Cross-Coupling

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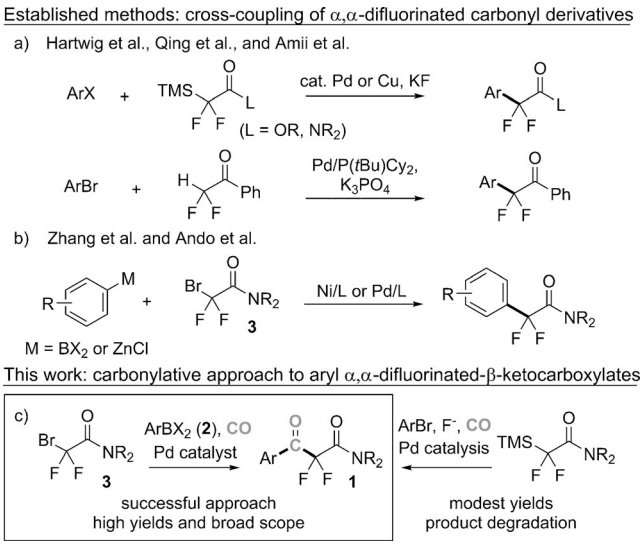
Direct Access to α,α-Difluoroacylated Arenes by Palladium-Catalyzed Carbonylation of (Hetero)Aryl Boronic Acid Derivatives

*Thomas L. Andersen, Mette W. Frederiksen, Katrine Domino, and Troels Skrydstrup**

Abstract: *A palladium-catalyzed carbonylative coupling of (hetero)aryl boronates or boronic acid salts with carbon monoxide and α-bromo-α,α-difluoroamides and bromo-α,α-difluoroesters is described herein. The method is useful for the synthesis of a diverse selection of (hetero)aryl α,α-difluoro-β-ketoamides and α,α-difluoro-β-ketoesters, which are useful building blocks for the generation of functionalized difluoroacylated and difluoroalkyl arenes. The method could be further extended to a one-pot protocol for the formation of difluoroacetophenones.*

The introduction of fluorine atoms as substitutes for hydrogen is an important strategy for the modulation of the biological activity of a pharmaceutically relevant molecules.[1] Considerable efforts have been devoted to the development of new synthetic methodologies for accessing fluorinated compounds. This includes the CF_2 group, which can function as a bioisostere for e.g. $-C(CH_3)_2$, an oxygen atom, or a carbonyl group.[2] In this aspect, the introduction of α,α-difluorinated carbonyls has attracted much attention, as such motifs in small building blocks are readily available.[3] For instance, palladium- or copper-catalyzed α-arylations of aryl halides with the enolates of α,α-difluorinated acetamides, phenones, or esters have been reported by the groups of Hartwig, Qing, and Amii, for accessing a wide range of aryl α,α-difluoroacetamides, α,α-difluoroketones, and α,α-difluoroesters (Scheme 1 a).[4] Alternatively, similar structures have been obtained by reversing the polarity of the coupling partners, for example, the coupling of α-halo-α,α-difluoroacetamides with the corresponding aryl zinc or boronic acid derivatives (Scheme 1 b).[5] The latter approach was also extended to include the formation of *gem*-difluorinated amides, esters, and phosphonates, as well as a similar strategy towards *gem*-difluoromethylation of (hetero)aryl boronic acids.[6]

So far no efforts have been directed to a carbonylative version of these transformations to generate α,α-difluoroacylated arenes such as **1** (Scheme 1 c). Such structures are not widely found and their overall absence in the pharmaceutical portfolio may be related to the challenges in their preparation.[7] Nevertheless, the α,α-difluorinated dicarbonyl moiety remains an excellent entry point for accessing a variety of functionalities and ring structures containing fluorine. For these reasons, we investigated the three-component palladium-catalyzed carbonylative α-arylation of α-silylated-α,α-difluoroacetamides to deliver structures such as the ketone **1** (Scheme 1 c). Whereas preliminary reactions revealed that this ketone was generated, it was accompanied by the product from simple protonation of the TMS enolate. In addition, a compound from enolate addition to **1** was produced, an event arising from the electron-withdrawing effect exerted by the fluorine atoms.[8] Attempts to control these unwanted side reactions were unsuccessful, and instead we resorted to employing boronic acid derivatives as the nucleophilic coupling partner, in combination with an α-bromo-α,α-difluoroacetamide (**3**) as the electrophile (Scheme 1 c). Such an approach would bypass the issue of product reactivity, as the boronic ester coupling partner would be less nucleophilic towards the α,α-difluoroacylated arene products.



