CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200903157

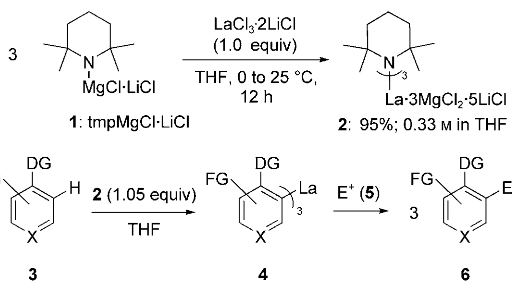
Atom-Economical Preparation of Aryl– and Heteroaryl–Lanthanum Reagents by Directed *ortho*-Metalation by Using tmp_3[La]**

Stefan H. Wunderlich and Paul Knochel*[a]

The *ortho*-metalation of aromatics and heteroaromatics is a powerful method for the functionalization of these ring systems.[1] Although lithium bases[2] and several ate-bases[3] allow the preparation of various *ortho*-metalated products, there is still a need for more chemoselective bases. Recently, we reported that the reaction of tmpMgCl•LiCl (**1**; tmp = 2,2,6,6-tetramethylpiperidyl)[4,5] or tmpLi[6] with metallic chlorides, such as $ZnCl_2$,[7] $AlCl_3$,[8] $MnCl_2$•2LiCl,[9] $FeCl_2$•2LiCl, or $FeCl_3$[10] provides highly chemoselective bases that tolerate a range of functional groups. The presence of $MgCl_2$ and LiCl in these bases ensures good solubility in THF and a high kinetic basicity (compare tmp_2Zn•$2MgCl_2$•2LiCl with tmpZnCl•LiCl).[7d]

Organolanthanum derivatives are relatively inexpensive organometallic intermediates of low toxicity.[11] They are usually prepared by transmetalation reactions starting from lithium or magnesium reagents as has been pioneered by Imamoto.[11,12] Several lanthanum amides have been reported, mainly for the performance of hydroamination reactions[11,13] or for structural studies.[11,14] Herein, we wish to report a new base, that is, tmp_3La•$3MgCl_2$•5LiCl (**2**, abbreviated, for the sake of clarity, to tmp_3[La]). The reaction of tmp_3[La] (**2**) with functionalized arenes and heteroarenes of type **3** allows an expedient access to functionalized aryl and heteroaryl derivatives of type **4** under mild conditions. These unsaturated lanthanum derivatives display a unique reactivity pattern and react with various electrophiles (**5**) producing a range of polyfunctional products of type **6**.

The new base **2** is readily prepared by the reaction of tmpMgCl•LiCl[4] (**1**; 3.0 equiv) with the THF soluble complex $LaCl_3$•2LiCl[15] in THF for 12 h. The resulting dark brown solution (0.33 M in THF; 95 % yield as determined by titration)[7a] is stable under argon for at least 2 months without decomposition (Scheme 1).



Scheme 1. Preparation of **2** and its reactivity with unsaturated substrates of type **3** leading to triorganolanthanum reagents of type **4**. E = electrophile, DG = directing group, FG = functional group, X = CH or heteroatom.

The new base **2** is highly chemoselective and tolerates methyl esters without special precautions. It also displays good atom economy[16] since all three tmp groups can be used for a directed metalation. Thus, the reaction of methyl 3-fluorobenzoate (**3a**) with **2** (0.35 equiv) in THF at −5 °C (45 min) affords the triaryllanthanum species **4a**.[17] This lanthanum organometallic reacts smoothly with hindered carbonyl derivatives, such as 2,6-dibenzylidenecyclohexanone (**5a**, 1.0 equiv, −5 °C, 1 h) giving the spirolactone **6a** in 87 % yield. Similarly, the reaction of **4a** with 2-furoyl chloride (**5b**, 1.1 equiv, −5 °C, 1 h) smoothly leads to the ketone **6b** in 85 % yield. Remarkably, no further addition of **4a** to **6b** was observed (Scheme 2).[18]

