



Cite this: *Dalton Trans.*, 2022, **51**, 5004

Received 27th January 2022,  
Accepted 1st March 2022

DOI: 10.1039/d2dt00266c

rsc.li/dalton

## Synthesis of carbon-11 radiolabelled transition metal complexes using $^{11}\text{C}$ -dithiocarbamates†

Sara Cesarec,<sup>a</sup> Fraser Edgar,<sup>a,b</sup> Titan Lai,<sup>a</sup> Christophe Plisson,<sup>c</sup>  
Andrew J. P. White<sup>a</sup> and Philip W. Miller<sup>\*a</sup>

**A novel radiolabelling method exploiting  $^{11}\text{C}$ -dithiocarbamate ligands has been used to generate  $^{11}\text{C}$ -labelled Au(i), Au(III), Pd(II) and Pt(II) complexes in high radiochemical yields (71–99%). Labelled complexes were prepared in a rapid one-pot procedure via the substitution reaction of  $^{11}\text{C}$ -dithiocarbamate ligands with appropriate transition metal chloride precursors.**

Positron emission tomography (PET) is a functional imaging technique that enables the visualisation and quantification of radiolabelled position emitting tracer compounds *in vivo*.<sup>1,2</sup> PET provides a wealth of information on the biodistribution, kinetic and metabolic profiles of tracers for a range of clinical applications in oncology, cardiology and neurology, enabling more accurate diagnoses and improved interventions.<sup>3–5</sup> PET is also used in drug discovery programmes where knowledge of the pharmacokinetic behaviour of novel radiolabelled drug candidates can accelerate selection and improve dosing regimens.<sup>6</sup>

Carbon-11, along with fluorine-18, is a key positron emitting radionuclide commonly used for the synthesis of small organic molecule-based PET tracers.<sup>7,8</sup> Its physical characteristics: high positron yield (>99%), 20.4 min half-life, favourable positron energy ( $E_{\text{max}} = 0.960$  MeV), high yielding cyclotron production routes and high theoretical molar activities mean that carbon-11 is at the forefront of novel PET radiotracer development.<sup>9,10</sup> However, the short half-life of carbon-11 presents significant time challenges and hence limits the number of chemical reactions that can be completed within a short

reaction window (*ca.* <60 min). To add to this challenge, [ $^{11}\text{C}$ ]  $\text{CO}_2$  is the main precursor to almost all carbon-11 labelled compounds, and is often transformed to more reactive [ $^{11}\text{C}$ ]  $\text{CH}_3\text{I}$  *via* a reduction and free-radical iodination process. [ $^{11}\text{C}$ ]  $\text{CH}_3\text{I}$  is then added to a target molecule *via* a nucleophilic substitution reaction to generate the  $^{11}\text{C}$ -methylated tracer. In recent years, much effort has been devoted to expanding the scope of  $^{11}\text{C}$  chemistry beyond simple *N*-, *S*-, and *O*-methylation reactions and into developing new  $^{11}\text{C}$  precursors and labelling strategies. For example, notable progress has been made in the  $^{11}\text{C}$ -labelling of carbonyl groups with [ $^{11}\text{C}$ ]CO,<sup>11</sup> [ $^{11}\text{C}$ ]CO<sub>2</sub>,<sup>12</sup> and [ $^{11}\text{C}$ ]COF<sub>2</sub>,<sup>13</sup> cyano groups using [ $^{11}\text{C}$ ]HCN<sup>14,15</sup> and trifluoromethyl groups with [ $^{11}\text{C}$ ]HCF<sub>3</sub>.<sup>16</sup>

