



Cite this: *Chem. Commun.*, 2019, 55, 13358

Received 4th September 2019,  
Accepted 10th October 2019

DOI: 10.1039/c9cc06905d

rsc.li/chemcomm

# Rhodium-mediated $^{18}\text{F}$ -oxyfluorination of diazoketones using a fluorine-18-containing hypervalent iodine reagent†

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**Geminal  $^{18}\text{F}$ -oxyfluorination of diazoketones was performed in the presence of rhodium mediators. The reactions were performed using a hypervalent iodine-based [ $^{18}\text{F}$ ]fluoro-benziodoxole reagent. By this methodology various  $\alpha$ -[ $^{18}\text{F}$ ]fluoro ethers were obtained in high radiochemical yield (up to 98%) and molar activity ( $216\text{ GBq } \mu\text{mol}^{-1}$ ).**

Organofluorine compounds have found a lot of recent applications in the pharmaceutical<sup>1</sup> and agrochemical industries<sup>2</sup> as well as in medical diagnostics.<sup>3</sup> A high demand of structurally diverse organofluorine compounds in drug discovery<sup>1</sup> and crop-protection<sup>2b</sup> has led to a revolutionary development of new methodologies in the synthesis of organofluorine compounds.<sup>4</sup> In recent years this development has been focused on the use of new reagents and catalytic methods for the synthesis of organofluorines with high selectivity under mild reaction conditions.<sup>4</sup> However, fluorine-18 labelling of organic compounds for Positron Emission Tomography (PET)<sup>3</sup> (which is one of the most important fields of organofluorine chemistry in medical diagnostics), has experienced less benefits of the development of synthetic organofluorine chemistry than the other fields mentioned above. Indeed, bridging the gap between recent advances in organofluorine chemistry and fluorine-18 labelling of PET tracers<sup>5</sup> has become one of the greatest challenges in synthetic methodology.<sup>3a,6</sup> The main difficulty is to adapt the use of new reagents and catalysts to the conditions of fluorine-18 labelling in a clinical environment. Some of the most important challenges of the adaptation (translation) of stoichiometric scale fluorine-19 chemistry to fluorine-18 labelling methods are: (i) downscaling the amounts of the fluorinating reagents to micromolar sometimes picomolar scale; (ii) requirement of very high fluorine-18 isotopic purity of the product (which is characterized by the molar activity); and (iii) the brief timescale of the synthesis dictated

by the half-life of fluorine-18 (109.7 minutes). A typical problem with downscaling (see (i) above) of the reactions is that certain side-reactions (leading to insignificant decrease of the yields in stoichiometric fluorine-19 reactions) may prevail in the case of using minute amounts of fluorine-18 reagents, completely inhibiting the formation of the desired  $^{18}\text{F}$ -fluorinated products. Fluorine isotope exchange is, of course, not an issue in the development of new reactions with the natural fluorine isotope. However, exchange of fluorine-18 isotope with fluorine-19 (arising from fluorinated reactants or ambient fluorine-19 sources) leads to low molar activity of a  $^{18}\text{F}$ -labelled product limiting its use as a PET tracer (see (ii) above).

As a part of our organofluorine chemistry program,<sup>7</sup> we have studied the use of the increasingly popular hypervalent iodine-based fluorinating reagents<sup>8</sup> for fluorine-18 labelling.<sup>7f</sup> [ $^{18}\text{F}$ ]Fluoro-benziodoxole is a versatile electrophilic reagent, which can be easily generated (from [ $^{18}\text{F}$ ]Bu<sub>4</sub>NF) and purified in a standard clinical environment.<sup>7f</sup> A particularly attractive feature of [ $^{18}\text{F}$ ]fluoro-benziodoxole, [ $^{18}\text{F}$ ]1, is that it can be used for fluorine-18 labelling with a remarkably high molar activity,<sup>7f</sup> which is several orders of magnitude higher than the molar activity reported for other electrophilic fluorinating reagents, such as [ $^{18}\text{F}$ ]F<sub>2</sub> and related reagents.<sup>9</sup>

