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LETTERS

Dichlorobis(triphenylphosphine)nickel-catalyzed cross-coupling of aryl chlorides with intramolecularly stabilized group 13 metal alkylating reagents

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Abstract

The intramolecularly stabilized alkyl and aryl aluminum complexes **1**, **4** and **11**, as well as the indium compounds **6**, **9** and **10** cross-couple with a variety of chloroarenes at 80°C in the presence of $NiCl_2(PPh_3)_2$ to give selectively the respective alkylated arenes in high yields. Addition of organic or inorganic bases lowers the reaction temperature to 50°C. © 2000 Elsevier Science Ltd. All rights reserved.

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Although palladium-catalyzed cross-coupling of aryl iodides, bromides and pseudohalides with organometallics in the Stille,[1] Suzuki,[2] Negishi[3] and related processes are extremely useful for C–C bond formation in academic research,[4] their utilization in industrial plants is still limited owing to the high cost of the substrates. It is thus understandable that extensive research has lately been conducted to modify the palladium catalysts in a way that they may activate inexpensive aryl chlorides in the above named coupling processes.[5] In the course of our studies on the cross-alkylation of aryl halides with intramolecularly stabilized dimethylaluminum reagents,[6] we found that some chloroarenes do undergo the coupling reaction when the electron-rich [1,3-bis(diisopropylphosphino)propane]palladium is used as catalyst.[7] This complex has, however, the disadvantages of being air sensitive and expensive, and it fails to affect unsubstituted aryl bromides.

In this communication we report the use of $NiCl_2(PPh_3)_2$ (that has previously been used in coupling reactions of Grignard reagents[8]) as an efficient catalyst for the cross-alkylation of several monomeric and dimeric dialkylaluminum and indium complexes with a variety of aryl chlorides. This catalyst is also capable of the activation of bromoarenes.

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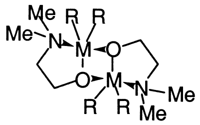


1: M = Al R = Me

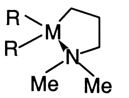
2: M = Al R = Et

3: M = Al R = i-Bu

4: M = Al R = Ph

5: M = Ga R = Me

6: M = In R = Me

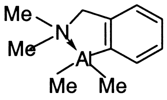


7: M = Al R = Me

8: M = Ga R = Me

9: M = In R = Me

10: M = In R = Et



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When, for example, a solution of 104 mg (0.64 mmol) of 1-chloronaphthalene, 186 mg (0.64 mmol) of **1**,[6a] and 21 mg (0.032 mmol) of $NiCl_2(PPh_3)_2$ in 4.5 ml of benzene was heated at 78°C under N_2 for 3 h, followed by quenching with 4 ml of 5% aq HCl, the resulting mixture consisted (according to GC and ^1H NMR analyses) of 95% of 1-methylnaphthalene and 3% of the unsubstituted hydrocarbon. Under similar conditions 1-bromonaphthalene gave quantitative yields of 1-methylnaphthalene after 2 h. A series of similar cross-coupling experiments conducted with several representative chloroarenes and alkylating agents **1**–**11**[6a,9–12] are summarized in Table 1.