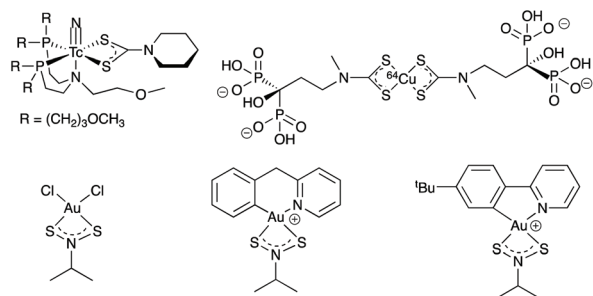
The novel  $^{11}\text{C}$  precursor [ $^{11}\text{C}$ ]CS<sub>2</sub><sup>17</sup> has been developed by us and used to access  $^{11}\text{C}$ -labelled organosulfur compounds that would be challenging to prepare with established precursors. To date, our group and others have used this method to generate  $^{11}\text{C}$ -labelled organic molecules including: dithiocarbamates, thioureas, isothioureas, thiocyanates, thiazolones, and the progesterone agonist Tanaproget.<sup>18–21</sup> Dithiocarbamate compounds in particular have found wide ranging applications as precursors to nanomaterials,<sup>22</sup> agrochemicals<sup>23</sup> and therapeutics.<sup>24</sup> They are readily prepared *via* the reaction of carbon disulfide and primary or secondary amines in the presence of organic or inorganic bases. Dithiocarbamates are non-selective ligands known to form complexes with all the transition metals in a range of oxidation states, typically forming thermodynamically stable bidentate chelates.<sup>25,26</sup> The formation of dithiocarbamate complexes is normally fast and straightforward, and often simply involve mixing the dithiocarbamate with transition metal precursors in solvent at room temperature. The ease of formation of dithiocarbamates and their chelating abilities, coupled with their technically simple and fast complexation reactions have led to their investigation as ligands for the development of imaging agents with <sup>99m</sup>Tc,<sup>27–29</sup> <sup>64</sup>Cu,<sup>30</sup> and other metal ions (Fig. 1).<sup>31</sup> Dithiocarbamate complexes have also received recurrent interest as therapeutics for targeting cancer, in particular Au(i) and Au(III) complexes have

<sup>a</sup>Department of Chemistry, Imperial College London, Molecular Sciences Research Hub, White City Campus, Wood Lane, London, W12 0BZ, UK.  
E-mail: philip.miller@imperial.ac.uk

<sup>b</sup>School of Biomedical Engineering and Imaging Sciences, King's College London, 4th Floor Lambeth Wing, St Thomas' Hospital, London, UK

<sup>c</sup>Inivicro, Burlington Danes Building, Hammersmith Hospital, Du Cane Road, London, UK

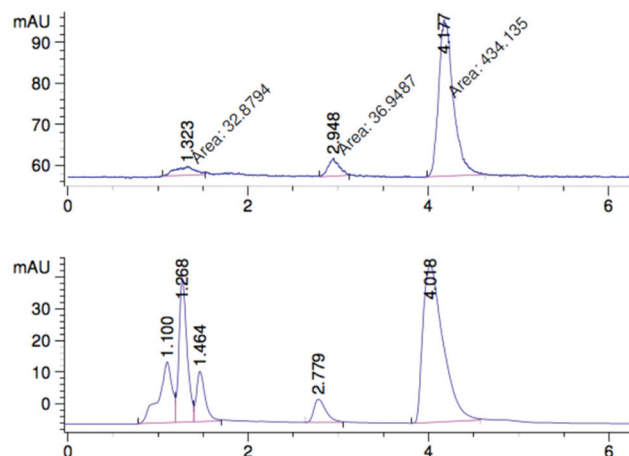
† Electronic supplementary information (ESI) available. CCDC 2130302–2130303. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/d2dt00266c



**Fig. 1**  $^{99m}\text{Tc}$  and  $^{64}\text{Cu}$  nuclear imaging agents bearing dithiocarbamate chelators (top). A range of  $\text{Au(III)}$  dithiocarbamate complexes that have anti-cancer properties (bottom).

