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JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
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Polycationic Ligands in Gold Catalysis: Synthesis and Applications of Extremely π-Acidic Catalysts

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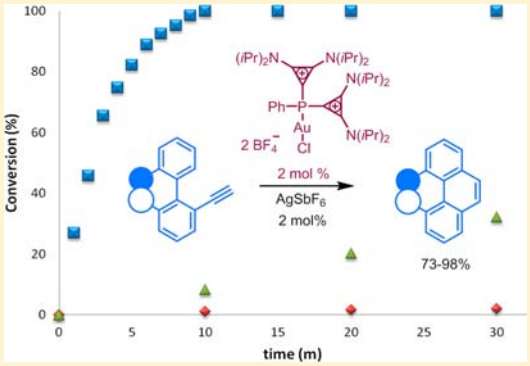
Supporting Information

ABSTRACT: Very often ligands are anionic or neutral species. Cationic ones are rare, and, when used, the positively charged groups are normally appended to the periphery of the ligand. Here, we describe a dicationic phosphine with no spacer between the phosphorus atom and the two positively charged groups. This structural feature makes its donor ability poorer than that of phosphites and only comparable to extremely toxic or pyrophoric compounds such as PF_3 or $P(CF_3)_3$. By exploiting these properties, a new Au catalyst has been developed displaying a dramatically enhanced capacity to activate π-systems. This has been used to synthesize very sterically hindered and naturally occurring 4,5-disubstituted phenanthrenes. The present approach is expected to be applicable to the development and improvement of many other transition metal catalyzed transformations that benefit from extremely strong π-acceptor ligands. The mechanism of selected catalytic transformations has been explored by density functional calculations.



1. INTRODUCTION

Phosphines are arguably the most important ancillary ligands in organometallic chemistry probably due to the easy modification of their electronic and steric properties in a predictable manner. Specifically, in homogeneous catalysis this tuning is a key attribute that allows a remarkable degree of control over the outcome of transition metal promoted transformations. Just to mention some examples, bulky phosphines are known to stabilize low-coordinated intermediates,[1] electron-rich ones facilitate oxidative additions,[2] and the employment of strong acceptor ligands favors the coordination of substrates or other coligands. Unfortunately, while steric hindrance can be modified quite independently, the tuning of electron properties is more subtle and any change in the σ-donation ability of a ligand is coupled with a variation of its π-acceptor properties, normally, in an opposite direction.[3]

Many electron-rich phosphines with different steric requirements are available. If moderate π-acceptor ligands are necessary, phosphites or polyhalogenated phosphines can be still employed, but there are only a few phosphorus-based ligands that are feeble σ-donor and strong π-acceptor ligands. In fact, only PF_3, $P(CF_3)_3$, and PCl_3 can be considered members of this category. However, despite this potential, their coordination chemistry is unexploited[4] for obvious reasons: PF_3 is a very poisonous gas, difficult to prepare and to handle, $P(CF_3)_3$ is a liquid with a quite low boiling point (17.3 °C, 760 mm) that burns in contact with air, and PCl_3 is a very irritant liquid readily prone to hydrolysis.[5] Moreover, the metal complexes resulting from their coordination are often as reactive or even more so than the corresponding free ligands.

As part of our program devoted to the development of more amenable extreme electron-poor phosphines with potential applications in catalysis, we envisaged a new strategy based on the introduction of positively charged homo- or heteroaromatic moieties directly attached to the central phosphorus atom.[6] This article discloses the successful implementation of this concept through the synthesis of (dialkylamino)-cyclopropenium substituted phosphines. Specifically, when two of these three-member ring substituents are introduced, the donor ability of the resulting ligand **1**—a bench stable crystalline solid—perfectly matches that of $P(CF_3)_3$. Taking advantage of these properties, we also develop herein a new gold catalyst **6** able to transform in excellent yields *ortho*-biaryl substituted alkynes into bent phenantrenes containing substituents in both internal positions, 4 and 5. We also demonstrate the impact of this catalyst on the synthesis of phenanthrene-derived natural occurring products such as Bulbophylantrin, Marylaurencinol A, Ochrolide, and Coelogininin. Finally, we report density functional theory (DFT) calculations to analyze the electronic structure of the catalyst and to elucidate the mechanism of a prototypical cycloisomerization reaction catalyzed by **6**.

2. RESULTS AND DISCUSSION

2.1. Bis[(di*iso*propylamino)cyclopropenium]-Substituted Phosphines. In phosphines, the nonshared electron pair at phosphorus accounts for the σ-donor ability while the

Received: July 9, 2013
Published: December 5, 2013

   dx.doi.org/10.1021/ja411146x | J. Am. Chem. Soc. 2013, 135, 18815−18823

σ^*(P−C) orbital accepts electron density from the metal through π-backdonation. In a first approach, introduction of a positively charged substituent directly on phosphorus lowers the energy of both orbitals by the inductive effect. Consequently, the resulting phosphine must be a worse σ-donor but a better π-acceptor ligand. This rationale is correct in general lines but still incomplete. If the positively charged group is an aromatic system, it will contain low-lying π^* orbitals that can interact with the lone pair at phosphorus and thereby change its shape. This can be viewed as a back-donation from phosphorus to its substituents, which will reduce the overlap with the orbitals of the metal (M) and weaken or, in an extreme case, even cancel the σ component of the P-M bond. This scenario explains why all monocationic phosphines that are known to form complexes with metals depict phosphite-type behavior.[7] Obviously, when two or more -onium substituents are attached to the central P-atom, the resulting polycationic phosphines should be even poorer donating ligands. Probably for this reason these compounds rarely coordinate to metals. In fact, the only two complexes reported to date containing polycationic ligands share the same $[L\rightarrow PtCl_3]^{n+}$ (n = 1,2) structure and their stability presumably relies on the exquisite π-back-donation capacity of the anionic Pt-moiety which is able to overcompensate the feeble σ-bond component.[6b,8] However, for a general impact on catalysis, polycationic ligands able to coordinate a broader metal panoply are required.

