

Article

A copper-masked monosubstituted carbene as a general transmetalating agent toward stable carbene complexes

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SUMMARY

Metal complexes bearing carbene ligands $L_nM=CR^1R^2$ are relevant intermediates in catalytic transformations. Diamino and N-heterocyclic carbenes ($R^1, R^2 = NR_2$) are widespread and among the most useful ligands in catalysis. Albeit examples of isolated complexes are known, the stability significantly decrease when one of the carbenic substituents is a hydrogen, i. e., for the case of monosubstituted carbenes and there is no general straightforward method of preparing these types of compounds. We have discovered that the copper complex $[Tp^{Ms}Cu(C(H)NEt_2)]$ (1) readily transfers the aminocarbene $:C(H)NEt_2$ to other complexes of metals such as rhodium, iridium, palladium, platinum, copper or gold, leading to complexes bearing the $M-C(H)NEt_2$ moiety. Experimental data allows proposing that this monosubstituted aminocarbene (MAC) ligand displays a nucleophilicity similar to NHC ligands bearing bulky substituents, but with a considerably lower volume. These features allow unprecedented reactivity patterns such as the generation of the first stable monosubstituted carbene adduct of $Rh_2(OAc)_4$, a well-known catalyst for carbene transfer reactions. DFT studies carried out on the transfer of the MAC ligand from $[Tp^{Ms}Cu(C(H)NEt_2)]$ to *trans*- $[PdCl_2(NCMe)(PPh_3)]$ have allowed to ascertain that the transmetalation process involves several intermediates in which the Tp^{Ms} ligand shifts between κ^2 and κ^3 coordination modes.

Carbene transfer – carbene transmetalation – monosubstituted carbene - copper carbene – rhodium carbene – gold carbene – palladium carbene – platinum carbene - transfer mechanism – DFT studies

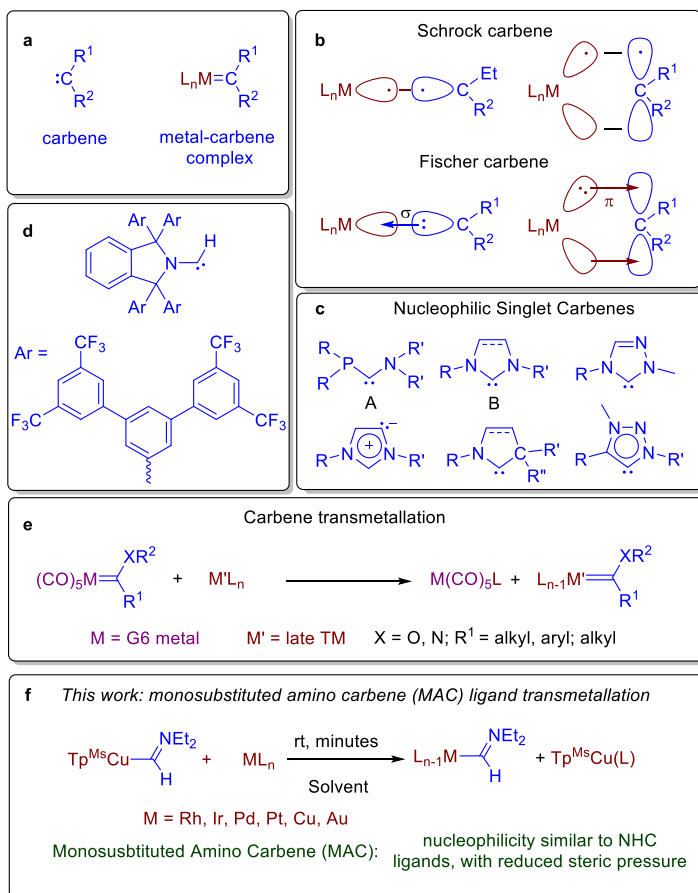
THE BIGGER PICTURE

Carbenes are a class of ligand with exceptional importance in transition metal chemistry, not only from a structural perspective but also for their key role in catalytic transformations. N-heterocyclic carbenes and diaminocarbenes are ubiquitous in metal-catalyzed reactions that form new C-C or C-X bonds. Here, we introduce a simple system based on an isolable copper compound bearing a monosubstituted aminocarbene ligand (MAC) that transfer such moiety to other metal centers at room temperature within minutes, leading to the formation of the corresponding metal-MAC derivatives. This ligand displays exceptional properties since it is highly nucleophilic such as other very bulky carbenes but with a quite reduced size, opening new ways to tailor carbene-metal catalysts.

INTRODUCTION

Carbenes constitute a class of ligands of great importance in chemistry (Scheme 1a).^{1,2} Historically they have been classified into two general types: Schrock carbenes and Fischer carbenes (Scheme 1b).^{3,4} The formers are nucleophilic in nature due to the dominant orbital interactions between the metal and the carbene formally in the triplet state. In contrast, traditional Fischer carbenes usually display a certain degree of electrophilicity and contain a singlet carbene which receives reduced back donation from the metal and are often stabilized by the presence of an electron-donating heteroatom linked to the carbene carbon.

There are many transformations, either stoichiometric or catalytic, in which a carbene ligand actively participates in a neat chemical transformation in the coordination sphere of the metal.⁵ At variance with that, the use of carbenes with a spectator role, as ancillary ligands, has been propelled more than three decades ago, after seminal work by Bertrand (Scheme 1c, A)⁶ and Arduengo (Scheme 1c, B), which provided not only the preparation but also the isolation of singlet carbenes.⁷ Since then, a considerable number of different singlet carbenes have been reported along with their use as ligands in metal complexes,^{8,9} which eventually display catalytic properties,^{10,11} or even as organocatalysts per se.¹² Scheme 1c displays representative, non-exhaustive, examples of those singlet carbenes, usually containing one or two heteroatoms directly connected to the carbenic carbon atom. Those carbenes are very often disubstituted, the presence of relatively bulky substituents as the R groups being also frequent, thus influencing the steric pressure exerted around the metal center. We are aware of only one example of a monosubstituted carbene of this kind, described by Bertrand and co-workers (Scheme 1d),¹³ which required a substantial elaboration to provide the steric protection required for the stability of the isolated carbene.



Scheme 1. Types of carbene ligands, transmetalation reactions and the new process involving the transfer of the nucleophilic, low volume monosubstituted aminocarbene (MAC) ligand to different transition metals.