Furthermore, the metalation of ethyl 3-chlorobenzoate (**3b**) proceeds within 3.5 h at 0 °C, and the reaction with dicyclopropyl ketone (**5c**; activated with $LaCl_3$•2LiCl (0.25 equiv)) leads to the lactone **6c** in 69 % yield (Table 1, entry 1). Additionally, ethyl 3-bromobenzoate (**3c**) can be converted into the lanthanated species within 2.5 h at 25 °C and subsequent treatment with ethyl oxalyl chloride (**5d**) gives the ketone **6d** in 67 % yield (Table 1, entry 2). Inter-

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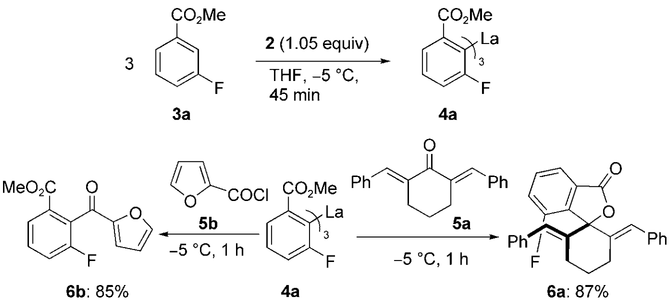
[a] S. H. Wunderlich, Prof. Dr. P. Knochel
Department Chemie und Biochemie
Ludwig-Maximilians-Universität München
Butenandtstrasse 5–13, Haus F, 81377 München (Germany)
Fax: (+49) 89-2180-77680
E-mail: paul.knochel@cup.uni-muenchen.de

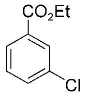
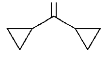
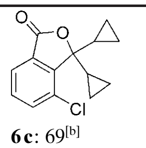
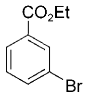
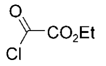
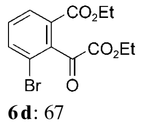
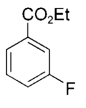
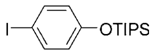
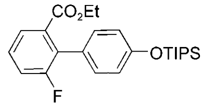
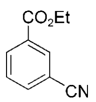
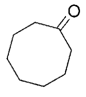
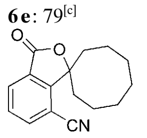
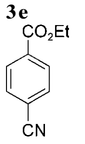
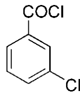
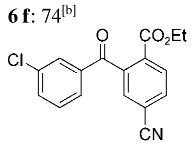
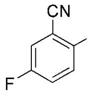
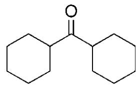
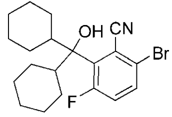
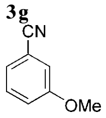
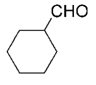
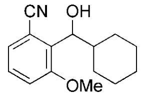
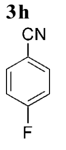
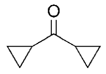
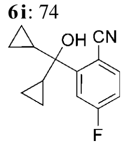
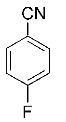
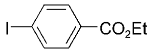
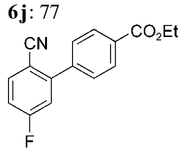
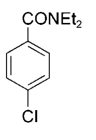
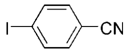
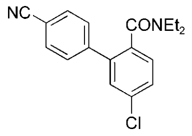
[**] tmp = 2,2,6,6-tetramethylpiperidyl; tmp_3[La] = tmp_3La•$3MgCl_2$•5LiCl.

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200903157.



Scheme 2. Typical metalation conditions of a functionalized arene, such as **3a** with **2** and its reaction with a hindered ketone (**5a**) or an acid chloride (**5b**).

Table 1. Lanthanation of aromatic substrates by using **2** and subsequent reactions with electrophiles.

