.

[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]benzene (5a) and [(1*Z*)-1-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]benzene (6a)

From styrenes **1a** (1035 mg, 5 mmol) or **2a** (1255 mg, 5 mmol) as a colorless oil; yield (**5** + **6**): 500 mg (41%, from **1a**), 903 mg (74%, from **2a**); ratio **5a**/**6a** 90:10.

IR (Nujol): 1660 (C=C) cm^{-1}.

Anal. Calcd for $C_{13}H_{15}F_3O$: C, 63.93; H, 6.19. Found: C, 64.38; H, 5.83.

Regioisomer 5a

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 [OC(*C*H$_3$)$_3$], 84.3 [O*C*(CH$_3$)$_3$], 121.4 (q, *J* = 276.6 Hz, CF_3), 122.0 (q, *J* = 4.4 Hz, *C*H=CCF$_3$), 128.3 (Ar), 128.5 (Ar), 129.7 (Ar), 133.4 (Ar), 140.2 (q, *J* = 32.2 Hz, *C*-CF_3).

Regioisomer 6a

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4 [OC(*C*H$_3$)$_3$], 82.2 [O*C*(CH$_3$)$_3$], 106.2 (q, *J* = 33.7 Hz, C=*C*HCF$_3$), 127.9 (Ar), 128.2 (Ar), 129.0 (Ar), the other signals are identical to those of the regioisomer **5a**.

1-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-4-methylbenzene (5b) and 1-[(1*Z*)-1-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-4-methylbenzene (6b)

From styrenes **1b** (1200 mg, 5 mmol) or **2b** (1325 mg, 5 mmol) as a colorless oil; yield (**5** + **6**): 52 mg (4%, from **1b**), 632 mg (49%, from **2b**); ratio **5b**/**6b** 83:17.

IR (Nujol): 1660 (C=C) cm^{-1}.

Anal. Calcd for $C_{14}H_{17}F_3O$: C, 65.10; H, 6.63. Found: C, 65.40; H, 6.33.

Regioisomer 5b

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.38 [s, 9 H, OC(CH$_3$)$_3$], 2.41 (s, 3 H, CH_3), 6.65 (s, 1 H, CH=CCF$_3$), 7.22 (d, *J* = 8.4 Hz, 2 H, Ar), 7.61 (d, *J* = 8.4 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (CH_3), 28.8 [OC(*C*H$_3$)$_3$], 84.0 [O*C*(CH$_3$)$_3$], 121.6 (q, *J* = 276.7 Hz, CF_3), 122.0 (q, *J* = 3.7 Hz, *C*H=CCF$_3$), 129.0 (Ar), 129.7 (Ar), 130.5 (Ar), 138.5 (Ar), 139.4 (q, *J* = 32.2 Hz, *C*-CF_3).

Regioisomer 6b

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 [s, 9 H, OC(CH$_3$)$_3$], 2.40 (s, 3 H, CH_3), 5.31 (q, *J* = 7.8 Hz, 1 H, $CHCF_3$), 7.54 (d, *J* = 8.1 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.2 (CH_3), 29.3 [OC(*C*H$_3$)$_3$], 82.0 [O*C*(CH$_3$)$_3$], 105.5 (q, *J* = 32.9 Hz, C=*C*HCF$_3$), 121.7 (q, *J* = 274.5 Hz, CF_3), 128.4 (Ar), 129.5 (Ar), 130.9 (Ar), 139.3 (Ar), the other signals are identical to those of the regioisomer **5b**.

1-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-4-chlorobenzene (5c) and 1-[(1*Z*)-1-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-4-chlorobenzene (6c)

From styrenes **1c** (1205 mg, 5 mmol) or **2c** (1425 mg, 5 mmol) as a colorless oil; yield (**5** + **6**): 1153 mg (83%, from **1c**), 1168 mg (84%, from **2c**); ratio **5c**/**6c** 86:14.

IR (Nujol): 1660 (C=C) cm^{-1}.

Anal. Calcd for $C_{13}H_{14}ClF_3O$: C, C 56.02; H, 5.06. Found: C, 55.63; H, 4.78.

Regioisomer 5c

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.7 [OC(*C*H$_3$)$_3$], 84.6 [O*C*(CH$_3$)$_3$], 120.7 (q, *J* = 4.4 Hz, *C*H=CCF$_3$), 121.4 (q, *J* = 276.6 Hz, CF$_3$), 128.6 (Ar), 131.0 (Ar), 131.9 (Ar), 134.2 (Ar), 140.7 (q, *J* = 32.2 Hz, *C*-CF$_3$).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –67.2 (s, CF$_3$).

Regioisomer 6c

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.3 [OC(*C*H$_3$)$_3$], 82.5 [O*C*(CH$_3$)$_3$], 106.5 (q, *J* = 32.9 Hz, C=*C*HCF$_3$), 123.0 (q, *J* = 270.1 Hz, CF$_3$), 128.5 (Ar), 129.1 (Ar), 135.8 (Ar), 136.6 (Ar), 161.2 (q, *J* = 5.9 Hz, *C*=CHCF$_3$).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –56.9 (d, *J* = 7.6 Hz, CF$_3$).

1-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-4-nitrobenzene (5d)

From styrene **1d** (1250 mg, 5 mmol) as a yellow oil; yield: 1200 mg (83%).

IR (Nujol): 1360, 1540 (NO$_2$), 1670 (C=C) cm^{-1}.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 [OC(*C*H$_3$)$_3$], 85.9 [O*C*(CH$_3$)$_3$], 119.7 (q, *J* = 3.7 Hz, *C*H=CCF$_3$), 120.8 (q, *J* = 277.4 Hz, CF$_3$), 123.6 (Ar), 130.3 (Ar), 140.0 (Ar), 143.2 (q, *J* = 32.9 Hz, *C*-CF$_3$), 147.2 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –67.5 (s, CF$_3$).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}F_3NNaO_3$: 312.0823; found: 312.0832.

