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N-Arylpyridiniophosphines: Synthesis, Structure, and Applications in Au(I) Catalysis

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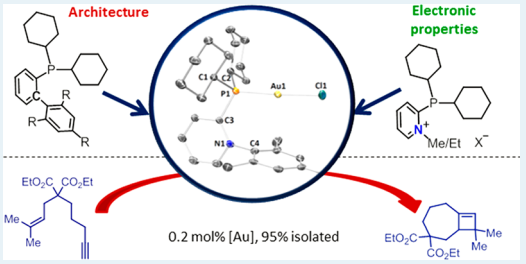
Supporting Information

ABSTRACT: The synthesis and characterization through NMR and X-ray crystallography of a series of *N*-arylpyridiniophosphines and their corresponding Au(I)-derivatives are reported. Because of their acceptor properties, pyridiniophosphines efficiently enhance the electrophilicity of the Au atom in the complexes they form. In our study, this is translated into higher reactivity of the corresponding Au catalysts, which is demonstrated in two mechanistically differentiated cycloisomerizations. Moreover, the steric protection and probably also the electronic stabilization provided by the *N*-aryl substituents make the active Au-species more robust and slow down its rate of decay. This allows for an appreciable reduction of the catalyst loadings.



KEYWORDS: *ligand design, α-cationic phosphines, Buchwald phosphines, Au(I)-catalysis, cycloisomerizations*

INTRODUCTION

The success harvested by Buchwald biarylphosphines in forming highly active Pd-catalysts is generally attributed to the unique combination of electronic and steric properties derived from their structural design. Specifically, their strong σ-donor ability together with the effective steric shielding of the metal by the biaryl rest facilitate the formation of low coordinated species [L_1Pd], which display enhanced reactivity toward both oxidative addition and reductive elimination. As a consequence, the employment of Buchwald ligands is associated with short reaction times, low catalyst loadings, mild reaction conditions, and a broad substrate scope in a wide range of C−C and C−N coupling reactions.[1]

The privileged architecture of dialkylbiarylphosphanes has also found widespread use in the area of Au-catalysis.[2] Both the steric protection of the active metal center and the weak but still stabilizing electronic interaction between the Au atom and the π-system of the lateral arene probably account for the robustness of the catalysts derived from these architectures.[3] It is also worth mentioning that because of the bulkiness of Buchwald ligands the formation of diaurated species, which have been recognized as resting states or even dead ends of the catalytic cycles leading to enyne cycloisomerizations, is less favored.[4]

Our research group has been involved during the past few years in the design and synthesis of α-cationic phosphines of various structure.[5] These ancillary ligands are unique in that the positive charge that they bear is directly attached to the donor phosphorus center, and for this reason, they display reduced σ-donor ability and enhanced π-acceptor character if compared with their neutral counterparts. These distinguishing attributes have been employed in our group to develop a series of mainly Au-[6] and Pt-,[7] but also Rh-catalysts[8] of enhanced catalytic activities.[9] However, the use of α-cationic ligands is not free of shortcomings: as a general rule, the reduced donation from the phosphorus center to the metal makes the bond between these two atoms significantly weaker. Moreover, the Coulomb repulsion between the ligand and the usually also positively charged metal center is expected to reduce the stability of the catalytically relevant species even more. As a result, although catalysts derived from α-cationic ligands exhibit unmatched reactivity, they are more prone to decomposition than those based on typical phosphines. This is particularly true in the case of monodentate ancillary ligands where stabilizing chelate effects are not present.[5]

Stimulated by the beneficial effects of Buchwald ligands in Au-promoted transformations[2] and expecting that a pendent aryl substituent directed toward the metal should also provide additional robustness to the complexes derived from cationic phosphines, we envisaged the design of a new generation of α-cationic phosphines that incorporates the privileged biaryl architecture. Herein, we bring this idea into practice with the synthesis of *N*-arylpyridiniophosphines. As can be observed in Figure 1, these salts can be considered as formal derivatives of

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dialkylbiarylphosphanes in which the bridging carbon atom has been substituted by a nitrogen center.[10]

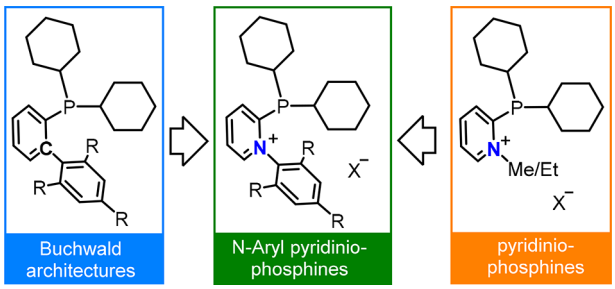


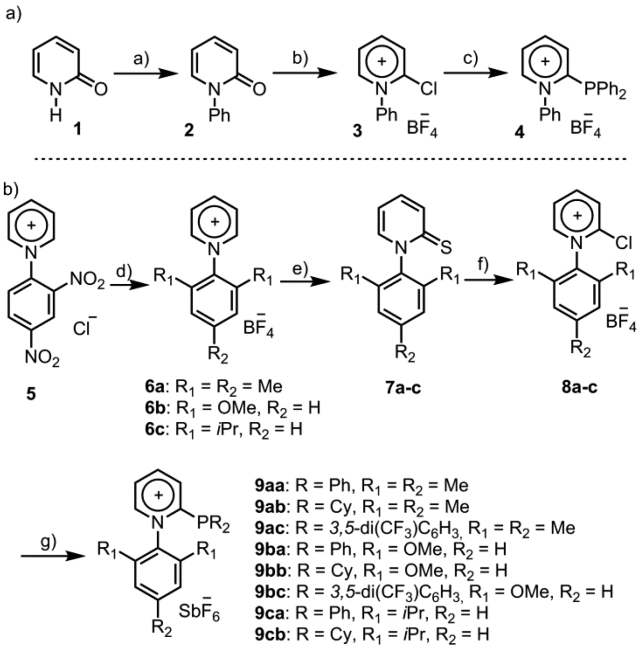
Figure 1. Design of *N*-arylpyridiniophosphines.

