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Synthetic Methods

Efficient Copper-Catalyzed Direct Intramolecular Aminotrifluoromethylation of Unactivated Alkenes with Diverse Nitrogen-Based Nucleophiles

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Abstract: A mild, convenient, and step-economical intramolecular aminotrifluoromethylation of unactivated alkenes with a variety of electronically distinct, nitrogen-based nucleophiles in the presence of a simple copper salt catalyst, in the absence of extra ligands, is described. Many different nitrogen-based nucleophiles (e.g., basic primary aliphatic and aromatic amines, sulfonamides, carbamates, and ureas) can be employed in this new aminotrifluoromethylation reaction. The aminotrifluoromethylation process allows straightforward access to diversely substituted CF_3-containing pyrrolidines or indolines, in good to excellent yields, through a direct difunctionalization strategy from the respective acyclic starting materials. Mechanistic studies were conducted and a plausible mechanism was proposed.

Introduction

Azaheterocycles, such as pyrrolidine and indoline, are an omnipresent component of a wide range of naturally occurring and biologically active molecules.[1] Among these molecules, skeletons that contain the trifluoromethyl (CF_3) group have been extensively used as important building blocks for the synthesis of anticholinergic, antiemetic, and antispastic drugs, as well as enzyme inhibitors, because of their unique properties, such as increased metabolic stability, lipophilicity, and bioavailability.[2] As a result, great synthetic efforts have been exerted to develop efficient methods for the incorporation of CF_3 into azaheterocyclic structures.[3] Despite these important achievements, most literature methods for the construction of trifluoromethylated pyrrolidines or indolines involve the reaction of precyclized substrates with trifluoromethyl-containing organic compounds.[3] In the context of efficient chemical syntheses with high step economy and increasing interest in this class of compounds for the exploration of new fluorine-containing pharmaceutical candidates, it would be of great synthetic interest to develop a convenient and step-economical route for facile access to trifluoromethylated pyrrolidines or indolines, preferably by using simple catalytic systems and readily available acyclic starting materials.

Recently, transition-metal-mediated or -catalyzed trifluoromethylation reactions have emerged as important synthetic tools for the synthesis of new potential pharmaceutical candidates.[3] In particular, since the pioneering studies in 2011, carried out by the groups of Buchwald,[4a] Liu,[4b] and Wang[4c], efficient trifluoromethylation of simple alkenes with trifluoromethylating reagents[5,6] has been successfully established.[7] Based on this mode of activation, some successful examples have been shown for the trifluoromethylation of alkenes by a direct difunctionalization strategy to construct two vicinal chemical bonds. Consequently, oxytrifluoromethylation[8,9] and carbotrifluoromethylation[10] of simple alkenes have been achieved to afford a series of CF_3-containing compounds. Specifically, the groups of Liu[10a] and Sodeoka[10b,c] have independently developed an elegant intramolecular aryltrifluoromethylation of alkenes with a palladium/ytterbium catalyst system and a Cu^I/Togni's reagent system, respectively (Scheme 1 a). Buchwald et al. have successfully demonstrated intramolecular copper-catalyzed oxytrifluoromethylation of alkenes with oxygen-based nucleophiles in the presence of a bidentate ligand, but this catalytic system was incompatible with nitrogen-based nucleophiles, such as secondary amides or sulfonamides (Scheme 1 a).[9a] Thus, compared with oxytrifluoromethylation and carbotrifluoromethylation, it still remains a great challenge to perform intramolecular difunctionalization-type trifluoromethylation of unactivated alkenes with different types of nitrogen-based nucleophiles.[11] Although, during the preparation of this manuscript, an aminotrifluoromethylation of unactivated alkenes was reported by the Sodeoka group, only electron-rich secondary aromatic amines were utilized as the nitrogen source.[11a] Given the paucity of reports about intramolecular aminotrifluoromethylation, we were interested in the use of transition-metal catalysts in the presence of hypervalent iodine CF_3 reagents for direct intramolecular aminotrifluoromethylation of unactivated alkenes with diverse nitro-

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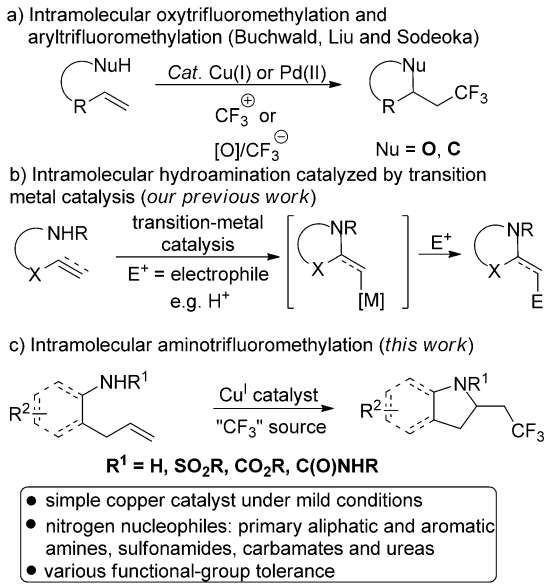


Scheme 1. Transition-metal catalyzed intramolecular reactions of unactivated alkenes.

gen-based nucleophiles, which include primary amines, sulfonamides, carbamates, and ureas. In this scenario, two major challenges must be overcome to accomplish the desired reaction:

1) primary electron-rich amines are susceptible to oxidation at nitrogen in the presence of hypervalent iodine reagents,[12] which could possibly result in undesirable side reactions that stem from the free-amine nucleophile.
2) it is very challenging to search for a simple catalytic system that can accommodate a variety of electronically distinct amines (from free amines to the various protected amines) as the nucleophilic component of the reaction due to a number of factors, which include the different thermodynamic stabilities of N–H σ-bonds and distinct inherent nucleophilicity of nitrogen atoms,[13] thereby displaying a significantly distinct reactivity toward unactivated alkenes.

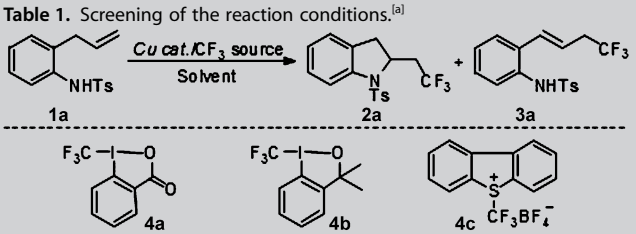
To circumvent these potential issues, the development of direct catalytic aminotrifluoromethylation of unactivated alkenes with a wide range of nitrogen-based nucleophiles with distinct inherent nucleophilicity is still highly desirable.

