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Access to Aryl and Heteroaryl Trifluoromethyl Ketones from Aryl Bromides and Fluorosulfates with Stoichiometric CO

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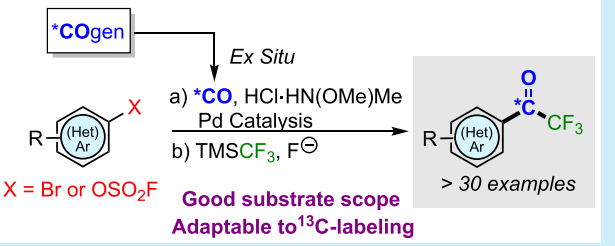
ABSTRACT: We report a sequential one-pot preparation of aromatic trifluoromethyl ketones starting from readily accessible aryl bromides and fluorosulfates, the latter easily prepared from the corresponding phenols. The methodology utilizes low pressure carbon monoxide generated *ex situ* from COgen to generate Weinreb amides as reactive intermediates that undergo monotrifluoromethylation affording the corresponding aromatic trifluoromethyl ketones (TFMKs) in good yields. The stoichiometric use of CO enables the possibility for accessing ^{13}C-isotopically labeled TFMK by switching to the use of ^{13}COgen.



The incorporation of fluorine into bioactive molecules for the enhancement or alteration of their chemical and biological properties is a strategy commonly applied in the pharmaceutical and agrochemical industry. About 60% of the top-selling pharmaceuticals display at least one fluorine-containing motif.[1] Trifluoromethyl ketones (TFMKs) connected to an aryl or heteroaryl ring possess an electron-poor carbonyl group capable of forming stable hydrates, in addition to displaying enhanced lipophilicity compared to the corresponding methyl ketone. These properties render this motif useful in drug design and in its utilization as enzyme inhibitors (Scheme 1a).[2,3] Efavirenz, a drug used for the treatment of HIV, exhibits a reduced TFMK and can be found on the World Health Organization's model list of essential medicines reported in 2019. The trifluoromethyl ketone substructure has also been exploited as a starting point for the synthesis of (i) fluorinated heterocycles by condensation reactions, (ii) F-containing olefins with Wittig reagents, (iii) α-fluoro amines by reductive amination, and (iv) fluorinated alkanes through reductions or alkylations.[2]

Considering the importance of aryl and heteroaryl trifluoromethyl ketones, it is somewhat surprising that only few synthetic routes to these structures have been reported. The traditional strategies rely on rather harsh conditions such as the addition of either organolithium or organomagnesium reagents to trifluoroacetyl electrophiles (Scheme 1b).[4] These methods have limited functional group tolerance and often require cryogenic reaction temperatures. Because of the trifluoromethyl ketone's electrophilic nature, further addition of the nucleophile to the carbonyl group is a common side reaction. The group of Wu recently reported on the Pd-catalyzed carbonylative trifluoromethylation of aromatic iodides to yield the corresponding TFMKs, relying on the participation of a specific organocopper reagent $(PPh_3)_3CuCF_3$ under 20 bar of pressure of carbon monoxide (CO).[5]

Bearing in mind the toxicity of CO, it would be advantageous from a safety point of view to investigate synthetic routes that circumvent the use of pressurized gas cylinders, as well as reaction conditions requiring high CO pressures. In this study, we wish to report on a two-step, one-pot catalytic protocol for accessing aryl and heteroaryl trifluoromethyl ketones from the corresponding aryl bromides or phenols via their fluorosulfates,[6] without the need for highly reactive intermediates, specialized reagents, or pressurized lecture bottles. This carbonylative methodology can be carried out with just stoichiometric quantities of CO with respect to the aryl electrophile using the commercially available CO surrogate, COgen.[7] Moreover, it is adaptable to the full incorporation of ^{13}CO to afford isotopically labeled TFMK with carbon-13.

