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Ruthenium-Catalyzed Site-Selective Trifluoromethylations and (Per)Fluoroalkylations of Anilines and Indoles

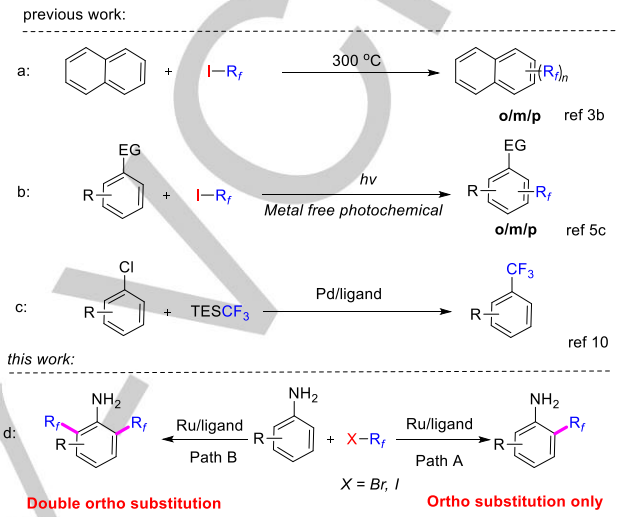
Yang Li,[a b] Helfried Neumann,[a] and Matthias Beller*[a]

Abstract: Introducing (per)fluoroalkyl groups into arenes continues to be an interesting, but challenging area in organofluorine chemistry. We herein report a novel ortho-selective C-H perfluoroalkylation including trifluoromethylations of anilines and indoles without the need of protecting groups using R_fI and R_fBr as commercially available reagents. The availability and price of the starting materials as well as the inherent selectivity make this novel methodology attractive for the synthesis of diverse (per)fluoroalkylated building blocks, e.g. for bio-active compounds and materials.

The incorporation of (per)fluoroalkyl moieties into (hetero)arenes has been demonstrated to significantly improve their physical and biological properties for various applications.[1,2] Hence, in recent years there is an increasing interest to prepare such molecules by thermal[3, 4] and photochemical reactions,[5-7] as well as others.[8-11] Despite these notable achievements, still more practical and convenient methodologies are lacking and there is a need using sophisticated reagents and/or tedious purification due to selectivity problems. Indeed, regio- and chemoselective functionalizations are of crucial importance, because isolation of the resulting pure fluorinated isomers is often very difficult. To avoid these problems, synthetic methods have been developed for the synthesis of perfluoroalkyl arenes starting from the corresponding aryl halides.[10] However, the direct preparation of the desired compounds from arenes via C-H functionalization would be more desirable due to their availability and process step economy.

Among the different perfluoroalkylation reagents, especially the corresponding halides R_fX constitute valuable substrates. Since the original work by Fuchikami and Ojima using perfluoroalkyl halides in the presence of copper bronze,[12] several transition metal-catalyzed perfluoroalkylations of arenes have been reported.[13-15] However, in general products are obtained as mixtures, which were often not even isolated and purified. In this respect, the recent work of Zhao and co-workers is noteworthy, who reported a *para*-selective perfluoroalkylation of anilides in the presence of $Mo(CO)_6$ as catalyst.[16]

Based on our interest in perfluoroalkylation reactions,[17, 18] herein we present the first general and practical methodology for highly *ortho*-selective, direct C-H perfluoroalkylation of anilines under mild reaction conditions (Scheme 1). To the best of our knowledge, there have been no examples reported, which allow introducing R_f groups with high site selectivity.



Scheme 1. Selected methods for introducing trifluoromethyl and perfluoroalkyl groups into arenes.

Recently, our group reported platinum-, nickel- and cobalt-based catalysts for such reactions. However, in no case the regioselectivity problem could be resolved. Hence, we continued to search for more suitable transition metal catalysts. Following this strategy, we used the reaction of 4-methoxyaniline (**1a**) and *n*-C_4F_9I (**2a**) as a model system. In an initial screening of catalysts, ruthenium carbene complexes revealed to be active. In general, 5 mol% of the catalyst and 2.0 equiv. of base (to trap HX) were used in organic solvents at 100 °C for 12 h. As shown in Table 1, optimization of reaction conditions, including pre-catalysts, bases, and solvents gave the desired product 4-methoxy-2-(perfluorobutyl)-aniline (**3a**) in >80% yield. ^{19}F NMR investigations after the reaction clearly demonstrated that only the mono-substituted aniline **3a** is formed. However, in the presence of an excess of **2a**, tiny amounts (<5%) of double perfluoroalkylation products can be formed.

