EurJOC
European Journal of Organic Chemistry

A Journal of
ChemPubSoc Europe

Accepted Article

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To be cited as: Eur. J. Org. Chem. 10.1002/ejoc.201601196

Link to VoR: http://dx.doi.org/10.1002/ejoc.201601196

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Cu-Mediated Trifluoromethylation of Aromatic α-Diazo Esters by Yagupolskii-Umemoto's Reagent

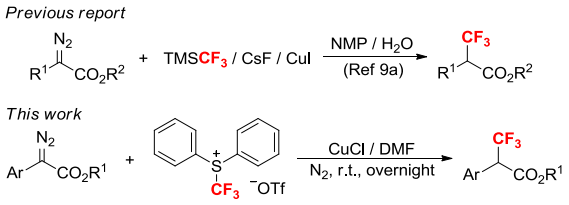
Xiao-Qian Hu, Jia-Bin Han, and Cheng-Pan Zhang*[a]

Abstract: Room temperature reductive trifluoromethylation of aromatic α-diazo esters by Yagupolskii-Umemoto's reagent ([Ph_2SCF_3][OTf]) in DMF in the presence of excess CuCl furnished a variety of α-trifluoromethyl arylacetates in up to 93% yield. The prior reaction of [Ph_2SCF_3][OTf] (**2a**) with CuCl before addition of α-diazo esters was imperative for the conversion, which might pre-generate the key [Cu(I)CF_3] intermediate according to the outcomes of the control experiments. When the long-chain perfluoroalkyl diphenylsulfonium triflates (**2b-e**) were employed instead of **2a**, the reaction of aromatic α-diazo ester under the same conditions followed by treatment with $NaHCO_3$ afforded a series of fluorinated α,β-unsaturated esters in good yields. This protocol allows for a facile, convenient, and practical access to α-trifluoromethyl arylacetates and their analogues, implying that the "$^+R_{fn}$" reagents are compatible with α-diazo esters in the presence of an appropriate reductant.

Introduction

The last several decades have witnessed the explosive growth of organofluorides.[1] Fluorine has emerged as one of the most important elements in a large number of biological molecules (e.g. pharmaceuticals and agrochemicals) and functional materials.[1] Although it ranks 13th in abundance among all elements in the earth's crust, the naturally-occurring fluorine-containing organic compounds have been very rarely reported.[2] Since the introduction of fluorine atoms into organic molecules can impart a great many of unique chemical, physicochemical, and biological properties, the development of highly effective fluorination and fluoroalkylation methods to furnish the target compounds is of great importance.[2] To date, the metal-mediated direct trifluoromethylation has become one of the most prevalent approaches to the synthesis of fluorine-containing molecules,[2-4] which includes the traditionally nucleophilic, electrophilc, and radical trifluoromethylation,[3] and the contemporarily oxidative and reductive trifluoromethylation.[4] To boost different sorts of trifluoromethylation, the development of new CF_3 transfer sources and the exploration of new property of the known ones are of permanent significance.

The Yagupolskii-Umemoto's reagents ([Ar_2SCF_3][X]), first synthesized by Yagupolskii et al and then modified by Umemoto, Shreeve and others, represent an important class of electrophilic "$^+CF_3$" transfer reagents, which were initially applied to trifluoromethylate multifarious nucleophiles.[3] Later, they were confirmed to be effective participants in the reductive trifluoromethylation of alkenes, alkynes, arenes, and other systems.[4b] Compared to the cyclic Umemoto and Togni's reagents, the acyclic Yagupolskii-Umemoto's reagents were much less studied even though they have similar oxidative properties.[4b] Recently, [Ar_2SCF_3][OTf] were used as powerful arylation reagents in the Pd-catalyzed Suzuki-Miyaura and Mizoroki-Heck-type reactions.[5] Despite the advances made, [Ar_2SCF_3][OTf] still have a narrow scope of application in organic synthesis in comparison with other "$^+CF_3$" reagents. Further exploitation of [Ar_2SCF_3][OTf] is sought-after because these reagents have advantages such as good stability, non-moisture sensitivity, nonvolatility, easy preparation, and simple handling.[3,4b]



On the other hand, α-diazo compounds have been widely used in the construction of cyclopropanes, heterocycles, olefins, and other useful molecules over the past few years.[6,7] The direct functionalization of the non-fluorinated α-diazo compounds by fluoroalkylation reagents has also achieved great success.[8] For instance, the Cu-mediated trifluoromethylthiolation of α-diazo esters by $AgSCF_3$, the Cu-mediated gem-difluoroolefination of diazo compounds by $TMSCF_3$ or $Ph_3P^+CF_2CO_2^-$, the metal-free gem-difluoroolefination of diazo compounds by $TMSCF_3$ or $TMSCF_2Br$, and the Ag-mediated trifluoromethoxylation of α-diazo esters by "$^-OCF_3$" anion have synthesized plenty of useful fluorine-containing building blocks.[8]

The CuI-mediated trifluoromethylation of α-diazo esters by $TMSCF_3$ / CsF was first disclosed by Hu and coworkers.[9a] This method required the volatile and moisture-sensitive $TMSCF_3$ reagent and a scavenger to "trap" the iodine anion, leading to the operation less uncomplicated. Very recently, the Rh-catalyzed geminal oxytrifluoromethylation of α-diazo ketones by ROH and Togni's reagent was reported, in late stage of which proceeded via an electrophilic trifluoromethylation.[9b] Although the Cu-mediated reductive Sandmeyer reaction of aryldiazonium salts and 5-(trifluoromethyl)-5H-dibenzo[b,d]thiophen-5-ium trifluoromethanesulfonate (Umemoto's reagent) was accomplished, the similar transformation of α-diazo esters with "$^+CF_3$" reagents has never been reported.[9c-d] In consideration of

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the easy preparation of $[Ph_2SCF_3][OTf]$ and the versatility of *α*-diazo compounds, we imagined whether the direct trifluoromethylation of *α*-diazo esters by $[Ph_2SCF_3][OTf]$ could provide a convenient way to yield *α*-CF_3 esters.