We have recently shown in a stoichiometric study that the Pd-catalyzed carbonylative trifluoromethylation of aryl bromides is not a viable route for accessing TFMK using common CF_3 reagents under low CO pressures.[8] By combining these results with the recent advances reported by the Buchwald group and our own research group within low pressure aminocarbonylations, a sequential one-pot method to prepare aryl and heteroaryl TFMK was explored.[9] We envisaged preparation of a stable acyl species from the corresponding aryl

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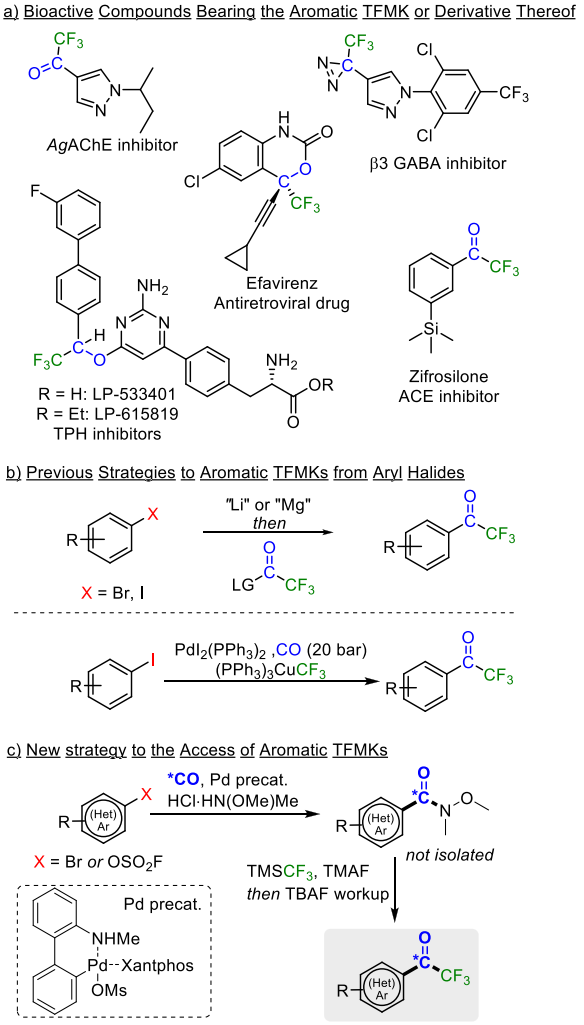
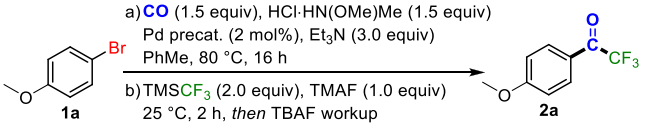
Scheme 1. Synthesis of Aromatic Trifluormethyl Ketones from Aryl Halides



bromide or fluorosulfate and *ex situ* generated CO from COgen in our two-chamber reactor, COware, that upon treatment with $TMSCF_3$ would afford the corresponding TFMK.[10,11] Previous work from the group of Leadbeater revealed that Weinreb amides are viable candidates, and as such we set out to investigate this possibility.[12]

Initial efforts were performed with 4-bromoanisole as the test substrate. After careful optimization of the reaction parameters, the corresponding TFMK was obtained in an 80% NMR yield with 14% unreacted Weinreb amide (Table 1, entry 1). TFMK and the Weinreb amide were in general the only two products observed in the crude reaction mixtures. The optimal reaction conditions for the initial Pd-catalyzed aminocarbonylation consisted of heating a reaction mixture of the aryl bromide, the hydrochloride salt of *N,O*-dimethylhydroxylamine (1.5 equiv), triethylamine (Et_3N, 1.5 equiv), and the fourth generation Buchwald-type palladacycle precatalyst (Xantphos Pd G4, 2 mol %) in toluene (PhMe, 0.5 M) at 80 °C overnight in the presence of CO (1.5 equiv). COgen premix containing COgen, $Pd(OAc)_2$ (0.5 mol %), and $HBF_4P(t\text{-}Bu)_3$ (0.5 mol %) in conjunction with base (Cy_2NMe) was used to release CO *ex situ* in 20 mL COware. Subsequent addition of the Ruppert-Prakash reagent, $TMSCF_3$ (2.0 equiv), with an activator (TMAF, 1.0 equiv) for 2 h at 25

