Cross-Coupling of Aryl Halides and Triflates with Group 13-Metal Alkylating Reagents by Palladium–Molybdenum and Palladium–Tungsten Mixed-Metal Catalysts

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Received 27 June 2005

palladium-containing Abstract: The {MoPdcp[µclusters $(CO)_{2}$ [[μ_{3} -(CO)](PPh_{3})}, (1) and $\{PdWcp[\mu-(CO)_2][\mu_3 (CO)](PPh_3)_2$ (2) catalyze the cross-methylation and ethylation of aryl halides and triflates with the respective intramolecularly stabilized dialkylaluminum, gallium and indium reagents 3-7 at temperatures between 78 °C and 120 °C. Unlike the conventional mononuclear palladium catalysts, complexes 1 and 2 promote the coupling of aryl chlorides and show no signs of homocoupling or hydrogenolysis even when the alkylating moieties contain β -hydrogen atoms. The catalytic activity and selectivity of the mixed-metal clusters is attributed to synergism between the different metal nuclei of the catalysts.

Key words: cross-coupling, mixed-metal catalysts, palladium, molybdenum, tungsten

In the course of our studies on cross-coupling of aryl and vinyl halides with intramolecularly stabilized group 13metal alkylating reagents, we have shown that the mixedcomplexes $[(CO)_4Fe(\mu-PPh_2)Pd(\mu-Cl)]_2$ metal and $[(CO)_3Co](\mu$ -CO)Pd[μ -Ph₂PCH₂)]₂ are not only efficient and selective catalysts for the cross-alkylation of bromoand iodoarenes but, in contrast to the common conventional mononuclear palladium complexes, they affect also chloroarenes.¹ We have now found that some other palladium-containing heteronuclear clusters are equally efficient. We investigated two such complexes: (4Mo-Pd)(Pd–Pd)tetra- μ -carbonyldi- μ_3 -carbonylbis(η^5 -2,4-cyclopentadien-1-yl)bis[(triphenylphosphine)palladium]dimolybdenum (1) and (Pd-Pd)(4Pd-W)tetra-µ-carbonyldi- μ_3 -carbonylbis(η^5 -2,4-cyclopentadien-1-yl)bis[(triphenylphosphine)palladium]ditungsten (2).² These clusters proved even more stable, easier to handle and more selective than the aforementioned Pd-Fe and Pd-Co complexes. They, and some of their analogs, have already been shown to act as catalysts in various hydrogen-transfer reactions (alkene and alkyne hydrogenation, hydrosilation, hydroformylation and oligomerization),³ as well as in carbonylation of nitroarenes.⁴ Typically, when a solution of 1-bromonaphthalene (0.96 mmol) in anhydrous benzene is heated at reflux with [Me₂AlOCH₂CH₂NMe₂]₂ (3; 1.94

SYNTHESIS 2006, No. 1, pp 0111–0114 Advanced online publication: 16.12.2005

DOI: 10.1055/s-2005-921749; Art ID: Z12205SS

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mmol), PPh₃ (0.20 mmol) and **1** (0.05 mmol) for two hours followed by quenching with 5% hydrochloric acid, 98% of 1-methylnaphthalene is isolated. Further examples of cross-coupling reactions catalyzed by **1** as illustrated in Scheme 1 are summarized in Table 1. Similar experiments were conducted in the presence of cluster **2**. Representative results from this study are listed in Table 2.

ArX + $(R_2ML)_2$ (1) 1 or 2, PR'₃, C₆H₆, 78 °C (2) ag HCl Ar + MCl₃ + L'

Scheme 1 M = Al, Ga, In; $L = OCH_2CH_2NMe_2$; L' = ligand residue after hydrolysis; X = halogen or triflate group; R = alkyl group of reagents 3–7; R' = Ph or*t*-Bu