Results and Discussion

Indeed, the reaction of ethyl 2-diazo-2-(4-methoxyphenyl)acetate (**1a**) with a mixture of trifluoromethyl diphenylsulfonium triflate (**2a**) (2 equiv) and Cu powder (4 equiv) in DMF, which was already reacted at 50 °C for 2 h, provided ethyl 3,3,3-trifluoro-2-(4-methoxyphenyl)propanoate (**3a**) in 13% yield (entry 1, **Table 1**). The use of additive such as CuCl, CuBr, CuI, CuSCN, or KI (1 equiv) in the reaction of **1a** with **2a** and Cu powder gave comparable or lower yields of **3a** (entry 2, **Table 2** and SI). Encouragingly, if **2a** (1.5 equiv) reacted with CuCl (2.25 equiv) for 15 min followed by treatment with **1a** at room temperature for another 5 h, **3a** was synthesized in 46% yield (entry 3, **Table 1**). Varying the amount of CuCl from 2.25 to 4.5 equiv, **3a** was obtained in 66% yield (entry 4, **Table 1**). Notably, reaction of **1a** with a mixture of **2a** (1.8 equiv) and CuCl (5.4 equiv) in DMF at room temperature under a N_2 atmosphere overnight gave **3a** in 86% yield (75% isolated yield) (entry 5, **Table 1**). Further increment of the molar ratio of CuCl to **2a** did not improve the yield of **3a** (entries 6 and 7, **Table 1**). However, slightly decreasing the amount of CuCl from 5.4 to 5.0 equiv in the reaction with **2a** (1.8 equiv) caused a lower yield of **3a** (entry 8, **Table 1**). The prior reaction of **2a** with CuCl was essential for the entire conversion since the simultaneous addition of **1a**, **2a**, and CuCl in DMF led to **3a** in 17% yield (see SI-Table 6), wherein the homo-coupling of **1a** was predominant. If **2a** was treated with CuCl in DMF for 10-15 min before addition of **1a**, **3a** was formed in 85-86% yield. Prolonging the reaction time of **2a** and CuCl from 15 to 30 min or longer lowered the yield of **3a**. CuBr was another suitable initiator for the reaction. When **1a** reacted with a mixture of **2a** and CuBr in DMF at room temperature overnight, **3a** was constructed in 70% yield (entry 9, **Table 1**). Other copper salts such as CuI, CuSCN, $Cu(OAc)_2$, IPrCuCl, CuOTf, and $[(MeCN)_4Cu]PF_6$ were less effective for the reaction, which provided **3a** in much lower yields (entries 10-15, **Table 1**). Furthermore, addition of 0.1 mL of H_2O (ca. 56 equiv) to the reaction mixture of **1a**, **2a**, and CuCl in DMF afforded **3a** in a comparable yield (65% (entry 16) vs 66% (entry 4), **Table 1**), suggesting that the moisture didn't harm the reaction. Nevertheless, if the reaction was run in air, only 12% of **3a** was obtained (entry 16, **Table 1**). Other electrophilic "$^+CF_3$" sources such as Umemoto's reagent (**2a'**) and Togni's reagent (**2a''**) were also amenable to the conversion. Reaction of **1a** with a mixture of CuCl (4.5 equiv) and **2a'** or **2a''** (1.5 equiv) in DMF provided **3a** in 63% or 45% yield, respectively (entries 18 and 19, **Table 1**).

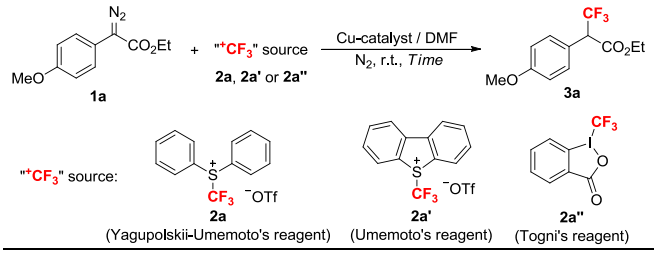


Table 1 Trifluoromethylation of **1a** by "$^+CF_3$" reagents in DMF in the presence of Cu salts.[a]

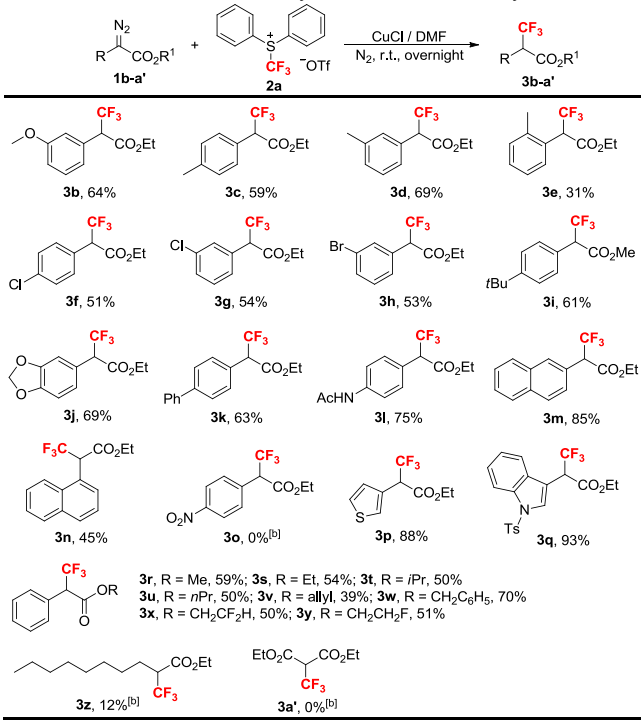
Entry	[$^+CF_3$] source	[Cu] salts	**1a : [$^+CF_3$] : [Cu]**[b]	Yield (**3a**, %)[c]
1[d]	**2a**	Cu powder	1 : 2 : 4	13
2[e]	**2a**	Cu / CuCl	1 : 2 : 4	7
3[f]	**2a**	CuCl	1 : 1.5 : 2.25	46
4	**2a**	CuCl	1 : 1.5 : 4.5	66
5	**2a**	CuCl	1 : 1.8 : 5.4	**86 (75)**
6	**2a**	CuCl	1 : 1.9 : 5.7	73
7	**2a**	CuCl	1 : 2.0 : 6.0	78
8	**2a**	CuCl	1 : 1.8 : 5.0	73
9	**2a**	CuBr	1 : 1.8 : 5.4	70
10	**2a**	CuI	1 : 1.8 : 5.4	19
11	**2a**	CuSCN	1 : 1.8 : 5.4	13
12	**2a**	$Cu(OAc)_2$	1 : 1.8 : 5.4	22
13	**2a**	IPrCuCl	1 : 1.8 : 3.6	0
14	**2a**	CuOTf	1 : 1.5 : 4.5	25
15	**2a**	$[(MeCN)_4Cu]PF_6$	1 : 1.5 : 4.5	23
16[g]	**2a**	CuCl	1 : 1.5 : 4.5	65
17[h]	**2a**	CuCl	1 : 1.8 : 5.4	12
18	**2a'**	CuCl	1 : 1.5 : 4.5	63
19	**2a''**	CuCl	1 : 1.5 : 4.5	45

[a] Reaction conditions: **2a**, **2a'**, or **2a''** / Cu salt / DMF (2 mL) / r.t. / N_2 / 10-15 min, then **1a** (0.1 mmol) / DMF (1 mL) / r.t. / overnight. [b] Molar ratio. [c] Yields were determined by HPLC using ethyl 3,3,3-trifluoro-2-(4-methoxyphenyl)propanoate (**3a**) as the external standard (t_R = 4.251 min, λ_{max} = 227.5 nm, CH_3CN : H_2O = 70 : 30 (v / v)). Isolated yield is depicted in the parentheses. [d] Reaction conditions: **2a** / Cu / DMF (2 mL) / 50 °C / N_2 / 2 h, then **1a** (0.1 mmol) / DMF (1 mL) / 50 °C / overnight. [e] Reaction conditions: **2a** / Cu / CuCl (1 equiv) / DMF (2 mL) / 50 °C / N_2 / 2 h, then **1a** (0.1 mmol) / DMF (1 mL) / r.t. / overnight. [f] 5 h. Yield was determined by ^{19}F NMR using $C_6H_5CF_3$ as an internal standard. [g] 0.1 mL of water was added with the addition of **1a**. [h] The reaction was run in air.