Table 1. Optimization of Sequential One-Pot Synthesis of Aromatic Trifluoromethyl Ketones[a]



entry	deviation	yield[b]
1	none	80%
2	3.0 equiv of $TMSCF_3$	59%
3	$TMSCF_3$ added slowly over 1 h	46%
4	0 °C in second step	62%
5	40 °C in second step	58%
6	$TESCF_3$ instead of $TMSCF_3$	48%[c]
7	1.4 equiv of TMAF	75%
8	0.6 equiv of TMAF	49%
9	CsF instead of TMAF	0%
10	TBAF (1 M in THF) instead of TMAF	0%
11	Na_2CO_3 instead of Et_3N	65%
12	K_2CO_3 instead of Et_3N	72%
13	$Pd(OAc)_2$/Xantphos	21%
14	dioxane as solvent	37%
15	CPME as solvent	65%

[a]Reactions were performed using 0.50 mmol of 4-bromoanisole. CO released *ex situ* from COgen premix using Cy_2NMe in PhMe. [b]^1H NMR yield using 1,3,5-trimethoxybenzene as internal standard. [c]Mixture of TFMK and *O*-TES-hemiaminal. PhMe = toluene. Pd precat. = Xantphos Pd G4. TMAF = tetramethylammonium fluoride. TBAF = tetrabutylammonium fluoride. $TMSCF_3$ = trimethyl(trifluoromethyl)silane.

°C followed by workup with TBAF led to the target product in a sequential one-pot fashion. Performing the reaction with 3.0 equiv of $TMSCF_3$, slow addition of $TMSCF_3$, or addition of $TMSCF_3$ at 0 or 40 °C all led to deteriorated yields (entries 2–5). $TESCF_3$ was less effective for promoting this transformation (entry 6). Increasing the amount of the activator resulted in a slightly decreased yield of 75% (entry 7), while lowering the number of activator equivalents afforded a yield of 49% of the desired product (entry 8). Other fluoride-based activators such as CsF or TBAF (1 M in THF) did not show any activity at all illustrating the importance of TMAF (entries 9 and 10). Substituting Et_3N with Na_2CO_3 or K_2CO_3 afforded the product in a yield of 65% and 72%, respectively (entries 11 and 12). Replacing the precatalyst with $Pd(OAc)_2$ and Xantphos resulted in a large decrease in yield (entry 13). Finally, dioxane and CPME were screened, but these efforts only led to product yields of 37% and 65%, respectively (entries 14 and 15).

Next, we proceeded to investigate the generality of this transformation (Scheme 2). Isolation of trifluoroacetophenone **2a** from the test system after column chromatography could be achieved in a 72% yield. Similarly, the 3,5-di- and 3,4,5-trimethoxy substituted bromobenzene gave **2b** and **2c** in yields of 52% and 40%, respectively. Various *O*-functionalized 4-bromophenol substrates were efficiently converted into the corresponding TFMKs in yields ranging between 45% and 59% (compounds **2d**–**2f**). Compound **2g** was isolated in a yield of 77%, and the corresponding carbon-13 labeled derivative ^{13}C-**2g** could be readily prepared with ^{13}COgen. Trimethylsilyl (TMS) substituted bromobenzenes were also converted into the corresponding TFMK. The 4-TMS product **2h** was isolated in a 39% yield while the 3-TMS product zifrosilone