In recent years, we have successfully developed a transition-metal-catalyzed hydroamination of a series of unactivated alkenes or alkynes and related tandem reactions (Scheme 1 b).[14] Inspired by these works, and considering the mechanism of copper-catalyzed trifluoromethylation of alkenes with electrophilic trifluoromethylating reagents to generate α-CF_3-alkyl radical intermediates,[4,9] we envisioned that an overall copper-catalyzed direct difunctionalization strategy might be applicable to various nitrogen-based nucleophiles under the right set of conditions. Herein we describe that a simple copper catalyst, in the absence of extra ligands, efficiently catalyzes direct intramolecular aminotrifluoromethylation of unactivated alkenes with different types of nitrogen-based nucleophile to build a variety of trifluoromethylated five-membered rings, in good to excellent yields, under mild reaction conditions (Scheme 1 c). Significantly, many different nitrogen-based nucleophiles (e.g., basic primary aliphatic and aromatic amines, sulfonamides, carbamates, and ureas) can be employed in this new aminotrifluoromethylation reaction that would be challenging reagents in related transition-metal-catalyzed hydroamination-type[13] reactions of unsaturated amines. The aminotrifluoromethylation process allows straightforward access to diversely substituted CF_3-containing pyrrolidines or indolines through a direct difunctionalization strategy from the respective acyclic starting materials in a step-economical fashion.

Results and Discussion

We initiated our study by examination of the reaction of **1a** in the presence of commercially available Togni's reagent (**4a**)[5] with a CuI catalyst. It was interesting to find that CuI (25 mol%) could catalyze this reaction in dichloroethane (DCE) at 75 °C to provide the desired product **2a** in 75% yield, along with a trace amount of allylic trifluoromethylated product **3a** (Table 1, entry 1). Encouraged by this result, we screened different Cu salts for this aminotrifluoromethylation reaction (Table 1, entries 2–7), and found that CuI was most beneficial for the reaction. Next, a solvent screen revealed DCE to be optimal to give maximum yield of **2a** (Table 1, entry 1 versus entries 8–10), which suggests a significant solvent effect for this

Table 1. Screening of the reaction conditions.[a]



	Catalyst	[CF_3] source	Solvent	**2a** [%][b]	**3a** [%][b]
1	CuI	**4a**	DCE	75	6
2	CuCl	**4a**	DCE	58	4
3	CuBr	**4a**	DCE	33	3
4	$[Cu(CH_3CN)_4][BF_4]$	**4a**	DCE	60	18
5	$[Cu(CH_3CN)_4][PF_6]$	**4a**	DCE	42	25
6	$CuOTf{\cdot}0.5C_6H_6$	**4a**	DCE	31	0
7	$Cu(OTf)_2$	**4a**	DCE	14	6
8	CuI	**4a**	CH_3CN	10	7
9	CuI	**4a**	dioxane	–[c]	–[c]
10	CuI	**4a**	toluene	–[c]	–[c]
11[d]	CuI	**4a**	DCE	80	6
12[e]	CuI	**4a**	DCE	71	6
13	CuI	**4b**	DCE	–[c]	–[c]
14	CuI	**4c**	DCE	–[c]	–[c]
15	–[f]	**4a**	DCE	–[c]	–[c]

[a] Reaction conditions: **1a** (0.05 mmol), **4** (0.1 mmol), catalyst (25 mol%), solvent (0.4 mL), 75 °C, 32 h, under argon. [b] Determined by ^{19}F NMR spectroscopy with $PhCF_3$ as an internal standard. [c] Product was not detected. [d] CuI (50 mol%) was used. [e] CuI (10 mol%) was used. [f] No catalyst. Ts = *p*-toluenesulfonyl, Tf = trifluoromethanesulfonyl.

reaction. We next studied this reaction under the optimal reaction conditions with different loadings of CuI and found that the load could be reduced to 10 mol% without any remarkable effect on the yield of **2a** (Table 1, entries 11 and 12). To our surprise, by changing the CF_3 reagent from **4a** to **4b** or Umemoto's reagent (**4c**), only a trace amount of the desired product was detected (Table 1, entries 13 and 14). A control experiment revealed that none of the desired product was observed in the absence of copper catalyst (Table 1, entry 15), which unambiguously revealed that the copper catalyst is essential for this reaction. It is also noteworthy that this reaction could be catalyzed by a simple copper salt without the use of extra ligands, in sharp contrast to the copper-catalyzed oxytrifluoromethylation of alkenes.[9a]

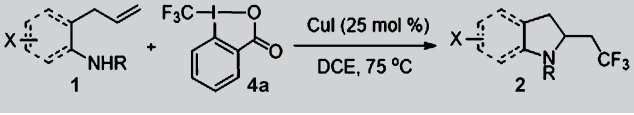
With an optimized protocol in hand, the substrate scope was investigated; the results are shown in Table 2. With a series of substituted *N*-sulfonyl-2-allylanilines **1** as the substrates, we found that functional groups (X = Cl, Me, OMe) at the *para* position of the phenyl ring were well tolerated and a variety of substituted CF_3-containing indolines **2b–d** were obtained in good yields (Table 2, entries 2–4). Furthermore, a variety of substituents on the nitrogen atom (benzene-, methane-, and 4-nitrophenyl-sulfonyl, and 4-$MeOC_6H_4SO_2$), were also found to be compatible with this catalytic system, to give the corresponding products **2e–h** in good to excellent yields (Table 2, entries 5–8), although an increased catalyst loading (CuI [50 mol%]) was required for full substrate conversion in the presence of the Ns substituent (Table 2, entry 7). It is interesting to note that the protocol could be extended to the copper-catalyzed aminotrifluoromethylation reaction of 4-pentenylsulfonamides **1i–k** for the synthesis of highly substituted trifluoromethylated pyrrolidines **2i–k**, and the product yields were relatively insensitive to the nature of the substitution on the carbon backbone (Table 2, entries 9–11).

