



Lanthanide assisted cross-coupling of aryl bromides with triethylaluminum

Margarita Shenglof,^a Dmitri Gelman,^a Gary A. Molander^b and Jochanan Blum^{a,*}

^aDepartment of Organic Chemistry, The Hebrew University, Jerusalem 91904, Israel

^bRoy and Diana Vagelos Laboratories, Department of Chemistry, University of Pennsylvania, Philadelphia, Pennsylvania, PA 19104-6323, USA

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Abstract—Cerium trichloride, as well as some other lanthanide salts, promote the palladium-catalyzed cross-coupling of triethylaluminum with bromoarenes. The lanthanide compounds also increase the selectivity by diminishing the undesired hydrodebromination process.

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Palladium- and nickel-catalyzed cross-coupling of aryl and vinyl halides with metal or metalloid alkyls is one of the most useful methods for C–C bond formation.¹ For this reason derivatives of nearly all common metals have been investigated as alkylating reagents. Organoaluminum compounds were utilized during the early stages of the development of cross-coupling processes, but thereafter gained only little popularity. Their ability to interact with many solvents leads frequently to side products and to low selectivity. Furthermore, the tendency of trialkylaluminum compounds R_3Al , which contain β -hydrogen atoms in the alkyl moieties, to disproportionate into alkenes and aluminum hydrides² is responsible for substantial hydrodehalogenation of the aryl halides. Recently, we have shown that these shortcomings can be overcome to a significant extent by replacement of the trialkylaluminum by Lewis base-intramolecularly stabilized dialkylaluminum derivatives using either phosphine-free nickel complexes³ or palladium-containing mixed-metal clusters⁴ as catalysts. We now report on an alternative method for selective activation of trialkylaluminum in cross-coupling processes based on the observation that lanthanide compounds promote a variety of C–C bond forming reactions,⁵ and that they are capable of undergoing transmetalation with metal alkyls, including derivatives of aluminum.⁶



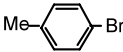
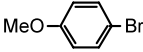
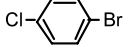
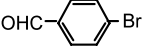
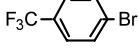
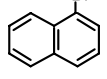
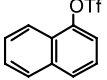
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* Corresponding author. Tel.: +972-2-6585329; fax: +972-2-6513832; e-mail: jblum@chem.huji.ac.il

Interaction of equimolar quantities of 1-bromonaphthalene and triethylaluminum in the presence of 5 mol% of $PdCl_2(PPh_3)_2$ in THF at 22°C afforded after 6 h 16% of 1-ethylnaphthalene and 5% of naphthalene. Upon addition of an equimolar amount of dry $CeCl_3$, the yield of 1-ethylnaphthalene increased to 88% and that of the dehalogenated naphthalene decreased to 0.6%. (The remaining 11% was the unreacted aryl bromide.) When the time was extended to 10 h full conversion was achieved without change in the selectivity. A similar increase in rate and in the selectivity was observed also when other aryl bromides or triflates were treated with the $Et_3Al/CeCl_3$ couple. Some representative results are listed in Table 1. Table 1 indicates that the rate is affected to some extent by electronic factors. Introduction of electron donating groups (entries 3 and 4) causes the reaction to slow down whereas electron attracting functions (entries 5 and 6) increase the rate. The behavior of 4-(trifluoromethyl)bromobenzene in the cross-coupling is obscure. The reaction is also affected by steric hindrance. 2-Bromotoluene reacts slower than the unsubstituted bromobenzene and the unhindered 4-bromotoluene (cf., entries 1, 2 and 3). Entry 9 indicates that the cross-coupling takes place also with triflates, however, in a less selective fashion than with the bromides.

Lanthanide-deficient blank experiments with the substrates listed in Table 1 gave usually less than half of the ethylated products as the $CeCl_3$ -mediated reactions. Apart from $CeCl_3$, salts of lanthanum, lutetium and ytterbium revealed a positive effect (although a smaller

Table 1. Cross-ethylation of some aryl bromides and a triflate, with $\text{Et}_3\text{Al}/\text{CeCl}_3$, $\text{ArX} \rightarrow \text{ArEt} + \text{ArH}$ under comparable conditions^a

Entry	Substrate	Yield of ArEt, (%) ^{b,c}	Yield of ArH, (%) ^{b,c}	Selectivity, (%)
1		71	2.8	96
2		33	1.7	95
3		64	2.9	96
4		45	1.9	96
5		87	3.7	96
6		77	5.0	94
7		30	0.0	100
8		88	0.6	99
9		86	13	87

^a Reaction conditions: aryl bromide or triflate (1.6 mmol), Et_3Al (1.6 mmol), anhydrous CeCl_3 (1.6 mmol), $\text{PdCl}_2(\text{PPh}_3)_2$ (0.079 mmol), THF (12.7 ml), N_2 atmosphere, 22°C. After 6 h the reaction mixture is diluted with 25 ml Et_2O and quenched with 2 ml MeOH and 5 ml 15% aq. HCl.