In this paper we report our studies on geminal  $^{18}\text{F}$ -oxyfluorination of diazocarbonyl compounds with [ $^{18}\text{F}$ ]fluoro-benziodoxole, [ $^{18}\text{F}$ ]1 (Fig. 1c). Previously, Gouverneur and co-workers reported a difluorination reaction of diazocarbonyls using [ $^{18}\text{F}$ ]Et<sub>4</sub>NF as a nucleophilic fluorine-18 source and pTolIF<sub>2</sub> as an electrophilic fluorine-19 source (Fig. 1a).<sup>6b</sup> Subsequently, Doyle and co-workers<sup>6d</sup> described a copper-catalysed asymmetric nucleophilic  $^{18}\text{F}$ -fluorination of diazocarbonyls (Fig. 1b) in good radiochemical yields and molar activity. The methodology of using an electrophilic [ $^{18}\text{F}$ ]fluoro-benziodoxole reagent ([ $^{18}\text{F}$ ]1) is based on our<sup>7c</sup> recent rhodium catalysed geminal oxyfluorination method. Using this methodology a biologically relevant  $\alpha$ -fluoro ether motif<sup>2a</sup> can be introduced in a single reaction step in a multicomponent process (Fig. 1c).

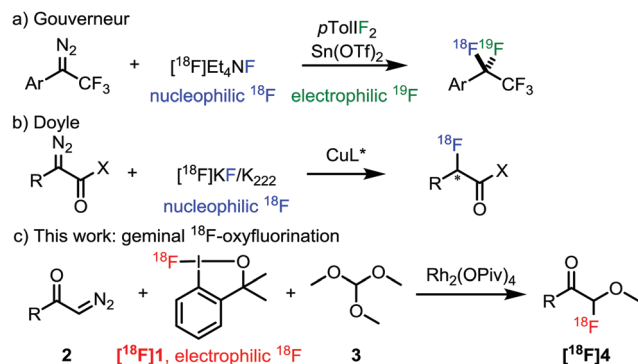
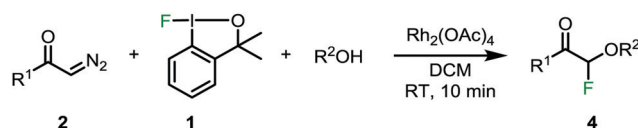
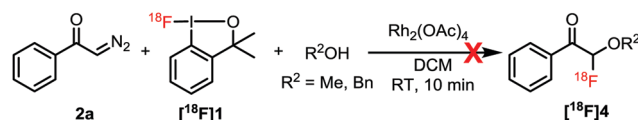
As mentioned above stoichiometric amounts of diazocarbonyl compounds (2), alcohols and fluoro-benziodoxole (1) react readily

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† Electronic supplementary information (ESI) available: Experimental procedures, characterization data and radiochemistry. See DOI: 10.1039/c9cc06905d



Fig. 1  $^{18}\text{F}$ -Fluorination of diazo compounds.Fig. 2 Geminal oxyfluorination of diazoketones with stoichiometric amounts of fluoro-benziodoxole **1**.<sup>7c</sup>Fig. 3 Attempted  $^{18}\text{F}$ -labelling of diazoketones using alcohols as nucleophiles.

in the presence of a rhodium catalyst to give geminal oxyfluorinated products **4** (Fig. 2).<sup>7c</sup> However, repeating the reaction with minute amounts of  $^{18}\text{F}$ **1**, formation of oxyfluorinated products  $^{18}\text{F}$ **4** could not be detected (Fig. 3). Variation of the reaction conditions and application of different alcohols was not helpful. We hypothesized that an unfavourable downscaling effect (see problem (i) above) prevented the formation of the expected oxyfluorinated products  $^{18}\text{F}$ **4**. As **1** is an electrophilic reagent, it readily reacts with nucleophiles. The reaction of **1** with stoichiometric amounts of alcohols is very slow at room temperature. However, micromolar amounts of  $^{18}\text{F}$ **1** probably reacted completely with the enormous excess of the alcohol component instead of the vinyl-ether intermediate (see below) of the desired reaction. In order to avoid this side reaction, we employed trimethyl orthoformate **3** as a nucleophile.

