ROYAL SOCIETY
OF CHEMISTRY

COMMUNICATION

Check for updates

Bis[cyclic (alkyl)(amino)carbene] isomers: Stable *trans*-bis(CAAC) *versus* facile olefin formation for *cis*-bis(CAAC)†

Braulio M. Puerta Lombardi,‡[a] Ethan R. Pezoulas,‡[a] Roope A. Suvinen, [b]
Alexander Harrison,[a] Zachary S. Dubrawski, [a] Benjamin S. Gelfand, [a]
Heikki M. Tuononen *[b] and Roland Roesler *[a]

Isomeric bis(aldiminium) salts with a 1,4-cyclohexylene framework were synthesized. The first isolable bis(CAAC) was prepared from the *trans*-stereoisomer and its ditopic ligand competency was proven by conversion to iridium(I) and rhodium(I) complexes. Upon deprotonation, the *cis*-isomer yielded an electron rich olefin *via* a classic, proton-catalyzed pathway. The C=C bond formation from the desired *cis*-bis(CAAC) was shown to be thermodynamically very favorable and to involve a small activation barrier. Compounds that can be described as insertion products of the *cis*-bis(CAAC) into the E−H bonds of NH_3, CH_3CN and H_2O were also identified.

First reported in 2005,[1] cyclic (alkyl)(amino)carbenes (CAACs) have been rapidly incorporated into the main-group and organometallic ligand toolkit. Their exceptional σ-donating and π-accepting abilities led to the isolation of a flurry of compounds of fundamental and applied interest.[2] Prominent examples include homoleptic late transition metal compounds in low oxidation states,[3] main-group and organoradical spin carriers,[4] elements in unusual oxidation states,[5] and high-performing transition metal catalysts.[6] The growing library of accessible CAACs is facilitating steric and electronic profile tuning of their complexes for tailored applications.[7–9] Along with the much used five-membered Me_2CAAC,[1] CyCAACs,[1] and AdCAAC,[10] other examples include CAACs incorporating imine or phosphine pendant arms,[11] six-membered CAAC-6,[12] and bicyclic BiCAACs[13] (Chart 1). The steady expansion of the CAAC library was facilitated by the straightforward access to the respective aldiminium-salt precursors starting from ubiquitous building blocks, *via* an elegant protonation-cyclization-hydroiminiumation sequence reported by Bertrand.[14]

Despite the growing library of CAAC ligands and the tremendous success of bis(NHC)[15] (NHC = *N*-heterocyclic carbene) and bisphosphine analogs,[16] no bis(CAAC) has been reported to date. We reasoned that this notable absence could be remedied in few synthetic steps, by formally derivatizing CyCAAC,[1] which was shown to be a competent ligand. The cyclohexyl scaffold could be used to build two desirable bis(CAAC)s: A bidentate *cis*-stereoisomer and a ditopic *trans*-stereoisomer (Chart 1). Our investigations targeting these derivatives will be reported herein.

Aldiminium precursors **3a** and **4a** were obtained in gram quantities *via* standard CAAC-building protocols,[14] adapted to accommodate the second CAAC moiety (Scheme 1). A commercially available isomeric mixture of cyclohexane-1,4-dimethanols was converted to cyclohexyl-1,4-dicarboxaldehydes and, following condensation with $DippNH_2$ (Dipp = 2,6-diisopropylphenyl), pure *trans*-diimine **1a** could be isolated in 29% overall yield. Double deprotonation of this precursor with *n*-butyllithium followed by reaction of the resulting aza-allyl anion with 3-bromo-2-methylpropene generated *cis*- and *trans*-**2a**, which were isolated as a mixture.

