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Authors: Julio Pérez, Rebeca Arevalo, Ramón López, Larry Falvello, and Lucía Riera

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Building C(sp^3) Molecular Complexity on 2,2'-Bipyridine and 1,10-Phenanthroline in Rhenium Tricarbonyl Complexes

Rebeca Arevalo,[a][b] Ramón López,[c] Larry R. Falvello,[d] Lucía Riera[a][e] and Julio Perez*[a][e]

[a] R. Arevalo, L. Riera, J. Perez
Departamento de Química Orgánica e Inorgánica
Universidad de Oviedo
Julián Clavería, 8, 33006, Oviedo (Spain)
E-mail: japm@uniovi.es
[b] R. Arevalo current address
Department of Chemistry and Chemical Biology
University of California, Merced
5200 N. Lake Road, 95343 Merced, CA (USA)
[c] R. López
Departamento de Química Física y Analítica
Universidad de Oviedo
Julián Clavería, 8, 33006, Oviedo (Spain)
[d] L. R. Falvello
Departamento de Química Inorgánica
Instituto de Ciencia de Materiales de Aragón (ICMA), Universidad de Zaragoza–CSIC
50009 Zaragoza (Spain)
[e] J. Perez, L. Riera
Centro de Investigación en Nanomateriales y Nanotecnología-CINN
CSIC- Universidad de Oviedo-Principado de Asturias
Avda.de la Vega 4–6, 33940, El Entrego (Spain)

Supporting information for this article is given via a link at the end of the document: General considerations; preparation of transition-metal complexes; spectroscopic and computational data (PDF). Crystallographic data for **8** (CCDC 1567450), **13** (CCDC 1567451) and **14** (CCDC 1567452) (CIF).

Abstract: The reactions of [Re(N-N)(CO)$_3$(PMe$_3$)]OTf (N-N= 2,2'-bipyridine, bipy; 1,10-phenanthroline, phen) compounds with *t*BuLi and with LiHBEt$_3$ have been explored. Addition to the N-N chelate took place with different site-selectivity depending on both chelate and nucleophile. Thus, with *t*BuLi, an unprecedented addition to C5 of bipy, a regiochemistry non-accessible for free bipy, was obtained, while coordinated phen underwent *t*BuLi addition to C2 and C4. Remarkably, when LiHBEt$_3$ reacted with [Re(bipy)(CO)$_3$(PMe$_3$)]OTf, hydride addition to the 4 and 6 positions of bipy triggered an intermolecular cyclodimerization of two dearomatized pyridyl rings. In contrast, hydride addition to the phen analog resulted on partial reduction of one pyridine ring. The resulting neutral Re(I) products showed a varied reactivity with HOTf and with MeOTf to yield cationic complexes. These strategies rendered access to Re(I) complexes containing bipy- and phen-derived chelates with several C(sp^3) centers.

Introduction

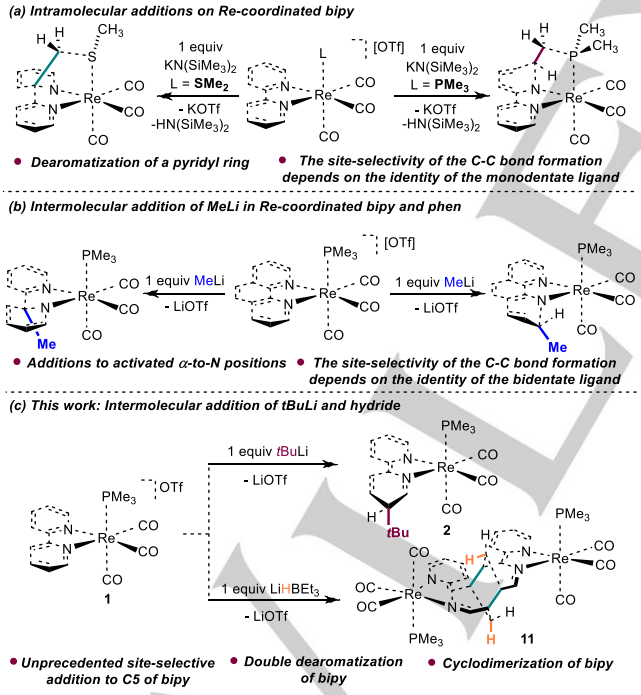
Substituted bipy and phen ligands are ubiquitous in coordination and organometallic complexes, many of which have applications in contemporary research fields, such as catalysis, photochemistry, luminescent materials or medicinal chemistry.[1] The introduction of substituents in the chelate backbones allows to tune the steric and electronic properties of their metal complexes. Hence, the ability to access a variety of substitution patterns plays an important role in the rationalization of structure-activity relationships[2] and the development of functional molecules with improved properties.[3] Chemical modification of bipy and phen beyond their decoration with substituents and, especially, functionalization of the coordinated ligands in their metal complexes, remains uncharted territory. As the interest in functional molecules incorporating C(sp^3) centers grows, so does the need for synthetic methods that provides access to 3-dimensional analogs of flat aromatic compounds. While moving from the 2D to the 3D chemical space has had great impact in the pharmacological properties of APIs (Active Pharmaceutical Ingredients),[4] the consequences of replacing a bipy or phen chelate by a 3D analog in a transition metal complex are unknown.[5]

The synthesis of C(sp^3)-containing analogs of bipy and phen by classic organic methods[6] might be challenging, and certain substitution patterns are difficult to attain. The main purpose of the synthesis of new bipy and phen derivatives is their use as chelate ligands in the preparation of metal complexes. Hence, a logical approach would involve exploiting the steric and electronic environment that a metal fragment imparts on the chelate to build C(sp^3) centers and unique substitution patterns. This strategy would enable direct access to the metal-chelate complex by post-coordination functionalization. Seminal work by Tzalis and Tor established that the coordination to a transition metal fragment could turn on S$_N$Ar reactivity that was unknown for free halogenated phen.[7] However, prior to our work, post-coordination functionalization of the parent bipy and phen ligands in metal complexes has never been exploited. Cationic Re(I) tricarbonyl complexes of the type *fac*-[Re(N-N)(CO)$_3$L]$^+$ (N-N = bipy, phen) are attractive targets to implement this strategy as they are currently employed as CO_2 reduction catalysts,[8] anticancer agents,[9] luminescent materials,[10] and bioimaging agents[11] among other areas of research.[12] The creation of C(sp^3) centers in their bipy or phen ligands at different ring positions will expand their chemical landscape and the range of their properties and applications.

From a fundamental point of view, it is unknown how coordinated bipy and phen ligands in transition-metal complexes behave upon addition of strong nucleophiles. These studies

could be impactful in catalysis, particularly on bipy or phen transition-metal precatalysts that are employed in combination with carbon-based nucleophiles or hydride-donor reagents.[13] Such reactions can be deleterious and be involved in catalyst deactivation, or beneficial if the active species contains a chelate resulting from nucleophilic addition that is more active than the precursor with parent bipy or phen.