While in the *palladium*-catalyzed cross-methylation of aryl bromides[6] and chlorides[7] both aluminum-bound methyl groups can take part in the process, only one of the alkyl functions is applicable in the $NiCl_2(PPh_3)_2$-catalyzed cross-coupling. When, for example, 1-chloronaphthalene was reacted with just half an equivalent of **1** (i.e. 0.25 mol of the reagent per each mol of substrate) the yield after 48 h was only 42% (entry 8), and did not exceed 50% even after extension of the reaction time. Table 1 indicates that both unsubstituted and substituted chlorobenzenes undergo cross-methylation with **1**. Substrates with electron-withdrawing substituents react faster than those with electron-donating groups (cf. entries 4–6 vs. entries 2,3). Likewise, 2-chloronaphthalene reacts faster than the 1-isomer in which the chlorine atom is sterically hindered. The cross-coupling with **1** tolerates the presence of cyano as well as keto- and ester-carbonyl moieties (entries 4–6), but in chlorobenzaldehyde both vulnerable groups are affected by the reagent (entry 7). The indium analog of **1**, complex **6**, reacts much slower than the aluminum reagent (see entries 1, 9, 14 and 15), and the gallium complex **5** hardly reacts at all ($1\text{-}C_{10}H_7Cl$ forms only 1% of $1\text{-}C_{10}H_7Me$ after 24 h). The monomeric methylating reagents **7**–**11** react usually faster than the dimeric analogs. The aluminum and gallium complexes react, however, in a non-selective fashion. Thus, compound **7** yields during the reaction with $1\text{-}C_{10}H_7Cl$ mainly naphthalene and only 27% of the methylated product (entry 16). Likewise, the monomeric gallium complex gives both methylated and unsubstituted naphthalene (entry 17). The indium methylating reagent **9** (which reacts much faster than **6**), yields solely 1-methylnaphthalene (entry 18). Also, complex **11**, which is more bulky than **7**, forms the expected product in a highly selective manner (entry 20). The $NiCl_2(PPh_3)_2$-catalyzed reactions of chloroarenes with analogs of **1** in which the Me moiety has been replaced by Et, *i*-Bu and Ph have also been studied. While the phenylated complex **4** reacts with 2-chloronaphthalene to give solely 2-phenylnapthalene (entry 13), reagents **2** and **3** which may lose ethylene and *i*-butene, respectively, to give aluminum hydrides,[13] form naphthalene as the major product (entries 11, 12). Rather unexpectedly, reagent **7** also gives mainly naphthalene, but the indium complexes **9** and **10** cross-couple with 1-chloronaphthalene in a highly selective manner to give exclusively 1-methyl- and 1-ethylnaphthalene, respectively (entries 18, 19).

Table 1
Cross-coupling of some representative aryl chlorides with complexes **1**–**11** in the presence of $NiCl_2(PPh_3)_2$[a]

Entry	Substrate	Alkylating reagent	Substrate:metal atom[b]	Reaction time (h)	Products (yield, %)
1	C_6H_5Cl[c]	**1**	1:1	5	C_6H_5Me (91)
2	4-MeC_6H_4Cl[c]	**1**	1:1	20	1,4-$C_6H_4Me_2$ (24)[d]
3	4-$MeOC_6H_4Cl$	**1**	1:2	20	4-$MeOC_6H_4Me$ (46)[d]
4	4-ClC_6H_4CN	**1**	1:2	6	4-MeC_6H_4CN (96)
5	4-ClC_6H_4COMe	**1**	1:2	4	4-MeC_6H_4COMe (91)
6	4-$ClC_6H_4CO_2Et$	**1**	1:2	4	4-$MeC_6H_4CO_2Et$ (81)
7	4-ClC_6H_4CHO	**1**	1:2	3.5	4-$MeC_6H_4CH(OH)Me$ (91)[e]
8	1-$C_{10}H_7Cl$	**1**	2:1	48	1-$C_{10}H_7Me$ (42)[d]
9	1-$C_{10}H_7Cl$	**1**	1:1	8	1-$C_{10}H_7Me$ (92)[f]
10	2-$C_{10}H_7Cl$	**1**	1:2	3	2-$C_{10}H_7Me$ (95)[f]
11	2-$C_{10}H_7Cl$	**2**	1:2	24	2-$C_{10}H_7Me$ (36), $C_{10}H_8$ (60)
12	2-$C_{10}H_7Cl$	**3**	1:2	24	2-$C_{10}H_7Me$ (22), $C_{10}H_8$ (76)
13	2-$C_{10}H_7Cl$	**4**	1:2	8	2-$C_{10}H_7Ph$ (93)
14	C_6H_5Cl[c]	**6**	1:1	20	C_6H_5Me (66)[d]
15	1-$C_{10}H_7Cl$	**6**	1:2	24	1-$C_{10}H_7Me$ (7)[d]
16	1-$C_{10}H_7Cl$	**7**	1:2	3	1-$C_{10}H_7Me$ (27), $C_{10}H_8$ (70)
17	1-$C_{10}H_7Cl$	**8**	1:2	5	1-$C_{10}H_7Me$ (43), $C_{10}H_8$ (55)
18	1-$C_{10}H_7Cl$	**9**	1:2	5	1-$C_{10}H_7Me$ 91)
19	1-$C_{10}H_7Cl$	**10**	1:2	5	1-$C_{10}H_7Me$ (95)
20	1-$C_{10}H_7Cl$	**11**	1:2	5	1-$C_{10}H_7Me$ (94)[f]