After optimization of the reaction conditions, we found that conducting the reaction of diazoketone **2a** with  $^{18}\text{F}$ **1** in the presence of  $\text{Rh}_2(\text{OPiv})_4$  in neat **3**,  $^{18}\text{F}$ -oxyfluorinated product  $^{18}\text{F}$ **4a** was obtained in excellent (98%) RCY (Table 1, entry 1). Deviations from these conditions led to a decreased amount of  $^{18}\text{F}$ **4a** or lack of  $^{18}\text{F}$ -oxyfluorination reaction. When methanol was used as a solvent instead of **3**, formation of  $^{18}\text{F}$ **4a** was not observed (entry 2), which is consistent with the above-mentioned findings (Fig. 3). Interestingly, traces (2%) of fluorine-18 labelled benzyloxylated product were formed using benzyl alcohol instead of **3** (entry 3). When a 1 : 1 mixture of DCM and orthoformate **3**

Table 1 Deviation of reaction conditions<sup>a</sup>

| Entry | Deviation                                                                            | RCY <sup>b</sup> (%)               |
|-------|--------------------------------------------------------------------------------------|------------------------------------|
| 1     | None                                                                                 | 98 ± 1 ( <i>n</i> = 2)             |
| 2     | Methanol instead of <b>3</b>                                                         | 0 ( <i>n</i> = 2)                  |
| 3     | Benzyl alcohol instead of <b>3</b>                                                   | 2 ± 2 ( <i>n</i> = 2) <sup>c</sup> |
| 4     | DCM/ <b>3</b> 1 : 1                                                                  | 0 ( <i>n</i> = 2)                  |
| 5     | $\text{Rh}_2(\text{OAc})_4$ instead of $\text{Rh}_2(\text{OPiv})_4$                  | 90 ± 2 ( <i>n</i> = 2)             |
| 6     | $\text{Rh}_2(\text{esp})_2$ instead of $\text{Rh}_2(\text{OPiv})_4$                  | 21 ± 1 ( <i>n</i> = 2)             |
| 7     | $\text{Rh}_2(\text{TPA})_4$ instead of $\text{Rh}_2(\text{OPiv})_4$                  | 26 ± 9 ( <i>n</i> = 2)             |
| 8     | No Rh                                                                                | 0 ( <i>n</i> = 2)                  |
| 9     | $^{18}\text{F}$ <b>Bu</b> <sub>4</sub> <b>NF</b> instead of $^{18}\text{F}$ <b>1</b> | 0 ( <i>n</i> = 2)                  |

<sup>a</sup> Unless otherwise stated, to a mixture of  $\text{Rh}_2(\text{OPiv})_4$  (0.5 mg, 0.8 μmol) and  $^{18}\text{F}$ **1** was added a solution of **2a** (2 mg, 14 μmol) in **3** (500 μL) before stirring at room temperature for 10 minutes. <sup>b</sup> RCY was estimated by radio-HPLC analysis of the crude reaction mixture. N.B. Previously, this value was referred as radiochemical conversion (RCC).<sup>10</sup> <sup>c</sup> The corresponding benzyloxylated product was formed.

