

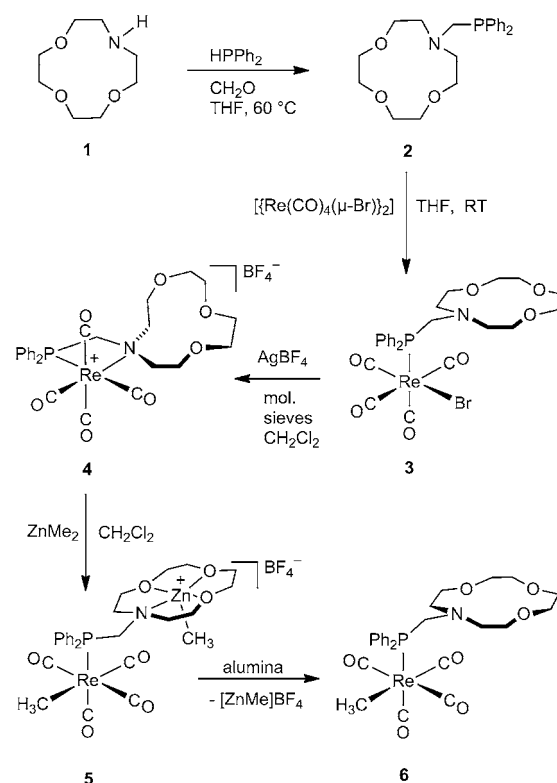
A Versatile Ligand Platform that Supports Lewis Acid Promoted Migratory Insertion**

Amaruka Hazari, Jay A. Labinger,* and John E. Bercaw*

In light of increasing crude oil prices and global energy demands, routes for obtaining fuels and chemical precursors from methane, coal, or biomass by using synthesis gas, which is a mixture of CO and H₂, are emerging as viable processes.^[1,2] The main large-scale processes for utilization of syngas are methanol synthesis, hydrogen production, and the Fischer–Tropsch reaction. A severe limitation of the last of these, which affords complex mixtures of hydrocarbons and oxygenates, is the inability to control the hydrocarbon product distribution and to select for a particular product.^[3] Although the prospect of developing homogeneous catalysts for selective conversion of synthesis gas to hydrocarbons or oxygenates has generated extensive research for over 40 years, no practical syngas-to-C₂₊ conversion has yet been realized; formation of the first C–H bond as well as C–C bonds appear to be the major hurdles that need to be overcome.^[4–7]

In previous work, we succeeded in facilitating both C–H and C–C bond forming reactions by appending Lewis acids to ligands in Re and Mn carbonyl complexes; however, those systems have not proven viable for catalytic CO reduction, as bonds between the Lewis acid (mostly boron) and oxygen in the resulting products are too robust, preventing non-destructive release of any organic product.^[8–10] A versatile ligand platform that can support a wide variety of Lewis acidic metals in close proximity to a M–CO reaction site would aid in the effort to balance reactivity with sufficient lability for closing a catalytic cycle. We report herein on a rhenium carbonyl complex of a phosphine-functionalized aza crown ether ligand,^[11,12] which upon coordination of Group 2 Lewis acids undergoes facile migratory insertions to form Lewis acid-stabilized acyl complexes that react with H₂O and Brønsted acids to liberate C₂ organic compounds.

Conversion of the commercially available aza crown ether **1** to phosphino-aza crown ether **2** followed by reaction with [Re(CO)₄(μ-Br)]₂ generated phosphine complex **3** (Scheme 1).^[13] Treatment of **3** with AgBF₄ in CH₂Cl₂ resulted in cationic complex **4**, the large upfield ³¹P NMR shift (δ –41) of which is characteristic of phosphorus in a four-membered



Scheme 1. Synthesis of complexes 2–6.

ring,^[14] suggesting that the N of the aza crown ether has occupied the vacant coordination site on Re. Reaction of **4** with ZnMe₂ in CH₂Cl₂ resulted in both methylation at Re and insertion of Zn into the macrocycle to give **5**; the zinc-free methyl complex **6** was obtained by passing a THF solution of **5** over alumina. The proposed structures of both **4** and **5** were confirmed by X-ray crystallography (Figure 1).^[15,23]

