CHEMISTRY
A EUROPEAN JOURNAL

DOI: 10.1002/chem.200901432

Deprotonative Metalation of Functionalized Aromatics Using Mixed Lithium–Cadmium, Lithium–Indium, and Lithium–Zinc Species

Katia Snégaroff,[a] Jean-Martial L'Helgoual'ch,[a] Ghenia Bentabed-Ababsa,[a, c] Tan Tai Nguyen,[a] Floris Chevallier,[a] Mitsuhiro Yonehara,[b] Masanobu Uchiyama,*[b] Aïcha Derdour,[c] and Florence Mongin*[a]

Abstract: In situ mixtures of $CdCl_2$·TMEDA (0.5 equiv; TMEDA = *N*,*N*,*N*′,*N*′-tetramethylethylenediamine) or $InCl_3$ (0.33 equiv) with [Li(tmp)] (tmp = 2,2,6,6-tetramethylpiperidino; 1.5 or 1.3 equiv, respectively) were compared with the previously described mixture of $ZnCl_2$·TMEDA (0.5 equiv) and [Li(tmp)] (1.5 equiv) for their ability to deprotonate anisole, benzothiazole, and pyrimidine. [$(tmp)_3CdLi$] proved to be the best base when used in tetrahydrofuran at room temperature, as demonstrated by subsequent trapping with iodine. The Cd–Li base then proved suitable for the metalation of a large range of aromatics including benzenes bearing reactive functional groups ($CONEt_2$, CO_2Me, CN, COPh) or heavy halogens (Br, I), and heterocycles (from the furan, thiophene, pyrrole, oxazole, thiazole, pyridine, and diazine series). Five-membered heterocycles benefiting from doubly activated positions were similarly dideprotonated at room temperature. The aromatic lithium cadmates thus obtained were involved in palladium-catalyzed cross-coupling reactions or simply quenched with acid chlorides.

Keywords: ab initio calculations · cadmium · cross-coupling · lithium · metalation

Introduction

Lithium bases such as alkyllithiums or hindered lithium dialkylamides have been largely employed for the deproto-metalation of aromatic rings.[1] Even if the less nucleophilic second category is more suitable for the metalation of aromatics bearing reactive functions (e.g., ester or cyano groups) or sensitive π-deficient heterocycles, either extremely low reaction temperatures or in situ electrophilic trapping are required due to the high reactivity of the corresponding (hetero)aryllithiums.

Recourse to softer magnesium diamides can improve the chemoselectivity of deprotonation reactions, but to the detriment of their efficiency.[2] In contrast, enhanced reactivities can be attained by adding to the lithium bases neutral Lewis bases, such as *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA), which are able to simplify their aggregation state.[1]

The use of metal additives to get more efficient or more chemoselective bases is a challenging field. Various types of $[(R)_n(R')_{n'}MLi]$ (M = metal, R, R′ = alkyl, amino, chloro, etc.) compounds already prepared behave as superbases since such species exhibit behaviors that cannot be reproduced by the monometallic compounds on their own. Among them, LIC–KOR (LIC = butyllithium, KOR = potassium *tert*-butoxide) first described by Schlosser[3] and Lochmann,[4] and BuLi–Li(DMAE) (DMAE = 2-dimethylaminoethoxide) introduced by Caubère[5] and developed further by Gros and Fort in the pyridine series[6] are well-known examples of powerful [RR′MLi] mixtures of organolithiums and M alkali-metal alkoxides.

[a] Dr. K. Snégaroff, Dr. J.-M. L'Helgoual'ch, Dr. G. Bentabed-Ababsa, T. T. Nguyen, Dr. F. Chevallier, Prof. F. Mongin
Chimie et Photonique Moléculaires
UMR 6510 CNRS—Université de Rennes 1
Bâtiment 10A, Case 1003, Campus Scientifique de Beaulieu
35042 Rennes Cedex (France)
Fax: (+33) 2-2323-6955
E-mail: florence.mongin@univ-rennes1.fr

[b] M. Yonehara, Prof. M. Uchiyama
The Institute of Physical and Chemical Research, RIKEN
2-1 Hirosawa, Wako-shi, Saitama 351-0198 (Japan)
Fax: (+81) 48-467-2879
E-mail: uchi_yama@riken.jp

[c] Dr. G. Bentabed-Ababsa, Prof. A. Derdour
Laboratoire de Synthèse Organique Appliquée
Faculté des Sciences de l'Université
BP 1524 Es-Senia, Oran 31000 (Algeria)

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.200901432.

More recently, $[(R)_n(R')_{n'}MLi]$-type compounds with M different from an alkali metal have also been described for their metalation ability.[7] These species display a large panel of reactivities, depending on both the metal M and the groups connected to it. By combining soft organometallic compounds with alkali (or alkaline-earth metal) additives, bases have been prepared and used to generate functionalized aromatic compounds. Examples are $[R_2Zn(tmp)Li\cdot(tmeda)]$ (R = *t*Bu, Bu; tmp = 2,2,6,6-tetramethylpiperidino) (described by the groups of Kondo, Uchiyama, Mulvey, and Hevia),[8] $[(tmp)_2Zn]\cdot 2MgCl_2\cdot 2LiCl$,[9] $[(tmp)ZnCl]\cdot LiCl$[10] (Knochel), $[iBu_3Al(tmp)Li]$ (Uchiyama and Mulvey),[11] $[Al(tmp)_3]\cdot 3LiCl$ (Knochel),[12] $[(Me_3SiCH_2)_2Mn(tmp)Li\cdot(tmeda)]$ (Mulvey),[13] and $[MeCu(tmp)(CN)Li_2]$ (Uchiyama and Wheatley).[14]

We recently accomplished the deproto-metalation of a large range of aromatics including heterocycles by using a newly developed lithium–cadmium base, $[(tmp)_3CdLi]$.[15] Herein, the details of our investigations into the choice of the base are described. In addition, different kinds of trapping for the aromatic cadmium species including palladium-catalyzed cross-couplings are recorded.

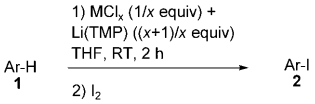
Results and Discussion

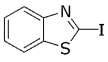
Wittig and co-workers reported the synthesis of $[Ph_3BeLi]$, $[Ph_3MgLi]$, $[Ph_3ZnLi]$, $[Ph_7Zn_2Li_3]$, $[Ph_3CdLi]$, and $[Ph_3HgLi]$ and their ability to deprotonate fluorene in diethyl ether.[16] Quenching with CO_2 and subsequent acidic workup afforded diphenyleneacetic acid in yields of 0 (after 2 weeks reaction time), 47 (after 3 d), 16 (after 10 d), 44 (after 10 d), 64 (after 3 d), and 84% (after 3 d), respectively. In 1951 these results were analyzed as a measure of the dissociation of such complexes into the original diphenylmetal and phenyllithium. The more recent discovery of the basic properties of lithium magnesates[7] and zincates[7,8] led us to consider these results from another angle, and prompted us to study the deproto-metalation of aromatic rings using lithium-metal ate bases with bigger central metals.

In a recent study we showed that the in situ prepared mixture of $ZnCl_2\cdot$TMEDA and 3 equiv of [Li(tmp)] was a 1:1 mixture of [Li(tmp)] and $[(tmp)_2Zn]$.[17] Even if not associated in the form of a zincate, the combination behaves synergically, allowing efficient and chemoselective deprotonation reactions. To seek more efficient and direct methods for introducing functionalities into aromatic rings including heterocycles, we focused on the deprotonative metalation using the corresponding mixtures with cadmium[18] and indium[19] instead of zinc to investigate the effect of a different size of metal ion.

We thus attempted reactions using in situ prepared mixtures of $CdCl_2\cdot$TMEDA[20] or $InCl_3$,[21] and [Li(tmp)] (3 or 4 equiv, respectively; Table 1). Using anisole (**1a**), veratrole (**1b**), benzothiazole (**1c**), and pyrimidine (**1d**) as substrate, the metalation reactions performed in tetrahydrofuran (THF) at room temperature by combining $CdCl_2\cdot$TMEDA (0.50 equiv) and [Li(tmp)] (1.5 equiv), followed by subsequent trapping with elemental iodine after 2 h, proceeded in good yields (71 to 97%). Under the same conditions, the experiments carried out with $InCl_3$ (0.33 equiv) and [Li(tmp)] (1.3 equiv) provided the expected iodo derivatives **2a–c** in medium yields (48 to 57%), but from pyrimidine (**1d**) the corresponding 4,4′-dimer proved to be the sole product formed.

Table 1. Metalation of substrates **1a–d** using different mixtures followed by trapping with I_2.



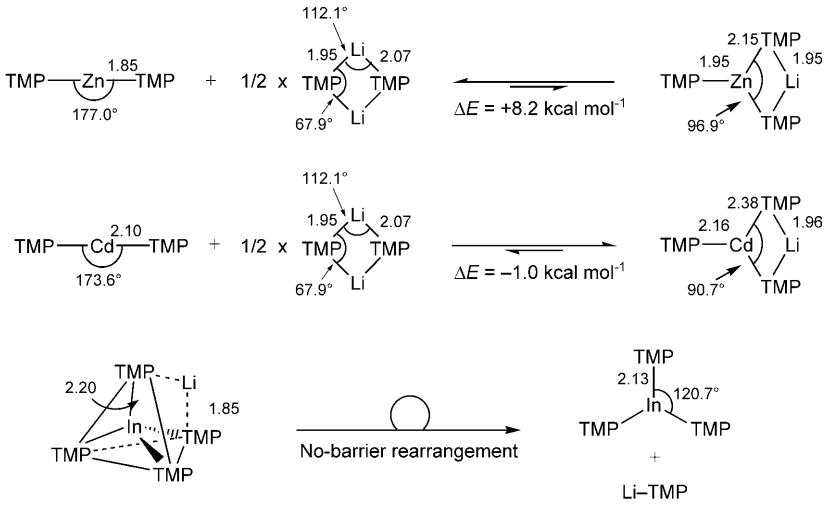
Entry	Substrate **1**		Product **2**		Yield [%] M = Cd[a]	M = In[b]	M = Zn[c]
1		**1a** (R = H) **1b** (R = OMe)		**2a** **2b**	75 79	48 52	84[d] –
2		**1c**		**2c**	97	57	52
3		**1d**		**2d**	71	0	57

[a] The cadmium source was $CdCl_2\cdot$TMEDA ($x = 2$). [b] The indium source was $InCl_3$ ($x = 3$). [c] The zinc source was $ZnCl_2\cdot$TMEDA ($x = 2$). The procedure was as previously described.[17] [d] In ref. [15a] we reported a 30% yield for this reaction, probably due to water-contaminated $ZnCl_2\cdot$TMEDA.