Scheme 1. Recent developments in catalytic difluoroalkylation protocols and novel carbonylative approach. TMS = trimethylsilyl.

We initially investigated the carbonylative coupling of the aryl boronic acid neopentylglycol ester **2a** and bromodifluoroacetamide **3a** (Table 1). In this setup, CO gas was generated from COgen in a separate reaction chamber and in a slight excess (1.6 equiv).[9] After optimization of the coupling conditions, formation of **1a** occurred in the presence of $[Pd(PPh_3)_4]$ with Xantphos as a secondary ligand by heating the reactions to 100 °C in toluene with water as a cosolvent (9:1). CuI was employed as a cocatalyst along with an excess of K_2CO_3 (entry 1). The coupling also proceeded by

[*] T. L. Andersen, M. W. Frederiksen, K. Domino, Prof. Dr. T. Skrydstrup
Carbon Dioxide Activation Center (CADIAC), Department of Chemistry and the Interdisciplinary Nanoscience Center (iNANO), Aarhus University
Gustav Wieds Vej 14, 8000 Aarhus C (Denmark)
E-mail: ts@chem.au.dk

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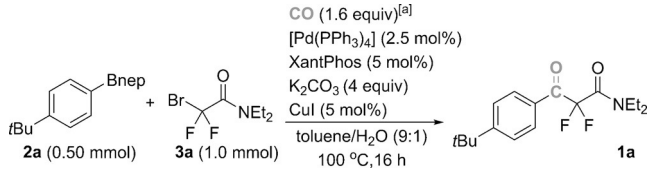
Table 1: Optimization of the carbonylative assembly of boronic ester **2a** and bromide **3a**.

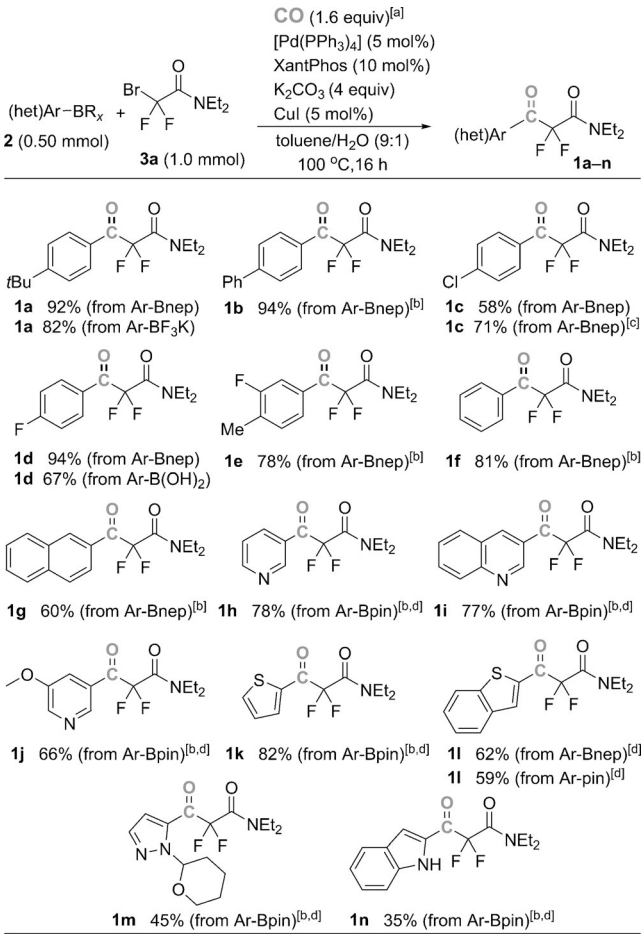


Entry	Deviations from standard cond.	Yield [%][b]
1	none	99
2	with $ArB(OH)_2$	52
3	with $ArBF_3K$	27
4	without Xantphos	37
5	PPh_3 instead of Xantphos	32
6	$P(tBu)_3$ instead of Xantphos	56
7	dppf instead of Xantphos	58
8	$Pd(OAc)_2$ instead of $[Pd(PPh_3)_4]$	39
9	$[Pd(PPh_3)_2Cl_2]$ instead of $[Pd(PPh_3)_4]$	53
10	without CuI	75
11	without water as co-solvent	69
12	5 mol% $[Pd(PPh_3)_4]$ and 10 mol% Xantphos	99 [92][c]