Both Ca²⁺ and Sr²⁺ were rapidly taken up into the macrocycle by simple addition of [CaI₂(thf)₄] or [SrI₂(thf)₅] to a CD₂Cl₂ solution of **6** to form **7a** and **7b**, respectively, followed by slow (ca. 1 day) insertion of CO into the Re–Me bond to give acyl complexes **8a** and **8b** (Scheme 2). These transformations were conveniently followed by ¹H and ³¹P NMR spectroscopy.^[13] Upon addition of Ca²⁺, the ³¹P NMR signal for **6** at δ 2 shifted upfield to give a single broad signal at δ –11.3 ppm; subsequently the ¹H signal corresponding to the Re–Me protons gradually disappeared and was replaced by a new singlet at δ 2.74, which is consistent with the formation of an acyl complex. The ¹³C NMR spectrum included a diagnostic acyl peak at δ 299 ppm (d, J_{C–P} = 8.8 Hz), suggesting formation of the Lewis acid-stabi-

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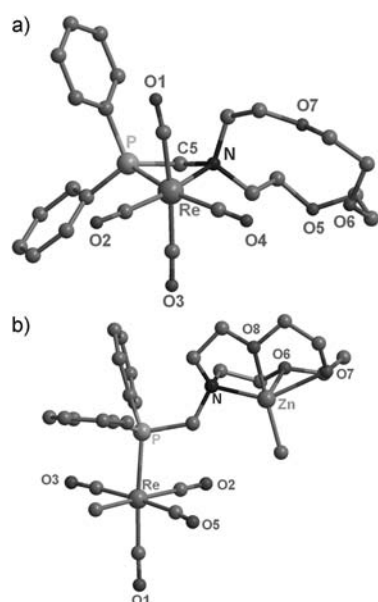
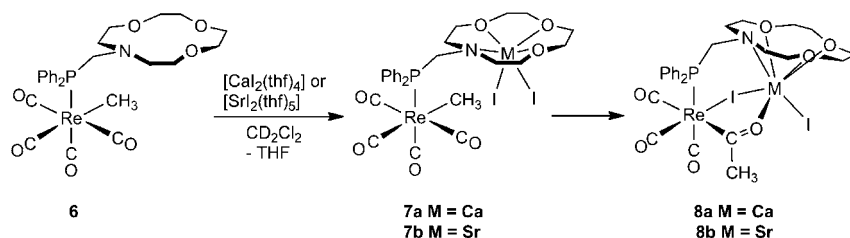


Figure 1. XRD structural representation of a) 4·0.6 Et₂O and b) 5·0.5 C₆H₆; solvent molecules are omitted for clarity. Selected bond lengths [Å] and angles [°]: 4: Re–N 2.2959(18), Re–P 2.4211(6), N–C5 1.511(3), P–C5 1.839(2); N–Re–P 66.96(5), N–C5–P 101.57(14). 5: Zn–O8 2.0675(16), Zn–O6 2.1862(18), Zn–N 2.2450(17), Zn–O7 2.3723(17); N–Zn–O7 140.63(7), O6–Zn–O8 88.08(7).



Scheme 2. Ca²⁺ and Sr²⁺ mediated methyl migration.

lized acyl complex **8a**; the IR spectrum was consistent with a *fac*-tricarbonyl complex,^[16] and an XRD study confirmed the proposed structure (Figure 2).^[17,23] The Ca²⁺ center in **8a** is seven-coordinate, interacting with the acyl oxygen and both iodides as well as the O and N donor atoms of the macrocycle.

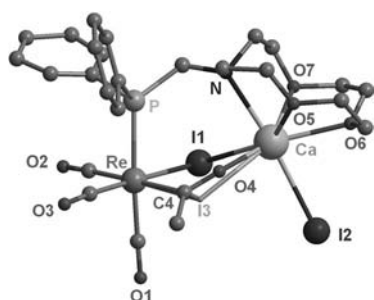


Figure 2. XRD structural representation of **8a**. The structure is disordered: **8a** co-crystallizes with 20% of a second species in which the bridging acyl is replaced by a second bridging iodine. Selected bond lengths [Å] and angles [°]: Re–C4 2.25(10), C4–O4 1.24(3), Ca–O5 2.416(10), Ca–O6 2.475(9), Ca–O7 2.426(9), Ca–N 2.576(10), Ca–O4 2.237(9); Re–I–Ca 92.23(5), Re–C4–O4 119.2(17).

A bridging iodide occupies the site on Re vacated by migratory insertion, forming a five-membered ring that incorporates both Ca and Re.