To obtain information about the active species of the new basic mixtures, NMR spectroscopy and DFT studies were carried out. By recording the NMR spectrum of the mixture generated from $CdCl_2\cdot$TMEDA and [Li(tmp)] (3 equiv), it was observed that [Li(tmp)] was not present, and the formation of the lithium cadmate $[(tmp)_3CdLi]$ was inferred. This possibility, different to what has been observed with zinc, was supported by the B3LYP-calculated equilibrium between [Li(tmp)] and $[(tmp)_2Cd]$ on one side and $[(tmp)_3CdLi]$ on the other.[15a]

Various attempts to get information about the structure of the species formed from $InCl_3$ and [Li(tmp)] (4 equiv) by NMR spectroscopy were unsuccessful. DFT calculations were performed for the equilibrium between [Li(tmp)] and $[(tmp)_3In]$ on one side and $[(tmp)_4InLi]$ on the other side. Although the structure of $[(tmp)_4InLi]$ was obtained at the HF/3-21G level, the re-optimization of this complex at the higher level such as B3LYP/6-31G* led to the collapse of the indium-ate complex. We confirmed that the tetracoordi-

nated ate structure is not the global minimum by making an artificial ideal tetrahedral geometry of [(tmp)$_4$InLi] (Scheme 1). Geometry optimization then caused smooth migration of one of the tmp ligands without energy barrier,



Scheme 1. Bond lengths (in Å) at B3LYP/6-31G* (SVP basis set for Zn, Cd, or In).

and dissociation of the ate structure into a trigonal non-ate complex and [Li(tmp)]. Recourse to the theoretical calculation indicated that the lithium indate was unlikely to form. Similar results experimentally observed in the case of pyrimidine (**1d**) by using either the In–Li base or [Li(tmp)][22] also suggested the presence of organolithiums in the reaction mixture.

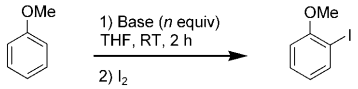
The synergy of the reactions using [(tmp)$_3$CdLi] was demonstrated with anisole (**1a**) as substrate using either [Li(tmp)] (1 equiv) or [(tmp)$_2$Cd] (1 equiv). Under the same reaction conditions, the iodide **2a** was isolated in 9% yield using the former, and did not form using the latter, whereas a 75% yield was obtained using the mixed base. A possible effect of lithium chloride[23] or TMEDA[24] on the course of the reaction was discarded. Indeed, using [Li(tmp)] (1 equiv) with either LiCl (2 equiv) or TMEDA (1 equiv) or both did not result in significant changes (14% yield in the presence of TMEDA alone, but only traces of **2a** identified in the presence of LiCl).

Since lithium zincates bearing alkyl and amino groups are efficient bases,[7,8] [(tmp)$_3$CdLi] was compared with [BuCd(tmp)$_2$Li], [Bu$_2$Cd(tmp)Li], and [Bu$_3$CdLi] (as well as with the corresponding zinc–lithium mixtures). Using anisole (**1a**) as substrate, metalation took place but in decidedly lower yields, decreasing as the number of tmp groups also decreased (Table 2). These results strongly suggested that [(tmp)$_3$CdLi] was the best species rather than other lithium cadmates for the deprotonation reaction.

The deprotonation–trapping sequence was then applied to functionalized benzenes (Table 3). Due to their electrophilic functional group, *N*,*N*-diethylbenzamide (**1e**),[2] methyl benzoate (**1f**),[2,8a] and benzonitrile (**1g**)[8a] have scarcely been metalated at room temperature. When possible, for example, using [(tmp)$_2$Mg][2] or [*t*Bu$_2$Zn(tmp)Li][8a] in THF, an excess of base has to be used. The compatibility of the Cd–Li base (0.5 equiv) with reactive functional groups allowed the expected iodides **2e–g** to be formed in good yields under the conditions optimized above (entries 1 and 2). The ketone function was still tolerated in the reaction, as shown from benzophenone (**1h**; entry 3). The chemoselective accumulation of the metalated derivatives of 4-bromoanisole (**1i**), 4-iodoanisole[25] (**1j**), and methyl 4-bromobenzoate (**1k**) also proved feasible, with complete regioselectivity for the position far from the heavy halogen atom (entries 4 and 5).

We next demonstrated that the cadmate base was suitable for the metalation of a large

Table 2. Metalation of substrate **1a** using different mixtures followed by trapping with I$_2$.



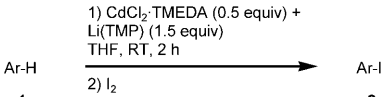
1a **2a**

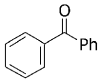
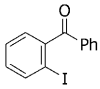
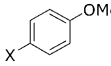
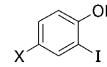
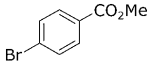
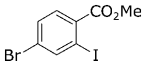
Entry	Base	Yield [%]			
		M = Cd		M = Zn	
		0.5 equiv	1 equiv	0.5 equiv	1 equiv
1	[(tmp)$_3$MLi][a]	75	–	84	–
2	[BuM(tmp)$_2$Li]	34	57	–	79
3	[Bu$_2$M(tmp)Li]	7	14	–	20
4	[Bu$_3$MLi]	9	–	–	0

[a] [(tmp)$_3$CdLi] or [Li(tmp)]+[(tmp)$_2$Zn].

range of aromatic heterocycles (Table 4). Benzo[*b*]thiophene (**1l**) has previously been magnesated at room temperature using [(tmp)MgCl]·LiCl,[26] and zincated using the in situ prepared mixture of [(tmp)$_2$Zn] and [Li(tmp)].[17a] Its cadmation was achieved in an excellent yield by using the Cd–Li base, as demonstrated by trapping with iodine. Benzo[*b*]furan (**1m**) behaved similarly to extend the list of benzo[*b*]furan organometallics prepared at room temperature[27] (entry 1). The room-temperature zincation of benzothiazole (**1c**) and benzoxazole (**1n**) using either [(tmp)$_2$Zn]·2MgCl$_2$·2LiCl[9a] or the in situ prepared mixture of [(tmp)$_2$Zn] and [Li(tmp)][17a] has previously been reported. The cadmation proceeded quantitatively starting from benzothiazole (**1c**), whereas a lower 63% yield was noted in the case of benzoxazole (**1n**), probably in relation to the in

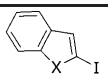
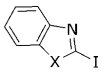
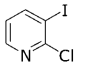
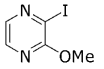
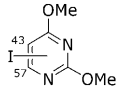
Table 3. Metalation of substrates **1e–k** using [(tmp)$_3$CdLi] followed by trapping with I_2.



Entry	Substrate **1**		Product **2**		Yield [%]
1		**1e** (R = NEt_2) **1f** (R = OMe)		**2e** (R = NEt_2) **2f** (R = OMe)	91 62 (89)[a]
2		**1g**		**2g**	68
3		**1h**		**2h**	66
4		**1i** (X = Br) **1j** (X = I)		**2i** (X = Br) **2j** (X = I)	97 83
5		**1k**		**2k**	60

[a] Using $CdCl_2$·TMEDA (1 equiv) + [Li(tmp)] (3 equiv).

Table 4. Metalation of substrates **1c,l–q** using [(tmp)$_3$CdLi][a] followed by trapping with I_2.

Entry	Substrate **1**		Product **2**		Yield [%]
1		**1l** (X = S) **1m** (X = O)		**2l** (X = S) **2m** (X = O)	97 84
2		**1c** (X = S) **1n** (X = O)		**2c** (X = S) **2n** (X = O)	97 63
3		**1o**		**2o**	52
4		**1p**		**2p**	47
5		**1q**		**2q/2′q**	84

[a] Conditions: $CdCl_2$·TMEDA (0.5 equiv) + [Li(tmp)] (1.5 equiv), THF, RT, 2 h.

situ opening of the formed 2-metalated species to give 2-isocyanophenolate (entry 2).[28]

Due to easy elimination of the metal halide to give pyridyne,[29] deproto-metalation of 2-chloropyridine (**1o**) can barely be achieved at room temperature. Chemoselectivity was present upon reaction with the sterically hindered cadmate, but not regioselectivity,[30] and the main iodide **2o** resulting from the metalation at the chloro-adjacent site was only isolated in 52% yield (Table 4, entry 3).

The good chemoselectivity observed during the Cd–Li base-mediated deprotonation prompted us to attempt to use it for the metalation of diazines, which are prone to nucleophilic addition.[31] Whereas [Li(tmp)] has to be used at −75 °C to avoid the formation of a dimer,[31] the mixed base can be employed at room temperature for the cadmation of methoxypyrazine (**1p**), and the metalated heterocycle is subsequently intercepted by iodine (Table 4, entry 4). The situation becomes more complex, for example, when using 2,4-dimethoxypyrimidine (**1q**) since the 5-position can be attacked using [Li(tmp)] at −75 °C,[31] and the 6-position using [(tmp)MgCl]·LiCl at room temperature.[32] The [(tmp)$_3$CdLi]-promoted reaction took place in a satisfying yield using the Cd–Li base, but with a complete lack of regioselectivity, leading to the 5- and 6-iodo derivatives **2q** and **2′q** in a 43:57 ratio (entry 5).

N-Boc pyrrole (**1r**; Boc = *tert*-butoxycarbonyl) was converted into the iodide **2r** in 68% yield.[33] As we found diiodide **3r** among the byproducts detected in the crude, we were encouraged to attempt the use of 1 equiv of base instead of 0.5 equiv. Under the same reaction conditions, the dimetalation[34] was favored, and diiodide **3r** was isolated in 60% yield (Table 5, entries 1 and 2). Since the introduction of two substituents in one step is challenging, the behavior of other five-membered aromatic heterocycles benefiting from doubly activated positions was studied (Table 5, entries 3–5). Thiazole (**1s**)[17a,35] and thiophene (**1t**)[26,35,36] undergo monodeprotonation at room temperature when exposed to DAMgCl (DA = diisopropylamino),[35] [Bu_3MgLi]·TMEDA,[36] or [(tmp)MgCl]·LiCl.[26] When subjected to the in situ prepared mixture of [$(tmp)_2Zn$] and [Li(tmp)],[17a] the dimetalation of thiazole (**1s**) was not avoided, even when using $^1/_3$ equiv of base;

Table 5. Metalation of substrates **1r–u** using [(tmp)$_3$CdLi] followed by trapping with I_2.