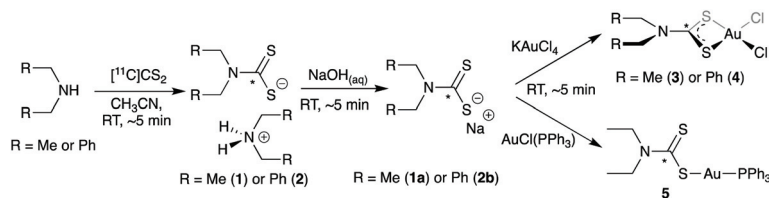
displayed anti-cancer properties for a range of tumour cell lines.<sup>32–36</sup> Given the extensive coordination chemistry of dithiocarbamates, we hypothesised that the generation of  $^{11}\text{C}$ -labelled dithiocarbamates would facilitate access to a diverse range of  $^{11}\text{C}$ -labelled transition metal complexes with generic and straightforward labelling protocols. Such labelled complexes could therefore aid in the understanding of the behaviour of transition metal-based therapeutics and result in the development of new PET imaging agents. Herein, we report a proof-of-principle strategy for labelling a range of late transition metal complexes *via* coordination with  $^{11}\text{C}$ -labelled dithiocarbamates.

$^{11}\text{C}$ Carbon disulfide was produced as previously reported *via* the high temperature gas phase reaction of  $^{11}\text{C}[\text{CH}_3\text{I}]$  with elemental sulfur.<sup>18</sup> Passing the gaseous  $^{11}\text{C}\text{CS}_2$  into an acetonitrile solution of secondary amine, either diethylamine or dibenzylamine, resulted in the quantitative trapping of  $^{11}\text{C}$



**Fig. 2** A representative radio-HPLC trace (top) and UV-HPLC trace (bottom) of the crude reaction mixture for the formation of  $[\text{AuCl}_2(^{11}\text{C})\text{S}_2\text{CNEt}_2]$  (**3**) (4.177 min) with co-injection of the unlabelled reference compound  $[\text{AuCl}_2(\text{S}_2\text{CNEt}_2)]$  (4.018 min).

$\text{CS}_2$  and formation of the carbon-11 labelled ammonium dithiocarbamate salts:  $^{11}\text{C}$  $N,N$ -diethyldithiocarbamate (**1**) and  $^{11}\text{C}$  $N,N$ -dibenzylthiocarbamate (**2**) (Scheme 1).  $\text{Au(III)}$  and  $\text{Au(I)}$  complexes were selected for proof-of-concept labelling studies owing to their abilities to form well-defined and stable bidentate or monodentate dithiocarbamate complexes, and also because of their potential for developing imaging agents to complement therapeutic gold-dithiocarbamate complexes. Addition of aqueous  $\text{NaOH}$  solution to  $^{11}\text{C}$  $N,N$ -diethyldithiocarbamate (**1**) followed by a solution of the gold precursor  $\text{K}[\text{AuCl}_4]$  and stirring for 5 min at room temperature resulted in the rapid and efficient labelling of  $[\text{AuCl}_2(^{11}\text{C})\text{S}_2\text{CNEt}_2]$  (**3**).

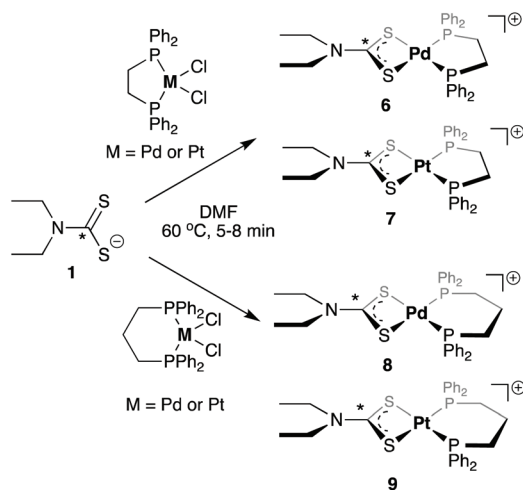


**Scheme 1** Radiosynthesis of  $^{11}\text{C}$ -labelled  $\text{Au(III)}$  and  $\text{Au(I)}$  complexes *via* the reaction of  $^{11}\text{C}$ diethyldithiocarbamate (**1a**) or  $^{11}\text{C}$ dibenzylthiocarbamate (**2b**) with  $\text{K}[\text{AuCl}_4]$  or  $\text{AuCl(PPh}_3\text{)}$  precursors.