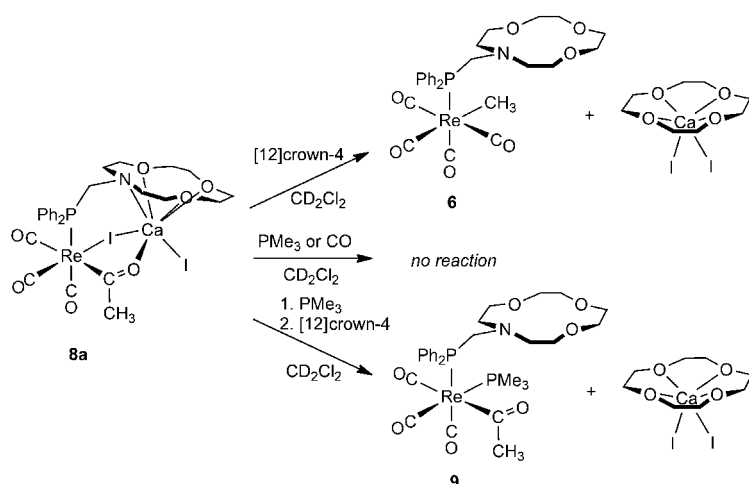
The analogous Sr-containing acyl **8b** was insoluble in CD₂Cl₂ and consequently precipitated from solution during the course of the reaction, but was sufficiently soluble in CD₃CN to obtain ¹H and ¹³C NMR spectra. The signals of these spectra are somewhat broadened at room temperature, but characteristic signals for the acyl carbon (δ = 298) and protons (δ = 2.75) were readily identified. Furthermore, the signal for the methylene protons linking P and N appears as two distinct sets of doublets of doublets as a result of coupling both to phosphorus and to each other; the chemical non-equivalence is expected for the proposed iodide-bridged structure.^[13]

Uptake of Li⁺ and In³⁺ into the macrocycle could also be effected by treatment of **6** with LiBF₄ or [InCl₃(thf)₃], as evidenced by rapid appearance of new, broad ³¹P NMR signals upfield (by 9–12 ppm) from that of **6**, but no further changes indicating insertion were observed. Addition of [MgX₂(thf)] (X = Cl, Br or I) to **6** did result in NMR signals that suggest formation of migratory insertion products, but these reactions did not proceed to completion, even after extended reaction times.^[13] These differences in reactivity may be a consequence of the relative sizes of the Lewis acids.

Ca²⁺ and Sr²⁺, the largest ions, are likely to be situated the furthest outside the macrocycle (the Ca sits 1.529 Å above the mean plane in **8a**) and thus closest to the Re–CO reaction site, whereas the smaller Li⁺, Mg²⁺, and In³⁺ would be expected to better fit inside the macrocycle.

The five-membered Re–acyl–Ca–I ring in **8a** is closely related to the early examples of acyl complexes formed by promotion with AlX₃,^[18–21] but whereas the latter undergo facile displacement of the Al–X–M bridges by CO, no reaction was observed when complex **8a** was exposed to an atmosphere of CO or treated with PMe₃. However, addition of [12]crown-4 to a solution of **8a** and PMe₃ did afford Ca-free acyl complex **9** (Scheme 3), which was characterized by NMR and IR spectroscopy (including an acyl stretch at 1567 cm^{–1});^[13] it decomposed in solution to a complex mixture of products over a period of 12 h, precluding its isolation. On treating **8a** with [12]crown-4 in the absence of added PMe₃, sequestration of CaI₂ resulted in the rapid reformation of methyl complex **6** (the reverse of migratory insertion).

The observations of Scheme 3 suggest that the role of the Re–I–M bridge in the kinetic acceleration and/or thermodynamic stabilization of migratory insertion products **8** is of importance comparable to that of the Lewis acid–acyl interaction. Indeed, no observable reaction took place upon treatment of complex **6** with a halide-free Lewis acid, Ca(OTf)₂, in acetonitrile over a period of several days. (The use of acetonitrile for this reaction was necessitated by the insolubility of Ca(OTf)₂ in CH₂Cl₂. This better-coordinating solvent might well interfere with the desired Lewis acid–oxygen interactions; however, the reaction of **6** with [CaI₂–



Scheme 3. Sequestration of Ca^{2+} from the macrocycle.

(thf)₄] in acetonitrile did lead to the formation of an acyl complex after several days.) Likewise, in situ generation of $\text{Ca}(\text{OTf})_2$ in CD_2Cl_2 , by addition of AgOTf to a solution of **6** and $[\text{CaI}_2(\text{thf})_4]$, led to no insertion.