A strategy commonly employed to add those carbene ligands to a given metal center is the transfer of such unit from another metal complex, in the so-called transmetalation process, pioneered by Fischer and Beck in 1970 with a molybdenum-to-iron carbene transfer (Scheme 1e).^{14,15,16} In the context of singlet carbenes shown in Scheme 1c, silver^{17,18,19} and copper^{20,21,22} have been extensively employed in transmetalation reactions. This procedure overcomes some of the problems occurring with the alternative strategy of the *in situ* generation of the free carbene that usually requires the use of strong bases and rigorous inert conditions.⁷

Based on the above, we targeted the development of a chemical system that could promote the incorporation of a carbene group into the coordination sphere of transition metals with two conditions: (a) the carbene ligand should display electronic properties similar to those shown in Scheme 1c, i. e. , they should behave as nucleophilic ancillary ligands with a high σ donation and low or none π back-donation, and (b) the size of the ligand should be considerably smaller, thus modifying steric properties with low or no effect in electronics. Herein we describe the use of a copper complex of composition $[\text{Tp}^{\text{Ms}}\text{Cu}=\text{C}(\text{H})\text{NEt}_2]$ which efficiently transfers the monosubstituted amino-carbene $\text{C}(\text{H})\text{NEt}_2$ group (MAC) to several metal centers such as Rh, Pd, Pt, Cu or Au, leading to a series of stable $\text{M}-\text{C}(\text{H})\text{NEt}_2$ complexes (Scheme 1f). Experimental data and DFT calculations have allowed proposing this carbene

ligand as similar to other NHC ligands in terms of nucleophilicity but with much lower steric pressure. The singular properties of this MAC ligand permit the isolation of elusive complexes such as dirhodium monosubstituted carbenes, the first example being now described.

RESULTS and DISCUSSION

Transmetalation of the aminocarbene C(H)NEt₂ (MAC) from copper to G9-G11 metals.

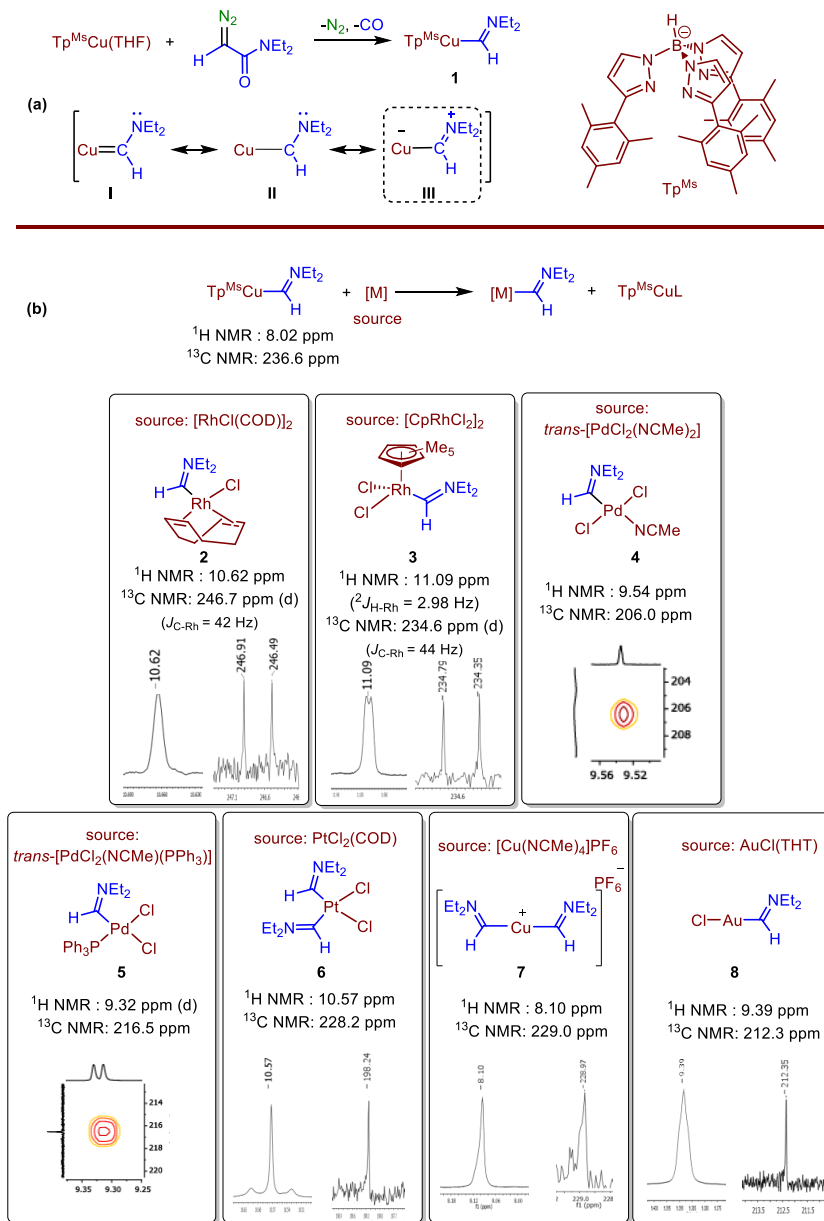
We have recently communicated the synthesis and isolation of a very stable monosubstituted copper-carbene complex of composition [Tp^{M_s}Cu-C(H)(NEt₂)] (**1**) (Tp^{M_s} = hydrotris(3-mesityl)pyrazolylborate ligand) obtained by reaction of [Tp^{M_s}Cu(THF)] with *N,N*-diethyl diazoacetamide [N₂=C(H)(CONEt₂)] (Scheme 2a).²³ Complex **1** results from a decarbonylation process of a transient in situ formed carbene species [Tp^{M_s}Cu=C(H)(CONEt₂)]. At variance with the latter, which displays electrophilic character at the carbenic carbon and undergoes intramolecular carbene insertion reactions into C-H bonds, complex **1** failed in transferring the carbene moiety to nucleophiles such as olefins, alcohols or amines, among others, even at temperatures as high as 70 °C. Structural parameters from X-ray studies, particularly the d(C-N) of 1.28 Å, allows proposing a substantial contribution of resonance form III (Scheme 2a), with a C=N bond. This agrees with a low back-donation from copper to the carbene group, in line with a predominant sigma-donor character of the monosubstituted aminocarbene (MAC) ligand.