**Table 1** Summary of results for  $^{11}\text{C}$ -labelling of  $\text{Au(III)}$ ,  $\text{Au(I)}$ ,  $\text{Pd(II)}$  and  $\text{Pt(II)}$  complexes

Entry	Transition metal Precursor	$^{11}\text{C}$ -labelling precursor	$^{11}\text{C}$ -labelled transition metal complex	RCY <sup>a</sup>
1	$\text{K}[\text{AuCl}_4]$	$^{11}\text{C}[\text{S}_2\text{CNEt}_2]^-$	$[\text{AuCl}_2(^{11}\text{C})\text{S}_2\text{CNEt}_2]$ ( <b>3</b> )	86% ( $n = 2$ )
2	$\text{K}[\text{AuCl}_4]$	$^{11}\text{C}[\text{S}_2\text{CNBn}_2]^-$	$[\text{AuCl}_2(^{11}\text{C})\text{S}_2\text{CNBn}_2]$ ( <b>4</b> )	71% ( $n = 2$ )
3	$[\text{AuCl(PPh}_3\text{)}]$	$^{11}\text{C}[\text{S}_2\text{CNEt}_2]^-$	$[\text{Au}(^{11}\text{C})\text{S}_2\text{CNEt}_2(\text{PPh}_3)]$ ( <b>5</b> )	86% ( $n = 3$ )
4	$[\text{PdCl}_2(\text{dppe})]$	$^{11}\text{C}[\text{S}_2\text{CNEt}_2]^-$	$[\text{Pd}(^{11}\text{C})\text{S}_2\text{CNEt}_2(\text{dppe})]^+$ ( <b>6</b> )	96% ( $n = 3$ )
5	$[\text{PtCl}_2(\text{dppe})]$	$^{11}\text{C}[\text{S}_2\text{CNEt}_2]^-$	$[\text{Pt}(^{11}\text{C})\text{S}_2\text{CNEt}_2(\text{dppe})]^+$ ( <b>7</b> )	89% ( $n = 3$ )
6	$[\text{PdCl}_2(\text{dppp})]$	$^{11}\text{C}[\text{S}_2\text{CNEt}_2]^-$	$[\text{Pd}(^{11}\text{C})\text{S}_2\text{CNEt}_2(\text{dppp})]^+$ ( <b>8</b> )	99% ( $n = 3$ )
7	$[\text{PtCl}_2(\text{dppp})]$	$^{11}\text{C}[\text{S}_2\text{CNEt}_2]^-$	$[\text{Pt}(^{11}\text{C})\text{S}_2\text{CNEt}_2(\text{dppp})]^+$ ( <b>9</b> )	94% ( $n = 3$ )

<sup>a</sup> Non-isolated radiochemical yield (RCY) determined by analytical radio-HPLC of the crude product.