Thus, it seems that at least two -onium substituents will be necessary to engender very strong π-acceptor properties in a phosphine, but importantly, not all positively charged substituents will be equally appropriate. Those endowed with the highest lowest unoccupied molecular orbital (LUMO) should minimize the undesired (onium-π^*)-(P-lone pair) overlap and should therefore be most prone to coordinate an array of transition metals. For these reasons, the bis-(di*iso*propylaminocyclopropenium)-substituted phosphine **1** was selected as the most promising target ligand.[9] This compound could be prepared in a two-step sequence: First, condensation of the readily available chlorocyclopropenium tetrafluoroborate **2** with phenylphosphine **3** in refluxing tetrahydrofuran afforded salt **4** in 76% yield. Deprotonation of **4** with a strong base such as potassium hexamethyldisilazide at −30 °C and in situ trapping of the phosphalkene intermediate with a second equivalent of **2** finally yielded **1** as an air and water stable white solid (Figure 1a). Its dicationic character was reflected in the shielding of the P center (^{31}P NMR resonance at δ = −48.3 ppm) comparable to that in a dicationic bis(imidazolium) substituted sister compound (δ = −50.8 ppm).[10] Subsequently, single crystal X-ray diffraction analysis unambiguously confirmed the proposed connectivity for **1** (Figure 1b).

We were pleased to observe that **1** was not only able to react with K_2PtCl_4 to give complex **5**, but also with neutral metal fragments such as AuCl to afford compound **6**. Encouraged by this distinctive reactivity, the Tolman cone angle (θ) and the electronic parameter (TEP) of **1** were determined. From the X-ray structure of **5**, θ[11] was calculated to be 183° while the TEP[12] was estimated to be 2101 cm^{-1}. This value reveals the tremendous influence of the two cyclopropenium substituents on the donor capacity of **1**. In fact, **1** can be ranked as weaker donor than any phosphite ligand; only $P(CF_3)_3$ depicts similar donor properties (Figure 2).

2.2. Catalysis. The electrophilic activation of alkynes by gold species has emerged as an extremely powerful tool for the synthesis of complex organic molecules through the promotion of structural rearrangements.[13] The low-lying LUMO and the poor back-donation capacity of cationic Au species account for their high efficiency in promoting these processes. It seems then reasonable to assume that this natural π-acidity of Au catalysts can be significantly enhanced by the introduction of strong π-acceptor ancillary ligands such as **1**.

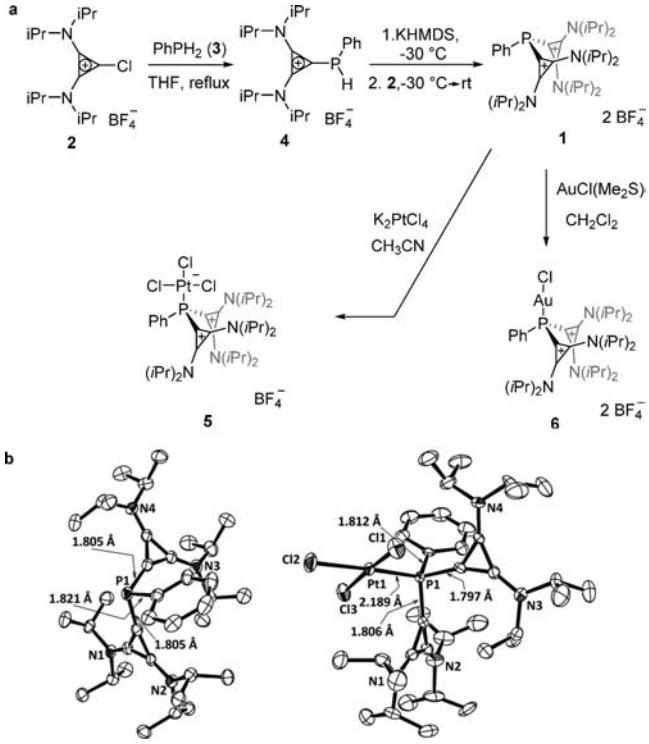


Figure 1. (a) Synthesis, structure, and complexation of **1**. (b) X-ray crystal structures of **1** and **5** in the solid state; hydrogen atoms and tetrafluoroborate counteranions are omitted for clarity.

Recently, we developed an efficient protocol for the previously known Pt(II)-catalyzed 6-*endo*-dig cyclization of 2-ethynyl-1,1′-biphenyls into polysubstituted phenanthrenes that dramatically expanded its scope.[6a,14] Unfortunately, when using biphenyls precursors of 4 and/or 5 substituted phenanthrenes, the yields of the desired products dropped significantly, or no cycloisomerization could be detected. The torsion imposed onto the phenanthrene system by the unfavorable steric interactions between the two internal substituents is probably responsible for the difficulties attending the synthesis of these seemly simple molecules. Hence, an even stronger activation of the alkyne moiety by a metal catalyst appears necessary to overcome this limitation and thus provide a useful entry for the synthesis of 4,5-disubstituted phenanthrenes. This route will intrinsically lead to the formation of only the desired compound, in contrast with the established methodology based on the irradiation of stilbenes in the presence of an external oxidant that affords mixtures of positional isomers.[15]