EXPERIMENTAL SECTION

Synthesis and Characterization of *N*-Arylpyridinio-phosphines. We previously reported a three-step route for the synthesis of *N*-phenylpyridiniophosphines starting from pyridone **1** consisting of an initial *N*-phenylation with iodobenzene to afford **2**,[11] which was transformed into the corresponding chloropyridinium salt **3** by treatment with oxalyl chloride. Finally, nucleophilic attack of diphenylphosphine to the 2-chloropyridinium ring of **3** efficiently afforded the desired α-pyridinium phosphine **4** (Scheme 1a).[10b] This protocol however encounters serious difficulties delivering *N*-arylpyridones in acceptable yields when the aryl rests to be incorporated at the N-position are bulkier than just a phenyl group. For this reason, the development of an alternative synthetic strategy was crucial. At that juncture, we decided to prepare *N*-arylpyridinium salts **6a–x** following the classical but very reliable Zincke synthesis, by reaction of appropriate anilines with dinitro substituted pyridinium salt **5**.[12] The necessary chloride functionality at the *ortho*-position to nitrogen was further installed through a two-step sequence consisting of the deprotonation of salts **6a–c** with LiHMDS at −100 °C followed by trapping of the in situ formed pyridin-2-ylidene with elemental sulfur. This leads to thiopyridones **7a–c**, which were subsequently transformed into the desired chloropyridinium salts **8a–c** by reaction with oxalyl chloride.[13] The scaling up of the synthetic sequence just described to gram scale was possible for all substitution patterns. Finally, condensation of **8a–c** with a range of secondary phosphines under microwave irradiation rendered the target *N*-arylpyridiniophosphines **9** as white to light brown solids in moderate to good yields. Due to the low basicity of bis(3,5-bis(trifluoromethyl)phenyl)-phosphine, the nucleophilic substitution at the pyridinium ring does not proceed to any appreciable extent; however, **9bc** is obtained in moderate yield when the polyfluorinated phosphine is previously deprotonated with KH to enhance its nucleophilicity (see Scheme 1b and the Supporting Information).

Evaluation of Stereoelectronic Properties. The X-ray analyses of single crystals of compounds **9aa**, **9ac**, **9ba**, and **9cb** are displayed in Figure 2. In the solid state, the sum of angles around P1 (304.9°, **9aa**; 308.2°, **9ac**; 305.7°, **9ba**; and 304.0°, **9cb**) are comparable to that observed in PPh_3 (309°). These similar degrees of pyramidalization indicate retention of the free electron pair at phosphorus despite the added positive charge. Also informative is the comparison of the metrical parameters of pyridiniophosphines with their parent Buchwald

Scheme 1. Synthesis of *N*-Arylpyridiniophosphines[a]



[a]Reagents and conditions: (a) iodobenzene (1 equiv), CuBr (10 mol %), Cs_2CO_3 (2.1 equiv), DMSO, 60 °C, 95%; (b) oxalyl chloride (3 equiv), $Cl(CH_2)_2Cl$, and then $NaBF_4$ (4 equiv), 71%; (c) Ph_2PH (2 equiv), THF, 65 °C, 71%; (d) $ArNH_2$, *n*-Butanol, 72 h, reflux, and then $NaBF_4$ (excess), **6a** (62%); **6b** (43%); **6c** (34%); (e) LiHMDS (1 equiv), S_8 (0.25 equiv), THF, **7a** (64%); **7b** (70%); **7c** (74%); (f) oxalyl chloride (3 equiv), DMF (0.1 mL), $Cl(CH_2)_2Cl$, **8a** (57%); **8b** (97%); **8c** (99%); (g) Method A: R_2PH (3 equiv), THF, 120 °C, μwave, 12 h, and then $NaSbF_6$, **9aa** (50%); **9ab** (55%); **9ba** (69%); **9bb** (69%); **9ca** (53%); **9cb** (32%); Method B: KH (8 equiv), R_2PH (1 equiv), THF, −78 °C → r.t., and then $NaSbF_6$,12 h, **9ac** (70%); **9bc** (44%).

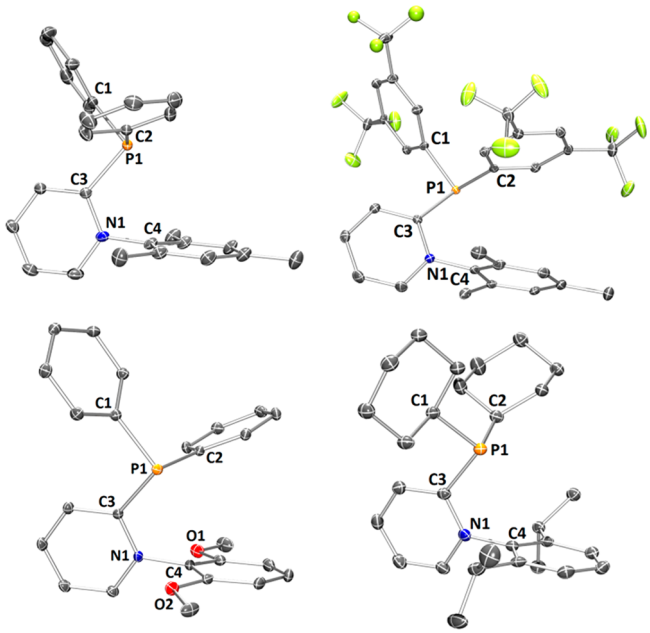


Figure 2. Crystal structures of **9aa**, **9ac**, **9ba**, and **9cb**. Hydrogen atoms and SbF_6 anions were omitted for clarity; ellipsoids are set at 50% probability.[15]

