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View Article Online
View Journal | View Issue



Cite this: Chem. Sci., 2019, 10, 5990

All publication charges for this article have been paid for by the Royal Society of Chemistry

Received 18th February 2019 Accepted 3rd May 2019

DOI: 10.1039/c9sc00829b

rsc.li/chemical-science

Trifluoromethylthiolation—arylation of diazocarbonyl compounds by modified Hooz multicomponent coupling†

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A new Zn-mediated trifluoromethylthiolation-based bifunctionalization reaction is developed. In this process, simultaneous $C-SCF_3$ and C-C bond formation takes place in a multicomponent reaction, in which an aryl and a SCF_3 group arise from different reagents. Our studies show that the reaction mechanism is similar to the Hooz multicomponent coupling. The process involves *in situ* generation of BAr_3 , which reacts with a diazocarbonyl compound, and the reaction is terminated by an electrophilic SCF_3 transfer. The reaction can also be extended to fluorination based bifunctionalization which proceeds with somewhat lower yield than the analogous trifluoromethylthiolation reaction.

The Hooz multicomponent reaction is based on coupling of diazocarbonyl compounds with organoboranes and electrophiles (Scheme 1).1 This and related reactions2 involve the formation of an adduct of the diazocarbonyl and the organoboron reagent followed by 1,2-migration of an alkyl substituent from the boron and being terminated by the reaction of an electrophile with the generated boron enolate (Scheme 1). The reaction is very useful for the synthesis of α,α' -bifunctionalized carbonyl compounds with formation of one or two new carboncarbon bonds. As a part of our research program in organofluorine chemistry, we have developed several bifunctionalization methods³ based on the introduction of F/CF₃/SCF₃ groups. Recently, our interest⁴ turned to the synthesis of α, α' -(geminal) bifunctionalized species by using diazocarbonyl compounds^{1d,5} and electrophilic fluorine (F/CF₃/SCF₃) transfer reagents in multicomponent reactions.

Development of new methods for the synthesis of SCF₃ compounds is particularly important, as functionalized trifluoromethylthiolates are attractive species in pharmaceutical industry, in crop protection and even in Positron Emissional Tomography (PET) based medical diagnostics. The broad interest in synthesis of structurally diverse SCF₃ compounds on the favorable properties of the trifluoromethylthiolation group. Trifluoromethylthiolates can modify the binding properties and lipophilicity (Hansch parameter $\pi=1.43$) of bioactive small molecules. For instance, the activity of cephalosporin antibiotics can be substantially improved by installing a SCF₃ functionality in cefazaflur, and

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tiflorex is a more efficient anorectic drug (Fig. 1) than its -CF₃ analog.¹⁰

Many excellent methods have been reported recently for mono-trifluoromethylthiolation of organic substrates. 6a-c,7,11 Our efforts have been focused on the development of trifluoromethylthiolation based bifunctionalization reactions to create structural complexity in a single multicomponent reaction. We have recently reported an efficient Rh-catalyzed procedure for geminal oxy-trifluoromethylthiolation of diazocarbonyl compounds (Scheme 2a). 4c In the present study we aimed to develop a trifluoromethylthiolation based

The Hooz multicomponent reaction $R' \stackrel{\bigcirc}{\longrightarrow} R'' + R'' - B \stackrel{\bigcirc}{\nearrow} R'' + E^{+} \stackrel{\longleftarrow}{\longrightarrow} SCF_{3} \text{ is possible?} \qquad R' \stackrel{\bigcirc}{\longrightarrow} R''$ $Via \bigcirc \bigcirc \bigcirc \bigcirc \bigcirc (R'')_{2}B \bigcirc (R'')_{3} \stackrel{\bigcirc}{\longrightarrow} B(R'')_{3} \stackrel{\bigcirc}{\longrightarrow} B(R'')_{2} \stackrel{\bigcirc}{\longrightarrow} R''$

Scheme 1 The Hooz multicomponent reaction of organoboranes and electrophiles E⁺.