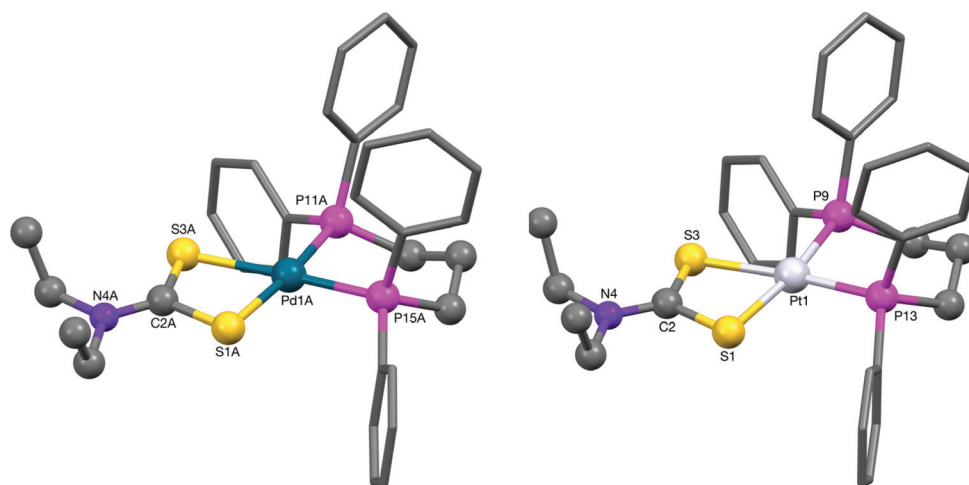


**Scheme 2** Radiosynthesis of  $^{11}\text{C}$ -labelled Pd(II) and Pt(II) complexes via the reaction of  $[^{11}\text{C}]\text{N,N}$ -diethyldithiocarbamate (**1**) with  $[\text{MCl}_2(\text{dppe})]$  or  $[\text{MCl}_2(\text{dppp})]$ ,  $\text{M} = \text{Pd}$  or  $\text{Pt}$ .

$\text{S}_2\text{CNET}_2$ ] (**3**) (Scheme 1, Table 1 entry 1 and Fig. 2) in 86% RCY. The reaction conditions for the formation of unlabelled of Au(III)–DTC complexes typically need to be carefully controlled owing to possible DTC ligand exchange reactions and formation of undesired  $[\text{Au}(\text{DTC})_2][\text{AuCl}_4]$  complexes. We expect, however, that the formation of such  $^{11}\text{C}$  labelled  $[\text{Au}(\text{DTC})_2]^+$  bischelates would be limited owing to the stoichiometry of  $^{11}\text{C}$  labelling reactions making them statistically unlikely to form in any significant amounts. The labelled  $[^{11}\text{C}]\text{N,N}$ -dibenzylthiocarbamate (**2**) was also found to react with  $\text{K}[\text{AuCl}_4]$  to give the analogous complex  $[\text{AuCl}_2][^{11}\text{C}]\text{S}_2\text{CNBN}_2$ ] (**4**) (Scheme 1, Table 1 entry 2), however, the average RCY of 71% obtained for **4** was reduced compared to complex **3**.

Based on the higher RCYs for complex **3** using  $[^{11}\text{C}]\text{N,N}$ -diethyldithiocarbamate, all remaining labelling studies were performed with this ligand. Reaction of **1** with the Au(I) precursor  $[\text{AuCl}(\text{PPh}_3)]$  to form  $[\text{Au}([^{11}\text{C}]\text{S}_2\text{CNET}_2)(\text{PPh}_3)]$  (**5**) under the same reaction conditions was also equally efficient giving a RCY of 86%, and demonstrating the method can also be used to form simple mono-dentate Au(I) complexes.

In order to expand the scope of these  $^{11}\text{C}$ -labelling reactions with other transition metals, a range of well-defined Pd(II) and Pt(II) diphosphine complexes were also investigated. Pd(II) and Pt(II) diphosphine complexes are known to form stable cationic chelating dithiocarbamate complexes,<sup>37,38</sup> and therefore present as suitable complexes for preliminary labelling reactions. We focused on labelling a small library of four Pd(II) and Pt(II) complexes containing the diphosphine ligands, 1,2-bis-diphenylphosphinoethane (dppe) and 1,3-bis-diphenylphosphinopropane (dppp), (Scheme 2). Unlabelled reference complexes were prepared via the reaction of sodium  $\text{N,N}$ -diethyldithiocarbamate with Pd(II) or Pt(II) diphosphine chloride salts.<sup>37,38</sup> Single crystal X-ray crystal structures were obtained for the reference complexes  $[\text{Pd}(\text{S}_2\text{CNET}_2)(\text{dppp})]\text{Cl}$  and  $[\text{Pt}(\text{S}_2\text{CNET}_2)(\text{dppp})]\text{Cl}$  (Fig. 3). The square planar molecular structures of the two complexes are isostructural and confirm the expected chelation of the dithiocarbamate ligand, varying only slightly in the bond lengths and angles at their respective metal centres (Table 2) and are similar to previously published DTC complexes.<sup>38,39</sup> Unlike the labelling reactions of the Au precursors that proceeded at room temperature, the reaction of  $^{11}\text{C}$ -dithiocarbamate **1** with  $[\text{PdCl}_2(\text{dppe})]$  or  $[\text{PtCl}_2(\text{dppe})]$  required heating to 60 °C to give appreciable RCYs within 5–8 min in DMF to facilitate solubility. Under these conditions the labelled complexes  $[\text{Pd}([^{11}\text{C}]\text{S}_2\text{CNET}_2)(\text{dppe})]\text{Cl}$  (**6**) and  $[\text{Pt}([^{11}\text{C}]\text{S}_2\text{CNET}_2)(\text{dppe})]\text{Cl}$  (**7**) were obtained in high RCYs of 96% and 89% respectively (Scheme 2, Table 1 entries 4 and 5). Labelling of the



