Homogeneous Catalysis

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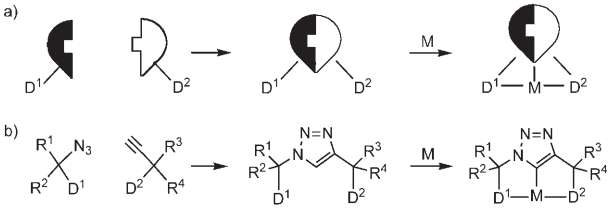
Pincer Click Ligands**

*Elaine M. Schuster, Mark Botoshansky, and Mark Gandelman**

Tridentate pincer-type ligands of the general form D^1CD^2 (where D^1 and D^2 are groups containing coordinating atoms) have been used to spectacular effect in coordination, mechanistic, synthetic, and supramolecular chemistry, as well as in nanoscience and in the development of sensors and molecular switches.[1] Most significantly, the realization that pincer ligands offer both a unique, highly protective environment for the coordinated metal center and opportunities to fine-tune the steric and electronic properties of the metal atom has generated extensive research into the use of these complexes as catalysts.[2] As a result, many important and challenging catalytic processes based on such systems have been developed. It is generally accepted that the reactivity, selectivity, and catalytic performance of pincer-based systems rely to a great extent on the characteristics of the donor groups D in the carefully selected ligand. The optimization of tailor-made catalysts involves extensive experimental investigation, in which the laborious synthesis of the ligands is often a serious bottleneck. In particular, the synthesis of nonsymmetrically substituted D^1CD^2 ligands (D^1 and D^2 are different groups) represents a considerable challenge, as their preparation usually includes a series of steps and separations that commonly result in low yields.[3]

Consequently, the development of efficient and powerful methods for the rapid synthesis of a wide variety of tailor-made ligands is of high importance. Although several methods for the preparation of bidentate ligand libraries have been reported,[4] a strategy for the building of a tridentate ligand library is, to the best of our knowledge, still unknown. Here, we report a conceptually new general approach for the efficient and facile preparation of a novel family of tridentate pincer ligands of the D^1CD^2 type. The tridentate mode of coordination was shown by the preparation and structural characterization of transition-metal complexes of these new ligands. Palladium complexes of this readily prepared set of representative ligands proved to be highly efficient catalysts in the Heck reaction.

Traditionally, pincer ligands are prepared by attaching donor atoms to a ligand backbone. We developed an entirely different synthetic route that allowed access to a broad range of tailor-made pincer ligands. In designing our approach, we considered a methodology which would allow the selective and facile incorporation of two complementary monomeric donor groups D^1 and D^2 by covalent assembly to afford a pincer-type system D^1CD^2. The resulting molecule must also have a potential carbanion between the donor groups so as to bind the metal center in a pincer-type mode (Scheme 1a).



Scheme 1. General approach to pincer click ligands.

We anticipated that the Huisgen dipolar cycloaddition of azides and alkynes to yield triazoles could be ideal for this purpose.[5] This reaction can be carried out under ambient conditions and with exclusive regioselectivity for the 1,4-disubstituted triazole product when mediated by catalytic amounts of Cu^I salts.[6] Coined the "click" reaction, it has found a wide variety of applications,[7] including the preparation of libraries of monophosphine and chiral phosphine ligands.[8] Our idea was to "click" two monomeric groups with coordinating atoms and functionalized with azidomethyl and propargyl units, respectively, under Sharpless conditions to provide a pincer-type ligand framework. The resulting triazole-based ligand possesses two coordinating "arms" in the 1,4-positions, and the relatively acidic C–H bond between them is suitable for directed insertion of a metal atom (Scheme 1b).

Importantly, in contrast to traditional synthetic methods, hetero-tridentate ligands (D^1CD^2) are selectively obtained in such an approach, since only this covalent assembly is possible under the conditions of the "click" reaction. Clearly, application of this "click" strategy to a separately prepared series of monodentate ligand units functionalized with azido and alkynyl groups, respectively, in a systematic combinatorial manner will result in a wide variety of triazole-based pincer ligands.

Thus, to evaluate the feasibility of our approach, a number of azido- and alkynyl-based monomers were prepared (Scheme 2). While some of these compounds are commercially available, the rest can be prepared in a simple manner by short synthetic protocols.[9] The syntheses of azide **1** and propynylphosphynes **3**[8b] are presented in Scheme 3.