Layering benzene solutions of this mixture with acetonitrile resulted in selective crystallization of *trans*-**2a** as large colorless blocks in 10% yield. This compound was then subjected to the hydroiminiumation procedure, leading to dialdiminium tetrafluoroborate salt **3a**. *cis*-Dialdiminium tetrafluoroborate **4a** was more conveniently obtained by carrying on the hydroiminiumation
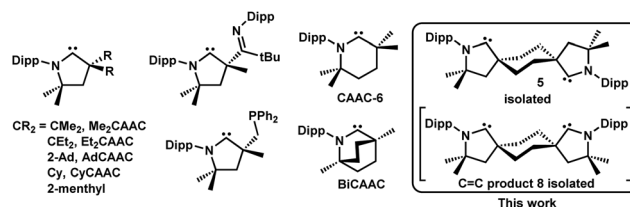
a Department of Chemistry, University of Calgary, 2500 University Drive NW, Calgary, AB, T2N 1N4, Canada. E-mail: roesler@ucalgary.ca
b Department of Chemistry, Nanoscience Centre, University of Jyväskylä, P.O. Box 35, FI-40014 Jyväskylä, Finland. E-mail: heikki.m.tuononen@jyu.fi

† Electronic supplementary information (ESI) available. CCDC 2131007–2131017. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d2cc01476a
‡ These authors contributed equally to this work.

Chart 1 Selected examples of CAACs.
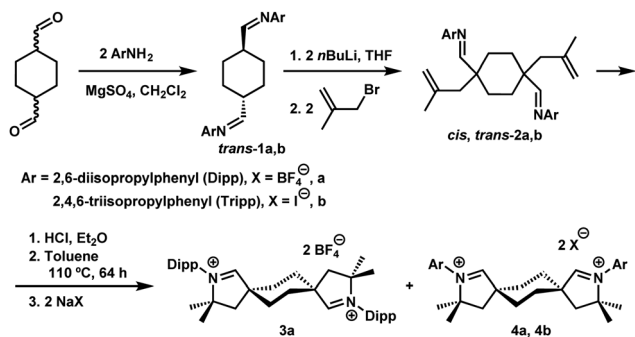
Scheme 1 Succession of reactions leading to the synthesis of bis(CAAC) precursors **3a** and **4a,b**.

Scheme 2 Synthesis of free dicarbene **5** and its metal complexes **6** and **7**.

reaction with a mixture of *cis*- and *trans*-**2a**. Extraction of the product mixture with CHCl$_3$ and recrystallization by layering CH$_2$Cl$_2$ solutions with hexanes yielded **4a** in 67% yield. The configuration of the aldiminium fragments was readily assessed by ^{1}H NMR, based on coupling patterns for the cyclohexylene linker protons (in CD$_2$Cl$_2$, **3a** exhibits two doublet resonances at 1.93 and 2.65 ppm and **4a** features a pair of multiplets at 2.20 and 2.52 ppm), and confirmed by single-crystal X-ray diffraction (Fig. 1).

Addition of two equivalents of potassium hexamethyldisilazide (KHMDS) to *trans*-aldiminium salt **3a** in THF produced the expected dicarbene **5** (Scheme 2 and Fig. 2), displaying a characteristic ^{13}C NMR resonance corresponding to the carbenic carbons at 315.2 ppm in C$_6$D$_6$. Under an inert atmosphere, **5** could be handled at room-temperature and no decomposition was observed by ^{1}H NMR after storing the solid at -40 °C for a month. The ditopic nature of **5** was probed *via* reaction with IrCl(CO)(PPh$_3$)$_2$ or [Rh(cod)Cl]$_2$ in benzene, which yielded complexes **6** (Fig. 3) and **7** (Fig. S67, ESI†), respectively, as yellow, crystalline precipitates. The four ligands in **6** adopt a
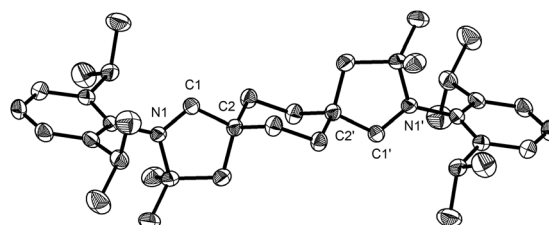