[a] CO gas was generated from 9-methyl-9*H*-fluorene-9-carbonyl chloride in a separate reaction chamber; see the Supporting Information section. [b] As determined by ^1H NMR spectroscopy using mesitylene as an internal standard. [c] Yield of isolated product. Bnep = boronic acid neopentylglycol ester, dppf = 1,1′-bis(diphenylphosphanyl)ferrocene, Xantphos = 9,9′-dimethyl-4,5-bis(diphenylphosphino)xanthene.

employing either the corresponding boronic acid or the BF_3K salt, however, in both cases the yields were lower (entries 2 and 3). Similarly, conducting the reaction in the absence of Xantphos or with additional PPh_3 or dppf led to a lower product formation. Substituting Xantphos for $P(tBu)_3$ provided full conversion of the starting boronic ester, but resulted in a more complex product distribution (entries 4–7). Several palladium sources were also investigated, but led to no improvement over using $[Pd(PPh_3)_4]$ (entry 8 and 9). The omission of CuI led to a decrease in yield, although product formation was still observed to a large extent. However, a more reliable and reproducible turnover was observed in the presence of copper. The same trend was observed when water was omitted as a cosolvent, thus leading to a lowered yield (entries 10 and 11). Finally, by increasing the catalyst loading, **1a** could be isolated in a 92% yield in a reproducible fashion (entry 12).

To establish the applicability of the protocol, a range of aryl boronic esters were coupled with **3a** under similar reaction conditions. It was found that simple aryl substituents such as a phenyl or the coupling of a naphthalene derivative was well tolerated, thus leading to the corresponding β-keto-α,α-difluoroacetamides (**1b** and **1g**; Scheme 2). The presence of halogen substituents such as fluoride on the aryl group was equally well tolerated, thus leading to **1d** and **1e** in good yields. As was seen for **1a**, it was also possible to employ the corresponding aryl boronic acid to form **1d**, albeit in a lower yield when compared to that of the boronic ester. Having a chloride in the *para*-position led to a drop in the yield of **1c** when compared to that of the fluorine analogue, possibly because of halogen activation by the transition metal. However, the yield could be increased to 71% by lowering



Scheme 2. Scope of α,α-difluoro-β-ketoamides. [a] CO gas was generated from 9-methyl-9*H*-fluorene-9-carbonyl chloride in a separate reaction chamber. See the Supporting Information section. [b] Average of two runs. [c] Reaction run at 90 °C. [d] Reaction run at 80 °C without CuI. Bpin = boronic acid pinacol ester.

the reaction temperature to 90 °C. It is well-known that heterocyclic boronic acids and ester derivatives are prone to protodeboronation and dimerization events, which are most likely accelerated in the presence of heat, base, and metal catalysts.[10] Therefore, and not surprisingly, attempts to couple 3-pyridineboronic acid neopentylglycol ester led to a low yield (30%) of the corresponding α,α-difluorinated β-ketoamide **1h** under unaltered coupling conditions.