Tables 1 and 2 indicate a general resemblance between the activities of 1 and 2 although a few differences, such as the level of activation of 1-chloronaphthalene (entries 1 in both Tables) are remarkable. There are also some similarities to the mixed Pd-Fe and Pd-Co heteronuclear catalysts described in our previous paper,¹ but in sharp contrast, neither 1 nor 2 ever led to the formation of any hydrogenolysis products of the aryl halides. While bromoand iodoarenes, as well as aryl triflate, smoothly couple with 3 at 78 °C during a few hours, electron-neutral and electron-rich chloroarenes hardly react under these conditions but require a temperature of 120 °C (see Table 1, entries 1,6 and Table 2, entries 1 and 3). Chloroarenes with electron-attracting substituents react at 78 °C but require usually ≥ 20 hours for the completion of the process. The cross-coupling of aryl triflates depends on the structure of the aromatic skeleton; while naphthyl triflate reacts rather fast (e.g., Table 1, entry 5) derivatives of phenol react slowly even in the presence of electron-attracting substituents (see entries 15 in both Table 1 and Table 2).

The analogous gallium and indium compounds **5**–7 can successfully replace the aluminum-containing alkylating reagent **3**. With the exception of one case in which 4- $IC_6H_4CF_3$ is used as substrate (Table 2, entry 13) the cross-coupling with the gallium reagent takes place only slightly slower than with **3**. Alkylation with the indium reagents **6** and **7** proceeds equally well as, or even better than, the corresponding aluminum compounds, **3** and **4**

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 Table 1
 Cross-Alkylation of Some Aryl Halides and Triflates with 3–6 in the Presence of Catalyst 1^a

Entry	Substrate	Alkylating reagent	Phosphine	Reaction time (h)	Product	Yield (%) ^b
1	$1 - C_{10}H_7Cl$	3	$P(t-Bu)_3$	1 ^c	$1-C_{10}H_7Me$	21
2	$1-C_{10}H_7Br$	3	PPh ₃	2	$1-C_{10}H_7Me$	98
3	$1-C_{10}H_7Br$	5	PPh ₃	2	$1-C_{10}H_7Me$	86
4	$1 - C_{10}H_7I$	3	PPh ₃	1	$1-C_{10}H_7Me$	47
5	$2-C_{10}H_7OTf$	3	PPh ₃	2	$2-C_{10}H_7Me$	100 ^d
6	4-ClC ₆ H ₄ Me	3	$P(t-Bu)_3$	6 ^c	$1,4-C_{6}H_{4}Me_{2}$	43 ^e
7	4-ClC ₆ H ₄ CO ₂ Me	3	$P(t-Bu)_3$	20	4-MeC ₆ H ₄ CO ₂ Me	31
8	4-ClC ₆ H ₄ CF ₃	3	$P(t-Bu)_3^{f}$	20	4-MeC ₆ H ₄ CF ₃	43
9	$4-ClC_6H_4NO_2$	3	PPh ₃	20	4-MeC ₆ H ₄ NO ₂	99 ^d
10	$4-BrC_6H_4CH_3$	3	PPh ₃	2	$1,4-MeC_6H_4Me_2$	27
11	$4-BrC_6H_4CF_3$	3	PPh ₃	2	4-MeC ₆ H ₄ CF ₃	100 ^d
12	$4-BrC_6H_4CF_3$	5	PPh ₃	2	4-MeC ₆ H ₄ CF ₃	77
13	$4-BrC_6H_4CF_3$	6	PPh ₃	2	4-MeC ₆ H ₄ CF ₃	99 ^d
14	$4-IC_6H_4CF_3$	3	PPh ₃	1	4-MeC ₆ H ₄ CF ₃	89
15	4-TfOC ₆ H ₄ NO ₂	3	PPh ₃	1	4-MeC ₆ H ₄ NO ₂	25

^a Reaction conditions: substrate (0.96 mmol), alkylating reagent (1.94 mmol), **1** (0.05 mmol), PPh₃ (0.20 mmol), anhyd benzene (15 mL), 78 °C unless stated otherwise, N₂ atmosphere.

^b Unless stated otherwise, the figures refer to isolated yields and were the average of at least two experiments that did not differ by more than 5%. The missing percentage reflects on the unreacted substrates.

° At 120 °C.

^d Yields were determined by GC.

e Yield: 98% after 15 h.

^f In the presence of PPh₃ the yield was 24%.