Release of a C_2 organic product generated by Lewis acid-mediated C–C coupling from the Re center was readily achieved. Addition of 5–20 equivalents of water to a CD_2Cl_2 solution of acyl complex **8a** or **8b** resulted in rapid liberation of acetaldehyde, which was identified by its ^1H NMR signals (δ 2.17 d; δ 9.76 q), and formation of Re–I complex **12**, the identity of which was confirmed by comparison of spectroscopic data to those of an independently synthesized sample.^[13] Larger amounts of water led to a different reaction: addition of 50 equivalents of water to a CD_2Cl_2 solution of **8a** gave new complex **13**, which underwent deinsertion to **6** over a period of several hours, and no acetaldehyde was observed. The crystal structure of **13** (Figure 3) reveals that the terminal iodide on Ca in **8a** has been replaced by two water molecules to give an eight-coordinate Ca^{2+} center.^[22,23]

In contrast, addition of 50 equivalents of acidified water (2% HOTf) to **8a** does afford acetaldehyde, as does protonation of **8a** with HOTf in the absence of added water. In each case, a single (as assessed by ^{31}P NMR) as yet unidentified metal species is formed. These observations suggest the sequence of steps shown in Scheme 4, in which the acyl oxygen of **8a** is protonated to afford hydroxycarbene intermediate **10**, followed by a 1,2-hydride shift and nucleophilic

attack by iodide at Re to release acetaldehyde (pathway A). We suggest that coordination of water to the Ca^{2+} center is required to generate sufficient acid strength for the protonation of **8a** to take place. With larger amounts of added water (in the absence of deliberately added acid) the effective pH is apparently too high (a consequence of the leveling effect), and pathway B, aquation of Ca^{2+} followed by its removal and deinsertion, is followed instead.

Complex **8a** is unaffected by the addition of methanol, but treatment of **8a** with HOTf and an excess of MeOH leads to the formation of 1,1-dimethoxyethane along with some methyl iodide (Scheme 5). Again, hydroxycarbene complex **10** is the probable first intermediate; it reacts with methanol to give methoxycarbene complex **14**, which undergoes addition of methanol to afford **15**

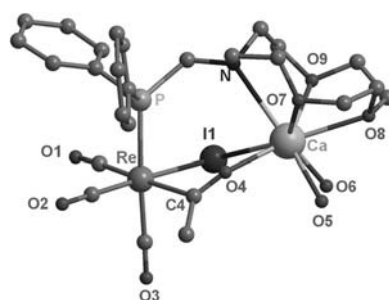
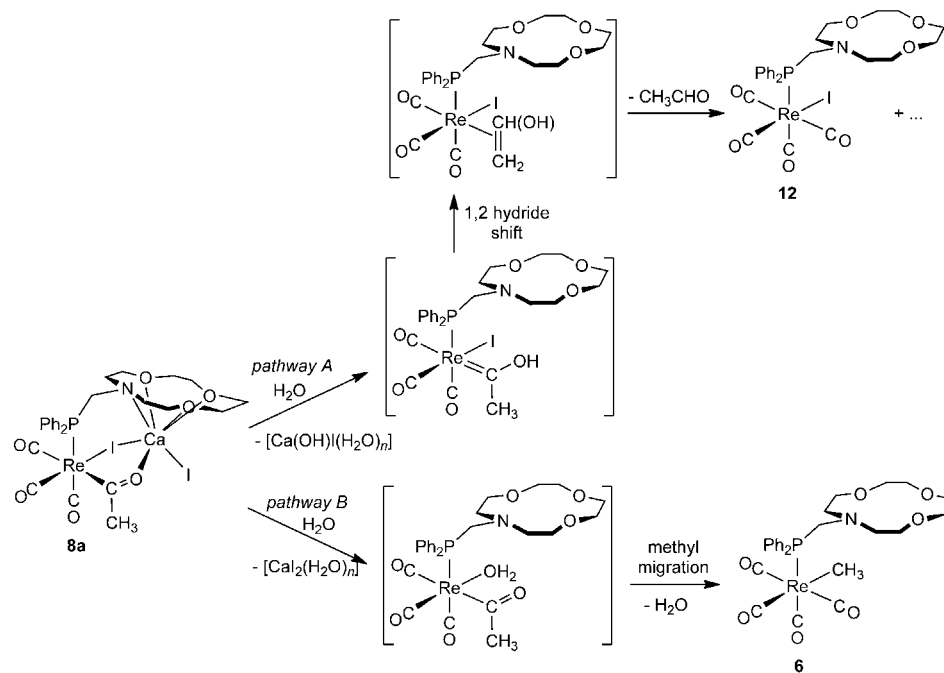
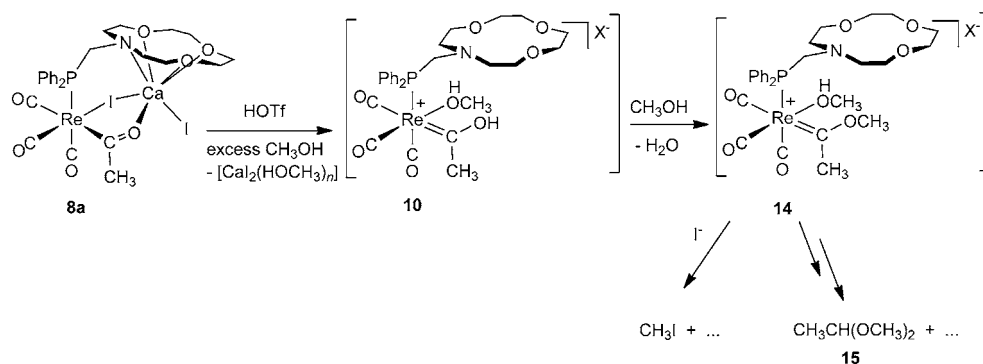