Entry	Substrate **1**		Product **2**[a] or **3**[b]		Yield [%]
1		**1r**		**2r**	68
2	**1r**			**3r**	60
3		**1s**		**3s**	50
4		**1t**		**3t**	74
5		**1u**		**3u**	81

[a] Metalation conditions: $CdCl_2$·TMEDA (0.5 equiv) + [Li(tmp)] (1.5 equiv), THF, RT, 2 h. [b] Metalation conditions: $CdCl_2$·TMEDA (1 equiv) + [Li(tmp)] (3 equiv), THF, RT, 2 h.

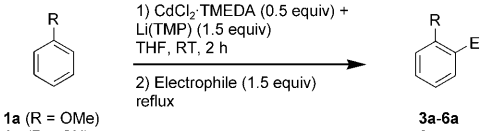
using 1 equiv of [(tmp)$_3$CdLi] enabled diiodide **3s** to be isolated in 50% yield. Better yields of 74 and 81% were obtained for the thiophene diiodides **3t** and **3u**, respectively, under the same reaction conditions. Furan is amenable to magnesation at room temperature using either [Bu_4MgLi_2][27a] or [(tmp)MgCl·LiCl.][26] When using [(tmp)$_3$CdLi], its monocadmation occurred but attempts to dimetalate it were disappointing, in contrast to what has recently been observed using the stronger [(tmeda)Na(CH_2SiMe_3)(tmp)Mg(tmp)].[37]

Electrophiles known to react with alkali and alkali-earth organometallic compounds were then employed to trap the cadmate generated from anisole (**1a**; Table 6). Reaction with 4-(trifluoromethyl)benzaldehyde (entry 1), trimethylsilyl chloride (entry 2), phenyl disulfide (entry 3), and allyl bromide (entry 4) at the reflux temperature of THF afforded the expected functionalized anisoles **3a**–**6a**, but in moderate yields ranging from 22 to 35%. The cadmate formed from benzonitrile (**1g**) did not react with 4-(trifluoromethyl)benzaldehyde, trimethylsilyl chloride, or phenyl disulfide under the same reaction conditions, and the allyl derivative **6g** was isolated in a low 30% yield.

To extend the synthetic applications of the aryl- and heteroarylcadmates, it was decided to involve them in palladium-catalyzed cross-coupling reactions with aromatic bromides. To our knowledge, cross-coupling reactions using cadmium compounds have only been described starting from organocadmium chlorides, and are known to produce, in addition to the expected products, homocoupling products derived from both substrates.[38] The first reactions of our optimization study (Table 7) were carried out at the reflux temperature of THF using the 2-metalated thiophene or methyl benzoate, 2-bromopyridine, and a catalytic amount of palladium(0) tetrakis(triphenylphosphine); the expected products **4t1**,**e** were produced in moderate to good yields (entries 1 and 2).

Because the results of reactions performed with palladium(0) tetrakis(triphenylphosphine)[39] are dependent on the quality of the latter, we searched out a procedure using in situ generated palladium(0). Reactions were then attempted to reproduce the result obtained from 2-metalated thiophene and 2-bromopyridine. Palladium(II) chloride (2 mol%) was the first precatalyst used for this purpose, and monodentate triphenylphosphine (4 mol%; Table 7, entry 3) and bidentate 1,1′-bis(diphenylphosphino)ferrocene (dppf, 2 mol%; entry 4) were compared. The latter proved superior, with triphenylphosphine only allowing the cross-coupling when used in a larger amount (10 mol%; entry 5). We then turned to the cross-coupling between 2-metalated furan and 4-bromoanisole. Since the reaction failed using

Table 6. Metalation of substrates **1a**,**g** using [(tmp)$_3$CdLi] followed by trapping using 4-(trifluoromethyl)benzaldehyde, trimethylsilyl chloride, phenyl disulfide, and allyl bromide.



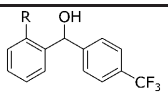
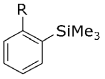
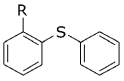
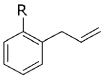
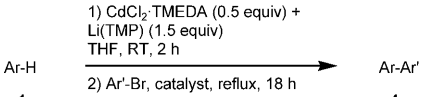
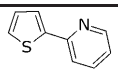
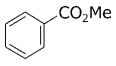
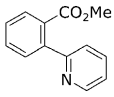
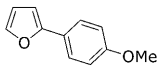
Entry	Substrate	Electrophile	Product		Yield [%]
1	**1a**	4-(F_3C)C_6H_4CHO		**3a**	35
	1g			**3g**	0
2	**1a**	Me_3SiCl		**4a**	22
	1g			**4g**	0
3	**1a**	PhSSPh		**5a**	27
	1g			**5g**	0
4	**1a**	$BrCH_2CH{=}CH_2$		**6a**	35
	1g			**6g**	30

Table 7. Metalation of substrates **1t**,**e**,**v** using [(tmp)$_3$CdLi] followed by cross-coupling.



Entry	Substrate **1**	Catalyst	Product **4**		Yield [%]
1	 **1t**	[$Pd(PPh_3)_4$] (2 mol%)		**4t1**	72
2	 **1e**	[$Pd(PPh_3)_4$] (4 mol%)		**4e**	35
3	**1t**	$PdCl_2$ (2 mol%), PPh_3 (4 mol%)	**4t1**		0[a]
4	**1t**	$PdCl_2$ (2 mol%), dppf (2 mol%)	**4t1**		26
5	**1t**	$PdCl_2$ (2 mol%), PPh_3 (10 mol%)	**4t1**		38
6	 **1v**	$PdCl_2$ (2 mol%), dppf (2 mol%)		**4v1**	0
7	**1v**	$Pd(OAc)_2$ (2 mol%), dppf (2 mol%)	**4v1**		10
8	**1v**	$Pd(OAc)_2$ (4 mol%), dppf (2 mol%)	**4v1**		51
9	**1v**	$Pd(OAc)_2$ (6 mol%), dppf (2 mol%)	**4v1**		83

[a] No improvement was observed using [$PdCl_2(PPh_3)_2$] (2 mol%).

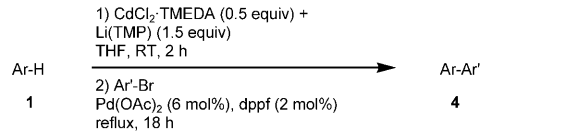
palladium(II) chloride (2 mol%) in the presence of dppf (2 mol%; entry 6), we suspected an inefficient reduction of palladium(II) chloride, and therefore decided to test the use of another precatalyst. We chose palladium(II) acetate, for which mixtures with tertiary phosphines are known to spontaneously generate palladium(0) complexes.[40] A low 10% yield was obtained by using a 1:1 $Pd(OAc)_2$/dppf ratio (2 mol% each; entry 7), but increasing this ratio to 2:1 and 3:1 resulted in improved yields of 51 and 83%, respectively (entries 8 and 9).

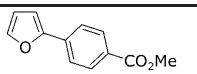
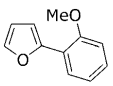
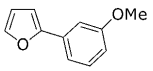
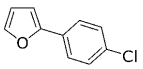
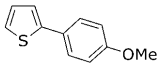
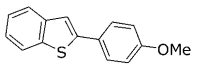
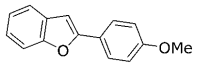
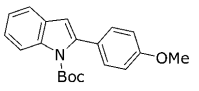
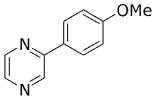
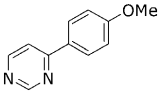
To evaluate the scope of this reaction, experiments employing 2-metalated furan (Table 8, entries 1–4) or thiophene (entry 5), and different aryl bromides were first conducted under the same reaction conditions. The expected 2-arylated heterocycles **4v2**–**4v5** and **4t2** were isolated, albeit in medium yields due to concomitant formation of homocoupling products. Similar results were noted for the deprotonation/cross-coupling sequences starting from the other aromatic heterocycles **1l**,**m**,**w**,**x** (entries 6–9). From pyrimidine (**1d**), a lower yield (29%) was obtained, probably in relation to the lower stability of the metalated species (entry 10).

It is acknowledged that organocadmium halides can be trapped by acid chlorides to provide ketones.[18] This possibility was attempted from the furanylcadmate using aliphatic acid chlorides, and the results clearly show that nonenolizable electrophiles are more suitable for the reactions (Table 9, entries 1–3). Methyl chloroformate allowed direct access to furan ester **5v4**, albeit in a low yield that could be due to the volatility of the product (entry 4).

Gilman and Nelson reported in 1936 the reaction of diphenylcadmium with benzenesulfonyl chloride to give a

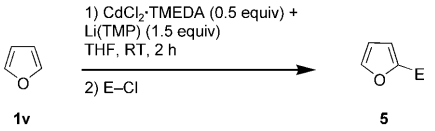
Table 8. Metalation of substrates **1d**,**v**,**t**,**l**,**m**,**w**,**x** using [$(tmp)_3CdLi$] followed by cross-coupling.