In previous studies we showed that bipy and phen coordinated to cationic *fac*-rhenium(I) tricarbonyl[14] or *cis*-molybdenum(II) dicarbonyl[14a,14e] fragments are not chemically inert ligands[15] and can undergo, under very mild conditions, the addition of internal nucleophiles generated by deprotonation of appropriately positioned co-ligands (Scheme 1a). As a result of the additions being intramolecular, the C(sp^3) centers were built on the chelate positions closest to the metal fragment- C2 upon deprotonation of SMe_2[16] and C6 upon deprotonation of N-alkylimidazoles,[14] PMe_3[17] or α-methyl-*N*-heterocycles.[18] Outer-sphere MeLi addition to coordinated bipy and phen ligands of *fac*-[Re(N-N)$(CO)_3(PMe_3)$]OTf (N-N = bipy, phen, Scheme 1b) complexes[17b] suggests that chelate identity plays a role on the site-selectivity of the addition. Unfortunately, the target of the few intermolecular additions to metal-bonded bipy and phen reported were the most electrophilic α-to-N positions,[17b,19] and nucleophilic additions to the β-to-N positions remain elusive. Whether or not the nature of the nucleophile can change the site-selectivity of the addition to metal-bonded bipy and phen remains unknown.



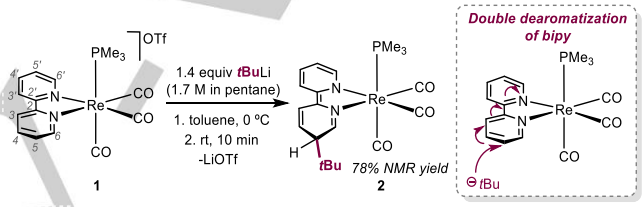
Scheme 1. Strategies to build C(sp^3)-derivatives of bipy and phen ligands by post-coordination addition in rhenium tricarbonyl complexes.

In this work we describe the reactivity of *t*BuLi and $LiHBEt_3$ with *fac*-[Re(N-N)$(CO)_3(PMe_3)$]OTf (N-N = bipy and phen) complexes (Scheme 1c). In all the cases examined, intermolecular additions to the chelates took place yielding neutral Re(I) complexes containing non-planar chelates with C(sp^3) centers and unprecedented substitution patterns. Remarkably, hydride additions triggered a cyclodimerization of bipy and the partial reduction of one of the pyridyl rings in phen.

Results and Discussion

Divergent site-selectivity in the addition *t*BuLi to Re(I) bipy and phen complexes

To explore the reactivity of cationic rhenium(I) complexes containing bipy and phen ligands toward bulkier nucleophiles than MeLi, *t*BuLi (1.7 M in pentane) was added to a suspension of [Re(bipy)$(CO)_3(PMe_3)$]OTf (**1**) in toluene at 0 °C, resulting in the formation of a dark red solution. Filtration in hexane and removal of the volatiles in vacuo afforded a highly air- and moisture-sensitive red powder in good yield (78%), identified as the neutral complex **2**, in which the *tert*-butyl group has been added to the 5 position of the bipy ligand (Scheme 2).



Scheme 2. Site-selective addition of *t*BuLi on the C5 of the bipy ligand of **1** to yield a product with a doubly-dearomatized ligand.

The IR vCO bands of **2** (2019, 1924, 1894 cm^{-1} in toluene) were consistent with a neutral complex. The ^1H, and ^{13}C NMR spectra of **2** in benzene-d_6 showed signals consistent with an asymmetric complex containing a *t*Bu-substituted *N*,*N*-chelate with two dearomatized pyridyl rings. The ^{13}C NMR signals of the *t*Bu group showed crosspeaks with the ^1H NMR signal at 3.00 ppm allowing its assignment to the *t*Bu-bonded C–H of the chelate. This C–H group showed a crosspeak with the H4 of the chelate (5.01 ppm) in the ^1H, ^1H-COSY spectrum, supporting the *t*Bu group to be bonded to the 5 position of the chelate (see SI for a detailed assignment of NMR signals). A NOE between H5 and PMe_3 supported the bulky *t*Bu group in **2** to be on the opposite face from the PMe_3 ligand. The ^1H NMR signals of the chelate occurred between 6.95 (H6) and 3.00 (H5) ppm for the substituted ring, and between 7.82 (H9) and 5.63 (H10) ppm for the unsubstituted ring, indicating the dearomatization of both rings.

To explore the changes in the electron distribution that resulted from the dearomatization of the pyridyl rings, the structures of the cation in **1** and of **2** were optimized by DFT (Figure 1) and Nucleus-Independent Chemical Shift (NICS)[20] calculations on the chelate were carried out.

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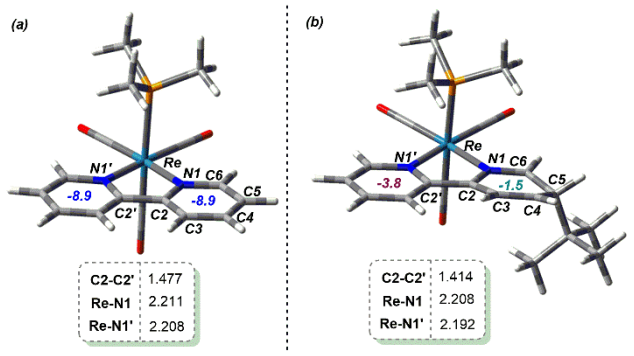


Figure 1. PCM-B3LYP/6-31+G(d) (LANL2DZ for Re) optimized structures of (a) the cation in **1** and (b) **2**. Numbers in tables are calculated bond distances in Å and numbers in the pyridyl rings are calculated NICS(1) in ppm.

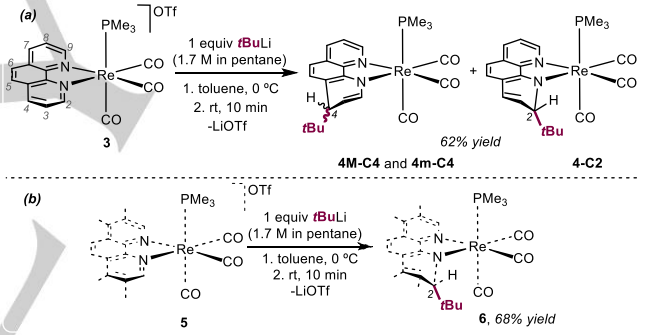
A C2–C2' interpyridyl ring distance of 1.414 Å in **2**, significantly contracted from that in the cation of **1** (1.477 Å), suggested a stronger bond, and is closer to those reported for 2-electron reduced bipy ligands (1.396(10) Å when coordinated to yttrium).[21] NICS values of -1.5 for the substituted ring, and of -3.8 for the non-substituted ring of **2** stand in sharp contrast with the -8.9 value found for both rings of $[Re(bipy)(CO)_3(PMe_3)]^+$. These results indicate a strong disruption of the aromaticity of both pyridyl rings in the bipy ligand of **1** upon addition of *t*BuLi.

To gain further insight into the formation of **2**, the reaction of *t*BuLi with **1** was monitored by ^{1}H NMR spectroscopy in THF-d_8 at -60 °C. Formation of **2** as the major organometallic species was observed, and other regio- or stereoisomers could not be identified (see Figure S9 of the SI). This result supports that the addition of *t*BuLi to **1** was site- and stereoselective to yield **2** and that it is unlikely that **2** was formed by *t*Bu shifts from other regioisomers.