Next, a combination of *α*-diazo ester and a mixture of **2a** (1.8 equiv) / CuCl (5.4 equiv) in DMF at room temperature overnight was employed to test the scope of the reaction. To our delight, various ethyl 2-diazo-2-arylacetates (**1b-n**) treated with a mixture of **2a**, CuCl, and DMF under the standard conditions, which was priorly reacted at room temperature for 10 min, gave the corresponding ethyl 2-trifluoro-2-arylacetates (**3b-n**) in good yields. The steric and electronic nature of the substituents on the aryl groups had a considerable influence on the reaction. For instance, treatment of ethyl 2-diazo-2-(*p*-tolyl)acetate (**1c**) and

ethyl 2-diazo-2-(*m*-tolyl)acetate (**1d**) with a mixture of **2a** and CuCl in DMF at room temperature under N_2 overnight provided **3c** in 59% yield and **3d** in 69% yield, respectively, while the reaction of ethyl 2-diazo-2-(o-tolyl)acetate (**1e**) under the same conditions afforded **3e** in 31% yield. Similarly, ethyl 2-diazo-2-(naphthalen-2-yl)acetate (**1m**) reacted with a mixture of **2a**, CuCl, and DMF under the standard conditions to supply **3m** in 85% yield, and the reaction of ethyl 2-diazo-2-(naphthalen-1-yl)acetate (**1n**) provided **3n** in 45% yield. These results indicated that the steric hindrance of aryl groups of *α*-diazo arylacetates suppressed the reaction. In addition, the electron-donating groups on the phenyl rings of alkyl 2-diazo-2-arylacetates (e.g. **1j** and **1l**) benefited the reaction, giving higher yields of the desired products than the non-substituted congener (e.g. **1s**). However, when the highly electron-deficient ethyl 2-diazo-2-(4-nitrophenyl)acetate (**1o**) reacted with a mixture of **2a**, CuCl, and DMF under the standard conditions, no desired product (**3o**) was formed. Furthermore, reactions of the electron-rich *α*-diazo heteroarylacetates such as ethyl 2-diazo-2-(thiophen-3-yl)acetate (**1p**) and ethyl 2-diazo-2-(1-tosyl-indol-3-yl)acetate (**1q**) with a mixture of **2a** and CuCl in DMF afforded respective **3p** in 88% yield and **3q** in 93% yield. Besides, other alkyl *α*-diazo esters such as methyl (**1r**), isopropyl (**1t**), propyl (**1u**), allyl (**1v**), benzyl (**1w**), 2',2'-difluoroethyl (**1x**), and 2'-fluoroethyl (**1y**) 2-diazo-2-phenylacetates were all successfully transformed, which produced **3r** and **3t-y** in 39-70% yields. Unfortunately, the reaction was less effective to aliphatic *α*-diazo esters as ethyl 2-diazodecanoate (**1z**) and diethyl 2-diazomalonate (**1a'**) reacted with **2a** / CuCl under the standard conditions to give trace or none of the desired products, which were determined by ^{19}F NMR analysis of the reaction mixture.

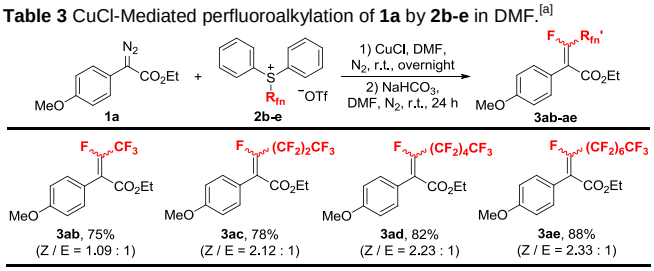
Table 2 CuCl-Mediated trifluoromethylation of *α*-diazo esters by **2a** in DMF.[a]



[a] Reaction conditions: **2a** (0.54 mmol) / CuCl (1.62 mmol) / DMF (3 mL) / r.t. / N_2 / 10 min, then **1** (0.30 mmol) / DMF (1.5 mL) / r.t. / overnight. [b] Yields were determined by ^{19}F NMR using ^{-}OTf anion as an internal standard.

In addition to **2a**, other long-chain perfluoroalkyl diphenylsulfonium salts were investigated in the reaction (**Table 3**). It was distinctive that reaction of **1a** or **1m** with **2b** under the standard conditions gave a mixture of *α*-pentafluoroethylated ester and *β*-F eliminated product, which were determined by NMR spectroscopy (see SI). To prohibit the *β*-F elimination, efforts were made by addition of water, $Et_3N•3HF$, or CsF to the reaction mixture of **1m** and **2b**. However, only a few changes in the product distribution of the reaction were observed (see SI). The previous report had disclosed that adventitious water in the reaction of *α*-diazo ester and "$CuCF_3$" could facilitate the formation of trifluoromethylated product.[9a] Moreover, by simple treatment of a reaction mixture of **1a** and **2b** with $NaHCO_3$ in DMF at room temperature for 24 h, ethyl 3,4,4,4-tetrafluoro-2-(4-methoxyphenyl)but-2-enoate (**3ab**) was obtained in 75% yield.[10] Similar results were also observed for **2c**, **2d**, and **2e**, which provided **3ac**, **3ad**, and **3ae** in 78-88% yields. The molar ratio of *Z*- and *E*-isomers of **3ab-ae** was determined by ^{19}F NMR analysis of the isolated products.[11] Interestingly, when the reaction mixture of **1a** and **2a** was treated with $NaHCO_3$ in DMF at room temperature for 24 h, **3a** was recovered, suggesting the ease of formation of *β*-F eliminated products with long-chain perfluoroalkyl groups.

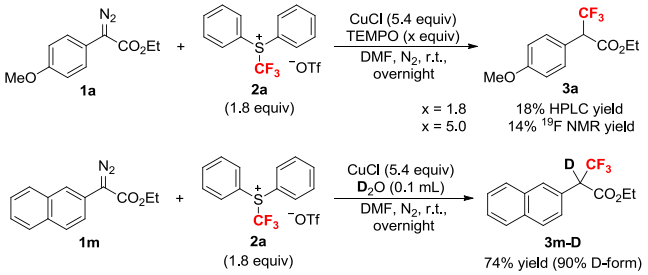
Table 3 CuCl-Mediated perfluoroalkylation of **1a** by **2b-e** in DMF.[a]



[a] Reaction conditions: 1) **2b-e** (0.54 mmol) / CuCl (1.62 mmol) / DMF (3 mL) / r.t. / N_2 / 10 min, then **1a** (0.30 mmol) / DMF (1.5 mL) / r.t. / overnight; 2) $NaHCO_3$ (0.9 mmol) / r.t. / N_2 / 24 h. The molar ratio of *Z*- and *E*-isomers was determined by ^{19}F NMR analysis of the isolated products according to the literatures.[11] **2b**: $R_{fn} = CF_2CF_3$; **2c**: $R_{fn} = (CF_2)_3CF_3$; **2d**: $R_{fn} = (CF_2)_5CF_3$; **2e**: $R_{fn} = (CF_2)_7CF_3$.