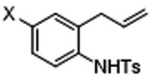
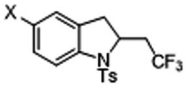
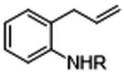
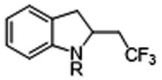
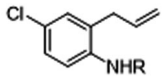
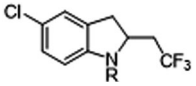
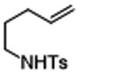
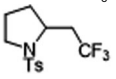
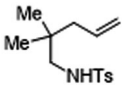
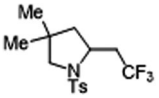
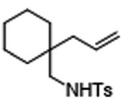
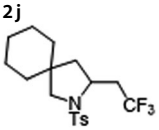
Encouraged by the aforementioned aminotrifluoromethylation reaction of alkenes with sulfonamides, we next turned our attention to expand the scope of the nucleophile to free primary amines, although we anticipated some challenges associated with primary amine oxidation in the presence of hypervalent iodine reagents.[12] To our delight, upon optimizing the reaction conditions by variation of the catalyst, catalyst loading, hypervalent iodine CF_3 reagent, and solvent (Table 3), we identified the following protocol as optimal: CuI (10 mol%), **4a** (1.5 equiv), DCE, 75 °C. The reaction of 2-allyl-4-chloroaniline (**1l**) gave **2l** in 71% yield (Table 3, entry 1).

With these optimized reaction conditions in hand, we investigated the scope of the reaction by using different types of substituted 2-allylanilines **1** (Table 4). A range of diversely functionalized 2-allylanilines, which included those with electron-withdrawing and electron-donating groups at different positions of the phenyl ring, gave the corresponding products **2l–q** in moderate to excellent yields. Additionally, 2-allyl-4,6-dichloroaniline (**1r**), which bears two chloro substituents, gave **2r** in 90% yield. To further investigate the scope of application, we tested aliphatic amines as viable nucleophiles for this reaction. It was found that the copper-catalyzed aminotrifluoromethylation reaction of alkenes tolerated aliphatic amines and substitution at the allylic olefinic carbon atoms to give trifluoromethylated pyrrolidines **2s** and **2t** in good yields. In consideration of the relatively low yields of products **2n**, **2q**, and **2t**, we improved the results by changing the solvent and modifying the reaction temperature.[15] We were pleased to find that when the solvent was changed from DCE to *t*BuOH, in all cases, the product yields were remarkably improved, even when CuI (5 mol%) was used (Table 4, entries 3, 6, and 9).

As an extension to the above aminotrifluoromethylation reaction, other protected amines could be employed as nucleophiles. Our preliminary results showed that, under conditions

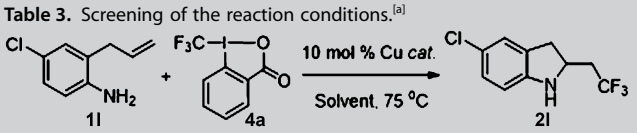
Table 2. CuI-catalyzed aminotrifluoromethylation of unactivated alkenes with sulfonamides.[a]



	1	2	*t* [h]	Yield [%][b]
				
1	**1a** X = H	**2a** X = H	32	75
2	**1b** X = Cl	**2b** X = Cl	10	70
3	**1c** X = Me	**2c** X = Me	10	81
4	**1d** X = OMe	**2d** X = OMe	10	75
				
5	**1e** R = Bs	**2e** R = Bs	24	71
6	**1f** R = Ms	**2f** R = Ms	16	90
7[c]	**1g** R = Ns	**2g** R = Ns	16	81
				
8	**1h** R = 4-$MeOC_6H_4SO_2$	**2h** R = 4-$MeOC_6H_4SO_2$	16	77
				
9	**1i**	**2i**	10	91
				
10	**1j**	**2j**	16	80
				
11	**1k**	**2k**	9	76

[a] Reaction conditions: **1** (0.5 mmol), **4a** (1.0 mmol), CuI (25 mol%), DCE (4 mL), 75 °C, under argon. [b] Isolated yield based on the starting alkene. [c] CuI (50 mol%) was used. Bs = benzenesulfonyl, Ms = methanesulfonyl, Ns = 4-nitrophenylsulfonyl.

Table 3. Screening of the reaction conditions.[a]



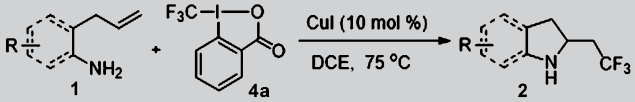
	Catalyst	Solvent	Yield [%][b]
1	CuI	DCE	71
2	CuCl	DCE	52
3	CuBr	DCE	65
4	$[Cu(CH_3CN)_4][BF_4]$	DCE	27
5	$[Cu(CH_3CN)_4][PF_6]$	DCE	10
6	$CuOTf{\cdot}0.5C_6H_6$	DCE	15
7	$Cu(OTf)_2$	DCE	25
8	CuI	CH_3CN	38
9	CuI	dioxane	44
10	CuI	toluene	–[c]

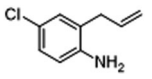
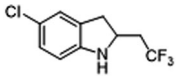
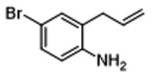
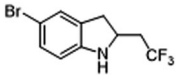
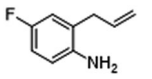
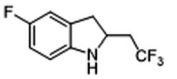
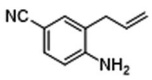
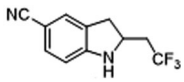
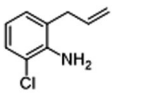
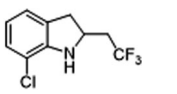
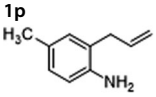
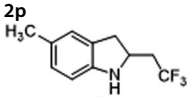
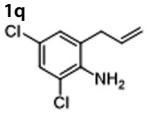
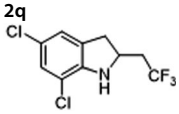
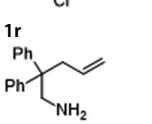
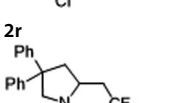
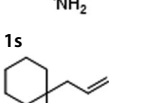
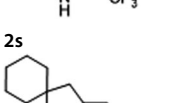
[a] Reaction conditions: **1l** (0.05 mmol), **4a** (0.1 mmol), catalyst (10 mol%), solvent (0.4 mL), 75 °C, 32 h, under argon. [b] Determined by ^{19}F NMR spectroscopy with $PhCF_3$ as an internal standard. [c] Product was not detected.