Fig. 2 Solid-state structure of **5** with 50% probability thermal ellipsoids and hydrogen atoms omitted for clarity. Selected bond lengths [Å] and angles [°]: N1–C1 1.3065(16), C1–C2 1.5232(17); N1–C1–C2 105.92(10).

square planar coordination geometry at iridium, with PPh$_3$ *trans* to the carbene, as previously observed in analogous IrCl(CO)(NHC)(PPh$_3$) complexes.[17] The spectral signature of **6** ($\delta_{carbene}$ 255 ppm, δ_{CO} 174 ppm, δ_P 22 ppm, ν_{CO} 1950 cm^{-1}) is also similar to that of IrCl(CO)(NHC)(PPh$_3$) ($\delta_{carbene}$ 178 ppm, δ_{CO} 171 ppm, δ_P 25 ppm, ν_{CO} 1945 cm^{-1}).[17]

Addition of two equivalents of Et$_3$N, iPr$_2$NEt, LiHMDS, LDA, MeLi or Me$_3$SiCH$_2$Li to a suspension **4a** in THF of led to intractable mixtures. When lithium-2,2,6,6-tetramethylpiperidide (LiTMP) was employed, an elimination reaction took place, regenerating *cis*-**2a**. A similar behavior was reported by Bertrand for CAAC-6.[12] Immediately upon addition of two equivalents of KHMDS to **4a** at -78 °C, (Fig. S55 and S56, ESI†), a singlet resonance was detected at
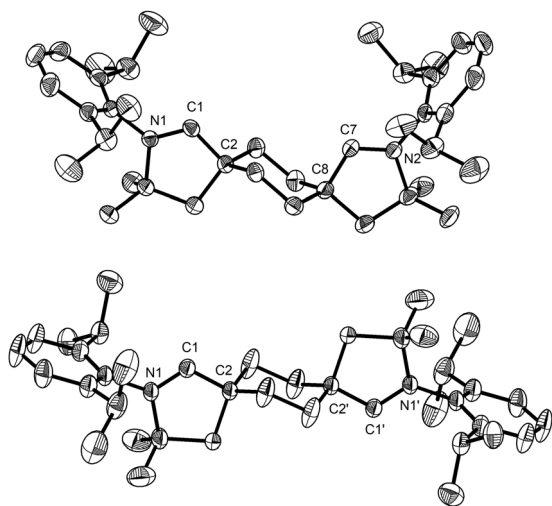

Fig. 1 Solid-state structures of the dications in **3a** (top) and **4a** (bottom) with 50% probability ellipsoids and hydrogen atoms omitted for clarity. Selected bond lengths [Å] and angles [°]: **3a**: C1–N1 1.272(4), C1–C2 1.491(4); N1–C1–C2 114.7(2); **4a**: C1–N1 1.275(2), C1–C2 1.482(3); N1–C1–C2 114.76(17).
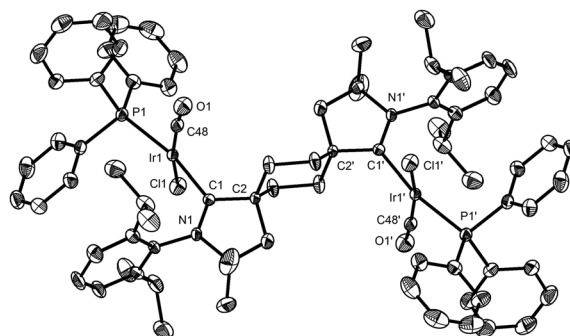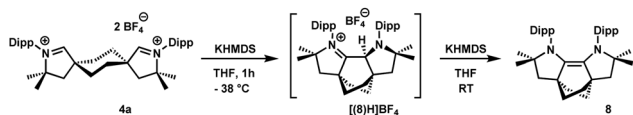

Fig. 3 Solid-state structure of **6** with 50% probability thermal ellipsoids and hydrogen atoms omitted for clarity. Selected bond lengths [Å] and angles [°]: Ir1–C1 2.035(3), Ir1–P1 2.3111(8), O1–C48 1.100(3), C1–Ir1–P1 168.68(7), C48–Ir1–Cl1 168.69(9), N1–C1–C2 109.3(2).