(compare entries 11 and 13 in Table 1 and entries 9 and 10 in Table 2), and even the indium containing ethylation reagent 7 reacts at an unusually high rate. Both the nature of the solvent and the phosphine additive have a substantial effect on the cross-coupling with 3. For example, the relative initial rates of the formation of 1-methylnaphthalene from 1-bromonaphthalene and 3 in benzene, THF and nhexane are 1.0, 0.15 and 0.06, respectively. Although complexes 1 and 2 promote the reaction shown in Scheme 1 without additives, an increase in yield is observed upon addition of up to 4 mol of PPh₃ per each mol of the catalyst. Under the conditions of Table 2, 1-bromonaphthalene yields after one hour 20% of 1-methylnaphthalene in the absence of added phosphine, and 76% of the product when PPh_3 (0.20 mmol) is added. A similar effect was observed with catalyst **1**. Excess of PPh₃ acts, however, as an inhibitor. A 2:1 molar ratio of phosphine/ catalyst reduces the yield in experiment 2 of Table 2 to ca 10% and a 6:1 ratio completely stalls the reaction. The optimum phosphine/catalyst ratio was shown to be 1.4. We recall our observation that the cross-coupling catalyst $[(CO)_4Fe(\mu-PPh_2)Pd(\mu-Cl)]_2$ is best activated by a fivefold molar excess of PPh₃.¹ ¹H, ¹³C and ³¹P NMR measurements indicated that the addition of PPh₃ (as well as other tertiary phosphines) to 1 and 2 neither replace the cyclopentadienyl moieties nor do they exchange the existing PPh₃ ligands. Therefore, we assume that the phosphine replaces part of the carbonyl groups. Support in this assumption is found in the changes of the IR spectra of 1 and 2 upon heating with PPh₃. The strong v_{CO} bands of 1 at 1916, 1840 and 1784 cm⁻¹ (see refs.^{2,5}) form new peaks at 1890, 1852, 1828, 1788 and 1763 cm⁻¹ and those of complex 2 at 1916, 1846, 1820 and 1776 cm⁻¹ (see refs.^{2,5}) condense to three bands at 1859, 1795 and 1782 cm⁻¹. Because it is known that the triply bridged μ_3 -COs undergo facile exchange with different ligands⁶ we presume that they are replaced at the outset of the process. The addition of $P(t-Bu)_3$ to 1 and 2 usually causes a slight rate increase in the cross-coupling of the aryl bromides, -iodides and -triflates. It has however, a rather significant effect on the reaction of the electron-neutral and electron-rich chloroarenes that hardly react at all with PPh₃. Even the reaction rates of electron-poor aryl chlorides are approximately doubled when PPh_3 is replaced by $P(t-Bu)_3$ (see e.g., Table 1, entry 8, including footnote f).

The cross-coupling reactions are not affected by small quantities (5 mol%) of azobis(isobutyronitrile) or benzoyl

 Table 2
 Cross-Alkylation of Some Aryl Halides and a Triflate with 3–7 in the Presence of Catalyst 2^a

Entry	Substrate	Alkylating reagent	Phosphine	Reaction time (h)	Product	Yield (%) ^b
1	$1-C_{10}H_7Cl$	3	$P(t-Bu)_3$	1°	$1-C_{10}H_7Me$	77
2	$1-C_{10}H_7Br$	3	PPh ₃	1	$1-C_{10}H_7Me$	76
3	4-ClC ₆ H ₄ Me	3	$P(t-Bu)_3$	6 ^c	$1,4-C_6H_4Me_2$	27
4	4-ClC ₆ H ₄ CF ₃	3	$P(t-Bu)_3$	20	$4-MeC_6H_4CF_3$	62
5	2-ClC ₆ H ₄ NO ₂	3	PPh ₃	20	2-MeC ₆ H ₄ NO ₂	98 ^d
6	4-ClC ₆ H ₄ NO ₂	3	PPh ₃	20	4-MeC ₆ H ₄ NO ₂	99 ^d
7	4-ClC ₆ H ₄ NO ₂	2	PPh ₃	20	4-EtC ₆ H ₄ NO ₂	95 ^d
8	4-BrC ₆ H ₄ CH ₃	3	PPh ₃	6 ^e	4-MeC ₆ H ₄ NO ₂	38
9	4-BrC ₆ H ₄ CF ₃	3	PPh ₃	2	$4-MeC_6H_4CF_3$	65
10	4-BrC ₆ H ₄ CF ₃	6	PPh ₃	2^{f}	$4-MeC_6H_4CF_3$	99 ^d
11	4-IC ₆ H ₄ CF ₃	3	PPh ₃	1	4-MeC ₆ H ₄ CF ₃	63
12	4-IC ₆ H ₄ CF ₃	4	PPh ₃	2	4-EtC ₆ H ₄ CF ₃	60
13	4-IC ₆ H ₄ CF ₃	5	PPh ₃	2	4-MeC ₆ H ₄ CF ₃	27
14	$4-IC_6H_4CF_3$	7	PPh ₃	2	4-MeC ₆ H ₄ CF ₃	97
15	4-TfOC ₆ H ₄ NO ₂	3	PPh ₃	1	4-MeC ₆ H ₄ NO ₂	11