identical to those of the aminotrifluoromethylation detailed above, the reaction of alkenyl benzyl carbamates **1u** and **1v**, which bear electron-donating (Me) and -withdrawing (Cl) groups, gave trifluoromethylated products **2u** and **2v** in 50 and 65% yields, respectively (Scheme 2a). In addition, Boc-protected alkenyl carbamate **1w** showed a similar reactivity to give **2w** in 42% yield (Scheme 2b). Next, we turned our attention to expand the scope of the nucleophile to include the more challenging urea protecting group. Because of the preferred copper(I)-catalyzed intramolecular diamination process under similar conditions,[16] effective suppression of this reaction was needed to obtain satisfactory chemoselectivity. We were delighted to find that when **1x** was employed under the standard conditions with **4a** the desired trifluoromethylated product **2x** was obtained in 44% isolated yield without any diamination product (Scheme 2), which demonstrated that the aminotrifluoromethylation step is much faster than the diamination process in our catalytic system. Our data indicate that the present Cu-catalyzed aminotrifluoromethylation process is a rather general reaction that can be extended to many more protected amines.

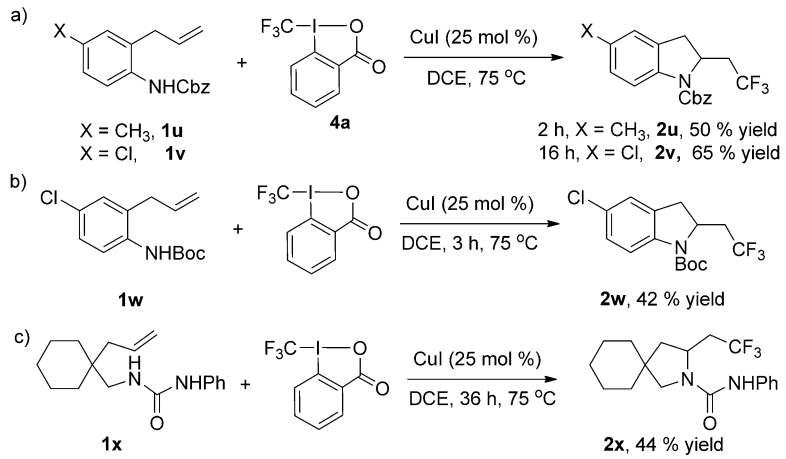
On the basis of the well-established reactivity of copper(I)-catalyzed allylic trifluoromethylation of unactivated alkenes,[4] a proposed mechanism for this Cu^I-catalyzed aminotrifluoromethylation reaction is depicted in Scheme 3. Reaction of **4a** with Cu^I generates a CF_3 radical,[10d] followed by radical addition and single-electron oxidation to give intermediate **B**.[9a] Subsequent trapping of the resultant carbocation with a nitrogen nucleophile (Scheme 3, **path A**) leads to the desired product **2**. Several control experiments were conducted to gain some insight into the mechanism for this Cu^I-catalyzed aminotrifluoromethylation reaction. 2,2,6,6-Tetramethyl-1-piperidinyloxy (TEMPO), a well-known radical scavenger,[4c,7c,8g] was reacted with **4a** in the presence of stoichiometric CuI under the standard reaction conditions (Scheme 4a), and the TEMPO-trapped complex **5** was obtained in 70% yield on the basis of ^{19}F NMR spectroscopic analysis. Moreover, the inhibition experiment of **1a** was conducted with the addition of TEMPO (2.0 equiv) under the standard reaction conditions and the desired product was afforded in only 9% yield, along with **5** in 60% yield (Scheme 4b), which revealed that the CF_3 radical is likely to be the reactive species under the current reaction conditions. Considering the fact that a small amount of allylic trifluoromethylated product **3** was formed through the elimination of intermediate **B**[4] in almost all cases, intramolecular hydroamination of **3** to give the final product **2** may be facilitated by copper catalyst in this catalytic system (Scheme 3, **path B**).[17] However, no reaction of **3a** in the presence of CuI (25 mol%) under the standard conditions was observed

Table 4. CuI-catalyzed aminotrifluoromethylation of unactivated alkenes with free amines.[a]

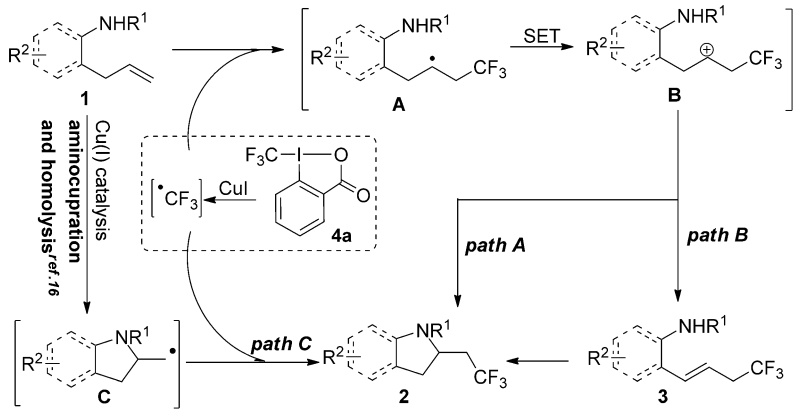


	1	2	t [h]	Yield [%][b]
1	 **1l**	 **2l**	16	71
2	 **1m**	 **2m**	10	80
3	 **1n**	 **2n**	10	50 (60)[c]
4	 **1o**	 **2o**	9	83
5	 **1p**	 **2p**	3	86
6	 **1q**	 **2q**	10	42 (50)[c]
7	 **1r**	 **2r**	3	90
8	 **1s**	 **2s**	16	80
9	 **1t**	 **2t**	12	53 (70)[d]