[a] Reaction conditions: 0.64 mmol chloro compound, the appropriate amount of the alkylating agent and 0.032 mmol of $NiCl_2(PPh_3)_2$ in 4.5 ml of benzene; 80°C; quenching with excess 5% aq HCl.

[b] Calculated for each metal atom as if complexes **1**–**6** reacted as monomeric species.

[c] In C_6D_6.

[d] The missing percentages reflect the unreacted starting chloroarene.

[e] Contaminated with 7% of 4-$MeC_6H_4CH_2OH$.

[f] Contaminated with 1–3% of naphthalene.

Finally, it is notable that unlike the Suzuki reaction,[2] the cross-coupling with stabilized group 13 metal reagents does not require the presence of a base. However, the addition of some bases enhances the reaction rate and lowers the temperature. While, for example, 1-chloronaphthalene, **1**, and $NiCl_2(PPh_3)_2$ (substrate:reagent:catalyst = 1:1:0.02) form upon heating at 50°C for 24 h, 64% of 1-methylnaphthalene and 2% of the unsubstituted hydrocarbon, the addition of 0.06 equivalents of NBu_3, Cs_2CO_3 or K_3PO_4 leads to the formation of 96, 92 and 91% of the methylated product, respectively, under the same experimental conditions.

Acknowledgements

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12. Compounds **2**–**4** were prepared by stirring a solution or suspension of 37 mmol of trialkylaluminum and 37 mmol of 2-dimethylaminoethanol in 200 ml pentane at −20°C for 3 h under Ar followed by stirring for 12 h at 25°C, removal of the solvent and recrystallization of the residue from pentane at −40°C. **2**: Yield 87%; mp 91°C; 300 MHz ^{1}H NMR (C_6D_6): δ 0.05 (q, 8, $J=9$ Hz), 1.39 (t, 12, $J=9$ Hz), 1.88 (s, 12), 1.98 (t, 4, $J=6$ Hz), 3.49 (t, 4, $J=6$ Hz); 100 Mz ^{13}C NMR (C_6D_6): δ 1.17, 11.82, 45.30, 57.33, 59.82. **3**: Yield: 43%; mp 114°C; 300 MHz ^{1}H NMR (C_6D_6): δ 0.03 (d, 8, $J=9$ Hz), 1.25 (d, 24, $J=6$ Hz), 1.95–1.98 (m, 4), 1.99 (t, 4, $J=6$ Hz), 3.55 (t, 4, $J=6$ Hz); 100 Mz ^{13}C NMR (C_6D_6): δ 23.70, 27.84, 29.90, 46.21, 57.66, 60.20. **4**: Yield: 68%; mp ∼200°C; 300 MHz ^{1}H NMR (C_6D_6): δ 1.55 (s, 12), 1.77 (t, 4, $J=6$ Hz), 3.19 (t, 4, $J=6$ Hz), 7.41–7.54 (m, 12), 8.14 (m, 8); 100 Mz ^{13}C NMR (C_6D_6): δ 45.77, 55.84, 58.98, 127.21, 127.59, 128.08, 138.47. Further analytical data of compounds **2**–**4** will be published elsewhere.
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