ChemComm

COMMUNICATION

View Article Online
View Journal | View Issue

Cite this: *Chem. Commun.*, 2025, **61**, 18717

Received 8th October 2025,
Accepted 23rd October 2025

DOI: 10.1039/d5cc05744b

rsc.li/chemcomm

Ligand exchange of tris(2,4-di-*tert*-butylphenyl) phosphite: a practical and efficient route to organo gold(I) complexes

David Vesseur,*[a] Shuo Li,[a] Sonia Mallet-Ladeira[b] and Didier Bourissou *[a]

Tris(2,4-di-*tert*-butylphenyl)phosphite (2,6-^{t}Bu$_2$-PhO)$_3$P is used as a stable, easily displaceable ancillary ligand in the preparation of organo Au(I) complexes. The phosphite gold(I) precursors are bench-stable and readily accessible. They undergo high-yielding ligand exchange with a variety of ligands such as phosphines, N-heterocyclic carbenes and bidentate ligands. This ligand exchange strategy overcomes the limitations associated with traditional gold halide-based synthetic routes and is compatible with different organogold fragments. The protocol is scalable, operationally simple and broadly applicable.

Until the 21st century, gold was widely regarded as catalytically inert and was largely treated as a chemical curiosity. This perception changed in 1998 when Teles *et al.* demonstrated that Au(I) phosphine complexes could efficiently catalyze the addition of alcohols to alkynes under mild conditions, achieving turnover numbers up to 10^5.[1] Over the following two and a half decades, gold complexes have emerged as exceptionally powerful catalysts, capable of promoting transformations that are often otherwise inaccessible.[2] Early developments in the field primarily employed gold complexes bearing simple ligands. However, as the transformations became more sophisticated, so did the ancillary ligands. For many advanced transformations and fundamental studies, the use of more elaborated ligands has become essential. While these ligands enable novel, valuable, and often unprecedented reactivity, the synthesis of the corresponding organogold complexes can present significant challenges.

We recently reported that bidentate ligands can be used to stabilize Au(I) difluorocarbene complexes, which undergo [2+2] and [2+4] cycloadditions with alkenes and 1,3-dienes.[3] These Au(I) difluorocarbene complexes were generated *via* fluoride abstraction from the corresponding Au(I) trifluoromethyl precursors. However, the preparation of these bidentate Au(I) trifluoromethyl complexes in high purity was challenging when using existing protocols for the preparation of Au(I) trifluoromethyl complexes.[4,5] Additionally, we were unable to find an effective method for their purification.

By far, the most widely used method for the preparation of organo Au(I) complexes involves a "ligand exchange first" (Fig. 1A). Weakly bound sulphide ligands (*e.g.*, Me_2S, THT) are first displaced from gold(I) halide precursors by more strongly coordinating ligands. This exchange is highly favorable due to the low bond dissociation energy (BDE) of the Au–S bond.[6] The resulting Au(I) halide complex is then subjected to functionalization conditions to install the desired organic group. However, this sequence can pose challenges when the target ligand or complex is unstable under the conditions required for functionalization. An alternative approach is to functionalize the gold center first and perform ligand exchange subsequently (Fig. 1B).[7] This method, though conceptually

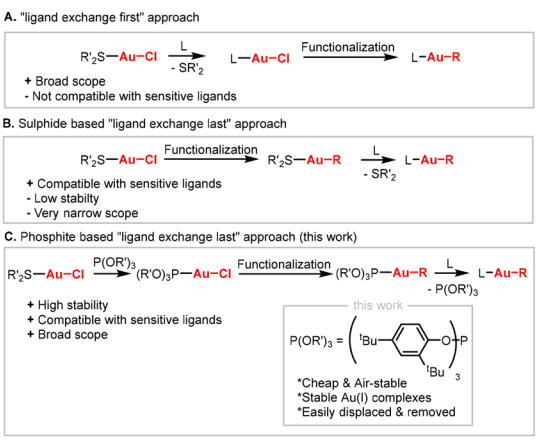
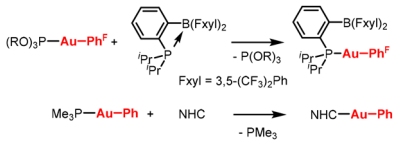


Fig. 1 (A) Classical approach for the synthesis of Au(I) complexes. (B) Functionalization of (R_2S)Au(I) complexes before ligand exchange. (C) Functionalization of [(RO)$_3$P]AuCl followed by ligand exchange.