Aiming to rationalize the site-selectivity observed in the reaction, the energies of the regioisomers resulting from *t*BuLi addition at C2 (**2-C2**), C3 (**2-C3**), C4 (**2-C4**) and C6 (**2-C6**) of the bipy in **1** and their kinetic barriers in THF were calculated by DFT (PCM-B3LYP-D3/6-31+G(d) (LANL2DZ for Re), Figure S137). Remarkably, while addition of MeLi was selective to the 2 position of bipy,[17b] the product from addition of *t*BuLi, **2-C2**, was found to be the most unstable (1.2 kcal/mol) of the regioisomers. This instability can be attributed to the steric clash between the *t*Bu substituent and the $\{Re(CO)_3(PMe_3)\}$ fragment, which was neglectable when the smaller MeLi reagent was employed. Accordingly, **2-C6** also showed a higher energy (-8.6 kcal/mol) than the **2**, **2-C3** and **2-C4** regioisomers where the *t*Bu substituent is further away from the metal fragment. Notably, **2** and **2-C3** (-11.5 and -11.3 kcal/mol respectively) showed a similar stability, and were slightly more stable than **2-C4** (-10.4 kcal/mol), despite the fact that the former contain two dearomatized pyridyl rings while in **2-C4** only the attacked ring was dearomatized. The kinetic barriers for each regioisomer are between 22.8 and 23.9 kcal/mol with the barrier leading to **2** (22.8 kcal/mol) only 0.5 kcal/mol lower than that leading to **2-C3** (23.3 kcal/mol). The small difference between the computed kinetic barriers deter us form attempting to use them as a rationale for the encountered regiochemistry. These calculations were carried out for the direct addition of *t*BuLi to the coordinated bipy. Note that known nucleophilic additions to free pyridines, from the venerable Chichibabin reaction[22] to the recent Hartwig fluoridation,[23] start with the coordination of the pyridine nitrogen to the metal of the main group nucleophile (e.g., Li in RLi). For the bipy and phen ligands in this work, their coordination to rhenium precludes such a process. Coordinated bipy or other polypyridines are known to undergo inner sphere reactions in which the alkyl group migrates from the metal to the proximal carbon atoms of the coordinated pyridine ring. In the saturated complexes reported here, devoid of labile ligands, such a possibility can be ruled out.

Nucleophilic addition on position 5 of coordinated 2,2'-bipyridine has no precedent, and additions on 3 and 5 positions of pyridyl rings are extremely rare due to the higher electrophilicity of positions 4, 2 and 6.[24] *t*BuLi adds to the 2 and 6 positions of non-coordinated pyridine[25] and bipy,[26] highlighting the ability of the $\{Re(CO)_3(PMe_3)\}^+$ fragment to enable additions with an unprecedented site-selectivity.

To explore how the nature of the diimine –phen vs bipy– affects the site-selectivity of the addition of *t*BuLi, complex $[Re(phen)(CO)_3(PMe_3)]OTf$ (**3**) was treated with *t*BuLi. The product was isolated as a dark blue powder in 62% yield that was identified as a mixture of three regioisomers (**4M-C4**, **4m-C4** and **4-C2**) from addition of *t*BuLi to the 4 (in **4M-C4**, **4m-C4**) and 2 (in **4-C2**) positions of the phen ligand (Scheme 3a).



Scheme 3. (a) Addition of *t*BuLi to C4 and C2 of the phen ligand in **3** to yield a mixture of three regioisomers and (b) site-selective addition of *t*Bu on C2 of the Me_4phen ligand in **5**.

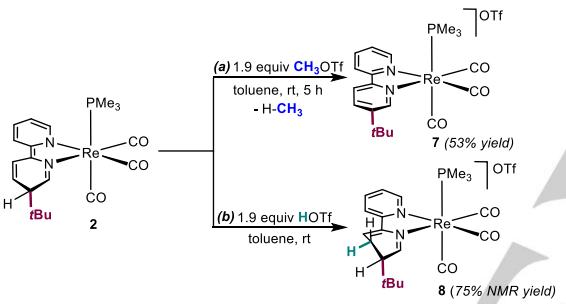
The 2D ^{1}H-^{1}H NOESY showed a NOE of the H2 of **4-C2** and the H4 of **4M-C4** with the PMe_3 ligand, indicating *t*Bu addition to the less sterically hindered phen face of the complex while the *t*Bu group in **4m-C4** is proposed to be on the same face than PMe_3. The **4M-C4**:**4m-C4**:**4-C2** ratio was 2.7:1.7:1.0 (from ^{31}P NMR integration) and remained constant over 16 hours at room temperature. Remarkably, the addition of *t*BuLi to phen in complex **3** took place at positions 2 and 4 of phen (see Table S7 for the DFT calculated bond distances), in contrast to the addition to bipy in complex **1**, which took place exclusively at 5. It can be conceived that the addition to positions 3 and 8 of phen are energetically penalized, as they would involve the dearomatization of the additional fused phenyl ring (see Table S9 for NICS values).

To investigate the effect of substituents at phen, *t*BuLi was added to $[Re(Me_4phen)(CO)_3(PMe_3)]OTf$ (**5**, Me_4phen = 3,4,7,8-tetramethyl-1,10-phenanthroline). The product was isolated as a blue powder in 68% yield and was identified on the basis of NMR spectroscopy as a single regioisomer, **6**, containing the

*t*Bu group on the 2 position of the chelate opposite to the PMe_3 ligand (Scheme 3b). Therefore, the presence of four methyl groups does not deprive the coordinated phenanthroline of its electrophilic reactivity towards *t*BuLi. As a result of the steric blocking of the methyl groups and their electron-donating effect on positions 4 and 7 of phen, addition of *t*BuLi was selective toward the position 2 of the chelate, despite its proximity to the $\{Re(CO)_3(PMe_3)\}^+$ fragment. This result highlights the impact that subtle modifications of the electronics and sterics of the phen ligand have on the site-selectivity of these additions.

Reaction with electrophiles of the products from tBuLi addition

The products of the reactions discussed above are neutral complexes with dearomatized chelates containing one amido-like nitrogen atom. Aiming to explore their reactivity toward electrophiles, a slight excess of MeOTf (1.9 equiv) was added to a solution of crude **2** at room temperature. The product precipitated after 5 hours and was isolated as an orange solid in 53% yield that was identified as [Re($^{5\text{-}t\text{Bu}}$bipy)$(CO)_3(PMe_3)$]OTf (**7**, $^{5\text{-}t\text{Bu}}$bipy = 5-tert-butyl-2,2'-bipyridine) on the basis of NMR spectroscopy (Scheme 4a).



Scheme 4. (a) Rearomatization of complex **2** by reaction with MeOTf and (b) protonation at the carbon 4 of the chelate in **2**.

The IR vCO of **7** (2037, 1950, 1922 cm^{-1} in THF) are substantially higher than those of **2** (see above), in agreement with the formation of a cationic complex. The NMR spectra of **7** in CD_2Cl_2 showed signals consistent with the presence of an asymmetric complex (*e*. *g*. 3 signals at 195.1, 194.7 and 188.2 ppm in the ^{13}C NMR spectrum for the CO ligands). The ^1H NMR spectrum showed 6 signals (from 8.96 to 7.69 ppm, integrating 1H five of them and 2H the other) for the 5-*tert*-butyl-2,2'-bipyridine. Remarkably, the lack of the ^1H NMR signal of H5 supported the rearomatization of the chelate in **2** by formal hydride abstraction upon reaction with MeOTf. *Tert*-butyl substitution at C5 was confirmed by the coupling pattern of H6 in the ^1H NMR spectrum (broad singlet at 8.90 ppm), consistent with the absence of a $^3J_{HH}$ coupling with the 5 position, and the lack of the C5 ^{13}C NMR signal in the ^{13}C-DEPT-135 NMR spectrum.