Scheme 3 Synthesis of **8** via [(**8**)H]BF₄.

318.0 ppm by ^{13}C NMR, suggesting the formation of a CAAC. It rapidly disappeared upon warming to -38 °C with concurrent emergence of a new set of resonances suggestive of a less symmetric compound. In the ^{1}H NMR spectrum, a singlet at 5.08 ppm, within the range observed for protonated NHC-CAAC dimers (4.90–5.32 ppm in CD₃CN;[18] 4.58, 4.72 ppm in CDCl₃),[19] was assigned to the protonated olefin intermediate [(**8**)H]BF₄ (Scheme 3). Ultimately, warming up the mixture to room temperature led to the formation of a higher-symmetry compound, confirmed via X-ray crystallography to be olefin **8** (Fig. S68, ESI†); whole-molecule disorder precluded a detailed discussion of bonding parameters. Similar electron-rich olefins were recently reported by Sarkar.[20] Solutions of **8** in toluene were stable up to 110 °C and the solid could be handled in air. The substantial steric crowding in **8** forces the nitrogen atoms to become pyramidalized (sum of nitrogen bond angles 351.4(4)°). Furthermore, two methyl groups within the Dipp fragments are forced into close proximity to the opposing aryl ring, giving rise to a strongly shielded ^{1}H NMR resonance at -0.02 ppm.

DFT studies showed that, upon single deprotonation of **4a** to a free mono-CAAC, the cyclohexane backbone readily changes conformation from chair to twist boat ($\Delta G_{c\text{-}tb}^{\ddagger} = 24$ kJ mol^{-1}, Fig. S72, ESI†). A second conformational change from twist boat to boat, accompanied by the formation of a C–C bond to give [**8**(H)]$^+$, is similarly facile ($\Delta G_{tb\text{-}b}^{\ddagger} = 12$ kJ mol^{-1}). The two-step transformation is overall exergonic ($\Delta G = -72$ kJ mol^{-1}) and expected to take place rapidly even at -38 °C due to the associated small energy barriers. The calculated ^{1}H NMR chemical shifts of [**8**(H)]$^+$ are in good agreement with the experimental values, with a characteristic singlet at 5.91 ppm vs. 5.08 ppm observed experimentally for the protonated olefin. A hypothetical cis-bis(CAAC) resulting from double deprotonation of **4a** gave a potential energy surface similar to single deprotonation, with greater energy barriers for conformational changes of the cylochexane ring ($\Delta G_{c\text{-}tb}^{\ddagger} = 52$ and $\Delta G_{tb\text{-}b}^{\ddagger} = 40$ kJ mol^{-1}, Fig. S73, ESI†). This likely stems from the increased repulsion associated with two carbon atoms with lone pairs. The formation of **8** from the cis-bis(CAAC) is overall highly exergonic ($\Delta G = -262$ kJ mol^{-1}) as a C=C double bond is formed between the two carbenic carbon atoms.

The calculations support the intermediacy of [**8**(H)]BF₄ en route from **4a** to **8**. Furthermore, even though double deprotonation of **4a** could take place prior to conformational changes, the energy barriers associated with the cyclohexane ring flip are minor. This suggests that the cis-bis(CAAC) species obtained via double deprotonation of **4a** is not isolable under any conditions. While these results might initially seem surprising, they become less so upon comparison with data calculated for the

dimerization of Me₂CAAC, which show $\Delta G_{dimer} = -75$ and -99 kJ mol^{-1} for cis and trans product geometries, respectively. Thus, dimerization of two CAACs is always thermodynamically favored but generally kinetically blocked by very high activation barriers ($\Delta G_{cis}^{\ddagger} = 189$ and $\Delta G_{trans}^{\ddagger} = 188$ kJ mol^{-1}) that arise in large part from the entropic penalty of dimerization ($-T\Delta S = 81$ kJ mol^{-1}). No such penalty exists when the two CAAC moieties are part of the same molecule, which supports the facile formation of **8**.