Among the different ruthenium salts and complexes applied, a variety of defined metathesis catalysts proved to be effective for this transformation. In line with this observation, adding 1,3-bis(2,6-diisopropylphenyl)-imidazolium bromide as NHC carbene ligand to simple ruthenium trichloride led to a reasonable active catalyst system (Table 1, entries 8-9). Nevertheless, commercially available **Ru-1** provided the highest product yield. Thus, in the presence of this precursor the influences of base (Table 1, entries 10-14) and solvents (Table 1, entries 15-18) including THF, MeCN, MePh and DMF were studied. Best results (86% of **3a**) were obtained using K_2CO_3 in 1,4-dioxane with an increased amount of **2a** (1.3 mmol; Table 1, entry 19).

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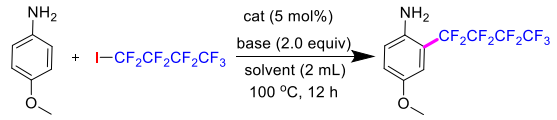
Obviously, the stoichiometry of the perfluoroalkylation reagent and the choice of base (Table 1, entries 10-11) have the major influence on the efficiency of this reaction. Thus, a control experiment using simple $RuCl_3{\cdot}H_2O$ (5% mol) in the presence of the carbene ligand (10 mol%) and K_2CO_3 as base was performed using 1.3 equiv. of R_fI. Indeed, the desired product **3a** is obtained in 73% yield (Table 1, entry 20). As expected without the metal catalyst, the background reaction occurred only to a negligible extent (Table 1, entry 21).

Table 1. Ru-catalyzed perfluoroalkylation of 4-methoxyaniline. [a]

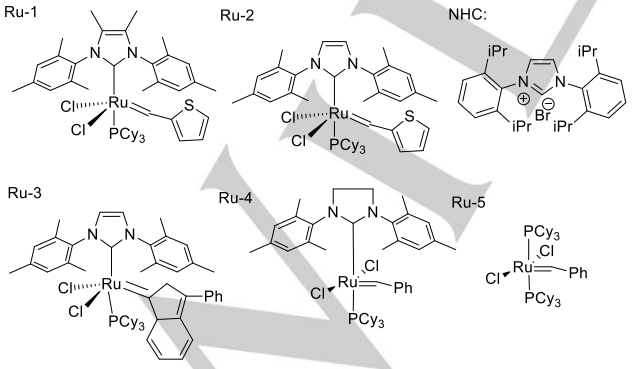


1a 2a 3a

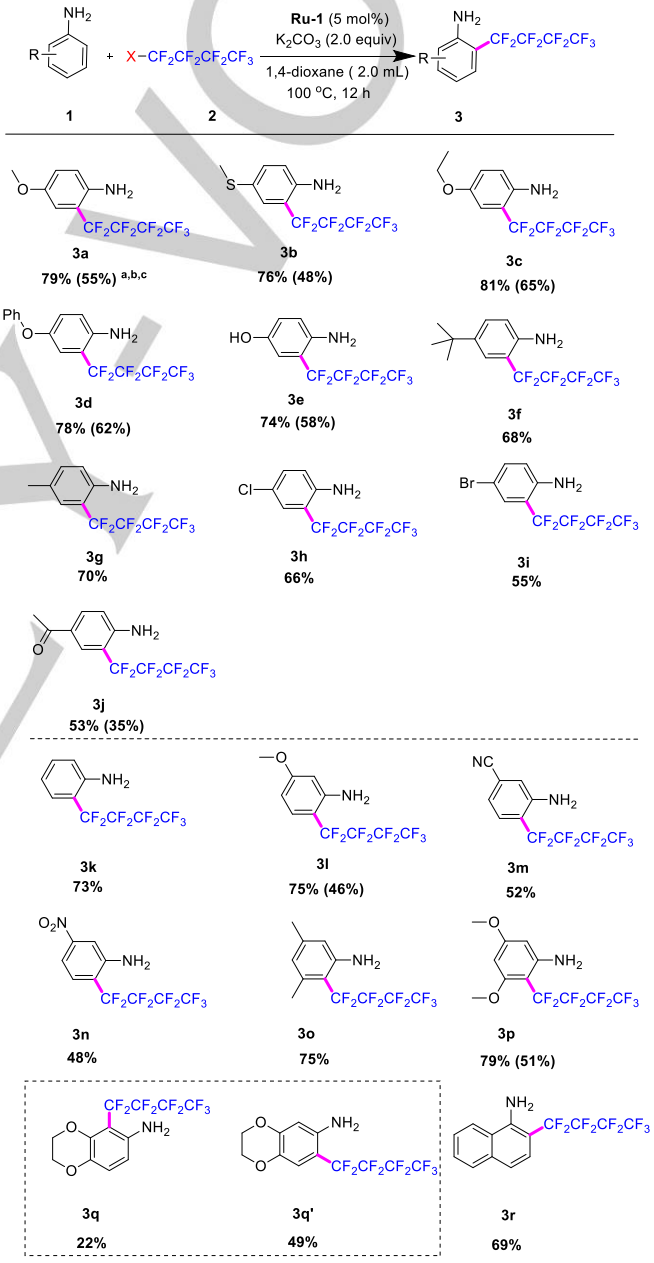
Entry	Catalyst	Base	Solvent	Yield (%) [b]
1	$RuCl_3 \cdot 3H_2O$	$NaHCO_3$	1,4-dioxane	6
2	$[RuCl_2(p\text{-Cymene})]_2$	$NaHCO_3$	1,4-dioxane	19
3	Ru-1	$NaHCO_3$	1,4-dioxane	45
4	Ru-2	$NaHCO_3$	1,4-dioxane	36
5	Ru-3	$NaHCO_3$	1,4-dioxane	31
6	Ru-4	$NaHCO_3$	1,4-dioxane	26
7	Ru-5	$NaHCO_3$	1,4-dioxane	19
8[c]	Ru-5	$NaHCO_3$	1,4-dioxane	38
9[c]	$RuCl_3 \cdot 3H_2O$	$NaHCO_3$	1,4-dioxane	41
10	Ru-1	$KHCO_3$	1,4-dioxane	51
11	Ru-1	K_2CO_3	1,4-dioxane	72
12	Ru-1	Na_2CO_3	1,4-dioxane	58
13	Ru-1	Na_2HPO_4	1,4-dioxane	16
14	Ru-1	Et_3N	1,4-dioxane	22
15	Ru-1	K_2CO_3	THF	49
16	Ru-1	K_2CO_3	MeCN	23
17	Ru-1	K_2CO_3	MePh	35
18	Ru-1	K_2CO_3	DMF	14
19[d]	**Ru-1**	**K_2CO_3**	**1,4-dioxane**	**83 (79)[e]**
20	$RuCl_3 \cdot 3H_2O$	K_2CO_3	1,4-dioxane	73
21	free	K_2CO_3	1,4-dioxane	8