Substituted bipy and phen ligands have been traditionally prepared by synthetic strategies that involve the addition of strong nucleophiles followed by an oxidation step,[27] metal-catalyzed C-C dehydrogenative coupling,[28] or cross coupling from 2-halopyridines[29] among other synthetic methods.[30] Subsequent metalation with a suitable transition-metal source affords the complex of interest. Certain substitution patterns can be challenging to attain as these syntheses rely on the electronic and steric properties of the chelate and the nucleophile or on the availability of the coupling partners. A method to synthesize 5-*tert*-butyl-2,2´-bipyridine has not been previously reported. This result posits post-coordination intermolecular additions of alkyl lithium reagents as a powerful synthetic method that enables access to metal compounds containing ligands challenging to access on its free form.

To further explore the reactivity of **2** with electrophiles, 1.9 equiv of HOTf were added to a crude toluene solution of the complex at room temperature. An orange solid instantaneously precipitated and was identified as compound **8** based on NMR and IR spectroscopy (Scheme 4b). The ^1H, ^{13}C and COSY NMR spectra of **8** displayed signals consistent with the presence of an asymmetric *N*,*N*-chelate containing a dearomatized pyridyl ring with a *t*Bu group adjacent to a CH_2 (signal at 19.2 ppm in the ^{13}C NMR spectrum and in opposite phase to the CH groups in the DEPT-135 and in the phase edited ^1H, ^{13}C-HSQC spectra), supporting protonation at C4 of the substituted pyridyl ring in **2**. Further supporting this assignment, the ^{13}C NMR spectrum showed a signal at 175.8 ppm that was assigned to the C(H)=N group in position 6 on the substituted pyridyl ring.

Slow diffusion of hexane into a concentrated solution of **8** in CH_2Cl_2 yielded orange crystals that were suitable for X-ray diffraction analysis. In addition to **8**, the crystals contained LiOTf, resulting from the employment of excesses of *t*BuLi and HOTf in the synthesis. The two rhenium cationic complexes (depicted in Figure 2) differed in the configuration of the *t*Bu-substituted pyridyl ring. In addition, the asymmetric unit included four triflate anions, two lithium cations, and two interstitial sites, each modelled as a one-quarter-occupied dichloromethane molecule, with one of them equally divided into two disordered congeners.

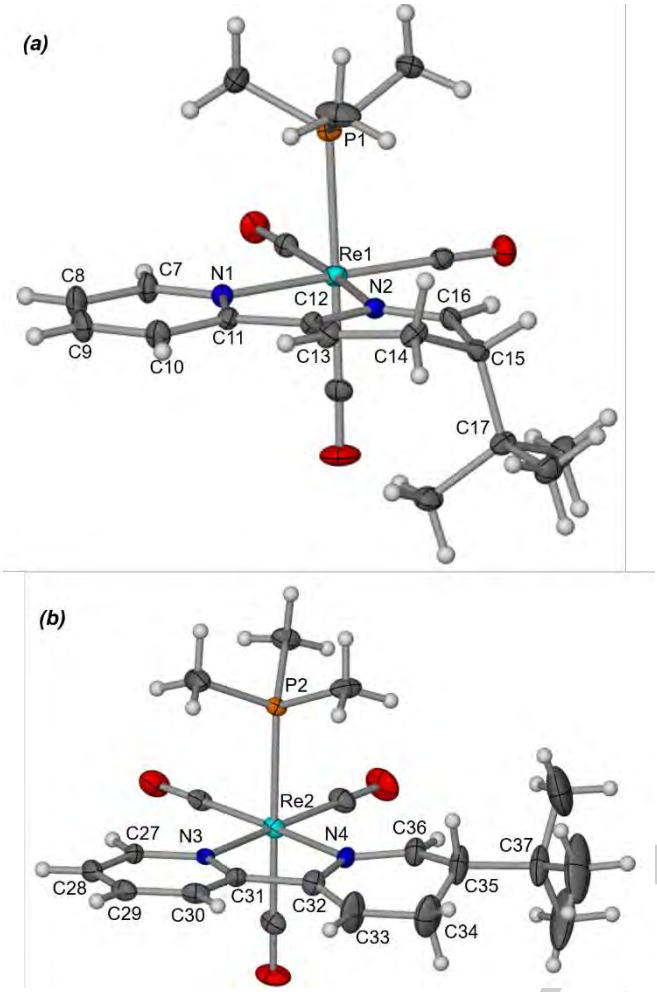
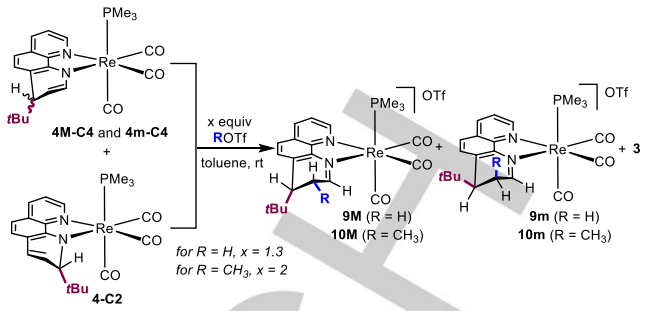


Figure 2. (a) and (b) Solid-state structures of the two cationic Re(I) ring isomers present in a single-crystal of product **8** (thermal ellipsoids at 30% probability).

Each rhenium complex showed a distorted octahedral geometry and contained an *N*,*N*-chelate with a 5-*tert*-butyl substituted dearomatized pyridyl ring with a methylene group on the 4 position. Distances were similar in both isomers, therefore, only the values of the isomer shown in Figure 2a will be discussed in what follows. Re1–N1 and Re1–N2 distances have values of 2.179(4) Å and 2.166(4) Å respectively, consistent with both nitrogen atoms being imino donors. The C11–C12 bond distance (1.471(6) Å) is consistent with a single bond, in contrast with the calculated distance in complex **2** (1.414 Å), supporting re-aromatization of the non-substituted ring upon protonation. Bond distances N2–C16 and C12–C13 are typical for double bonds (1.301(6) Å and 1.334(7) Å respectively) while C13–C14 (1.478(7) Å), C14–C15 (1.512(7) Å) are characteristic of single bonds, consistent with protonation at C4.

The **4-C2**, **4M-C4** and **4m-C4** mixture also reacted with MeOTf and with HOTf in toluene at room temperature. The products were isolated as orange solids and were fully characterized by 1D and 2D NMR. NMR spectroscopy showed the presence of three species on each of the reaction crudes, two of them from protonation (**9M**, **9m**), or methylation (**10M**, **10m**) at the 3 position of the chelates in **4M-C4** and **4m-C4** respectively (Scheme 5). The third product was identified as the precursor **3**.



Scheme 5. Functionalization of the position 3 of the chelate in the mixture **4M-C4**, **4m-C4**, **4-C2** upon reaction with MeOTf or HOTf.