Anal. Calcd for $C_{13}H_{14}F_3NO_3$: C, 53.98; H, 4.88. Found: C, 53.69; H, 4.77.

1-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-3-nitrobenzene (5e) and 1-[(1*Z*)-1-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-3-nitrobenzene (6e)

From styrene **1e** (1255 mg, 5 mmol) as a yellow oil; yield (**5** + **6**): 1012 mg (70%); ratio **5e**/**6e** 91:9.

IR (Nujol): 1360, 1540 (NO$_2$), 1660 (C=C) cm^{-1}.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_{14}F_3NNaO_3$: 312.0823; found: 312.0818.

Anal. Calcd for $C_{13}H_{14}F_3NO_3$: C, 53.98; H, 4.88. Found: C, 53.87; H 4.68.

Regioisomer 5e

^1H NMR (400 MHz, $CDCl_3$): δ = 1.36 [s, 9 H, OC(CH$_3$)$_3$], 6.68 (s, 1 H, CH=CCF$_3$), 7.56 (t, *J* = 8.1 Hz, 1 H, Ar), 7.88 (d, *J* = 8.1 Hz, 1 H, Ar), 8.16 (dd, *J* = 8.1, 1.5 Hz, 1 H, Ar), 8.70 (br s, 1 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 [OC(*C*H$_3$)$_3$], 85.6 [O*C*(CH$_3$)$_3$], 119.4 (q, *J* = 3.7 Hz, *C*H=CCF$_3$), 121.4 (q, *J* = 276.6 Hz, CF$_3$), 123.1 (Ar), 124.2 (Ar), 129.4 (Ar), 135.0 (Ar), 135.5 (Ar), 142.6 (q, *J* = 32.9 Hz, *C*-CF$_3$), 148.2 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –67.3 (s, CF$_3$).

Regioisomer 6e

^1H NMR (400 MHz, $CDCl_3$): δ = 1.27 [s, 9 H, OC(CH$_3$)$_3$], 5.43 (q, *J* = 7.6 Hz, 1 H, CHCF$_3$), 7.66 (t, *J* = 8.0 Hz, 1 H, Ar), 7.85 (d, *J* = 8.0 Hz, 1 H, Ar), 8.27 (dd, *J* = 8.0 Hz, *J* = 1.3 Hz, 1 H, Ar), 8.43 (br s, 1 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.4 [OC(*C*H$_3$)$_3$], 83.2 [O*C*(CH$_3$)$_3$], 108.1 (q, *J* = 33.7 Hz, C=*C*HCF$_3$), 122.6 (Ar), 124.5 (Ar), 129.5 (Ar), 133.4 (Ar), 138.0 (Ar), 148.1 (Ar), 159.5 (q, *J* = 5.1 Hz, *C*=CHCF$_3$), the other signals are identical to those of the regioisomer **5e**.

^{19}F NMR (282 MHz, $CDCl_3$): δ = –57.3 (d, *J* = 7.6 Hz, CF$_3$).

1-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-2-methoxybenzene (5f)

From styrene **2f** (1405 mg, 5 mmol) as a colorless oil; yield: 1363 mg (97%).

IR (Nujol): 1660 (C=C) cm^{-1}.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.7 [OC(*C*H$_3$)$_3$], 55.4 (OCH$_3$), 83.8 [O*C*(CH$_3$)$_3$], 110.4 (Ar), 117.0 (q, *J* = 3.7 Hz, *C*H=CCF$_3$), 120.1 (Ar), 121.5 (q, *J* = 275.9 Hz, CF$_3$), 122.2 (Ar), 129.8 (Ar), 130.8 (Ar), 139.7 (q, *J* = 32.2 Hz, *C*-CF$_3$), 157.1 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –67.49 (s, CF$_3$).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{17}F_3NaO_2$: 297.1078; found: 297.1073.

Anal. Calcd for $C_{14}H_{17}F_3O_2$: C, 61.31; H, 6.25. Found: C, 61.33; H 5.93.

1-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-3-methoxybenzene (5g) and 1-[(1*Z*)-1-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-3-methoxybenzene (6g)

From styrene **1g** (1405 mg, 5 mmol) as a colorless oil; yield (**5** + **6**): 1205 mg (88%); ratio **5g**/**6g** 92:8.

IR (Nujol): 1660 (C=C) cm^{-1}.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{17}F_3NaO_2$: 297.1078; found: 297.1073.

Anal. Calcd for $C_{14}H_{17}F_3O_2$: C, 61.31; H, 6.25. Found: C, 61.35; H, 6.03.

Regioisomer 5g

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 [OC(*C*H$_3$)$_3$], 55.2 (OCH$_3$), 84.3 [O*C*(CH$_3$)$_3$], 114.6 (Ar), 114.7 (Ar), 121.4 (q, *J* = 276.6 Hz, CF$_3$), 122.0 (q, *J* = 4.4 Hz, *C*H=CCF$_3$), 122.3 (Ar), 129.3 (Ar), 134.6 (Ar), 140.2 (q, *J* = 32.2 Hz, *C*-CF$_3$), 159.5 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –67.2 (s, CF$_3$).

Regioisomer 6g

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.3 [OC(*C*H$_3$)$_3$], 55.2 (OCH$_3$), 82.3 [O*C*(CH$_3$)$_3$], 105.1 (q, *J* = 32.9 Hz, C=*C*HCF$_3$), 113.2 (Ar), 115.5 (Ar), 120.2 (Ar), 159.3 (Ar), the other signals are identical to those of the regioisomer **5g**.

1-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-4-methoxybenzene (5h) and 1-[(1*Z*)-1-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-4-methoxybenzene (6h)

From styrene **2h** (1405 mg, 5 mmol) as a colorless oil; yield (**5** + **6**): 1247 mg (91%); ratio **5h**/**6h** 67:33.