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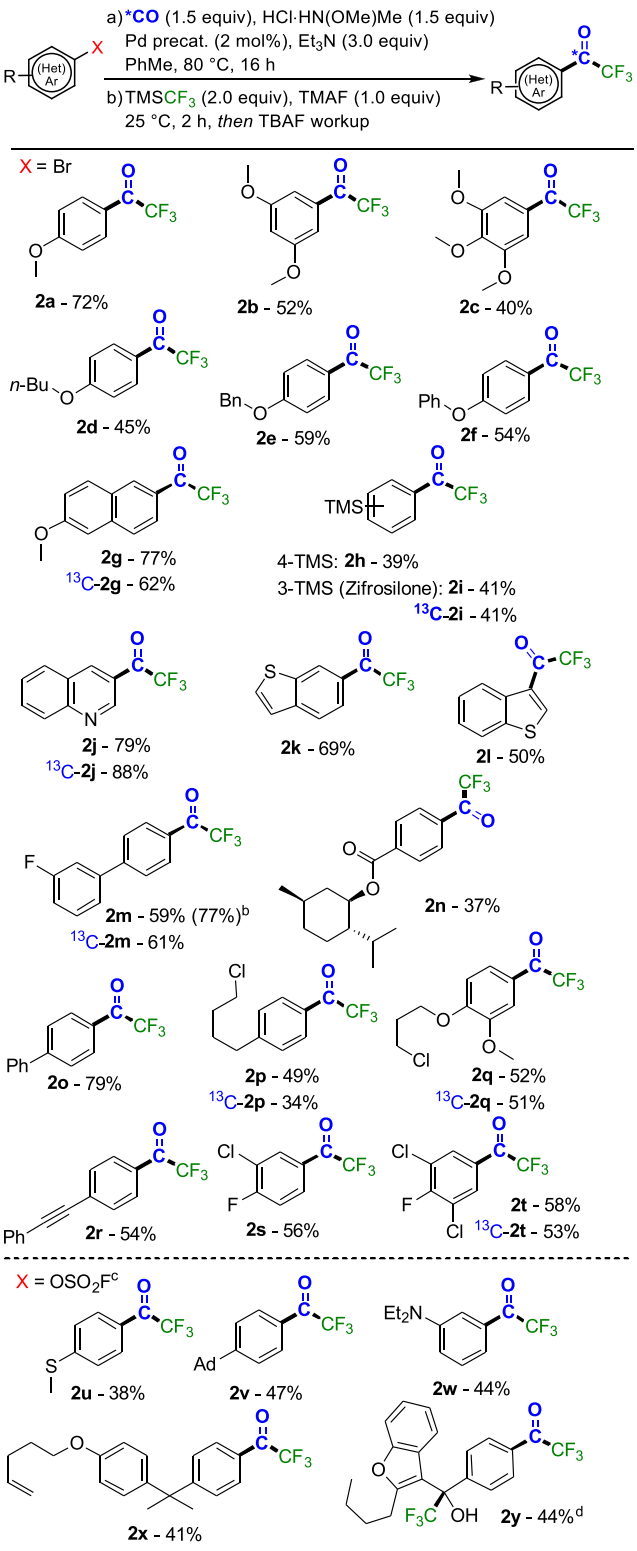
Scheme 2. Scope of Aromatic Trifluoromethyl Ketones[a]



[a]Reactions were performed on a 0.50 mmol scale, and isolated yields for the nonlabeled products are based on the average of two runs. Reactions leading to the ^{13}C-labeled compounds were run only once, and yields are based on isolated product. [b]Reaction performed on 5 mmol scale; see Supporting Information for experimental details. [c]3 mol % of Xantphos Pd G4 instead of 2 mol %, and K_2CO_3 instead of Et_3N. [d]4.0 equiv of $TMSCF_3$ were used instead of 2.0 equiv. See Supporting Information for experimental details.

(**2i**), a clinical candidate as acetylcholinesterase (ACE) inhibitor,[3b] and its ^{13}C-labeled analog ^{13}C-**2i** could both be prepared in identical yields. Heteroaryl bromides, such as quinoline and benzothiophene, proved to be viable substrates for this methodology (**2j**−**2l** and ^{13}C-**2j**).