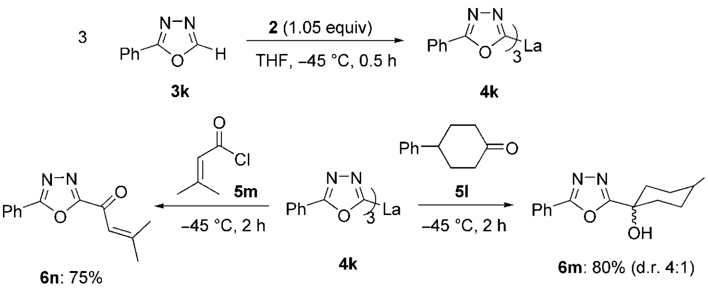
	Substrate	T [°C], t [h]	Electrophile	Product/Yield [%][a]
1	 **3b**	0, 3.5	 **5c**	 **6c**: 69[b]
2	 **3c**	25, 2.5	 **5d**	 **6d**: 67
3	 **3d**	0, 0.5	 **5e**	 **6e**: 79[c]
4	 **3e**	0, 1.25	 **5f**	 **6f**: 74[b]
5	 **3f**	−25, 3	 **5g**	 **6g**: 68
6	 **3g**	−35, 0.5	 **5h**	 **6h**: 66
7	 **3h**	25, 1.5	 **5i**	 **6i**: 74
8	 **3i**	0, 1	 **5c**	 **6j**: 77
9	 **3i**	0, 1	 **5j**	 **6k**: 73[c]
10	 **3j**	0, 2	 **5k**	 **6l**: 80[c]

[a] Yield of the analytically pure isolated product. [b] $LaCl_3$·2LiCl (0.25 equiv) was used. [c] $[Pd(PPh_3)_4]$ (2.5 mol %) was used.

estingly, the triaryllanthanum species undergo Pd-catalyzed cross-coupling reactions without the need of any additional transmetalation. Thus, the lanthanum species **4d**, obtained by the metalation of ethyl 3-fluorobenzoate (**3d**) within 30 min at 0 °C, reacts directly with the aryl iodide **5e** in the presence of $[Pd(PPh_3)_4]$ (2.5 mol %) giving the biphenyl **6e** in 79 % yield (Table 1, entry 3). Moreover, ethyl 3-cyanobenzoate (**3e**) is regioselectively metalated at the 2-position within 1.25 h at 0 °C. After the reaction with cyclooctanone (**5f**; activated with $LaCl_3$·2LiCl (0.25 equiv)), the spirolactone **6f** is isolated in 74 % yield (Table 1, entry 4). Additionally, the lanthanation of ethyl 4-cyanobenzoate (**3f**) proceeds within 3 h at −25 °C and the reaction with 3-chlorobenzoyl chloride provides the ketone **6g** in 68 % yield (Table 1, entry 5). Furthermore, 2-bromo-5-fluoro-benzonitrile (**3g**) is converted into the lanthanum species **4g** within 30 min at −35 °C. Treatment of **4g** with dicyclohexyl ketone provides the alcohol **6h** in 66 % yield (Table 1, entry 6). 3-Methoxybenzonitrile (**3h**) is readily lanthanated at the 2-position within 1.5 h at 25 °C and subsequent treatment with cyclohexane carbaldehyde (**5i**) gives the product **6i** in 74 % yield (Table 1, entry 7). Additionally, the metalation of 4-fluorobenzonitrile (**3i**) is accomplished within 1 h at 0 °C giving the triaryllanthanum species **4i**. The alcohol **6j** is obtained in 77 % yield after the addition of **4i** to dicyclopropyl ketone (**5c**), whereas the cross-coupling product **6k** is isolated in 73 % yield by using $[Pd(PPh_3)_4]$ (2.5 mol %) and ethyl 4-iodobenzoate (**5j**) (Table 1, entries 8 and 9). Finally, the lanthanation of 4-chloro-*N*,*N*-diethylbenzamide (**3j**) proceeds smoothly within 2 h at 0 °C and the subsequent Pd-catalyzed cross-coupling with 4-iodobenzonitrile (**5l**) afforded the biphenyl **6l** in 80 % yield (Table 1, entry 10).