Figure 3. XRD structural representation of **13**; the iodide counteranion is not shown. Selected bond lengths [Å] and angles [°]: Re–C4 2.345(10), C4–O4 1.176(10), Ca–N 2.803(8), Ca–O4 2.282(7), Ca–O7 2.432(7), Ca–O8 2.537(7), Ca–O9 2.453(7); Re–I–Ca 94.47(4), Re–C4–O4 116.4(7).



Scheme 4. Reactivity of **8a** with H_2O . Pathway A is accompanied by the formation of an unidentified precipitate; presumably this side reaction provides the additional equivalent of CO required to form **12**.



Scheme 5. Reactivity of **8a** with MeOH/HOTf.

along with an unidentified metal species. Competing nucleophilic attack at the O–Me bond of **14** by iodide leads to the formation of methyl iodide.

In conclusion, we have shown that Ca²⁺ and Sr²⁺ cations can be readily incorporated into a macrocycle appended to a phosphine ligand attached to a rhenium carbonyl complex, and thus be suitably positioned to act as Lewis acids that promote otherwise unfavorable transformations of coordinated CO, under mild conditions. These Lewis acids appear to form weaker intermediate M–O bonds and exhibit greater substitutional lability than the boron-based systems studied previously, thereby enabling the facile release of organic products from the metal center, although that release has not yet been accomplished nondestructively, in a manner compatible with a closed catalytic cycle. To achieve that goal, we are continuing to investigate the behavior of a wide range of Lewis acids, using this and other ligand architectures.