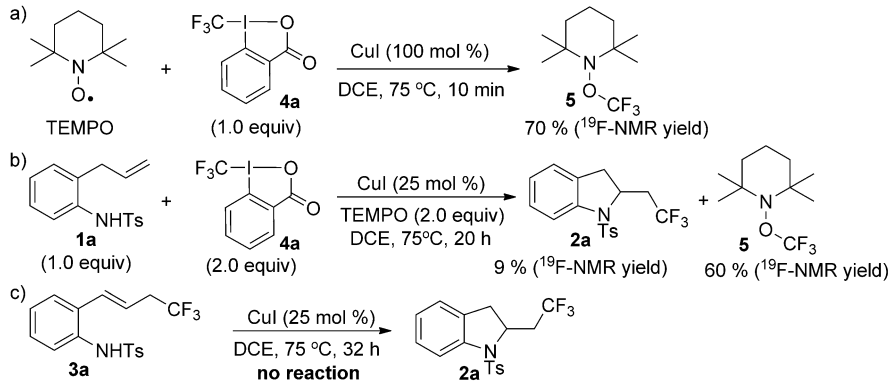
[a] Reaction conditions: **1** (0.5 mmol), **4a** (0.75 mmol), CuI (10 mol%), DCE (4 mL), 75 °C, under argon. [b] Isolated yield based on the starting alkene. [c] Reaction conditions: **1** (0.5 mmol), **4a** (0.6 mmol), CuI (5 mol%), *t*BuOH (4 mL), 40 °C, 10 h, under argon. [d] Reaction conditions: **1** (0.5 mmol), **4a** (0.6 mmol), CuI (5 mol%), *t*BuOH (4 mL), 12 h, 75 °C, under argon.



Scheme 2. The aminotrifluoromethylation of other protected amines



Scheme 3. Proposed mechanism for the aminotrifluoromethylation reaction of unactivated alkenes.



Scheme 4. Control experiments.

(Scheme 4c), which revealed that a mechanism that involves copper-catalyzed intramolecular hydroamination of **3** to give the final product is unlikely. On the other hand, an alternative catalytic mechanism, which proceeds by the formation of a primary carbon radical **C** through an aminocupration followed by homolysis of the C–Cu bond,[18] and subsequent coupling of this intermediate and a CF_3 radical, cannot be ruled out at the present stage (Scheme 3, **path C**). Therefore, the exact mechanism for the aminotrifluoromethylation reaction remains unclear at present and deserves further detailed studies.

Conclusion

We have developed a mild, convenient, and step-economical intramolecular aminotrifluoromethylation of unactivated alkenes with a variety of electronically distinct nitrogen-based nucleophiles (from free amines to various protected amines) in the presence of a simple copper salt catalyst, in the absence of extra ligands. This protocol provides a highly efficient method for the synthesis of trifluoromethylated pyrrolidines or indolines in good to excellent yields. A very broad substrate scope from simple starting materials renders the method a valuable addition to the arsenal for the synthesis of trifluoromethyl-containing azaheterocycles. Further studies to gain insight into the mechanism and to induce stereocontrol in the aminotrifluoromethylation of unactivated alkenes are underway in our laboratory.

Experimental Section

General procedure a: CuI-catalyzed aminotrifluoromethylation of unactivated alkenes with sulfonamides

Sulfonamide substrate (0.5 mmol, 1.0 equiv), CuI (23.8 mg, 0.125 mmol, 25 mol%), **4a** (316.0 mg, 1.0 mmol, 2.0 equiv) were added to a 25 mL Schlenk tube equipped with a magnetic stirrer bar. The tube was evacuated and backfilled with argon (×4) and then DCE (4.0 mL) was added to the tube by syringe, under argon. The sealed tube was stirred at 75 °C. After reaction completion (monitored by TLC), the solvent was removed under vacuum and the residue was purified by silica gel column chromatography (petroleum ether/CH_2Cl_2 = 10:1–1:5) to give the desired products **2a–k** and **2u–x**.

Compound 2a:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.69 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 2H), 7.26–7.21 (m, 1H), 7.18 (d, J = 8.0 Hz, 2H), 7.07–7.03 (m, 2H), 4.47–4.40 (m, 1H), 2.97–2.87 (m, 2H), 2.77 (dd, J = 16.4, 2.8 Hz, 1H), 2.51–2.40 (m, 1H), 2.35 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.53, 140.89, 134.36, 130.77, 129.90, 128.25, 127.28, 125.79 (q, J(C,F) = 275.9 Hz), 125.40, 125.25, 117.40, 56.95 (q, J(C,F) = 3.3 Hz), 40.75 (q, J(C,F) = 26.6 Hz), 34.29, 21.66 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.08 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{17}H_{17}F_3NO_2S$: 356.0932 $[M+H]^+$; found: 356.0922.

Compound 2b:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.62 (d, J = 8.4 Hz, 1H), 7.55 (d, J = 8.4 Hz, 2H), 7.26–7.20 (m, 3H), 7.03 (s, 1H), 4.46–4.39 (m, 1H), 2.97–2.88 (m, 2H), 2.76 (dd, J = 16.8, 3.2 Hz, 1H), 2.52–2.40 (m, 1H), 2.38 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.84, 139.66, 133.97, 132.69, 130.52, 130.07, 128.38, 127.27, 125.65 (q, J(C,F) = 275.8 Hz), 125.57, 118.30, 57.26 (q, J(C,F) = 3.2 Hz), 40.68 (q, J(C,F) = 29.6 Hz), 34.08, 21.71 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.08 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{17}H_{16}ClF_3NO_2S$: 390.0542 $[M+H]^+$; found: 390.0538.

Compound 2c:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.44 (m, 3H), 7.09 (d, J = 8.0 Hz, 2H), 6.95 (d, J = 8.4 Hz, 1H), 6.78 (s, 1H), 4.35–4.30 (m, 1H), 2.85–2.74 (m, 2H), 2.61 (dd, J = 16.8, 2.6 Hz, 1H), 2.38–2.30 (m, 1H), 2.28 (s, 3H), 2.20 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.43, 138.44, 135.15, 134.28, 130.98, 129.89, 128.85, 127.30, 126.00, 125.82 (q, J(C,F) = 275.8 Hz), 117.28, 57.08 (q, J(C,F) = 3.1 Hz), 40.67 (q, J(C,F) = 26.7 Hz), 34.22, 21.66, 21.08 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.07 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{18}H_{19}F_3NO_2S$: 370.1089 $[M+H]^+$; found: 370.1091.