^a Reaction conditions as in Table 1.

^b Unless stated otherwise the yields refer to isolated products. The missing percentage reflects on the unreacted started material.

° At 120 °C.

^d The yields were determined by GC.

e Yield: 14% after 2 h.

f Yield: 93% after 1 h.

peroxide. This indicates that no free radical steps are involved in the reactions. In analogy to the process promoted by the aforementioned Pd-Fe and Pd-Co clusters,¹ the cross-couplings described herein seem to be governed by a synergistic effect between the metal nuclei of the catalysts. None of the starting materials of 1 and 2, $Mo(CO)_6$, $W(CO)_6$ and $PdCl_2(PhCN)_2$ promotes the cross-coupling of 1-bromonaphthalene with 3 and no evidence whatsoever could be found for the dissociation of 1 and 2 into catalytically active mononuclear palladium-phosphine complexes.

In conclusion, the Pd-Mo and Pd-W mixed-metal clusters 1 and 2 (Figure 1) proved to be highly efficient and selective catalysts for cross-coupling of aryl halides with intramolecularly stabilized aluminum, gallium and indium methylating and ethylating reagents 3-7 (Figure 2). The catalysts are superior to the current palladium and nickel catalysts as they are more stable, highly selective and do not promote any hydrogenolysis of the haloarenes even in the presence of ethylating reagents. Because 1 and 2 are applicable to aryl chlorides, they provide an important addition to the repertoire of catalysts that promote crosscoupling processes of industrial interest (see, e.g., ref.⁷).



Figure 1

(4Mo-Pd)(Pd-Pd)Tetra- μ -carbonyldi- μ_3 -carbonylbis(η^5 -2,4-cyclopentadien-1-yl)bis-[(triphenylphosphine)palladium]dimolybdenum (1),⁸ (Pd–Pd)(4Pd–W)tetra- μ -carbonyl-di- μ_3 -carbonylbis(η^5 -2,4-cyclopentadien-1-yl)bis[(triphenylphosphine)palladium]ditungsten (2),⁸ bis{ μ -[2-(dimethylamino)ethanolato-N, O:O]}tetramethyldialuminum (3),⁹ bis{ μ -[2-(dimethylamino)ethanolato-N, O:O] tetraethyldialuminum (**4**),¹⁰ bis{ μ -[2-methylamino)ethanolato-N,O:O] tetramethyldigallium (5),¹¹ bis{ μ -[2-methylami-

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4: M = Al, R = Et 5: M = Ga, R = Me

Figure 2

no)ethanolato-N,O:O]}tetramethylindium (**6**),¹² and bis{ μ -[2-methylamino)ethanolato-N,O:O]}tetraethylindium (**7**),¹ were prepared according to literature procedures.

Cross-Coupling of Aryl Halides and Triflates; General Procedure

A thick-walled pressure tube was charged under exclusion of air with the alkylating reagent (1.94 mmol), the aromatic substrate (0.96 mmol), the catalyst (0.05 mmol), the appropriate tertiary phosphine (0.20 mmol) and anhyd benzene (15 mL) and heated at the required temperature for the desired length of time. The mixture was cooled to r.t., diluted with Et_2O and treated with an excess of 5% aq HCl. Phase separation, extraction of the aqueous phase with Et_2O and filtration of the extracts through a millipore filter gave the product which was analyzed and compared by IR, NMR and GC–MS with authentic samples.

Acknowledgment

We thank the United States-Israel Binational Science Foundation for financial support of this study through grant No. 2000013.

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