[a] Reaction conditions: **1a** (1.0 mmol), **2** (1.2 mmol), catalyst (5 mol%), base (2.0 mmol), solvent (2.0 mL), 100 °C, 12 h. [b] Determined by ^{19}F NMR analysis using (trifluoromethoxy)benzene as internal standard. [c] 7 mol% NHC ligand was added. [d] **2** (1.3 mmol). [e] Isolated yield in brackets.

Structure of catalysts and ligands:



Regarding the mechanism, we propose the initial formation of a perfluoroalkyl radical via a metal-catalyzed single electron transfer process (SET) is occurring. Such SET processes are well known for several ruthenium complexes.[19] The excellent regioselectivity observed in the model reaction should be a result of the coordination of aniline to the metal center, which determines preferential formation of the ortho-perfluoroalkylated product **2a**. To understand this selectivity and the underlying reaction mechanism, several control experiments were carried out under standard conditions (see SI, Table S1). In contrast to aniline, phenol and anisole do not react under identical conditions, which highlights the importance of the amino group for this transformation.



[a] Reaction conditions: aniline (1.0 mmol), *n*-C_4F_9I (1.3 mmol), **Ru-1** (5 mol%), K_2CO_3 (2.0 eq). and 1,4-dioxane (2.0 mL), 100 °C, 12 h. [b] Isolated yield. [c] *n*-C_4F_9Br (1.5 mmol) used for the reaction in brackets.

Scheme 2. Selective Ru-catalyzed perfluoroalkylation of anilines.

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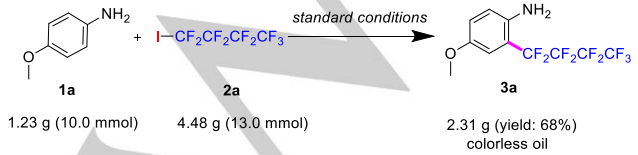
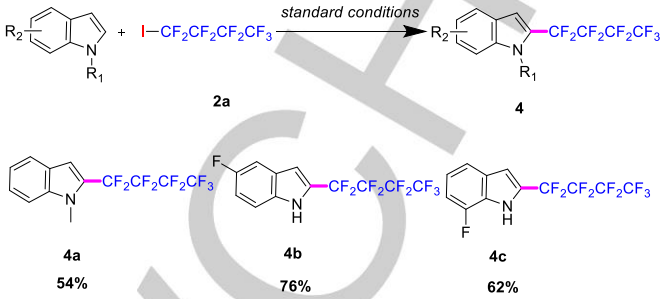
In these latter cases the starting materials were retained in >98%. Interestingly, the use of *N*,*N*-dimethylaniline led to a mixture of perfluoroalkylated products, which could not be isolated in pure form due to the similar physical properties of the regioisomers. To isolate and/or identify any organometallic intermediate of the catalytic cycle, the complex **Ru-1** (0.1 mmol) was mixed with n-C_4F_9I (0.1 mmol) in 1,4-dioxane (1 mL) and stirred at 100 °C for several hours. Analysis of the crude mixture by ^{19}F NMR revealed unfortunately no obvious changes (see SI for more details).