To our delight, the prepared azido and alkynyl monomers smoothly undergo copper(I)-catalyzed [2+3] cycloaddition

[*] E. M. Schuster, Dr. M. Botoshansky, Dr. M. Gandelman
Schulich Faculty of Chemistry
Technion-Israel Institute of Technology
Technion City, Haifa 32000 (Israel)
Fax: (+972) 4-829-5703
E-mail: chmark@tx.technion.ac.il

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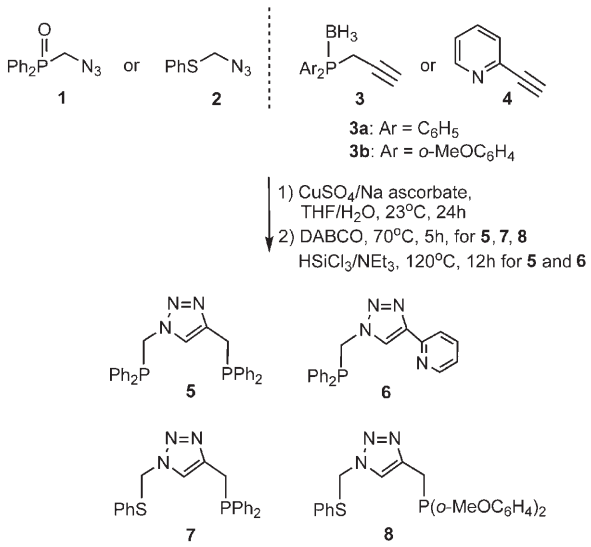
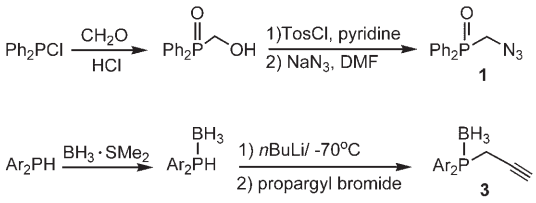


Scheme 2. Combinatorial synthesis of **5**–**8**.

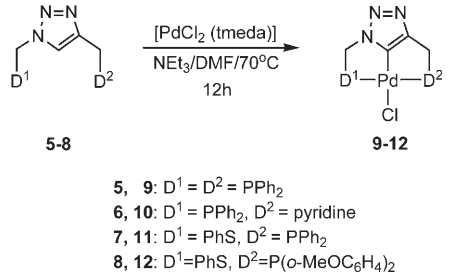


Scheme 3. Synthesis of **1** and **3**. Tos = toluene-4-sulfonyl.

reactions under "click" conditions. Representative examples of the ligands prepared by this approach are reported here, including PCP (phosphorus-phosphorus based, **5**), PCN (phosphorus-nitrogen based, **6**), and PCS (phosphorus-sulfur based, **7** and **8**) binding modes (Scheme 2). The typical reaction takes place in a THF/water solution without the need to exclude air, and results in full conversion of the starting materials into the protected ligands after stirring the reaction for 24 h at room temperature. Phosphines should be protected (for example, as the corresponding borane complexes or as oxides) to prevent an undesirable Staudinger reaction with the azides in the "click" reaction. A final deprotection of the phosphine group by 1,4-diazabicyclo[2.2.2]octane (DABCO) in the case of the borane complex[10] or reduction with trichlorosilane in the case of the phosphine oxide[11] results in the corresponding pincer click ligands (PCLs) in an overall yield of up to 80%.

In our opinion, this unprecedented approach to assembly of the pincer ligands has numerous important advantages. The use of the Sharpless "click" conditions ensure operationally simple and reliable reaction protocols, broad functional group tolerance, high yields, and easy purification of the products. In addition, our approach allows the selective straightforward synthesis of tailor-made hetero-tridentate ligands of the type D^1CD^2 exclusively, and the donor sites D^1 and D^2 can be easily varied. Moreover, the triazole unit in the backbone of the ligand offers an interesting alternative to the traditional phenyl-based framework: it might be further functionalized or additional metal ions could be coordinated to the nitrogen atom after the creation of the pincer complex.[12]

Most importantly, the new PCLs demonstrate typical tridentate coordination upon reaction with late-transition metals. From spectroscopic considerations, PCP ligand **5** was initially examined. When a solution of **5** in DMF was added to $[PdCl_2(tmeda)]$ (tmeda = tetramethylethylenediamine) in a 1:1 ratio, the gradual development of a deep orange color was observed at 70 °C. ^{31}P NMR spectroscopic analysis shows complete and selective conversion of the starting ligand into the desired PCP-Pd complex **9** after 12 h (Scheme 4).



Scheme 4. Synthesis of complexes **9**–**12**.

This complex was characterized in solution by multinuclear NMR techniques. The ^{31}P NMR spectrum of **9** shows two doublets at $\delta = 33.1$ and 23.4 ppm, with a typical *trans*-phosphorus–phosphorus coupling constant of $J = 462.0$ Hz. The *ipso* carbon atom gives rise to a broad signal centered at $\delta = 163.0$ ppm in the ^{13}C NMR spectrum, thus indicating a carbon–metal bond.

The molecular structure of complex **9** was confirmed by X-ray analysis.[13] Yellow crystals of **9** suitable for single-crystal X-ray analysis were obtained by slow diffusion of diethyl ether into a solution of the complex in dichloromethane. The palladium atom is located at the center of a distorted square-planar structure, with the chloride group occupying a position *trans* to the carbon atom of the triazole ring (Figure 1). The two phosphine groups are located in mutual *trans* positions, with a P-Pd-P angle of 157.02.