was used, formation of  $^{18}\text{F}$ **4a** was not observed (entry 4). This emphasizes the importance of using **3** as solvent for the reaction. We have also tested different rhodium complexes in the reaction (entries 5–7). Application of  $\text{Rh}_2(\text{OAc})_4$  instead of  $\text{Rh}_2(\text{OPiv})_4$  (entry 5) led to a slight decrease of the RCY (90%), probably because of the lower solubility of  $\text{Rh}_2(\text{OAc})_4$  in **3**. When we switched to  $\text{Rh}_2(\text{esp})_2$  or  $\text{Rh}_2(\text{TPA})_4$  the RCY values were substantially decreased (entries 6 and 7). The presence of a rhodium complex, such as  $\text{Rh}_2(\text{OPiv})_4$  is essential for the  $^{18}\text{F}$ -oxyfluorination reaction, as in the absence of rhodium  $^{18}\text{F}$ **4a** was not formed (entry 8). In addition, the oxyfluorination process requires the presence of an electrophilic fluorinating reagent, such as  $^{18}\text{F}$ **1**. Thus formation of  $^{18}\text{F}$ **4a** was not observed when  $^{18}\text{F}$ **1** was replaced by a nucleophilic fluorine-18 source  $^{18}\text{F}$ **Bu**<sub>4</sub>**NF** (entry 9). Probably due to steric reasons, trimethyl orthoformate **3** is a much weaker nucleophile than MeOH. This is beneficial for the present fluorine-18 labelling method, as, unlike MeOH, **3** did not solvolyse the micromolar amounts of  $^{18}\text{F}$ **1** (compare entries 1 and 2). However, using orthoformates instead of alcohols as nucleophiles in this multi-component reaction imposes some limitations as well. For example, application of triethyl orthoformate (instead of **3**) did not result in α- $^{18}\text{F}$ fluoro ether product. This can be explained by the increase of the steric hindrance in triethyl orthoformate leading to further lowering of the nucleophilicity of the reagent compared to MeOH or trimethyl orthoformate (see mechanistic discussion below, Fig. 6).

With the optimized conditions in hand, we sought to explore the substrate scope of this labelling reaction (Fig. 4) using different diazocarbonyl compounds (**2**). Under these conditions diazoketone **2b**, bearing a naphthyl substituent, gave about as high RCY (94%) as **2a** (98%). Diazoketones with electron-withdrawing halogen substituents, such as bromine and fluorine, reacted smoothly, and products  $^{18}\text{F}$ **4c** and  $^{18}\text{F}$ **4d** were obtained in 91% and 96% RCY respectively. However, in the presence of a



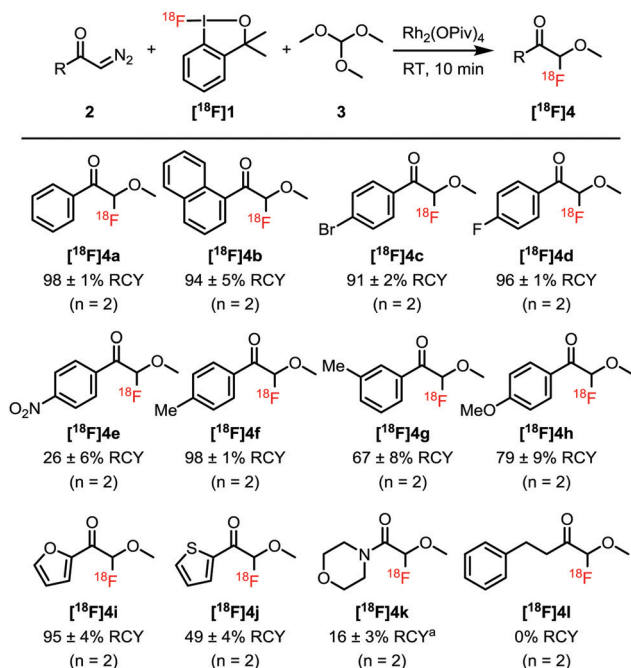


Fig. 4 Substrate scope in Rh-mediated electrophilic  $^{18}\text{F}$ -labelling of diazoketones. RCY estimated by radio-HPLC analysis of the crude reaction mixture starting from  $[^{18}\text{F}]\text{1}$ . <sup>a</sup> The reaction was performed at 90 °C.