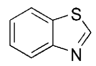
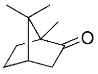
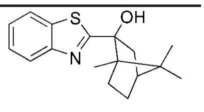
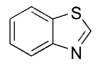
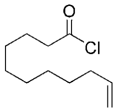
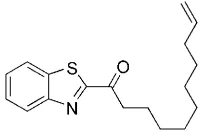
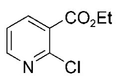
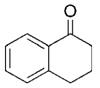
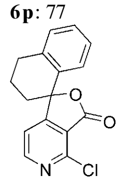
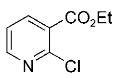
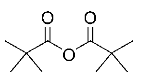
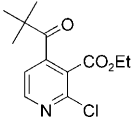
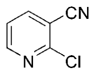
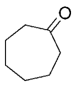
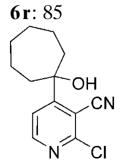
Heterocyclic systems are also readily metalated by using **2**. Thus, the treatment of 2-phenyl-1,3,4-oxadiazole (**3k**) with **2** (0.35 equiv) in THF (−45 °C, 30 min) gives the desired metalated species **4k**. In contrast to the corresponding magnesiated or lithiated heterocycle,[7a] no fragmentation of this sensitive heterocycle resulting in the formation of benzonitrile is observed. Quenching the reaction with 4-phenylcyclohexanone (**5l**, 1.0 equiv, −45 °C, 1 h) leads to the desired tertiary alcohol **6m** in 80 % yield. Alternatively, the reaction of **4k** with 3,3-dimethyl acryloyl chloride (**5m**, 1.1 equiv, −45 °C, 1 h) provides the ketone **6n** in 75 % yield (Scheme 3).

The metalation of both electron-rich and -poor heterocycles can be performed as summarized in Table 2. Thus, the



Scheme 3. Metalation of 2-phenyl-[1,3,4]-oxadiazole (**3k**) with **2** and its reaction with a ketone (**5l**) and an acid chloride (**5m**).

Table 2. Lanthanation of heteroaromatics of type **3** by using **2** and subsequent reactions with electrophiles.

	Substrate	T [°C], t [h]	Electrophile	Product/Yield [%][a]
1	 **3l**	0, 0.5	 **5n**	 **6o**: 83 (d.r. 9:1)
2	 **3l**	0, 0.5	 **5o**	 **6p**: 77
3	 **3m**	–20, 0.75	 **5p**	 **6q**: 74
4	 **3m**	–20, 0.75	 **5q**	 **6r**: 85
5	 **3n**	–30, 0.75	 **5r**	 **6s**: 71

[a] Yield of the analytically pure isolated product.

metalation of benzothiazole (**3l**) proceeds smoothly within 30 min at 0°C. The subsequent reactions with camphor (**5n**) or the acid chloride **5o** give the products **6o** and **6p** in 83 and 77% yield, respectively (Table 2, entries 1 and 2). Moreover, the reaction of ethyl 2-chloronicotinate (**3m**) with **2** gives the fully metalated species **4m** within 45 min at –20°C.[19] The lactone **6q** is obtained in 74% yield after quenching with α-tetralone (**5p**, Table 2, entry 3). Surprisingly, the addition of **4m** to the sterically hindered anhydride **5q** leads to the *tert*-butyl ketone **6r** in 85% yield (Table 2, entry 4). Additionally, 2-chloro-3-cyanopyridine (**3n**) undergoes a smooth metalation at –30°C within 45 min and subsequent treatment with cycloheptanone (**5r**) gives the tertiary alcohol **6s** in 71% yield (Table 2, entry 5).