Given the simplicity of the MAC ligand in terms of size, and the aforementioned reported capabilities of copper-carbene complexes toward transmetalation reactions, we decided to investigate the potential of complex **1** toward that end. It is of note that previous reports on this topic usually employ di-coordinated copper complexes of type LCu(carbene), at variance with the tetra-coordinated, distorted tetrahedral geometry observed in complex **1**. In a series of experiments carried out at NMR scale, solutions with equimolar mixtures of [Tp^{M_s}Cu=C(H)(NEt₂)] and [RhCl(COD)]₂, [CpRhCl₂]₂, *trans*-[PdCl₂(NCMe)₂], *trans*-[PdCl₂(NCMe)(PPh₃)], *cis*-[PtCl₂(COD)], [Cu(NCMe)₄][PF₆]₂ or [AuCl(THT)] led to the smooth formation of complexes **2-8** (Scheme 2b), at room temperature, in a time range of 5-30 min. In all cases, the disappearance of the carbenic Cu-C-H resonances of **1** and the appearance of new signals, both in the ¹H and ¹³C NMR spectra for the corresponding M-C-H moiety were observed. As shown in Scheme 2, the MAC ligand can be readily transferred from **1** to the acceptor metal complex, in some cases leading to a bis-carbene complex (**6**, **7**). The hydrogen chemical shift, originally found at 8.02 ppm for the parent copper complex **1**, shifted toward higher chemical shifts within the 9.00-11.35 ppm range (Scheme 2b). The ¹³C chemical shift for the carbenic carbon nucleus moved from 236.6 to an interval limited by 206.0 (**4**) and 246.7 (**2**). For the case of the platinum complex **6**, the J_{Pt-C} value of 1245 Hz allows proposing a *cis* geometry (vide infra for X-ray confirmation).²⁴ It is worth mentioning that other transition metals bearing similar aminocarbene ligands have been reported; however, they were synthesized by limited scope methods and in no case using a transmetalation strategy.²⁵⁻³⁵

Isolation and structural characterization of MAC complexes.

Once the *in-situ* generation of the metal-MAC complexes was assessed, we turned our attention to their isolation. The use of acetonitrile as reaction solvent led to the precipitation of the copper complex [Tp^{M_s}Cu(NCMe)], affording, in most cases, clean

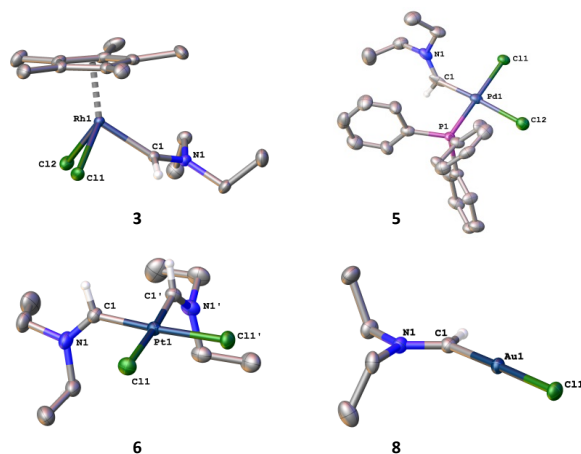
solutions of the new complexes **2-8** which were isolated in 15-80% yields upon workup (see Supplemental Information for full description).



Scheme 2. In situ NMR-scale (CD_2Cl_2) transmetalation of the monosubstituted aminocarbene (MAC) to G9-G11 metals. 2D NMR correspond to HSQC experiments. See Supplemental Information for full set of spectroscopic data.

Single crystals of complexes $[\text{Cp}^*\text{Rh}(\text{MAC})(\text{Cl})_2]$ (**3**), $[\text{PdCl}_2(\text{MAC})(\text{PPh}_3)]$ (**5**), $[\text{PtCl}_2(\text{MAC})_2]$ (**6**) and $[\text{AuCl}(\text{MAC})]$ (**8**) were grown. Figure 1 shows their structures as well as relevant bond distances and angles, from which several trends can be extracted. The metal-MAC M-C1 bond distance fits well with the existence of a single bond, and a nearly non-existent back-donation from the metal to the carbene ligand. The C-N bond distances of the MAC ligand fall within the range typical for a carbon-nitrogen double bond, similarly to that of 1.28 Å previously described for the parent

copper complex **1**. These bond lengths reflect the important donation of the lone electron pair on the nitrogen of the amino group to the vacant p orbital of the carbenic carbon atom. Angles around the N atom are consistent with a sp^2 hybridization and a distorted trigonal planar geometry. All in all, structural data allows drawing the structure of the M-MAC unit with a single M-C bond and a double carbon-nitrogen bond, assuming a prevalent sigma-donor character of the carbene ligand. Albeit charge separation could be drawn showing ionic structures similar to III in Scheme 2 for the parent complex **1**, we believe that for the sake of clarity charges can be omitted. The information gained from structural determination unambiguously demonstrate the role of the MAC ligand as a strong sigma donor with very low acceptor capabilities, in a similar manner to the ligands shown in Scheme 1c. To reinforce such statement, the next section provides additional experimental evidence toward that end.



Complex	M-C1 (Å)	C1-N1 (Å)	Σ (angles around N1)
[Cp*Rh(MAC)(Cl) ₂] (3)	1.9838(11)	1.2967(14)	359.97°
[PdCl ₂ (MAC)(PPh ₃)] (5)	1.968(11)	1.270(13)	359.90°
[PtCl ₂ (MAC) ₂] (6)	1.950(3)	1.288(4)	359.90°
[AuCl(MAC)] (8)	1.980(4)	1.287(4)	360.00°

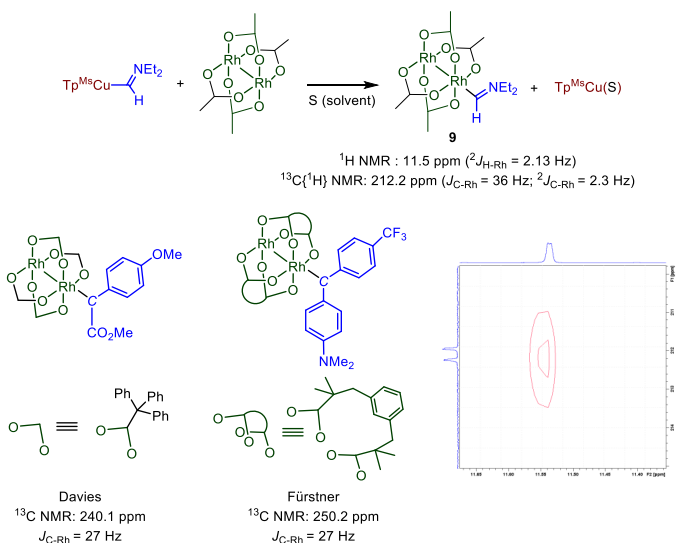
Figure 1. Molecular structures of complexes 3, 5, 6 and 8 and relevant distances and angles.