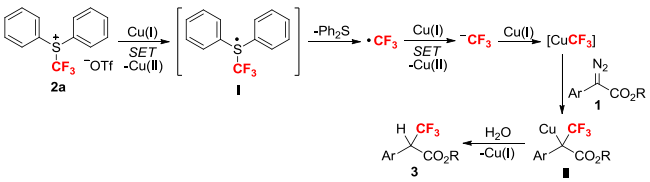
To probe the possible reaction mechanism, the control experiments were performed (**Scheme 1**). A mixture of **2a**, CuCl, TEMPO (1.8 or 5.0 equiv), and DMF reacted at room temperature for 10 min followed by addition of **1a** provided **3a** in 18% HPLC yield or 14% ^{19}F NMR yield. Meanwhile, the TEMPO-CF_3 adduct was formed and determined by ^{19}F NMR analysis of the reaction mixture (see SI). Nevertheless, if TEMPO (5.0 equiv) was contemporaneously added with **1a** to the reaction mixture of **2a**, CuCl, and DMF, which was already reacted at room temperature for 10 min, **3a** was obtained in 57% ^{19}F NMR yield. These results suggested that the radical process might be involved in the reaction, which predominated at the beginning of the reaction. Moreover, ^{19}F NMR measurement of the reaction mixture of **2a**, CuCl, and DMF indicated that most of **2a** was

consumed in the first 20 min (see SI). Addition of D_2O (0.1 mL) to the reaction mixture of **1a** and **2a** / CuCl at the beginning of the reaction or at the stage of adding **1a** gave **3a** in 74% or 71% yield (90% deuterated form, **Scheme 1**), implying that the *α*-proton of **3a** is originated from the residual moisture in the solvent.

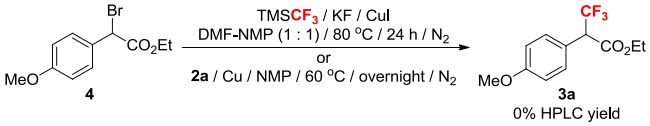


Scheme 1 The control experiments of Cu(I)-mediated trifluoromethylation.

Based on the results above and the previous reports,[4b,12] a plausible reductive trifluoromethylation mechanism was suggested for the reaction (**Scheme 2**). First, **2a** is reduced by CuCl via a single electron transfer (SET), generating **I** and Cu(II) salt. Intermediate **I** is unstable which rapidly decomposes to $\bullet CF_3$ radical and releases diphenyl sulfide. The $\bullet CF_3$ radical is very easy to be reduced by a second equivalent of Cu(I) catalyst to form $^-CF_3$ anion, which combines with another equivalent of Cu(I) catalyst to produce $[Cu(I)CF_3]$. Then $[Cu(I)CF_3]$ reacts with *α*-diazo ester (**1**) yielding the insertion metal-complex (**II**), which is protonated to eventually afford the trifluoromethylated product (**3**). In the cases of perfluoroalkyl diphenylsulfonium salts, the *β*-F elimination of the insertion metal-complex might compete with the protonation, leading to a mixture of products. Nevertheless, the exact details of the reaction mechanism are still unclear.



Scheme 2 A proposed reaction mechanism for Cu(I)-mediated trifluoromethylation of **1a** with **2a**



Scheme 3 Synthesis of **3a** from ethyl 2-bromo-2-(4-methoxyphenyl)acetate (**4**) and $TMSCF_3$ or **2a**

It should be mentioned that trifluoromethylation of benzyl halides and their derivatives ($ArCH_2X$) at the benzylic position has been well documented.[13] However, trifluoromethylation of the analogues (ArCH(R)X) that possess substituents on the benzylic carbon is scarcely known.[13] We found that ethyl 2-bromo-2-(4-methoxyphenyl)acetate (**4**) reacted with $TMSCF_3$ or **2a** by the known procedures failing to give the desired product (**3a**) (**Scheme 3**), although these procedures had successfully trifluoromethylated the non-substituted benzyl halides at the benzylic position.[13d,13h] These results illustrated the reliability and practicability of our method in the construction of tertiary $C_{benzylic}$-CF_3 bonds.

Conclusions

In conclusion, we have found that aromatic *α*-diazo esters could be trifluoromethylated by Yagupolskii-Umemoto's reagent (**2a**) in the presence of CuCl. The reaction at room temperature furnished numerous *α*-trifluoromethyl arylacetates in good yields. The prior reaction between **2a** and CuCl before addition of *α*-diazo esters was very necessary for the entire conversion. Using perfluoroalkyl diphenylsulfonium triflates instead of **2a**, the reaction afforded a mixture of *α*-perfluoroalkylated and *β*-defluorinated products, which was further treated with $NaHCO_3$ to solely provide the *β*-defluorinated compounds. A plausible reductive trifluoromethylation mechanism was suggested for the reaction according to the outcomes of the control experiments and the previous reports.[4b,12] This protocol is simply operational without the use of extra iodine anion "scavenger",[9a] which, alternatively, supplies a facile and practical access to *α*-trifluoromethyl arylacetates under mild conditions. Most importantly, the reaction has demonstrated a good compatibility of "$^+R_{fn}$" reagents with *α*-diazo compounds in the presence of a certain reductant.

Experimental Section

Procedure A (typical): In a nitrogen-filled glovebox, an oven-dried tube (20 mL) were charged with **2a** (218 mg, 0.54 mmol), CuCl (160 mg, 1.62 mmol), and DMF (3 mL) with vigorous stirring. After 10 minutes, a solution of **1** (0.30 mmol) in DMF (1.5 mL) was introduced via syringe. The mixture was reacted at room temperature overnight and extracted with dichloromethane (3 × 25 mL). The combined organic layers were washed with H_2O (3 × 50 mL), dried over anhydrous Na_2SO_4, and concentrated to dryness under reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 20 : 1 (v / v) as eluents to give **3** as the desired product.

Ethyl 3,3,3-trifluoro-2-(4-methoxyphenyl)propanoate (**3a**),[9a] yellow oil, 59 mg, 75% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.5 Hz, 2H), 6.92 (d, *J* = 8.0 Hz, 2H), 4.29-4.17 (m, 3H), 3.81 (s, 3H), 1.26 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -68.1 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4 (q, *J* = 2.6 Hz), 159.3, 129.6, 122.8 (q, *J* = 278.3 Hz), 120.4, 113.3, 60.9, 54.2, 53.8 (q, *J* = 28.4 Hz), 12.8.

Ethyl 3,3,3-trifluoro-2-(3-methoxyphenyl)propanoate (**3b**), yellow oil, 50 mg, 64% yield. ^1H NMR (500 MHz, $CDCl_3$) δ 7.31 (t, *J* = 8.5 Hz, 1H), 7.03-7.01 (m, 2H), 6.94 (dm, *J* = 7.7 Hz, 1H), 4.31-4.17 (m, 3H), 3.82 (s, 3H), 1.26 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.6 (d, *J* = 8.9 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 166.0 (q, *J* = 2.6 Hz), 159.9, 130.7, 129.9, 123.7 (q, *J* = 280.4 Hz), 121.8, 115.2, 114.7, 62.0, 55.5 (q, *J* = 29.1 Hz), 55.3, 13.9. IR (KBr): 2984, 2841, 1748, 1603, 1587, 1494, 1467, 1439, 1373, 1349, 1315, 1265, 1152, 1109, 1076, 1026, 973, 945, 879, 840, 783, 718, 695, 602 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{12}H_{13}F_3O_3$: 262.0817, found: 262.0807.