3′-Fluoro-4-bromobiphenyl was converted into the corresponding TFMK **2m** in a yield of 59%, and 61% for the ^{13}C-isotope labeled compound (^{13}C-**2m**). Compound **2m** represents a two-step precursor to LP-533401 and a three-step precursor to LP-615819 (Scheme 1), both reported to display inhibitory activities toward the tryptophan hydroxylase (TPH).[3d] No double addition of the trifluoromethyl anion to a substrate bearing a carboxylate ester in the 4-position of an aryl bromide was observed (compound **2n**). 4-Bromobiphenyl was converted efficiently to **2o** in a 79% yield. As evident from **2p** and **2q**, alkyl chloride substituents are well tolerated and represent a useful handle for further modification of the TFMK. The corresponding ^{13}C-labeled compounds ^{13}C-**2p** and ^{13}C-**2q** were likewise prepared. An alkynyl substituted substrate was converted into the TFMK **2w** in a 54% yield. Lastly, aromatic TFMKs **2s**, **2t**, ^{13}C-**2t** possessing fluoride and chloride substituents were synthesized, which can serve as electrophiles for S_NAr or cross-coupling reactions. **2s** and **2t** have been reported as interesting and convenient intermediates for the synthesis of cyclopentene and spirocyclic compounds, respectively, both investigated for their application as pesticides and insecticides.[13]

We also investigated aryl fluorosulfates as potential electrophiles in this transformation (Scheme 2 bottom). The corresponding fluorosulfate obtained from 4-phenylphenol proved worthwhile in this transformation providing the TFMK **2o** in an isolated yield of 79%, which is identical to the yield of the corresponding aryl bromide transformation. Slightly altered reaction conditions were used, such as the catalyst loading was increased to 3 mol % of Xantphos Pd G4, and Et_3N was replaced with K_2CO_3.

4-Thiomethyl, 4-adamantyl, and 3-(*N*,*N*-diethylamino) substituted phenylfluorosulfate substrates afforded the products **2u**−**2w** in moderate yields. A substrate possessing the bisphenol A core led to the TFMK **2x** with a yield of 41%. A second addition of CF_3 was realized onto the internal ketone affording the **2y** in a 44% yield.

We next focused our efforts to scale up the reaction. Conversion of 5 mmol of aryl bromide **1m** into the trifluoromethyl ketone **2m** only led to a 39% isolated yield along with the corresponding unreacted Weinreb amide (54% isolated yield). Instead, the reaction mixture was filtered and concentrated after the initial aminocarbonylation. NMR analysis of the filter cake suggested that the insoluble hydrochloride salt of triethylamine was selectively removed. The concentrated filtrate was redissolved in toluene with TMAF into which $TMSCF_3$ was added dropwise. This approach led to the isolation of 1.04 g (77%) of **2m** (Scheme 2).[14]

Having established a methodology to access (hetero)aryl trifluoromethyl ketones, we proceeded to investigate the chemical use of **2m** as a model substrate for TFMKs in general (Scheme 3). The [1,2]-addition of cyclopropylacetylene onto the carbonyl functionality is important for the synthesis of Efavirenz.[3c] Therefore, the copper-catalyzed addition of cyclopropylacetylene was performed to furnish the carbinol product **3m** in an 84% yield.[15] A $NaBH_4$ reduction of **2m** followed by an S_NAr reaction with 2-amino-4,6-

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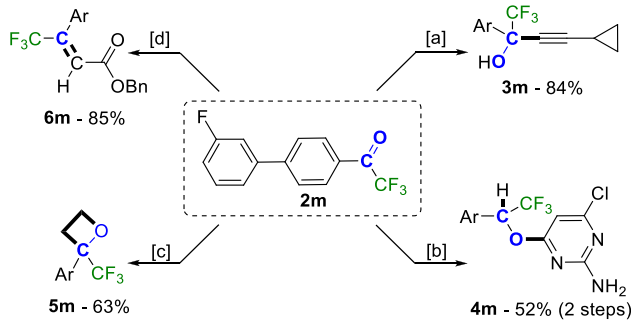
Scheme 3. Post-modification Studies of 2m