Next, we were interested to explore the substrate scope of anilines of this novel methodology. Thus, reactions of various substituted anilines with *n*-C_4F_9I were examined. Based on the optimization *vide supra*, the following conditions were applied:1.3 equiv. of **2**, 5 mol% **Ru-1**, 2.0 equiv. of K_2CO_3 in 1,4-dioxane (2.0 mL) at 100 °C for 12 h under N_2. Initially, we focused on the functional group tolerance of the catalyst. For this purpose, several electron-rich *para*-substituted anilines (-OMe, -SMe, -OEt, OPh, -*t*-Bu, -OH) were reacted with *n*-C_4F_9I to afford smoothly the corresponding products in good to excellent yields (Scheme 2, **3a**-**3i**). Apart from *n*-C_4F_9I, also using *n*-C_4F_9Br gave the target compounds, albeit in somewhat lower yields. In addition, anilines with electron-withdrawing groups (-Cl, -Br, -Ac) provided the perfluoroalkylated products in moderate to good yields. Notably, halide and ketone substituents on the aniline ring remained untouched demonstrating the excellent chemo-selectivity of the system. In general, the reactivity of the latter substrates is lower than those of electron-rich anilines. Next, we investigated reactions of aniline, 1-naphthylamine, 1,3-disubstituted, and 1,3,5-trisubstituted anilines. In all these cases, the control of regioselectivity is significantly more challenging. Nevertheless, using parent aniline **1j** as substrate perfluoroalkylation occurred specifically in the *ortho*-position giving **3j** in 73% isolated yield. Other isomers (<5%) could not be observed. Next, anilines with *meta*-substitution pattern were tested in this process. Again, both electron-rich (-OMe) and -withdrawing (-CN, -NO_2) substrates expressed good activities for the perfluoroalkylation reaction and only one regioisomer was obtained (Scheme 2, **3l**-**3n**). In addition, anilines with two substituents, such as 3,5-dimethyl and 3,5-dimethoxy can be conveniently employed in this reaction with high site-selectivity (Scheme 2, **3o**, **3p**). Finally, when using 2,3-dihydrobenzo[b][1,4]dioxin-6-amine **1q** we obtained two ortho-substituted regioisomers in 49 and 22% yield (Scheme 2, **3q, 3q'**), respectively. Similarly to the model system, also for these substrates *n*-C_4F_9Br could be successfully used as perfluoroalkyl source and the *ortho*-perfluoroalkylated anilines were obtained in moderate to good yields (Scheme 2, **3k**, **3l**, **3p**). In all these cases the perfluoroalkylated products are easily obtained in pure form due to the high selectivity of the process.



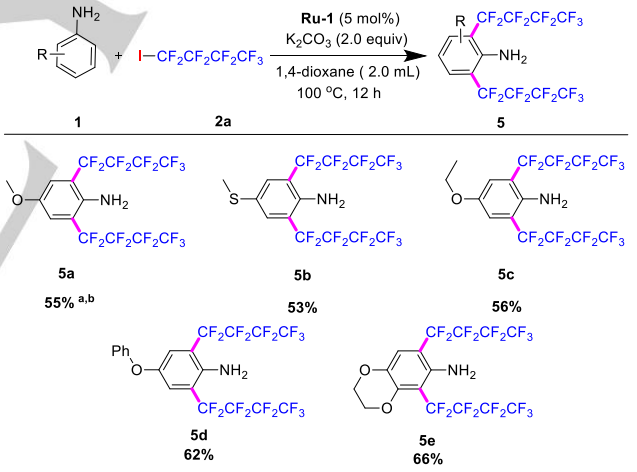
Scheme 3. Gram-scale synthesis of **3a**.

To demonstrate the synthetic utility of our protocol on multi-g-scale, the reaction of 4-methoxyaniline (10.0 mmol) with *n*-C_4F_9I (13.0 mmol) was performed and gave the corresponding product only in slightly lower yield (Scheme 3).



Scheme 4. Ru-catalyzed perfluoroalkylation of indoles.

Indoles are an important class of heterocyclic compounds. Indeed, numerous natural products contain this electron-rich scaffold. Thus, we explored the reactivity of **4a-c** with **2a** in this process. We were pleasured to find that selective perfluorobutylation occurred selectively at the C-2 position with or without N protection (Scheme 4).



[a] Reaction conditions: aniline (1.0 mmol), *n*-C_4F_9I (3.0 mmol), **Ru-1** (5 mol%), K_2CO_3 (2.0 eq.) and 1,4-dioxane (2.0 mL), 100 °C, 12 h. [b] Isolated yield.

Scheme 5. Ru-catalyzed double-perfluoroalkylation of anilines.