In an attempt to address this issue, we focused on the performance of precatalysts **6** containing the more π-acid Au(I) center and the extremely strong π-acceptor ligand **1**. Initial trials were carried out using 2-ethynyl-2′,6-dimethylbiphenyl **7** as model substrate (Figure 3a). After screening the reaction using a series of five solvents (THF, MTBE, toluene, acetonitrile, and dichloromethane), different catalyst loadings, and silver salts for the abstraction of the chloride moiety of **6**,

dx.doi.org/10.1021/ja411146x | J. Am. Chem. Soc. 2013, 135, 18815−18823

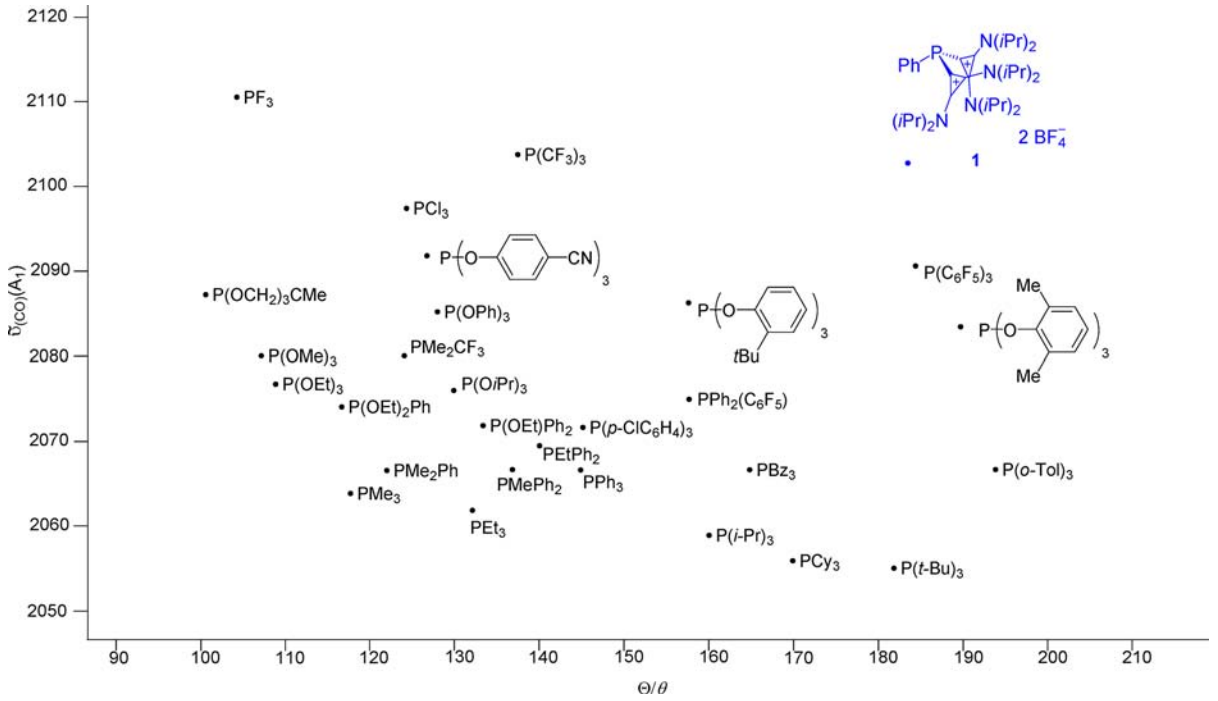


Figure 2. Tolman stereoelectronic map for P-based ligands. Comparison with other phosphines and phosphites highlights the exceptional π-acceptor properties of **1** (shown in blue).

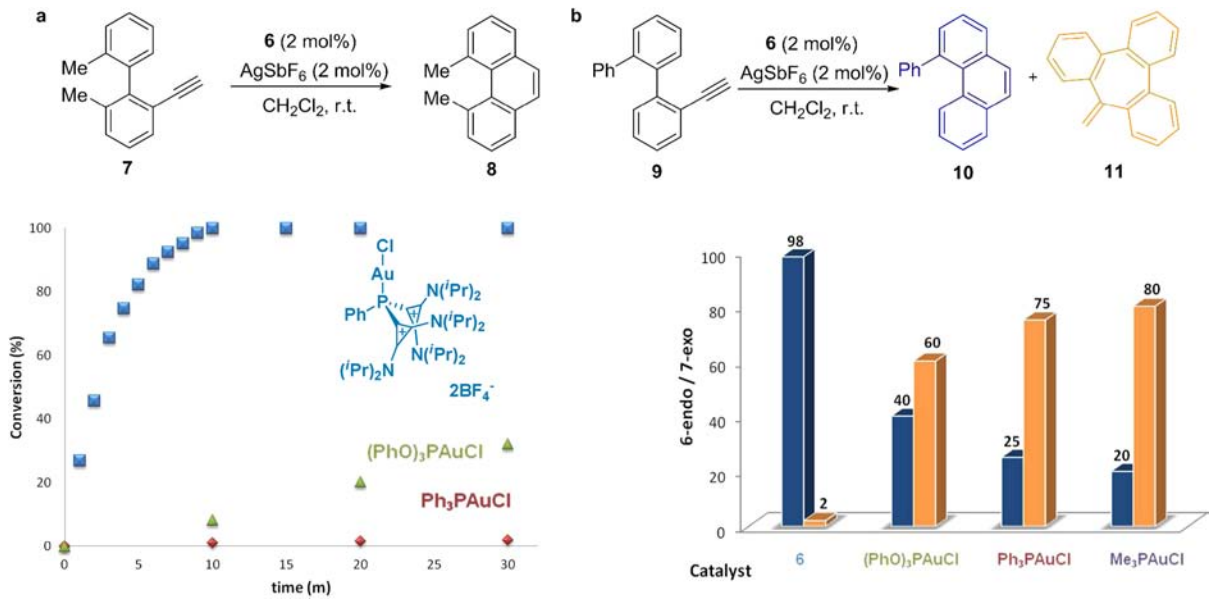


Figure 3. Ligand effect on the Au-catalyzed cyclization of 2-ethynylbiphenyls into phenanthrenes. (a) Plot of conversion versus time in the reaction of 2-ethynyl-6,2′-dimethylbiphenyl into 4,5-dimethylphenanthrene. Conditions: **7** (0.05 M), Au precatalysts 2 mol %, $AgSbF_6$ 2 mol %, CH_2Cl_2, room temperature. Conversions were determined by GC. (b) Effect of phosphine ligands with different donor−acceptor properties on the Au-catalyzed cyclization of biphenyl **9**. Product ratios and yields measured after complete consumption of the starting material. Isolated yields of the **10**/**11** mixtures: 92%, (**6**); 89%, $(PhO)_3P$; 93%, Ph_3P; 90%, Me_3P.