Compound 2d:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59 (d, J = 8.8 Hz, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.19 (d, J = 8.1 Hz, 2H), 6.78 (dd, J = 8.8, 2.4 Hz, 1H), 6.60 (d, J = 2.4 Hz, 1H), 4.45–4.38 (m, 1H), 3.78 (s, 3H), 2.94–2.77 (m, 2H), 2.67 (dd, J = 16.8, 2.4 Hz, 1H), 2.49–2.40 (m, 1H): 2.35 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.92, 144.35, 134.24, 134.17, 132.75, 129.85, 127.38, 125.78 (q, J(C,F) = 276.0 Hz), 118.76, 113.47, 111.01, 57.31 (q, J(C,F) = 3.2 Hz), 55.74, 40.59 (q, J(C,F) = 26.6 Hz), 34.41, 21.66 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.07 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{18}H_{19}F_3NO_3S$: 386.1038 $[M+H]^+$; found: 386.1036.

Compound 2e:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.63–7.57 (m, 3H), 7.46–7.44 (m, 1H), 7.34–7.30 (m, 2H), 7.18–7.14 (m, 1H), 6.98 (d, J = 4.0 Hz, 2H), 4.41–4.34 (m, 1H), 2.90–2.78 (m, 2H), 2.68 (dd, J = 16.4, 3.0 Hz, 1H), 2.43–2.29 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 140.71, 137.27, 133.59, 130.80, 129.32, 128.31, 127.23, 125.76 (q, J(C,F) = 275.9 Hz), 125.47, 125.42, 117.44, 57.02 (q, J(C,F) = 3.2 Hz), 40.69 (q, J(C,F) = 26.6 Hz), 34.24 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.06 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{16}H_{15}F_3NO_2S$: 342.0776 $[M+H]^+$; found: 342.0778.

Compound 2f:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35 (d, J = 8.4 Hz, 1H), 7.19–7.16 (m, 2H), 4.60–4.53 (m, 1H), 3.51 (dd, J = 16.8, 9.8 Hz, 1H), 3.02 (dd, J = 16.8, 4.0 Hz, 1H), 2.95–2.83 (m, 1H), 2.83 (s, 3H), 2.53–2.39 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.50, 132.05, 130.43, 128.57, 125.89, 125.60 (q, J(C,F) = 276.0 Hz), 116.75, 57.69 (q, J(C,F) = 3.2 Hz), 40.69 (q, J(C,F) = 26.7 Hz), 35.76, 34.39 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −62.97 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{11}H_{10}ClF_3NO_2S$: 312.0073 $[M-H]^-$; found: 312.0078.

Compound 2g:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.25 (d, J = 8.8 Hz, 2H), 7.87 (d, J = 8.8 Hz, 2H), 7.70 (d, J = 8.4 Hz, 1H), 7.31–7.26 (m, 1H), 7.12–7.11 (m, 2H), 4.51–4.45 (m, 1H), 2.98–2.87 (m, 2H), 2.83 (dd, J = 16.8, 2.8 Hz, 1H), 2.56–2.42 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 150.68, 142.93, 139.82, 130.65, 128.64, 128.46, 126.09, 125.85, 125.54 (q, J(C,F) = 275.9 Hz), 124.50, 117.27, 57.38 (q, J = 3.2 Hz), 40.68 (q, J(C,F) = 27.0 Hz), 34.21 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.06 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{16}H_{14}F_3N_2O_4S$: 387.0626 $[M+H]^+$; found: 387.0624.

Compound 2h:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.59–7.57 (m, 3H), 7.18 (dd, J = 8.0, 4.0 Hz, 1H), 7.02 (s, 1H), 6.86 (d, J = 8.8, 2H), 4.45–4.39 (m, 1H), 3.80 (s, 3H), 2.97–2.87 (m, 2H), 2.75 (dd, J = 16.0, 4.0 Hz, 1H), 2.49–2.39 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 163.70, 139.64, 132.71, 130.33, 129.27, 128.27, 128.18, 125.57 (q, J(C,F) = 275.8 Hz), 125.45, 118.18, 114.48, 57.11 (q, J(C,F) = 3.2 Hz), 55.61, 40.52 (q, J(C,F) = 26.8 Hz), 34.04 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.09 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{17}H_{16}ClF_3NO_3S$: 406.0492 $[M+H]^+$; found: 406.0492.

Compound 2i:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, J = 8.4 Hz, 2H), 7.34 (d, J = 8.0 Hz, 2H), 3.75–3.69 (m, 1H), 3.45–3.39 (m, 1H), 3.19–3.13 (m, 1H), 3.06–2.93 (m, 1H), 2.43 (s, 3H), 2.32–2.16 (m, 1H), 1.80–1.75 (m, 3H), 1.53–1.46 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.05, 133.74, 130.02, 127.72, 125.87 (q, J(C,F) = 275.8 Hz), 54.75 (q, J(C,F) = 3.2 Hz), 49.14, 40.61 (q, J(C,F) = 26.3 Hz), 31.72, 24.04, 21.66 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.78 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{13}H_{17}F_3NO_2S$: 308.0932 $[M+H]^+$; found: 308.0922.

Compound 2j:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.61 (d, J = 8.0 Hz, 2H), 7.23 (d, J = 8.0 Hz, 2H), 3.62–3.54 (m, 1H), 3.29–3.24 (m, 1H), 3.07 (d, J = 10.8 Hz, 1H), 2.94 (dd, J = 10.6, 1.0 Hz, 1H), 2.32 (s, 3H), 2.26–2.11 (m, 1H), 1.75 (dd, J = 12.8, 7.2 Hz, 1H), 1.48 (dd, J = 12.8, 8.4 Hz, 1H), 0.93 (s, 3H), 0.33 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.09, 133.82, 129.93, 127.79, 126.10 (q, J(C,F) = 275.6 Hz), 61.21, 54.64 (q, J(C,F) = 3.3 Hz), 46.92, 41.05 (q, J(C,F) = 26.4 Hz), 37.59, 26.37, 25.56, 21.65 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.76 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{15}H_{21}F_3NO_2S$: 336.1245 $[M+H]^+$; found: 336.1220; m/z calcd for $C_{15}H_{20}F_3NNaO_2S$: 358.1065 $[M+Na]^+$; found: 358.1055.