IR (Nujol): 1670 (C=C) cm^{-1}.

Anal. Calcd for $C_{14}H_{17}F_3O_2$: C, 61.31; H, 6.25. Found: C, 61.85; H, 5.88.

Regioisomer 5h

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.36 [s, 9 H, $OC(CH_3)_3$], 3.85 (s, 3 H, OCH_3), 6.60 (s, 1 H, $CH=CCF_3$), 6.91 (d, *J* = 8.8 Hz, 2 H, Ar), 7.65 (d, *J* = 8.8 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 [$OC(CH_3)_3$], 55.2 (OCH_3), 83.8 [$OC(CH_3)_3$], 113.7 (Ar), 121.6 (q, *J* = 275.9 Hz, CF_3), 121.7 (q, *J* = 4.4 Hz, *C*H=CCF_3), 125.9 (Ar), 131.2 (Ar), 138.4 (q, *J* = 32.2 Hz, *C*-CF_3), 159.7 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –66.7 (s, CF_3).

Regioisomer 6h

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.28 [s, 9 H, $OC(CH_3)_3$], 3.86 (s, 3 H, OCH_3), 5.25 (q, *J* = 7.8 Hz, 1 H, $CHCF_3$), 6.90 (d, *J* = 8.9 Hz, 2 H, Ar), 7.43 (d, *J* = 8.9 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.3 [$OC(CH_3)_3$], 55.3 (OCH_3), 82.0 [$OC(CH_3)_3$], 104.9 (q, *J* = 32.9 Hz, C=*C*HCF_3), 113.5 (Ar), 123.2 (q, *J* = 269.3 Hz, CF_3), 129.3 (Ar), 130.3 (Ar), 160.9 (Ar), 162.3 (q, *J* = 5.9 Hz, *C*=$CHCF_3$).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –56.5 (d, *J* = 7.8 Hz, CF_3).

1-Bromo-[(1*Z*)-2-*tert*-butoxy-3,3,3-trifluoroprop-1-enyl]benzene (5i)

From styrene **1i** (1425 mg, 5 mmol) or **2i** (1650 mg, 5 mmol) as a colorless oil; yield: 1050 mg (65%, from **1i**), 1131 mg (70%, from **2i**).

IR (Nujol): 1665 (C=C) cm^{-1}.

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 [$OC(CH_3)_3$], 84.7 [$OC(CH_3)_3$], 121.1 (q, *J* = 274.5 Hz, CF_3), 121.4 (q, *J* = 4.4 Hz, *C*H=CCF_3), 124.1 (Ar), 127.0 (Ar), 129.7 (Ar), 131.9 (Ar), 132.5 (Ar), 133.8 (Ar), 141.5 (q, *J* = 32.9 Hz, *C*-CF_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –68.4 (s, CF_3).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{13}H_{14}BrF_3NaO$: 345.0078; found: 345.0072.

Anal. Calcd for $C_{13}H_{14}BrF_3O$: C, 48.32; H, 4.37. Found: C, 48.46; H 4.31.

Methyl 4-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]benzoate (5j)

From styrenes **1j** (1320 mg, 5 mmol) or **2j** (1545 mg, 5 mmol) as a colorless oil; yield: 936 mg (62%, from **1j**), 1102 mg (73%, from **2j**).

IR (Nujol): 1670 (C=C), 1720 (C=O, CO_2Me) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.31 [s, 9 H, $OC(CH_3)_3$], 3.78 (s, 3 H, CO_2CH_3), 6.66 (s, 1 H, $CH=CCF_3$), 7.67 (d, *J* = 8.6 Hz, 2 H, Ar), 8.01 (d, *J* = 8.6 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 [$OC(CH_3)_3$], 60.1 (CO_2CH_3), 85.0 [$OC(CH_3)_3$], 121.1 (q, *J* = 4.4 Hz, *C*H=CCF_3), 121.2 (q, *J* = 276.6 Hz, CF_3), 141.6 (q, *J* = 32.9 Hz, *C*-CF_3), 129.2 (Ar), 129.7 (Ar), 131.7 (Ar), 137.4 (Ar), 165.3 (CO_2CH_3).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –67.4 (s, CF_3).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{17}F_3NaO_3$: 325.1027; found: 325.1022.

Anal. Calcd for $C_{15}H_{17}F_3O_3$: C, 59.60; H, 5.67. Found: C, 59.51; H, 5.71.

4-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-1,2-dimethoxybenzene (5k) and 4-[(1*Z*)-1-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]-1,2-dimethoxybenzene (6k)

From styrene **2k** (1555 mg, 5 mmol) as a colorless oil; yield (**5** + **6**): 1490 mg (98%); ratio **5k**/**6k** 67:33.

IR (Nujol): 1660 (C=C) cm^{-1}.

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{15}H_{19}F_3NaO_3$: 327.1184; found: 327.1179.

Anal. Calcd for $C_{15}H_{19}F_3O_3$: C, 59.20; H, 6.29. Found: C, 59.19; H, 6.26.

Regioisomer 5k

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.35 [s, 9 H, $OC(CH_3)_3$], 3.90 (s, 6 H, 2 OCH_3), 6.57 (s, 1 H, $CH=CCF_3$), 6.85 (d, *J* = 8.3 Hz, 1 H, Ar), 7.13 (dd, *J* = 8.3, 1.8 Hz, 1 H, Ar), 7.35 (d, *J* = 1.8 Hz, 1 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.8 [$OC(CH_3)_3$], 55.8 (2 OCH_3), 83.9 [$OC(CH_3)_3$], 110.7 (Ar), 112.4 (Ar), 121.5 (q, *J* = 275.9 Hz, CF_3), 122.0 (q, *J* = 4.4 Hz, *C*H=CCF_3), 123.1 (Ar), 126.1 (Ar), 138.5 (q, *J* = 32.2 Hz, *C*-CF_3), 148.5 (Ar), 149.3 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –66.7 (s, CF_3).