**Fig. 3** Isostructural X-ray crystal structures of the square planar dithiocarbamate complexes:  $[\text{Pd}(\text{S}_2\text{CNET}_2)(\text{dppp})]\text{Cl}$  (one of the two independent complex cations present in the crystal of **8**, left) and  $[\text{Pt}(\text{S}_2\text{CNET}_2)(\text{dppp})]\text{Cl}$  (**9**, right), counter ions and solvent molecules have been removed for clarity.



**Table 2** Selected bond lengths (Å) and angles (°) data for complexes in crystals of [Pd(S<sub>2</sub>CNEt<sub>2</sub>)(dppp)]Cl (**8**) and [Pt(S<sub>2</sub>CNEt<sub>2</sub>)(dppp)]Cl (**9**)

Selected bond lengths (Å) for [Pd(S <sub>2</sub> CNEt <sub>2</sub> )(dppp)]Cl ( <b>8</b> )		Selected bond lengths (Å) [Pt(S <sub>2</sub> CNEt <sub>2</sub> )(dppp)]Cl ( <b>9</b> )	
Pd(1A)–P(15A)	2.2701(11)	Pt(1)–P(9)	2.2501(10)
Pd(1A)–P(11A)	2.2846(11)	Pt(1)–P(13)	2.2526(10)
Pd(1A)–S(1A)	2.3487(12)	Pt(1)–S(1)	2.3541(10)
Pd(1A)–S(3A)	2.3498(11)	Pt(1)–S(3)	2.3529(10)
Selected bond angles (°)		Selected bond angles (°)	
P(15A)–Pd(1A)–P(11A)	92.10(4)	P(9)–Pt(1)–P(13)	92.84(4)
S(1A)–Pd(1A)–S(3A)	75.25(4)	S(3)–Pt(1)–S(1)	74.99(4)

related Pd(II) and Pt(II) dppp complexes was discovered to be slightly more efficient resulting in near quantitative RCYs for both [Pd([<sup>11</sup>C]S<sub>2</sub>CNEt<sub>2</sub>)(dppp)]Cl (**8**) and [Pt([<sup>11</sup>C]S<sub>2</sub>CNEt<sub>2</sub>)(dppp)]Cl (**9**) (Scheme 2, Table 1 entries 6 and 7).

## Conclusions

In conclusion, a small range of novel <sup>11</sup>C-labelled late transition metal complexes has been prepared *via* the substitution reaction of <sup>11</sup>C-dialkyldithiocarbamates with metal chloride precursors. The method was discovered to be an efficient, rapid and practical one-pot process that was amenable to labelling Au(I), Au(III), Pd(II) and Pt(II) complexes in high RCYs. The versatility of such dithiocarbamates for coordination to transition metals opens the possibility for the generation of a wide range of labelled complexes that could find applications as PET imaging agents beyond the scope of conventional radiolabelled small organic molecules or could be used to complement a better understanding of the biology of transition metal-based therapeutics. We are currently investigating other DTC complexes that we anticipate could be translated to further <sup>11</sup>C radiolabelling studies and PET imaging applications.