Cefazaflur (cephalosporin antibiotic)

Tiflorex (anoretic drug)

Fig. 1 Examples of SCF₃ containing drugs.

[†] Electronic supplementary information (ESI) available: Experimental procedures, characterization and NMR spectra of the products. See DOI: 10.1039/c9sc00829b

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Scheme 2 Trifluoromethylthiolation based bifunctionalization of diazocarbonyl compounds (a–d) including reactions with C-C and $C-SCF_3$ coupling (b–d).

bifunctionalization reaction involving carbon–carbon coupling. There are relatively few reactions reported in the literature, in which bifunctionalization of diazoketones involve simultaneous C–SCF₃ and C–C bond formation. A recent example is published by Wang and coworkers¹² for the asymmetric trifluoromethylthiolation of sulfonium ylides *via* sigmatropic rearrangement (Scheme 2b), which is based on the Doyle–Kirmse¹³ reaction. Our idea was to develop a new multicomponent reaction, in which the SCF₃ and aryl groups arise from different reagents. Considering the tremendous problems in functional group incompatibility in such multicomponent couplings, we hypothesized that the Hooz reaction (Scheme 1) could be a suitable platform for the realization of this transformation.

Our initial studies were performed under the typical conditions¹ of Hooz multicomponent reactions (Scheme 2c). In this process, diazoketone 2a, dibenzenesulfonimide¹⁴ 1 (as electrophile) were reacted with various organoboron species (including phenylboronic acid/boroxine and BPh₃). However, the reaction proceeded with low yield (up to 15%) even under strictly inert conditions (see below). When we modified the typical conditions of the Hooz reaction by application of tetraphenylborate derivatives (such as 3c) and Zn(NTf₂)₂ (4), the SCF₃/Ph-bifunctionalized product 5a was obtained in high yield (Scheme 2d).

After careful optimization we found that the reaction proceeds in 81% yield when excess amounts of diazoketone 2a (1.5 equiv.) and phenyl source 3c (1.5 equiv.) were reacted with SCF₃ transfer reagent 1 in the presence of (0.5 equiv.) Zn-salt (4) and molecular sieves at -10 °C (Table 1, entry 1). Deviations from these optimal conditions led to decreased yields or the formation of SCF₃ product 5a could not be observed. Reduction of the amount of Zn-mediator 4 (entry 2) led to a decrease of the yield of 5a (37%) and without 4, formation of 5a was not observed at all (entry 3). As mentioned above, $Rh_2(OAc)_4$ was an

Table 1 Deviation from the optimal reaction conditions for the α,α' -trifluoromethylthiolation—phenylation of diazoketone $2a^{\alpha}$

$$\begin{array}{c} O \\ Ph \\ \downarrow \\ N_2 \\ PhO_2 \\ \hline \\ PhO_2 \\ \hline \\ PhO_2 \\ \hline \\ N-SCF_3 \\ + Bu_4 \\ \hline \\ Ph \\ D_1 \\ \hline \\ Ph \\ Ph \\ \hline \\ Ph \\ Ph \\ \hline \\ CH_2 \\ \hline \\ Cl_2, 3 \\ Å \\ ms \\ \hline \\ Ph \\ \hline \\ SCF_3 \\ \hline \\ 2a \ (1.5 \ equiv.) \\ \hline \\ 1 \ (1.0 \ equiv.) \\ \hline \\ 3c \ (1.5 \ equiv.) \\ \hline \\ 3c \ (1.5 \ equiv.) \\ \hline \\ 2a \ (1.5 \ equiv.) \\ \hline \end{array}$$