However, by employing the more stable 3-pyridineboronic acid pinacol ester and by lowering the reaction temperature to 80 °C in the absence of CuI, **1h** could be isolated in 78% yield in a reproducible fashion (Sceme 2). This result suggests that an intimate relationship is operating between the boronic ester hydrolysis rate, the rate of alkyl bromide activation, and transmetallation, and that successful coupling relies on the fine-tuning of these parameters. Meanwhile, a range of heteroaromatic boronic acid derivatives could be coupled with these modified reaction conditions, to give for example, quinolone and pyridine derivatives **1i** (77%) and **1j** (66%), respectively. Furthermore, even notoriously challenging coupling partners such as 2-thienyl- and 2-benzothienyl boronic acid esters were viable substrates, thus leading to **1k**

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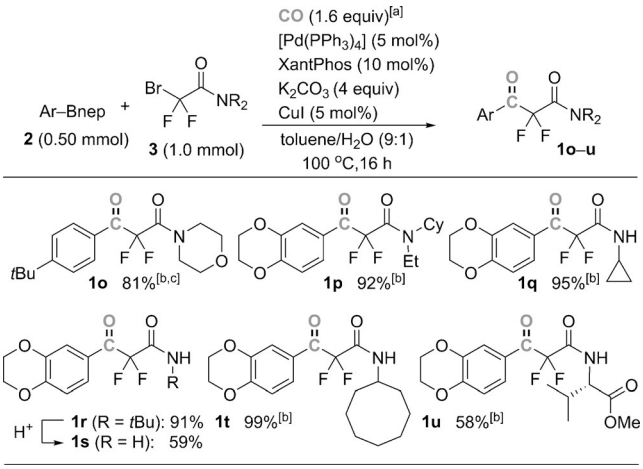
and **1l** in an 82 and 59% yield, respectively.[11] Useful yields of **1m** and **1n** could be obtained when 2-boronato derivatives of nitrogen-containing heterocycles such as an N-substituted pyrazole or a free indole were employed.[12]

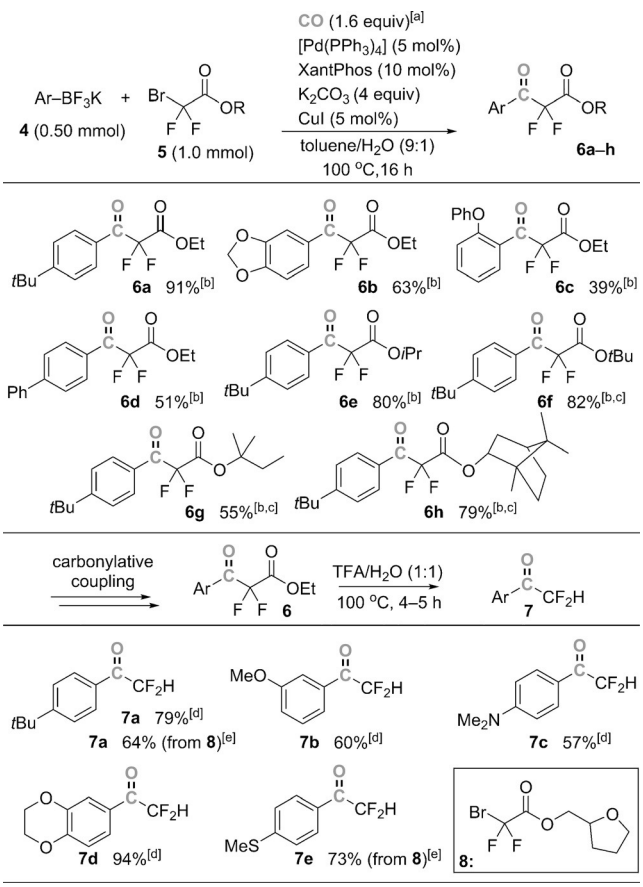
In a similar fashion, we investigated the tolerance for substitutions on the amide coupling partner. These acetamides are readily available in one synthetic step from the corresponding ethyl ester or carboxylic acid. In general, it was found that tertiary amides underwent the carbonylative coupling to give the corresponding β-ketoamides in high yields (**1o** and **1p**; Scheme 3). Secondary amides could also



Scheme 3. N-Substituted α-bromo-α,α-difluoroacetamides. [a] CO gas was generated from 9-methyl-9*H*-fluorene-9-carbonyl chloride in a separate reaction chamber; see Supporting Information section. [b] Average of two runs. [c] Reaction run at 110°C and with 7.5 mol% CuI.

be employed with high yield, even with increasingly sterically demanding N-substituents (**1q–t**). Rapid deprotection of the secondary *tert*-butyl amide **1r** with catalytic $MeSO_3H$ provided a convenient approach to the formation of the primary α,α-difluorinated-β-ketoamide **1s**. Finally, the amino-acid derivative **1u** could be prepared in a high yield from the corresponding amide.