## Author contributions

C. S. carried out the synthetic chemistry and <sup>11</sup>C-radiochemistry. F. E. and T. L. assisted in the isolation and crystallisation of complexes. P. W. M. and C. P. supervised <sup>11</sup>C-radiolabelling experiments. A. J. P. W. conducted the single crystal X-ray structure determinations. P. W. M. supervised the project. All authors contributed to the writing and proofreading of the manuscript.

## Conflicts of interest

There are no conflicts to declare.

## Acknowledgements

We are grateful to Imperial College London for the award of a studentship to C. S. and to the King's College London & Imperial College London EPSRC Centre for Doctoral Training in Medical Imaging (EP/L015226/1) for funding F. E. We are also grateful to the EPSRC (EP/L025140/1) and the Royal Society (RG110449) for funding.

## Notes and references

- M. E. Phelps, *Proc. Natl. Acad. Sci. U. S. A.*, 2000, **97**, 9226–9233.
- M. M. Khalil, *Basic science of PET imaging*, 2016.
- W. A. Weber, M. Schwaiger and N. Avril, *Nucl. Med. Biol.*, 2000, **27**, 683–687.
- T. H. Schindler, H. R. Schelbert, A. Quercioli and V. Dilsizian, *JACC Cardiovasc. Imaging*, 2010, **3**, 623–640.
- K. Heurling, A. Leuzy, M. Jonasson, A. Frick, E. R. Zimmer, A. Nordberg and M. Lubberink, *Brain Res.*, 2017, **1670**, 220–234.
- P. M. Matthews, E. A. Rabiner, J. Passchier and R. N. Gunn, *Br. J. Clin. Pharmacol.*, 2012, **73**, 175–186.
- P. W. Miller, N. J. Long, R. Vilar and A. D. Gee, *Angew. Chem., Int. Ed.*, 2008, **47**, 8998–9033.
- X. Deng, J. Rong, L. Wang, N. Vasdev, L. Zhang, L. Josephson and S. H. Liang, *Angew. Chem.*, 2019, **131**, 2604–2631.
- K. Dahl, C. Halldin and M. Schou, *Clin. Transl. Imaging*, 2017, **5**, 275–289.
- N. S. Goud, A. Bhattacharya, R. K. Joshi, C. Nagaraj, R. D. Bharath and P. Kumar, *J. Med. Chem.*, 2021, **64**, 1223–1259.
- J. Eriksson, G. Antoni, B. Långström and O. Itsenko, *Nucl. Med. Biol.*, 2021, **92**, 115–137.
- C. Taddei and A. D. Gee, *J. Labelled Compd. Radiopharm.*, 2018, **61**, 237–251.
- J. E. Jakobsson, S. Lu, S. Telu and V. W. Pike, *Angew. Chem., Int. Ed.*, 2020, **59**, 7256–7260.
- W. Zhao, H. G. Lee, S. L. Buchwald and J. M. Hooker, *J. Am. Chem. Soc.*, 2017, **139**, 7152–7155.
- Y. Xu and W. Qu, *Eur. J. Org. Chem.*, 2021, **2021**, 4653–4682.
- M. B. Haskali and V. W. Pike, *Chem. – Eur. J.*, 2017, **23**, 8156–8160.
- P. W. Miller and D. Bender, *Chem. – Eur. J.*, 2012, **18**, 433–436.
- T. Haywood, S. Kealey, S. Sánchez-Cabezas, J. J. Hall, L. Allott, G. Smith, C. Plisson and P. W. Miller, *Chem. – Eur. J.*, 2015, **21**, 9034–9038.
- T. Haywood, S. Cesarec, S. Kealey, C. Plisson and P. W. Miller, *MedChemComm*, 2018, **9**, 1311–1314.
- S. Merchant, L. Allott, L. Carroll, V. Tittrea, S. Kealey, T. H. Witney, P. W. Miller, G. Smith and E. O. Aboagye, *RSC Adv.*, 2016, **6**, 57569–57579.