Regioisomer 6k

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.27 [s, 9 H, $OC(CH_3)_3$], 3.90 (s, 6 H, 2 OCH_3), 5.26 (q, *J* = 7.8 Hz, 1 H, $CHCF_3$), 6.84 (d, *J* = 8.2 Hz, 1 H, Ar), 7.01 (d, *J* = 2.0 Hz, 1 H, Ar), 7.05 (dd, *J* = 8.2, 2.0 Hz, 1 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 29.3 [$OC(CH_3)_3$], 55.9 (2 OCH_3), 82.1 [$OC(CH_3)_3$], 105.1 (q, *J* = 33.7 Hz, C=*C*HCF_3), 110.6 (Ar), 111.0 (Ar), 120.6 (Ar), 123.1 (q, *J* = 270.8 Hz, CF_3), 130.6 (Ar), 148.4 (Ar), 150.3 (Ar), 162.1 (q, *J* = 5.9 Hz, *C*=$CHCF_3$).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –56.5 (d, *J* = 7.8 Hz, CF_3).

2-[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]pyridine (5l)

Obtained from styrene **1l** (1225 mg, 5 mmol) as a colorless oil; yield: 884 mg (72%).

IR (Nujol): 1660 (C=C) cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 [s, 9 H, $OC(CH_3)_3$], 6.75 (s, 1 H, $CH=CCF_3$), 7.11 (dd, *J* = 7.8, 4.9 Hz, 1 H_{Py}), 7.61 (td, *J* = 7.8, 1.6 Hz, 1 H_{Py}), 7.89 (d, *J* = 7.8 Hz, 1 H_{Py}), 8.55 (d, *J* = 7.8 Hz, 1 H_{Py}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 28.6 [$OC(CH_3)_3$], 84.9 [$OC(CH_3)_3$], 121.1 (q, *J* = 276.6 Hz, CF_3), 122.7 (q, *J* = 4.4 Hz, *C*H=CCF_3), 122.7 (Py), 125.0 (Py), 135.9 (Py), 142.5 (q, *J* = 32.9 Hz, *C*-CF_3), 149.5 (Py), 153.0 (Py).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –67.7 (s, CF_3).

HRMS (ESI): *m*/*z* $[M + Na]^+$ calcd for $C_{12}H_{14}F_3NNaO$: 268.0925; found: 268.0920.

Anal. Calcd for $C_{12}H_{14}F_3NO$: C, 58.77; H, 5.75. Found: C, 58.57; H, 5.50.

1-Substituted 4-(3,3,3-Trifluoroprop-1-ynyl)benzenes 7c and 7h; General Procedure

A one-neck, 50-mL round-bottomed flask was charged with anhyd THF (10 mL) and styrene **1** (5 mmol) and cooled down to 0 °C. Then a cooled to 0 °C soln of *t*-BuOK (670 mg, 6 mmol) in anhyd THF (12 mL) was added dropwise with stirring. The mixture was stirred at r.t. for 24 h and then poured into H_2O (200 mL). The products were extracted with pentane (3 × 20 mL). The combined extracts were washed with H_2O (2 × 50 mL) and brine (50 mL) and dried (Na_2SO_4). Pentane was evaporated in vacuo, and the residue was passed through a short filter with silica gel (pentane).

1-Chloro-4-(3,3,3-trifluoroprop-1-ynyl)benzene (7c)

From styrene **1c** (1205 mg, 5 mmol) as a colorless liquid; yield: 724 mg (71%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.37 (d, *J* = 8.6 Hz, 2 H, Ar), 7.49 (d, *J* = 8.6 Hz, 2 H, Ar).

1-Methoxy-4-(3,3,3-trifluoroprop-1-ynyl)benzene (7h)
From styrene **1h** (1185 mg, 5 mmol) as a colorless liquid; yield: 640 mg (64%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 (s, 3 H, OCH_3), 6.89 (d, *J* = 8.9 Hz, 2 H, Ar), 7.49 (d, *J* = 8.9 Hz, 2 H, Ar).

1-Nitro-4-(3,3,3-trifluoroprop-1-ynyl)benzene (7d)
A one-neck, 50-mL, round-bottomed flask was charged with CH_2Cl_2 (10 mL), styrene **1d** (1.250 mg, 5 mmol), H_2O (5 mL), NaOH (240 mg, 6 mmol), and benzyltriethylammonium chloride (23 mg, 1 mmol). The mixture was refluxed for 48 h with vigorous stirring until styrene **1d** disappeared (TLC monitoring). The organic layer was separated and the aqueous phase was extracted with CH_2Cl_2 (20 mL). The combined extracts were washed with H_2O (2 × 50 mL) and brine (50 mL) and dried (Na_2SO_4). CH_2Cl_2 was evaporated in vacuo and the residue was passed through a short filter with silica gel (CH_2Cl_2–pentane, 1:1) to give **7d** as colorless crystals; yield: 925 mg (86%); mp 75–76 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 8.9 Hz, 2 H, Ar), 8.27 (d, *J* = 8.9 Hz, 2 H, Ar).

[(1*Z*)-2-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]benzenes 5c,d,h and [(1*Z*)-1-*tert*-Butoxy-3,3,3-trifluoroprop-1-enyl]benzenes 6c,d,h from Acetylenes 7c,d,h and Potassium *tert*-Butoxide; General Procedure
A one-neck, 10-mL, round-bottomed flask was charged with anhyd DMF (2 mL) and the corresponding acetylene **7** (1 mmol) and cooled down to 0 °C. Then a soln of *t*-BuOK (135 mg, 1.2 mmol) in anhyd DMF (2 mL) at 0 °C was added dropwise with stirring. The mixture was stirred at r.t. for 24 h and then poured into H_2O (200 mL). The products were extracted with CH_2Cl_2 (3 × 20 mL). The combined extracts were washed with H_2O (2 × 50 mL) and brine (50 mL) and dried (Na_2SO_4). CH_2Cl_2 was evaporated in vacuo, affording crude material in near quantitative yields. The structures of the products and the ratio of regioisomers **5** and **6** in the mixtures were determined using ^{1}H NMR and ^{19}F NMR by comparison with corresponding data of styrene reactions.