[a] *Université de Toulouse, CNRS, Laboratoire Hétérochimie Fondamentale et Appliquée (LHFA, UMR 5069), 118 Route de Narbonne, 31062 Cedex 09 Toulouse, France. E-mail: d.vesseur@uva.nl, didier.bourissou@utoulouse.fr*

[b] *Université de Toulouse, CNRS, Institut de Chimie de Toulouse (UAR 2599), 118 Route de Narbonne, 31062 Cedex 09 Toulouse, France*



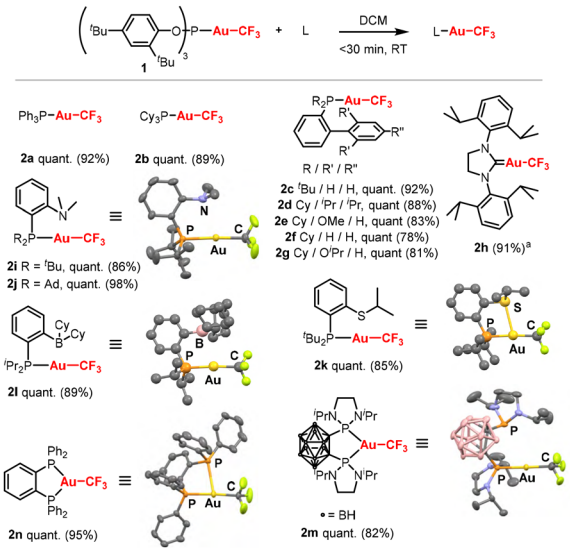
Scheme 1 Examples of ligand exchange with phosphite and phosphine ligands. R = 2,4-^{t}Bu$_2$-Ph, PhF = 4-(CF$_3$)Ph.

attractive, is limited by the instability of organogold sulphide intermediates, which are often prone to decomposition and cannot be readily isolated or stored—thereby restricting the scope of accessible organogold species. To overcome these limitations, it is desirable to employ a ligand that forms stable Au(I) complexes while still featuring a sufficiently low BDE to allow facile substitution. Although a few isolated examples of such ligand exchange at Au(I) have been reported (Scheme 1),[8] a systematic investigation aimed at developing a general synthetic protocol remains lacking.

From the few reported examples of ligand exchange, we envisioned that Au(I) complexes featuring the (2,4-^{t}Bu$_2$-PhO)$_3$P ancillary ligand could serve as excellent and general organogold sources. While Au(I) phosphite complexes tend to be moderately stable, this is largely offset in the case of (2,6-^{t}Bu$_2$-PhO)$_3$P, where the steric bulk contributes to improved stability. Owing to its poor donor properties, this phosphite forms relatively weak Au–P bonds,[6] and it is thus expected to be easily displaced by other ligands. Furthermore, this ligand is inexpensive, commercially available, air-stable, and it forms bench-stable Au(I) complexes. Notably, it is also highly soluble in aliphatic solvents, in contrast to most organogold complexes, which greatly facilitates purification after ligand exchange.

Herein, we report a general strategy for the synthesis of organo gold(I) complexes using (2,4-^{t}Bu$_2$-PhO)$_3$P as an ancillary ligand that allows for facile ligand exchange (Fig. 1C). [(2,4-^{t}Bu$_2$-PhO)$_3$P]AuR complexes are easily prepared and can be stored for prolonged periods. Due to the relatively low BDE of the phosphite and Au(I) centre, the ligand is rapidly and quantitatively displaced by phosphine or carbene ligands, enabling efficient access to a wide variety of Au(I) complexes bearing diverse ligands and functional groups. The displaced phosphite can be readily removed, further simplifying product isolation and purification.