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- [1] A. Y. Khodakov, W. Chu, P. Fongarland, *Chem. Rev.* **2007**, *107*, 1692.
- [2] C. K. Rofer-DePoorter, *Chem. Rev.* **1981**, *81*, 447.
- [3] *United Nations Development Program. World Energy Assessment Report: Energy and the Challenge of Sustainability*, United Nations, New York, **2000**.
- [4] G. C. Demitras, E. L. Muettert, *J. Am. Chem. Soc.* **1977**, *99*, 2796.
- [5] A. R. Cutler, P. K. Hanna, J. C. Vites, *Chem. Rev.* **1988**, *88*, 1363.
- [6] B. D. Dombek, *Adv. Catal.* **1983**, *32*, 325.
- [7] N. M. West, A. J. M. Miller, J. A. Labinger, J. E. Bercaw, *Coord. Chem. Rev.* **2011**, *255*, 881.
- [8] A. J. M. Miller, J. A. Labinger, J. E. Bercaw, *J. Am. Chem. Soc.* **2008**, *130*, 11874.
- [9] A. J. M. Miller, J. A. Labinger, J. E. Bercaw, *Organometallics* **2010**, *29*, 4499.
- [10] N. M. West, J. A. Labinger, J. E. Bercaw, *Organometallics* **2011**, *30*, 2690.
- [11] S. J. McLain, *J. Am. Chem. Soc.* **1983**, *105*, 6355.
- [12] S. J. McLain, *Inorg. Chem.* **1986**, *25*, 3124.
- [13] See the Supporting Information for full experimental and spectroscopic details.
- [14] P. E. Garrou, *Chem. Rev.* **1981**, *81*, 229.
- [15] Crystal data for **4**: [C₂₅H₂₈NO₇PRE]⁺·[BF₄]⁻·0.6(C₄H₁₀O), triclinic, *P* $\bar{1}$, *a* = 9.2994(5), *b* = 9.9376(4), *c* = 17.5007(8) Å, α = 87.062(2), β = 84.077(3), γ = 75.087(3)°, *V* = 1553.97(13) Å³, *Z* = 2, ρ_{calcd} = 1.712 Mg m⁻³, *F*(000) = 792, μ = 4.031 mm⁻¹, reflections measured: 101 244, independent reflections: 12 609 [*R*_{int} = 0.0432], *R*₁ = 0.0305 [*I* > 2σ(*I*)], *wR*₂ = 0.051 (all data), residual electron density 2.438/–2.718 e Å⁻³. For **5**: [C₂₇H₃₁NO₇PREZn]⁺·[BF₄]⁻·0.5(C₆H₆), triclinic, *P* $\bar{1}$, *a* = 11.5843(6), *b* = 17.2038(8), *c* = 17.2154(9) Å, α = 88.971(3), β = 77.007(3), γ = 89.071(3)°, *V* = 3342.3(3) Å³, *Z* = 4, ρ_{calcd} = 1.775 Mg m⁻³, *F*(000) = 1764, μ = 4.452 mm⁻¹, reflections measured: 338 688, independent reflections: 49 331 [*R*_{int} = 0.0454], *R*₁ = 0.0587 [*I* > 2σ(*I*)], *wR*₂ = 0.0907 (all data), residual electron density 8.977/–4.817 e Å⁻³.
- [16] An acyl CO stretching peak was not observed in the IR spectrum. Presumably, strong bonding to the Lewis acid lowers the energy of this peak to a point where it is obscured by the peaks that are due to phenyl vibrations.
- [17] Crystal data for **8a**: 0.8(C₂₆H₃₁NO₇PCaI₂Re)·0.2(C₂₄H₂₈NO₆PCaI₃Re), monoclinic, *P*₂₁, *a* = 11.8734(4), *b* = 14.0152(5), *c* = 12.0094(5) Å, β = 109.605(2), *V* = 1882.61(12) Å³, *Z* = 2, ρ_{calcd} = 1.821 Mg m⁻³, *F*(000) = 979, μ = 5.252 mm⁻¹, reflections measured: 40053, independent reflections: 9988 [*R*_{int} = 0.0455], *R*₁ = 0.0602 [*I* > 2σ(*I*)], *wR*₂ = 0.1322 (all data), residual electron density 3.262/–2.835 e Å⁻³.
- [18] E. Lindner, G. von Au, *Angew. Chem.* **1980**, *92*, 843; *Angew. Chem. Int. Ed. Engl.* **1980**, *19*, 824.
- [19] S. B. Butts, S. H. Strauss, E. M. Holt, R. E. Stimson, N. W. Alcock, D. F. Shriver, *J. Am. Chem. Soc.* **1980**, *102*, 5093.
- [20] S. B. Butts, E. M. Holt, S. H. Strauss, N. W. Alcock, R. E. Stimson, D. F. Shriver, *J. Am. Chem. Soc.* **1979**, *101*, 5864.
- [21] T. G. Richmond, F. Basolo, D. F. Shriver, *Inorg. Chem.* **1982**, *21*, 1272.
- [22] Crystal data for **13**: [C₂₆H₃₁NO₇PCaI₂Re]⁺[I]⁻, monoclinic, *C*2/*c*, *a* = 50.446(6), *b* = 8.8199(11), *c* = 17.567(2) Å, β = 93.862(7)°, *V* = 7798.2(17) Å³, *Z* = 8, ρ_{calcd} = 1.969 Mg m⁻³, *F*(000) = 4424, μ = 5.127 mm⁻¹, reflections measured: 116 605, independent reflections: 9367 [*R*_{int} = 0.0436], *R*₁ = 0.0818 [*I* > 2σ(*I*)], *wR*₂ = 0.1320 (all data), residual electron density 4.437/–3.910 e Å⁻³.
- [23] Data were collected at 100 K using a Bruker KAPPA APEX II diffractometer with MoK α radiation (γ = 0.71073 Å). Structure solution and refinements were performed with the SHELXS-97 program. Refinement of *F*² against all reflections. CCDC 850303 (**4**), 822258 (**5**), CCDC 854071 (**8a**), and CCDC 854702 (**13**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.