Synthesis of 1,1,1-Trifluoroacetone 8c and Heterocycles 9–17 from *tert*-Butoxystyrenes; General Procedure
A one-neck, 25-mL round-bottomed flask was charged with the corresponding *tert*-butoxystyrene (1 mmol) and CH_2Cl_2 (3 mL). Then 1 M Br_2 in CH_2Cl_2 (1.1 mL) was added dropwise with vigorous stirring. After the Br_2 had been added, CH_2Cl_2 was evaporated in vacuo. The residue was dissolved in MeCN (2 mL) and the soln of the corresponding nucleophile (1 mmol) in MeCN (2 mL) was added. Then the mixture was stirred at r.t. for 2 h and refluxed for another 8 h. The mixture was cooled to r.t. and the reaction was quenched with 25% NH_3 soln (0.2 mL). (In case of **15**, after cooling down to r.t., the MeCN was evaporated to one quarter. The formed precipitate of the hydrobromide was filtered off and washed with MeCN and Et_2O). The solvents were removed in vacuo and the residue was purified by column chromatography (silica gel, CH_2Cl_2–MeOH).

3-Bromo-3-(4-chlorophenyl)-1,1,1-trifluoroacetone (8c)
Isolated in crude form from the reaction of **5c**/**6c** (86:14, 278 mg, 1 mmol) with Br_2 and evaporation of CH_2Cl_2; brown oil; yield: 256 mg (~85%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77 (s, 1 H, CHBr), 7.41 (d, *J* = 8.6 Hz, 2 H, Ar), 7.45 (d, *J* = 8.6 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 44.6 (Ar), 115.2 (q, *J* = 292.8 Hz, CF_3), 129.6 (Ar), 130.6 (Ar), 134.0 (Ar), 136.4 (Ar), 183.0 (q, *J* = 35.9 Hz, CF_3-*C*=O).

3-Phenyl-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (9a)
From **5a**/**6a** (91:9, 244 mg, 1 mmol) as a viscous brown oil; yield: 121 mg (46%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.85 (t, *J* = 7.7 Hz, 1 H, Im), 7.27–7.34 (m, 1 H, Im), 7.43–7.48 (m, 2 H, Ar), 7.50–7.55 (m, 3 H, Ar), 7.70 (d, *J* = 7.7 Hz, 1 H, Im), 7.95 (d, *J* = 7.7 Hz, 1 H, Im).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 114.8 (Imd), 119.1 (Imd), 121.6 (q, *J* = 2.9 Hz, *C*=CCF_3), 121.7 (q, *J* = 269.3 Hz, CF_3), 123.2 (Imd), 123.6 (Imd), 124.4 (Ar), 131.3 (Ar), 133.4 (Ar), 133.7 (q, *J* = 38.1 Hz, *C*-CF_3), 145.0 (Imd), 148.4 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.4 (s, CF_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_9F_3N_2Na$: 285.0616; found: 285.0610.

Anal. Calcd for $C_{14}H_9F_3N_2$: C, 64.12; H, 3.46. Found: C, 63.98; H, 3.54.

3-(4-Chlorophenyl)-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (9c)
From **5c**/**6c** (86:14, 278 mg, 1 mmol) as a viscous brown oil; yield: 155 mg (52%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.88 (t, *J* = 7.7 Hz, 1 H, Im), 7.28–7.35 (m, 1 H, Im), 7.41 (d, *J* = 8.3 Hz, 2 H, Ar), 7.52 (d, *J* = 8.3 Hz, 2 H, Ar), 7.69 (d, *J* = 7.7 Hz, 1 H, Im), 7.93 (d, *J* = 7.7 Hz, 1 H, Im).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 114.1 (Imd), 118.8 (Imd), 122.0 (q, *J* = 269.3 Hz, CF_3), 123.0 (q, *J* = 2.9 Hz, *C*=CCF_3), 123.8 (Imd), 125.2 (Ar), 126.6 (Imd), 129.6 (Ar), 131.7 (Ar), 132.9 (q, *J* = 37.3 Hz, *C*-CF_3), 136.0 (Ar), 144.5 (Imd).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.5 (s, CF_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_8ClF_3N_2Na$: 319.0226; found: 319.0220.

Anal. Calcd for $C_{14}H_8ClF_3N_2$: C, 56.68; H, 2.72. Found: C, 56.51; H, 2.67.

3-(4-Nitrophenyl)-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (9d)
From **5d** (289 mg, 1 mmol) as a yellow powder; yield: 163 mg (53%); mp 137–138 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.98 (t, *J* = 7.7 Hz, 1 H, Im), 7.38–7.44 (m, 1 H, Im), 7.73 (d, *J* = 8.6 Hz, 2 H, Ar), 7.77 (d, *J* = 7.7 Hz, 1 H, Im), 8.01 (d, *J* = 7.7 Hz, 1 H, Im), 8.43 (d, *J* = 8.6 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 114.8 (Imd), 119.1 (Imd), 121.6 (q, *J* = 2.9 Hz, *C*=CCF_3), 121.7 (q, *J* = 269.3 Hz, CF_3), 123.6 (Imd), 124.4 (Ar), 127.2 (Imd), 131.3 (Ar), 133.4 (Ar), 133.7 (q, *J* = 38.1 Hz, *C*-CF_3), 145.0 (Imd), 148.4 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.4 (s, CF_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_8F_3N_3NaO_2$: 330.0466; found: 330.0461.