Given our interest in (L)Au(I)CF$_3$ complexes,[3] we started our investigation with the phosphite complex (2,4-^{t}Bu$_2$-PhO)$_3$PAuCF$_3$ **1**, which is readily accessible by reacting (2,6-^{t}Bu$_2$-PhO)$_3$PAuCl with AgF and TMSCF$_3$.[4b,9] Upon mixing complex **1** with PPh$_3$ in dichloromethane (DCM), ligand exchange was monitored by the disappearance of complex **1** and the appearance of free (2,4-^{t}Bu$_2$-PhO)$_3$P in the ^{31}P NMR spectrum. After 30 minutes, complete conversion to the desired product **2a** was confirmed by both ^{31}P and ^{19}F NMR spectroscopy (Scheme 2). Complex **2a** was isolated in 92% yield by simple washing of the crude mixture with pentane. The displaced phosphite ligand could also be recovered if desired.[9] Using the more electron-rich PCy$_3$ ligand, similar results were obtained (**2b**, 89%). Biaryl ligands, which are often used in Au(I) catalysis and mechanistic

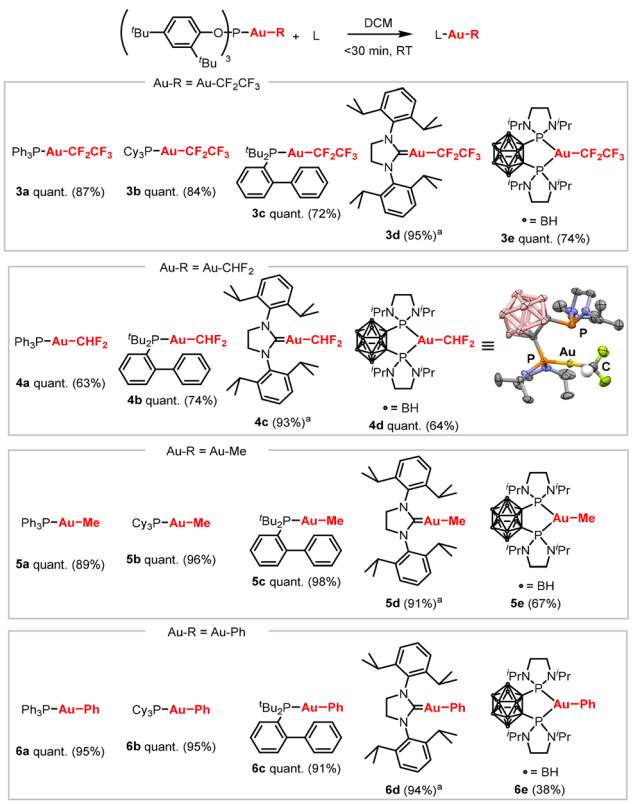


Scheme 2 Scope of the ligand exchange with (2,4-^{t}Bu$_2$-PhO)$_3$PAuCF$_3$. Reaction conditions: (2,4-^{t}Bu$_2$-PhO)$_3$PAuCF$_3$ (0.05 mmol, 1.0 eq.), L (0.05 mmol, 1.0 eq.), DCM (0.05 M), rt, <30 minutes. Quantitative conversion determined by ^{31}P NMR spectroscopy, isolated yields in brackets. Molecular structure of **2i**, **2k**, **2l**, **2m** and **2n** with the hydrogen atoms omitted for clarity. [a] Reaction performed in toluene (0.05 M).