| Entry | Deviation from the standard conditions | Yield ^b (%) |
|-------|---|------------------------|
| 1 | None | 81 |
| 2 | $0.25 \text{ equiv. } Zn(NTf_2)_2$ (4) | 37 |
| 3 | Without $Zn(NTf_2)_2$ (4) | <5 |
| 4 | $Rh_2(OAc)_4$ (5 mol%) instead of 4 | 0 |
| 5 | Pd(OAc) ₂ (15 mol%) instead of 4 | 30 |
| 6 | Zn(OTf) ₂ instead of 4 | <5 |
| 7 | 0.5 equiv. of 3c | 28 |
| 8 | Na(BPh ₄) instead of 3c | 52 |
| 9 | (PhBO) ₃ (3a) instead of 3c, without 4 | 0 |
| 10 | BPh ₃ (3b) instead of 3c, without 4 | 15 |
| 11 | ZnPh ₂ instead of 3c | <5 |
| 12 | ZnPh2 instead of 4 and BPh3 3b instead of 3c | 0 |
| 13 | PhMe as the solvent | 71 |
| 14 | THF as the solvent | 35 |
| 15 | MeCN as the solvent | 0 |
| 16 | Without 3Å ms | 59 |
| 17 | 22 °C instead of -10 °C | 66 |

 a To reagent 1 (0.1 mmol), $Bu_4N(BPh_4)$ (3c) (0.15 mmol), $Zn(NTf_2)_2$ (4) (0.05 mmol) and 80 mg 3Å molecular sieves (ms) was added a solution of diazoketone 2a (0.15 mmol) in CH_2Cl_2 (1.0 ml) at $-10\,^{\circ}C$. This mixture was stirred at $-10\,^{\circ}C$ for 2 h before allowing it to warm up to RT overnight. b Isolated yield.

excellent catalyst in the geminal oxy-trifluoromethylthiolation of diazocarbonyl compounds^{4c} (Scheme 2a). However, phenyltrifluoromethylthiolation of 2a did not occur, when Zn-mediator 4 was replaced by a Rh-catalyst (entry 4).

When Pd(OAc)₂ was used instead of 4, a complex reaction mixture was obtained, from which 5a could be isolated in 30% yield (entry 5). According to the analysis of the crude reaction mixture by ¹⁹F NMR, in this process a large amount (up to 35%) of Ph-SCF₃ was formed indicating that two components (1 and **3c)** of the three-component reaction may react directly in a Pdcatalyzed process. Other Zn-salts in place of 4, such as Zn(OTf)₂, were not able to mediate the reaction (entry 6). Using Na(BPh₄) instead of Bu₄N(BPh₄) 3c led to a decrease of the yield (52%) probably because of its poor solubility in DCM (entry 8). This gave the idea to study various solubilizing reagents together with Na(BPh₄) (see below). As mentioned above, phenylboroxine 3a was inefficient as phenyl source (entry 9) and application of BPh₃ (3b) (typical Hooz conditions) instead of 3c/4 led to a poor yield (15%) of 5a (entry 10). A boron-based phenyl source is important for the bifunctionalization reaction, as ZnPh₂ instead of 3c gave no product 5a (entry 11). The combination of BPh₃ (3b) and phenylzinc reagent ZnPh2 did not result in product 5a formation, indicating that phenyl transfer cannot happen from an external phenylzinc source in the presence of BPh3 (entry 12). We briefly screened the solvent effects as well. The reaction proceeds with good yield (71%) in toluene (entry 13) but in more

polar solvent, such as in THF (entry 14) the yield is lower (35%) and we did not observe any formation of 5a in acetonitrile (entry 15). The dry conditions are apparently important for the high yield of 5a, as without molecular sieves the yield dropped to 59% (entry 16). At room temperature instead of -10 °C, the yield was decreased to 66% (entry 17).