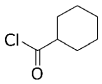
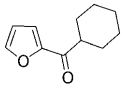
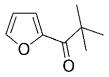
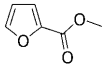
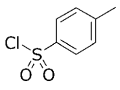
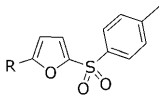
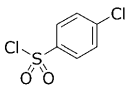
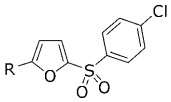
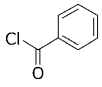
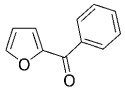
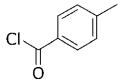
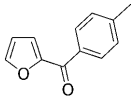
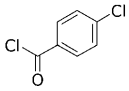
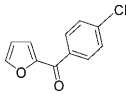
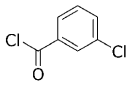
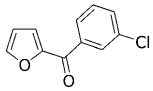
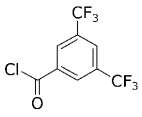


Entry	Substrate **1**		Product **4**		Yield [%]
1		**1v**		**4v2**	41
2		**1v**		**4v3**	42
3		**1v**		**4v4**	57
4		**1v**		**4v5**	46
5		**1t**		**4t2**	63[a]
6		**1l**		**4l**	50[b]
7		**1m**		**4m**	42[c]
8		**1w**		**4w**	56
9		**1x**		**4x**	59
10		**1d**		**4d**	29

[a] 2,5-Bis(4-methoxyphenyl)thiophene was isolated in 16% yield. [b] 2,2′-Bis(benzo[*b*]thiophene) was isolated in 25% yield. [c] 2,2′-Bis(benzo[*b*]furan) was isolated in 12% yield.

Table 9. Metalation of substrate **1v** using [$(tmp)_3CdLi$] followed by trapping with acid chlorides.



Entry	E–Cl	Product **5**		Yield [%]
1			**5v1**	0
2			**5v2**	21
3			**5v3**	60
4			**5v4**	15
5			**5v5** (R = H) **5′v5** (R = Cl)	17[a] 5
6			**5v6** (R = H) **5′v6** (R = Cl)	18[a] 6
7			**5v7**	76
8			**5v8**	42
9			**5v9**	49
10			**5v10**	51
11			**5v11**	63[b]

[a] 2-Chlorofuran and 2,5-dichlorofuran could form and be evaporated under reduced pressure (b.p. 77[42a] and 115 °C,[42b] respectively). [b] Bis-[3,5-bis(trifluoromethyl)phenyl] furan-2,5-diyl diketone (**5′v11**) also formed, and was isolated in 3% yield.

mixture of diphenylsulfone, benzenesulfinic acid, and chlorobenzene.[41] The furanylcadmate was involved in similar reactions with tosyl chloride and 4-chlorobenzenesulfonyl chloride. The expected diarylsulfones **5v5–5v6** were isolated in moderate yields (17–18%; Table 9, entries 5 and 6). Concomitant formation of 2-chlorofuran and 2,5-dichlorofuran was suspected, even if not isolated due to their volatility.[42] Indeed, 5-(arylsulfonyl)-2-chlorofurans **5′v5–5′v6** were also accessed in 5–6% yield, probably through electrophilic trapping of the 2,5-dimetalated species through the two different modes. The disulfone was not detected, which suggests that benzenesulfonyl chlorides more likely act as chlorinating agents.

Different diarylketones were finally obtained in medium to good yields when different benzoyl chlorides were chosen to intercept the furanylcadmate (Table 9, entries 7–11).

Conclusion

In summary, efficient deprotonative cadmation reactions of functionalized aromatics including heterocycles were realized using the newly developed (tmp)Cd-ate base. The latter proved compatible with reactive functional groups ($CONEt_2$, CO_2Me, CN, COPh), heavy halogens (Br, I), and sensitive aromatic aza-heterocycles. Heterocycles benefiting from doubly activated positions were similarly dideprotonated at room temperature.

The aromatic lithium cadmates were evidenced by using iodine; the species were then involved in palladium-catalyzed cross-coupling reactions or simply quenched with acid chlorides to extend the synthetic applications of the method.

Due to the toxicity of cadmium compounds we are attempting to develop new mixed lithium-metal bases of ate-type that are still efficient and chemoselective, profiting from the present study.

Experimental Section

All of the reactions occurred in Schlenk tubes under an argon atmosphere. THF was distilled over sodium/benzophenone, and CH_2Cl_2 was distilled over CaH_2. Nuclear magnetic resonance spectra were acquired on Bruker ARX-200 (200 and 50 MHz for ^1H and ^{13}C, respectively) and Bruker AC-300 (300 and 75 MHz for ^1H and ^{13}C, respectively) spectrometers. High-resolution mass spectra measurements were performed at the Centre Régional de Mesures Physiques de l'Ouest (CRMPO) in Rennes using a Micromass MS/MS ZABSpec TOF instrument in EI mode. Liquid chromatography separations were achieved on silica gel Merck Geduran Si 60 (40–63 mesh).

$CdCl_2$·TMEDA:[20] TMEDA (3.25 mL, 22 mmol) was added to a stirred suspension of flame-dried $CdCl_2$ (2.0 g, 11 mmol) in dry CH_2Cl_2 (50 mL). The mixture was heated at reflux for 2 h under argon before it was evaporated under reduced pressure. The residual solid was washed under argon with CH_2Cl_2 (20 mL) and ethanol (20 mL). Solvent evaporation under vacuum gave $CdCl_2$·TMEDA (2.4 g, 73%) as a white solid. ^1H NMR ([D$_6$]DMSO, 200 MHz): $\delta = 2.29$ (s, 12H), 2.45 ppm (s, 4H); ^{13}C NMR ([D$_6$]DMSO, 75 MHz): $\delta = 46.6$ (4C), 56.0 ppm (2C).

General procedure for the deprotocadmation (using [(tmp)$_3$CdLi])–iodination of aromatics: BuLi (about 1.6 M hexanes solution, 6.0 mmol) was added to a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (1.0 mL, 6.0 mmol) in THF (5 mL). After the solution had been stirred for 15 min at 0 °C, $CdCl_2$·TMEDA (0.60 g, 2.0 mmol) was added, and the mixture was stirred for 15 min at this temperature before introduction of the substrate (4.0 mmol). After the mixture had been stirred for 2 h at room temperature, a solution of I_2 (1.5 g, 6.0 mmol) in THF (5 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of $Na_2S_2O_3$ (5 mL) and extraction with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure before being purified by means of column chromatography on silica gel.

2-Chloro-3-iodopyridine (2o): Yellow solid; m.p. 98–100 °C; ^1H NMR ($CDCl_3$, 200 MHz): $\delta = 6.96$ (dd, $J = 4.7$, 7.7 Hz, 1H), 8.20 (dd, $J = 1.7$, 7.7 Hz, 1H), 8.41 ppm (dd, $J = 1.7$, 4.7 Hz, 1H). These data are consistent with those obtained for a commercial sample.

2-Iodo-3-methoxypyrazine (2p): Pale yellow solid; m.p. 62 °C; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 4.02$ (s, 3H), 7.93 (d, $J = 2.7$ Hz, 1H), 7.98 ppm (d, $J = 2.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 55.1$, 107.7, 137.4, 139.5, 159.3 ppm; elemental analysis calcd (%) for $C_5H_5IN_2O$: C 25.45, H 2.14, N 11.87; found: C 25.49, H 2.12, N 11.54.

5-Iodo-2,4-dimethoxypyrimidine (2q): White solid; m.p. 99–100 °C; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 3.98$ (s, 3H), 4.03 (s, 3H), 8.44 ppm (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 55.1$, 55.2, 77.2, 164.8, 165.4, 168.8 ppm. The ^1H NMR data are consistent with the literature.[43]

6-Iodo-2,4-dimethoxypyrimidine (2′q): White solid; m.p. 72 °C; ^1H NMR ($CDCl_3$, 300 MHz,): $\delta = 3.93$ (s, 3H), 3.98 (s, 3H), 6.87 ppm (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 54.1$, 55.3, 112.5, 127.8, 163.6, 170.6 ppm.[44]

General procedure for the dideprotocadmation (using [(tmp)$_3$CdLi])–diiodination of aromatics: BuLi (about 1.6 M hexanes solution, 6.0 mmol) was added to a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (1.0 mL, 6.0 mmol) in THF (5 mL). After the solution had been stirred for 15 min at 0 °C, $CdCl_2$·TMEDA (0.60 g, 2.0 mmol) was added, and the mixture was stirred for 15 min at this temperature before introduction of the substrate (2.0 mmol). After the mixture had been stirred for 2 h at room temperature, a solution of I_2 (1.5 g, 6.0 mmol) in THF (5 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of $Na_2S_2O_3$ (5 mL) and extraction with CH_2Cl_2 (3 × 20 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure before being purified by means of column chromatography on silica gel.

General procedure for the deprotocadmation (using [(tmp)$_3$CdLi]) of aromatics followed by trapping with different electrophiles: BuLi (about 1.6 M hexanes solution, 3.0 mmol) was added to a stirred, cooled (0 °C) solution of 2,2,6,6-tetramethylpiperidine (0.51 mL, 3.0 mmol) in THF (3 mL). After the solution had been stirred for 15 min at 0 °C, $CdCl_2$·TMEDA (0.30 g, 1.0 mmol) was added, and the mixture was stirred for 15 min at this temperature before introduction of the substrate (2.0 mmol). After the mixture had been stirred for 2 h at room temperature, the electrophile (3.0 mmol) was added at 0 °C. The mixture was stirred overnight at 60 °C before addition of brine (5 mL) and extraction with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure before being purified by means of column chromatography on silica gel.