Compound 2k:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, J = 8.4 Hz, 2H), 7.32 (d, J = 8.0 Hz, 2H), 3.65–3.57 (m, 1H), 3.42–3.29 (m, 1H), 3.24 (d, J = 10.8 Hz, 1H), 3.12 (d, J = 10.8 Hz, 1H), 2.41 (s, 3H), 2.33–2.21 (m, 1H), 1.91 (dd, J = 12.4, 6.8 Hz, 1H), 1.52 (dd, J = 12.0, 8.8 Hz, 1H), 1.43–1.03 (m, 8H), 0.73–0.67 (m, 1H), 0.54–0.48 ppm (m, 1H);

^{13}C NMR (100 MHz, $CDCl_3$): δ = 144.05, 133.72, 129.89, 127.51, 126.13 (q, J(C,F) = 275.6 Hz), 58.33, 53.90 (q, J = 3.0 Hz), 45.26, 41.47, 41.20 (q, J(C,F) = 26.4 Hz), 36.36, 33.89, 25.84, 23.74, 22.90, 21.64 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −63.70 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{18}H_{25}F_3NO_2S$: 376.1558 $[M+H]^+$; found: 376.1547.

General procedure b: CuI-catalyzed aminotrifluoromethylation of unactivated alkenes with free amines

CuI (10 or 5 mol%), **4a** (237.0 mg, 0.75 mmol, 1.5 equiv) were added to a 25 mL Schlenk tube equipped with a magnetic stirrer bar. The tube was evacuated and backfilled with argon (×4), then the solution of substrate (0.50 mmol, 1.0 equiv) in DCE or *t*BuOH (4.0 mL) was added to the tube by syringe, under argon. The contents of the sealed tube were stirred at 40 or 75 °C. Upon completion of the reaction (monitored by TLC), the solvent was removed under vacuum and the residue was purified by silica gel column chromatography (petroleum ether/CH_2Cl_2 = 50:1–1:1) to give the desired products **2l**–**t**.

Compound 2l:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04 (d, J = 0.4 Hz, 1H), 6.99 (dd, J = 8.0, 2.0 Hz, 1H), 6.52 (d, J = 8.0 Hz, 1H), 4.23–4.15 (m, 1H), 4.04 (br s, 1H), 3.22 (dd, J = 15.8, 8.4 Hz, 1H), 2.74 (dd, J = 15.8, 9.2 Hz, 1H), 2.55–2.33 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 148.94, 129.43, 127.57, 126.46 (q, J(C,F) = 275.7 Hz), 124.89, 123.72, 110.01, 54.53 (q, J(C,F) = 2.4 Hz), 41.40 (q, J(C,F) = 26.5 Hz), 36.29 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −64.24 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{10}H_{10}ClF_3N$: 236.0454 $[M+H]^+$; found: 236.0451.

Compound 2m:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.17 (s, 1H), 7.13 (d, J = 8.4 Hz, 1H), 6.48 (d, J = 8.4 Hz, 1H), 4.22–4.15 (m, 1H), 4.11 (s, 1H), 3.22 (dd, J = 15.8, 8.4 Hz, 1H), 2.74 (dd, J = 15.8, 8.8 Hz, 1H), 2.52–2.36 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.36, 130.46, 129.87, 127.68, 126. 42 (q, J(C,F) = 275.5 Hz), 110.72, 110.57, 54.43 (q, J = 2.7 Hz), 40.39 (q, J(C,F) = 26.4 Hz), 36.21 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −64.20 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{10}H_{10}BrF_3N$: 279.9949 $[M+H]^+$; found: 279.9950.

Compound 2n:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.83–6.81 (m, 1H), 6.76–6.71 (m, 1H), 6.53 (dd, J = 8.4, 4.4 Hz, 1H), 4.22–4.18 (m, 1H), 3.88 (br s, 1H), 3.23 (dd, J = 15.6, 8.4 Hz, 1H), 2.75 (dd, J = 15.6, 9.2 Hz, 1H), 2.57–2.35 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 157.29 (q, J(C,F) = 234.3 Hz), 146.27, 129.23 (d, J(C,F) = 8.1 Hz), 126.48 (q, J(C,F) = 275.5 Hz), 113.77 (d, J(C,F) = 23.1 Hz), 112.15 (d, J(C,F) = 23.8 Hz), 109.56 (d, J(C,F) = 8.3 Hz), 54.80 (q, J(C,F) = 2.7 Hz), 40.43 (q, J(C,F) = 26.5 Hz), 36.63 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −64.28 (s, 3F), −125.91 ppm (s, 1F); HRMS (ESI): m/z calcd for $C_{10}H_{10}F_4N$: 220.0749 $[M+H]^+$; found: 220.0741.

Compound 2o:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28 (d, J = 8.4 Hz, 1H), 7.24 (s, 1H), 6.55 (d, J = 8.4 Hz, 1H), 4.72 (s, 1H), 4.31–4.24 (m, 1H), 3.28 (dd, J = 16.0, 9.2 Hz, 1H), 2.77 (dd, J = 16.0, 8.4 Hz, 1H), 2.54–2.34 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.17, 133.52, 128.12, 127.97, 126.27 (q, J(C,F) = 275.5 Hz), 120.64, 108.44, 100.31, 53.98 (q, J(C,F) = 2.9 Hz), 40.45 (q, J(C,F) = 26.5 Hz), 35.39 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −64.15 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{11}H_{10}F_3N_2$: 227.0796 $[M+H]^+$; found: 227.0793.

Compound 2p:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04 (dd, J = 8.0, 0.4 Hz, 1H), 6.97 (dd, J = 7.2, 0.8 Hz, 1H), 6.68–6.64 (m, 1H), 4.30 (s, 1H), 4.28–4.20 (m, 1H), 3.33 (dd, J = 16.0, 8.8 Hz, 1H), 2.85 (dd, J = 16.0, 9.2 Hz, 1H), 2.61–2.36 ppm (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.36, 129.00, 127.57, 126.37 (q, J(C,F) = 275.5 Hz), 122.90, 120.02, 114.88, 54.06 (q, J = 2.9 Hz), 40.48 (q, J(C,F) = 26.5 Hz), 37.15 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −64.26 ppm (s, 3F). HRMS (ESI): m/z calcd for $C_{10}H_{10}ClF_3N$: 236.0454 $[M+H]^+$; found: 236.0444.