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As mentioned above, the reactions proceeded with high yield with $\mathrm{Bu_4N}(\mathrm{BPh_4})$ **3c**, which is soluble in DCM, while the yield dropped, when sparingly soluble $\mathrm{Na}(\mathrm{BPh_4})$ was employed (*c.f.* entries 1 and 8). Therefore, we attempted to increase the yield (52%) of the reaction with $\mathrm{Na}(\mathrm{BPh_4})$ using phase transfer (PT) catalysts (Table 2). Using $\mathrm{Bu_4N}(\mathrm{BPh_4})$ **3c** and $\mathrm{Bu_4N}(\mathrm{NTf_2})$ in 10 mol% as PT catalyst (Table 2 entries 2 and 3) increased the yield to 66% and 64%, respectively. However, the yields with $\mathrm{Na}(\mathrm{BPh_4})$ in the presence of PT catalysts were still lower than with $\mathrm{Bu_4N}(\mathrm{BPh_4})$ **3c** as the phenyl source.

With the optimized reaction conditions in hand we investigated the substrate scope of this reaction by varying the diazocarbonyl and the organoboron reagents. Diazoketones bearing halogen or EWD nitro substituents (Table 3, entries 2-4) on the aryl ring (2b-d) reacted with high yields (73-84%), similarly to phenyl derivative 2a (entry 1), affording the corresponding SCF₃ derivatives **5b-d**. The aromatic iodo substituent in **2c** (entry 3) remained unchanged under the reaction affording 5c, which has a useful handle for subsequent Pd-catalyzed coupling reactions. With the presence of an electron donating methoxy group (2e) in the substrate, the yield (60%) was somewhat lower than for the phenyl derivative 5a. Aryldiazoketone 2f containing a similar tetrazole motif as cefazaflur (Fig. 1) reacted smoothly providing 5f in 68% yield (entry 6). Due to the low solubility of 2f in DCM, this reaction was conducted at room temperature instead of -10 °C. Furane based diazoketone 2g reacted with high yield (84%) affording the SCF_3 product 5g (entry 7). Disubstituted diazoketone 2h also underwent the phenylationtrifluoromethylthiolation reaction affording 5h, in which the phenyl and SCF3 groups are attached to a quaternary carbon (entry 8). This reaction occurred with lower yield (30%) compared to the formation of the tertiary substituted trifluoromethylthio derivatives, such as 5a, probably because of steric reasons (see below). Not only aromatic but even aliphatic

 Table 2 Phase transfer experiments for the 1,1-trifluoromethyl-thio-lation-phenylation^a

$$\begin{array}{c} O \\ Ph \\ N_2 \end{array} + \begin{array}{c} PhO_2S \\ PhO_2S \\ PhO_2S \end{array} + \begin{array}{c} N-SCF_3 \end{array} + \begin{array}{c} WA \\ Ph \\ Ph \\ Ph \\ Ph \end{array} \begin{array}{c} Ph \\ Ph \\ Ph \\ Ph \end{array} \begin{array}{c} PT \ cat. \ (10 \ mol\%) \\ Zn(NTf_2)_2 \ (4) \\ CH_2Cl_2, \ 3 \ \mathring{A} \ ms \\ CH_2Cl_2, \ 3 \ \mathring{A} \ ms \\ SCF_3 \end{array} \begin{array}{c} Ph \\ SCF_3 \end{array}$$

| Entry | Phase transfer (PT) catalyst | Yield ^b of 5a (%) |
|-------|---------------------------------|------------------------------|
| 1 | None | 52 |
| 2 | $Bu_4N(BPh_4)$ | 66 |
| 3 | $Bu_4N(NTf_2)$ | 64 |

^a Standard conditions according to Table 1, entry 1. ^b Isolated yield.