- 21 H. Ishii, T. Yamasaki, J. Yui, Y. Zhang, M. Hanyu, M. Ogawa, N. Nengaki, A. B. Tsuji, Y. Terashima, K. Matsushima and M. R. Zhang, *Bioorg. Med. Chem. Lett.*, 2020, **30**, 126998.
- 22 J. C. Sarker and G. Hogarth, *Chem. Rev.*, 2021, **121**, 6057–6123.
- 23 J. P. Zubrod, M. Bundschuh, G. Arts, C. A. Brühl, G. Imfeld, A. Knäbel, S. Payraudeau, J. J. Rasmussen, J. Rohr, A. Scharmüller, K. Smalling, S. Stehle, R. Schulz and R. B. Schäfer, *Environ. Sci. Technol.*, 2019, **53**, 3347–3365.
- 24 L. Kaul, R. Süß, A. Zannettino and K. Richter, *iScience*, 2021, **24**, 1–14.
- 25 G. Hogarth, *Prog. Inorg. Chem.*, 2005, **53**, 71–561.
- 26 G. Hogarth, *Mini-Rev. Med. Chem.*, 2012, **12**, 1202–1215.
- 27 J. K. Bordoloi, D. Berry, I. U. Khan, K. Sunassee, R. T. M. De Rosales, C. Shanahan and P. J. Blower, *Dalton Trans.*, 2015, **44**, 4963–4975.
- 28 N. Salvatorese, D. Carta, C. Marzano, G. Gerardi, L. Melendez-Alafort and C. Bolzati, *J. Med. Chem.*, 2018, **61**, 11114–11126.
- 29 C. Bolzati, M. Cavazza-Ceccato, S. Agostini, F. Refosco, Y. Yamamichi, S. Tokunaga, D. Carta, N. Salvatorese, D. Bernardini and G. Bandoli, *Bioconjugate Chem.*, 2010, **21**, 928–939.
- 30 R. Torresmartinderosales, R. Tavaré, R. L. Paul, M. Jauregui-Osoro, A. Protti, A. Glaria, G. Varma, I. Szanda and P. J. Blower, *Angew. Chem., Int. Ed.*, 2011, **50**, 5509–5513.
- 31 D. J. Berry, R. Torres Martin de Rosales, P. Charoenphun and P. J. Blower, *Mini-Rev. Med. Chem.*, 2012, **12**, 1174–1183.
- 32 L. Cattaruzza, D. Fregona, M. Mongiat, L. Ronconi, A. Fassina, A. Colombatti and D. Aldinucci, *Int. J. Cancer*, 2011, **128**, 206–215.
- 33 B. Bertrand, M. R. M. Williams and M. Bochmann, *Chem.-Eur. J.*, 2018, **24**, 11840–11851.
- 34 M. Altaf, A. A. Isab, J. Vančo, Z. Dvořák, Z. Trávníček and H. Stoeckli-Evans, *RSC Adv.*, 2015, **5**, 81599–81607.
- 35 J. Quero, S. Cabello, T. Fuertes, I. Mármol, R. Laplaza, V. Polo, M. C. Gimeno, M. J. Rodríguez-Yoldi and E. Cerrada, *Inorg. Chem.*, 2018, **57**, 10832–10845.
- 36 L. Ronconi, L. Giovagnini, C. Marzano, F. Bettio, R. Graziani, G. Pilloni and D. Fregona, *Inorg. Chem.*, 2005, **44**, 1867–1881.
- 37 G. Exarchos, S. D. Robinson and J. W. Steed, *Polyhedron*, 2001, **20**, 2951–2963.
- 38 G. Exarchos, S. D. Robinson and J. W. Steed, *Polyhedron*, 2000, **19**, 1511–1517.
- 39 J. W. Wiench, C. Michon, A. Ellern, P. Hazendonk, A. Iuga, R. J. Angelici and M. Pruski, *J. Am. Chem. Soc.*, 2009, **131**, 11801–11810.