nitro group in the diazoketone substrate, the RCY dropped considerably for the formation of  $[^{18}\text{F}]\text{4e}$  (26%). The reaction also proceeded with good to excellent RCY in the presence of electron-donating substituents in the aromatic ring of the diazoketone. Thus, 4-methyl-substituted diazoketone **2f** reacted to give  $[^{18}\text{F}]\text{4f}$  in excellent (98%) RCY, whereas its isomer **2g** afforded  $[^{18}\text{F}]\text{4g}$  in 67% RCY. Diazoketone **2h**, bearing a 4-methoxy substituent, afforded the corresponding product  $[^{18}\text{F}]\text{4h}$  in 79% RCY. The reaction could also be applied to heterocyclic diazoketones, such as furane (**2i**) and thiophene (**2j**) derivatives. Thus, labelled compound  $[^{18}\text{F}]\text{4i}$  was obtained in excellent (95%) RCY, while thiophene containing product  $[^{18}\text{F}]\text{4j}$  was only obtained in 49% RCY. Not only diazoketones but diazoamide derivative **2k** can also be used as a substrate. Thus,  $[^{18}\text{F}]\text{4k}$  could be obtained in 16% RCY, when the reaction was performed at 90 °C (instead of room temperature, which was typically used). The low RCY and the high temperature required for the reaction indicates a lower reactivity for the diazoamide substrates compared to the diazoketones. Fluorine-18 labelling of aliphatic diazoketones was not successful. For example, we were not able to obtain  $[^{18}\text{F}]\text{4l}$ . This result was surprising as the reaction with the natural fluorine isotope using equimolar amounts of **1** and **2l** in trimethyl orthoformate gave **4l**. Most probably, a so far unknown side reaction prevented formation of  $[^{18}\text{F}]\text{4l}$ .

The optimized procedure was employed to determine the activity yield (AY) and molar activity ( $A_m$ ) of an isolated labelled compound.<sup>10</sup> These studies were performed with diazoketone **2c** bearing an aromatic bromine substituent. The aromatic bromide functionality in product  $[^{18}\text{F}]\text{4c}$  can be used in subsequent Suzuki–Miyaura coupling as a prosthetic group.<sup>3b,6i</sup> For determination of the AY and  $A_m$ , 2.70 GBq of  $[^{18}\text{F}]\text{1}$  was reacted with **2c** affording

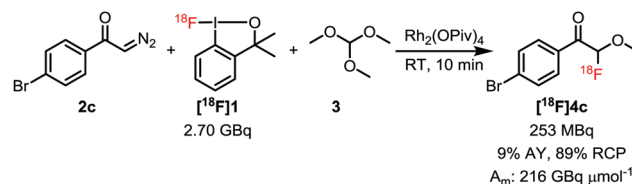


Fig. 5 Isolation and molar activity determination of  $[^{18}\text{F}]\text{4c}$ .

$[^{18}\text{F}]\text{4c}$  in 38% RCY. After isolation by semi-preparative HPLC we obtained 253 MBq of purified  $[^{18}\text{F}]\text{4c}$  (AY = 9% with respect to  $[^{18}\text{F}]\text{1}$ ) with a radiochemical purity (RCP) of 89%. This activity of purified  $[^{18}\text{F}]\text{4c}$  corresponds to a molar activity ( $A_m$ ) of 216 GBq  $\mu\text{mol}^{-1}$ , determined 110 minutes after the end of the bombardment (Fig. 5). This value is in the range of our<sup>7f</sup> previously reported value for labelling with  $[^{18}\text{F}]\text{1}$  and it is orders of magnitude higher than those obtained using electrophilic  $^{18}\text{F}$ -fluorination reagents derived from  $[^{18}\text{F}]\text{F}_2$ .<sup>9b,d,f</sup>

Based on our previous experimental<sup>7c,11</sup> and DFT modelling<sup>12</sup> studies on the rhodium catalysed oxyfluorination of diazocarbonyl compounds with alcohols, we propose a catalytic cycle for using trimethyl orthoformate as a nucleophile (Fig. 6).