α-Bromo-α,α-difluorinated esters (**5**) represent another interesting motif for this coupling reaction, and an attempt was made to extend the optimized reaction conditions to these starting materials (Scheme 4). Unfortunately, direct translation of such conditions led only to a modest yield (49%) of the α,α-difluoro-β-ketoester **6a**, upon attempted coupling between the ethyl ester and 4-*t*-butylphenylboronic acid neopentylglycol ester. Better results were obtained when the corresponding potassium trifluoroborate was employed, thus leading to **6a** in a 91% yield upon isolation. This trend proved to be general and a range of aryl trifluoroborates could be used to generate the desired compounds **6a–d**.[13] Attention was then turned to the ester coupling partner. Initially, we found that the isopropyl ester furnished the desired product **6e** in a high yield of 80%. When more bulky esters were employed, it was beneficial to increase the amount of copper salt. Under these reaction conditions, sterically encumbered esters derived from *t*BuOH, *tert*-amyl alcohol, and (−)-borneol provided the corresponding α,α-



Scheme 4. Synthesis of α,α-difluoro-β-keto esters and α,α-difluoro acetophenones. [a] CO gas was generated from 9-methyl-9*H*-fluorene-9-carbonyl chloride in a separate reaction chamber; see Supporting Information section. [b] Average of two runs. [c] 10% CuI. [d] Decarboxylation conducted on the corresponding ethyl ester **6** without purification in TFA/H_2O (1:1) at 100°C. [e] Decarboxylation occurred spontaneously after coupling of **4** with ester **8**. TFA = trifluoroacetic acid.

difluorinated-β-ketoesters **6f–h** in 82, 55, and 79% yield, respectively.

Finally, the possibility of performing a one-pot, acid-mediated decarboxylation of the α,α-difluorinated-β-ketoesters into their corresponding α,α-difluoroacetophenone counterparts was examined. These structures are commonly obtained from a Friedel–Crafts acylation of arenes with difluoroacetonitrile (Houben–Hoesch reaction), or by metalation of an aryl halide followed by electrophilic quenching with, for example, ethyl 2,2-difluoroacetate. In the present case, we found that filtration and concentration of the crude mixture from the coupling reaction with the ethyl ester **5** (R = Et) and subsequent heating in a TFA/H_2O (1:1) mixture, promoted an efficient decarboxylation. This way, the difluoroacetophenones **7a–d** could be obtained in good to excellent yields. When ester **8** was examined, the corresponding difluoroacetophenones **7a** and **7e** were identified as the only coupling products, arising from in situ decarboxylation.

Aryl α,α-difluoro-β-ketoamides and α,α-difluoro-β-esters provide an excellent platform for the synthesis of functionalized fluoroalkylated arenes. For instance, facile access to the

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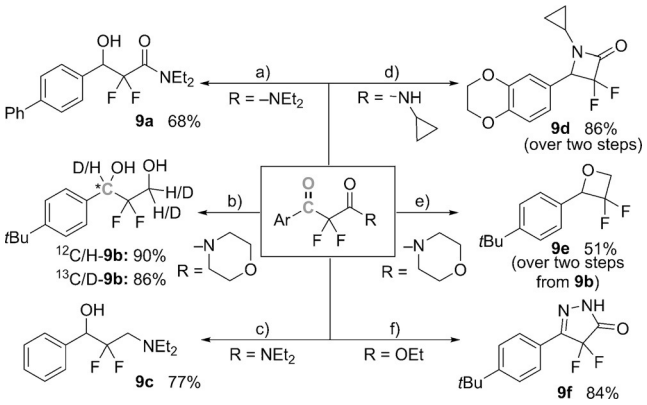
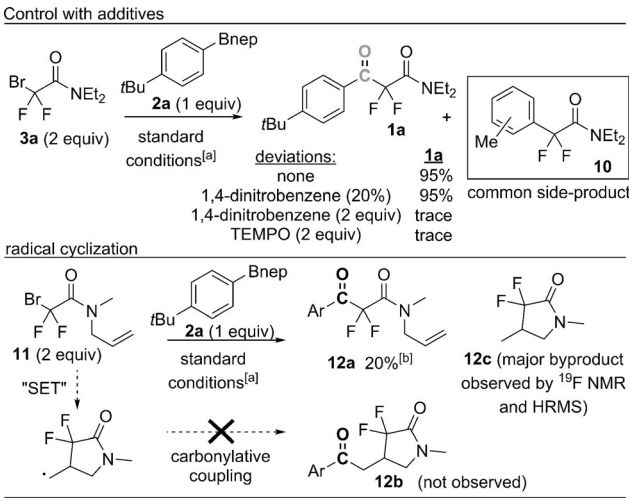
fluorinated alcohol **9a** could be achieved by reduction of **1b** with $NaBH_4$ (Scheme 5). Alternatively, when the morpholine amide **1o** was employed under similar reaction conditions, the corresponding α,α-difluorinated diol ^{12}C/H-**9b** was formed in