The ^{1}H NMR spectra of **9M**, **9m** and **10M**, **10m** in CD_2Cl_2 showed signals consistent with the presence of a dearomatized pyridyl ring in each complex of the mixtures. Similar NMR signal patterns for **M** and **m** compounds support that they are diastereomers containing the *t*Bu group on the 4 position and differing on the configuration at this carbon, with the **M** compounds having the *t*Bu group on the opposite face to the PMe_3. The ^{1}H and ^{13}C NMR spectra supported that C4 and C3 were sp^3-hybridized (at 41.6 and 30.2 ppm respectively in the ^{13}C NMR spectrum of **9M**). In agreement with the crosspeaks observed in the ^{1}H, ^{1}H-COSY, ^{1}H, ^{13}C-HSQC and ^{1}H, ^{13}C-HMBC experiments, protonation or methylation occurred at the position 3 of the chelate. The ^{1}H NMR signal of H3 in **10M** and **10m** was a singlet, supporting a cis disposition of H3 and H4 in both compounds.

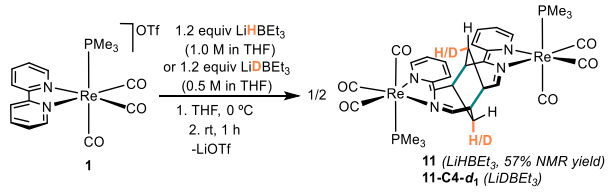
Remarkably, the mixtures from protonation or methylation did not contain rhenium complexes derived from **4-C2**. It is proposed that **3** was formed in both reactions from rearomatization of **4-C2** by *t*Bu abstraction. This process can be more favored in **4-C2** than in **4M-C4**, **4m-C4**, due to an increased steric conflict between the *t*Bu and the metal fragment $\{Re(CO)_3PMe_3\}^+$. Notably, the ratios of the products from protonation (the **9M**:**9m**:**3** ratio was 2.9:1.5:1.0) and methylation (**10M**:**10m**:**3** ratio = 2.2:1.8:1.0) were different than that of the starting materials (**4M-C4**:**4m-C4**:**4-C2** ratio was 2.7:1.7:1.0) suggesting that, not **only 4-C2**, but also **4M-C4** and **4m-C4** regenerated **3** to some extent.

Rhenium complexes containing dearomatized pyridyl rings from intramolecular nucleophilic addition have been protonated or methylated at the amido nitrogen.[14a,14b] Examples of protonation at a carbon atom have been found in complexes containing dearomatized 4,4'-X_2-2,2'-bipyridine (X = OMe,[14a] NMe_2),[14e] for which the preference for carbon (over the amido nitrogen) protonation was attributed to the presence of the resonance electron-donating groups, which increased the nucleophilicity of ring carbons. The *tert*-butyl substituent in the chelates of **4M-C4** and **4m-C4** could be playing a similar role, leading to functionalization of the 3 position upon both protonation and methylation.

Divergent reactivity in the additions of hydride to Re(I) bipy and phen complexes

Soluble hydridoborates are widely employed reagents in reduction reactions and in the creation of transition metal-hydride bonds, however, their reactions with coordinated bipy and phen are unknown. To further explore the influence of the

nucleophile on the identity of the products of intermolecular addition to bipy and phen Re(I) complexes, the reaction with $LiHBEt_3$ was studied. Addition of 1.2 equiv of $LiHBEt_3$ to a THF solution of **1** at 0 °C resulted in a color change from yellow to purple followed by the formation of a red solution after stirring for 1 hour at room temperature. IR monitoring of the reaction showed a shift of the vCO bands to lower frequencies (from 2034, 1934, 1913 in **1** to 2014, 1918, 1891 cm^{-1} in THF) consistent with the formation of a neutral product. The product, **11**, was formed in 57% yield (determined by ^1H NMR spectroscopy, see below) from intermolecular cyclodimerization of two dearomatized pyridyl rings, in turn formed upon hydride addition to the position 4 of the bipy ligand in **1** (Scheme 6). The air- and moisture-sensitivity of **11** precluded its isolation and crystallization. Consequently, the strongest support for the structure of **11** comes from the structural determination by X-ray diffraction of its protonated derivative (see below).

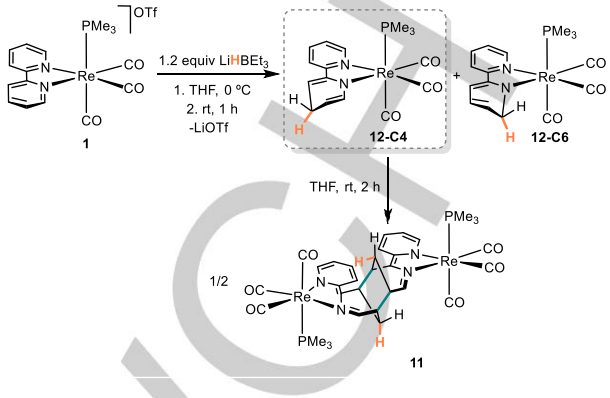


Scheme 6. Cyclodimerization of the bipy in **1** triggered by $LiHBEt_3$ or $LiDBEt_3$ addition.

The NMR spectra of the reaction crude in benzene-d_6 were consistent with the formation of **11** as a single species and showed signals for a C_2-symmetric complex. Each rhenium center contained a *N*,*N*-chelate from double dearomatization of bipy (^1H NMR signals of the non-substituted pyridyl ring occur from 7.88 to 5.57 ppm) with three sp^3 carbons on the 3, 4 and 5 positions. Position 4 could be unequivocally assigned to a methylene group (δ ^1H NMR 1.86 and 1.06 ppm, 1H each, and δ ^{13}C NMR 21.9 ppm) from addition of hydride to this position. Crucially, signals for the 3 and 5 positions were assigned to methine groups (δ ^1H NMR 2.63 and 2.28, 1H each, and δ ^{13}C NMR 42.3 and 36.7 ppm respectively), consistent with C–C bond formation between these positions, while the 2 and 6 carbons retained their sp^2 hybridization (occurring at 117.6 and 136.5 ppm respectively in the ^{13}C NMR spectrum).

When the reaction was carried out with $LiDBEt_3$[31] (>99% D-incorporation) under the same conditions, the d_1-isotopologue **11-C4-d_1** was formed. Complex **11-C4-d_1** showed >99% deuterium incorporation on the ^1H NMR signal at 1.06 ppm, assigned to one of the two diasterotopic H atoms in the methylene on the 4 position of the chelate, as evidenced by the loss of coupling of the signal at 1.86 ppm. This result supports the formation of the methylene group in **11** from addition of hydride to bipy.

To identify the intermediates involved in the formation of **11**, the addition of $LiHBEt_3$ to **1** was carried out at -78 °C and the crude 1D and 2D NMR spectra were registered in THF-d_8 at 0 °C. The NMR spectra of the purple solution revealed the presence of two rhenium complexes in a 3 to 1 ratio (from ^1H NMR integration) each containing one dearomatized 2-pyridyl ring. The products were identified as **12-C4** (major) and **12-C6** (minor) from hydride addition to the 4 and 6 positions respectively of the bipy ligand in **1** (Scheme 7).[22e]

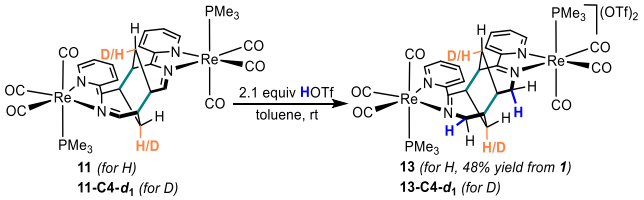


Scheme 7. Proposed pathway for the formation of **11**.