In all cases for the **2-8** series of complexes, the ethyl groups of the MAC ligand provide two separate sets of NMR resonances in solution, similarly to that found for complex **1**. The lack of symmetry in the molecules account for such difference, albeit a rotation of the C=N bond could promote their equivalency in solution, which is not observed. In addition, 1D NOESY experiments carried out on **1** and **8** as representative examples have shown NOE effects between the carbenic proton and only one of the ethyl groups, the other resulting unaffected (see Supplemental Information for full description). This is the result of the lack of C=N rotation, in solution, at least in the NMR timescale and it is consistent with the double bond character observed in the solid state.

There are two additional comments that arise from the above data. The platinum-based complex shows the two carbene ligands in a *cis*-disposition. Actually, this is what could be expected for a complex with two chloride and two carbene ligands, based on their *trans* influence. However, the already reported $[\text{PtCl}_2(\text{NHC})_2]$ display a *trans* disposition of the NHC ligands,³⁶ due to their high steric demand. It is only because of the small size of the MAC ligand that complex **6** shows the electronically preferred *cis* geometry. The gold complex **8** contains the special feature of the observation of aurophilic interactions, and the formation of zig-zag chains supported by weak Au-Au connections at distances of 3.27-3.32 Å, similar to those observed for $[\text{AuCl}(\text{NHC})]$.³⁷

Capture of the elusive dirhodium tetraacetate monosubstituted carbene complex $\text{Rh}_2(\text{OAc})_4(\text{MAC})$ (**9**).

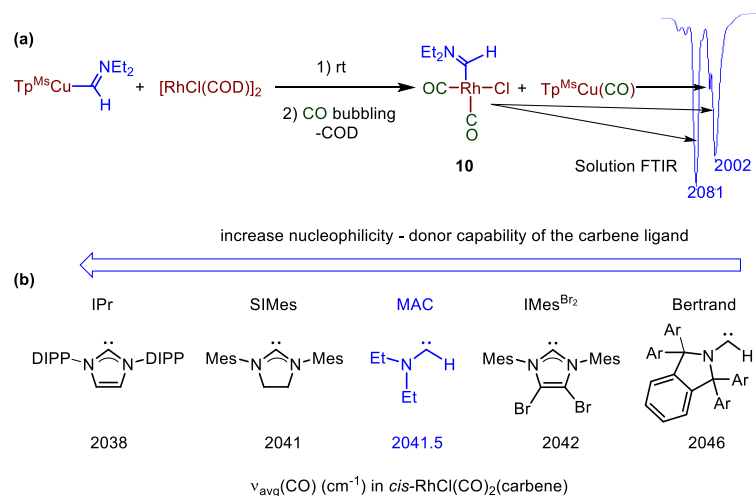
The exceptional capabilities of complex **1** to transfer the MAC ligand has been explored in the synthesis of monosubstituted carbene metal complexes largely pursued but yet unreported. To illustrate such potential, we have focused on $[\text{Rh}_2(\text{OAc})_4]$, a complex which displays an excellent activity for the transfer of carbene groups from diazo compounds. After half a century since such reactivity was reported by Teysié and co-workers,³⁸ a large family of derivatives of composition $[\text{Rh}_2(\text{L})_4]$ has grown over the years for the incorporation of carbene moieties to a plethora of substrates. The rhodium-carbene intermediates have been detected or isolated, albeit always showing disubstitution at the carbenic carbon, by Davies and Berry³⁹ and by Fürstner.⁴⁰ To the best of our knowledge, experimental evidence for a monosubstituted dirhodium-carbene species is yet unreported. On this basis, we have run the reaction of complex **1** with $[\text{Rh}_2(\text{OAc})_4]$, which has led to the formation of complex $[\text{Rh}_2(\text{OAc})_4(\text{MAC})]$ (**9**). Addition of a second equivalent resulted in no incorporation of the MAC ligand to the other rhodium center. As shown in Scheme 3, the carbene resonances appear centered at 11.5 (d, $^2J_{\text{H-Rh}} = 2.1$ Hz) and 212.2 ppm (dd, $^1J_{\text{C-Rh}} = 36$ Hz and $^2J_{\text{C-Rh}} = 2.3$ Hz) in the ^1H and ^{13}C NMR spectra, respectively. The signal corresponding to the carbenic carbon nucleus appears at lower chemical shift than those reported by Davies and Berry (240.1 ppm) and Fürstner (250.2 ppm), with donor-acceptor and donor-donor substituents, respectively (Scheme 3). Interestingly, the observation of two constants corresponding to the coupling to both rhodium nuclei is only found with complex **9**, at variance with the other two known examples shown in Scheme 3, which only display coupling to one rhodium nucleus. Reported $[\text{Rh}_2(\text{O-O})_4(\text{NHC})]$ adducts show no coupling^{41,42} of the carbenic carbon with rhodium nuclei, whereas phosphite $[\text{Rh}_2(\text{O-O})_4(\text{P}(\text{OR})_3)]$ adducts display two distinct coupling constants with both rhodium centers.⁴³ Complex **9** constitutes the first example of a dirhodium-monosubstituted carbene complex that has been detected and spectroscopically characterized.



Scheme 3. Generation of the dirhodium-monosubstituted carbene complex 9.
 The HSQC spectrum shows the correlation between the carbenic C-H moiety.

Electronic properties of the MAC ligand.

Once assessed the nucleophilic character of the MAC ligand derived from already presented structural data, we wondered how it compares to other nucleophilic carbene ligands. Toward that end, we employed one of the strategies reported to evaluate the electronic properties of NHC ligands, consisting in the generation of a complex of composition $\text{cis}[\text{RhCl}(\text{CO})_2(\text{carbene})]$,⁴⁴ and measuring the average $\nu(\text{CO})$ for the two carbonyl absorptions in the IR spectrum. We thus generated complex $\text{cis}[\text{RhCl}(\text{CO})_2(\text{MAC})]$ (**10**) upon consecutive reaction of **1** with $[\text{RhCl}(\text{COD})]_2$ followed by CO bubbling through the solution (Scheme 4a). Solution FTIR studies showed two $\nu(\text{CO})$ bands centered at 2081 and 2002 cm^{-1} , which provide a $\nu_{\text{avg}}(\text{CO})$ value of 2041.5 cm^{-1} . Its comparison with those reported⁴⁴ for other $\text{cis}[\text{RhCl}(\text{CO})_2(\text{carbene})]$ complexes containing nucleophilic carbene ligands is shown in Scheme 4b. The MAC ligand displays electronic properties very similar to NHC ligands such as SIMes or IMes^{Br2}, which are disubstituted carbenes with a substantial steric pressure exerted by the mesityl flanking substituents at the N atoms. In line with these measurements, MAC ligand is more nucleophilic than the monosubstituted carbene described by Bertrand, but less than the commonly employed IPr. In any case, experimental data seems to assess that this very simple, monosubstituted ligand provides electron density to the metal comparable with those more elaborated, disubstituted NHC ligands.