Ethyl 3,3,3-trifluoro-2-(p-tolyl)propanoate (**3c**),[9a] yellow oil, 41 mg, 55% yield. ^1H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 2H), 4.33-4.17 (m, 3H), 2.37 (s, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -67.8 (d, *J* = 8.6 Hz, 3F). ^{13}C NMR (100 MHz,

$CDCl_3$) δ 166.3 (q, *J* = 2.6 Hz), 139.2, 129.6, 129.3, 126.5, 123.8 (q, *J* = 277.5 Hz), 62.0, 55.2 (q, *J* = 28.5 Hz), 21.1, 13.9.

Ethyl 3,3,3-trifluoro-2-(m-tolyl)propanoate (**3d**),[14a] yellow oil, 51 mg, 69% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38-7.19 (m, 4H), 4.33-4.14 (m, 3H), 2.36 (s, 3H), 1.25 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -67.6 (d, *J* = 8.6 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3 (q, *J* = 2.6 Hz), 138.7, 130.1, 130.0, 129.3, 128.8, 126.5, 123.8 (q, *J* = 278.4 Hz), 62.0, 55.5 (q, *J* = 28.4 Hz), 21.3, 13.9.

Ethyl 3,3,3-trifluoro-2-(o-tolyl)propanoate (**3e**),[9a] yellow oil, 23 mg, 31% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.5 Hz, 1H), 7.34-7.28 (m, 3H), 4.69 (q, *J* = 8.0 Hz, 1H), 4.33-4.19 (m, 2H), 2.47 (s, 3H), 1.28 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.2 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6 (q, *J* = 2.6 Hz), 137.4, 130.9, 129.0, 128.4, 128.2, 126.6, 124.1 (q, *J* = 278.3 Hz), 61.9, 50.6 (q, *J* = 28.4 Hz), 19.9, 13.9.

Ethyl 2-(4-chlorophenyl)-3,3,3-trifluoropropanoate (**3f**),[9a] yellow oil, 41 mg, 51% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.40-7.37 (m, 4H), 4.31-4.18 (m, 3H), 1.26 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.7 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (q, *J* = 2.6 Hz), 135.5, 130.8, 129.2, 127.9, 123.5 (q, *J* = 278.3 Hz), 62.3, 54.9 (q, *J* = 29.3 Hz), 13.9.

Ethyl 2-(3-chlorophenyl)-3,3,3-trifluoropropanoate (**3g**),[9a] yellow oil, 43 mg, 54% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.40-7.31 (m, 3H), 4.32-4.17 (m, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -67.5 (d, *J* = 8.6 Hz, 3F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.6 (q, *J* = 2.8 Hz), 134.8, 131.2, 130.1, 129.6, 129.5, 127.7, 123.4 (q, *J* = 280.4 Hz), 62.3, 55.1 (q, *J* = 29.1 Hz), 13.9.

Ethyl 2-(3-bromophenyl)-3,3,3-trifluoropropanoate (**3h**), yellow oil, 49 mg, 53% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.55 (dm, *J* = 8.0 Hz, 1H), 7.40 (d, *J* = 7.6 Hz, 1H), 7.27 (t, *J* = 8.0 Hz, 1H), 4.32-4.17 (m, 3H), 1.27 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -67.5 (d, *J* = 8.6 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6 (q, *J* = 2.6 Hz), 132.5, 132.5, 131.4, 130.4, 128.1, 123.4 (q, *J* = 277.5 Hz), 122.8, 62.4, 55.1 (q, *J* = 28.4 Hz), 13.9. IR (KBr): 2922, 1749, 1571, 1476, 1432, 1373, 1348, 1217, 1159, 1111, 1078, 1025, 999, 784, 713 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{11}H_{10}BrF_3O_2$: 309.9816, found: 309.9812.

Methyl 2-(4-(tert-butyl)phenyl)-3,3,3-trifluoropropanoate (**3i**), yellow oil, 50 mg, 61% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.0 Hz, 2H), 7.37 (d, *J* = 8.0 Hz, 2H), 4.32 (q, *J* = 8.5 Hz, 1H), 3.77 (s, 3H), 1.33 (s, 9H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.8 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8 (q, *J* = 2.6 Hz), 152.3, 129.1, 126.2, 126.0, 123.7 (q, *J* = 277.5 Hz), 55.0 (q, *J* = 28.5 Hz), 52.8, 34.6, 31.2. IR (KBr): 2962, 1755, 1438, 1362, 1304, 1224, 1203, 1155, 1110, 1012, 826 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{14}H_{17}F_3O_2$: 274.1181, found: 274.1178.

Ethyl 2-(benzo[d][1,3]dioxol-5-yl)-3,3,3-trifluoropropanoate (**3j**), yellow oil, 57 mg, 69% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (s, 1H), 6.87 (dd, *J* = 8.0 Hz, *J* = 1.2 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 5.98 (s, 2H), 4.30-4.15 (m, 3H), 1.26 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -68.0 (d, *J* = 8.6 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (q, *J* = 2.5 Hz), 148.4, 148.1, 123.7 (q, *J* = 277.5 Hz), 123.6, 122.8, 109.5, 108.5, 101.5, 62.1, 55.1 (q, *J* = 28.4 Hz), 13.9. IR (KBr): 2919, 2852, 2129, 1748, 1633, 1611, 1447, 1396, 1374, 1348, 1244, 1153, 1025, 977, 933, 870, 808, 785, 733, 687, 598 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{12}H_{11}F_3O_4$: 276.0609, found: 276.0602.

Ethyl 2-([1,1'-biphenyl]-4-yl)-3,3,3-trifluoropropanoate (**3k**), white solid, 58 mg, 63% yield. M.p.: 59-61 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 7.5 Hz, 2H), 7.54 (d, *J* = 8.0 Hz, 2H), 7.47 (t, *J* = 7.5 Hz, 2H), 7.39 (t, *J* = 7.5 Hz, 1H), 4.41-4.21 (m, 3H), 1.30 (t, *J* = 7.0 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.5 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (q, *J* = 2.6 Hz), 142.2, 140.2, 129.9, 128.9, 128.3, 127.7, 127.6, 127.2, 123.8 (q, *J* = 278.4 Hz), 62.2, 55.3 (q, *J* = 28.4 Hz), 13.9. IR (KBr): 1743, 1412, 1375, 1346, 1303, 1252, 1206, 1166, 1104, 1028, 844, 825, 763, 734, 690, 665 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{17}H_{15}F_3O_2$: 308.1024, found: 308.1012.

Ethyl 2-(4-acetamidophenyl)-3,3,3-trifluoropropanoate (**3l**), white solid, 65 mg, 75% yield, petroleum ether / ethyl acetate = 5 : 1 (v / v) as eluents for column chromatography. M.p.: 128-130°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (s, 1H), 7.53 (d, *J* = 7.5 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 4.29-4.15 (m, 3H), 2.16 (s, 3H), 1.25 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.8 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 166.2 (q, *J* = 2.6 Hz), 138.9, 130.1, 124.9, 123.7 (q, *J* = 278.3 Hz), 120.1, 62.1, 54.9 (q, *J* = 28.4 Hz), 24.5, 13.9. IR (KBr): 3253, 1736, 1664, 1600, 1558, 1515, 1372, 1347, 1323, 1255, 1220, 1157, 1109, 1028, 844, 825, 763, 737, 530 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{13}H_{14}F_3NO_3$: 289.0926, found: 289.0923.