Compound 2q:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.96 (s, 1H), 6.89 (d, J = 8.0 Hz, 1H), 6.57 (d, J = 7.6 Hz, 1H), 4.21–4.13 (m, 1H), 3.94 (br s, 1H), 3.23 (dd, J = 15.4, 8.4 Hz, 1H), 2.75 (dd, J = 15.4, 8.8 Hz, 1H), 2.55–2.38 (m, 2H), 2.30 ppm (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.93, 128.69, 128.09, 127.85, 126.37 (q, J(C,F) = 275.4 Hz), 125.50, 109.31, 54.36 (q, J = 2.9 Hz), 40.54 (q, J(C,F) = 26.3 Hz), 36.56, 20.90 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −64.21 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{11}H_{13}F_3N$: 216.1000 $[M+H]^+$; found: 216.0997.

Compound 2r:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.04–7.03 (m, 1H), 6.93 (s, 1H), 4.28–4.20 (m, 2H), 3.30 (dd, J = 16.0, 8.8 Hz, 1H), 2.82 (dd, J = 16.0, 9.2 Hz, 1H), 2.59–2.35 ppm (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 146.19, 130.20, 127.10, 126.25 (q, J(C,F) = 275.5 Hz), 123.76, 123.36, 114.80, 54.30 (q, J = 2.8 Hz), 40.34 (q, J(C,F) = 26.7 Hz), 36.98 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −64.28 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{10}H_9Cl_2F_3N$: 270.0064 $[M+H]^+$; found: 270.0057.

Compound 2s:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.34–7.17 (m, 10H), 3.79 (d, J = 11.2 Hz, 1H), 3.55–3.58 (m, 1H), 3.43 (d, J = 11.6 Hz, 1H), 2.92 (dd, J = 12.8, 6.4 Hz, 1H), 2.37–2.25 (m, 2H), 2.18–2.11 (m, 1H), 1.99 ppm (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 147.06, 145.94, 128.77, 128.58, 127.09, 126.87, 126.56 (q, J(C,F) = 275.7 Hz), 126.50, 126.41, 57.53, 56.44, 51.63 (q, J = 2.6 Hz), 44.92, 41.36 ppm (q, J(C,F) = 25.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$): δ = −64.14 (s, 3F); HRMS (ESI): m/z calcd for $C_{18}H_{19}F_3N$: 306.1470 $[M+H]^+$; found: 306.1465.

Compound 2t:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.43 (br s, 1H), 2.75–2.85 (m, 2H), 2.38–2.17 (m, 4H), 1.89 (s, 1H), 1.44–1.41 ppm (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 126.64 (q, J(C,F) = 275.3 Hz), 58.24, 52.11, 45.25, 42.98, 40.52 (q, J(C,F) = 26.6 Hz), 38.43, 37.00, 26.14, 24.04, 23.60 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): δ = −64.31 ppm (s, 3F); HRMS (ESI): m/z calcd for $C_{11}H_{19}F_3N$: 222.1470 $[M+H]^+$; found: 222.1461.

Compound 2u:

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.76 (br s, 1H), 7.48–7.36 (m, 5H), 7.02 (s, 2H), 5.34 (s, 2H), 4.80–4.78 (m, 1H), 3.40 (dd, J = 16.4, 9.6 Hz, 1H), 2.97 (d, J = 16.4 Hz, 1H), 2.66 (br s, 1H), 2.40–2.26 ppm (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.32, 138.68, 136.05, 133.03, 129.20, 128.66, 128.51, 128.36, 128.22, 125.95 (q, J(C,F) = 275.9 Hz), 125.76, 115.27, 67.54, 54.34, 38.18, 33.74, 20.82 ppm;

^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -63.24$ ppm (br s, 3F); HRMS (ESI): *m/z* calcd for $C_{19}H_{18}F_3NNaO_2$: 372.1187 $[M+Na]^+$; found: 372.1182.

Compound 2v:

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.73$ (br s, 1H), 7.42–7.35 (m, 5H), 7.14 (br s, 2H), 5.29 (s, 2H), 4.81–4.76 (m, 1H), 3.39 (dd, $J = 16.8$, 9.6 Hz, 1H), 2.96 (d, $J = 16.8$ Hz, 1H), 2.64 (br s, 1H), 2.38–2.24 ppm (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 152.31$, 139.79, 135.76, 131.07, 128.77, 128.57, 128.43, 128.34, 127.87, 125.82 (q, J(C,F) = 275.8 Hz), 125.27, 116.45, 67.88, 54.60, 38.10, 33.58 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -63.29$ ppm (br s, 3F); HRMS (APCI): *m/z* calcd for $C_{17}H_{16}ClF_3N$: 326.0923 $[M-CO_2+H]^+$; found: 326.0856.

Compound 2w:

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.66$ (br s, 1H), 7.13 (d, $J = 10.8$ Hz, 2H), 4.70 (s, 1H), 3.38 (dd, $J = 16.8$, 9.6 Hz, 1H), 2.92 (d, $J = 16.8$ Hz, 1H), 2.64 (s, 1H), 2.37–2.23 (m, 1H), 1.56 ppm (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 151.55$, 140.18, 130.96, 127.90, 127.71, 125.85 (q, J(C,F) = 275.7 Hz), 125.14, 116.26, 82.11, 54.43 (q, $J = 3.1$ Hz), 38.34, 33.60, 28.33 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -63.62$ ppm (br s, 3F); HRMS (APCI): *m/z* calcd for $C_{10}H_{10}ClF_3N$: 236.0454 $[M-CO_2-C_4H_8+H]^+$; found: 236.0441.

Compound 2x:

^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.30$ (d, $J = 7.6$ Hz, 2H), 7.21–7.17 (m, 2H), 6.95 (t, $J = 7.2$ Hz, 1H), 6.21 (s, 1H), 4.19–4.11 (m, 1H), 3.30 (d, $J = 9.2$ Hz, 1H), 3.15–3.08 (m, 1H), 3.03 (d, $J = 9.2$ Hz, 1H), 2.11 (dd, $J = 13.0$, 7.6 Hz, 1H), 2.03–1.91 (m, 1H), 1.51–1.30 ppm (m, 11H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 154.69$, 138.89, 129.04, 126.41 (q, J(C,F) = 275.8 Hz), 123.31, 119.91, 57.24, 51.74 (q, J(C,F) = 3.1 Hz), 43.21, 42.42, 38.60 (q, J(C,F) = 26.2 Hz), 36.61, 34.83, 26.07, 23.85, 22.98 ppm; ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -63.20$ ppm (s, 3F); HRMS (ESI): *m/z* calcd for $C_{18}H_{24}F_3N_2O$: 341.1841 $[M+H]^+$; found: 341.1834.

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