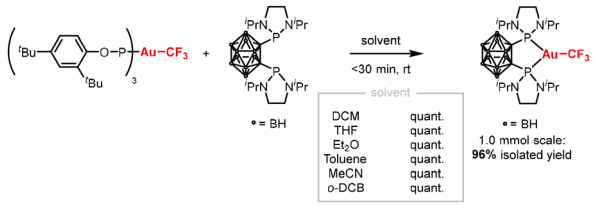
studies, also worked very well, delivering complexes **2c–2g** in 78–92% yields. Expanding beyond phosphorus-based ligands, a NHC ligand was tested. SIPr proved compatible, yielding complex **2h** in 91% isolated yield. Having demonstrated the generality of this approach with monodentate ligands, we then turned our attention to more elaborated ligands where traditional synthetic methods can pose problems. We first investigated phosphine-amine (P^N) ligands, which have become a staple of Au(I)/Au(III) redox chemistry due to their ability to stabilise both oxidation states and facilitate redox cycling.[10] Both *tert*-butyl- and adamantyl-substituted P^N ligands reacted smoothly with complex **1**, affording **2i** and **2j** in 86% and 98% yield, respectively. A phosphine-sulphide ligand[11] also performed well, providing **2k** in 85% yield. We then explored a phosphine–borane ligand containing a Lewis acidic boron center, known for its rich and unusual coordination properties.[12] Previous studies have shown that functionalization of Au(I) complexes bearing such ambiphilic ligands is challenging due to the sensitivity of the borane moiety.[7b] Using the ligand exchange strategy, the desired complex **2l** was readily obtained in 89% yield. Finally, we examined bidentate diphosphine ligands. Mononuclear diphosphine–Au(I) complexes are rarely observed due to the strong preference of gold(I) for linear geometries, often resulting instead in digold species featuring aurophilic Au···Au interactions,[13] Nevertheless, such monometallic diphosphine complexes have attracted interest for their ability to enhance backdonation from gold, particularly with *o*-carboranyl-based ligands.[3,14,15] Using 1, 2-bis(diaminophosphino)-1,2-dicarba-closododecaborane, we successfully obtained complex **2m** in 82% yield and high purity. Single-crystal X-ray diffraction (scXRD) analysis showed coordination of a single phosphine donor to the Au(I) center, while NMR spectroscopy indicated rapid exchange in solution. Excitingly, when

1,2-bis(diphenylphosphino)benzene was used, the monometallic complex **2n** was obtained with an excellent yield (95%). In the solid state, **2n** adopts a T-shape (not a Y-shape) with dissymmetric coordination of the two phosphorus atoms. Possibly, the bulkiness of the (2,6-^{t}Bu$_2$-PhO)$_3$P prevents the ligation of a second gold centre. This suggests that the (2,6-^{t}Bu$_2$-PhO)$_3$P ligand may enable access to other mononuclear Au(I) complexes with bidentate ligands, which would otherwise be inaccessible with alternative gold sources.

To demonstrate that the reaction is not limited to trifluoromethyl Au(I) complexes, other organic groups were investigated (Scheme 3). To show the generality of the reaction, five different ligands were tested: the simple phosphines PPh$_3$ and PCy$_3$, JohnPhos, SIPr as a C-based ligand and the *o*-carboranyl diphosphine as a bidentate ligand. First, the ligand exchange was extended to Au(I) equipped with a pentafluoroethyl group which are underdeveloped compared to their trifluoromethyl analogues. In all cases, the reaction proceeded smoothly, affording complexes **3a–3e** in high isolated yields (72–95%). To exemplify further the utility of our ligand exchange methodology, the difluoromethyl substituent was also investigated. A previous study found that while Au(I) difluoromethyl complexes



Scheme 3 Scope of the ligand exchange of (2,4-^{t}Bu$_2$-PhO)$_3$PAuR with selected ligands triphenyl phosphine (PPh$_3$), tricyclohexyl phosphine (PCy$_3$), (2-biphenyl)di-*tert*-butylphosphine (JohnPhos), 1,3-bis(2,6- diisopropylphenyl)-4,5-dihydroimidazol-2-ylidene (SIPr), and *o*-carborane diphosphine (P^P). Reaction conditions: (2,4-^{t}Bu$_2$-PhO)$_3$PAuR (0.05 mmol, 1.0 eq.), L (0.05 mmol, 1.0 eq.), DCM (0.05 M), rt, <30 minutes. Quantitative conversion determined by ^{31}P NMR spectroscopy, isolated yields in brackets. [a] Reaction performed in toluene (0.05 M).