(2-Methoxyphenyl)[4-(trifluoromethyl)phenyl]methanol (3a): Yellow oil; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 3.13$ (d, $J = 5.7$ Hz, 1H), 3.82 (s, 3H), 6.08 (d, $J = 5.4$ Hz, 1H), 6.91 (d, $J = 8.2$ Hz, 1H), 6.97 (td, $J = 0.9$, 7.5 Hz, 1H), 7.22 (dd, $J = 1.6$, 7.5 Hz, 1H), 7.30 (m, 1H), 7.51 (d, $J = 8.2$ Hz, 2H), 7.58 ppm (d, $J = 8.3$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = 55.4$, 71.8, 110.8, 120.9, 124.2 (q, $J_F = 272$ Hz), 125.1 (q, $J_F = 3.8$ Hz, 2C), 126.7, 127.8, 129.1, 129.2 (q, $J_F = 32.3$ Hz, 2C), 131.2, 147.3, 156.6 ppm. These data are consistent with the literature.[45]

2-(Trimethylsilyl)anisole (4a): Colorless oil; ^1H NMR ($CDCl_3$, 300 MHz): $\delta = 0.27$ (s, 9H), 3.81 (s, 3H), 6.84 (d, $J = 8.2$ Hz, 1H), 6.96 (dt, $J = 0.9$, 7.3 Hz, 1H), 7.36 ppm (m, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta = -1.0$

(3C), 55.0, 109.5, 120.4, 127.9, 130.7, 134.9, 164.3 ppm. These data are consistent with the literature.[46]

2-(Phenylthio)anisole (5a): Colorless liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.89 (s, 3H), 6.90 (m, 2H), 7.10 (dd, J=1.7, 7.7 Hz, 1H), 7.23–7.30 (m, 2H), 7.33–7.39 ppm (m, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=55.9, 110.8, 121.2, 124.1, 127.05, 128.3, 129.1 (2C), 131.5 (2C), 131.6, 134.4, 157.3 ppm. These data are consistent with the literature.[47]

2-Allylanisole (6a): Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.40 (d, J=6.6 Hz, 2H), 3.84 (s, 3H), 5.06 (m, 2H), 6.02 (m, 1H), 6.87 (d, J=8.2 Hz, 1H), 6.93 (dd, J=1.0, 7.4 Hz, 1H), 7.17 (m, 1H), 7.23 ppm (dd, J=1.5, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=34.2, 55.3, 110.3, 115.3, 120.5, 127.3, 128.6, 129.7, 137.0, 157.2 ppm. These data are consistent with the literature.[48]

2-Allylbenzonitrile (6g): Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.62 (d, J=6.7 Hz, 2H), 5.11–5.17 (m, 2H), 5.91–6.00 (m, 1H), 7.30–7.35 (m, 2H), 7.52–7.55 (m, 1H), 7.63 ppm (d, J=7.6 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=38.5, 112.5, 117.4, 117.9, 126.8, 129.7, 132.8, 132.9, 134.9, 143.8 ppm. These data are consistent with the literature.[49]

General procedure for the deprotocadmation (using [(tmp)$_3$CdLi])–cross-coupling ([Pd(PPh$_3$)$_4$]) of aromatics: BuLi (about 1.6 M hexanes solution, 6.0 mmol) was added to a stirred, cooled (0°C) solution of 2,2,6,6-tetramethylpiperidine (1.0 mL, 6.0 mmol) in THF (5 mL). After the solution had been stirred for 15 min at 0°C, $CdCl_2$·TMEDA (0.60 g, 2.0 mmol) was added, and the mixture was stirred for 15 min at this temperature before introduction of the substrate (4.0 mmol). After the mixture had been stirred for 2 h at room temperature, the heterocyclic bromide (6.0 mmol) and [Pd(PPh$_3$)$_4$] were added to the reaction mixture, which was stirred for 18 h at reflux. The solution was cooled before addition of water (0.5 mL) and filtration over Celite. The mixture was dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified by means of flash chromatography on silica gel.

2-(Thiophen-2-yl)pyridine (4t1): White solid; m.p. 61–63°C. The physical and spectroscopic data are consistent with those obtained for a commercial sample.

Methyl 2-(pyridin-2-yl)benzoate (4e): Colorless oil; ^{1}H NMR ($CDCl_3$, 200 MHz): δ=3.64 (s, 3H), 7.20 (ddd, J=1.2, 5.0, 7.6 Hz, 1H), 7.48 (m, 4H), 7.70 (td, J=1.8, 7.7 Hz, 1H), 7.78 (d, J=7.6 Hz, 1H), 8.60 ppm (dd, J=1.0, 5.0 Hz, 1H). These data are consistent with the literature.[50] ^{13}C NMR ($CDCl_3$, 50 MHz): δ=51.9, 122.0, 122.6, 128.2, 129.6, 129.7, 131.0, 131.5, 136.2, 140.8, 148.9, 158.4, 169.2 ppm.

General procedure for the deprotocadmation (using [(tmp)$_3$CdLi])–cross-coupling (Pd(OAc)$_2$+dppf) of aromatics: BuLi (about 1.6 M hexanes solution, 6.0 mmol) was added to a stirred, cooled (0°C) solution of 2,2,6,6-tetramethylpiperidine (1.0 mL, 6.0 mmol) in THF (5 mL). After the solution had been stirred for 15 min at 0°C, $CdCl_2$·TMEDA (0.60 g, 2.0 mmol) was added and the mixture was stirred for 15 min at this temperature before introduction of the substrate (4.0 mmol). After the mixture had been stirred for 2 h at room temperature, the heterocyclic bromide (6.0 mmol), $Pd(OAc)_2$ and dppf were added to the reaction mixture, which was stirred for 18 h at reflux. The solution was cooled before addition of water (0.5 mL) and filtration over Celite. The mixture was dried over $MgSO_4$, filtered, concentrated under reduced pressure, and purified by means of flash chromatography on silica gel.

Methyl 4-(furan-2-yl)benzoate (4v2): Orange solid; m.p. 114°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.92 (s, 3H), 6.50 (dd, J=1.5, 3.4 Hz, 1H), 6.78 (br d, J=3.4 Hz, 1H), 7.51 (br d, J=1.5 Hz, 1H), 7.72 (d, J=8.7 Hz, 2H), 8.05 ppm (d, J=8.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=52.2, 107.4, 112.1, 123.5 (2C), 128.7, 130.2 (2C), 134.9, 143.3, 153.0, 166.9 ppm. These data are consistent with the literature.[51]

2-(2-Methoxyphenyl)furan (4v3): Brown liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.95 (s, 3H), 6.49 (dd, J=1.8, 3.3 Hz, 1H), 6.94–7.05 (m, 3H), 7.24 (m, 1H), 7.46 (dd, J=0.6, 1.7 Hz, 1H), 7.85 ppm (dd, J=1.7, 7.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=55.5, 109.9, 111.1, 111.7, 120.1, 120.9, 126.1, 128.1, 141.2, 150.4, 155.4 ppm. These data are consistent with the literature.[52]

2-(3-Methoxyphenyl)furan (4v4): Brown liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.72 (s, 3H), 6.34 (dd, J=1.8, 3.4 Hz, 1H), 6.53 (dd, J=0.7, 3.4 Hz, 1H), 6.70 (m, 1H), 7.15 (m, 3H), 7.34 ppm (dd, J=0.7, 1.8 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=55.3, 105.3, 109.1, 111.6, 113.2, 116.4, 129.7, 132.2, 142.1, 153.8, 159.9 ppm. These data are consistent with the literature.[53]

2-(4-Chlorophenyl)furan (4v5): Yellow solid; m.p. 65–66°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=6.64 (dd, J=0.7, 3.4 Hz, 1H), 6.78 (dd, J=1.8, 3.4 Hz, 1H), 7.35 (d, J=8.8 Hz, 2H), 7.47 (dd, J=0.7, 1.8 Hz, 1H), 7.60 ppm (dd, J=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=105.4, 111.8, 125.0 (2C), 128.8 (2C), 126.0, 132.9, 142.3, 152.9 ppm. These data are consistent with the literature.[54]

2-(4-Methoxyphenyl)thiophene (4t2): Brown solid; m.p. 104°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.84 (s, 3H), 6.92 (d, J=8.8 Hz, 2H), 7.05 (dd, J=3.6, 5.0 Hz, 1H), 7.21 (m, 2H), 7.54 ppm (d, J=8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=55.1, 114.4 (2C), 122.2, 124.0, 127.4, 127.4, 128.0 (2C), 144.5, 159.3 ppm. These data are consistent with the literature.[55]

2-(4-Methoxyphenyl)benzo[*b*]thiophene (4l): White solid; m.p. 200°C; ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ=3.81 (s, 3H), 7.04 (d, J=8.7 Hz, 2H), 7.34 (m, 2H), 7.76 (m, 4H), 7.94 ppm (m, 1H); ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ=55.2, 114.5 (2C), 118.5, 122.3, 123.3, 124.1, 124.2, 124.6, 127.3 (2C), 138.1, 140.6, 143.1, 159.5 ppm. These data are consistent with the literature.[56]

2-(4-Methoxyphenyl)benzo[*b*]furan (4m): White solid; m.p. 153°C; ^{1}H NMR ([D$_6$]DMSO, 300 MHz): δ=3.82 (s, 3H), 7.06 (d, J=9.0 Hz, 2H), 7.26 (m, 3H), 7.60 (m, 2H), 7.85 ppm (d, J=9.0 Hz, 2H); ^{13}C NMR ([D$_6$]DMSO, 75 MHz): δ=55.2, 100.1, 110.8, 114.4 (2C), 120.7, 122.3, 123.3, 123.9, 126.2 (2C), 129.0, 153.9, 155.3, 159.7 ppm. These data are consistent with the literature.[57]

***N*-Boc-2-(4-methoxyphenyl)indole (4w)**: Beige solid; m.p. 87–88°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.26 (s, 9H), 3.73 (s, 3H), 6.41 (br s, 1H), 6.83 (d, J=8.8 Hz, 2H), 7.10–7.27 (m, 4H), 7.43 (m, 1H), 8.11 ppm (m, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=27.7 (3C), 55.4, 83.4, 109.6, 113.3 (2C), 115.3, 120.4, 122.9, 124.1, 127.5, 129.4 (2C), 130.0, 137.4, 140.5, 150.4, 159.3 ppm. These data are consistent with the literature.[58]

(4-Methoxyphenyl)pyrazine (4x): Beige solid; m.p. 95°C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.85 (s, 3H), 7.01 (d, J=8.9 Hz, 2H), 7.96 (d, J=8.9 Hz, 2H), 8.42 (d, J=2.4 Hz, 1H), 8.56 (br m, 1H), 8.60 ppm (br s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=55.5, 114.6 (2C), 128.4 (2C), 128.9, 141.7, 142.2, 144.0, 152.6, 161.3 ppm. These data are consistent with the literature.[59]

4-(4-Methoxyphenyl)pyrimidine (4d): Yellow liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=3.84 (s, 3H), 7.10 (d, J=8.4 Hz, 2H), 8.02 (d, J=5.0 Hz, 1H), 8.19 (d, J=8.4 Hz, 2H), 8.78 (d, J=5.0 Hz, 1H), 9.17 ppm (s, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=55.3, 114.4 (2C), 116.1, 128.1, 128.6 (2C), 157.6, 158.6, 161.8, 162.1 ppm. These data are consistent with the literature.[60]

General procedure for the deprotocadmation (using [(tmp)$_3$CdLi])–trapping of aromatics with RCOCl, ArSO$_2$Cl, and ArCOCl: BuLi (about 1.6 M hexanes solution, 6.0 mmol) was added to a stirred, cooled (0°C) solution of 2,2,6,6-tetramethylpiperidine (1.0 mL, 6.0 mmol) in THF (5 mL). After the solution had been stirred for 15 min at 0°C, $CdCl_2$·TMEDA (0.60 g, 2.0 mmol) was added and the mixture was stirred for 15 min at this temperature before introduction of furan (0.29 mL, 4.0 mmol). After the mixture had been stirred for 2 h at room temperature, the electrophile (RCOCl, $ArSO_2Cl$, or ArCOCl) (8.0 mmol) was added at 0°C. The mixture was stirred overnight at room temperature before addition of an aqueous saturated brine solution (20 mL) and extraction with Et_2O (3×20 mL). The combined organic layers were washed with brine (2×10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure before being purified by column chromatography on silica gel.