During the initial optimization of this procedure, we found small amounts of double perfluoroalkylation. Following this original observation, we investigated the reaction of aniline **1a** with a larger excess of **2a**. Surprisingly, the di-*ortho*-perfluoroalkylated aniline **5a** is obtained in 55% isolated yield using 3.0 equiv. of **2a**. As shown in Scheme 5, other anilines **1a-d, q** presented similar reactivity and gave the desired *ortho/ortho*-disubstituted compounds in 53-66% isolated yield. It should be noted that such 2,6-difuctionalized anilines are otherwise very difficult to access.

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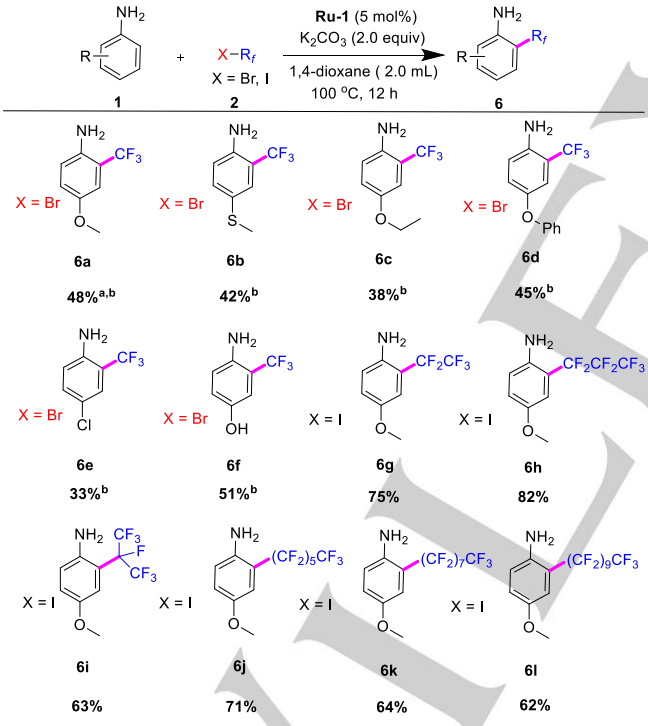
Regarding the various perfluoroalkylation reactions, certainly trifluoromethylation is the most important transformation, especially for the synthesis of new bio-active compounds. Hence, diverse state-of-the-art reagents for laboratory scale synthesis including Umemoto´s,[20] Togni´s,[21] Langlois´,[22] and Ruppert-Prakash´s reagent[23] as well as $CuCF_3$[23] were developed in the past decades. However, due to their price and availability, the use of these reagents on >kg-scale is highly problematic. In contrast, CF_3Br is available on multi-100 kg-scale and less expensive compared to the above-mentioned reagents. Nevertheless, we want to make clear that also this reagent has ozone depleting properties, which are forbidden by the Montreal protocol. Hence, appropriate safety measures should be taken. As shown in Scheme 6, CF_3Br allows for ortho-selective functionalization of para-substituted anilines with acceptable yields (Scheme 6, **6a**-**6f**). Similarly, using **Ru-1** other perfluoroalkyl iodides (C_2F_5I, C_3F_7I, $C_6F_{13}I$, $C_8F_{17}I$, and $C_{10}F_{21}I$) reacted well with 4-methoxyaniline (**1a**) to give the corresponding target compounds in moderate to good yields and excellent selectivities (Scheme 6, **6g**, **6h**, **6i**, **6j**, **6k**, **6l**). In the context of building blocks for bio-active compounds, it is worth mentioning that heptafluoroisopropyl iodide **2i** afforded the corresponding product in 63% yield (Scheme 6, **6i**).



[a] Reaction conditions: **1** (1.0 mmol), R_fX (1.3 mmol), **Ru-1** (5 mol%), K_2CO_3 (2.0 eq). and 1,4-dioxane (2.0 mL), 100 °C 12 h. [b] 4 mL solution of CF_3Br in 1,4-dioxane (0.06 mol/L) was used, and yield based on CF_3Br.

Scheme 6. Substrate scope of trifluoromethyl and perfluoroalkyl halides.

In conclusion, we have developed an efficient and practical *ortho*-selective mono- and di(per)fluoroalkylation methodology of free anilines and indoles. In the presence of the stable and commercially available pre-catalyst **Ru-1** various *meta*- and *para*-substituted anilines, including mono- and disubstituted ones, gave the corresponding products without the need for protecting groups in high purity. The availability of the starting materials and the high selectivity make the process attractive for the synthesis of all kinds of perfluoroalkyl-substituted anilines, including trifluormethyl derivatives.

Experimental Section

Perfluoroalkylation of anilines with *n*-C_4F_9I: aniline (1.0 mmol), *n*-C_4F_9I (1.3 mmol), **Ru-1** (5 mol%), K_2CO_3 (2.0 eq). and 1,4-dioxane (2.0 mL) were added to a reaction tube. Then, the tube was degassed with argon three times and heated at 100 °C for 12 h. After cooling to room temperature, the solvent was removed under vacuum conditions, and the products were purified through silica gel chromatography by using hexane and ethyl acetate as the eluents.