Anal. Calcd for $C_{14}H_8F_3N_3O_2$: C, 54.73; H, 2.62. Found: C, 54.42; H, 2.50.

3-(3-Nitrophenyl)-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (9e)
From **5e**/**6e** (91:9, 289 mg, 1 mmol) as a yellow powder; yield: 129 mg (42%); mp 110–112 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.97 (t, *J* = 7.7 Hz, 1 H, Im), 7.37–7.42 (m, 1 H, Im), 7.75 (d, *J* = 7.7 Hz, 1 H, Im), 7.79 (t, *J* = 7.8 Hz, 1 H, Ar), 7.86 (d, *J* = 7.8 Hz, 1 H, Ar), 7.96 (d, *J* = 7.7 Hz, 1 H, Im), 8.38 (s, 1 H, Ar), 8.39 (d, *J* = 7.8 Hz, 1 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 114.7 (Imd), 119.0 (Imd), 121.4 (q, *J* = 2.9 Hz, *C*=CCF_3), 121.7 (q, *J* = 270.1 Hz, CF_3), 123.5 (Ar), 124.6 (Imd), 125.2 (Ar), 127.1 (Imd), 128.6 (Ar), 130.5 (Ar), 133.6 (q, *J* = 37.2 Hz, *C*-CF_3), 136.6 (Ar), 144.8 (Imd), 148.7 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.5 (s, CF_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_8F_3N_3NaO_2$: 330.0466; found: 330.0461.

Anal. Calcd for $C_{14}H_8F_3N_3O_2$: C, 54.73; H, 2.62. Found: C, 54.58; H, 2.61.

3-(2-Methoxyphenyl)-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (9f)

From **5f** (274 mg, 1 mmol) as a yellow powder; yield: 91 mg (31%); mp 90–92 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.76 (s, 3 H, OCH_3), 6.83 (t, *J* = 7.7 Hz, 1 H, Im), 7.08 (d, *J* = 7.8 Hz, 1 H, Ar), 7.12 (t, *J* = 7.8 Hz, 1 H, Ar), 7.27–7.34 (m, 1 H, Im), 7.39 (d, *J* = 7.8 Hz, 1 H, Ar), 7.53 (td, *J* = 7.8 Hz, *J* = 1.6 Hz, 1 H, Ar), 7.68 (d, *J* = 7.7 Hz, 1 H, Im), 7.72 (d, *J* = 7.7 Hz, 1 H, Im).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.2 (OCH_3), 111.3 (Ar), 113.1 (Imd), 115.4 (Ar), 118.5 (Imd), 121.0 (Ar), 121.5 (q, *J* = 2.9 Hz, *C*=CCF_3), 122.1 (q, *J* = 268.6 Hz, CF_3), 125.1 (Imd), 126.1 (Imd), 131.7 (Ar), 132.8 (q, *J* = 37.3 Hz, *C*-CF_3), 132.9 (Ar), 144.5 (Imd), 157.7 (Ar).

Anal. Calcd for $C_{15}H_{11}F_3N_2O$: C, 61.64; H, 3.79. Found: C, 61.54; H, 3.60.

3-(3-Methoxyphenyl)-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (9g)

From **5g**/**6g** (92:8, 274 mg, 1 mmol) as a viscous brown oil; yield: 149 mg (51%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.81 (s, 3 H, OCH_3), 6.82 (t, *J* = 7.7 Hz, 1 H, Im), 6.98 (d, *J* = 1.8 Hz, 1 H, Ar), 7.02 (d, *J* = 8.1 Hz, 2 H, Ar), 7.24–7.30 (m, 1 H, Im), 7.42 (t, *J* = 8.1 Hz, 1 H, Ar), 7.66 (d, *J* = 7.7 Hz, 1 H, Im), 7.97 (d, *J* = 7.7 Hz, 1 H, Im).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 113.9 (Imd), 115.3 (Ar), 115.9 (Ar), 118.6 (Imd), 122.1 (q, *J* = 269.3 Hz, CF_3), 122.5 (Ar), 124.2 (Imd), 126.4 (Imd), 127.9 (Ar), 130.3 (Ar), 132.4 (q, *J* = 37.3 Hz, *C*-CF_3), 144.3 (Imd), 160.0 (Ar).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.4 (s, CF_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{12}F_3N_2O$: 293.0902; found: 293.0896.

Anal. Calcd for $C_{15}H_{11}F_3N_2O$: C, 61.64; H, 3.79. Found: C, 61.72; H, 3.90.

3-(4-Methoxyphenyl)-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (9h)

From **5h**/**6h** (72:28, 274 mg, 1 mmol) as yellow crystals; yield: 89 mg (27%); mp 87–88 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.89 (s, 3 H, OCH_3), 6.85 (t, *J* = 7.7 Hz, 1 H, Im), 7.07 (d, *J* = 8.7 Hz, 2 H, Ar), 7.27–7.33 (m, 1 H, Im), 7.39 (d, *J* = 8.7 Hz, 2 H, Ar), 7.70 (d, *J* = 7.7 Hz, 1 H, Im), 7.95 (d, *J* = 7.7 Hz, 1 H, Im).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 55.4 (OCH_3), 113.7 (Imd), 114.7 (Ar), 118.6 (Imd), 122.1 (q, *J* = 270.1 Hz, CF_3), 124.0 (Imd), 124.2 (q, *J* = 2.2 Hz, *C*=CCF_3), 126.3 (Imd), 131.1 (Ar), 131.7 (Ar), 132.3 (q, *J* = 36.6 Hz, *C*-CF_3), 144.2 (Imd), 160.7 (Ar).

Anal. Calcd for $C_{15}H_{11}F_3N_2O$: C, 61.64; H, 3.79. Found: C, 61.42; H, 3.50.