we found optimum conditions (2 mol % of **6** and $AgSbF_6$, CH_2Cl_2, room temperature), under which the desired 4,5-dimethylphenantrene **8** was obtained in excellent yield (97%) after only 10 min. For comparison, Figure 3a also depicts the conversion-versus-time plot for the archetypal Au precatalysts Ph_3PAuCl (red) and $(PhO)_3PAuCl$ (green) under otherwise identical conditions. The vastly superior behavior of **6** demonstrates the remarkable ability of **1** to increase the π-acidity of Au (see the Computational Section for a detailed theoretical analysis). In addition, the advantages derived from the employment of **6** as precatalyst are not only of kinetic nature. Figure 3b shows the product distribution when **9** is employed as substrate in the presence of different Au precatalysts. Whereas Me_3PAuCl, Ph_3PAuCl or $(PhO)_3PAuCl$ lead to the formation of cycloheptatriene **11** as the major product through a parasite 7-*exo*-dig process, **6** furnished the desired 4-phenylphenanthrene **10** with excellent selectivity. This switch from an originally preferred pathway to another

dx.doi.org/10.1021/ja411146x | J. Am. Chem. Soc. 2013, 135, 18815−18823

Table 1. Scope of the Au-Catalyzed Cycloisomerization of Ortho-Alkynylated Biaryls Employing Catalyst 6

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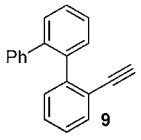
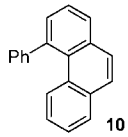
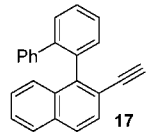
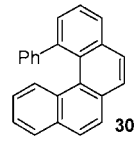
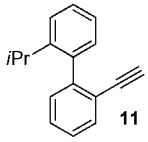
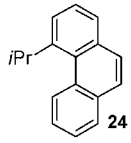
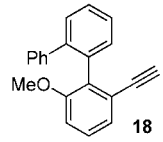
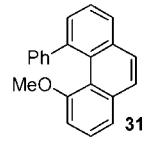
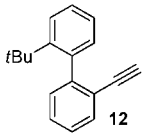
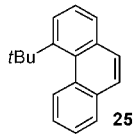
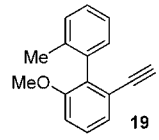
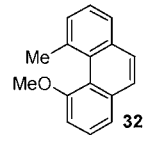
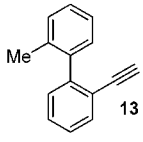
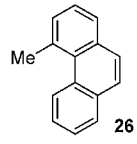
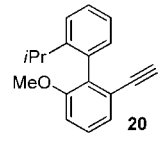
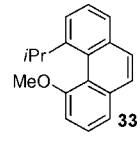
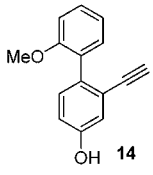
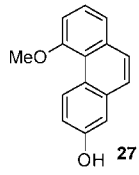
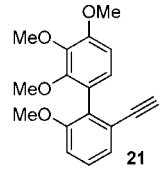
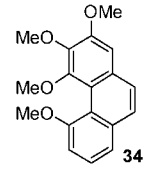
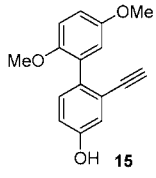
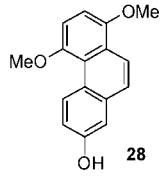
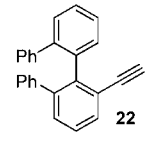
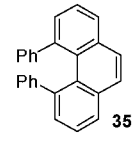
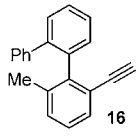
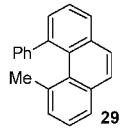
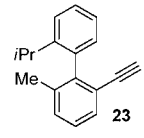
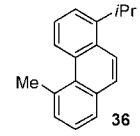
1	 9	 10	88%	8	 17	 30	73%
2	 11	 24	74%	9	 18	 31	93%
3	 12	 25	95%	10	 19	 32	91%
4	 13	 26	92%	11	 20	 33	87%
5	 14	 27	93%	12	 21	 34	98%
6	 15	 28	91%	13	 22	 35	90%
7	 16	 29	96%	14	 23	 36	55%†

Conditions: biphenyl (0.05M), **6** (2 mol %), $AgSbF_6$ (2 mol %) CH_2Cl_2, room temperature. *Isolated yield. †Four products were detected by GC–MS analysis of the reaction crude (4-methyl-8-*iso*propylphenanthrene **36**, 66%; 4-methyl-5-*iso*propylphenanthrene **37**, 22%; 4-methyl-6-*iso*propylphenanthrene **38**, 3%; 4-methylphenanthrene **26**, 7%). Preparative HPLC allowed the isolation of the four compounds and subsequent NMR analysis. The structure of the major isomer, **36**, was also confirmed by X-ray difraction analysis of a monocrystal.

one depending on the π-acidity of the catalysts is consistent with the following mechanistic interpretation.[16] The reaction is thought to commence with a nucleophilic attack of the arene ring on the activated alkyne. A strong activation of the alkyne by the catalysts will give rise to a rather early transition state where steric issues are not crucial; hence, the 6-*endo*-dig cyclization takes place almost exclusively. In the case of weaker π-acid catalysts, a closer approach of the reacting fragments is needed to reach the transition state. Sterics may then play an important role and increase the barrier to the 6-*endo*-dig cyclization so that the competitive 7-*exo*-dig process gets favored.

Having identified the optimized reaction conditions, further experiments were conducted to explore the generality of this cycloisomerization protocol regarding functional group tolerance and the size of the groups that could be introduced. We

dx.doi.org/10.1021/ja411146x | J. Am. Chem. Soc. 2013, 135, 18815–18823

first prepared a collection of 2-ethynylbiphenyls **9**−**14** only substituted at position 2′ (see the Supporting Information) and performed a reactivity screen. The results were highly encouraging as all the substrates were completely converted to the desired phenanthrenes **23**−**28** in good to excellent yields (Table 1, entries 1−6). Interestingly, methyl-, phenyl-, methoxy-, *iso*-propyl-, and even *tert*-butyl-substituents in position 4 were found to be compatible with the cyclization process. Moreover, the presence of free −OH groups was tolerated, although competitive coordination of the oxygen atom to Au could have been an issue.