The initial step of the above oxyfluorination reaction is most probably the formation of rhodium carbene **B** from  $\text{Rh}_2(\text{OPiv})_4$  and diazoketone **2** via intermediate **A**.<sup>13</sup> Alcohols and ethers readily form onium ylides with electrophilic rhodium carbenes (such as **B**).<sup>14</sup> Thus, nucleophilic attack of trimethyl orthoformate

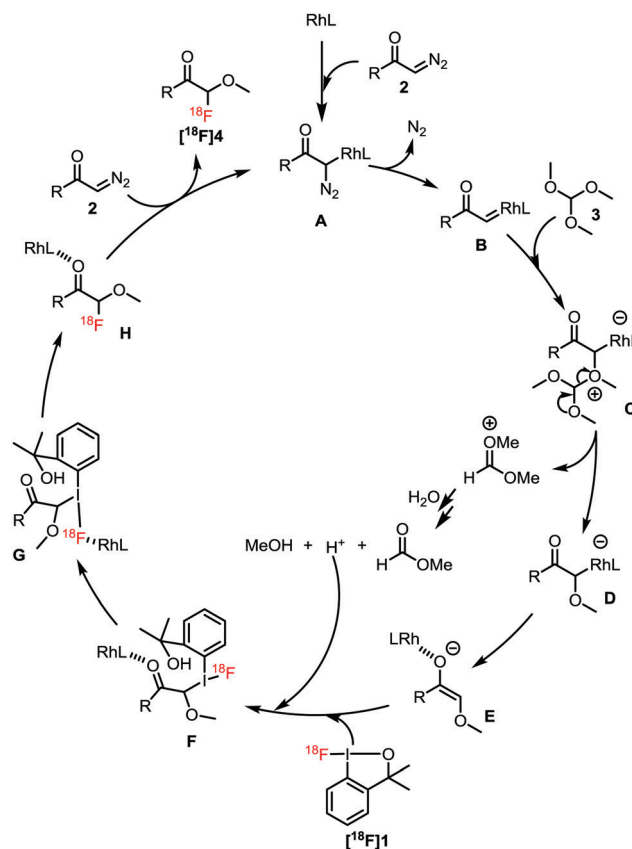


Fig. 6 Suggested mechanism for  $^{18}\text{F}$ -fluorination of diazoketones.



3 on rhodium carbene **B** leads to the formation of rhodium ylide **C**. Obviously, **3** is more sterically hindered, and thus a weaker nucleophile than the corresponding alcohols, which were used in our previous studies<sup>7c</sup> for oxyfluorination with the natural isotope in **1**. Formation of ylide **C** is affected by the lower nucleophilicity of trimethyl orthoformate **3** vs. MeOH or other alcohols. Our DFT modelling studies have shown that rhodium ylides,<sup>12</sup> such as **C**, readily rearrange to vinyl ethers, such as **E**. The key step of the oxyfluorination reaction<sup>12a</sup> is the electrophilic addition of [<sup>18</sup>F]**1** to vinyl ether **E** to form intermediate **F**. As mentioned above, a possible reason for the unsuccessful oxyfluorination of **2** with MeOH (Fig. 3) is that the micromolar amounts of [<sup>18</sup>F]**1** reacted with the large excess of MeOH instead of vinyl ether **E**. After rhodium migration and isomerization of the I–F bond to form intermediate **G**, C–F bond formation by displacement of the hypervalent iodine gives **H**.<sup>12a</sup> Finally, dissociation of rhodium gives the final oxyfluorinated product [<sup>18</sup>F]**4**.

In summary, we have presented an efficient fluorine-18 labelling method for the one-step synthesis of the biologically relevant  $\alpha$ -[<sup>18</sup>F]fluoro ether motif.<sup>2a</sup> The reaction is based on the downscaling/translation of our rhodium-catalysed oxyfluorination of diazoketones. The key reagent is [<sup>18</sup>F]fluoro-benziodoxole, [<sup>18</sup>F]**1**, which is an electrophilic <sup>18</sup>F-fluorinating reagent generated in an operationally simple process from [<sup>18</sup>F]Bu<sub>4</sub>NF in the standard clinical environment. The fluorine-18 oxyfluorination reactions were performed rapidly typically under mild reaction conditions, affording fluorine-18 labelled compounds in up to 98% RCY. A preparative <sup>18</sup>F-oxyfluorination experiment gave the  $\alpha$ -[<sup>18</sup>F]fluoro ether product with a molar activity of 216 GBq  $\mu$ mol<sup>−1</sup>, which is a higher value compared to typical molar activities reported for fluorine-18 products obtained using other electrophilic fluorinating reagents. We hope that this study contributes to the application of electrophilic fluorinating reagent [<sup>18</sup>F]**1** extending the reagent scope of fluorine-18 labelling of PET tracers to hypervalent iodines.