Scheme 4 Reaction conditions: (2,4-^{t}Bu$_2$-PhO)$_3$PAuCF$_3$ (0.05 mmol, 1.0 eq.), 1,2-bis(diaminophosphino)-1,2-dicarba-closododecaborane (0.05 mmol, 1.0 eq.), solvent (0.05 M), rt, <30 minutes. Ligand exchange of (2,4-^{t}Bu$_2$-PhO)$_3$PAuCF$_3$ with the diphosphine carborane ligand in different solvents. Quantitative conversion determined by ^{31}P NMR spectroscopy. Reaction conditions for 1.0 mmol scale: (2,4-^{t}Bu$_2$-PhO)$_3$PAuCF$_3$ (1.0 mmol, 1.0 eq.), P^P ligand (1.0 mmol, 1.0 eq.), DCM (1.0 M), rt, <30 minutes.

can be synthesized *via* alternative methods, isolation was often hampered by decomposition during purification.[16] The (2,4-^{t}Bu$_2$-PhO)$_3$PAuCHF$_2$ precursor itself could be prepared and easily extracted from the reaction mixture with pentane due to its high solubility in aliphatic solvents. Ligand exchange proceeded quantitatively, furnishing the targeted (L)Au(I)CHF$_2$ complexes **4a–4d**, which were easily purified by simple pentane washes.[9] Then, organic groups without fluorides were tested to demonstrate that the ligand exchange approach goes beyond electron-deficient substituents. The reaction worked well for both methyl-substituted complexes **5a–5e** (67–98% yields) and phenyl-substituted complexes **6a–6e** (38–95% yields) (Scheme 3).[17]

All reactions were carried out in dichloromethane, a solvent in which organo Au(I) complexes are typically stable and highly soluble. It might however be desirable to use alternative solvents. Therefore, the ligand exchange methodology was tested in a range of different solvents, with different polarities and potential coordinating abilities (Scheme 4). In all cases, quantitative conversion was achieved within 30 minutes, as determined by ^{31}P NMR spectroscopy. Lastly, the reaction was successfully scaled up to 1 mmol (0.7 g) scale, yielding the desired complex in 96% yield. These results underscore the robustness and synthetic practicality of the ligand exchange methodology.

In conclusion, Au(I) complexes bearing the labile phosphite ligand (2,4-^{t}Bu$_2$-PhO)$_3$P have proven to be excellent precursors for the synthesis of organo Au(I) complexes *via* a straightforward and easy-to-operate ligand exchange protocol. This "ligand exchange last" strategy offers several advantages over the more commonly employed "ligand exchange first" approach, benefiting from the air-stability, low cost and ease of removal of the phosphite (2,4-^{t}Bu$_2$-PhO)$_3$P. A broad scope of ligands and organic groups was explored, which afforded the desired Au(I) complexes in high yield and purity. Overall, this ligand exchange approach provides a practical and efficient route to organo gold(I) complexes which would otherwise be difficult to prepare using known synthetic methods.

Financial support from the Centre National de la Recherche Scientifique, the Université de Toulouse, the Agence Nationale de la Recherche (ANR-19-CE07-0037), and the Chinese

Scholarship Council (PhD fellowship to S. L.) is gratefully acknowledged. The NMR service of ICT, UAR 2599 (Pierre Lavedan), is acknowledged for assistance with the variabletemperature NMR experiments.

Conflicts of interest

There are no conflicts to declare.

Data availability

The data supporting this article have been included as part of the supplementary information (SI). Supplementary information: details of the experimental methods, NMR spectra and X-ray analyses. See DOI: **https://doi.org/10.1039/d5cc05744b**.