With these results in hand, we then focused our attention on the reactivity of biphenyl substrates that simultaneously bear substituents at positions 2′ and 6. To our delight, full conversions and high isolated yields of the desired phenanthrenes were also obtained after short reaction times (Table 1, entries 7−14). X-ray structure analysis of compounds **8**, **30**, and **35** further demonstrates the exquisite ability of **6** to accomplish the desired cyclizations encompassing sterically demanding substrates. The clash between substituents in positions 4 and 5 generates destabilizing twists of up to 31.7° within the phenanthrene moiety (measured through the C4−C4a−C5a−C5 torsion) but nonetheless, the desired ring closure takes place cleanly (Figure 4).

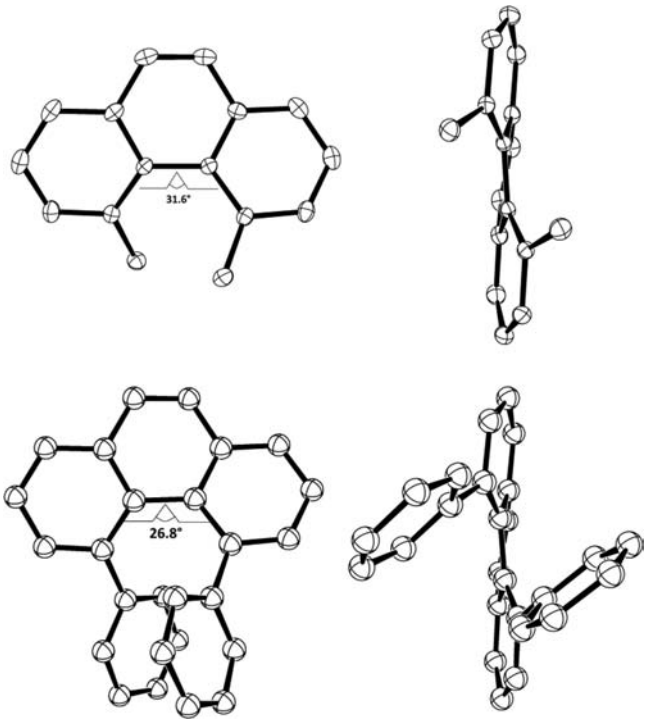


Figure 4. X-ray crystal structures of **8** and **35** in the solid state. Dihedral angles between the two terminal rings are defined in terms of the torsion angle C4−C4a−C5a−C5. Hydrogen atoms are omitted for clarity, and ellipsoids are shown at 50% probability.

Interestingly, the biphenyl substrate **23** behaves differently when submitted to the standard reaction conditions. Up to four different products with phenanthrene architecture could be isolated from the reaction mixture in which the isopropyl group ended up in positions 5 (**37**), 6 (**38**), 8 (**36**), or was not even present as shown by the isolation of **26**. Apparently, with this sterically very hindered substrate, new competitive reaction pathways emerge leading to the formation of more stable products, possibly through migration of the isopropyl moiety. Efforts directed toward the understanding of this phenomenon are currently underway.

2.3. Synthetic Applications. A large number of naturally occurring polyoxygenated phenanthrenes with different substitution patterns have been isolated from plants belonging to the *Orchidaceae* family.[17] They exhibit interesting biological activities as antiinflammatory, antiallergic, antimicrobial, antifungal, and cytotoxic reagents. In view of their relevance, we decided to explore the utility of our methodology for the synthesis of some representative examples. Specifically, we focused on the preparation of the synthetically more challenging 4,5-disubstituted derivatives.

As first targets, we chose Bulbophylantrin **39**,[18] a diphenol isolated from the orchid *Bulbophyllum leopardium* and its 9,10-dihydro- derivative Marylaurencinol A **40**,[19] recently obtained from *Cymbidium* Great Flower Marie Laurencin. Our total synthesis of these products started from the already described 2-bromo-3-hydroxy-benzaldehyde **41**[20] which was cross-coupled with the benzyl-protected boronic acid **42**[21] to form the corresponding biphenyl derivative **43**. Treatment with Ohira−Bestmann reagent[22] generated the desired alkyne **44** that was subsequently submitted to the key Au-catalyzed cycloisomerization. In line with our expectations, the desired phenanthrene **45** was obtained in excellent yield after a few minutes. Removal of the benzyl group by hydrogenolytic cleavage in ethyl acetate cleanly afforded Bulbophyllantrin **39**. Hydrogenation in a more polar solvent such as methanol not only caused cleavage of the benzyl ether but also reduction of the phenanthrene skeleton at the more activated 9- and 10-positions giving Marylaurencinol A. This material crystallized quite readily and X-ray analysis could be performed confirming the expected connectivity (Scheme 1).

The naturally occurring phenantropyrone Ochrolide **53**, first isolated from the orchid *Coelogine orchracea*, was also selected as an interesting synthetic target. In this case, the final molecule is planar however, it can be envisaged that if the twisted phenanthrene **52** could be obtained, removal of the benzyl-protecting groups should also spontaneously induce the desired transesterification (Scheme 2). After preparation of the two coupling partners **46** and **47** (see the Supporting Information), a Negishi reaction afforded the corresponding biphenyl derivative **48** in which the aldehyde moiety is already deprotected. Subsequently, the Ohira−Bestmann reaction produced the expected alkyne **49**.