The ^1H NMR spectrum of the mixture showed signals consistent with **12-C4**, **12-C6** being asymmetric complexes, each containing a CH_2 group on position 4 (at 3.45 ppm, 2H) or 6 (two doublets at 4.35 and 4.03 ppm, 1H each) from hydride addition to bipyridine ligands. Stirring the purple solution of **12-C4**, **12-C6** at room temperature for two hours resulted in a color change to red and a slight shift of the IR vCO bands (from 2010, 1913, 1882 to 2014, 1918, 1891 cm^{-1} in THF) indicating the formation of **11**. Because complex **11** contains a methylene group only on the 4 position of the chelate, it can only be formed by cyclodimerization of **12-C4** and not of **12-C6**. While the fate of complex **12-C6** could not be elucidated based on experimental evidence, it can be proposed that it undergoes a 1,3-hydride shift[30] to form **12-C4** a process that could be driven by the cyclodimerization of the latter to yield **11**.

Dimerization of pyridyldiimine (PDI) ligands triggered by intramolecular alkyl migration to the pyridyl ring has been reported in manganese(II),[33] aluminium(III)[34] and chromium(II)[35] alkyl complexes. An analogous transformation involving bipy was unknown and could be thought to be more energetically demanding as it involves the dearomatization of a second pyridyl ring.

Attempting to access derivatives of **11** with enhanced stability, HOTf (2.1 equiv with respect to 1) was added to an in-situ prepared toluene solution of **11** at room temperature. A pale yellow solid precipitated and was isolated in a 48% yield (calculated from **1**) and identified as complex **13**. Its formation involved rearomatization of the non-substituted pyridyl rings in **11** triggered by the protonation of the 6 positions in the cyclodimerized rings (Scheme 8).



Scheme 8. Protonation at C6 of complexes **11** or **11-C4-*d*$_1$** to yield dicationic Re(I) complexes.

The IR vCO bands of **13** (2032, 1944, 1920 cm^{-1} in CH_2Cl_2) supported the formation of a cationic Re(I) complex and the NMR spectra in CD_2Cl_2 showed signals consistent with the presence of a C_2-symmetric complex. The ^{1}H NMR spectrum showed four signals between 9.05 and 7.82 ppm consistent with re-aromatization of the non-substituted pyridyl rings upon protonation. The ^{13}C NMR spectrum showed signals consistent with the presence of four sp^3-hybridized carbon atoms in the 3, 4, 5 and 6 positions of the cyclodimerized pyridyl rings. Remarkably, the signal at 66.0 ppm was identified as a methylene group on the 6 position of the chelate, formed by protonation at that position.

To further prove that protonation of **11** takes place at position 6, HOTf was added to complex **11-C4-*d*$_1$** yielding the *d*$_1$-isotopologue of **13**, **13-C4-*d*$_1$** (Scheme 8). 1D and 2D NMR spectroscopy showed that **13-C4-*d*$_1$** incorporated D only at the position 4 of the chelate, while the methylene group at position 6 showed no D-incorporation, as expected from protonation at this position.

Yellow crystals of **13** suitable for X-ray diffraction were grown from slow diffusion of hexane into a concentrated CD_2Cl_2 solution of **13** at -20 °C. The asymmetric unit contained three triflate anions, a molecule of THF, a molecule of water, a $[H_3O]^+$ cation, and the dinuclear Re(I) dication depicted in Figure 3. The latter was formed by C–C coupling between the 3 positions and the 5 positions of **12-C4** followed by protonation at the 6 positions. As previously found for the products from PDI dimerization,[33-35] the 3, 4 and 5 positions of the coupled rings defined a cyclohexane ring in a chair configuration. As a result of the selective 3-3 and 5-5 C–C bond formation, the tetradentate *N*-chelate adopted a *U*-shaped configuration.

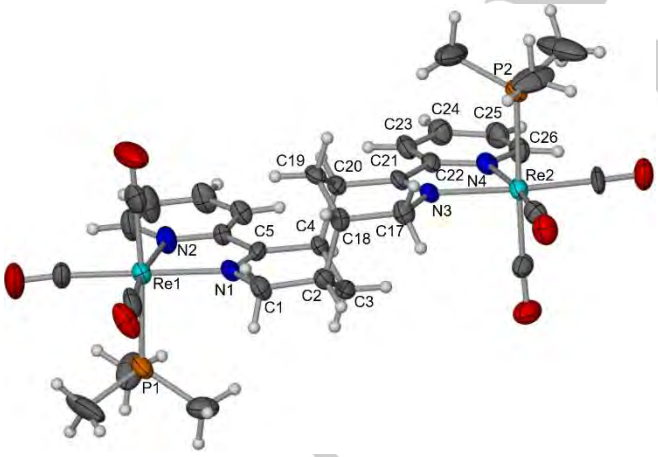
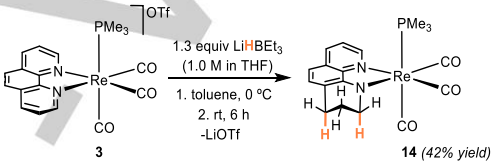


Figure 3. Solid-state structure of the dication in **13** (thermal ellipsoids at 30% probability).

Bond distances in both rhenium subunits are statistically identical and only the values for the Re2 subunit are employed in the discussion. Re–N3 and Re–N4 distances have similar values (2.143(9) Å and 2.17(1) Å respectively) and are consistent with both nitrogen atoms having imino character. In agreement, the N3–C21 distance (1.27(1) Å) supported the presence of a double bond. C20–C21, C19–C20, C18–C19 and C17–C18 bond distances (in the range of 1.52(2)-1.54(2) Å) were consistent with single bonds, while shorter C–C bond distances were found in the non-substituted ring (C24–C25 was 1.38(2) Å and C23–C24 was 1.39(2) Å), supporting its aromaticity.

To extend the study of the hydride addition reaction to the phenanthroline analogue of **1**, $LiHBEt_3$ (1.3 equiv) was added to a toluene suspension of [Re(phen)(CO)$_3$(PMe$_3$)]OTf (**3**) at 0 °C. After 6 hours stirring at room temperature a dark green solution was formed. Upon removal of the volatiles and dissolution of the residue in toluene, the color of the solution changed to dark blue and a brown residue remained insoluble in toluene. Filtration and work-up of the blue solution afforded the product, as a blue powder in a 42% yield that was identified as complex **14**, where two double bonds of phen have been reduced yielding a 2,3,4-trihydro-1,10-phenanthroline ligand (Scheme 9).



Scheme 9. Partial reduction of a pyridyl ring in the phen ligand of **3**.