CCDC 2482843 (for **2i**), 2482844 (for **2k**), 2482845 (for **2l**), 2482839 (for **2m**), 2492890 (for **2n**) and 2482840 (for **4d**) contain the crystallographic data.[18a–f]

Notes and references

1 J. H. Teles, S. Brode and M. Chabanas, *Angew. Chem., Int. Ed.*, 1998, **37**, 1415–1418.
2 For some reviews, see: (*a*) A. S. K. Hashmi and G. J. Hutchings, *Angew. Chem., Int. Ed.*, 2006, **45**, 7896–7936; (*b*) A. S. K. Hashmi and M. Rudolph, *Chem. Soc. Rev.*, 2008, **37**, 1766–1775; (*c*) M. Rudolph and A. S. K. Hashmi, *Chem. Rev.*, 2012, **41**, 2448–2462; (*d*) R. Ciriminna, E. Falletta, C. Della Pina, J. H. Teles and M. Pagliaro, *Angew. Chem., Int. Ed.*, 2016, **55**, 14210–14217; (*e*) S. A. Shahzad, M. A. Sajid, Z. A. Khan and D. Canseco-Gonzalez, *Synth. Commun.*, 2017, **47**, 735–755; (*f*) S. Witzel, A. S. K. Hashmi and J. Xie, *Chem. Rev.*, 2021, **121**, 8868–8925; (*g*) W. Wang, C.-L. Ji, K. Liu, C.-G. Zhao, W. Li and J. Xie, *Chem. Soc. Rev.*, 2021, **50**, 1874–1912.
3 D. Vesseur, S. Li, N. Albouy, P. Lavedan, S. Mallet-Ladeira, K. Miqueu and D. Bourissou, *Angew. Chem., Int. Ed.*, 2025, **64**, e202515429.
4 (*a*) M. Blaya, D. Bautista, J. Gil-Rubio and J. Vicente, *Organometallics*, 2014, **33**, 6358–6368; (*b*) A. G. Tskhovrebov, J. B. Lingnau and A. Fürstner, *Angew. Chem., Int. Ed.*, 2019, **58**, 8834–8838; (*c*) M. Navarro, L. Delaurenti, A. Pita-Milleiro and J. Campos, *JACS Au*, 2025, **5**, 4604–4610; (*d*) Z. R. Wong, B. K. Mai, W. R. Berg, A. Kvitsinski, T. L. F. Correia, Y. Zhang, P. Liu and F. D. Toste, *Angew. Chem., Int. Ed.*, 2025, **64**, e202511941.
5 For a review dealing with gold trifluoromethyl complexes, see: J. Gil-Rubio and J. Vicente, *Dalton Trans.*, 2015, **44**, 19432–19442.
6 G. C. Fortman and S. P. Nolan, *Organometallics*, 2010, **29**, 4579–4583.
7 For selected examples, see: (*a*) R. Usón, A. Laguna, M. Laguna, B. R. Manzano, P. G. Jones and G. M. Sheldrick, *J. Chem. Soc., Dalton Trans.*, 1985, **11**, 2417–2420; (*b*) P. Espinet, S. Martín-Barrios, F. Villafañe, P. G. Jones and A. K. Fischer, *Organometallics*, 2000, **19**, 290–295; (*c*) J. Lloret Fillol, A. Kruckenberg, P. Scherl, H. Wadepohl and L. H. Gade, *Chem. – Eur. J.*, 2011, **17**, 14047–14062; (*d*) S. Martínez-Salvador, L. R. Falvello, A. Martín and B. Menjón, *Chem. – Eur. J.*, 2013, **19**, 14540–14552; (*e*) L. Gu, Y. Zheng, E. Haldón, R. Goddard, E. Bill, W. Thiel and M. Alcarazo, *Angew. Chem., Int. Ed.*, 2017, **56**, 8790–8794; (*f*) E. Martín-Encinas, V. Conejo-Rodríguez, J. A. Miguel, J. M. Martínez-Ilarduya, G. Rubiales, B. R. Knudsen, F. Palacios and C. Alonso, *Dalton Trans.*, 2020, **49**, 7852–7861.