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structures. If the expected slight shortening of the three C−N bonds around N1 compared with Csp^2−Csp^2 bonds in **9** is ignored, no other significant variation is observed. This means that the formal exchange of the biaryl rest by a N-arylpyridinium moiety has minimal influence on the ligand structure. Thus, the steric parameters in **9** remain identical to the ones of the parent (uncharged) Buchwald ligands. This is confirmed by comparison of the percent buried volume (% V_{Bur}) and the topographic steric maps for both families of ligands (see Figure 3 and the Supporting Information).[14]

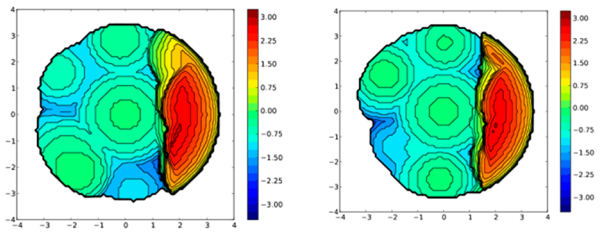
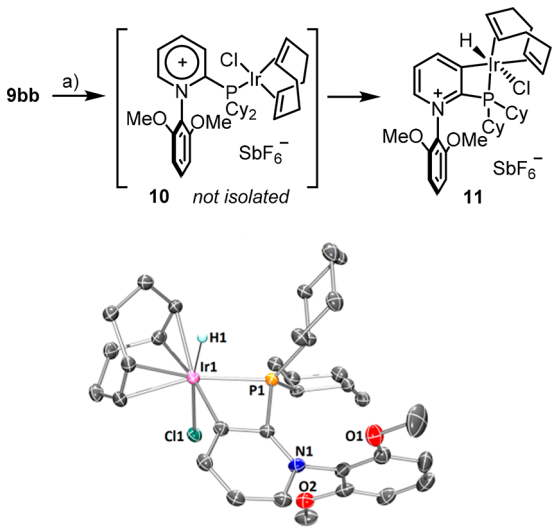


Figure 3. Steric maps for **9ab** (left) and SPhos (right). Both ligands are characterized by an identical %V_{Bur} = 49.

In a first attempt to determine the Tolman electronic parameter of the new cationic phosphines, ligand **9bb** was chosen as a proxy and reacted with $[IrCl(cod)]_2$ (Scheme 2).[16,17] The expected complex **10** could be detected by NMR

Scheme 2. Synthesis and X-ray Structure of Iridacycle 11[a]



[a]Reagents and conditions: (a) $[IrCl(cod)]_2$, CH_2Cl_2, 76%. Hydrogen atoms, except the hydride one, and SbF_6 anions omitted for clarity; ellipsoids are set at 50% probability.[15]

analysis; however, the reaction did not stop at that point, and instead, the Ir center oxidatively added to the *meta* C−H bond of the pyridinium moiety to afford the iridacyclobutane hydride complex **11**. The formation of this iridacycle was originally suggested by the appearance of a characteristic hydride signal at δ = −14.81 ppm ($^2J_{H-P}$ = 11.4 Hz) in the ^1H NMR spectrum and subsequently confirmed by X-ray crystallography (Scheme 2).

Because the oxidative addition process just described seems to be general for the pyridiniophosphine series of ligands, the oxidation potential E_p(ox) was chosen as an alternative parameter to rank the electronic properties of the new ligands. Cyclic voltammetry measurements afford values for the oxidation of ligands **4**, **9aa**, **9ab**, **9ca**, and **9cb** at the interval between 1.225 and 1.302 V (calibrated versus Fc^+/Fc), which are very similar potentials to the one measured for $(MeO)_3P$ (1.287 V). Although consideration of these values should be done with care because of the irreversible nature of the oxidation monitored, we can prudently assume that ligands of general structure **9** are defined by a basicity comparable to that characteristic of phosphites (Table 1). Hence, we conclude

Table 1. Electrochemical Oxidation Potentials[a]

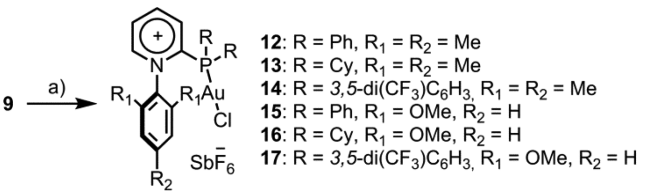
entry	ligand	E_p(ox)
1	SPhos	0.570
2	$(PhO_3)P$	1.287
3	**4**	1.285
4	**9aa**	1.302
5	**9ab**	1.271
6	**9ca**	1.287
7	**9cb**	1.225

[a]Oxidation peak potentials reported in V. Calibrated vs ferrocene/ferrocenium, Bu_4NPF_6 (0.1 M) in CH_2Cl_2.

that the formal exchange of the phenylene bridge by a pyridinium moiety in Buchwald-type phosphines significantly reduces the basicity of the parent ligands without altering, not even minimally, their unique steric properties.