3-(2-Bromophenyl)-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (9i)

From **5i** (323 mg, 1 mmol) as a viscous brown oil; yield: 174 mg (51%).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.89 (t, *J* = 7.7 Hz, 1 H, Im), 7.32–7.38 (m, 1 H, Im), 7.40–7.45 (m, 2 H, Ar), 7.47 (d, *J* = 7.7 Hz, 1 H, Im), 7.61 (d, *J* = 7.7 Hz, 1 H, Ar), 7.72–7.79 (m, 2 H, Ar, Im).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 113.9 (Imd), 118.6 (Imd), 121.8 (q, *J* = 269.3 Hz, CF_3), 123.1 (q, *J* = 2.9 Hz, C=CCF_3), 124.6 (Imd), 125.4 (Ar), 126.7 (Imd), 128.0 (Ar), 128.1 (Ar), 131.9 (Ar), 133.2 (Ar), 133.2 (q, *J* = 37.3 Hz, *C*-CF_3), 133.7 (Ar), 144.5 (Imd).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –60.5 (s, CF_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{14}H_9BrF_3N_2$: 340.9901; found: 340.9896.

Anal. Calcd for $C_{14}H_8BrF_3N_2$: C, 49.29; H, 2.36. Found: C, 49.42; H, 2.50.

6-Bromo-3-(4-chlorophenyl)-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (10)

From **5c**/**6c** (86:14, 278 mg, 1 mmol) as a white powder; yield: 165 mg (44%); mp 102.5–104.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.39 (dd, *J* = 9.6, 1.4 Hz, 1 H, Im), 7.42 (d, *J* = 8.3 Hz, 2 H, Ar), 7.56 (d, *J* = 8.3 Hz, 2 H, Ar), 7.59 (d, *J* = 9.6 Hz, 1 H, Im), 8.03 (d, *J* = 1.4 Hz, 1 H, Im).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 109.2 (Imd), 119.5 (Imd), 121.8 (q, *J* = 270.1 Hz, CF_3), 123.0 (q, *J* = 1.5 Hz, *C*=CCF_3), 123.9 (Imd), 124.5 (Ar), 129.8 (Ar), 130.3 (Imd), 131.6 (Ar), 133.6 (q, *J* = 37.3 Hz, *C*-CF_3), 136.5 (Ar), 142.8 (Imd).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.7 (s, CF_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_7BrClF_3N_2Na$: 396.9331; found: 396.9325.

Anal. Calcd for $C_{14}H_7BrClF_3N_2$: C, 44.77; H, 1.88. Found: C, 44.38; H, 1.77.

3-(4-Chlorophenyl)-5-methyl-2-(trifluoromethyl)imidazo[1,2-*a*]pyridine (11)

From **5c**/**6c** (86:14, 278 mg, 1 mmol) as a pale yellow powder; yield: 146 mg (47%); mp 106.7–108.9 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.41 (s, 3 H, CH_3), 6.70 (dd, *J* = 7.2, 1.1 Hz, 1 H, Im), 7.39 (d, *J* = 8.3 Hz, 2 H, Ar), 7.43 (s, 1 H, Im), 7.51 (d, *J* = 8.3 Hz, 2 H, Ar), 7.80 (d, *J* = 7.2 Hz, 1 H, Im).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.3 (CH_3), 116.8 (Imd), 116.9 (Imd), 122.0 (q, *J* = 269.3 Hz, CF_3), 122.4 (q, *J* = 2.2 Hz, *C*=CCF_3), 122.9 (Imd), 125.4 (Ar), 129.5 (Ar), 131.6 (Ar), 132.6 (q, *J* = 37.3 Hz, *C*-CF_3), 135.8 (Ar), 137.9 (Imd), 145.0 (Imd).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.5 (s, CF_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{11}ClF_3N_2$: 311.0563; found: 311.0557.

Anal. Calcd for $C_{15}H_{10}ClF_3N_2$: C, 57.99; H, 3.24. Found: C, 57.71; H, 3.18.

3-(4-Chlorophenyl)-2-(trifluoromethyl)imidazo[1,2-*a*]pyrimidine (12)

From **5c**/**6c** (86:14, 278 mg, 1 mmol) as a yellow powder; yield: 155 mg (52%); mp 117–120 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.02 (dd, *J* = 6.8, 4.1 Hz, 1 H, Pyrimidinyl), 7.43 (d, *J* = 8.6 Hz, 2 H, Ar), 7.53 (d, *J* = 8.6 Hz, 2 H, Ar), 8.34 (dd, *J* = 6.8, 1.9 Hz, 1 H, Pyrimidinyl), 8.65 (dd, *J* = 4.0, 1.9 Hz, 1 H, Pyrimidinyl).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 110.5 (Imd), 121.6 (q, *J* = 270.1 Hz, CF_3), 121.7 (q, *J* = 2.2 Hz, *C*=CCF_3), 124.0 (Ar), 129.7 (Ar), 131.6 (Ar), 132.1 (Imd), 133.7 (q, *J* = 37.3 Hz, *C*-CF_3), 136.5 (Ar), 147.2 (Imd), 152.6 (Imd).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.7 (s, CF_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{13}H_7ClF_3N_3Na$: 320.0178; found: 320.0173.

Anal. Calcd for $C_{13}H_7ClF_3N_3$: C, 52.45; H, 2.37. Found: C, 51.49; H, 2.24.

3-(4-Chlorophenyl)-2-(trifluoromethyl)-9*H*-imidazo[1,2-*a*]-benzimidazole (13)

From **5c**/**6c** (86:14, 278 mg, 1 mmol) as yellow crystals; yield: 124 mg (37%); mp 262–265 °C.

