Cyclopropenylidene Carbene Ligands in Palladium C−N Coupling Catalysis

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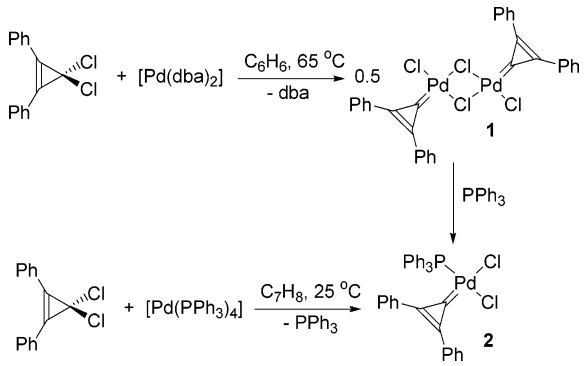
Summary: Palladium complexes supported by a 2,3-diphenylcyclopropenylidene carbene ligand are efficient and robust catalysts for C−N coupling reactions.

Palladium-catalyzed C−N bond formation has developed into a versatile way of producing aryl amines from aryl halides,[1] probably the best known methodology being the Buchwald−Hartwig amination reaction, which makes use of palladium complexes supported by strong σ-donor phosphine or N-heterocyclic carbene (NHC) ligands.[2] Recently, we became aware of the earlier suggestion[3,4] that the cyclopropenylidene carbene ligand can function as an extremely strong σ donor and poor π acceptor, and this led us to explore the use of palladium cyclopropenylidene complexes as catalysts for C−C coupling reactions.[5] Our findings, that such complexes are indeed highly active and efficient catalysts in the case of Heck and Suzuki reactions, have encouraged us to begin to explore their use in C−N coupling, and in this communication we report our promising initial findings.

Previous routes to palladium cyclopropenylidene complexes have relied on oxidative addition of 1,1-dichloro-2,3-diphenylcyclopropene to palladium black over extended periods at elevated temperature.[6] In our hands, this route led to capricious results, and more reliable synthesis is achieved using well-defined soluble Pd(0) sources, with the added advantage of reduced reaction times. In this way, the chloro-bridged dimeric complex **1** may be synthesized in 68% yield by oxidative addition of 1,1-dichloro-2,3-diphenylcyclopropene to [Pd(dba)$_2$] (dba = dibenzylideneacetone) over 15 h at 65 °C (Scheme 1).

Scheme 1. Synthesis of Palladium Cyclopropenylidene Complexes



Addition of a monomeric phosphine rapidly splits this dimer to produce monomeric complexes. For example, addition of PPh_3 rapidly forms complex **2**, which may also be synthesized by our previously reported route using [Pd(PPh$_3$)$_4$] as the Pd(0) source.[5] These complexes show excellent stability; for example, **2** is indefinitely stable in air at room temperature and is thermally robust in the solid state to ca. 200 °C. The reason for this stability is likely to lie in the possibility of a contribution from a resonance form in which a two-π-electron aromatic cationic cyclopropenium moiety is formed (Figure 1).

Catalytic reactions were performed under previously reported standard conditions;[7] results for complex **2** with a range of substrates are presented in Table 1. Conversion is moderate to good across a variety of activated and unactivated aryl bromides with morpholine (runs 1−6). At lower temperature, yields are reduced but some conversion is observed even at 25 °C (compare runs 1−3). Bulkier primary aryl amines (runs 7 and 8) and secondary amines (runs 9 and 10) are also efficiently coupled.

Complex **1** was screened with a more focused range of aryl halides and amines; the effect of adding phosphines to produce **2** and related complexes in situ was also investigated.[8] Some activity is seen for all derivatives with aryl bromides. It can also be seen that similar results are obtained if complexes are isolated or formed in situ (compare Table 1, run 1, and Table 2, run 2), suggesting that the same catalytically active species is formed. In general, improved results are observed as more basic phosphine ancillary ligands are used, so that with alkyl phosphines the amination of aryl chlorides is also successful with excellent conversion (runs 9−11). With these systems,

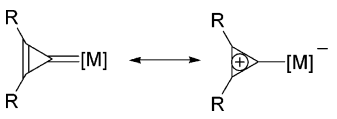


Figure 1. Resonance stabilization of cyclopropenylidene ligands.