In summary, we have reported a new convenient procedure for preparing polyfunctional aryl and heteroaryl lanthanum derivatives tolerating important functional groups, such as a methyl ester, a cyano group, and halogen atoms. These triaryl- and triheteroaryllanthanum species react with various electrophiles. Especially interesting is the direct Pd-catalyzed cross-coupling reaction with aryl iodides. Remarkably, addition reactions to aldehydes or ketones afford sterically hindered alcohols or lactones and the acylation reactions with acid chlorides and an anhydride provide the expected ketones in satisfactory yields. The excellent atom economy of the reaction is worth mentioning, since only 0.33 equivalent of La is required for this metalation procedure. Further investigations of these lanthanation reactions applied to more complex unsaturated substrates are currently underway in our laboratories.

Experimental Section

Preparation of reagent 2: In a dry and argon-flushed 250 mL Schlenk flask, freshly titrated tmpMgCl·LiCl (100 mmol, 1.18 M, 85 mL) was purged and cooled to 0°C. Then, $LaCl_3$·2LiCl (0.5 M in THF, 66 mL, 33 mmol) was added over 5 min. The resulting mixture was stirred for 30 min at 0°C, warmed to 25°C and stirred for another 12 h. The resulting solution of **2** was concentrated in vacuo and was titrated prior to use at 0°C with benzoic acid (0.5 M in THF) by using 4-(phenylazo)diphenylamine as the indicator. A concentration of 0.33 M in THF was obtained.

Synthesis of 2,6-dibenzylidene-7′-fluoro-spiro[cyclohexane-1,1′-isobenzofuran]-3′-one (6a): A dry and argon-flushed 25 mL Schlenk tube, equipped with a magnetic stirring bar was charged with a solution of **3a** (308 mg, 2 mmol) in dry THF (2 mL) and cooled to –5°C. A solution of **2** (0.33 M in THF, 2.2 mL, 0.73 mmol) was added dropwise and the reaction mixture was stirred at –5°C for 45 min. The metalation progress was monitored by GC analysis of reaction aliquots that were quenched with allyl bromide. Then, compound **5a** (550 mg, 2.0 mmol) was added, and the resulting mixture was stirred for 1 h at –5°C. After standard workup, the solvent was evaporated in vacuo. The crude product was purified by column chromatography (pentane/ether = 8:1) to give **6a** (690 mg, 87% yield) as a colorless solid.

Acknowledgements

We thank the Fonds der Chemischen Industrie, the European Research Council (ERC) and the Deutsche Forschungsgemeinschaft (DFG) for financial support. We also thank Evonik AG (Hanau), BASF AG (Ludwigshafen), W. C. Heraeus GmbH (Hanau), and Chemetall GmbH (Frankfurt) for the generous gift of chemicals.

Keywords: acylation · cross-coupling · directed metalation · lanthanum · metal amides

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[1] a) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879; b) R. Chinchilla, C. Nájera, M. Yus, *Chem. Rev.* **2004**, *104*, 2667.

[2] a) P. Beak, V. Snieckus, *Angew. Chem.* **2004**, *116*, 2256; *Angew. Chem. Int. Ed.* **2004**, *43*, 2206; b) M. Schlosser, *Angew. Chem.* **2005**,

117, 380; *Angew. Chem. Int. Ed.* **2005**, *44*, 376; c) A. Turck, N. Plé, F. Mongin, G. Quéguiner, *Tetrahedron* **2001**, *57*, 4489; d) F. Mongin, G. Quéguiner, *Tetrahedron* **2001**, *57*, 4059.