diazoketones (2i-j) could be used as substrates (entries 9 and 10). The successful bifunctionalization of 2i-i could be due to the mild reaction conditions without added base leaving the αketo hydrogens unchanged. In particular, nonyl derivative 2i reacted with high yield (83%), while the bifunctionalization of cyclopentyl derivative 2j occurred with a lower yield (48%). Unlike in the Rh-catalyzed oxy-trifluoromethylthiolation reaction,4c diazoester 2k underwent the phenylation-trifluoromethylthiolation reaction smoothly (entry 11) affording 5k in good yield (78%). This result, together with the above mentioned observation (Table 1, entry 4), shows that the trifluoromethylthiolation based bifunctionalization of diazocarbonyl compounds in Rh-catalyzed and in Hooz-type reactions proceed with substantially different mechanisms (see below). A ten-fold scale up of the reaction of diazoester 2k with 1 and 3c (entry 11) could be performed without significant change of the yield (74%). When diazoacetamide 2m was employed, bifunctionalized product 5m was obtained in high yield (entry 12). However, diazomalonate 2n could not be converted to the corresponding product 5n (entry 13), in which the phenyl and

Table 3 1,1-Trifluoromethylthiolation—phenylation of diazo compounds 2 with SCF $_3$ -source 1 and Bu $_4$ N(BPh) $_4$ (3a) a

$$\begin{array}{c} \begin{array}{c} O \\ R^{1} \\ \end{array} & \begin{array}{c} PhO_{2}S \\ R^{2} \end{array} & \begin{array}{c} PhO_{2}S \\ PhO_{2}S \end{array} & \begin{array}{c} Bu_{4}N \\ Ph \\ Ph \end{array} & \begin{array}{c} Ph \\ Ph \\ Ph \end{array} & \begin{array}{c} Dh \\ Ph \\ Ph \end{array} & \begin{array}{c} Dh \\ CH_{2}CI_{2}, 3 \text{ A ms} \end{array} & \begin{array}{c} O \\ R^{2} \\ SCF_{3} \end{array} \\ \begin{array}{c} Ph \\ SCF_{3} \end{array} \\ \begin{array}{c} 2 \\ \end{array} & \begin{array}{c} Dh \\ CH_{2}CI_{2}, 3 \text{ A ms} \end{array} & \begin{array}{c} O \\ R^{2} \\ SCF_{3} \end{array} & \begin{array}{c} Ph \\ SCF_{3} \end{array} & \begin{array}{c}$$

| 2 | 1 | 3c -10 °C to R1 | 5 |
|-------|---|-----------------------------------|--------------------------------|
| Entry | Diazocarbonyl compound 2 | Carbonyl compound 5 | Yield ^b of 5 (%) |
| 1 | O N ₂ | ScF ₃ | 81 |
| 2 | N_2 | F Sb SCF ₃ | 80 |
| 3 | O N ₂ | Ph 5c SCF ₃ | 73 |
| 4 | $\bigcap_{O_2N} \bigcap_{\mathbf{2d}} N_2$ | O ₂ N SCF ₃ | 84 |
| 5 | MeO 2e N ₂ | MeO Ph | 60 |
| 6 | $\sum_{\substack{N,N \\ N}}^{N}\sum_{j=1}^{N}\sum_{k=1}^{N}\sum_{k=1}^{N}\sum_{j=1}^{N}\sum_{k=1}^{N}\sum_{j=1}^{N}\sum_{k=1}^{N}\sum_$ | N.N. SCF ₃ | 68 ^c |
| 7 | O N ₂ | O Ph O 5g SCF ₃ | 84 |

Table 3 (Contd.)

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$$R^{1} = \begin{pmatrix} O \\ R^{2} \end{pmatrix} + \begin{pmatrix} PhO_{2}S \\ PhO_{2}S \end{pmatrix} + \begin{pmatrix} PhO_{2}S \\ PhO_{2}S \end{pmatrix} + \begin{pmatrix} Ph \\ Ph \\ Ph \end{pmatrix} + \begin{pmatrix} Ph \\ Ph \\ Ph \end{pmatrix} + \begin{pmatrix} Ph \\ Ph \\ Ph \end{pmatrix} + \begin{pmatrix} Ph \\ CH_{2}CI_{2}, 3 \text{ Å ms} \\ -10 \text{ °C to RT} \end{pmatrix} + \begin{pmatrix} O \\ Ph \\ R^{2}SCF_{3} \end{pmatrix}$$