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Keywords: anilines • ortho • perfluoroalkylation • Ru catalyst • site-selective

[1] a) P. Kirsch, In Modern Fluoroorganic Chemistry, Wiley-VCH, Weinheim, Germany, **1996**. b I. Ojima, Fluorine in Medicinal Chemistry and Chemical Biology, Wiley-Blackwell: Chichester, UK; 2009.

[2] a) C. N. Neumann, T. Ritter, *Angew. Chem. Int. Ed.* **2015**, *54*, 3216-3218; *Angew. Chem.* **2015**, *127*. 3261-3263; b) J. A. Ma, D. Cahard, *Chem. Rev.* **2004**, *104*, 6119-6119.

[3] a) A. B. Cowell, C. Tamborski, *J. Fluorine Chem.* **1981**, *17*, 345-356; b) L. K. San, E. V. Bukovsky, I. V. Kuvychko, A. A. Popov, S. H. Strauss, O. V. Boltalina, *Chem. Eur. J.* **2014**, *20*, 4373-4379.

[4] a) Y. Macé, E. Magnier, *Eur. J. Org. Chem.* **2012**, 2479-2494; b) T. Kitazume, T. Ikeya, *J. Org. Chem.* **1988**, *53*, 2349-2350; c) D. Y. Mikhaylov, T. V. Gryaznova, Y. G. Budnikova, O. G. Sinyashin, *Russ. Chem. Bull.* **2010**, *59*, 1918-1920; d) M. Médebielle, S. Fujii, K. Kato, *Tetrahedron* **2000**, *56*, 2655-2664.

[5] a) D. -F. Jiang, C. Liu, Y. Guo, J. -C. Xiao, Q. -Y. Chen, *Eur. J. Org. Chem.* **2014**, *28*, 6303-6309; b) L. Cui, Y. Matusaki, N. Tada, T. Miura, B. Uno and A. Itoh, *Adv. Synth. Catal.* **2013**, *355*, 2203-2207; c) M. Nappi, G. Bergonzini and P. Melchiorre, *Angew. Chem. Int. Ed.* **2014**, *53*, 4921-4925; *Angew. Chem.* **2014**, *126*, 5021-5025; d) N. J. Straathof, H. P. Gemoets, X. Wang, J. C. Schouten, V. Hessel, T. Noel, *ChemSusChem* **2014**, *7*, 1612-1617; e) S. Barata-Vallejo, D. E. Yerien, A. Postigo, *Eur. J.Org. Chem.* **2015**, 7869-7875; f) C. -Y. He, J. -W. Gu, X. Zhang, *Tetrahedron Lett.* **2017**, *58*, 3939-3941.

[6] a) J. W. Beatty, J. J. Douglas, R. Miller, R. C. McAtee, K. P. Cole, C. R. J. Stephenson, *Chem* **2016**, *1*, 456-472; b) Y. Wang, J. Wang, G. X. Li, G. He, G. Chen, *Org. Lett.* **2017**, *19*, 1442-1445; c) E. Torti, S. Protti, M. Fagnoni, *Chem. Commun.* **2018**, *54*, 4144-4147; d) Y. Ouyang, X. H. Xu, F. L. Qing, *Angew. Chem. Int. Ed.* **2018**, *57*, 6926-6929; *Angew. Chem.* **2018**, *130,* 7042-7045; e) D. E. Yerien, M. V. Cooke, M. C. García Vior, S. Barata-Vallejo, A. Postigo, *Org. Biomol. Chem.* **2019**, *17*, 3741.

[7] a) D. E. Yerien, R. Conde, S. Barata-Vallejo, B. Camps, B. Lantaño, A. Postigo, *RSC Adv.* **2017**, *7*, 266-274; b) P. B. Arockiam, L. Guillemard, J. Wencel-Delord, *Adv. Synth. Catal.* **2017**, *359*, 2571-2579; c) I. Ghosh,

J. Khamrai, A. Savateev, N. Shlapakov, M. Antonietti, B. König, *Science* **2019**, *365*, 360-366.

[8] a) N. Kamigata, T. Ohtsuka, T. Fukushima, M. Yoshida, T. Shimizu, *J. Chem. Soc. Perkin Trans. 1* **1994**, 1339-1346; b) N. Kamigata, T. Ohtsuka, M. Yoshida, T. Shimizu, *Synth. Commun.* **1994**, *24*, 2049-2055; c) N. Kamigata, T. Ohtsuka, T. Shimizu, *Phosphorus Sulfur Silicon Relat. Elem.* **1994**, 95-96, 491-492; c) R. N. Loy, M. S. Sanford, *Org. Lett.* **2011**, *13*, 2548-2551; d) X. -T. Huang, Z. -Y. Long, Q. -Y. Chen, *J. Fluorine Chem.* **2001**, *111*, 107-113; e) C. Wakselman, M. Tordeux, *J. Chem. Soc. Chem. Commun.* **1987**, *22*, 1701-1703; f) K. Natte, R. V. Jagadeesh, L. He, J. Rabeah, J. Chen, C. Taeschler, S. Ellinger, F. Zaragoza, H. Neumann, A. Brückner, M, Beller, *Angew. Chem. Ed. Int.* **2016**, *55*, 2782-2786.