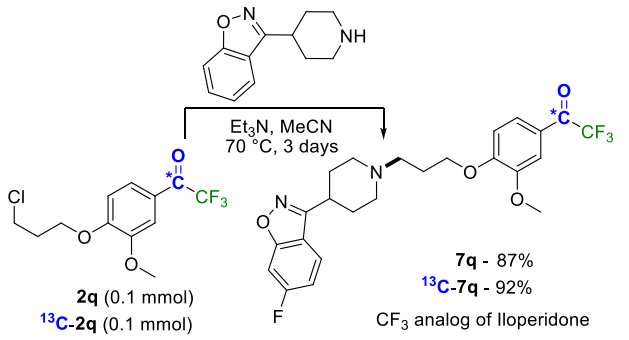


[a][1,2]-Addition. [b]Reduction and S_NAr reaction. [c]Johnson–Corey–Chaykovsky oxetane formation. [d]Wittig reaction. Ar = 3′-fluoro-[1,1′-phenyl]-4-yl. See Supporting Information for experimental details.

dichloropyrimidine yielded 52% of **4m** over 2 steps.[3d] Performing a Johnson–Corey–Chaykovsky reaction on **2m** afforded 63% of the corresponding trifluoromethyl oxetane **5m**, which is an isostere to the *tert*-butyl group.[16] A Wittig reaction on the ketone functionality of **2m** was conducted to afford the trifluorocrotyl product **6m** in an 85% yield. Comparing the chemical shift of the CF_3 group in the ^{19}F NMR spectrum with similar structures suggested that **6m** has been isolated almost exclusively as the *E*-isomer (*E*/*Z* > 99:1).[17]

Iloperidone is an antipsychotic pharmaceutical bearing an aromatic methyl ketone functionality.[18] We have demonstrated that the CF_3 analog of iloperidone **6q** can be synthesized from **2q** by simple S_N2 displacement of the chloride with a commercially available amine (Scheme 4). This approach

Scheme 4. Synthesis of a CF_3 Analog of Iloperidone[a]



[a]See Supporting Information for experimental details.

proved applicable in high yields, and the reported methodology thereby enables access to a ^{13}C-labeled CF_3 analog of iloperidone, ^{13}C-**6q**, in only three synthetic steps from 4-bromoguaiacol.

In summary, we have developed a direct procedure to access aryl and heteroaryl trifluoromethyl ketones applying Pd catalyzed carbonylation chemistry with *ex situ* generated CO from COgen to install the carbonyl moiety, and the Ruppert-Prakash reagent as the CF_3 source. With this methodology, ^{13}C-isotope labeled trifluoromethyl ketones can also be easily accessed, which is showcased by the synthesis of a ^{13}C-enriched CF_3 analog of iloperidone.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.0c01117.

Experimental procedures, product characterization, and spectral data (PDF)

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Notes

The authors declare the following competing financial interest(s): Troels Skrydstrup is co-owner of SyTracks A/S, which commercializes the two-chamber system (COware), COgen premix, and ^{13}COgen.

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■ REFERENCES

(1) For general fluorine properties, see: (a) Muller, K.; Faeh, C.; Diederich, F. *Science* **2007**, *317*, 1881−1886. (b) Wang, J.; Sánchez-Roselló, M.; Aceña, J. L.; del Pozo, C.; Sorochinsky, A. E.; Fustero, S.; Soloshonok, V. A.; Liu, H. *Chem. Rev.* **2014**, *114*, 2432−2506. (c) Zhou, Y.; Wang, J.; Gu, Z.; Wang, S.; Zhu, W.; Acena, J. L.; Soloshonok, V. A.; Izawa, K.; Liu, H. *Chem. Rev.* **2016**, *116*, 422−518.