Scheme 5. Functionalization of α,α-difluorinated-β-keto amides and -esters. a) $NaBH_4$ (2 equiv), methanol, 0 °C–RT. b) $NaBH_4$ (3.5 equiv), 1-propanol, 80 °C. c) BH_3·THF (5 equiv), THF, 0–80 °C. d) 1. $NaBH_4$ (3.7 equiv), methanol, 0 °C–RT. 2. PPh_3 (1.5 equiv), DIAD (1.5 equiv), THF, RT. e) 1. $NaBH_4$ (3.5 equiv), 1-propanol, 80 °C, 2. TsCl (1.1 equiv), Et_3N (2 equiv), CH_2Cl_2, 0 °C–RT. 3. *n*BuLi (1 equiv), ethanol, 0–70 °C. f) Hydrazine (1 equiv), ethanol, 80 °C. DIAD = diisopropyl azodicarboxylate, THF = tetrahydrofuran, Ts = 4-toluenesulfonyl.

an excellent yield. One advantage of the described approach to carbonylation is the ease of isotopic labeling of the carbonyl group introduced by substituting COgen for an isotope-labeled version. As such the ^{13}C-labeled version of **1o** was obtained by using the normal coupling conditions, and by reduction with $NaBD_4$, an $M+4$ version of the diol ^{13}C/D-**9b** could be prepared in a similar yield. When an analogous morpholine amide was subjected to reduction with BH_3·THF, the corresponding amino alcohol **9c** was obtained in good yield. The α,α-difluorinated dicarbonyls also serve as versatile precursors for the preparation of heterocyclic structures. By reaction of the ester **6a** with hydrazine, the 4,4-difluorinated pyrazoline-3-one **9f** could be prepared. Alternatively, easy access to difluorinated diols could be exploited for the synthesis of the *gem*-difluoro oxetane **9e**, through sequential tosylation and base-promoted ring closure of the compound ^{12}C/H-**9b**. Finally, the β-lactam **9d** was prepared from **1q** in an 86% overall yield by a two-step sequence involving ketone reduction followed by a Mitsunobu-type cyclization.

The mechanism for the transition metal catalyzed coupling of fluoroalkyl halides has been proposed in several cases. In the presence of either copper, palladium, or nickel, experimental data supports the formation of radicals on the fluorinated carbon by a single-electron transfer (SET) pathway.[3f,5b,14] To evaluate the possibility for such a pathway under our reaction conditions, the coupling of **2a** and **3a** was performed in the presence of 1,4-dinitrobenzene as a SET scavenger. Addition of 20% did not lead to any change in the yield of **1a**, whereas increasing the amount to 2 equivalents completely suppressed conversion of the starting material. Addition of TEMPO (2 equiv) led to formation of the



Scheme 6. Mechanistic investigations. [a] Standard conditions identical to Scheme 2. [b] As determined by NMR analysis. A small quantity of **12a** was isolated for the purpose of characterization. TEMPO = 2,2,6,6-tetramethylpiperidinyl-1-oxyl.