Diagnostic ^{1}H NMR signals supporting partial reduction of a pyridyl ring were three multiplets (2H each) occurring between 3.81 and 1.76 ppm that were assigned to three CH_2 groups in positions 2, 3 and 4 of the chelate. The rest of the signals of the chelate occurred as five multiplets (1H each) in the aromatic region (between 8.23 and 6.27 ppm). The ^{15}N chemical shifts for the nitrogen atoms in **14** were consistent with the presence of an amido nitrogen in the partially reduced pyridyl ring (at 80.1 ppm) and an imino nitrogen (at 230.6 ppm) in the intact ring.

Slow diffusion of hexane into a concentrated solution of **14** in toluene at -20 °C yielded single-crystals suitable for X-ray diffraction analysis. Complex **14** showed a distorted octahedral geometry and a partially reduced pyridyl ring in the *N*,*N*-chelate, as evidenced by the loss of planarity (Figure 4). Bond distances of 1.51(1) Å and 1.49(1) Å for C2–C3 and C3–C4 respectively were consistent with the presence of single bonds between the positions 2, 3 and 4 of the chelate. The sum of angles around N1 was 359.8(5)° supporting delocalization of the amido lone electron pair to the metal fragment and/or to the aromatic rings of the chelate.[17b]

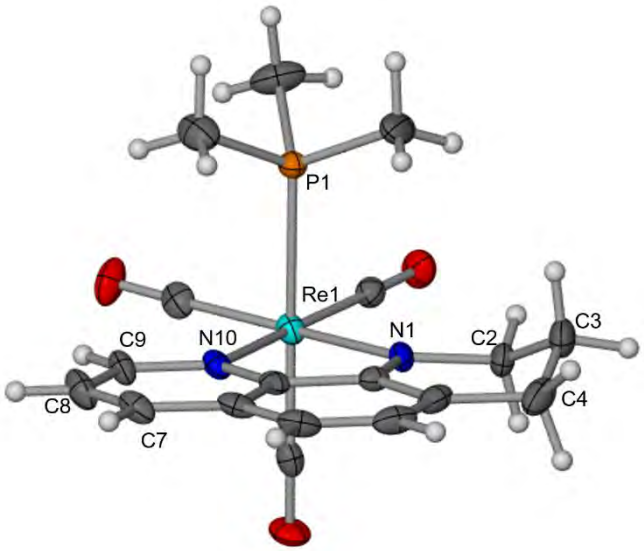


Figure 4. Solid-state structure of complex **14** (thermal ellipsoids at 30% probability).

Although the partial reduction of a monodentate pyridine ligand in a vanadium(III) complex with H_2 has been reported[36] the partial reduction of a phen ligand was unknown. The fact that only two double bonds of the pyridyl ring were reduced can be attributed to the conjugation of the remaining double bond with the amido nitrogen (N1) and with the aromatic rings of the chelate.

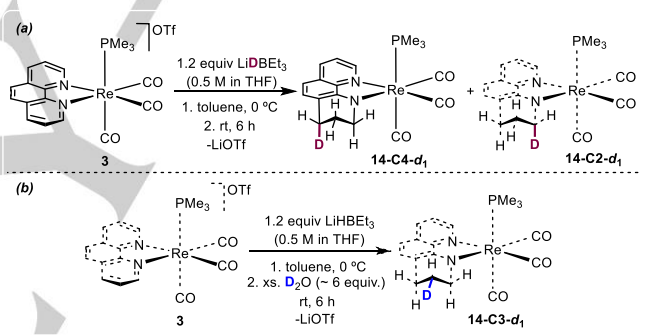
Metal complexes of group 4 containing the 2,3,4-trihydro-1,10-phenanthroline ligand are efficient precatalysts for olefin polymerization.[37] The main synthetic route to access these complexes involves two steps- first the synthesis of the free ligand that can be achieved by metal-catalyzed partial reduction of phen[6b-i] to yield 1,2,3,4-tetrahydro-1,10-phenanthroline followed by treatment with a metal alkyl precursor. In contrast, the strategy reported here for Re complexes avoids the need of using transition metal catalysts to access the partially reduced ligand.

To identify the intermediates involved in the formation of **14**, 1.1 equiv of $LiHBEt_3$ were added to **3** at 0 °C in THF-d_8 and the reaction was monitored by ^{1}H NMR spectroscopy at 0 °C. The 1D and 2D NMR spectra of the resulting dark green solution showed the presence of two Re(I) compounds in a 1.6:1.0 ratio (from ^{1}H NMR integration) identified as **15-C4** (major) and **15-C2** (minor) containing a dearomatized pyridyl ring from nucleophilic addition of hydride to the 4 and 2 positions respectively of the phen ligand in **3**. Remarkably, the **15-C4**, **15-C2** mixture is analogous to the **12-C4**, **12-C6** from hydride addition to the bipy complex **1** (Scheme 7), however, the evolution of the former at room temperature results in the partial reduction of the dearomatized pyridyl ring instead of its cyclodimerization. This behavior can be attributed to a higher barrier for cyclodimerization in the phen-derived complexes, due to the extra phenyl fused ring, that would be dearomatized upon cyclodimerization (see page S185 of the SI for the calculated NICS).

Stirring the solution of **15-C4**, **15-C2** at room temperature resulted on a color change from green to blue, consistent with the formation of **14**, and the precipitation of a brown solid. The ^{1}H and ^{31}P NMR spectra of the brown residue showed signals consistent with the presence of $[Re(phen)(CO)_3(PMe_3)]^+$ and two minor unidentified Re(I) phosphine compounds.

Aiming to track the origin of the H atoms involved in the reaction, D-labelling experiments were carried out. When $LiDBEt_3$ was added to **3** under the same conditions, a mixture of two d_1-isotopologues of **14** were formed in a 3.3:1.0 ratio. Based on the $^1J_{CD}$ couplings on the ^{13}C NMR spectrum, the products were isotopomers with deuterium incorporation at the methylene in position 4 (**14-C4-*d*$_1$**, major) and in position 2 (**14-C2-*d*$_1$**, minor) (Scheme 10a). The d_2-isotopologue with D-incorporation at both the 2 and 4 positions was not detected by NMR spectroscopy. This result supports that $LiHBEt_3$ only provided one of the three H atoms required to yield **14** from **3** and that both intermediates, **15-C4**, **15-C2** further reacted to afford the final product.

To explore the origin of the other two H atoms required to form **14** from **15-C4**, **15-C2**, D_2O was added to the mixture resulting on the isolation of the d_1-isotopologue of **14**, showing D-incorporation at the position 3 of the chelate (**14-C3-*d*$_1$**) (Scheme 10b). This result suggests that the methylene group at this position was formed upon protonation by trace water present in the reaction medium.

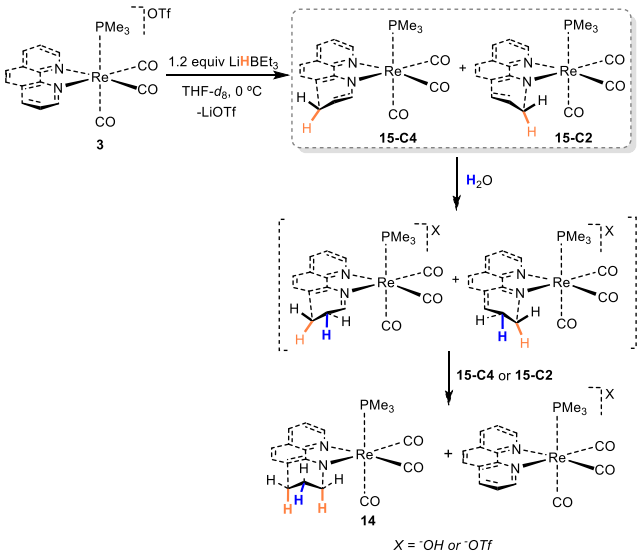


Scheme 10. D-Labelling experiments to rationalize the formation of **14** Reaction of **3** (a) with $LiDBEt_3$ and (b) with $LiHBEt_3$ followed by addition of D_2O.