Cyclohexyl furan-2-yl ketone (5v2): Colorless liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): δ=1.14–1.52 (m, 5H), 1.69 (m, 1H), 1.77–1.85 (m, 4H), 3.02 (tt, J=3.3, 12 Hz, 1H), 6.48 (dd, J=1.7, 3.6 Hz, 1H), 7.14 (dd, J=0.8, 3.6 Hz, 1H), 7.54 ppm (dd, J=0.8, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ=25.7 (2C), 25.8, 28.9 (2C), 46.3, 112.1, 117.0, 146.2, 152.3, 192.9 ppm. These data are consistent with the literature.[61]

2-Pivaloylfuran (5v3): Colorless oil; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=$ 1.34 (s, 9H), 6.49 (dd, $J=1.7$, 3.6 Hz, 1H), 7.20 (dd, $J=0.8$, 3.6 Hz, 1H), 7.52 ppm (dd, $J=0.8$, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=27.0$ (3C), 43.0, 111.7, 118.0, 145.0, 152.5, 194.9 ppm. These data are consistent with the literature.[62]

Methyl furan-2-carboxylate (5v4): Yellow liquid; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=3.87$ (s, 3H), 6.48 (dd, $J=1.8$, 3.5 Hz, 1H), 7.15 (dd, $J=$ 0.8, 3.5 Hz, 1H), 7.55 ppm (dd, $J=0.8$, 1.7 Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=51.9$, 111.8, 117.9, 144.6, 146.3, 159.1 ppm. These data are consistent with the literature.[63]

2-[(4-Tolyl)sulfonyl]furan (5v5): Pale yellow solid; m.p. 109°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=2.42$ (s, 3H), 6.48 (dd, $J=1.8$, 3.5 Hz, 1H), 7.17 (dd, $J=0.9$, 3.5 Hz, 1H), 7.33 (dd, $J=0.6$, 8.6 Hz, 2H), 7.52 (dd, $J=0.9$, 1.8 Hz, 1H), 7.87 ppm (dd, $J=1.8$, 8.4 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=21.7$, 77.3, 111.6, 117.0, 127.9 (2C), 130.0 (2C), 144.9, 147.3, 150.2 ppm. The spectroscopic data are consistent with the literature.[64]

2-Chloro-5-[(4-tolyl)sulfonyl]furan (5′v5): Yellow solid; m.p. 89–92°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=2.46$ (s, 3H), 6.28 (d, $J=3.6$ Hz, 1H), 7.14 (d, $J=3.6$ Hz, 1H), 7.34 (dd, $J=0.6$, 8.6 Hz, 2H), 7.86 ppm (d, $J=$ 8.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=21.7$, 108.6, 119.0, 128.1 (2C), 130.1 (2C), 136.4, 142.3, 145.2, 149.2 ppm. X-ray diffraction quality crystals of **5f** were obtained from $CHCl_3$.[65]

2-[(4-Chlorophenyl)sulfonyl]furan (5v6): Pale yellow solid; m.p. 104°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=6.51$ (dd, $J=1.8$, 3.6 Hz, 1H), 7.21 (dd, $J=0.9$, 3.6 Hz, 1H), 7.51 (dd, $J=2.0$, 8.8 Hz, 2H), 7.56 (dd, $J=0.9$, 1.8 Hz, 1H), 7.93 ppm (dd, $J=2.0$, 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=111.8$, 117.7, 129.4 (2C), 129.7 (2C), 138.4, 140.5, 147.7, 149.5 ppm; HRMS (EI): m/z calcd for $C_{10}H_7{}^{35}ClO_3S$: 241.9804; found: 241.9814.

2-Chloro-5-[(4-chlorophenyl)sulfonyl]furan (5′v6): Pale yellow solid; m.p. 124–125°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=6.32$ (d, $J=3.6$ Hz, 1H), 7.19 (d, $J=3.6$ Hz, 1H), 7.53 (dd, $J=2.0$, 8.8 Hz, 2H), 7.93 ppm (dd, $J=$ 2.0, 8.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=108.8$, 119.7, 129.6 (2C), 129.8 (2C), 137.9, 140.9, 142.9, 148.5 ppm. X-ray diffraction quality crystals of **5′f** were obtained from $CHCl_3$.[65]

Furan-2-yl 4-tolyl ketone (5v8): Orange solid; m.p. 70°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=2.42$ (s, 3H), 6.58 (dd, $J=1.8$, 3.6 Hz, 1H), 7.22 (dd, $J=0.6$, 3.6 Hz, 1H), 7.28 (d, $J=7.9$ Hz, 2H), 7.69 (dd, $J=0.6$, 1.8 Hz, 1H), 7.87 ppm (d, $J=7.9$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=21.7$, 112.3, 120.2, 129.2 (2C), 129.6 (2C), 134.5, 143.6, 147.2, 152.3, 182.6 ppm. These data are consistent with the literature.[66]

4-Chlorophenyl furan-2-yl ketone (5v9): Pale brown solid; m.p. 96–98°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=6.57$ (dd, $J=1.7$, 3.6 Hz, 1H), 7.22 (dd, $J=0.8$, 3.6 Hz, 1H), 7.43 (d, $J=8.8$ Hz, 2H), 7.68 (dd, $J=0.8$, 1.7 Hz, 1H), 7.91 ppm (d, $J=8.7$ Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=112.4$, 120.6, 128.7 (2C), 130.8 (2C), 135.4, 139.0, 147.2, 152.1, 181.0 ppm. These data are consistent with the literature.[62]

3-Chlorophenyl furan-2-yl ketone (5v10): Pale yellow solid; m.p. <40°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=6.61$ (dd, $J=1.7$, 3.6 Hz, 1H), 7.27 (dd, $J=0.7$, 3.6 Hz, 1H), 7.43 (t, $J=7.8$ Hz, 1H), 7.55 (ddd, $J=1.2$, 2.1, 8.0 Hz, 1H), 7.70 (dd, $J=0.8$, 1.7 Hz, 1H), 7.86 (ddd, $J=1.2$, 1.5, 7.7 Hz, 1H), 7.95 ppm (t, $J=1.7$ Hz, 1H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=112.4$, 120.9, 127.4, 129.3, 129.8, 132.5, 134.6, 138.7, 147.4, 152.0, 180.9 ppm. These data are consistent with the literature.[62]

3,5-Bis(trifluoromethyl)phenyl furan-2-yl ketone (5v11): Red oil; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=6.68$ (dd, $J=1.7$, 3.6 Hz, 1H), 7.38 (dd, $J=0.8$, 3.6 Hz, 1H), 7.77 (dd, $J=0.8$, 1.7 Hz, 1H), 8.09 (m, 1H), 8.47 ppm (dd, $J=0.5$, 1.0 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=113.0$, 121.5, 122.9 (q, $J_F=273$ Hz, 2C), 125.8 (septuplet, $J_F=4.0$ Hz), 129.5 (m, 2C), 132.1 (q, $J_F=34$ Hz, 2C), 138.5, 147.9, 151.7, 178.9 ppm; HRMS (EI): m/z calcd for $C_{13}H_6F_6O_2$: 308.0272; found: 308.0261.

Bis[3,5-bis(trifluoromethyl)phenyl]furan-2,5-diyl diketone (5′v11): Red solid; m.p. 173–174°C; ^{1}H NMR ($CDCl_3$, 300 MHz): $\delta=7.57$ (s, 2H), 8.14 (m, 2H), 8.49 ppm (dd, $J=1.5$ Hz, 4H); ^{13}C NMR ($CDCl_3$, 75 MHz): $\delta=$ 121.0 (2C), 122.7 (q, $J_F=273$ Hz, 4C), 126.6 (septuplet, $J_F=3.6$ Hz, 2C), 129.5 (m, 4C), 132.5 (q, $J_F=34$ Hz, 4C), 137.3 (2C), 153.3 (2C), 179.1 ppm (2C). X-ray diffraction quality crystals of **5′v11** were obtained from $CHCl_3$.[65]

General procedure for the deprotometalation (using an in situ prepared mixture of $InCl_3$ and 4 equiv of Li(TMP))–iodination of aromatics: BuLi (about 1.6M hexanes solution, 5.3 mmol) was added to a stirred, cooled (0°C) solution of 2,2,6,6-tetramethylpiperidine (0.97 mL, 5.3 mmol) in THF (2 mL). The solution was transferred at 0°C to anhydrous $InCl_3$ (0.30 g, 1.3 mmol) in THF (3 mL), and the mixture was stirred for 15 min at this temperature before introduction of the substrate (4.0 mmol). After the mixture had been stirred for 2 h at room temperature, a solution of I_2 (1.3 g, 5.3 mmol) in THF (5 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of $Na_2S_2O_3$ (5 mL) and extraction with Et_2O (3×20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure before being purified by means of column chromatography on silica gel.

[BuM(tmp)$_2$Li]: BuLi (about 1.6M hexanes solution, 4.0 mmol) was added to a stirred, cooled (0°C) solution of 2,2,6,6-tetramethylpiperidine (0.68 mL, 4.0 mmol) in THF (5 mL). After the solution had been stirred for 15 min at 0°C, MCl_2·TMEDA (2.0 mmol) was added, and the mixture was stirred for 15 min at this temperature before addition of BuLi (2.0 mmol). After the mixture had been stirred for 15 min at 0°C, the substrate (4.0 mmol) was introduced. After the mixture had been stirred for 2 h at room temperature, a solution of I_2 (1.5 g, 6.0 mmol) in THF (5 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of $Na_2S_2O_3$ (5 mL) and extraction with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure before being purified by means of column chromatography on silica gel.