corresponding TEMPO adduct with no formation of **1a** (Scheme 6).[15] In addition to these observations, it should be noted that fluoroalkylated toluene isomers such as **10** were observed as side products under the described reaction conditions.[16] Employing **11** as the starting material led to formation of **12a** in a low yield (20%).[17] The corresponding cyclized adduct **12b** was not observed, although we cannot exclude its formation in small quantities. Instead, **12c** was identified as the major side product as determined by NMR and MS analysis. Taken together, these results suggest that C-centered radicals are generated by a SET pathway. Recombination with a palladium(I) species furnishes an oxidative addition complex which ultimately leads to product formation. Alternatively, radical addition to the solvent may occur leading to formation of the toluene isomers **10**, or, when **11** is employed as the substrate, **12c** is formed by radical cyclization followed by H abstraction. The formation of **12a** suggests that recombination of the difluoroalkyl radical with palladium occurs on a timescale comparable to that of the intramolecular radical cyclization.

In summary, we have reported the development of a synthetic route to aryl α,α-difluoro-β-ketoamides and α,α-difluoro-β-esters by carbonylative cross-coupling. The method relies largely on starting materials, which are either commercially available or accessible in only few synthetic steps, and provides access to a variety of fluorinated small molecules. Furthermore, this chemistry can be extended to α,α-difluoroacetophenones in a one-pot fashion. Our palladium-catalyzed carbonylation reaction could grant ready access to a range of privileged structures to aid the drug discovery processes.

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Angew. Chem. **2016**, *128*, 10552–10556

[1] a) J. Wang, M. Sanchez-Rosello, J. L. Acena, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok, H. Liu, *Chem. Rev.* **2014**, *114*, 2432–2506; b) S. Purser, P. R. Moore, S. Swallow, V. Gouverneur, *Chem. Soc. Rev.* **2008**, *37*, 320–330.

[2] N. A. Meanwell, *J. Med. Chem.* **2011**, *54*, 2529–2591.

[3] For recent work in this area, see: a) Z. Feng, Q. Q. Min, H. Y. Zhao, J. W. Gu, X. Zhang, *Angew. Chem. Int. Ed.* **2015**, *54*, 1270–1274; *Angew. Chem.* **2015**, *127*, 1286–1290; b) J. Jung, E. Kim, Y. You, E. J. Cho, *Adv. Synth. Catal.* **2014**, *356*, 2741–2748; c) Y. L. Xiao, W. H. Guo, G. Z. He, Q. Pan, X. Zhang, *Angew. Chem. Int. Ed.* **2014**, *53*, 9909–9913; *Angew. Chem.* **2014**, *126*, 10067–10071; d) L. Wang, X. J. Wei, W. L. Jia, J. J. Zhong, L. Z. Wu, Q. Liu, *Org. Lett.* **2014**, *16*, 5842–5845; e) Y. M. Su, Y. Hou, F. Yin, Y. M. Xu, Y. Li, X. Q. Zheng, X. S. Wang, *Org. Lett.* **2014**, *16*, 2958–2961; f) A. Prieto, R. Melot, D. Bouyssi, N. Monteiro, *Angew. Chem. Int. Ed.* **2015**, *54*, 1885–1889; *Angew. Chem.* **2015**, *127*, 1905–1907; g) M.-H. Yang, D. L. Orsi, R. A. Altman, *Angew. Chem. Int. Ed.* **2015**, *54*, 2361–2365; *Angew. Chem.* **2015**, *127*, 2391–2395; h) N. Surapanich, C. Kuhakarn, M. Pohmakotr, V. Reutrakul, *Eur. J. Org. Chem.* **2012**, 5943–5952; i) Q. Chen, C. Wang, J. Zhou, Y. Wang, Z. Xu, R. Wang, *J. Org. Chem.* **2016**, *81*, 2639–2645.

[4] a) C. Guo, R.-W. Wang, F.-L. Qing, *J. Fluorine Chem.* **2012**, *143*, 135–142; b) C. Guo, R.-W. Wang, Y. Guo, F.-L. Qing, *J. Fluorine Chem.* **2012**, *133*, 86–96; c) K. Fujikawa, Y. Fujioka, A. Kobayashi, H. Amii, *Org. Lett.* **2011**, *13*, 5560–5563; d) S. I. Arlow, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2016**, *55*, 4567–4572; *Angew. Chem.* **2016**, *128*, 4643–4648; e) S. Ge, W. Chaladaj, J. F. Hartwig, *J. Am. Chem. Soc.* **2014**, *136*, 4149–4152; f) S. Ge, S. I. Arlow, M. G. Mormino, J. F. Hartwig, *J. Am. Chem. Soc.* **2014**, *136*, 14401–14404.