Scheme 4. Evaluation of the electronic properties of the MAC ligand.

To further analyze the electronic properties of MAC we have computed electrophilicity (ω) and nucleophilicity (N) indexes for the free MAC ligand (:C(H)NEt₂) and related carbenes as well (see the complete series and calculation details at the Supplemental Information, Figures S64 and S65). As shown in Figure 2, MAC appears as a strong nucleophile ($N > 3.0$ eV)⁴⁵ and a marginal electrophile ($\omega < 0.8$ eV).⁴⁶ Its nucleophilicity index (3.13 eV) is very similar to that of the monosubstituted aminocarbene described by Bertrand¹³ and the Fischer carbene :C(Ph)(OMe), but it is a much weaker electrophile ($\omega = 0.68$ eV).

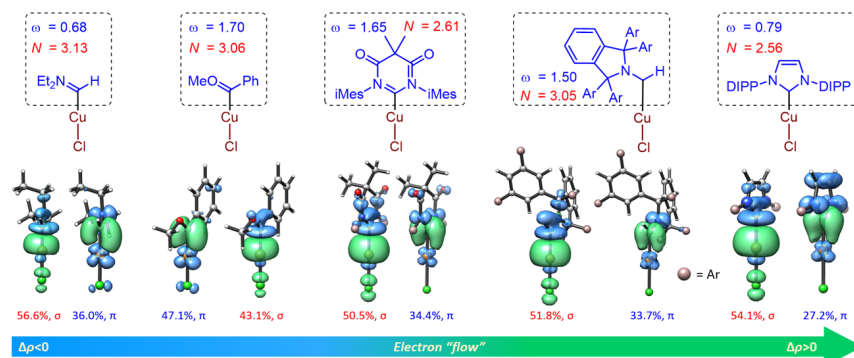
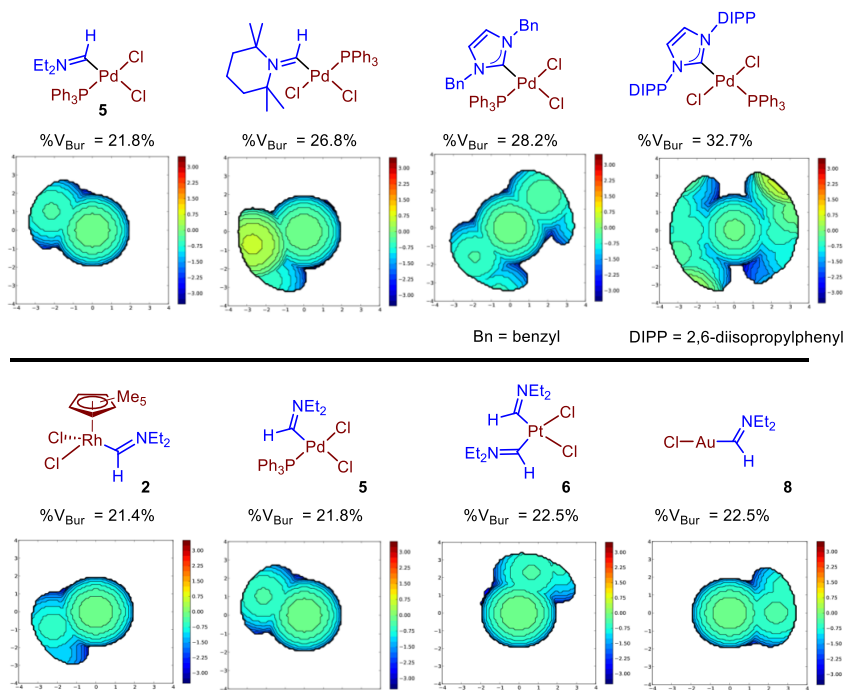


Figure 2. For the reported carbene series: top, computed global electrophilicity index (ω) and the relative nucleophilicity index (N) for the carbene fragments; bottom, ETS-NOCV isodensity surfaces $\Delta\rho_{1-2}$ (0.005 a.u.) for the deformation maps relative to the C-M bond of the most relevant NOCV pairs along with their σ or π % character computed as: $\% \Delta\varepsilon_{\text{orb}}(\sigma \text{ or } \pi) = \left[\frac{\sum_i \Delta\varepsilon_{\text{orb}}(\sigma \text{ or } \pi)}{\Delta\varepsilon_{\text{orb}}(\text{total})} \right] \cdot 100$.

The metal-carbene bond properties were analyzed by the Energy Decomposition Analysis - Natural Orbitals for Chemical Valence (EDA-NOCV) scheme, considering CuCl as the transition metal fragment binding the carbene ligand (complete analysis is available at the Supplemental Information Table S2). The percentage of σ and π contributions to the stabilizing orbital term ΔE_{orb} for CuCl-MAC bond is similar to those of the Bertrand's monosubstituted aminocarbene (Figure 2) and in line with similar analysis in group 11 complexes with N-heterocyclic carbenes.⁴⁷

Steric properties of the MAC ligand.