The stage was then set for the key Au-catalyzed cyclization. Although the formation of **51** could be observed, the benzyl-deprotected product **52** was also formed in similar quantities. It is well-known that Lewis acids promote deprotection of benzylated phenols having a carbonyl group in the ortho-position. Hence, the formation of **52** could be attributed to the exceptional Lewis acidity of Au when coordinated to phosphine **1**. Analytically pure **52** could be obtained after selective monodebenzylation of **49** with $AlCl_3$ followed by treatment with **6**/$AgBF_4$. In any case, Pd/C catalyzed cleavage of the benzyl ethers in **52** or mixtures containing **51** and **52** cleanly generated Ochrolide **53**. As expected, hydrogenation of **52** under more forcing conditions (H_2, 20 bar) also allowed the isolation of the 9,10-dihydrophenanthrene derivative Coeloginin **54**, another phenanthrenoid that was first isolated from the high-altitude Himalayan orchid *Coelogyne cristata*.[23]

2.4. Computational Results. Up to this point, our explanations and mechanistic arguments, although based on

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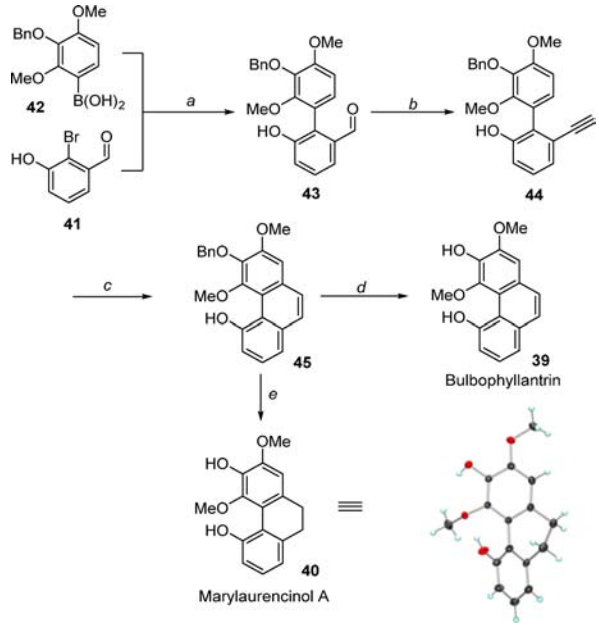
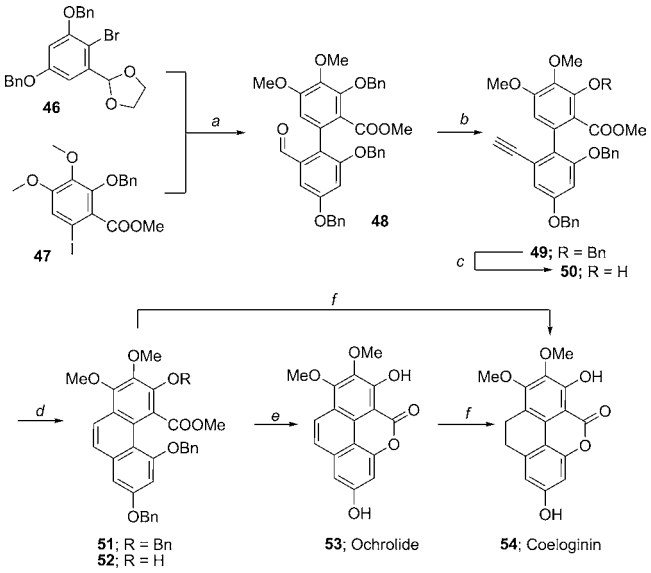
Scheme 1. Synthesis of Bulbophyllantrin and Marylaurencinol A



Conditions: (a) $Pd_2(dba)_3$ 5 mol %, Cy_3P 11 mol %, Cs_2CO_3 (2.5 equiv), dioxane:toluene (2:3), 85 °C, 16 h, 85%; (b) Ohira–Bestmann reagent (1.5 equiv), K_2CO_3 (2 equiv), MeOH, 16h, room temperature, 91%; (c) **6** 2 mol %, $AgSbF_6$ 2 mol %, CH_2Cl_2 (0.05 M), 10 min, room temperature, 90%; (d) Pd/C (10%), 20 mol %, AcOEt, 24 h, H_2 (1 atm.), 81%; (e) Pd/C (10%), 50 mol %, MeOH, 16 h, H_2 (1 atm.), 97%.

Scheme 2. Synthesis of Ochrolide and Coeloginin



Conditions: (a) **46**, n-BuLi, THF, 1 h; then $ZnCl_2$ and $Pd_2(dba)_3$ 2.5 mol %, 2-dicyclohexylphosphino-2′,6′-di(isopropyl)oxybiphenyl 6 mol % and **47**, 64% ; (b) Ohira–Bestmann reagent (1.5 equiv), K_2CO_3 (2 equiv), MeOH, 16 h, room temperature, 93%; (c) $AlCl_3$, benzene, reflux, 73%; (d) **6**/$AgSbF_6$ 5 mol %, $Cl(CH_2)_2Cl$, 75%; (e) Pd/C (10%), AcOEt, H_2 (1 atm), 93%; (f) Pd/C (10%), AcOEt, H_2 (20 atm), 92%.

kinetic data, have been qualitative in nature. Computational methods nowadays provide quantitative information that can be used to characterize synthetically inaccessible compounds and to elucidate reactions pathways.[24]

In an attempt to gain insight into the origin of the remarkable reactivity of the actual catalyst **55**, we studied its electronic structure by performing a fragment molecular orbital (MO) analysis employing the *Amsterdam Density Functional* (ADF) program package (see the Supporting Information).[25] In this analysis, the MOs are expanded in terms of Slater-type orbitals, employing a triple-ζ basis set with one polarization function (TZP); relativistic effects were included using the zero-order regular approximation (ZORA) approach,[26] as implemented in the ADF program package.

In catalyst **55**, the interaction between the fragment MOs from **1** and Au^+ generates a low-lying antibonding orbital (σ^* P–Au, LUMO) that has a strong contribution from the Au 6s orbital (46%) (see Figure 5 (left) and Figure S54 of the Supporting Information). For comparison, Figure 5 also depicts the LUMO of $[(MeO)_3PAu]^+$ (**56**) (right). In both cases, the LUMO has a similar shape (σ^* P–Au), but it lies much lower in **55** (−11.89 eV) than in **56** (−8.03 eV). As in both systems, the LUMO is the main orbital involved in the coordination with the alkyne substrate, its energetic position thus governs the π-acidity of both catalysts. Therefore, the lower LUMO energy confers a stronger π-acidity to **55** and accounts for its higher reactivity when compared with other phosphorus-containing Au complexes such as **56**.