[5] a) A. Tarui, S. Shinohara, K. Sato, M. Omote, A. Ando, *Org. Lett.* **2016**, *18*, 1128–1131; b) Z. Feng, Q. Q. Min, Y. L. Xiao, B. Zhang, X. Zhang, *Angew. Chem. Int. Ed.* **2014**, *53*, 1669–1673; *Angew. Chem.* **2014**, *126*, 1695–1699.

[6] a) Y. L. Xiao, B. Zhang, Z. Feng, X. Zhang, *Org. Lett.* **2014**, *16*, 4822–4825; b) Z. Feng, Q. Q. Min, X. Zhang, *Org. Lett.* **2016**, *18*, 44–47.

[7] The main synthetic routes to access these structures are generally multistep operations featuring for example, metal-mediated addition of α-bromo-α,α-dilfuoro acetates to aryl aldehydes followed by oxidation: see Ref. [3g]; or electrophilic α-fluorination of a previously assembled 1,3-dicarbonyl or enamine: a) O. D. Gupta, J. N. M. Shreeve, *Tetrahedron Lett.* **2003**, *44*, 2799–2801; b) W. M. Peng, J. N. M. Shreeve, *J. Org. Chem.* **2005**, *70*, 5760–5763; c) Z. Q. Xu, D. D. Desmarteau, Y. Gotoh, *J. Fluorine Chem.* **1992**, *58*, 71–79.

[8] Addition adducts of this type were in several cases isolated as a sideproduct.

[9] A detailed description of the experimental setup is included in the Supporting Information section. For example, from our group see: a) P. Hermange, A. T. Lindhardt, R. H. Taaning, K. Bjerglund, D. Lupp, T. Skrydstrup, *J. Am. Chem. Soc.* **2011**, *133*, 6061–6071; b) S. D. Friis, T. Skrydstrup, S. L. Buchwald, *Org. Lett.* **2014**, *16*, 4296–4299; c) T. L. Andersen, S. D. Friis, H. Audrain, P. Nordeman, G. Antoni, T. Skrydstrup, *J. Am. Chem. Soc.* **2015**, *137*, 1548–1555; d) D. U. Nielsen, C. Lescot, T. M. Gøgsig, A. T. Lindhardt, T. Skrydstrup, *Chem. Eur. J.* **2013**, *19*, 17926–17938.

[10] a) G. A. Molander, *J. Org. Chem.* **2015**, *80*, 7837–7848; b) D. M. Knapp, E. P. Gillis, M. D. Burke, *J. Am. Chem. Soc.* **2009**, *131*, 6961–6963.

[11] K. Billingsley, S. L. Buchwald, *J. Am. Chem. Soc.* **2007**, *129*, 3358–3366.

[12] The main limitations of the enclosed method were found to be the reluctance of alkyl boronates to undergo coupling. Similarly, no conversion was seen when alkyl chlorides were used as electrophiles.

[13] Aryl trifluoroborates bearing electron-deficient groups led in general to coupling yields ranging from 30–50%. The same was observed when the potassium 3-pyridyl trifluoroborate salt was employed.

[14] a) Z. S. Ye, K. E. Gettys, X. Y. Shen, M. J. Dai, *Org. Lett.* **2015**, *17*, 6074–6077; b) Z. Y. Yang, D. J. Burton, *J. Org. Chem.* **1992**, *57*, 4676–4683; c) Z. Y. Yang, D. J. Burton, *J. Org. Chem.* **1992**, *57*, 5144–5149.

[15] Although no effect was seen in the presence of 20% 1,4-dinitrobenzene, full consumption of the additive was observed.

[16] We are currently investigating the nature of this side-reaction.

[17] Y. Isono, S.-I. Iwamatsu, H. Nagashima, *J. Org. Chem.* **2001**, *66*, 315–319.

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