[Bu$_2$M(tmp)Li]: BuLi (about 1.6M hexanes solution, 2.0 mmol) was added to a stirred, cooled (0°C) solution of 2,2,6,6-tetramethylpiperidine (0.34 mL, 2.0 mmol) in THF (5 mL). After the solution had been stirred for 15 min at 0°C, MCl_2·TMEDA (2.0 mmol) was added, and the mixture was stirred for 15 min at this temperature before addition of BuLi (4.0 mmol). After the mixture had been stirred for 15 min at 0°C, the substrate (4.0 mmol) was introduced. After the mixture had been stirred for 2 h at room temperature, a solution of I_2 (1.5 g, 6.0 mmol) in THF (5 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of $Na_2S_2O_3$ (5 mL) and extraction with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure before being purified by means of column chromatography on silica gel.

[Bu$_3$MLi]: MCl_2·TMEDA (2.0 mmol) was added to a stirred, cooled (0°C) solution of BuLi (about 1.6M hexanes solution, 6.0 mmol) in THF (5 mL), and the mixture was stirred for 15 min at this temperature before introduction of the substrate (4.0 mmol). After the mixture had been stirred for 2 h at room temperature, a solution of I_2 (1.5 g, 6.0 mmol) in THF (5 mL) was added. The mixture was stirred overnight before addition of an aqueous saturated solution of $Na_2S_2O_3$ (5 mL) and extraction with CH_2Cl_2 (3×20 mL). The combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered, and concentrated under reduced pressure before being purified by means of column chromatography on silica gel.

2-Iodoanisole (**2a**), 1-iodo-2,3-dimethoxybenzene (**2b**), 2-iodobenzothiazole (**2c**), 4-iodopyrimidine (**2d**), *N*,*N*-diethyl-2-iodobenzamide (**2e**), methyl 2-iodobenzoate (**2f**), 2-iodobenzonitrile (**2g**), 2-iodobenzophenone (**2h**), 4-bromo-2-iodoanisole (**2i**), 2,4-diiodoanisole (**2j**), methyl 4-bromo-2-iodobenzoate (**2k**), 2-iodobenzo[*b*]thiophene (**2l**), 2-iodobenzo[*b*]furan (**2m**), 2-iodobenzoxazole (**2n**), *N*-Boc-2-iodopyrrole (**2r**), *N*-Boc-2,5-diiodopyrrole (**3r**), 2,5-diiodothiazole (**3s**), 2,5-diiodothiophene (**3t**), 2,5-diiodo-3,4-ethylenedioxythiophene (**3u**), 2-(4-methoxyphenyl)-furan (**4v1**), and furan-2-yl phenyl ketone (**5v7**) have been previously described.[15a]

Acknowledgements

We gratefully acknowledge the financial support of Région Bretagne (to K.S. and J.M.L.), MESRS of Algeria (to G.B.A.), MESR of France (to T.T.N.). We thank Mathieu Pucheault for helpful discussion.

[1] a) H. W. Gschwend, H. R. Rodriguez, *Org. React.* **1979**, *26*, 1–360; b) P. Beak, V. Snieckus, *Acc. Chem. Res.* **1982**, *15*, 306–312; c) V. Snieckus, *Chem. Rev.* **1990**, *90*, 879–933; d) T. G. Gant, A. I. Meyers, *Tetrahedron* **1994**, *50*, 2297–2360; e) M. Schlosser, *Organometallics in Synthesis*, 2nd ed. (Ed.: M. Schlosser), Wiley, New York, **2002**, Chapter I.

[2] See for example: P. E. Eaton, C. H. Lee, Y. Xiong, *J. Am. Chem. Soc.* **1989**, *111*, 8016–8018.

[3] M. Schlosser, *Pure Appl. Chem.* **1988**, *60*, 1627–1634.

[4] L. Lochmann, *Eur. J. Inorg. Chem.* **2000**, 1115–1126.

[5] P. Caubere, *Chem. Rev.* **1993**, *93*, 2317–2334.

[6] P. Gros, Y. Fort, *Eur. J. Org. Chem.* **2002**, 3375–3383.

[7] For reviews, see: a) R. E. Mulvey, *Organometallics* **2006**, *25*, 1060–1075; b) R. E. Mulvey, F. Mongin, M. Uchiyama, Y. Kondo, *Angew. Chem.* **2007**, *119*, 3876–3899; *Angew. Chem. Int. Ed.* **2007**, *46*, 3802–3824; c) R. E. Mulvey, *Acc. Chem. Res.* **2009**, *42*, 743–755.

[8] a) Y. Kondo, M. Shilai, M. Uchiyama, T. Sakamoto, *J. Am. Chem. Soc.* **1999**, *121*, 3539–3540; b) M. Uchiyama, T. Miyoshi, Y. Kajihara, T. Sakamoto, Y. Otani, T. Ohwada, Y. Kondo, *J. Am. Chem. Soc.* **2002**, *124*, 8514–8515; c) H. R. L. Barley, W. Clegg, S. H. Dale, E. Hevia, G. W. Honeyman, A. R. Kennedy, R. E. Mulvey, *Angew. Chem.* **2005**, *117*, 6172–6175; *Angew. Chem. Int. Ed.* **2005**, *44*, 6018–6021; d) W. Clegg, S. H. Dale, E. Hevia, G. W. Honeyman, R. E. Mulvey, *Angew. Chem.* **2006**, *118*, 2430–2434; *Angew. Chem. Int. Ed.* **2006**, *45*, 2370–2374; e) W. Clegg, S. H. Dale, R. W. Harrington, E. Hevia, G. W. Honeyman, R. E. Mulvey, *Angew. Chem.* **2006**, *118*, 2434–2437; *Angew. Chem. Int. Ed.* **2006**, *45*, 2374–2377; f) W. Clegg, S. H. Dale, A. M. Drummond, E. Hevia, G. W. Honeyman, R. E. Mulvey, *J. Am. Chem. Soc.* **2006**, *128*, 7434–7435; g) M. Uchiyama, Y. Kobayashi, T. Furuyama, S. Nakamura, Y. Kajihara, T. Miyoshi, T. Sakamoto, Y. Kondo, K. Morokuma, *J. Am. Chem. Soc.* **2008**, *130*, 472–480; h) W. Clegg, B. Conway, E. Hevia, M. D. McCall, L. Russo, R. E. Mulvey, *J. Am. Chem. Soc.* **2009**, *131*, 2375–2384.

[9] a) S. H. Wunderlich, P. Knochel, *Angew. Chem.* **2007**, *119*, 7829–7832; *Angew. Chem. Int. Ed.* **2007**, *46*, 7685–7688; b) S. Wunderlich, P. Knochel, *Chem. Commun.* **2008**, 6387–6389; c) S. H. Wunderlich, P. Knochel, *Org. Lett.* **2008**, *10*, 4705–4707; d) M. Mosrin, P. Knochel, *Chem. Eur. J.* **2009**, *15*, 1468–1477.

[10] M. Mosrin, P. Knochel, *Org. Lett.* **2009**, *11*, 1837–1840.

[11] a) M. Uchiyama, H. Naka, Y. Matsumoto, T. Ohwada, *J. Am. Chem. Soc.* **2004**, *126*, 10526–10527; b) J. Garcia-Alvarez, D. V. Graham, A. R. Kennedy, R. E. Mulvey, S. Weatherstone, *Chem. Commun.* **2006**, 3208–3210; c) J. Garcia-Alvarez, E. Hevia, A. R. Kennedy, J. Klett, R. E. Mulvey, *Chem. Commun.* **2007**, 2402–2404; d) B. Conway, E. Hevia, J. García-Álvarez, D. V. Graham, A. R. Kennedy, R. E. Mulvey, *Chem. Commun.* **2007**, 5241–5243; e) H. Naka, M. Uchiyama, Y. Matsumoto, A. E. H. Wheatley, M. McPartlin, J. V. Morey, Y. Kondo, *J. Am. Chem. Soc.* **2007**, *129*, 1921–1930; f) 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*, 16193–16200.

[12] S. H. Wunderlich, P. Knochel, *Angew. Chem.* **2009**, *121*, 1530–1533; *Angew. Chem. Int. Ed.* **2009**, *48*, 1501–1504.

[13] J. Garcia-Álvarez, A. R. Kennedy, J. Klett, R. E. Mulvey, *Angew. Chem.* **2007**, *119*, 1123–1126; *Angew. Chem. Int. Ed.* **2007**, *46*, 1105–1108.

[14] S. Usui, Y. Hashimoto, J. V. Morey, A. E. H. Wheatley, M. Uchiyama, *J. Am. Chem. Soc.* **2007**, *129*, 15102–15103.

[15] a) J.-M. L′Helgoual′ch, G. Bentabed-Ababsa, F. Chevallier, M. Yonehara, M. Uchiyama, A. Derdour, F. Mongin, *Chem. Commun.* **2008**, 5375–5377. See also: b) J.-M. L′Helgoual′ch, G. Bentabed-Ababsa, F. Chevallier, A. Derdour, F. Mongin, *Synthesis* **2008**, 4033–4035; c) G. Bentabed-Ababsa, F. Blanco, A. Derdour, F. Mongin, F. Trécourt, G. Quéguiner, R. Ballesteros, B. Abarca, *J. Org. Chem.* **2009**, *74*, 163–169.

[16] G. Wittig, F. J. Meyer, G. Lange, *Liebigs Ann. Chem.* **1951**, *571*, 167–201.

[17] a) J.-M. L′Helgoual′ch, A. Seggio, F. Chevallier, M. Yonehara, E. Jeanneau, M. Uchiyama, F. Mongin, *J. Org. Chem.* **2008**, *73*, 177–183. See also: b) A. Seggio, M.-I. Lannou, F. Chevallier, D. Nobuto, M. Uchiyama, S. Golhen, T. Roisnel, F. Mongin, *Chem. Eur. J.* **2007**, *13*, 9982–9989; c) A. Seggio, F. Chevallier, M. Vaultier, F. Mongin, *J. Org. Chem.* **2007**, *72*, 6602–6605.

[18] Organocadmium reagents have been mainly prepared by reaction of organic halides with cadmium metal or by transmetalation: a) P. R. Jones, P. J. Desio, *Chem. Rev.* **1978**, *78*, 491–516; b) P. O'Brien, M. A. Malik, *Sci. Synth.* **2004**, *3*, 91–131.