(2) Recent reviews on TFMKs: (a) Kelly, C. B.; Mercadante, M. A.; Leadbeater, N. E. *Chem. Commun.* **2013**, *49*, 11133. (b) Wu, W.; Weng, Z. *Synthesis* **2018**, *50*, 1958.

(3) For examples of TFMKs and derivatives thereof, see: (a) Camerino, E.; Wong, D. M.; Tong, F.; Körber, F.; Gross, A. D.; Islam, R.; Viayna, E.; Mutunga, J. M.; Li, J.; Totrov, M. M.; Bloomquist, J. R.; Carlier, P. R. *Bioorg. Med. Chem. Lett.* **2015**, *25*, 4405. (b) Cutler, N. R.; Seifert, R. D.; Schleman, M. M.; Sramek, J. J.; Szylleyko, O. J.; Howard, D. R.; Barchowsky, A.; Wardle, T. S.; Brass, E. P. *Clin. Pharmacol. Ther.* **1995**, *58*, 54. (c) Young, S. D.; Britcher, S.

https://dx.doi.org/10.1021/acs.orglett.0c01117
Org. Lett. XXXX, XXX, XXX−XXX

F.; Tran, L. O.; Payne, L. S.; Lumma, W. C.; Lyle, T. A.; Huff, J. R.; Anderson, P. S.; Olsen, D. B.; Carroll, S. S.; Pettibone, D. J.; O'Brien, J. A.; Ball, R. G.; Balani, S. K.; Lin, J. H.; Chen, I.-W.; Schleif, W. A.; Sardana, V. V.; Long, W. J.; Byrnes, V. W.; Emini, E. A. *Antimicrob. Agents Chemother.* **1995**, *39*, 2602. (d) Shi, Z.-C.; Devasagayaraj, A.; Gu, K.; Jin, H.; Marinelli, B.; Samala, L.; Scott, S.; Stouch, T.; Tunoori, A.; Wang, Y.; Zang, Y.; Zhang, C.; Kimball, S. D.; Main, A. J.; Sun, W.; Yang, Q.; Nouraldeen, A.; Yu, X.-Q.; Buxton, E.; Patel, S.; Nguyen, N.; Swaffield, J.; Powell, D. R.; Wilson, A.; Liu, Q. *J. Med. Chem.* **2008**, *51*, 3684. (e) Sirisoma, N. S.; Ratra, G. S.; Tomizawa, M.; Casida, J. E. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2979.

(4) (a) McGrath, T. F.; Levine, R. *J. Am. Chem. Soc.* **1955**, *77*, 3656. (b) Creary, X. *J. Org. Chem.* **1987**, *52*, 5026. (c) Kerdesky, F. A. J.; Basha, A. *Tetrahedron Lett.* **1991**, *32*, 2003. (d) Dolman, S. J.; Gosselin, F.; O'Shea, P. D.; Davies, I. W. *Tetrahedron* **2006**, *62*, 5092. (e) Yamazaki, T.; Terajima, T.; Kawasaki-Taskasuka, T. *Tetrahedron* **2008**, *64*, 2419. (f) Smits, H. *Syngenta Participations AG*, 2016, WO 2016/058896 A1.

(5) Zhu, F.; Yang, G.; Zhou, S.; Wu, X.-F. *RSC Adv.* **2016**, *6*, 57070.

(6) (a) Dong, J.; Krasnova, L.; Finn, M. G.; Sharpless, K. B. *Angew. Chem., Int. Ed.* **2014**, *53*, 9430. (b) Veryser, C.; Demaerel, J.; Bieliunas, V.; Gilles, P.; De Borggraeve, W. M. *Org. Lett.* **2017**, *19*, 5244. (c) Domino, K.; Veryser, C.; Wahlqvist, B. A.; Gaardbo, C.; Neumann, K. T.; Daasbjerg, K.; De Borggraeve, W. M.; Skrydstrup, T. *Angew. Chem., Int. Ed.* **2018**, *57*, 6858. (d) Schimler, S. D.; Froese, R. D. J.; Bland, D. C.; Sanford, M. S. *J. Org. Chem.* **2018**, *83*, 11178.