Synthesis of Au(I)-Complexes. Encouraged by this analysis and willing to exploit the stereoelectronic properties of the newly prepared pyridiniophosphines in catalysis, we first prepared a series of Au(I)-complexes **12**−**17** by phosphine displacement of Me_2S in $(Me_2S)AuCl$ (Scheme 3).[18] The

Scheme 3. Synthesis of Au-Complexes 12−17[a]



[a]Reagents and conditions: (a) $(Me_2S)AuCl$ (1 equiv), CH_2Cl_2, rt, 1h, **12** (98%); **13** (96%); **14** (98%); **15** (98%); **16** (96%); **17** (89%).

decision to employ Au-catalysis for the initial screening of *N*-arylpyridiniophosphines comes from our long-standing interest in Au-catalyzed processes that benefit from strong acceptor ligands.[6,19]

Indicative of the formation of the desired Au(I)-complexes is the displacement of the ^{31}P $\{^1H\}$NMR chemical shifts upon coordination from the range of δ = −7.3 to −1.7 ppm in the free cationic ligands to δ = 29.7−48.8 ppm in the corresponding Au-complexes (see the Supporting Information). The combination of massive steric overcrowding with a significantly reduced σ-donor ability is presumably the reason why the reaction of **9ca** and **9cb** with $(Me_2S)AuCl$ is not clean, thus precluding the isolation of the corresponding Au-complexes in analytically pure form.

The solid-state structures of complexes **12**, **13**, **14**, and **17**, determined by X-ray diffraction analysis, are depicted in Figure 4. The measured Au1−P1 bond lengths for these complexes

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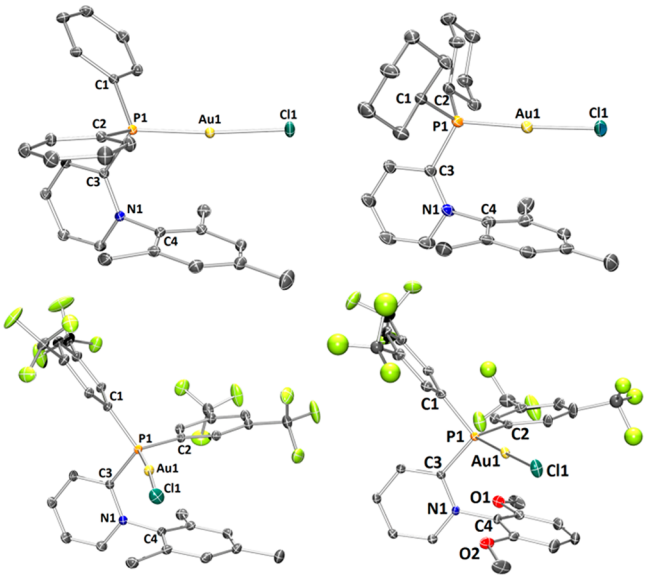
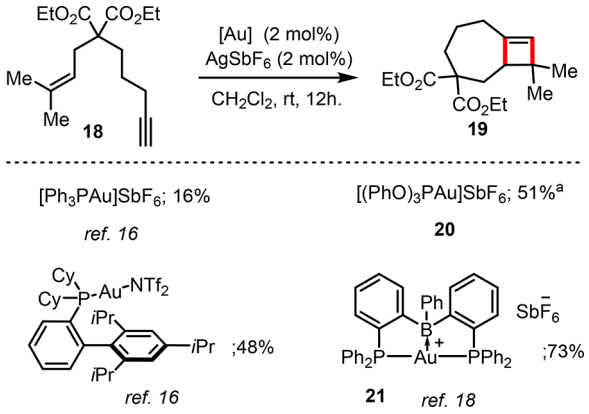


Figure 4. Crystal structures of **12**, **13**, **14**, and **17**. Hydrogen atoms and SbF_6 anions and solvent acetonitrile in the case of **14** were omitted for clarity; ellipsoids are set at 50% probability.[15]

vary from 2.12 to 2.23 Å, a slightly shorter range than that measured for the corresponding neutral analogues (P1−Au1, 2.22−2.30 Å).[3a] This is probably a consequence of the more internal electron pair at phosphorus in pyridiniophosphines, which imposes a shorter P1−Au1 distance to maximize orbital overlap. This agrees with the lower donor power of cationic phosphanes. Moreover, in all the structures measured a contact shorter than the sum of van der Waals radii (3.36 Å) is observed between the Au atom and the flanking aryl ring.[20] For **12** and **14**, it is the C_{ortho} closest to Au with distances of 3.136 and 3.177 Å respectively. In **13** the Au−C_{ipso} distance is the shortest, 3.149 Å, while in **17** the Au atom interacts preferentially with the oxygen atom of one of the methoxy-substituents (Au1−O2; 3.092 Å). In all cases the geometry of the P−Au−Cl fragment is slightly distorted from the expected linearity (P1−Au1−Cl1 angles: 172.8° in **12**; 176.8° in **13**; 176.0° in **14** and 177.2° in **17**). Most likely, this deviation originates from the steric requirements of the biaryl rest.