8 For examples, see: (*a*) E. Tomas-Mendivil, M. M. Hansmann, C. M. Weinstein, R. Jazzar, M. Melaimi and G. Bertrand, *J. Am. Chem. Soc.*, 2017, **139**, 7753–7756; (*b*) C. A. Theulier, Y. García-Rodeja, S. Mallet-Ladeira, K. Miqueu, G. Bouhadir and D. Bourissou, *Organometallics*, 2021, **40**, 2409–2414; (*c*) Y. K. Loh, M. Melaimi, D. Munz and G. Bertrand, *J. Am. Chem. Soc.*, 2023, **145**, 2064–2069.
9 See SI for details.
10 (*a*) A. Zeineddine, L. Estévez, S. Mallet-Ladeira, K. Miqueu, A. Amgoune and D. Bourissou, *Nat. Commun.*, 2017, **8**, 565; (*b*) B. Huang, M. Hu and F. D. Toste, *Trends Chem.*, 2020, **2**, 707–720; (*c*) P. Font, H. Valdés and X. Ribas, *Angew. Chem., Int. Ed.*, 2024, **63**, e202405824.
11 Y. Luo, K. Ji, Y. Li and L. Zhang, *J. Am. Chem. Soc.*, 2012, **134**, 17412–17415.
12 (*a*) S. Bontemps, G. Bouhadir, K. Miqueu and D. Bourissou, *J. Am. Chem. Soc.*, 2006, **128**, 12056–12057; (*b*) G. Bouhadir and D. Bourissou, *Chem. Soc. Rev.*, 2016, **45**, 1065–1079.
13 (*a*) M. C. Gimeno and M. A. Laguna, *Chem. Rev.*, 1997, **97**, 511–522; (*b*) M. A. Carvajal, J. J. Novoa and S. Alvarez, *J. Am. Chem. Soc.*, 2004, **126**, 1465–1477; (*c*) H. Schmidbaur and A. Schier, *Chem. Soc. Rev.*, 2012, **41**, 370–412.
14 (*a*) M. Joost, L. Estévez, S. Mallet-Ladeira, K. Miqueu, A. Amgoune and D. Bourissou, *Angew. Chem., Int. Ed.*, 2014, **53**, 14512–14516; (*b*) A. Zeineddine, F. Rekhroukh, E. D. Sosa Carrizo, S. Mallet-Ladeira, K. Miqueu, A. Amgoune and D. Bourissou, *Angew. Chem., Int. Ed.*, 2018, **57**, 1306–1310; (*c*) M. Rigoulet, D. Vesseur, K. Miqueu and D. Bourissou, *Angew. Chem., Int. Ed.*, 2022, **61**, e202204781; (*d*) D. Vesseur, K. Miqueu and D. Bourissou, *Chem. Commun.*, 2023, **59**, 5387–5390.
15 O. Crespo, M. C. Gimeno, A. Laguna and P. G. Jones, *J. Chem. Soc., Dalton Trans.*, 1992, 1601–1605.
16 P. García-Domínguez, *Organometallics*, 2021, **40**, 2923–2928.
17 Complexes 5a–5c, 5e, and 6e were found to be highly soluble in pentane. Therefore, the purification method was modified from a pentane wash to extraction with MeCN.
18 (*a*) CCDC 2482839: Experimental Crystal Structure Determination, 2025, DOI: **10.5517/ccdc.csd.cc2pbll7**; (*b*) CCDC 2482840: Experimental Crystal Structure Determination, 2025, DOI: **10.5517/ccdc.csd.cc2pblm8**; (*c*) CCDC 2482843: Experimental Crystal Structure Determination, 2025, DOI: **10.5517/ccdc.csd.cc2pblqc**; (*d*) CCDC 2482844: Experimental Crystal Structure Determination, 2025, DOI: **10.5517/ccdc.csd.cc2pblrd**; (*e*) CCDC 2482845: Experimental Crystal Structure Determination, 2025, DOI: **10.5517/ccdc.csd.cc2pblsf**; (*f*) CCDC 2492890: Experimental Crystal Structure Determination, 2025, DOI: **10.5517/ccdc.csd.cc2pbn7y**.