[19] Organoindium ate complexes have been mainly prepared by transmetalation and, more recently, by indium insertion: a) K. Hoffmann, E. Weiss, *J. Organomet. Chem.* **1973**, *50*, 25–31; b) P. H. Lee, S. W. Lee, D. Seomoon, *Org. Lett.* **2003**, *5*, 4963–4966; c) T. Hirashita, Y. Hayashi, K. Mitsui, S. Araki, *Tetrahedron Lett.* **2004**, *45*, 3225–3228; d) Y. H. Chen, P. Knochel, *Angew. Chem.* **2008**, *120*, 7760–7763; *Angew. Chem. Int. Ed.* **2008**, *47*, 7648–7651.

[20] For the synthesis of $CdCl_2$·TMEDA, see: G. Kedarnath, L. B. Kumbhare, V. K. Jain, P. P. Phadnis, M. Nethaji, *Dalton Trans.* **2006**, 2714–2718.

[21] Attempts to prepare $InCl_3$·TMEDA by adding TMEDA (2 equiv) to a solution of $InCl_3$ in THF gave a compound for which a correct microanalysis could not be obtained.

[22] N. Ple, A. Turck, K. Couture, G. Quéguiner, *J. Org. Chem.* **1995**, *60*, 3781–3786.

[23] For the catalytic effect of LiCl on ortholithiations, see: L. Gupta, A. C. Hoepker, K. J. Singh, D. B. Collum, *J. Org. Chem.* **2009**, *74*, 2231–2233, and references therein.

[24] TMEDA has previously been found as the most effective in accelerating the rates of deprotonation, but the effect remains small: R. R. Fraser, T. S. Mansour, *Tetrahedron Lett.* **1986**, *27*, 331–334.

[25] For previously described metalation of 4-iodoanisole at room temperature, see ref. [11a,e].

[26] A. Krasovskiy, V. Krasovskaya, P. Knochel, *Angew. Chem.* **2006**, *118*, 3024–3027; *Angew. Chem. Int. Ed.* **2006**, *45*, 2958–2961.

[27] a) For the magnesation using $[Bu_4MgLi_2]$, see: F. Mongin, A. Bucher, J. P. Bazureau, O. Bayh, H. Awad, F. Trécourt, *Tetrahedron Lett.* **2005**, *46*, 7989–7992; b) For the zincation using the in situ prepared mixture of $[(tmp)_2Zn]$ and [Li(tmp)], see ref. [17a]; c) For the alumination using $[iBu_3(tmp)AlLi]$, see ref. [11 a,e].

[28] O. Bayh, H. Awad, F. Mongin, C. Hoarau, L. Bischoff, F. Trécourt, G. Quéguiner, F. Marsais, F. Blanco, B. Abarca, R. Ballesteros, *J. Org. Chem.* **2005**, *70*, 5190–5196, and references therein.

[29] G. Queguiner, F. Marsais, V. Snieckus, J. Epsztajn, *Adv. Heterocycl. Chem.* **1991**, *52*, 187–304, and references therein.

[30] A similar result has previously been observed, even if to a lesser extent, by using lithium magnesates at −10 °C: H. Awad, F. Mongin, F. Trécourt, G. Quéguiner, F. Marsais, *Tetrahedron Lett.* **2004**, *45*, 7873–7877.

[31] F. Chevallier, F. Mongin, *Chem. Soc. Rev.* **2008**, *37*, 595–609, and references therein.

[32] M. Mosrin, N. Boudet, P. Knochel, *Org. Biomol. Chem.* **2008**, *6*, 3237–3239.

[33] The same yield had previously been obtained using the in situ prepared mixture of $[(tmp)_2Zn]$ and [Li(tmp)], see ref. [17a].

[34] Dimetalated species have been previously described using zincate- or manganate-type bases: a) W. Clegg, S. H. Dale, E. Hevia, L. M. Hogg, G. W. Honeyman, R. E. Mulvey, C. T. O'Hara, *Angew. Chem.* **2006**, *118*, 6698–6700; *Angew. Chem. Int. Ed.* **2006**, *45*, 6548–6550; b) L. M. Carrella, W. Clegg, D. V. Graham, L. M. Hogg, A. L. Kennedy, J. Klett, R. E. Mulvey, E. Rentschler, L. Russo, *Angew. Chem.* **2007**, *119*, 4746–4750; *Angew. Chem. Int. Ed.* **2007**, *46*, 4662–4666; c) D. R. Armstrong, W. Clegg, S. H. Dale, D. V. Graham, E. Hevia,

L. M. Hogg, G. W. Honeyman, A. R. Kennedy, R. E. Mulvey, *Chem. Commun.* **2007**, 598–600. See also ref. [13].
[35] M. Shilai, Y. Kondo, T. Sakamoto, *J. Chem. Soc. Perkin Trans. 1* **2001**, 442–444.
[36] O. Bayh, H. Awad, F. Mongin, C. Hoarau, F. Trécourt, G. Quéguiner, F. Marsais, F. blanco, B. Abarca, R. Ballesteros, *Tetrahedron* **2005**, *61*, 4779–4784.
[37] a) V. L. Blair, A. R. Kennedy, J. Klett, R. E. Mulvey, *Chem. Commun.* **2008**, 5426–5428. See also: b) D. V. Graham, E. Hevia, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, C. Talmard, *Chem. Commun.* **2006**, 417–419.
[38] a) E.-i. Negishi, T. Takahashi, S. Baba, D. E. Van Horn, N. Okukado, *J. Am. Chem. Soc.* **1987**, *109*, 2393–2401; b) N. Bumagin, A. B. Ponomarev, I. P. Beletskaya, *Zh. Org. Khim.* **1987**, *23*, 1345–1353. See also: c) J. A. Miller, R. P. Farrell, *Tetrahedron Lett.* **1998**, *39*, 7275–7278.
[39] D. R. Coulson, *Inorg. Synth.* **1972**, *13*, 121–123.
[40] C. Amatore, E. Carré, A. Jutand, M. A. M'Barki, *Organometallics* **1995**, *14*, 1818–1826.
[41] H. Gilman, J. F. Nelson, *Recl. Trav. Chim. Pays-Bas* **1936**, *55*, 518.
[42] a) A. F. Shepard, *J. Am. Chem. Soc.* **1930**, *52*, 2083–2090; b) O. W. Cass, U.S. Application No. 2430667, 1947.
[43] A. Wada, H. Yasuda, S. Kanatomo, *Synthesis* **1988**, 771–775.
[44] J. P. Horwitz, A. J. Tomson, *J. Org. Chem.* **1961**, *26*, 3392–3395.
[45] T. Zou, S-S. Pi, J-H. Li, *Org. Lett.* **2009**, *11*, 453–456.
[46] E. McNeil, T. E. Barder, S. L. Buchwald, *Org. Lett.* **2007**, *9*, 3785–3788.
[47] M. A. Fernandez-Rodriguez, Q. Shen, J. F. Hartwig, *Chem. Eur. J.* **2006**, *12*, 7782–7796.
[48] S. E. Denmark, N. S. Werner, *J. Am. Chem. Soc.* **2008**, *130*, 16382–16393.
[49] I. Tatsuya, Y. Yoshimi, T. Morita, Y. Tokunaga, M. Hatanaka, *Tetrahedron* **2008**, *64*, 263–269.
[50] D. Crich, M. Patel, *Tetrahedron* **2006**, *62*, 7824–7837.
[51] Y. Kobayashi, A. D. William, R. Mizojiri, *J. Organomet. Chem.* **2002**, *653*, 91–97.
[52] R. V. Ohri, A. T. Radosevich, K. J. Hrovat, C. Musich, D. Huang, T. R. Holman, F. D. Toste, *Org. Lett.* **2005**, *7*, 2501–2504.
[53] A; Pelter, M. Rowlands, G. Clements, *Synthesis* **1987**, 51–53.
[54] a) A. W. Johnson, *J. Chem. Soc.* **1946**, 895–899; b) A. R. Katritzky, J. Li, M. F. Gordeev, *J. Org. Chem.* **1993**, *58*, 3038–3041.
[55] a) M. Nilsson, C. Ullenius, *Acta Chem. Scand.* **1970**, *24*, 2379–2388; b) S.-K. Kang, J. S. Kim, S.-C. Choi, *J. Org. Chem.* **1997**, *62*, 4208–4209.
[56] a) C. F. Roberts, R. C. Hartley, *J. Org. Chem.* **2004**, *69*, 6145–6148; b) J. E. Banfield, W. Davies, N. W. Gamble, S. Middleton, *J. Chem. Soc.* **1956**, 4791–4796.
[57] A. Arcadi, S. Cacchi, M. Del Rosario, G. Fabrizi, F. Marinelli, *J. Org. Chem.* **1996**, *61*, 9280–9288.
[58] S. E. Denmark, J. D. Baird, *Org. Lett.* **2004**, *6*, 3649–3652.
[59] D. H. Huh, H. Ryu, Y. G. Kim, *Tetrahedron* **2004**, *60*, 9857–9862.
[60] N. Nishiwaki, K. Yamashita, M. Azuma, T. Adachi, M. Tamura, M. Ariga, *Synthesis* **2004**, 1996–2000.
[61] T. Kondo, M. Akazome, Y. Tsuji, Y. Watanabe, *J. Org. Chem.* **1990**, *55*, 1286–1291.
[62] R. Lerebours, A. Camacho-Soto, C. Wolf, *J. Org. Chem.* **2005**, *70*, 8601–8604.
[63] J.-E. Won, H.-K. Kim, J.-J. Kim, H.-S. Yim, M.-J. Kim, S.-B. Kang, H.-A. Chung, S.-G. Lee, Y.-J. Yoon, *Tetrahedron* **2007**, *63*, 12720–12730.
[64] K. Aboutayab, S. Caddick, K. Jenkins, S. Joshi, S. Khan, *Tetrahedron* **1996**, *52*, 11329–11340.
[65] CCDC 716974 (**5′v5**), 716976 (**5′v6**), and 716975 (**5′v11**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
[66] M. L. N. Rao, V. Venkatesh, D. Banerjee, *Tetrahedron* **2007**, *63*, 12917–12926.

Received: May 28, 2009
Published online: August 17, 2009