Catalysis. As a preliminary study to determine the relative electrophilicity of complexes **12**−**17** and test their potential as catalysts, we initially compared their performance in the [2 + 2] cycloaddition of 1,8-enyne **18** into cyclobutene **19**.[21,22] This benchmark reaction, originally reported by Gagosz, was chosen because the archetypical Au-catalyst, ($Ph_3PAu(SbF_6)$, 2 mol %) is only able to afford low conversion (16% yield); probably due to fast catalyst decomposition (Scheme 4). The use of XPhos as ancillary ligand under similar conditions improves the yield of **19** to 48% (24 h); very likely, the steric protection of the 2,4,6-tri(isopropylphenyl) flanking group and the stronger electron-donation of this ancillary ligand better safeguard the catalytic species from deactivation. On the other hand strong π-acceptor ligands such as phosphites also seem to be beneficial for this transformation. Compound **19** was obtained in 51% yield after only 90 min using 2 mol % of **20**, yet catalyst decomposition again prevented the reaction from proceeding to conclusion (Scheme 4). In terms of isolated yield of the desired product, the best catalytic system reported to date for this transformation is **21**, consisting of a monocationic Au center embedded in a robust chelating

Scheme 4. Ligand Effect on the Au-Catalyzed Cycloisomerization of 18 to Cyclobutene 19



[a]Reaction time, 90 min.

structure and further activated by an adjacent Lewis acidic borane.[23] Cyclobutene **19** was isolated in 73% yield employing 2 mol % of **21**; however, the reaction time needed to be prolonged for 12 h. All together, these experiments suggest that optimal results should be obtained by the use of a strong π-acceptor ancillary ligand, which additionally should be able to efficiently protect the active catalytic species from decomposition.

The conversion versus time plot for precatalysts **13**, **14**, **16**, SPhosAuCl, and **20** under otherwise identical conditions (2 mol % Au, r.t., CH_2Cl_2) is shown in Figure 5. All catalysts

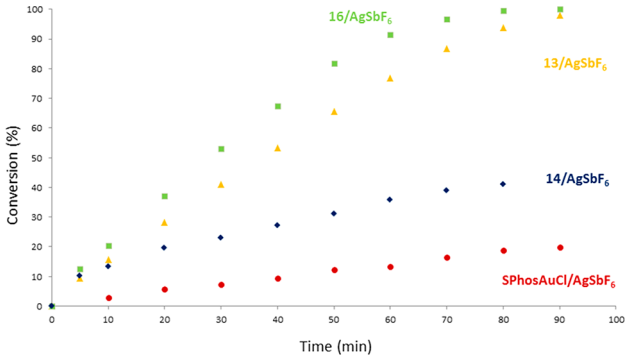


Figure 5. Ligand effect on the Au-catalyzed [2 + 2] cycloaddition of 1,8-enyne **18** into cyclobutene **19**. Conditions: **18** (0.1 M in CH_2Cl_2, 2 mol % [Au], 2 mol % $AgSbF_6$, r.t. Conversions determined by GC.

screened overtake the performance of SPhosAuCl, surely due to the augmented electrophilicity that they impart on the Au center. However, for precatalyst **14** the high initial activities decay after approximately 1 h, and only partial conversion into **19** is finally achieved. We speculate that for this system the protecting steric effect of the mesityl residue is not sufficient to compensate for the weakness of the P−Au bond. Note that the basicity of the P atom in **14** is significantly reduced because it bears three strongly electron-withdrawing groups: the pyridinium substituent and two 3,5-bis(trifluoromethyl)phenyl groups.

In contrast, catalysts **13** and **16**, both decorated with cyclohexyl substituents, exhibit excellent performance; their activities only seem to decay when no more substrate is available. In fact, after optimization of the reaction conditions,

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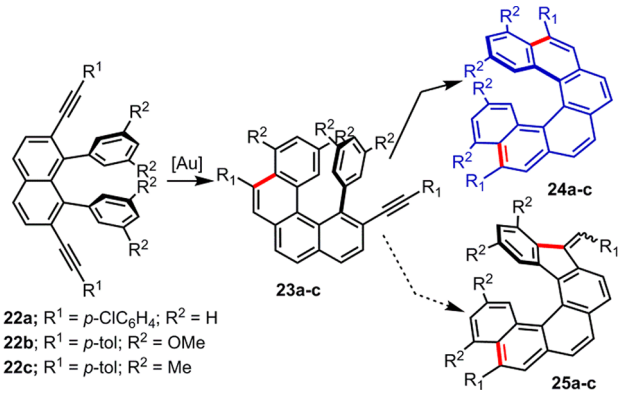
18 could be transformed into cyclobutene **19** (95% yield, 16 h) employing a catalyst loading of only 0.2 mol % of **16**.

Encouraged by this result, pyridiniophosphines were additionally screened in a more complex scenario. Our group has recently reported the enantioselective synthesis of [6]helicenes via double 6-*endo*-dig hydroarylation of appropriate diynes **22**.[6a,b] In order to obtain the desired reactivity, strong Lewis acidity at the metal is again required;[24] additionally, catalytic loadings of up to 10 mol % are necessary to ensure complete conversion of the starting material.[6a,b] Hence, we considered it interesting to test the performance of precatalysts **13**−**17** on this particular cycloisomerization.

The first set of results collected is shown in Table 2 (entries 1−7); a fixed catalyst loading of 5 mol % was employed. At

Table 2. Ligand Effect in the Synthesis of [6]Helicenes[a]



entry	subst.	catalyst (mol %)	yields (%)[b]	ratio **23:24:25**[c]
1	**22a**	Ph_3PAuCl (5)	49	59:22:19
2	**22a**	SPhosAuCl (5)	10	100:0:0
3	**22a**	$(PhO)_3PAuCl$ (5)	>95	1:65:34
4	**22a**	**13** (5)	>95	0:83:17
5	**22a**	**14** (5)	>95	0:31:69
6	**22a**	**16** (5)	>95	0:67:33
7	**22a**	**17** (5)	>95	0:45:55
8[d]	**22a**	**13** (2)	>95	0:83:17
9[e]	**22b**	**13** (1.5)	91[f]	0:100:0
10[e]	**22c**	**13** (1.5)	93[f]	0:100:0