[3] a) H. Naka, M. Uchiyama, Y. Matsumoto, A. E. H. Wheatley, M. McPartlin, J. V. Morey, Y. Kondo, *J. Am. Chem. Soc.* **2007**, *129*, 1921; b) R. E. Mulvey, F. Mongin, M. Uchiyama, Y. Kondo, *Angew. Chem.* **2007**, *119*, 3876; *Angew. Chem. Int. Ed.* **2007**, *46*, 3802; c) H. Naka, J. V. Morey, J. Haywood, D. J. Eisler, M. McPartlin, F. Garcia, H. Kudo, Y. Kondo, M. Uchiyama, A. E. H. Wheatley, *J. Am. Chem. Soc.* **2008**, *130*, 16193; d) M. Uchiyama, Y. Kobayashi, T. Furuyama, S. Nakamura, Z. Kajihara, T. Miyoshi, T. Sakamoto, Y. Kondo, K. Morokuma, *J. Am. Chem. Soc.* **2008**, *130*, 472; e) S. Usui, Y. Hashimoto, J. V. Morey, A. E. H. Wheatley, M. Uchiyama, *J. Am. Chem. Soc.* **2007**, *129*, 15102; f) F. Chevallier, F. Mongin, *Chem. Soc. Rev.* **2008**, *37*, 595; g) A. Seggio, F. Chevallier, M. Vaultier, F. Mongin, *J. Org. Chem.* **2007**, *72*, 6602; h) J-M. L'Helgoual'ch, A. Seggio, F. Chevallier, M. Yonehara, E. Jeanneau, M. Uchiyama, F. Mongin, *J. Org. Chem.* **2008**, *73*, 177; i) L. M. Carrella, W. Clegg, D. V. Graham, L. M. Hogg, A. R. Kennedy, J. Klett, R. E. Mulvey, E. Rentschler, L. Russo, *Angew. Chem.* **2007**, *119*, 4746; *Angew. Chem. Int. Ed.* **2007**, *46*, 4662; j) W. Clegg, S. H. Dale, E. Hevia, L. M. Hogg, G. W. Honeyman, R. E. Mulvey, C. T. O'Hara, L. Russo, *Angew. Chem.* **2008**, *120*, 743; *Angew. Chem. Int. Ed.* **2008**, *47*, 731; k) V. L. Blair, L. M. Carrella, W. Clegg, B. Conway, R. W. Harrington, L. M. Hogg, J. Klett, R. E. Mulvey, E. Rentschler, L. Russo, *Angew. Chem.* **2008**, *120*, 6304; *Angew. Chem. Int. Ed.* **2008**, *47*, 6208; l) V. L. Blair, W. Clegg, B. Conway, E. Hevia, A. Kennedy, J. Klett, R. E. Mulvey, L. Russo, *Chem. Eur. J.* **2008**, *14*, 65; m) P. Alborés, L. Carrella, W. Clegg, P. García-Álvarez, A. R. Kennedy, J. Klett, R. E. Mulvey, E. Rentschler, L. Russo, *Angew. Chem.* **2009**, *121*, 3367; *Angew. Chem. Int. Ed.* **2009**, *48*, 3317; n) V. L. Blair, L. M. Carrella, W. Clegg, J. Klett, R. E. Mulvey, E. Rentschler, L. Russo, *Chem. Eur. J.* **2009**, *15*, 856.

[4] a) A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem.* **2006**, *118*, 3024; *Angew. Chem. Int. Ed.* **2006**, *45*, 2958; b) W. Lin, O. Baron, P. Knochel, *Org. Lett.* **2006**, *8*, 5673; c) N. Boudet, J. R. Lachs, P. Knochel, *Org. Lett.* **2007**, *9*, 5525; d) N. Boudet, S. R. Dubbaka, P. Knochel, *Org. Lett.* **2008**, *10*, 1715; e) A. H. Stoll, P. Knochel, *Org. Lett.* **2008**, *10*, 113; f) M. Mosrin, P. Knochel, *Org. Lett.* **2008**, *10*, 2497; g) G. C. Clososki, C. J. Rohbogner, P. Knochel, *Angew. Chem.* **2007**, *119*, 7825; *Angew. Chem. Int. Ed.* **2007**, *46*, 7681; h) C. J. Rohbogner, G. C. Clososki, P. Knochel, *Angew. Chem.* **2008**, *120*, 1526; *Angew. Chem. Int. Ed.* **2008**, *47*, 1503.