Cyclic voltammetry of **8** in THF revealed two reversible redox waves ($E_{1/2} = -0.32$ and 0.49 vs. Fc/Fc$^+$, Fig. S59, ESI†), corresponding to the oxidation of **8** to its radical cation and further to the dication, respectively. Both oxidations are anodically-shifted in comparison to the values reported by Sarkar,[20] potentially due to the inductive effect of the N-aryl substituent in **8** leading to a less electron rich system. The C_2-symmetric radical cation was isolated as purple tetrafluoroborate salt **9** following the oxidation of **8** with [Ph₃C][BF₄]. It was characterized by EPR (Fig. S60, ESI†) and its structure was confirmed by X-ray crystallography (Fig. 4).

Attempting to destabilize the electron rich olefin **8** in favor of a free cis-bis(CAAC), the Dipp substituents in **4a** were replaced with Tripp (2,4,6-triisopropylphenyl) (Scheme 1). However, deprotonation of **4b** also led to C=C bond formation and this chemistry will not be detailed here. We then turned our attention to complex formation directly from **4a**, by employing metal reagents featuring Brønsted-basic ligands (Scheme 4). The reaction of NHC salt precursors with Cu₂O or Ag₂O to yield the corresponding metal complexes has been extensively explored.[21] Extrapolation of this method to CAACs is less common,[22] arguably due to the weaker acidity of aldiminium-CAAC salts. Heating an acetonitrile solution of **4a** with Cu₂O over several days in an NMR tube resulted in crystallization of colorless blocks that were identified as ether **12** by single-crystal X-ray diffraction (Fig. S71, ESI†). The structure is reminiscent of the (Me₂CAACH)₂O ether obtained as a side-product while preparing (Me₂CAAC)₂Ge.[23] Refluxing **4a** and Fe(HMDS)₂ in acetonitrile led to crystallization of **11** (Fig. S65, ESI†). The presence of (Me₃Si)₂NH in the NMR of the product mixture suggests that deprotonation may indeed take place. However, scaling up the reaction led to the isolation of **10** instead (Fig. S70, ESI†). The origin of the nitrogen atom is presumably (Me₃Si)₂NH, a byproduct from the reaction of Fe(HMDS)₂
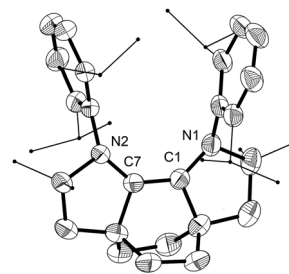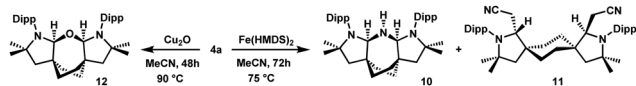
Fig. 4 Solid-state structure of the cation in **9** with 50% thermal ellipsoids and hydrogen atoms omitted for clarity. Selected bond lengths (Å) and angles (°): C1–C7 1.409(3), C1–N1 1.357(3), C7–N2 1.360(3).

Scheme 4 Reactivity of **4a** towards transition metal complexes with Brønsted-basic ligands.

and **4a**. Attempted complex formation using $Ca(HMDS)_2$, $Mg(SiTMS_3)_2$, $Pd(OAc)_2$, or $[PtMe_2(\mu\text{-}SMe_2)]_2$ gave intractable mixtures.