[a]Reactions were carried out in CH_2Cl_2 at r.t. and quenched after 45 min. [b]Combined yields of the mixture of **23a**, **24a** and **25a**. [c]Determined by ^1H NMR and/or HPLC. [d]1 h. [e]2 h for **24b** and 6 h for **24c**. [f]Isolated yield.

first sight, it can be appreciated that the SPhos or even Ph_3P ligands are too basic for this transformation; the reactions proceed slowly and tetrahelicene **23a**, the intermediate where only one of the two alkynes has been hydroarylated, accumulates. This is not surprising because the second cyclization is believed to be the rate-determining step of the complete process. Catalysts **14** and **17**, both bearing a pyridinium group and two bis(trifluoromethyl)phenyl substituents attached to the phosphorus center were subsequently tested. Both displayed exceedingly higher reactivities; after only 45 min the initial substrate has disappeared. It is of note, however, that low selectivity toward the formation of the desired [6]helicene is observed, as in this case fulvene **25a**, the product of one 5-*exo*-dig and one 6-*endo*-dig cyclization is the main compound obtained (Table 2, entries 5 and 7).

A much better balance between reactivity and selectivity is obtained with catalyst **13**. Complete conversion of **22a** was observed with a good 83:17 ratio favoring helicene **24a** (Table 2, entry 4). Moreover, the catalytic activity of the active gold species decays slowly, and accordingly, the catalyst loading could be reduced to 2 mol % with identical results (Table 2, entry 8). Further reduction of the catalyst loading to 1.5 mol % is still possible for more reactive substrates. These conditions suffice to transform **22b** and **22c** into [6]helicenes **24b** and **24c**, respectively, with excellent yields and complete *endo* selectivity. The X-ray structure of **24b** is depicted in Figure 6.

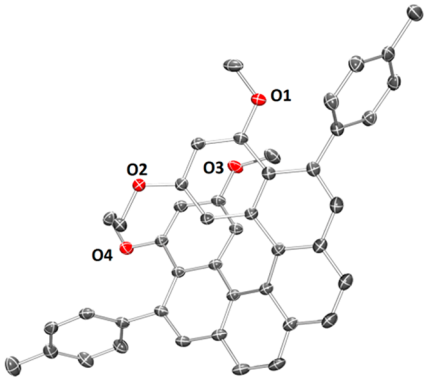


Figure 6. Crystal structure of **24b**. Hydrogen atoms were omitted for clarity; ellipsoids are set at 50% probability.[15]

These results additionally demonstrate the beneficial effects provided in Au-catalysis by the use of ancillary ligands able to combine a Buchwald-type structure with Lewis acidity at the P atom.

CONCLUSIONS

In summary, we report an efficient method for the preparation of *N*-arylpyridiniophosphines of different structures and the corresponding Au-derived complexes. Our experiments suggest exceptional electrophilicity at the Au center and importantly, much longer survival of the actual catalytic species if compared with those derived from *N*-alkylpyridinio phosphines.[10] This has been used to improve yields and significantly reduce the catalyst loadings in the chosen model transformations. We suspect that a potentially large number of Au-catalyzed transformations might benefit from the use of the ligands herein described. Ongoing research in our group targets this challenging field, as well as the application of *N*-arylpyridinio phosphines in processes catalyzed by other metals.[25]

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acscatal.8b03271.

Experimental, synthesis of new compounds, and analytical data (PDF)
X-ray data for **24b** (CIF)
X-ray data for **9aa** (CIF)
X-ray data for **9ab** (CIF)
X-ray data for **9ac** (CIF)
X-ray data for **9ba** (CIF)
X-ray data for **9cb** (CIF)
X-ray data for **11** (CIF)
X-ray data for **12** (CIF)
X-ray data for **13** (CIF)
X-ray data for **14** (CIF)

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X-ray data for **17** (CIF)

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Notes

The authors declare no competing financial interest.

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REFERENCES

(1) (a) Surry, D. S.; Buchwald, S. L. Biaryl Phosphane Ligands in Palladium-Catalyzed Amination. *Angew. Chem., Int. Ed.* **2008**, *47*, 6338−6361. (b) Martin, R.; Buchwald, S. L. Palladium-Catalyzed Suzuki−Miyaura Cross-Coupling Reactions Employing Dialkylbiaryl Phosphine Ligands. *Acc. Chem. Res.* **2008**, *41*, 1461−1473. (c) Barder, T. E.; Biscoe, M. R.; Buchwald, S. L. Structural Insights into Active Catalyst Structures and Oxidative Addition to (Biaryl)phosphine−Palladium Complexes via Density Functional Theory and Experimental Studies. *Organometallics* **2007**, *26*, 2183−2192.

(2) (a) Nieto-Oberhuber, C.; López, S.; Echavarren, A. M. Intramolecular [4 + 2] Cycloadditions of 1,3-Enynes or Arylalkynes with Alkenes with Highly Reactive Cationic Phosphine Au(I) Complexes. *J. Am. Chem. Soc.* **2005**, *127*, 6178−6179. (b) Nieto-Oberhuber, C.; López, S.; Muñoz, M. P.; Cárdenas, D.; Buñuel, E.; Nevado, C.; Echavarren, A. M. Divergent Mechanisms for the Skeletal Rearrangement and [2 + 2] Cycloaddition of Enynes Catalyzed by Gold. *Angew. Chem., Int. Ed.* **2005**, *44*, 6146−6148.