[5] P. García-Alvarez, D. V. Graham, E. Hevia, A. R. Kennedy, J. Klett, R. E. Mulvey, C. T. O'Hara, S. Weatherstone, *Angew. Chem.* **2008**, *120*, 8199; *Angew. Chem. Int. Ed.* **2008**, *47*, 8079.

[6] I. E. Kopka, Z. A. Fataftah, M. W. Rathke, *J. Org. Chem.* **1987**, *52*, 448.

[7] a) S. H. Wunderlich, P. Knochel, *Angew. Chem.* **2007**, *119*, 7829; *Angew. Chem. Int. Ed.* **2007**, *46*, 7685; b) S. H. Wunderlich, P. Knochel, *Org. Lett.* **2008**, *10*, 4705; c) S. H. Wunderlich, P. Knochel, *Chem. Commun.* **2008**, *47*, 6387; d) M. Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837.

[8] S. H. Wunderlich, P. Knochel, *Angew. Chem.* **2009**, *121*, 1530; *Angew. Chem. Int. Ed.* **2009**, *48*, 1501.

[9] S. H. Wunderlich, M. Kienle, P. Knochel, *Angew. Chem.* **2009**, *121*, 7392; *Angew. Chem. Int. Ed.* **2009**, *48*, 7256.

[10] a) S. H. Wunderlich, P. Knochel, *Angew. Chem.* **2009**, *121*, 9897; *Angew. Chem. Int. Ed.* **2009**, *48*, 9717; b) C. Bolm, J. Legros, J. LePiah, L. Zani, *Chem. Rev.* **2004**, *104*, 6217; c) T. Kauffmann, *Angew. Chem.* **1996**, *108*, 401; *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 386; d) H. Bürger, U. Wannagat, *Monatsh. Chemie* **1963**, *94*, 1007.

[11] a) G. A. Molander, *Chem. Rev.* **1992**, *92*, 29; b) G. A. Molander, *Chem. Rev.* **1996**, *96*, 307; c) A. Knief, A. M. Laval, G. A. Molander, *Chem. Rev.* **1999**, *99*, 745; d) *Lanthanides: Chemistry and uses in Organic Synthesis* (Ed.: S. Kobayashi), Springer, Berlin, **1999**; e) P. G. Steel, *J. Chem. Soc. Perkin Trans. 1* **2001**, 2727; f) S. Kobayashi, M. Sugiura, H. Kitagawa, W. W. L. Lam, *Chem. Rev.* **2002**, *102*, 2227; g) S. Kobayashi, K. Manabe, *Acc. Chem. Res.* **2002**, *35*, 209.

[12] a) T. Imamoto, Y. Sugiyura, N. Takiyama, *Tetrahedron Lett.* **1984**, *25*, 4233; b) T. Imamoto, N. Takiyama, K. Nakamura, *Tetrahedron Lett.* **1985**, *26*, 4763; c) T. Imamoto, Y. Sugiyura, N. Takiyama, T. Hatojima, Y. Kamiya, *J. Am. Chem. Soc.* **1989**, *111*, 4392; d) H. Schumann, M. Glanz, J. Gottfriedsen, S. Dechert, D. Wolff, *Pure Appl. Chem.* **2001**, *73*, 279; e) V. Dimitrov, K. Koslova, M. Genov, *Tetrahedron Lett.* **1996**, *37*, 6787; f) C. Alcaraz, U. Groth, *Angew. Chem.* **1997**, *109*, 2590; *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 2480; g) U. Groth, M. Jeske, *Angew. Chem.* **2000**, *112*, 586; *Angew. Chem. Int. Ed.* **2000**, *39*, 574; h) U. Groth, M. Jeske, *Synlett* **2001**, 129; i) S. Fischer, U. Groth, M. Jeske, T. Schutz, *Synlett* **2002**, 1922; j) W.-D. Z. Li, J.-H. Yang, *Org. Lett.* **2004**, *6*, 1849; k) D. Tsvelikhovsky, D. Gelman, G. A. Molander, J. Blum, *Org. Lett.* **2004**, *6*, 1995; l) M. Shenglof, D. Gelman, G. A. Molander, J. Blum, *Tetrahedron Lett.* **2003**, ***44***, 8593; m) P. Eckenberg, U. Groth, T. Köhler, *Liebigs Ann. Chem.* **1994**, 673; n) M. Hatano, T. Matsuma, K. Ishkihara, *Org. Lett.* **2005**, *7*, 573; o) S. Fukuzawa, T. Fujinami, S. Yamauchi, S. Sakai, *J. Chem. Soc. Perkin Trans. 1* **1986**, 1929; p) F. T. Edelmann, D. M. M. Freckmann, H. Schumann, *Chem. Rev.* **2002**, *102*, 1851.