We thank the Knut och Alice Wallenbergs Foundation (Dnr: 2018.0066) and Swedish Research Council (VR) for financial support and Carl Tryggers Foundation (CTS 17:458) for a postdoctoral fellowship to X. J.

## Conflicts of interest

There are no conflicts to declare.

## Notes and references

- Y. Zhou, J. Wang, Z. Gu, S. Wang, W. Zhu, J. L. Aceña, V. A. Soloshonok, K. Izawa and H. Liu, *Chem. Rev.*, 2016, **116**, 422.
- (a) F. Leroux, P. Jeschke and M. Schlosser, *Chem. Rev.*, 2005, **105**, 827; (b) P. Jeschke, *ChemBioChem*, 2004, **5**, 570.
- (a) X. Deng, J. Rong, L. Wang, N. Vasdev, L. Zhang, L. Josephson and S. H. Liang, *Angew. Chem., Int. Ed.*, 2019, **58**, 2580; (b) S. Preshlock, M. Tredwell and V. Gouverneur, *Chem. Rev.*, 2016, **116**, 719.
- (a) J. Charpentier, N. Früh and A. Togni, *Chem. Rev.*, 2015, **115**, 650; (b) T. Liang, C. N. Neumann and T. Ritter, *Angew. Chem., Int. Ed.*, 2013, **52**, 8214.
- M. G. Campbell, J. Mercier, C. Genicot, V. Gouverneur, J. M. Hooker and T. Ritter, *Nat. Chem.*, 2017, **9**, 1.
- (a) J. R. Wolstenhulme and V. Gouverneur, *Acc. Chem. Res.*, 2014, **47**, 3560; (b) E. Emer, J. Twilton, M. Tredwell, S. Calderwood, T. L. Collier, B. Liégault, M. Taillefer and V. Gouverneur, *Org. Lett.*, 2014, **16**, 6004; (c) S. Verhoog, C. W. Kee, Y. Wang, T. Khotavivattana, T. C. Wilson, V. Kersemans, S. Smart, M. Tredwell, B. G. Davis and V. E. Gouverneur, *J. Am. Chem. Soc.*, 2018, **140**, 1572; (d) E. E. Gray, M. K. Nielsen, K. A. Choquette, J. A. Kalow, T. J. A. Graham and A. G. Doyle, *J. Am. Chem. Soc.*, 2016, **138**, 10802; (e) M. K. Nielsen, C. R. Ugaz, W. Li and A. G. Doyle, *J. Am. Chem. Soc.*, 2015, **137**, 9571; (f) E. Lee, A. S. Kamlet, D. C. Powers, C. N. Neumann, G. B. Boursalian, T. Furuya, D. C. Choi, J. M. Hooker and T. Ritter, *Science*, 2011, **334**, 639; (g) M. S. Sanford and P. J. H. Scott, *ACS Cent. Sci.*, 2016, **2**, 128; (h) L. Trump, A. Lemos, B. Lallemand, P. Pasau, J. Mercier, C. Lemaire, A. Luxen and C. Genicot, *Angew. Chem., Int. Ed.*, 2019, **58**, 13149; (i) D. van der Born, A. Pees, A. J. Poot, R. V. A. Orru, A. D. Windhorst and D. J. Vugts, *Chem. Soc. Rev.*, 2017, **46**, 4709; (j) A. Pees, C. Sewing, M. J. W. D. Vosjan, V. Tadino, J. D. M. Herscheid, A. D. Windhorst and D. J. Vugts, *Chem. Commun.*, 2018, **54**, 10179; (k) Z. Yuan, R. Cheng, P. Chen, G. Liu and S. H. Liang, *Angew. Chem., Int. Ed.*, 2016, **55**, 11882.