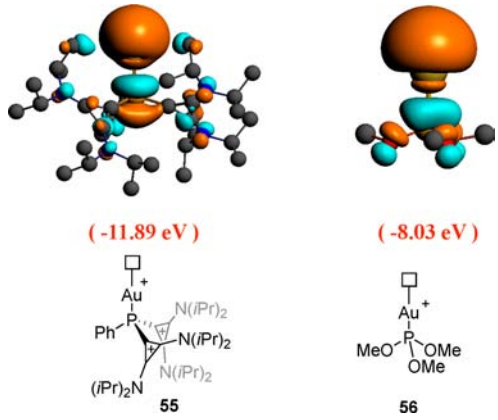


Figure 5. Left, LUMO of **55**; right, LUMO of $[(MeO)_3PAu]^+$ (**56**).

The mechanistic pathways for the cycloisomerization of **7** to **8** catalyzed by **55** (green) and $[Ph_3PAu]^+$ (**57**) (red) were explored by DFT calculations (see Figure 6). Geometry optimizations were carried out using BP86[27,28] functional in combination with def2-SVP basis sets.[29] In the case of gold, the 60 inner-shell core electrons were replaced by an effective core potential (ECP) generated for the neutral atom using quasi-relativistic methods, and the explicitly treated electrons were described by the standard def2-ECP basis set.[30] The resolution-of-identity (RI) approximation[31] was applied in conjunction with appropriate auxiliary basis sets to speed up the calculations. All low-energy conformations of the substrate and the catalyst were considered during initial screening, and all relevant stationary points were characterized as minima or first-order transition states by evaluating the harmonic vibrational frequencies at the same level (RI-BP86/def2-SVP) that had been applied for geometry optimization.

The influence of the solvent environment (dichloromethane, dielectric constant ε = 8.93) on the relative energies was

dx.doi.org/10.1021/ja411146x | J. Am. Chem. Soc. 2013, 135, 18815−18823

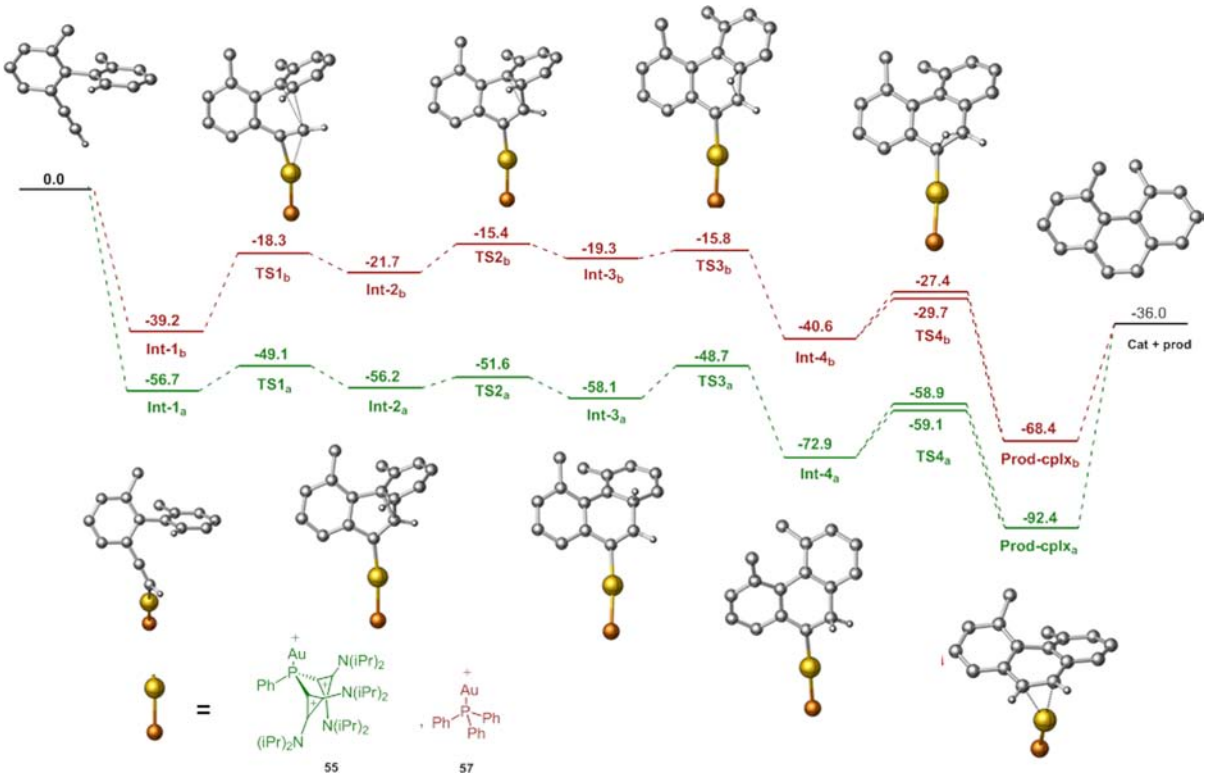


Figure 6. Free energy profiles (kcal/mol) for the cyclization of 2-ethynyl-2′,6-dimethylbiphenyl **7** to 4,5-dimethylphenanthrene **8**. The green and red lines represent the calculated profiles for catalysts **55** and **57**, respectively. Both diasteromeric protons were considered in the calculation of $\mathbf{TS4}_a$ and $\mathbf{TS4}_b$.

investigated through single-point calculations with the conductor-like screening model (COSMO)[32] at RI-BP86/def2-SVP level. To evaluate the best estimate of total energies, all located stationary points were reoptimized at RI-BP86 level employing the def2-TZVPP basis set. The empirical Grimme-type dispersion corrections were also incorporated during this step using the latest parametrization (DFT-D3).[33] Relative free energies (ΔG) at standard pressure (1 bar) and 273.15 K were determined at the RI-BP86/def2-SVP level. The required thermal and entropic contributions were evaluated within the rigid-rotor harmonic-oscillator approximation. All geometry optimizations were performed using the TURBOMOLE (version 6.4) suite of program.[34] To check the sensitivity of the computed energy profile, single-point energies at optimized RI-BP86/def2-TZVPP geometries were evaluated by using more advanced functionals (B3LYP, M06), and larger basis sets (def2-SVP, def2-TZVPP, and 6-31+G*).The single-point results (see the Supporting Information) confirm the qualitative conclusions drawn from the standard approach outlined above and will therefore not be discussed in the following.