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.07–7.14 (m, 2 H, C_6H_4), 7.34 (td, *J* = 6.8, 1.0 Hz, 1 H, C_6H_4), 7.48 (d, *J* = 8.1 Hz, 1 H, C_6H_4), 7.68 (s, 4 H, 4-ClC_6H_4), 12.17 (br s, 1 H, NH).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 111.9 (Het), 112.8 (Het), 120.6 (Het), 120.8 (q, *J* = 3.7 Hz, *C*=CCF$_3$), 122.7 (q, *J* = 267.9 Hz, CF_3), 124.3 (4-ClC_6H_4), 125.0 (Het), 126.9 (Het), 128.4 (q, *J* = 35.9 Hz, *C*-CF_3), 129.4 (4-ClC_6H_4), 132.1 (4-ClC_6H_4), 134.6 (Het), 136.1 (4-ClC_6H_4), 148.4 (Het).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –58.7 (s, CF_3).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{10}ClF_3N_3$: 336.0515; found: 336.0510.

Anal. Calcd for $C_{16}H_9ClF_3N_3$: C, 57.24; H, 2.70. Found: C, 57.48; H, 2.50.

5-(4-Chlorophenyl)-6-(trifluoromethyl)imidazo[2,1-*b*]thiazole (14)

From **5c**/**6c** (86:14, 278 mg, 1 mmol) as white crystals; yield: 182 mg (60%); mp 135.5–137.2 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.01 (d, *J* = 4.7 Hz, 1 H, Thiazolyl), 7.37 (d, *J* = 4.7 Hz, 1 H, Thiazolyl), 7.43 (d, *J* = 8.5 Hz, 2 H, Ar), 7.49 (d, *J* = 8.5 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 115.7 (Het), 117.2 (Het), 121.4 (q, *J* = 271.5 Hz, CF_3), 125.3 (q, *J* = 2.9 Hz, *C*=CCF$_3$), 125.9 (Ar), 129.4 (Ar), 130.4 (Ar), 133.1 (q, *J* = 37.3 Hz, *C*-CF_3), 135.7 (Ar), 149.4 (Het).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.4 (s, CF_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{12}H_6ClF_3N_2NaS$: 324.9790; found: 324.9785.

Anal. Calcd for $C_{12}H_6ClF_3N_2S$: C, 47.61; H, 2.00. Found: C, 47.35; H, 1.75.

5-(4-Chlorophenyl)-4-(trifluoromethyl)thiazol-2-amine Hydrobromide (15·HBr)

From **5c**/**6c** (86:14, 278 mg, 1 mmol) as white crystals; yield: 259 mg (72%); mp 165–167 °C (dec).

^{1}H NMR (400 MHz, DMSO-d_6): δ = 7.09 (br s, 3 H, NH_3^+), 7.37 (d, *J* = 8.5 Hz, 2 H, Ar), 7.46 (d, *J* = 8.5 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, DMSO-d_6): δ = 121.4 (q, *J* = 271.5 Hz, CF_3), 125.7 (Ar), 128.8 (Thiazolyl), 129.1 (Ar), 131.6 (Ar), 133.0 (q, *J* = 33.7 Hz, *C*-CF_3), 133.9 (Ar), 168.2 (Thiazolyl).

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{10}H_7ClF_3N_2S$: 278.9971; found: 278.9965.

5-(4-Chlorophenyl)-*N*-phenyl-4-(trifluoromethyl)thiazol-2-amine (16)

From **5c**/**6c** (86:14, 278 mg, 1 mmol) as white crystals; yield: 284 mg (80%); mp 128–129 °C.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.20–7.26 (m, 1 H, Ph), 7.38–7.48 (m, 8 H, Ar), 8.91 (br s, 1 H, NH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 120.7 (Ph), 121.0 (q, *J* = 272.3 Hz, CF_3), 125.0 (Ph), 127.0 (4-ClC_6H_4), 127.8 (Thiazolyl), 128.8 (4-ClC_6H_4), 129.8 (Ph), 131.1 (4-ClC_6H_4), 134.4 (q, *J* = 35.1 Hz, *C*-CF_3), 135.2 (4-ClC_6H_4), 139.9 (Ph), 166.1 (Thiazolyl).

^{19}F NMR (282 MHz, $CDCl_3$): δ = –59.8 (s, CF_3).

Anal. Calcd for $C_{16}H_{10}ClF_3N_2S$: C, 54.17; H, 2.84. Found: C, 54.35; H, 2.63.

5-(4-Chlorophenyl)-2-methyl-4-(trifluoromethyl)-4,5-dihydrothiazol-4-ol (17)

From **5c**/**6c** (86:14, 278 mg, 1 mmol) as white crystals; yield: 160 mg (54%); mp 181–183 °C (dec).

^{1}H NMR (400 MHz, acetone-d_6): δ = 2.34 (s, 3 H, CH_3), 5.46 (s, 1 H, C*H*, Ar), 6.33 (s, 1 H, OH), 7.37 (d, *J* = 8.4 Hz, 2 H, Ar), 7.54 (d, *J* = 8.4 Hz, 2 H, Ar).

^{13}C NMR (100 MHz, acetone-d_6): δ = 19.7 (CH_3), 57.1 (*C*H, Ar), 104.5 (q, *J* = 28.5 Hz, *C*-CF_3), 124.3 (q, *J* = 286.2 Hz, CF_3), 127.9 (Ar), 131.9 (Ar), 132.8 (Ar), 133.4 (Ar), 174.7 [S*C*(Me)=N].

^{19}F NMR (282 MHz, $CDCl_3$): δ = –82.1 (s, CF_3).

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{11}H_9ClF_3NNaOS$: 317.9943; found: 317.9938.

Anal. Calcd for $C_{11}H_9ClF_3NOS$: C, 44.68; H, 3.07. Found: C, 44.63; H, 2.82.

Acknowledgment

This project was supported by the Deutsche Forschungsgemeinschaft (DFG) through grant No: 436 RUS 113/858/0-1 and the Russian Foundation for Basic Research (grants No. 08-03-00736-a, RFBR-DFG 07-03-91562-NNIO_a).

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