Ethyl 3,3,3-trifluoro-2-(naphthalen-2-yl)propanoate (**3m**), yellow solid, 72 mg, 85% yield. M.p.: 43-46°C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (s, 1H), 7.90-7.89 (m, 3H), 7.57-7.53 (m, 3H), 4.50 (q, *J* = 8.5 Hz, 1H), 4.34-4.20 (m, 2H), 1.27 (t, *J* = 7.0 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.4 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (q, *J* = 3.4 Hz), 133.4, 133.2, 129.4, 128.8, 128.2, 127.7, 126.9, 126.8, 126.7, 126.3, 123.8 (q, *J* = 278.3 Hz), 62.2, 55.6 (q, *J* = 28.5 Hz), 13.9. IR (KBr): 3476, 3060, 2957, 2926, 2854, 1918, 1748, 1636, 1601, 1511, 1465, 1374, 1347, 1261, 1214, 1159, 1109, 1027, 966, 923, 893, 861, 844, 817, 751, 666, 633, 621, 563 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{15}H_{13}F_3O_2$: 282.0868, found: 282.0872.

Ethyl 3,3,3-trifluoro-2-(naphthalen-1-yl)propanoate (**3n**),[9a] yellow oil, 38 mg, 45% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 7.5 Hz, 1H), 7.63 (t, *J* = 8.0 Hz, 1H), 7.57-7.51 (m, 2H), 5.27 (q, *J* = 8.0 Hz, 1H), 4.30-4.19 (m, 2H), 1.22 (t, *J* = 7.0 Hz, 3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -66.7 (d, *J* = 8.6 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7 (q, *J* = 2.6 Hz), 134.1, 131.9, 130.0, 129.2, 127.3, 127.2, 126.1, 125.7, 125.3, 124.1 (q, *J* = 278.4 Hz), 122.5, 62.1, 49.9 (q, *J* = 28.4 Hz), 13.9.

Ethyl 3,3,3-trifluoro-2-(thiophen-3-yl)propanoate (**3p**), yellow oil, 62 mg, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 2.0 Hz, 1H), 7.35 (dd, *J* = 4.8 Hz, *J* = 3.2 Hz, 1H), 7.17 (d, *J* = 4.8 Hz, 1H), 4.47 (q, *J* = 8.4 Hz, 1H), 4.32-4.18 (m, 2H), 1.28 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -68.0 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (q, *J* = 2.6 Hz), 128.8, 127.8, 126.3, 125.9, 123.4 (q, *J* = 278.4 Hz), 62.2, 51.2 (q, *J* = 29.3 Hz), 13.9. IR (KBr): 2986, 2924, 1469, 1447, 1397, 1373, 1347, 1264, 1231, 1206, 852, 786, 726, 694, 651, 597 cm^{-1}. HRMS-EI (m/z) calcd. for $C_9H_9F_3O_2S$: 238.0275, found: 238.0272.

Ethyl 3,3,3-trifluoro-2-(1-tosyl-1H-indol-3-yl)propanoate (**3q**), yellow oil, 119 mg, 93% yield, petroleum ether / ethyl acetate = 10 : 1 (v / v) as eluents for column chromatography. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, *J* = 8.0 Hz, 1H), 7.86 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.60 (d, *J* = 8.0 Hz, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.31 (t, *J* = 8.0 Hz, 1H), 7.25 (d, *J* = 8.0 Hz, 2H), 4.60 (q, *J* = 8.0 Hz, 1H), 4.33-4.22 (m, 2H), 2.36 (s, 3H), 1.28 (t, *J* = 8.0 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.5 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.5 (q, *J* = 2.6 Hz), 145.4, 134.9, 134.7, 130.0, 129.3, 126.9, 126.7, 125.3, 123.7 (q, *J* = 278.4 Hz), 123.7, 119.4, 113.7, 110.6, 62.4, 47.4 (q, *J* = 30.1 Hz), 21.6, 13.9. IR (KBr): 3358, 3193, 2955, 2921, 2850, 1747, 1659, 1633, 1469, 1449, 1375, 1284, 1260, 1175, 1113, 1094, 1022, 981, 813, 762, 746, 704, 665, 618, 578 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{20}H_{18}F_3NO_4S$: 425.0909, found: 425.0912.

Methyl 3,3,3-trifluoro-2-phenylpropanoate (**3r**),[14b] yellow oil, 39 mg, 59% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (m, 2H), 7.41 (m, 3H), 4.35 (q, *J* = 8.4 Hz, 1H), 3.77 (s, 3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -67.7 (d, *J* = 8.6 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6 (q, *J* = 2.6 Hz), 129.5, 129.4, 129.3, 129.0, 123.7 (q, *J* = 277.5 Hz), 55.4 (q, *J* = 28.4 Hz), 52.8.

Ethyl 3,3,3-trifluoro-2-phenylpropanoate (**3s**),[14c] yellow oil, 38 mg, 54% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.41 (m, 3H), 4.35-4.14 (m, 3H), 1.26 (t, *J* = 7.5 Hz, 3H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.7 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1 (q, *J* = 2.8 Hz), 129.5, 129.2, 128.9, 123.7 (q, *J* = 280.4 Hz), 62.1, 55.6 (q, *J* = 28.2 Hz), 13.9.

Isopropyl 3,3,3-trifluoro-2-phenylpropanoate (**3t**), yellow oil, 37 mg, 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.40 (m, 3H), 5.11 (m, 1H), 4.29 (q, *J* = 8.4 Hz, 1H), 1.29 (d, *J* = 6.4 Hz, 3H), 1.19 (d, *J* = 6.4 Hz,

3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -67.6 (d, *J* = 8.6 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.6 (q, *J* = 2.6 Hz), 129.6, 129.4, 129.1, 128.8, 123.8 (q, *J* = 278.3 Hz), 69.9, 55.8 (q, *J* = 28.4 Hz), 21.5, 21.3.

Propyl 3,3,3-trifluoro-2-phenylpropanoate (**3u**), yellow oil, 37 mg, 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (m, 2H), 7.40 (m, 3H), 4.33 (q, *J* = 8.4 Hz, 1H), 4.20-4.10 (m, 2H), 1.70-1.61 (m, 2H), 0.89 (t, *J* = 7.2 Hz, 3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -67.6 (d, *J* = 8.6 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.2 (q, *J* = 2.6 Hz), 129.5 (m), 129.5, 129.2, 128.9, 123.7 (q, *J* = 278.4 Hz), 67.6, 55.6 (q, *J* = 28.4 Hz), 21.7, 10.1. IR (KBr): 3477, 3071, 3037, 2971, 2930, 2857, 2109, 1748, 1500, 1458, 1393, 1355, 1259, 1217, 1153, 1109, 1056, 1034, 991, 933, 894, 846, 759, 699, 682, 596 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{12}H_{13}F_3O_2$: 246.0868, found: 246.0870.

Allyl 3,3,3-trifluoro-2-phenylpropanoate (**3v**), yellow oil, 29 mg, 39% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.41 (m, 3H), 5.87 (m, 1H), 5.28 (d, *J* = 17.4 Hz, 1H), 5.24 (d, *J* = 10.7 Hz, 1H), 4.68 (m, 2H), 4.36 (q, *J* = 8.5 Hz, 1H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.6 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.8 (q, *J* = 2.6 Hz), 131.0, 129.5, 129.3, 129.0, 126.4, 123.7 (q, *J* = 278.3 Hz), 119.1, 66.4, 55.5 (q, *J* = 28.5 Hz). IR (KBr): 2956, 2923, 2852, 2110, 1748, 1650, 1633, 1500, 1457, 1424, 1373, 1347, 1216, 1154, 1109, 990, 939, 848, 758, 700, 596 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{12}H_{11}F_3O_2$: 244.0711, found: 244.0706.