| | • | - | |
|-------|--|---|-----------------------------|
| Entry | Diazocarbonyl compound 2 | Carbonyl compound 5 | Yield ^b of 5 (%) |
| 8 | O N ₂ | Ph SCF ₃ | 30^c |
| 9 | C_8H_{17} N_2 | C ₈ H ₁₇ Ph 5i SCF ₃ | 83 |
| 10 | $\bigcup_{\mathbf{2j}}^{O} N_2$ | O Ph 5j SCF ₃ | 48 |
| 11 | EtO N ₂ | EtO Ph 5k SCF ₃ | 78(74) ^d |
| 12 | $\bigcap_{0} \bigvee_{\mathbf{2m}}^{\mathbf{N}} N_{2}$ | N 5m SCF ₃ | 80 |
| 13 | N_2 EtO_2C CO_2Et CO_2Et | EtO ₂ C Ph EtO ₂ C 5n SCF ₃ | 0 |
| 14 | $O_2N $ | O ₂ N Fh | 55 ^{c,e,f} |

^a Unless otherwise stated: to 1 (0.1 mmol), Bu₄N(BPh₄) (3c) (0.15 mmol), Zn(NTf₂)₂ (4) (0.05 mmol) and 3Å ms (80 mg) was added a solution of 2 (0.15 mmol) in $\mathrm{CH_2Cl_2}$ (1.0 ml) at $-10\,^{\circ}\mathrm{C}$, stirred for 2 h before warmed up to RT overnight. ^b Unless otherwise stated isolated yield. ^c RT overnight. d 1.0 mmol scale. e Instead of 1, NFSI was used. f Yield of 6 (determined by ¹H-NMR analysis) contains side product 1-(4nitrophenyl)-2-phenylethan-1-one.

SCF₃ groups would be attached to a quaternary carbon. We have briefly studied the possibilities for a phenylation-fluorination reaction (entry 14) using NFSI instead of 1 as a fluorine-electrophile source with 2d as the substrate. This reaction occurred with a lower yield (55%) than the analogous process with 1 (entry 4, 84%). In addition, fluoro derivative 6 and (4-nitrophenyl)-2-phenylethan-1-one were formed in a 1:1 mixture, indicating that protonation of the key reaction intermediate is about as fast as fluorination. The observation that substantial amounts of protonation product formed in the fluorination (entry 12) compared to the trifluoromethylthiolation (entry 4) reaction under similar conditions confirms our previous conclusion¹⁵ that 1 is a more efficient electrophile than NFSI in bifunctionalization reactions (see also the control experiments below). Due to their similar polarity, the separation of the mixture of the fluorinated and protonated products was

cumbersome, which somewhat decreases the synthetic utility of this phenylation-fluorination-based bifunctionalization of diazoketones. The yield (55%) of 6 was determined after chromatography using a sample, which was contaminated with the protonated analog [1-(4-nitrophenyl)-2-phenylethan-1-one]. However, 6 could be further purified by selective oxidation of the protonated byproduct (see ESI†).

We have also varied the aryl source, BAr4, of the bifunctionalization reaction (eqn (1)-(4)). When the phenyl substituent of 3c was replaced by other aryl groups, we had to slightly modify the reactions conditions, such as the counter ion of the BAr₄ reagent and/or the reaction temperature. The yields with these reagents were lower (36-48%) than with 3c. When the chloro-phenyl derivative 3d and 1 were reacted with diazoester 2k or diazoketone 20, the corresponding bifunctionalized products 50 and 5p were formed in 48% and 47% yields, respectively (eqn (1) and (2)). These species have one (50) or two (5p) aromatic halogenide handles for further functionalization by cross-coupling reactions. The reaction with thiophene transfer reagent 3e was conducted at room temperature affording 5q in 45% yield (eqn (3)). Trifluoromethylthio product 5r with two different heterocyclic rings was obtained in 36% yield by reaction of 2g and 3e with 1 at room temperature (eqn We also attempted to perform alkylation-trifluoromethylthiolation reactions using Bu₄N(BBu₄), 3f. However, in this reaction (eqn (5)) formation of 5s was not observed, instead Bu-SCF₃ (7) was formed by the rapid reaction of 1 and 3f.