- (a) N. O. Ilchenko, B. O. A. Tasch and K. J. Szabó, *Angew. Chem., Int. Ed.*, 2014, **53**, 12897; (b) W. Yuan and K. J. Szabó, *Angew. Chem., Int. Ed.*, 2015, **54**, 8533; (c) W. Yuan, L. Eriksson and K. J. Szabó, *Angew. Chem., Int. Ed.*, 2016, **55**, 8410; (d) M. Luebecke, D. Bezhan and K. J. Szabó, *Chem. Sci.*, 2019, **10**, 5990; (e) A. Bermejo Gomez, M. Cortes, M. Luebecke, M. Johansson, C. Halldin, K. J. Szabó and M. Schou, *Chem. Commun.*, 2016, **52**, 13963; (f) M. A. Cortes Gonzalez, P. Nordeman, A. Bermejo Gomez, D. N. Meyer, G. Antoni, M. Schou and K. J. Szabó, *Chem. Commun.*, 2018, **54**, 4286.
- (a) S. V. Kohlhepp and T. Gulder, *Chem. Soc. Rev.*, 2016, **45**, 6270; (b) G. C. Geary, E. G. Hope and A. M. Stuart, *Angew. Chem., Int. Ed.*, 2015, **54**, 14911; (c) B. Yang, K. Chansaenpak, H. Wu, L. Zhu, M. Wang, Z. Li and H. Lu, *Chem. Commun.*, 2017, **53**, 3497.
- (a) J. Bergman and O. Solin, *Nucl. Med. Biol.*, 1997, **24**, 677; (b) H. Teare, E. G. Robins, E. Arstad, S. K. Luthra and V. Gouverneur, *Chem. Commun.*, 2007, 2330; (c) S. Forsback, O. Eskola, M. Haaparanta, J. Bergmann and O. Solin, *Radiachim. Acta*, 2008, **96**, 845; (d) H. Teare, E. G. Robins, A. Kirjavainen, S. Forsback, G. Sandford, O. Solin, S. K. Luthra and V. Gouverneur, *Angew. Chem., Int. Ed.*, 2010, **49**, 6821; (e) I. S. R. Stenhagen, A. K. Kirjavainen, S. J. Forsback, C. G. Jorgensen, E. G. Robins, S. K. Luthra, O. Solin and V. Gouverneur, *Chem. Commun.*, 2013, **49**, 1386; (f) F. Buckingham, A. K. Kirjavainen, S. Forsback, A. Krzyczmonik, T. Keller, I. M. Newington, M. Glaser, S. K. Luthra, O. Solin and V. Gouverneur, *Angew. Chem., Int. Ed.*, 2015, **54**, 13366.
- H. H. Coenen, A. D. Gee, M. Adam, G. Antoni, C. S. Cutler, Y. Fujibayashi, J. M. Jeong, R. H. Mach, T. L. Mindt, V. W. Pike and A. D. Windhorst, *Nucl. Med. Biol.*, 2017, **55**, v.
- (a) W. Yuan and K. J. Szabó, *ACS Catal.*, 2016, **6**, 6687; (b) M. Luebecke, W. Yuan and K. J. Szabó, *Org. Lett.*, 2017, **19**, 4548.
- (a) B. K. Mai, K. J. Szabó and F. Himo, *ACS Catal.*, 2018, **8**, 4483; (b) B. K. Mai, K. J. Szabó and F. Himo, *Org. Lett.*, 2018, **20**, 6646.
- C. Werlé, R. Goddard, P. Philipps, C. Farès and A. Fürstner, *J. Am. Chem. Soc.*, 2016, **138**, 3797.
- X. Guo and W. Hu, *Acc. Chem. Res.*, 2013, **46**, 2427.