Albeit at first sight the steric hindrance of the MAC ligand is significantly lower than that of the ligands shown in Schemes 1c or 4b, as representative examples, we have searched for evidence to demonstrate it. A valuable tool for such goal is the so-called percent buried volume ($\%V_{\text{Bur}}$) of a ligand,⁴⁸ which provides a measurement of the space blocked by a given ligand around the metal center. To achieve such value, crystallographic data must be employed where similar compounds with a given ligand can be compared. In this sense, we focused on complex *cis*-[PdCl₂(MAC)(PPh₃)] **5**, for which the molecular structure has been determined (Figure 1). We have searched for related *cis*-[PdCl₂(carbene)(PPh₃)] complexes in the literature, prepared by other routes,⁴⁹ and found that disubstituted NHC carbenes bearing DIPP or Mes groups attached to the N atoms exclusively provide the corresponding *trans*-[PdCl₂(NHC)(PPh₃)] complexes.⁵⁰ Only when less sterically demanding substituents such as IBn (Bn = benzyl) ligands were used, the *cis*-isomer was isolated.⁵¹ Scheme 5 displays the results of the calculation of the $\%V_{\text{Bur}}$ for complex **5** as well as two additional *cis*-[PdCl₂(carbene)(PPh₃)] complexes, where the carbene ligand corresponds with IBn or another monosubstituted carbene (:C(H)NR₂), derived from 2,2,6,6-tetramethylpiperidine.⁵² Complex **5** shows the lowest value of the $\%V_{\text{Bur}}$, with the MAC ligand occupying 21.8% of the volume. This value increases up to 26.8% for the pyrrolidine-derived carbene ligand and to 28.2% for the IBn ligand. For comparison, the $\%V_{\text{Bur}}$ for the IPr ligand in the *trans*-[PdCl₂(IPr)(PPh₃)] has been calculated as 32.7%. Therefore, the MAC ligand possesses a reduced volume compared with those of other carbene ligands shown in Scheme 4, although they are similar from an electronic point of view.



Scheme 5. Evaluation of the steric properties of the MAC ligand compared with other carbene ligands in a series of PdCl₂(carbene)(PPh₃) complexes (top) and within the series of new complexes **2**, **5**, **6** and **8**. The topographic map is drawn with the metal-carbene carbon axis in the center. All other ligands are removed for clarity, the V_{Bur} value correspond to the volume of a sphere centered at metal with a radius of 3.5 Å (convention) that is occupied by the carbene ligand.

A comparison within the four structurally characterized complexes **2**, **5**, **6** and **8** has also been done (Scheme 6). The calculated V_{Bur} remains limited within a narrow interval of 21.4–22.5%, despite the differences in the metal, coordination number and size of the other co-ligands in each complex. The parent complex **1**, with a highly sterically demanding TpMs ligand, also shows a V_{Bur} value of 22.3% for the MAC ligand. Overall, we can conclude that the volume of the MAC ligand around a metal center is quite reduced and is maintained independently of the ML_n core to which it is ligated.

NMR studies on the copper-to-palladium transmetalation reaction.

The transmetalation of the carbene group from copper complex **1** to *trans*- $[\text{PdCl}_2(\text{NCMe})(\text{PPh}_3)]$, generated upon dissolving $[\text{Pd}(\mu\text{-Cl})\text{Cl}(\text{PPh}_3)_2]$ in acetonitrile, was monitored at variable temperature by ^1H NMR. Both complexes were mixed at -40°C in a ratio Cu:Pd = 1:1. The evolution of the low field region corresponding to the Pd-CHNEt₂ resonance is shown in Figure 3. It was found that in the -40°C to -25°C temperature interval, the formation of complex *trans*- $[\text{PdCl}_2(\text{MAC})(\text{PPh}_3)]$ (*trans*-**5**) occurred, being the only species observed. This *trans*- isomer shows a similar chemical shift for the proton signal of the aminocarbene than that of *cis*-**5** but with a slightly higher coupling constant to phosphorous (*trans*-**5**, $J_{\text{H-P}} = 11.0$ Hz vs. *cis*-**5**, $J_{\text{H-P}} = 8.1$ Hz). At -25°C , the formation of complexes **4** and *cis*-**5** was observed. In the last temperature interval (-25°C to -10°C) both **4** and *trans*-**5** transform into the thermodynamically more stable complex *cis*-**5**, which is the final product of the reaction (Figure 3). To check the possible scenario in which the Cu(I) complex can be acting as a trapping agent of PPh₃ during the transmetalation step, and therefore being the cause of the formation of the phosphine-free complex **4**, independent experiments have been carried out. Neither the starting carbene complex $[\text{Tp}^{\text{Ms}}\text{Cu}\{\text{CH}(\text{NEt}_2)\}]$ nor $[\text{Tp}^{\text{Ms}}\text{Cu}(\text{THF})]$ react with PPh₃.

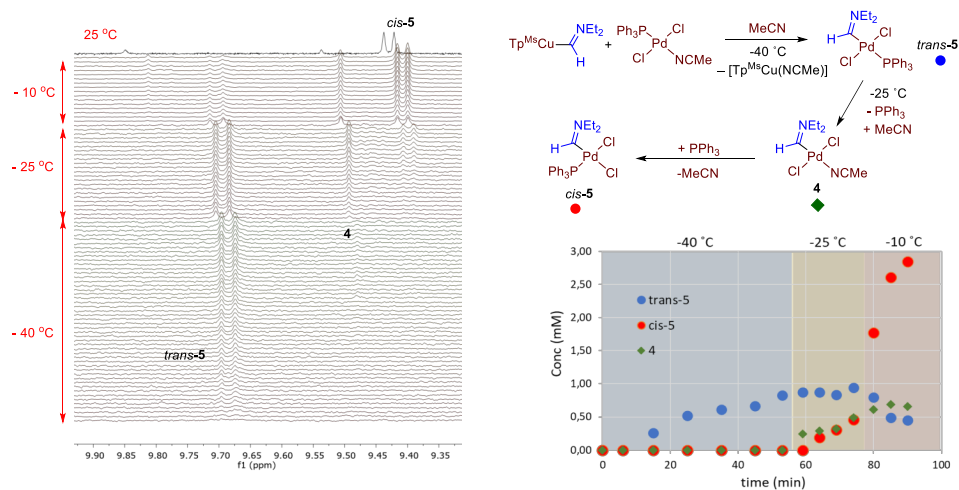


Figure 3. ^1H NMR monitoring of the transmetalation process from copper to palladium.

DFT calculations on the transmetalation reaction.

Transmetalation processes commented in the previous section are seemingly simple ligand exchange reactions in which the carbene ligand is transferred from the Cu(I) center of **1** to another transition metal center. However, DFT studies (B3LYP-D3 calculations in solution, see Computational Details at the Supplemental Information)

reveal a more complicated mechanistic scenario. The steps for the transmetalation of :C(H)(NEt₂) (MAC) from **1** to *trans*-[PdCl₂(NCMe)(PPh₃)] are shown in Figure 4, together with a 3D-view of the involved transition states. The Gibbs energy profile and optimized structures of all the species involved are collected in the Supplemental Information (Figures S54-S55).