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In order to get insights into the reaction mechanism, we performed a couple of control experiments (Scheme 3). First, we wanted to determine the sequence of the reactions among the four reaction components, such as 1, 2a, 3c and 4. Therefore, the systematic changes of the 11B NMR spectrum of the reaction of Bu₄N(BPh₄) 3c and Zn(NTf₂)₂ 4 was monitored. Pure 3c gave a sharp ¹¹B NMR signal at -6.6 ppm, which immediately disappeared, when an equimolar amount of Zn(NTf₂)₂ (4) was added (Scheme 3). The reaction of 3c and 4 led to appearance of a new, broad signal at 67.6 ppm. The value of the ¹¹B NMR shift and the broad shape of the signal indicated formation of BPh₃ 3b from Bu₄N(BPh₄) 3c by boron to zinc transmetallation. ¹⁶ In this process PhZnNTf₂ (8) was probably also formed. Phenylzinc derivative 8 rapidly reacted with residual water reversibly adsorbed by the molecular sieves to give benzene (9), which was observed by ¹H NMR in the reaction mixture. The other product of the hydrolysis of PhZnNTf₂ (8) is probably Zn(OH)NTf₂ (10). When the resulted reaction mixture was reacted with diazoketone 2a a new broad peak appeared at 45.6 ppm in the 11B NMR spectrum, which was assigned to vinyloxy-boronate 13.17 Species like 13 are known to form in the Hooz reaction via formation of adduct 11, followed by formation of 12 and a subsequent borotropic shift.1,17b Subsequent addition of dibenzenesulfonimide 1 to the reaction mixture led to the formation of trifluoromethylthiolation product 5a, which could be observed by ¹⁹F NMR. In this last step (13 \rightarrow 5a), the Zn-

Scheme 3 Suggested mechanism for the 1,1-trifluoro-methylthiolation—arylation of diazocarbonyl compounds. Chemical shifts (δ) are given in ppm.

mediator **4** or its hydroxy derivative **10** may play an important role. For example, the electrophilic SCF₃ transfer may be accelerated by coordination of Zn to the oxygen atom of **13**, which facilitates the cleavage of the boron–oxygen bond and delivery of **14**. As mentioned above, the three-component reaction of **2a**, BPh₃ (**3b**) and **1** proceeds with a notoriously low yield (Scheme 2c, and Table 1/entry 10). This yield could not be improved by using strictly dry conditions in the reaction. However, a high yield was observed for a large variety of diazocarbonyl compounds, when **3c/4** conditions were used involving: (a) *in situ* generation of BPh₃ (Scheme 3), (b) *in situ* removal of H₂O and (c) Zn-mediated assistance of the electrophilic attack on **13**.

Further control reactions (Scheme 4) confirmed the above mechanistic suggestions (Scheme 3). As mentioned above, Zn(OTf)₂ (16), which is a close analog of Zn(NTf₂)₂ (4) did not mediate the reaction of 2a, 3a and 1 to form 5a (Table 1, entry 6). This may be explained by the fact that the reaction of 16 and 3c did not lead to an *in situ* formation of BPh₃ **3b** (Scheme 4a), which is the prerequisite for the formation of 5a via 11 (Scheme 3). A further confirmation of the Hooz-type reaction mechanism via vinyloxyboronate intermediate 13 arose from the control reaction, when 1 was replaced by another electrophile, such as benzaldehyde derivative 17 (Scheme 4b). The result of this reaction was formation of 18, which most probably formed by reaction of 13 and 17 in the terminating step of the reaction. As mentioned above, the phenylation-fluorination reaction (Table 2, entry 12) with NFSI occurred with much lower yield than the corresponding phenylation-trifluoromethylthiolation with 1 (Table 2, entry 4). In the fluorination reaction, significant amounts of protonation product formed presumably because of competing electrophilic protonation of 13. This led us to the conclusion that 1 is a better electrophile than NFSI in this bifunctionalization reaction (see above).