[13] a) J.-S. Ryu, G. Y. Li, T. J. Marks, *J. Am. Chem. Soc.* **2003**, *125*, 12584; b) I. Aillaud, J. Collin, C. Duhayon, R. Guillot, D. Lyubov, E. Schulz, A. Trifonov, *Chem. Eur. J.* **2008**, *14*, 2189; c) R. Liu, C. Zhang, Z. Zhu, J. Luo, X. Zhou, L. Weng, *Chem. Eur. J.* **2006**, *12*, 6940; d) Q. Shen, W. Huang, J. Wang, X. Zhou, *Organometallics* **2008**, *27*, 301.

[14] a) P. B. Hitchcock, Q.-G. Huang, M. F. Lappert, X.-H. Wei, *J. Mater. Chem.* **2004**, *14*, 3266; b) L. Ma, J. Zhang, R. Cai, Z. Chen, L. Wenig, X. Zhou, *J. Organomet. Chem.* **2005**, *690*, 4926; c) D. Cui, M. Nishiura, Z. Hou, *Angew. Chem. Int. Ed.* **2005**, *44*, 959; d) W. J. Evans, D. B. Rego, J. W. Ziller, *Inorg. Chem.* **2006**, *45*, 3437; e) Y. Wu, S. Wang, X. Zhu, G. Yang, Y. Wei, L. Zhang, H.-B. Song, *Inorg. Chem.* **2008**, *47*, 5503; f) C. Döring, R. Kempe, *Eur. J. Inorg. Chem.* **2009**, 412.

[15] a) A. Krasovskiy, F. Kopp, P. Knochel, *Angew. Chem.* **2006**, *118*, 511; *Angew. Chem. Int. Ed.* **2006**, *45*, 497; b) K. C. Nicolaou, A. Krasovskiy, V. E. Trepanier, D. J.-K. Chen, *Angew. Chem.* **2008**, *120*, 4285; *Angew. Chem. Int. Ed.* **2008**, *47*, 4217; c) A. Metzger, A. Gavryushin, P. Knochel, *Synlett* **2009**, 1433.

[16] B. M. Trost, *Science* **1991**, *254*, 1471.

[17] In the absence of $MgCl_2$, no metalation of aromatic systems like **3a** and **3d** was observed at 0 °C by using $tmp_3La{\cdot}5LiCl$. When these reaction mixtures were warmed to 25 °C, the starting material was completely consumed within 30 min, but no metalated species could be identified. Unfortunately, the metalation of less-activated substrates like anisole or $PhNMe_2$ could not be achieved. For the use of alternative amines, see: C. J. Rohbogner, S. H. Wunderlich, G. C. Clososki, P. Knochel, *Eur. J. Org. Chem.* **2009**, 1781.

[18] R. K. Dieter, *Tetrahedron* **1999**, *55*, 4177.

[19] W. Schlecker, A. Huth, E. Ottow, J. Mulzer, *J. Org. Chem.* **1995**, *60*, 8414.

Received: November 17, 2009