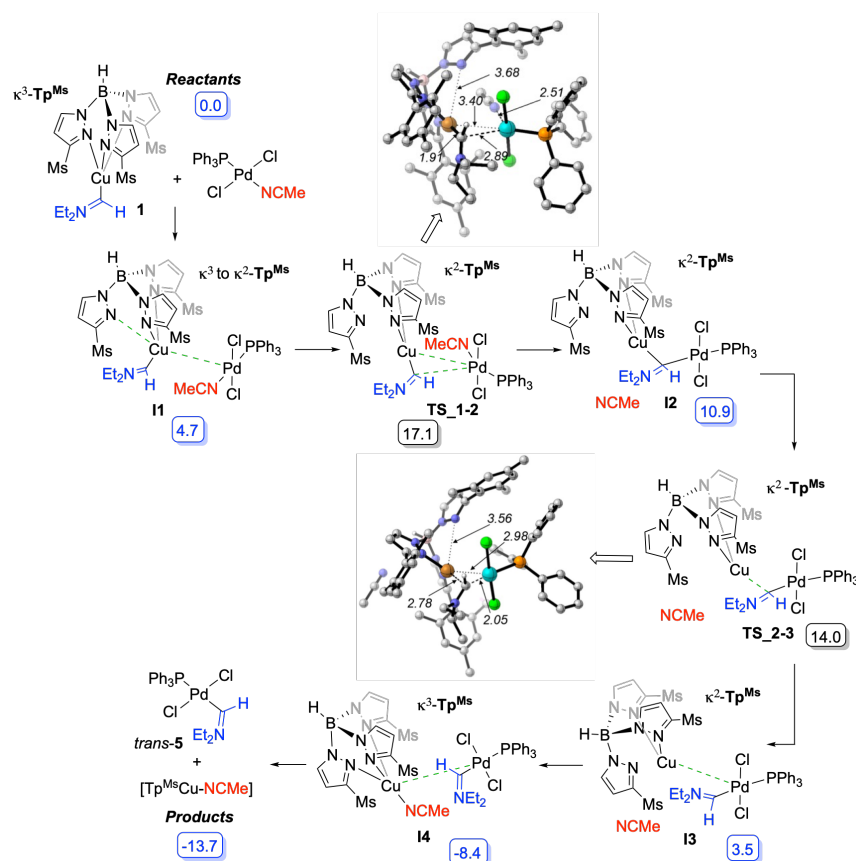
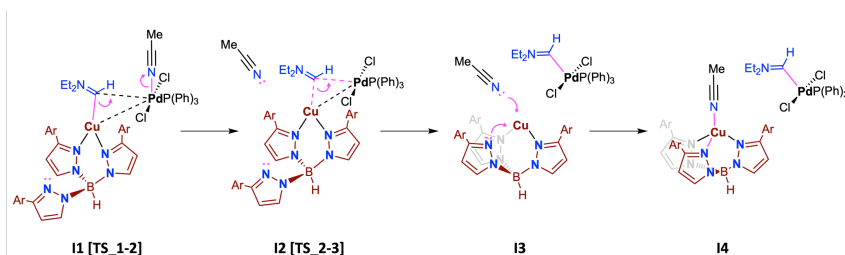


Figure 4. Reaction pathway for the transmetalation of MAC from **1 to *trans*-[PdCl₂(NCMe)(PPh₃)]. Numbers are relative Gibbs energies of each structure in acetonitrile solvent, in kcal mol⁻¹.**

The electronic rearrangements involved in the transmetalation have been identified by following the displacement of the centroids of the localized molecular orbital (CLMO) along the reaction coordinate, devising the arrow-pushing scheme depicted in Scheme 6 (see Supplemental Information, Figure S62).⁵³



Scheme 6. Arrow-pushing scheme of the transmetalation mechanism from the analysis of the displacement of the centroids of localized molecular orbitals (CLMOs). Dashed pink lines describe a three-center-two-electron Cu-carbene-Pd bond. Dashed black lines only indicate closeness between Pd and Cu atoms.

Calculations identify structures with the carbene ligand bridging both metals as key species in the transmetalation process. To reach such conformations, the two metals must approach to a distance around 3 Å. However, the presence of the mesityl arms in the Tp^{Ms} ligand creates a steric encumbrance that hinders the approach of both complexes. The intermetallic approach is driven by the strong donating character of the carbene that labilizes a Cu-N(pyrazolyl) bond, which elongates from 2.08 Å in $\text{Tp}^{\text{Ms}}\text{Cu}$ to 2.38 Å in $[\text{Tp}^{\text{Ms}}\text{Cu-C(H)(NEt}_2)]$, allowing an easy change of the Tp^{Ms} coordination from κ^3 to κ^2 when *trans*- $[\text{PdCl}_2(\text{NCMe})(\text{PPh}_3)]$ comes into play (intermediate **I1**, Cu-N = 3.81 Å; Cu-Pd distance of 5.21 Å, Figure 4). From this κ^2 - Tp^{Ms} intermediate, dissociation of the acetonitrile ligand in the Pd(II) complex via **TS_1-2** permits approaching of the Cu(I)-C(H)(NEt₂) unit to the palladium(II) center with formation of a Cu-carbene-Pd three-membered ring in **I2**.

In intermediate **I2** the carbene is bridging both metals (Cu-C and Pd-C distances of 1.95 and 2.26 Å, respectively), which fall at 2.80 Å to each other (not very far from the sum of the Cu-Pd covalent radii, 2.71 Å).⁵⁴ The CLMO analysis describes the three-membered Cu-Pd-carbene ring as simple three-center two electron species, in which the σ -lone pair of the bridging carbene is shared by the two metals (see Scheme 6 for a simple view of arrow pushing and the associated localized molecular orbital in Figure S63). No relevant displacement of Cu or Pd CLMOs along the metal-metal axis is observed, thus ruling out Cu-Pd donor-acceptor interactions. It is thought that metal-metal interactions facilitate transmetalation steps, although the nature of such interactions, usually named metallophilic interactions, has been matter of debate.⁵⁵ In analogy with our results, short metal-metal distances without intermetallic bond critical point were also reported for heterobimetallic Cr-Pd and Cr-Cu intermediates in carbene transmetalations,⁵⁶ or in models for Pd-Cu transmetalations.⁵⁷ All in all, despite the short distance between both metal centers, data available do not support the existence of noticeable metallophilic interactions beyond the 3c-2e bond.