(3) (a) Hashmi, A. S. K.; Bechem, B.; Loos, A.; Hamzic, M.; Rominger, F.; Rabaa, H. Gold Catalysis: Biarylphosphine Ligands as Key for the Synthesis of Dihydroisocoumarins. *Aust. J. Chem.* **2014**, *67*, 481−499. (b) Wang, W.; Hammond, G. B.; Xu, B. Ligand Effects and Ligand Design in Homogeneous Gold(I) Catalysis. *J. Am. Chem. Soc.* **2012**, *134*, 5697−5705. (c) Li, Q. S.; Wan, C. Q.; Zou, R. Y.; Xu, F. B.; Song, H. B.; Wan, X. J.; Zhang, Z. Z. Gold(I) η^2-Arene Complexes. *Inorg. Chem.* **2006**, *45*, 1888−1890. (d) Pérez-Galán, P.; Delpont, N.; Herrero-Gómez, E.; Maseras, F.; Echavarren, A. M. Metal-Arene Interactions in Dialkylbiarylphosphane Complexes of Copper, Silver and Gold. *Chem. - Eur. J.* **2010**, *16*, 5324−5332.

(4) (a) Ferrer, S.; Echavarren, A. M. Role of σ,π-Digold(I) Alkyne Complexes in Reactions of Enynes. *Organometallics* **2018**, *37*, 781−786. (b) Homs, A.; Obradors, C.; Leboeuf, D.; Echavarren, A. M. Dissecting Anion Effects in Gold(I)-Catalyzed Intermolecular Cycloadditions. *Adv. Synth. Catal.* **2014**, *356*, 221−228. (c) Simonneau, A.; Jaroschik, F.; Lesage, D.; Karanik, M.; Guillot, R.; Malacria, M.; Tabet, J. C.; Goddard, J. P.; Fensterbank, L.; Gandon, V.; Gimbert, Y. Tracking gold acetylides in gold(I)-catalyzed cycloisomerization reactions of enynes. *Chem. Sci.* **2011**, *2*, 2417−2422.

(5) (a) Alcarazo, M. Synthesis, Structure, and Applications of α-Cationic Phosphines. *Acc. Chem. Res.* **2016**, *49*, 1797−1805. (b) Alcarazo, M. α-Cationic Phosphines: Synthesis and Applications. *Chem. - Eur. J.* **2014**, *20*, 7868−7877.

(6) (a) Nicholls, L. D. M.; Marx, M.; Hartung, T.; González-Fernández, E.; Golz, C.; Alcarazo, M. TADDOL-Derived Cationic Phosphonites: Toward an Effective Enantioselective Synthesis of [6]Helicenes via Au-Catalyzed Alkyne Hydroarylation. *ACS Catal.* **2018**, *8*, 6079−6085. (b) González-Fernández, E.; Nicholls, L. D. M.; Schaaf, L. D.; Farès, C.; Lehmann, C. W.; Alcarazo, M. Enantioselective Synthesis of [6]Carbohelicenes. *J. Am. Chem. Soc.* **2017**, *139*, 1428−1431. (c) Haldón, E.; Kozma, Á.; Tinnermann, H.; Gu, L.; Goddard, R.; Alcarazo, M. Synthesis and reactivity of α-cationic phosphines: the effect of imidazolinium and amidinium substituents. *Dalton Trans* **2016**, *45*, 1872−1876. (d) Carreras, J.; Gopakumar, G.; Gu, L.; Gimeno, A. M.; Linowski, P.; Petuškova, J.; Thiel, W.; Alcarazo, M. Polycationic Ligands in Gold Catalysis: Synthesis and Applications of Extremely π-Acidic Catalysts. *J. Am. Chem. Soc.* **2013**, *135*, 18815−18823. (e) Petuškova, J.; Bruns, H.; Alcarazo, M. Cyclopropenylylidene-Stabilized Diaryl and Dialkyl Phosphenium Cations: Applications in Homogeneous Gold Catalysis. *Angew. Chem., Int. Ed.* **2011**, *50*, 3799−3802.

(7) (a) Dube, J. W.; Zheng, Y.; Thiel, W.; Alcarazo, M. α-Cationic Arsines: Synthesis, Structure, Reactivity, and Applications. *J. Am. Chem. Soc.* **2016**, *138*, 6869−6877. (b) Carreras, J.; Patil, M.; Thiel, W.; Alcarazo, M. Exploiting the π-Acceptor Properties of Carbene-Stabilized Phosphorus Centered Trications $[L_3P]^{3+}$: Applications in Pt(II) Catalysis. *J. Am. Chem. Soc.* **2012**, *134*, 16753−16758.

(8) Gu, L.; Wolf, L. M.; Zieliński, A.; Thiel, W.; Alcarazo, M. α-Dicationic Chelating Phosphines: Synthesis and Application to the Hydroarylation of Dienes. *J. Am. Chem. Soc.* **2017**, *139*, 4948−4953.

(9) For an additional theoretical analysis, see: García-Rodeja, Y.; Fernández, I. Understanding the Effect of α-Cationic Phosphines and Group 15 Analogues on π-Acid Catalysis. *Organometallics* **2017**, *36*, 460−466.

(10) (a) Marset, X.; Khoshnood, A.; Sotorríos, L.; Gómez-Bengoa, E.; Alonso, D. A.; Ramón, D. J. Deep Eutectic Solvent Compatible Metallic Catalysts: Cationic Pyridiniophosphine Ligands in Palladium Catalyzed Cross-Coupling Reactions. *ChemCatChem* **2017**, *9*, 1269−1275. (b) Tinnermann, H.; Wille, C.; Alcarazo, M. Synthesis, Structure, and Applications of Pyridiniophosphines. *Angew. Chem., Int. Ed.* **2014**, *53*, 8732−8736.

(11) Lv, X.; Bao, W. A β-Keto Ester as a Novel, Efficient, and Versatile Ligand for Copper(I)-Catalyzed C−N, C−O, and C−S Coupling Reactions. *J. Org. Chem.* **2007**, *72*, 3863−3867.