[9] a) I. Popov, S. Lindeman, O. Daugulis, *J. Am. Chem. Soc.* **2011**, *133*, 9286-9289; b) H. Morimoto, T. Tsubogo, N. D. Litvinas, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2011**, *50*, 3793-3798; *Angew. Chem.* **2011**, *123*, 3877-3882; c) M. G. Mormino, P. S. J. F. Hartwig, *Org. Lett.* **2014**, *16*, 1744-1747.

[10] E. J. Cho, T. D. Senecal, T. Kinzel, Y. Zhang, D. A. Watson, S. L. Buchwald, *Science* **2010**, *328*, 1679-1681.

[11] a) D. Leifert, D. G. Artiukhin, J. Neugebauer, A. Galstyan, C. A. Strassert, A. Studer, *Chem. Commun.* **2016**, *52*, 5997-6000; b) T. Shirai, M. Kanai and Y. Kuninobu, *Org. Lett.* **2018**, *20*, 1593-1596; c) L. Wu, F. Wang, P. Chen, G. Liu, *J. Am. Chem. Soc.* **2019**, *141*, 1887-1892.

[12] T. Fuchikami and I. Ojima, *J. Fluorine Chem.* **1983**, *22*, 541-556.

[13] a) X. Bao, L. Liu, J. Li and S. Fan, *J. Org. Chem.* **2018**, *83*, 463-468; b) S. Zhang, H. Neumann, M. Beller, *Chem. Eur. J.* **2018**, *24*, 67-70; c) K. Aikawa, Y. Nakamura, Y. Yokota, W. Toya and K. Mikami, *Chem. Eur. J.* **2015**, *21*, 91-100; d) T. Knauber, F. Arikan, G. V. Röschenthaler and L. J. Gooβen, *Chem. Eur. J.* **2011**, *17*, 2689-2697; e) M. Moreno-Mañas, R. Pleixats, S. Villarroya, *Synlett* **1999**, *12*, 1996-1998.

[14] a) L. Strekowski, H. Lee, S. -Y. Lin, A. Cyarny, D. V. Derveer, *J. Org. Chem.* **2000**, *65*, 7703-7706; b) K. A. McReynolds, R. S. Lewis, L. K. G. Ackerman, G. G. Dubinina, W.W.Brennessel, D. A. Vicic, *J. Fluorine Chem.* **2010**, *131*, 1108-1112; c) M. Oishi, H. Kondo and H. Amii, *Chem. Commun.* **2009**, 1909-1911; d) J. Monteiro, P. F. Carneiro, P. Elsner, D. M. Roberge, P. G. M. Wuts, K. C. Kurjan, B. Gutmann, C. O. Kappe, *Chem. Eur. J.* **2017**, *23*, 176-186.

[15] a) A. Hafner, A. Bihlmeier, M. Nieger, W. Klopper, S. Bräse, *J. Org. Chem.* **2013**, *78*, 7938-7948; b) R. N. Loy, M. S. Sanford, *Org. Lett,* **2011**, *13*, 2548-2551; c) N. D. Litvinas, P. S. Fier, J. H. Hartwig, *Angew. Chem. Int. Ed.* **2012**, *51*, 536-539; *Angew. Chem.* **2012**, *124*, 551-554.

[16] C. Yuan, P. Dai, X. Bao, Y. Zhao, *Org. Lett.* **2019**, *21*,6481-6484.

[17] L. He, K. Natte, J. Rabeah, C. Taeschler, H. Neumann, A. Brückner, M. Beller, *Angew. Chem. Int. Ed.* **2015**, *54*, 4320-4324; *Angew. Chem.* **2015**, *127*, 4394-4398.

[18] S. Zhang, N. Rotta-Loria, F. Weniger, J. Rabeah, H. Neumann, C. Taeschler, M. Beller, *Chem. Commun.* **2019**, *55*, 6723-6726.

[19] T. Koike, M. Akita, Visible-Light-Induced Redox Reactions by Ruthenium Photoredox Catalyst. Topics in Organometallic Chemistry. **2015**, *48*, 371-395.

[20] a) J. Jacquet, S. Blanchard, E. Derat, M. Desage-El Murr and L. Fensterbank, *Chem. Sci.* **2016**, *7*, 2030-2036; b) G. Dagousset, A. Carboni, E. Magnier and G. Masson, *Org. Lett.* **2014**, *16*, 4340-4343; c) W. An, N. Ha, H. M. Lee, Y. R. Malpani, D. -H. Lee, Y.-S. Jung and S. B. Han, *Adv. Synth. Catal.* **2015**, *357*, 3949-3960; d) R. Tomita, Y. Yasu, T. Koike and M. Akita, Beilstein *J. Org. Chem.* **2014**, *10*, 1099-1106.