Figure 6 depicts the calculated pathways for the cycloisomerization of **7** to **8**. For both catalysts, the reaction begins with the coordination of the alkyne to Au forming a catalyst-substrate complex **Int1**, which is much more exergonic when **55** is employed as catalyst, $\mathbf{Int1}_a$. The higher thermodynamic stability of $\mathbf{Int1}_a$ has its origin in the very low-lying LUMO of the catalyst **55** that favors the coordination of substrate (Figure 5). The next step along the reaction coordinate involves in both cases the nucleophilic attack of the arene ring on the activated alkyne to form the expected cyclopropyl intermediates $\mathbf{Int2}_{a/b}$. Judging from the computed relative free energies, this step is much easier when the strongly activating catalyst **55** is employed: The free energy of activation (relative to the preceding intermediate) is only 7.6 kcal/mol compared with 20.9 kcal/mol when using the archetypical catalyst **57**. This is the main reason why the use of ligand **1** significantly fosters the whole process. The following steps, cyclopropane ring-opening and 1,2-H shift to $\mathbf{Int4}_{a/b}$, are quite facile in both cases (free energy barriers of less than 10 kcal/mol) and do not depend much on the nature of the ancillary ligand.

The two intermediates $\mathbf{Int4}_{a/b}$ are more stable than their precursors $\mathbf{Int3}_{a/b}$ by 14.8 and 21.3 kcal/mol, respectively, and the energies for the following transition states $\mathbf{TS4}_a$ (−59.1 kcal/mol) and $\mathbf{TS4}_b$ (−29.7 kcal/mol) are much lower than those of $\mathbf{TS3}_a$ (−48.7 kcal/mol) and $\mathbf{TS3}_b$ (−15.8 kcal/mol), respectively. Thus, the formation of the Au-carbenes $\mathbf{Int4}_{a/b}$ is likely to be irreversible. In the final step, a second 1,2-hydrogen shift (involving either one of the diasteromeric H atoms) yields the phenanthrene−Au π-complexes, the dissociation of which will provide the desired product and regenerate the catalysts. The interaction between catalyst **55** and the product is calculated to be very strong (92.4 kcal/mol), which may be responsible for the catalyst deactivation of the catalysts observed at high substrate conversion, once the phenanthrene product accumulates (Figure 3a).

We have examined in an analogous manner the cycloisomerization of the substrate **9** to the 6-endo product **10** and the 7-*exo* product **11** using **55** and Me_3PAuCl as catalysts. The computed mechanistic pathway for the conversion **9** →**10** (see Figure S25 of the Supporting Information) is similar to that established for **7**→**8** (see Figure 6), with one minor modification: The cyclization does not proceed through the formation of a cyclopropyl intermediate, instead the six-membered ring is formed in one step. For both conversions,

dx.doi.org/10.1021/ja411146x | J. Am. Chem. Soc. 2013, 135, 18815−18823

55 outperforms the other considered catalysts (Ph_3PAuCl and Me_3PAuCl) by a large margin, with significantly lower rate-limiting barriers. When using catalyst **55**, the initial cyclization is computed to be more facile for **7** than for **9** (barriers of 7.6 and 13.8 kcal/mol, respectively).

We have also located pathways for the conversion **9** →**11** (see Figure S44 of the Supporting Information). When using **55** as catalyst, the relevant barriers are higher than those for the cyclization **9** →**10**, consistent with the observed preferential formation of the 6-*endo* product **10** (see Figure 3). When Me_3PAuCl is used as catalyst, the computed barriers are generally higher than in the case of **55** (as expected), but the qualitative preferences remain the same (6-*endo* product favored). Hence, the observed reversal of selectivity when changing the catalyst (see Figure 3) is not reproduced by the present calculations. Despite extensive scans of the potential energy surface, we apparently still miss a low-energy pathway for the Me_3PAuCl-catalyzed conversion **9** →**11**. Further work is needed to find such a pathway (possibly with the use of more extended model systems).

3. CONCLUSIONS

This study provides a conceptually new approach to the design of extreme π-acceptor ligands for transition metal catalysis based on the use of dicationic phosphines with two cyclopropenium groups directly attached to the phosphorus atom. The remarkable ability of this ligand to enhance the natural π-acidity of Au(I) was demonstrated in a series of examples, which achieve levels of reactivity and selectivity that clearly surpass the known catalytic systems. Moreover, and as an additional advantage, complex **6** can be weighed and handled in air and it is stable for months when stored under inert gas. Considering the multitude of transformations that might benefit from the use of extreme π-acceptor ligands, we believe that this approach shows a vast potential in the development and improvement of transition metal catalyzed reactions.

■ ASSOCIATED CONTENT

Supporting Information

Experimental procedures including characterization data for all new compounds, NMR spectra, CIF files for **1**, **5**, **8**, **30**, **35**, and **40**, as well as computational procedures and detailed computational results. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

Dedicated to Prof. Manfred Reetz on the occasion of his 70th birthday. The authors thank C. Farès for NMR spectroscopic assistance, C. W. Lehmann, R. Goddard, and J. Rust for X-ray crystallographic analysis, and A. Degge for HPLC assistance. A. Fürstner is thanked for continuous support and encouragement. Financial support for this work was provided by the Max Planck Gesellschaft, the Deutsche Forschung Gemeinschaft, the Spanish Ministerio de Educación y Ciencia (postdoctoral fellowship for J.C.) and the Chinese Scholarship Council (doctoral fellowship to L.G.).

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