In conclusion, two isomeric CAAC-aldiiminium salts **3a** and **4a**, derived from the same parent aldehydes, were synthesized on multi-gram scale. *trans*-Stereoisomer **3a** was doubly deprotonated to yield the first isolable bis(CAAC) **5**, which proved to easily form dinuclear metal complexes, as exemplified by iridium complex **6** and rhodium complex **7**. Upon double deprotonation with KHMDS, *cis*-stereoisomer **4a** formed the electron-rich olefin **8**. Experimental and computational studies suggest the process follows the classic Lewis-acid catalyzed NHC dimerization pathway. DFT calculations showed that the intramolecular C=C bond formation in a free *cis*-bis(CAAC) derived from **4a** is highly exergonic (-262 kJ mol^{-1} *vs.* -75 kJ mol^{-1} for *cis*-dimerization of Me$_2$CAAC) and involves, for entropic reasons, a small activation barrier that can be lowered even more by proton catalysis. Reaction of **4a** with metal complexes featuring Brønsted-basic ligands led to the identification of **10**, **11**, and **12**, which can be described as insertion products of a bis(CAAC) into the N–H, C–H and O–H bonds of NH_3, CH_3CN and H_2O, respectively. Whether their formation involves a free CAAC intermediate that has been observed at low-temperature by NMR, as described for mono(CAAC)s,[24] or the transient formation of metal complexes, remains to be investigated. 17 years after the first report of a CAAC ligand, our study adds the first bis(CAAC) ligand to the organometallic toolkit.

Conflicts of interest

There are no conflicts to declare.