Precipitation of $[Re(phen)(CO)_3(PMe_3)]^+$ upon formation of **14** from the **15-C4**, **15-C2** mixture suggests that both components of the mixture can act as hydride donors[38] and transfer a second equivalent of hydride to yield **14** and $[Re(phen)(CO)_3(PMe_3)]^+$.

Taking all the experimental evidence together, a pathway for the formation of **14** is proposed in Scheme 11. The addition of hydride takes place to the positions 2 and 4 of the phen ligand in the cationic complex **3** yielding the mixture of Re(I) neutral complexes **15-C2**, **15-C4**. Both neutral complexes undergo protonation on their 3 position by trace water in the reaction medium to yield a putative mixture of cationic Re(I) complexes containing two methylene groups on the 3 and 4 or 3 and 2 positions that has not been detected by NMR spectroscopy. However, a similar complex has been isolated from nucleophilic addition of *t*BuLi to bipy complex **1** followed by protonation (see above). The mixture of cationic complexes would then undergo an intermolecular hydride transfer from either **15-C4** or **15-C2** to yield product **14** and $[Re(phen)(CO)_3(PMe_3)]X$ (X = $^-$OH, $^-$OTf) as the byproducts from the hydride donation from **15-C4** or **15-C2**. A pathway involving a double hydride addition to **3** followed by protonation seems unlikely as it would involve the formation of a

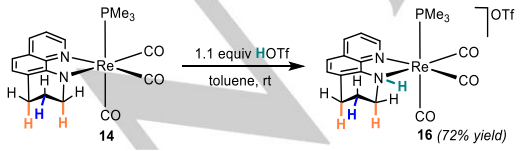
highly reactive carbanion on the position 3 of the chelate (see page S186 of the SI).



Scheme 11. Proposed pathway for the formation of **14**.

Both **15-C4** and **15-C2** could transfer a hydride to another molecule of **15-C4** or **15-C2** to afford **14**. The tendency to act as hydride donor is expected to be higher for **15-C2** than for **15-C4**, since species from hydride addition to C2 are usually formed as kinetic products that evolve to the thermodynamically more stable C4-hydride species by a 1,3-hydrogen shift.[32] These intermolecular hydride transfers between Re(I) complexes account for the moderate yield of the product (42%) as part of the Re complexes are being sacrificed by formation of $[Re(phen)(CO)_3(PMe_3)]^+$ upon hydride transfer. Complex **14** was obtained in similar yield even when the reaction was carried out with 2.2 equiv of $LiHBEt_3$ supporting that the performance of the rhenium complexes **15-C2**, **15-C4** as hydride donors could not be prevented.

To further explore the reactivity of complex **14**, HOTf (1.1 equiv) was added to a solution of **14** in toluene at room temperature resulting on the immediate formation of an orange oil. The product was isolated as an orange powder in 72% yield and was identified as the cationic Re(I) complex **16**, formed by protonation of the amido nitrogen in the partially reduced pyridyl ring of **14** (Scheme 12).



Scheme 12. Protonation at the amido nitrogen of complex **14**.

The ^1H and ^{13}C NMR spectra of **16** in CD_2Cl_2 showed signals consistent with the presence of an asymmetric complex. The ^1H NMR signals for the neutral bidentate *N,N*-chelate were slightly downfield shifted (between 9.05 and 7.52 ppm for the aromatic rings and between 4.10 and 2.02 ppm for the three methylene groups) with respect to those for the anionic chelate in **14**, further supporting the transformation of the neutral Re(I) complex into a cationic product. A broad singlet occurring at 6.78 ppm was assigned to the N–H group as it did not show any cross-peak with a C atom in the ^1H, ^{13}C-HSQC NMR spectrum.

Conclusion

In conclusion, $C(sp^3)$ centers in bipy and phen coordinated to $\{Re(CO)_3(PMe_3)\}^+$ have been built by addition of *t*BuLi and of $LiHBEt_3$. Nucleophilic additions to bipy and phen ligands rendered access to neutral Re(I) complexes with anionic bidentate *N,N*-chelates containing substituted sp^3-hybridized carbon atoms in different positions depending on the identity of both the nucleophile and the chelate.

Remarkably, hitherto unknown functionalization of position 5 of bipy was achieved when $[Re(bipy)(CO)_3(PMe_3)]OTf$ was reacted with *t*BuLi, yielding a neutral complex where both pyridyl rings in bipy were dearomatized. In contrast, addition of hydride triggered the intermolecular cyclodimerization of dearomatized pyridyl rings in bipy and the partial reduction of a pyridyl ring in phen, highlighting the impact of chelate identity on the reaction pathway. Furthermore, in most cases protonation or methylation of the neutral complexes generated an additional $C(sp^3)$ in the chelate, affording cationic Re(I) complexes with different substitution patterns on the chelate.

As transition-metal coordinated bipy and phen ligands emerge as chemically non-innocent ligands, this work provides insight into reaction pathways that can be turned on upon coordination and were unknown for the free ligands. These results posit post-coordination functionalization as a versatile strategy to incorporate sp^3 carbon atoms in different positions of polypyridyl ligands taking advantage of the environment that a metal fragment imparts on the chelates. This strategy has been successfully implemented as proof of concept in low-oxidation state $\{Re^I(CO)_3(PMe_3)\}$ complexes, where the spectroscopic signals of bipy and phen do not indicate any particular activation in the cationic starting materials, and, therefore, could be extended to other transition metal fragments. This discovery sets the pathway for future studies of rational design of metal fragments with modular ligands that enable fine tuning of the electronics and sterics to gain full control over the site of incorporation of the $C(sp^3)$ centers in polypyridyl ligands.

Acknowledgements

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Keywords: 2,2'-bipyridine • Carbonyl Ligands • 1,10-phenanthroline • Reactivity of Coordinated Ligands • Rhenium

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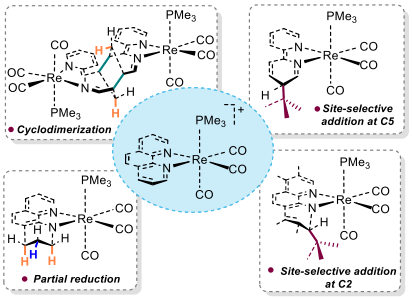

Everything is possible with bipy and phen in the game. Post-coordination functionalization of 2,2'-bipyridine (bipy) and 1,10-phenanthroline (phen) has been applied to the synthesis of {$Re^{I}(CO)_3$} complexes containing C(sp^3)-derivatives of the aromatic chelates. The additions of *t*BuLi and of $LiHBEt_3$ to Re-coordinated bipy and phen showed unprecedented site-selectivity and triggered reaction pathways such as cyclodimerization or reduction.