^b In all experiments the only byproduct was the bromide-free starting materials (ArH).

^c The yields were determined both by GC and by ^1H NMR. The figures are the average of at least two experiments that did not differ by more than 3%. As there are no other side products except the ArH, the missing percentage reflects on the unreacted starting material.

one than CeCl_3) on the palladium-catalyzed reaction of 1-bromonaphthalene with Et_3Al (Table 2). On the other hand, some lanthanide salts [e.g. EuCl_3 and $\text{Sm}(\text{OTf})_3$] act as inhibitors and cause the cross-coupling to slow down. It is notable that not only the type of lanthanide

metal, but also the nature of the counter-ion affects the cross-coupling. While e.g. the effect of CeCl_3 is really significant, that of CeBr_3 is much smaller. Likewise, the two ytterbium salts affect the reaction to a different extent.

Table 2. $\text{PdCl}_2(\text{PPh}_3)_2$ -catalyzed cross-coupling of 1-bromonaphthalene with Et_3Al in the presence of some lanthanide halides or triflates under comparable conditions^a

Entry	Lanthanide compound	Yield of 1-ethyl-naphthalene (%) ^b	Yield of naphthalene (%) ^b	Selectivity (%)
1	None ^c	16	5.0	76
2	CeCl_3	88	0.6	99
3	CeBr_3	27	3.7	88
4	LaCl_3	38	1.0	97
5	LuCl_3	32	1.0	97
6	$\text{Yb}(\text{OTf})_3$	40	1.4	97
7	YbCl_3	20	0.3	98

^a Reaction conditions as in Table 1 except that lanthanide compounds other than CeCl_3 were also used.

^b The yields were determined both by GC and ^1H NMR and were the average of at least two experiments that did not differ by more than 3%. The missing percentage reflects on the unreacted starting material after 6 h.

^c The same result was obtained when 1.6 mmol of either AlCl_3 or BF_3 etherate was added to the reaction mixture. Addition of 1.6 mmol of ZnCl_2 afforded 6% of 1-ethylnaphthalene and 1.7% of naphthalene.

The exact function of the lanthanide salt in the cross-coupling process is not quite clear. As AlCl_3 and BF_3 etherate have no effect whatsoever on either the cross-coupling of Et_3Al with 1-bromonaphthalene, or on the hydrodehalogenation of the latter compound, and freshly fused ZnCl_2 even reduces the rate and the selectivity, it is unlikely that the lanthanides function in our case (as they do in many other processes⁵) as Lewis acids. Although complexes of trialkylaluminum and some lanthanides are known⁷ we were unable to prove unequivocally by ^1H , ^{13}C and ^{27}Al NMR studies that Et_3Al and the diamagnetic LaCl_3 forms a discrete alkyl lanthanum compound. Yet we assume on the basis of the observation that alkyl lanthanide derivatives can act as active reagents in alkylation and cross-coupling processes,⁸ that transmetallation may also occur in our reactions.

Finally, we also examined the effect of a lanthanide salt [$\text{Eu}(\text{OTf})_3$] on the cross-coupling of an aryl chloride. We found that indeed the $\text{NiCl}_2(\text{PPh}_3)_2$ -catalyzed reaction of 1-chloronaphthalene⁹ with Me_3Al is enhanced by the added europium salt. While in the absence of the lanthanide compound 25% of 1-methylnaphthalene and 2% of naphthalene were formed after 6 h, the respective percentages of these products were 56 and 0.2 in its presence.

In summary, CeCl_3 and some other Ln^{+3} salts are useful additives for effective cross-coupling of bromoarenes with triethylaluminum. They both increase the reaction rate and diminish the disproportionation of the aluminum reagent which leads to undesired hydrogenolysis of the starting halide.

Acknowledgements

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