Benzyl 3,3,3-trifluoro-2-phenylpropanoate (**3w**), yellow oil, 62 mg, 70% yield. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (m, 2H), 7.42 (m, 3H), 7.36 (m, 3H), 7.30 (m, 2H), 5.28 (d, *J* = 12.5 Hz, 1H), 5.20 (d, *J* = 12.0 Hz, 1H), 4.41 (q, *J* = 8.5 Hz, 1H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.5 (d, *J* = 8.5 Hz, 3F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0 (q, *J* = 2.5 Hz), 134.9, 129.5, 129.3, 129.2, 129.0, 128.6, 128.6, 128.2, 123.7 (q, *J* = 278.4 Hz), 67.7, 55.5 (q, *J* = 28.4 Hz). IR (KBr): 3068, 3036, 2959, 2925, 1748, 1499, 1457, 1382, 1351, 1216, 1153, 1107, 1006, 893, 849, 751, 698, 604 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{16}H_{13}F_3O_2$: 294.0868, found: 294.0877.

2,2-Difluoroethyl 3,3,3-trifluoro-2-phenylpropanoate (**3x**), yellow oil, 40 mg, 50% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46-7.39 (m, 5H), 5.92 (tt, $^2J_{HF}$ = 54.8 Hz, *J* = 4.0 Hz, 1H), 4.47-4.27 (m, 3H). ^{19}F NMR (376MHz, $CDCl_3$) δ -67.8 (d, *J* = 7.1 Hz, 3F), -125.8 (dq, $^2J_{HF}$ = 53.8 Hz, $^3J_{HF}$ = 12.0 Hz, 2F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4 (q, *J* = 2.5 Hz), 129.5, 129.4, 129.1, 128.6, 123.4 (q, *J* = 278.3 Hz), 112.1 (t, *J* = 240.4 Hz), 63.3 (t, *J* = 29.3 Hz), 55.2 (q, *J* = 28.5 Hz). IR (KBr): 3357, 3071, 3039, 2958, 2922, 2851, 1763, 1659, 1632, 1501, 1458, 1422, 1358, 1260, 1217, 1158, 1108, 1030, 969, 934, 896, 850, 760, 701, 596, 578 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{11}H_9F_5O_2$: 268.0523, found: 268.0522.

2-Fluoroethyl 3,3,3-trifluoro-2-phenylpropanoate (**3y**), yellow oil, 38 mg, 51% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (m, 2H), 7.41 (m, 3H), 4.64 (m, 1H), 4.53-4.30 (m, 4H). ^{19}F NMR (471MHz, $CDCl_3$) δ -67.7 (d, *J* = 8.5 Hz, 3F), -225.0 (tt, $^2J_{HF}$ = 45.7 Hz, $^3J_{HF}$ = 28.7 Hz, 1F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.0 (q, *J* = 2.5 Hz), 129.5, 129.4, 129.0, 123.6 (q, *J* = 278.3 Hz), 80.7 (d, *J* = 169.8 Hz), 64.6 (d, *J* = 19.8 Hz), 55.3 (q, *J* = 29.3 Hz). IR (KBr): 3358, 3195, 3071, 3038, 2958, 2921, 2851, 1755, 1659, 1632, 1606, 1588, 1500, 1458, 1409, 1378, 1351, 1258, 1218, 1155, 1111, 1068, 1040, 1006, 981, 923, 900, 880, 833, 760, 701, 683, 596 cm^{-1}. HRMS-EI (m/z) calcd. for $C_{11}H_{10}F_4O_2$: 250.0617, found: 250.0625.

Procedure B: In a nitrogen-filled glovebox, an oven-dried tube (20 mL) were charged with **2b** (245 mg, 0.54 mmol), **2c** (299 mg, 0.54 mmol), **2d** (353 mg, 0.54 mmol), or **2e** (407 mg, 0.54 mmol), CuCl (160 mg, 1.62 mmol), and DMF (3 mL) with vigorous stirring. After 10 minutes, a solution of **1a** (66 mg, 0.30 mmol) in DMF (1.5 mL) was introduced via syringe. The mixture was reacted at room temperature under a N_2 atmosphere overnight. $NaHCO_3$ (76 mg, 0.90 mmol) was added and the resulting mixture was kept reacting at room temperature under N_2 for another 24 h. The mixture was extracted with dichloromethane (3 × 25 mL). The combined organic layers were washed with H_2O (3 × 50 mL), dried over anhydrous Na_2SO_4, and concentrated to dryness under reduced pressure. The residue was purified by column chromatography on silica gel using petroleum ether / ethyl acetate = 20 : 1 (v / v) as eluents to give **3ab** (66 mg, 75% yield), **3ac** (92 mg, 78% yield), **3ad** (121 mg, 82% yield), or **3ae** (156 mg, 88% yield), respectively.

Ethyl 3,4,4,4-tetrafluoro-2-(4-methoxyphenyl)but-2-enoate (**3ab**), a mixture of *Z*- and *E*-isomers, molar ratio of *Z* / *E* isomers = 1.09 : 1.00 (or 0.52 : 0.48), yellow oil, 66 mg, 75% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, *J* = 8.8 Hz, 0.82H), 7.25 (d, *J* = 8.8 Hz, 0.84H), 6.94 (d, *J* = 9.2 Hz, 0.78H), 6.91 (d, *J* = 8.8 Hz, 0.94H), 4.36-4.27 (m, 2H), 3.84 (s, 1.14H), 3.83 (s, 1.61H), 1.35-1.29 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -65.7 (d, *J* = 8.6 Hz, 1.59F), -68.6 (d, *J* = 10.5 Hz, 1.47F), -119.7 (q, *J* = 8.6 Hz, 0.52F), -134.0 (q, *J* = 10.5 Hz, 0.48F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.3, 163.9, 160.7, 160.5, 130.2, 130.1 (d, *J* = 5.4 Hz), 120.7, 120.4 (d, *J* = 4.5 Hz), 114.3, 114.0, 62.6, 62.4, 55.4, 55.3, 14.0, 13.8. IR (KBr): 3359, 2961, 2924, 2848, 1738, 1609, 1575, 1514, 1466, 1423, 1372, 1340, 1295, 1259, 1232, 1204, 1180, 1150, 1111, 1028, 973, 918, 836, 808, 697, 665, 637, 545 cm^{-1}. HRMS-ESI (m/z) calcd. for $[C_{13}H_{13}F_4O_3]^+$ ($[M + H]^+$): 293.0801, found: 293.0795.