a) no transmetallation to zinc triflate observed

$$Zn(OTf)_2$$
 + $Bu_4N(BPh_4)$ \longrightarrow BPh_3 + $PhZnOTf$ + Bu_4NOTf
16 $3c$ CD_2Cl_2 , RT, 1 h $3b$

b) replacement of 1 with 17 as the electrophile

c) competition experiment between 1 and NFSI

$$\begin{array}{c} \text{PhO}_2 \text{S.}_{\text{N.}} \text{SO}_2 \text{Ph} & \text{Bu}_4 \text{N}(\text{BPh}_4) \ (\textbf{3a}) \\ \text{OPh} & \text{SCF}_3 \\ \text{Ph} & \text{O.1 mmol} \end{array} \\ \begin{array}{c} \text{SCF}_3 \\ \text{0.1 mmol} \end{array} \\ \begin{array}{c} \text{Zn}(\text{NTf}_2)_2 \ (\textbf{4}) \\ \text{3 A ms, CH}_2 \text{Cl}_2 \end{array} \\ \begin{array}{c} \text{Ph} & \text{SCF}_3 \\ \text{SCF}_3 \end{array} \\ \begin{array}{c} \text{Ph} & \text{Ph} \\ \text{SCF}_3 \end{array} \\ \begin{array}{c} \text{SCF}_3 \\ \text{19} \\ \text{exclusive} \\ \text{product} \end{array} \\ \begin{array}{c} \text{NFSI} \\ \text{O.1 mmol} \end{array}$$

Scheme 4 Control experiments to support the mechanism given in Scheme 3.

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Indeed, when we performed a competitive reaction of 2a, 3a and equimolar amounts of 1 and NFSI, we observed exclusive formation of the trifluoromethylthiolated product 5a without formation of the fluorinated product 19.

An alternative to the above Hooz-type mechanism could be an initial reaction of the PhZn species 8 directly with the diazo compound 2a without involvement of BPh₃. However, this hypothesis seems to be in conflict with the attempted phenylation–trifluoromethylthiolation reactions with ZnPh₂ species without application of Zn(NTf₂)₂ 4 (Table 1, entries 11 and 12). In these reactions the bifunctionalized product 5a did not form.

In this report, we have described a new arylation-trifluoromethylthiolation reaction for an α,α' -bifunctionalization of diazocarbonyl compounds. This process can be performed as a multicomponent reaction, in which the aryl and SCF₃ groups arise from different reagents, from 3 and 1. This Hooz-type coupling is a novel approach for bifunctionalization based trifluoromethylthiolation, as for example the previously reported⁴⁶ Rh-catalyzed oxy-trifluoromethylthiolation. The arylation-trifluoromethylthiolation reaction is initiated by Zn assisted formation of BAr₃ from 3. According to our mechanistic studies the reaction follows a Hooz-type reaction mechanism, which is terminated by electrophilic SCF₃ transfer from 1. As far as we know this is the first Hooz-type reaction for the synthesis of organofluorines from electrophilic transfer reagents. The reaction can also be extended to the phenylation-fluorination process, using the fluorine analog (NFSI) of 1.

Conflict of interest

The authors declare no competing financial interest.

Acknowledgements

We thank the Knut och Alice Wallenbergs Foundation (Dnr: 2018.0066) and Swedish Research Council (VR) for financial support.

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