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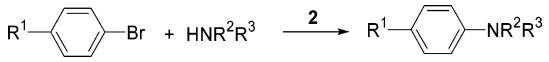
Table 1. Catalysis Data for Complex 2



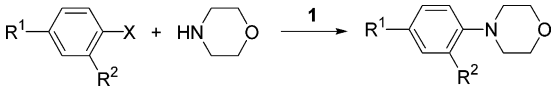
run[a]	R^1	R^2, R^3	yield[b]/%
1	CF_3	$-CH_2CH_2OCH_2CH_2-$	63
2[c]	CF_3	$-CH_2CH_2OCH_2CH_2-$	39
3[d]	CF_3	$-CH_2CH_2OCH_2CH_2-$	11
4	H	$-CH_2CH_2OCH_2CH_2-$	64
5	Me	$-CH_2CH_2OCH_2CH_2-$	50
6	OMe	$-CH_2CH_2OCH_2CH_2-$	23
7	CF_3	H, 2-C_6H_4(Me)	20
8	CF_3	H, 2,4,6-$C_6H_2(Me)_3$	51
9	CF_3	C_6H_5, C_6H_5	100
10	CF_3	C_6H_5, CH_3	45

[a] Conditions unless stated otherwise: 1.0 mmol of aryl bromide, 1.2 mmol of amine, 1.4 mmol of NaO^{t}Bu, 2.0 mol % Pd, 8 ml toluene, 100 °C, 18 h. [b] Determined by integration of ^{1}H NMR peaks vs mesitylene standard. [c] 50 °C. [d] 25 °C.

even deactivated and ortho-substituted aryl chlorides are aminated in excellent yields. To ensure that the cyclopropenylidene ligand is playing a crucial role, we tested a carbene-free complex containing only P^{t}Bu$_3$ donor ligands under identical conditions (runs 12 and 13); markedly inferior results were observed.[9]

A plot of percent conversion with time based on Table 2, run 2 (see the Supporting Information), reveals that complete conversion is achieved for a typical run within 3 h. It is also noteworthy that no induction period is observed, suggesting very rapid initiation. A similar observation is made for Heck and Suzuki coupling catalysis with these systems[5] and by Herrmann for cycloheptatrienylidene catalysts,[10] where good performance is attributed to the high thermal stability of the metal−carbene

Table 2. Catalysis Data for Complex 1



run[a]	phosphine	X, R^1, R^2	conversn[b] (yield)[c]/%
1	none	Br, CF_3, H	50 (30)
2	PPh_3	Br, CF_3, H	100 (62)
3	P(2-C_6H_4(Me))$_3$	Br, CF_3, H	100 (78)
4	PCy_3	Br, CF_3, H	100 (61)
5	P^{t}Bu$_3$	Br, CF_3, H	100 (89)
6	none	Cl, CF_3, H	0
7	PPh_3	Cl, CF_3, H	0
8	P(2-C_6H_4(Me))$_3$	Cl, CF_3, H	13 (3)
9	PCy_3	Cl, CF_3, H	100 (61)
10	P^{t}Bu$_3$	Cl, CF_3, H	100 (85)
11	P^{t}Bu$_3$	Cl, H, OMe	100 (97)
12[d]	P^{t}Bu$_3$	Cl, H, OMe	5 (3)
13[e]	P^{t}Bu$_3$	Cl, H, OMe	32 (30)

[a] Conditions unless stated otherwise: 1.0 mmol of aryl halide, 1.2 mmol of morpholine, 1.4 mmol of NaO^{t}Bu, 2.0 mol % Pd, 8 ml toluene, 100 °C, 18 h. [b] Determined by GC based on aryl halide. [c] Determined by GC vs authentic samples and confirmed by integration of ^{1}H NMR peaks vs mesitylene standard. Major side product when detected is ArH, in line with previous reports (see ref 7). [d] [Pd(PhCN)$_2$Cl$_2$] and 2 equiv of P^{t}Bu$_3$. [e] [Pd(PhCN)$_2$Cl$_2$] and 1 equiv of P^{t}Bu$_3$.

unit in their systems. We suggest the same rationale here, although the potential for electronic flexibility of the ligand between the illustrated resonance forms (Figure 1) depending on the requirements of catalytic intermediates may also be a factor.

In conclusion, our new cyclopropenylidene carbene catalysts show good activity for C−N coupling reactions. Work is underway to further modify this ligand type and fully map structure−property relationships for these and other palladium-catalyzed coupling reactions.

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Supporting Information Available: Text and figures giving experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) We note that a similar strategy with ortho-metalated phosphite catalysts has been reported. See: Bedford, R. B.; Blake, M. E. *Adv. Synth. Catal.* **2003**, *345*, 1107.

(9) However, in line with previous observations, 1 equiv of phosphine gives improved conversion compared to the case with 2 equiv. See: Hartwig, J. F.; Kawatsura, M.; Hauck, S. I.; Shaughnessy, K. H.; Alcazar-Roman, L. M. *J. Org. Chem.* **1999**, *64*, 5575.

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