Ethyl 3,4,4,5,5,6,6,6-octafluoro-2-(4-methoxyphenyl)hex-2-enoate (**3ac**), a mixture of *Z*- and *E*-isomers, molar ratio of *Z* / *E* isomers = 2.12 : 1.00 (or 0.68 : 0.32), yellow oil, 92 mg, 78% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 8.8 Hz, 0.57H), 7.24 (d, *J* = 8.8 Hz, 1.18H), 6.94 (d, *J* = 8.8 Hz, 0.62H), 6.89 (d, *J* = 8.8 Hz, 1.20H), 4.34-4.26 (m, 2H), 3.84 (s, 0.91H), 3.82 (s, 1.81H), 1.33-1.29 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.7 (t, *J* = 8.6 Hz, 2.10F), -80.8 (t, *J* = 8.6 Hz, 0.97F), -113.3 (m, 1.57F), -115.9 (m, 0.73F), -117.6 (m, 0.68F), -126.3 (m, 1.41F), -126.5 (d, *J* = 10.5 Hz, 0.69F), -131.6 (m, 0.32F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 162.9, 159.8, 159.4, 129.1 (m), 129.0 (d, *J* = 5.1 Hz), 124.2 (d, *J* = 12.9 Hz), 123.2 (d, *J* = 11.3 Hz), 119.9, 119.0 (d, *J* = 5.2 Hz), 113.3, 112.7, 61.5, 61.4, 54.3, 54.2, 13.0, 12.7. IR (KBr): 2963, 2938, 2845, 1741, 1610, 1575, 1514, 1466, 1446, 1356, 1232, 1186, 1116, 1028, 964, 837, 800, 748, 711, 603, 570 cm^{-1}. HRMS-ESI (m/z) calcd. for $[C_{15}H_{13}F_8O_3]^+$ ($[M + H]^+$): 393.0737, found: 393.0731.

Ethyl 3,4,4,5,5,6,6,7,7,8,8,8-dodecafluoro-2-(4-methoxyphenyl)oct-2-enoate (**3ad**), a mixture of *Z*- and *E*-isomers, molar ratio of *Z* / *E* isomers = 2.23 : 1.00 (or 0.69 : 0.31), yellow oil, 121 mg, 82% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.8 Hz, 0.57H), 7.24 (d, *J* = 8.8 Hz, 1.22H), 6.94 (d, *J* = 9.2 Hz, 0.60H), 6.90 (d, *J* = 8.8 Hz, 1.23H), 4.34-4.26 (m, 2H), 3.84 (s, 0.87H), 3.82 (s, 1.88H), 1.33-1.29 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.8 (m, 3F), -112.4 (m, 1.58F), -114.9 (m, 0.70F), -117.5 (m, 0.69F), -122.1 (m, 2F), -122.9 (m, 2F), -126.1 (m, 2F), -131.4 (m, 0.31F). ^{13}C NMR (126 MHz, $CDCl_3$) δ 164.0, 163.9, 160.9, 160.4, 146.6 (t, *J* = 27.3 Hz), 144.5 (t, *J* = 28.2 Hz), 130.1, 130.0 (d, *J* = 5.4 Hz), 125.3 (d, *J* = 13.6 Hz), 124.2 (d, *J* = 9.1 Hz), 120.9, 120.0 (d, *J* = 4.5 Hz), 114.3, 113.8, 62.5, 62.4, 55.3, 55.2, 14.0, 13.7. IR (KBr): 2964, 2940, 2844, 1739, 1610, 1513, 1467, 1446, 1363, 1331, 1237, 1205, 1143, 1030, 970, 890, 876, 860, 838, 812, 799, 728, 645, 586 cm^{-1}. HRMS-ESI (m/z) calcd. for $[C_{17}H_{13}F_{12}O_3]^+$ ($[M + H]^+$): 493.0673, found: 493.0667.

Ethyl3,4,4,5,5,6,6,7,7,8,8,9,9,10,10,10-hexadecafluoro-2-(4-methoxyphenyl)dec-2-enoate (**3ae**), a mixture of *Z*- and *E*-isomers, molar ratio of *Z* / *E* isomers = 2.33 : 1.00 (or 0.70 : 0.30), yellow oil, 156 mg, 88% yield. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.8 Hz, 0.57H), 7.24 (d, *J* = 8.4 Hz, 1.24H), 6.95 (d, *J* = 8.8 Hz, 0.59H), 6.90 (d, *J* = 8.4 Hz, 1.24H), 4.34-4.26 (m, 2H), 3.84 (s, 0.87H), 3.82 (s, 1.88H), 1.33-1.29 (m, 3H). ^{19}F NMR (376 MHz, $CDCl_3$) δ -80.8 (m, 3F), -112.3 (m, 1.56F), -114.9 (m, 0.68F), -117.5 (m, 0.70F), -121.9 (m, 6F), -122.7 (m, 2F), -126.1 (m, 2F), -131.4 (m, 0.30F). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.0, 162.9, 159.9, 159.4, 146.0 (t, *J* = 27.5 Hz), 143.3 (t, *J* = 28.4 Hz), 129.1 (d, *J* = 1.7 Hz), 129.0 (d, *J* = 6.0 Hz), 124.3 (d, *J* = 13.8 Hz), 119.9, 119.1 (d, *J* = 4.3 Hz), 113.3, 112.8, 61.5, 61.5, 54.3, 54.2, 13.0, 12.7. IR (KBr): 2963, 2940, 2844, 1740, 1610, 1575, 1514, 1466, 1446, 1368, 1291, 1238, 1212, 1148, 1035, 971, 862, 836, 801, 737, 708, 661, 532 cm^{-1}. HRMS-ESI (m/z) calcd. for $[C_{19}H_{13}F_{16}O_3]^+$ ($[M + H]^+$): 593.0609, found: 593.0603.

Acknowledgements

We thank Wuhan University of Technology, the Natural Science Foundation of Hubei Province (China) (2015CFB176), the "Chutian Scholar" Program from Department of Education of Hubei Province (China), the "Hundred Talent" Program of Hubei Province, and the Wuhan Youth Chen-Guang Project for financial support.

Keywords: fluorine • copper • reduction • diazo compounds • reaction mechanisms

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[10] The use of K_2CO_3 as base instead of $NaHCO_3$ in the same reaction provided **3ab** accompanied by unknown side products (see the ^{19}F NMR spectrum of the isolated product in Supporting Information).

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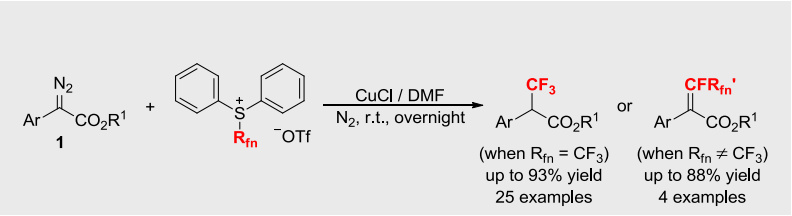
Trifluoromethylation

FULL PAPER



The first room temperature reductive trifluoromethylation of aromatic *α*-diazo esters by Yagupolskii-Umemoto's reagent ([Ph_2SCF_3][OTf]) in the presence of excess CuCl furnished a variety of *α*-trifluoromethyl arylacetates in up to 93% yield. When the long-chain perfluoroalkyl diphenylsulfonium triflates were employed instead of **2a**, the reaction of *α*-diazo ester under the same conditions followed by treatment with $NaHCO_3$ afforded a series of fluorinated *α*,*β*-unsaturated esters in good yields.

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Cu-Mediated Trifluoromethylation of Aromatic *α*-Diazo Esters by Yagupolskii-Umemoto's Reagent