References

1 V. Lavallo, Y. Canac, C. Präsang, B. Donnadieu and G. Bertrand, *Angew. Chem., Int. Ed.*, 2005, **44**, 5705–5709.
2 M. Soleilhavoup and G. Bertrand, *Acc. Chem. Res.*, 2015, **48**, 256–266; M. Melaimi, R. Jazzar, M. Soleilhavoup and G. Bertrand, *Angew. Chem., Int. Ed.*, 2017, **56**, 10046–10068; V. Nesterov, D. Reiter, P. Bag, P. Frisch, R. Holzner, A. Porzelt and S. Inoue, *Chem. Rev.*, 2018, **118**, 9678–9842; S. K. Kushvaha, A. Mishra, H. W. Roesky and K. C. Mondal, *Chem. – Asian J.*, 2022, e2021013.
3 S. Roy, K. C. Mondal and H. W. Roesky, *Acc. Chem. Res.*, 2016, **49**, 357–369.
4 M. M. Hansmann, M. Melaimi, D. Munz and G. Bertrand, *J. Am. Chem. Soc.*, 2018, **140**, 2546–2554; M. M. Hansmann, M. Melaimi and G. Bertrand, *J. Am. Chem. Soc.*, 2018, **140**, 2206–2213; T. Ullrich, P. Pinter, J. Messelberger, P. Haines, R. Kaur, M. M. Hansmann, D. Munz and D. M. Guldi, *Angew. Chem., Int. Ed.*, 2020, **59**, 7906–7914.
5 M. Arrowsmith, H. Braunschweig, M. A. Celik, T. Dellermann, R. D. Dewhurst, W. C. Ewing, K. Hammond, T. Kramer, I. Krummenacher, J. Mies, K. Radacki and J. K. Schuster, *Nat. Chem.*, 2016, **8**, 890–894; W. Lu, Y. Li and R. Kinjo, *J. Am. Chem. Soc.*, 2019, **141**, 5164–5168.
6 M. P. Wiesenfeldt, Z. Nairoukh, W. Li and F. Glorius, *Science*, 2017, **357**, 908–912; J. Morvan, M. Mauduit, G. Bertrand and R. Jazzar, *ACS Catal.*, 2021, **11**, 1714–1748.
7 Y. Gao, S. Yazdani, A. Kendrick IV, G. P. Junor, T. Kang, D. B. Grotjahn, G. Bertrand, R. Jazzar and K. M. Engle, *Angew. Chem., Int. Ed.*, 2021, **60**, 19871–19878.
8 D. Pichon, M. Soleilhavoup, J. Morvan, G. P. Junor, T. Vives, C. Crevisy, V. Lavallo, J. M. Campagne, M. Mauduit, R. Jazzar and G. Bertrand, *Chem. Sci.*, 2019, **10**, 7807–7811.
9 J. Morvan, F. Vermersch, Z. Zhang, L. Falivene, T. Vives, V. Dorcet, T. Roisnel, C. Crevisy, L. Cavallo, N. Vanthuyne, G. Bertrand, R. Jazzar and M. Mauduit, *J. Am. Chem. Soc.*, 2020, **142**(47), 19895–19901.
10 V. Lavallo, G. D. Frey, S. Kousar, B. Donnadieu and G. Bertrand, *Proc. Natl. Acad. Sci. U. S. A.*, 2007, **104**, 13569–13573.
11 J. Chu, D. Munz, R. Jazzar, M. Melaimi and G. Bertrand, *J. Am. Chem. Soc.*, 2016, **138**, 7884–7887.
12 C. M. Weinstein, G. P. Junor, D. R. Tolentino, R. Jazzar, M. Melaimi and G. Bertrand, *J. Am. Chem. Soc.*, 2018, **140**, 9255–9260.
13 E. Tomás-Mendivil, M. M. Hansmann, C. M. Weinstein, R. Jazzar, M. Melaimi and G. Bertrand, *J. Am. Chem. Soc.*, 2017, **139**, 7753–7756.
14 R. Jazzar, R. D. Dewhurst, J.-B. Bourg, B. Donnadieu, Y. Canac and G. Bertrand, *Angew. Chem., Int. Ed.*, 2007, **46**, 2899–2902; R. Jazzar, J.-B. Bourg, R. D. Dewhurst, B. Donnadieu and G. Bertrand, *J. Org. Chem.*, 2007, **72**, 3492–3499.
15 M. Poyatos, J. A. Mata and E. Peris, *Chem. Rev.*, 2009, **109**, 3677–3707; M. Poyatos and E. Peris, *Dalton Trans.*, 2021, **50**, 12748–12763.
16 In *Phosphorus(III) Ligands in Homogeneous Catalysis: Design and Synthesis*, ed. P. C. J. Kamer and P. W. N. M. van Leeuwen, Wiley, New York, 2012; A. L. Clevenger, R. M. Stolley, J. Aderibigbe and J. Louie, *Chem. Rev.*, 2020, **120**, 6124–6196.
17 C.-F. Fu, Y.-H. Chang, Y.-H. Liu, S.-M. Peng, C. J. Elsevier, J.-T. Chen and S.-T. Liu, *Dalton Trans.*, 2009, 6991–6998.
18 D. Munz, J. Chu, M. Melaimi and G. Bertrand, *Angew. Chem., Int. Ed.*, 2016, **55**, 12886–12890; J. Messelberger, A. Grünwald, S. J. Goodner, F. Zeilinger, P. Pinter, M. E. Miehlich, F. W. Heinemann, M. M. Hansmann and D. Munz, *Chem. Sci.*, 2020, **11**, 4138–4149.
19 D. Mandal, R. Dolai, R. Kumar, S. Suhr, N. Chrysochos, P. Kalita, R. S. Narayanan, G. Rajaraman, C. Schulzke, B. Sarkar, V. Chandrasekhar and A. Jana, *J. Org. Chem.*, 2019, **84**, 8899–8909.
20 M. K. Nayak, S. Suhr, N. Chrysochos, H. Rawat, C. Schulzke, V. Chandrasekhar, B. Sarkar and A. Jana, *Chem. Commun.*, 2021, **57**, 1210–1213.
21 I. J. B. Lin and C. S. Vasam, *Coord. Chem. Rev.*, 2007, **251**, 642–670; M. R. L. Furst and C. S. J. Cazin, *Chem. Commun.*, 2010, **46**, 6924.
22 Y. D. Bidal, O. Santoro, M. Melaimi, D. B. Cordes, A. M. Z. Slawin, G. Bertrand and C. S. J. Cazin, *Chem. – Eur. J.*, 2016, **22**, 9404–9409.
23 Y. Li, K. C. Mondal, H. W. Roesky, H. Zhu, P. Stollberg, R. Herbst-Irmer, D. Stalke and D. M. Andrada, *J. Am. Chem. Soc.*, 2013, **135**, 12422–12428.
24 G. D. Frey, V. Lavallo, B. Donnadieu, W. W. Schoeller and G. Bertrand, *Science*, 2007, **316**, 439–441.