Dissociation of the carbene from copper occurs in **TS_2-3** (Cu-C(carbene) = 2.78 Å; Pd-C(carbene) = 2.05 Å), although both metals are still at a short distance (Cu-Pd = 2.98 Å). This transition state connects with intermediate **I3** in which the two metals separate (Cu-Pd = 3.50 Å) and the carbene is fully transferred to the palladium center. The trispyrazolyl borate ligand keeps a κ^2 - Tp^{Ms} coordination in this step. Finally, the two complexes move further away (Cu-Pd distance of 6.05 Å in **I4**), allowing coordination of one acetonitrile molecule to the Cu(I) center, which recovers the initial κ^3 -coordination of the Tp^{Ms} ligand. In this way the transmetalation is completed and *trans*- $[\text{PdCl}_2(\text{MAC})(\text{PPh}_3)]$ (*trans*-**5**) is formed. Relative Gibbs energies of all the species in the transmetalation pathway (numbers in Figure 4) agree with a smooth energy landscape for the transformation, which takes place with an energy span of only 17.1 kcal mol⁻¹, in agreement with the fast reaction at room temperature. Cu to Pd

transmetalation has a thermodynamic driving force (ΔG of reaction = -13.7 kcal mol⁻¹).

As commented in the previous section, raising the temperature leads to the isomerization of *trans*-[PdCl₂(MAC)(PPh₃)] (*trans*-**5**) to *cis*-[PdCl₂(MAC)(PPh₃)] (*cis*-**5**) as the final product, with the concomitant formation of *trans*-[PdCl₂(MAC)(NCMe)] (**4**) (Figure 3). We have computationally evaluated the mechanism of the *trans*-**5** to *cis*-**5** isomerization. In *trans*-**5** the strong σ -donor MAC labilizes the *trans* PPh₃ ligand (Pd-P distance of 2.41 Å), provoking its low energy-demanding dissociation (15.4 kcal mol⁻¹). The coordination vacancy created in the Pd coordination sphere is filled by a solvent molecule (acetonitrile), yielding the detected intermediate *trans*-[PdCl₂(MAC)(NCMe)] (**4**). In a subsequent step the phosphine displaces a chloride ligand and finally the chloride reenter into the Pd coordination sphere displacing the acetonitrile and forming the final *cis*-**5** product. The overall Gibbs energy barrier for the isomerization is 17.3 kcal mol⁻¹, and the process is driven by the thermodynamic stability of the *cis*-**5** product, 7.4 kcal mol⁻¹ more stable than *trans*-**5**. The complete energy profile and 3D views of the optimized structures along the isomerization pathway can be found at the Supplemental Information (Figures S57 and S58).

To assess the feasibility of the transmetalation mechanism found for the Cu(I) to Pd(II) transmetalation of MAC for other metals, we have also computed the transmetalation from **1** to [AuCl(THT)]. Details are provided at the Supplemental Information (Figures S59 and S60). The main features of the process are the same than for the Pd(II) complex.

The picture for the carbene transmetalation than emerges from these computational studies is that it requires placing the migrating ligand bridging both metal centers. However, this is a necessary but not sufficient condition to achieve the transmetalation. Indeed, this disposition has been already proposed for Cu(I) to Pd(II) transmetalation of alkynyl ligands in Sonogashira couplings,⁵⁷ although in most of the reported cases transmetalation is not accomplished, but it stops without complete transfer of the alkynyl to the palladium. We have computationally analyzed one of such cases, the reaction of [Pd(η^3 -allyl)Cl(PPh₃)] with [Cu(C \equiv CPh)] (see Supplemental Information, Figure S61).⁵⁸ Stopping half-way in the transmetalation path, with bimetallic complexes being formed instead, has also been found in attempted Cr-Au carbene transmetalations.⁵⁹ Therefore, a moderate energy demanding approach of the two transition metal complexes to form the ligand bridging structure, and not too stable intermediates after its formation are required for a successful transmetalation. In our systems, ligand displacements and changes in the coordination mode of Tp^{M_s} contribute to the fulfillment of both conditions.

Of course, a third requirement concerns the stability of the transmetalated products, that must be more stable than the initial complexes, thus providing a thermodynamic driving force to the transmetalation process. Therefore, the balance between the energies of bonds broken and formed along the process is relevant for the fate of transmetalation. Computed ΔG of binding for all the ligands are collected at the Supplemental Information (Figure S66 and Table S3).

Conclusions

We have developed a novel transmetalating system using the complex [Tp^{M_s}Cu-C(H)(NEt₂)] that readily introduces the monosubstituted aminocarbene C(H)(NEt₂) ligand (MAC) in the coordination sphere of a variety of metal complexes (M = Rh, Pd, Pt, Cu, Au). This MAC ligand displays unique features since it resembles the nucleophilicity and donor ability associated to bulky N-heterocyclic carbene ligands but occupying a much-reduced volume around the coordination sphere than those NHC ligands. Those electronic and steric properties provide a certain stability to the metal-carbene complexes formed through this strategy, despite the monosubstituted

character of the carbene ligand. Application to $[\text{Rh}_2(\text{OAc})_4]$ has led to the formation of $[\text{Rh}_2(\text{OAc})_4(\text{MAC})]$, exemplifying the competence of the system. A computational study highlights some of the basic requirements to meet when designing new transmetalating systems: i) the migrating ligand should be able to bridge the metal centers; ii) the intermetallic approach should not be too energy demanding and the subsequent intermediate should not be too stable to stop the reaction; and iii) the entire process should be exergonic providing the thermodynamic driving force.

EXPERIMENTAL PROCEDURES

Resource availability

Lead contact

Further information and requests for resources and reagents should be directed to the lead contact, Pedro J. Pérez.

Materials availability

Information about all materials generated in this study are available from the lead contact without restriction.

Data and code availability

The accession numbers for the crystallographic data reported in this paper are CCDC 2290008, (3), 2289359 (5), 2333619 (6) and 2333619 (8). Copies of these data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif. Correspondence and requests for materials should be addressed to P. J. P.

Full experimental procedures are provided in the supplemental information.

SUPPLEMENTAL INFORMATION

Supplemental information can be found online at <https://doi.org/>

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AUTHOR CONTRIBUTIONS

P. J. P., T. R. B., A. C. A. and A. L. conceived the project and designed the experiments; M. A., F. V. and M. C. performed the experiments and analyzed the data; G. S. and A. L. performed the theoretical calculations; F. M. and F. V. collected the X-ray data and refined the structures; all authors discussed the results and edited the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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