(12) Zincke, T.; Heuser, G.; Moller, T. Über Dinitrophenylpyridiniumchlorid und dessen Umwandlungsprodukte. *Liebigs Ann.* **1904**, *333*, 296−345.

(13) Fürstner, A.; Seidel, G.; Kremzow, D.; Lehmann, C. W. Preparation of Metal−Imidazolidin-2-ylidene Complexes by Oxidative Addition. *Organometallics* **2003**, *22*, 907−909.

(14) (a) Falivene, L.; Credendino, R.; Poater, A.; Petta, A.; Serra, L.; Oliva, R.; Scarano, V.; Cavallo, L. SambVca ^{2}. A Web Tool for Analyzing Catalytic Pockets with Topographic Steric Maps. *Organometallics* **2016**, *35*, 2286−2293. (b) Clavier, H.; Nolan, S. P. Percent Buried Volume for Phosphine and N-heterocyclic Carbene Ligands: Steric Properties in Organometallic Chemistry. *Chem. Commun.* **2010**, *46*, 841−861.

(15) CCDC 1860878 (**24b**), 1862282 (**9aa**), 1862283 (**9ab**), 1862284 (**9ac**), 1862285 (**9ba**), 1862286 (**9cb**), 1862336 (**11**), 1862287 (**12**), 1862288 (**13**), 1862289 (**14**), 1862290 (**17**) contain the supplementary crystallographic data for this paper. This information can be obtained free of charge from The Cambridge Crystallographic data centre via www.ccdc.cam.ac.uk/data_request/cif.

(16) (a) Chianese, A. R.; Li, X.; Janzen, M. C.; Faller, J. W.; Crabtree, R. H. Rhodium and Iridium Complexes of N-Heterocyclic Carbenes via Transmetalation: Structure and Dynamics. *Organometallics* **2003**, *22*, 1663−1667. (b) Kelly, R. A., III; Clavier, H.; Giudice, S.; Scott, N. M.; Stevens, E. D.; Bordner, J.; Samardjiev, I.; Hoff, C. D.; Cavallo, L.; Nolan, S. P. Determination of N-Heterocyclic Carbene (NHC) Steric and Electronic Parameters using the [(NHC)Ir(CO)$_2$Cl] System. *Organometallics* **2008**, *27*, 202−210.

(17) Diebolt, O.; Fortman, G. C.; Clavier, H.; Slawin, A. M. Z.; Escudero-Adán, E. C.; Benet-Buchholz, J.; Nolan, S. P. Steric and Electronic Parameters Characterizing Bulky and Electron-Rich Dialkylbiarylphosphines. *Organometallics* **2011**, *30*, 1668−1676.

(18) See the Supplementary Information of: Mézailles, N.; Ricard, L.; Gagosz, F. Phosphine Gold(I) Bis-(trifluoromethanesulfonyl)-imidate Complexes as New Highly Efficient and Air-Stable Catalysts for the Cycloisomerization of Enynes. *Org. Lett.* **2005**, *7*, 4133−4136.

DOI: 10.1021/acscatal.8b03271
ACS Catal. 2018, 8, 10457−10463

(19) (a) Malhotra, D.; Mashuta, M. S.; Hammond, G. B.; Xu, B. A Highly Efficient and Broadly Applicable Cationic Gold Catalyst. *Angew. Chem., Int. Ed.* **2014**, *53*, 4456−4459. (b) Ebule, R.; Liang, S.; Hammond, G. B.; Xu, B. Chloride-Tolerant Gold(I)-Catalyzed Regioselective Hydrochlorination of Alkynes. *ACS Catal.* **2017**, *7*, 6798−6801.
(20) Bondi, A. van der Waals Volumes and Radii. *J. Phys. Chem.* **1964**, *68*, 441−451.
(21) Odabachian, Y.; Gagosz, F. Cyclobutenes as Isolable Intermediates in the Gold(I)-Catalysed Cycloisomerisation of 1,8-Enynes. *Adv. Synth. Catal.* **2009**, *351*, 379−386.
(22) (a) Grirrane, A.; García, H.; Corma, A.; Álvarez, E. Intermolecular [2 + 2] Cycloaddition of Alkyne-Alkene Catalyzed by Au(I) Complexes. What Are the Catalytic Sites Involved? *ACS Catal.* **2011**, *1*, 1647−1653. (b) López-Carrillo, V.; Echavarren, A. M. Gold(I)-Catalyzed Intermolecular [2 + 2] Cycloaddition of Alkynes with Alkenes. *J. Am. Chem. Soc.* **2010**, *132*, 9292−9294.
(23) Inagaki, F.; Matsumoto, C.; Okada, Y.; Maruyama, N.; Mukai, C. Air-Stable Cationic Gold(I) Catalyst Featuring a Z-Type Ligand: Promoting Enyne Cyclizations. *Angew. Chem., Int. Ed.* **2015**, *54*, 818−822.
(24) Mehler, G.; Linowski, P.; Carreras, J.; Zanardi, A.; Dube, J. W.; Alcarazo, M. Bis(cyclopropenium)phosphines: Synthesis, Reactivity, and Applications. *Chem. - Eur. J.* **2016**, *22*, 15320−15327.
(25) Hicks, J. D.; Hyde, A. M.; Cuezva, A. M.; Buchwald, S. L. Pd-Catalyzed N-Arylation of Secondary Acyclic Amides: Catalyst Development, Scope, and Computational Study. *J. Am. Chem. Soc.* **2009**, *131*, 16720−16734.

DOI: 10.1021/acscatal.8b03271
ACS Catal. 2018, 8, 10457−10463