[20] a) M. Fu, L. Chen, Y. Jiang, Z. -X. Jiang, Z. Yang, *Org. Lett.* **2016**, *18*, 348-351; b) Z. He, P. Tan, J. Hu, *Org. Lett.* **2016**, *18*, 72-75; c) S. P. Pitre, C. D. McTiernan, J. C. Scaiano, *Acc. Chem. Res.* **2016**, *49*, 1320-1330; d) J. Zheng, Z. Deng, Y. Zhang, S. Cui, *Adv. Synth. Catal.* **2016**, *358*, 746-751; e) L. -Z. Yu, Q. Xu, X. -Y. Tang, M. Shi, *ACS Catal.* **2016**, *6*, 526-531; f) N. Y. Yang, Z. L. Li, L. Ye, B. Tan, X. Y. Liu, *Chem. Commun*. **2016**, *52*, 9052-9055; g) K. Shen, Q. Wang, *Org. Chem. Front.* **2016**, *3*, 222-226; h) K. N. Lee, Z. Lei, C. A. Morales-Rivera, P. Liu, M. Y. Ngai, *Org. Biomol. Chem.* **2016**, 14, 5599-5605; i) Y. Kuninobu, M. Nishi, M. Kanai, *Org. Biomol. Chem.* **2016**, *14*, 8092-8100; j) D. Katayev, J. Vaclavik, F. Bruning, B. Commare, A. Togni, *Chem. Commun.* **2016**, *52*, 4049-4052; k) Y. L. Ji, J. J. Luo, J. H. Lin, J. C. Xiao, Y. C. Gu, *Org. Lett.* **2016**, *18*, 1000-1003.

[21] a) Q. Y. Lin, X. H. Xu, F. L. Qing, *J. Org. Chem.* **2014**, *79*, 10434-10446; b) C. Zhang, *Adv. Synth. Catal.* **2014**, *356*, 2895-2906; c) A. Maji, A. Hazra, D. Maiti, *Org. Lett.* **2014**, *16*, 4524-4527; d) L. Li, X. Mu, W. Liu, Y. Wang, Z. Mi, C. J. Li, *J. Am. Chem. Soc.* **2016**, *138*, 5809-5812; e) Q. Lefebvre, N. Hoffmann, M. Rueping, *Chem. Commun.* **2016**, *52*, 2493-2496; f) X. -H. Cao, X. Pan, P. -J. Zhou, J. -P. Zou, O. T. Asekun, *Chem. Commun.* **2014**, *50*, 3359; g) Y. Ji, T. Brueckl, R. D. Baxter, Y. Fujiwara, I. B. Seiple, S. Su, D. G. Blackmond, P. S. Baran, *Proc. Natl. Acad. Sci. USA*, **2011**, *108*, 14411-14415.

[22] a) M. Nagase, Y. Kuninobu, M. Kanai, *J. Am. Chem. Soc.* **2016**, *138*, 6103-6106; b) R. P. Singh, J. n. M. Shreeve, *Tetrahedron* **2000**, *56*, 7613-7632; c) B. Bayarmagnai, C. Matheis, E. Risto, L. J. Gooβen, *Adv. Synth. Catal.* **2014**, *356*, 2343-2348; d) H. Serizawa, K. Aikawa, K. Mikami, *Chem. Eur. J.* **2013**, *19*, 17692-17697; e) Y. Li, F. Liang, Q. Li, Y. C. Xu, Q. R. Wang, L. Jiang, *Org. Lett.* **2011**, *13*, 6082-6085; f) G. K. S. Prakash, A. K. Yudin, *Chem. Rev.* **1997**, *97*, 757-786.

[23] a) P. Novák, A. Lishchynskyi, V. V. Grushin, *Angew. Chem. Int. Ed.* **2012**, **51**, 7767-7770; *Angew. Chem.* **2012**, *124*, 7887-7890; b) A. Zanardi, M. A. Novikov, E. Martin, J. Benet-Buchholz, V. V. Grushin, *J. Am. Chem. Soc.* **2011**, *133*, 20901-20913.

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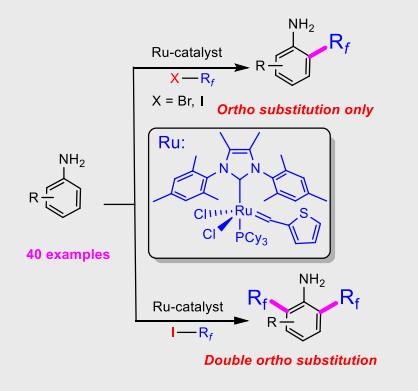

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