(7) Hermange, P.; Lindhardt, A. T.; Taaning, R. H.; Bjerglund, K.; Lupp, D.; Skrydstrup, T. *J. Am. Chem. Soc.* **2011**, *133*, 6061.

(8) Domino, K.; Johansen, M. B.; Daasbjerg, K.; Skrydstrup, T. *Organometallics* **2020**, *39*, 688.

(9) (a) Friis, S. D.; Skrydstrup, T.; Buchwald, S. L. *Org. Lett.* **2014**, *16*, 4296. (b) Martinelli, J. R.; Freckmann, D. M. M.; Buchwald, S. L. *Org. Lett.* **2006**, *8*, 4843.

(10) For selected reviews on $TMSCF_3$, see: (a) Liu, X.; Xu, C.; Wang, M.; Liu, Q. *Chem. Rev.* **2015**, *115*, 683. (b) Prakash, G. K. S.; Yudin, A. K. *Chem. Rev.* **1997**, *97*, 757.

(11) Bruno, N. C.; Niljianskul, N.; Buchwald, S. L. *J. Org. Chem.* **2014**, *79*, 4161.

(12) (a) Rudzinski, D. M.; Kelly, C. B.; Leadbeater, N. E. *Chem. Commun.* **2012**, *48*, 9610. (b) Nahm, S.; Weinreb, S. M. *Tetrahedron Lett.* **1981**, *22*, 3815. (c) Phetcharawetch, J.; Betterley, N. M.; Soorukram, D.; Pohmakotr, M.; Reutrakul, V.; Kuhakarn, C. *Eur. J. Org. Chem.* **2017**, *2017*, 6840. (d) Miele, M.; Citarella, A.; Micale, N.; Holzer, W.; Pace, V. *Org. Lett.* **2019**, *21*, 8261.

(13) (a) Koerber, K.; Datta, G. K.; Bindschaedler, P.; Von Deyn, W.; Braun, F.-J. *BASF SE*, 2017, WO 2017/016883 A1. (b) Speake, J. D.; Perales, J. B.; Fan, W.; Rolland, S. C. *Avista Pharma Solutions*, 2016, WO 2016/115315 A1. (c) Speake, J. D.; Pandi, B.; Ogbu, C. O.; Adams, J. A.; Moore, J. A., III; Perales, J. B.; Li, K., Avista Pharma Solutions Inc., 2017, WO 2017/201134 A1.

(14) Replacing TMAF with CsF as activator in this modified scale-up reaction led to no conversion of **1m** as judged by ^{1}H NMR analysis.

(15) Wang, L.; Liu, N.; Dai, B.; Ma, X.; Shi, L. *RSC Adv.* **2015**, *5*, 10089.

(16) Mukherjee, P.; Pettersson, M.; Dutra, J. K.; Xie, L.; am Ende, C. W. *ChemMedChem* **2017**, *12*, 1574.

(17) Yamazaki, T.; Mano, N.; Hikage, R.; Kaneko, T.; Kawasaki-Takasuka, T.; Yamada, S. *Tetrahedron* **2015**, *71*, 8059.

(18) (a) Strupczewski, J. T.; Bordeau, K. J.; Chiang, Y.; Glamkowski, E. J.; Conway, P. G.; Corbett, R.; Hartman, H. B.; Szewczak, M. R.; Wilmot, C. A.; Helsley, G. C. *J. Med. Chem.* **1995**, *38*, 1119. (b) Solanki, P. V.; Uppelli, S. B.; Pandit, B. S.; Mathad, V. T. *Org. Process Res. Dev.* **2014**, *18*, 342.

https://dx.doi.org/10.1021/acs.orglett.0c01117
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