The PCLs **6**–**8** exhibit similar reactivities as ligand **5** with $[PdCl_2(tmeda)]$ under the same reaction conditions, and give rise to the smooth formation of complexes **10**–**12** (Scheme 4). All complexes were fully characterized by spectroscopic techniques.[9]

The facile combinatorial access to a novel family of pincer click ligands and their corresponding metal complexes opens the way to the rapid and convenient screening of these systems in various catalytic transformations. With numerous PCL-based palladium complexes in hand, we performed preliminary studies to examine the influence of the ligand on catalytic activity in the Heck reaction. This carbon–carbon bond-forming reaction between aryl halides and alkenes in the presence of a base has found broad applications in synthetic chemistry.[14] Recently, several pincer-based palladium systems have proven to be highly efficient catalysts in the Heck reaction,[1,2] and as such the reaction serves as a "benchmark" for the evaluation of the activity of new pincer-

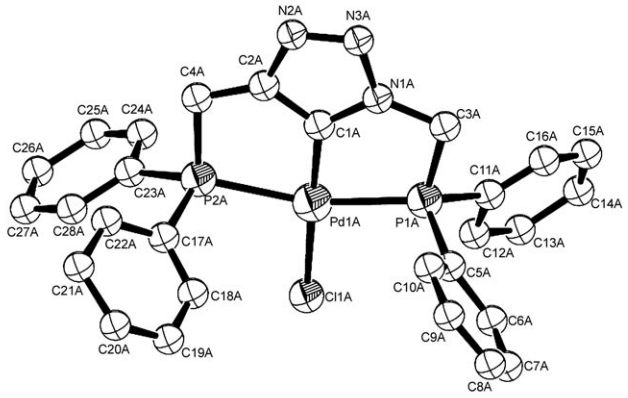
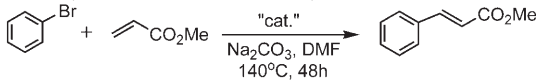


Figure 1. Perspective view of a molecule of **9**. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] and angles [°]: Pd1A-C1A 1.920(17), Pd1A-P1A 2.310(5), Pd1A-P2A 2.343(6), Pd1A-Cl1A 2.354(4), P1A-Pd1A-P2A 157.02(18), C1A-Pd1A-Cl1A 177.8(5).

type systems. There is a continuing search for more stable, efficient, and generally applicable catalysts as well as for simpler methods for their preparation.

In a typical experiment to compare the catalytic performance of complexes **9**–**12**, 6 mmol of methyl acrylate was added to 5 mmol of bromobenzene in dimethylformamide, followed by the addition of an equimolar amount of sodium carbonate (Table 1). The catalyst was added in amounts as

Table 1: Catalysis of the Heck reaction by **9**–**12**.[a]



Catalyst[b]	Yield [%]	TON
9	94	134 000
10	88	125 000
11	29	42 000
12	5	6900

[a] All reactions were carried out with 5 mmol of bromobenzene and 6 mmol of methyl acrylate. [b] Loading of 3.5×10^{-5} mmol of the complex (7×10^{-4} mol%).

low as 7×10^{-4} mol% and the resulting mixture was stirred at 140 °C, while the progression of the reaction was monitored by gas chromatography. Importantly, commercially available reagents and solvents were used without further purification, and complexes **9**–**12** are air stable. Our preliminary screening of the prepared pincer click ligands reveals that the PCN (**10**) and PCP (**9**) systems are incredibly efficient catalysts for the Heck reaction. Interestingly, from the yield and conversion, PCP complex **9** is among the most active and efficient catalysts for the Heck coupling with aryl bromides. Catalyst **9** mediates the reaction of bromobenzene with methyl acrylate to give the product in 94% yield and an observed turnover number (TON) of 134 000 after 48 h.

The substantially lower activity of the PCS systems (**11** and **12**) in the Heck reaction, as compared to **9** and **10**, is interesting in view of reported results obtained with analogous complexes having a phenyl backbone: PCP-based palladium complexes are highly active in the reaction of bromobenzene with methyl acrilate (TON of 132 900 after 63 h and 93% yield),[15a] while the SCS-Pd complex is ineffective with aryl bromides.[15b] As such, while a palladium center in the SCS frame is, likely, not sufficiently electron rich to insert into the C–Br bond of bromobenzene, our PCS systems are hybrids of the PCP and SCS counterparts. Instability of the PCS complexes **9** and **10** can probably be ruled out, as the same turnover frequencies (TOF = TON/time) are observed for these catalysts after 24 and 48 h. Further synthetic and mechanistic studies are required for a deeper understanding of these results.

In summary, we have developed a conceptually new approach to the synthesis of a novel, diverse family of pincer-type tridentate ligands. The use of "click chemistry" was found to be highly advantageous for the combinatorial synthesis of nontrivial ligands from relatively simple building blocks. Our PCL strategy allows the efficient preparation and screening of a broad range of organometallic catalysts for a variety of synthetic applications. This highly selective, rapid synthetic strategy provides not only a broad range of new pincer-type ligands, but also well-defined transition-metal-based catalysts. These advantages are exemplified here by the discovery of an air- and thermally stable triazole-based PCP–palladium complex **9**, which exhibits extremely high catalytic efficiency in the Heck reaction. Further applications of the PCL approach to other transformations catalyzed by organometallic reagents, including asymmetric catalysis, are currently underway.

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