Cite this: *Dalton Trans.*, 2014, **43**, 1408

Optimisation of a lithium magnesiate for use in the non-cryogenic asymmetric deprotonation of prochiral ketones†

Javier Francos, Silvia Zaragoza-Calero and Charles T. O'Hara*

A study has been conducted to determine whether lithium magnesiates are feasible candidates for the enantioselective deprotonation of 4-alkylcyclohexanones. The commercially available chiral amine (+)-bis-[(*R*)-1-phenylethyl]amine (**2**-H) was utilised to induce enantioselection. When transformed to its lithium salt and combined with $^t\text{Bu}_2\text{Mg}$, improved enantioselective deprotonation of 4-*tert*-butylcyclohexanone (with respect to the monometallic lithium amide) at 20 °C was observed. In an attempt to optimise the reaction further, different additives were added to the lithium amide. The best performing deprotonations at 0 °C were those in which $(\text{Me}_3\text{SiCH}_2)_2\text{Mg}$ (er pro-*S* 74 : 26) and $(\text{Me}_3\text{SiCH}_2)_2\text{Mn}$ (er pro-*S* 72 : 28) were added, hence the lithium magnesiate " $\text{LiMg}(\mathbf{2})(\text{CH}_2\text{SiMe}_3)_2$ " was used in the remainder of the study. The optimum solvent for the reaction was found to be THF. NMR spectroscopic studies of a D_8 -THF solution of " $\text{LiMg}(\mathbf{2})(\text{CH}_2\text{SiMe}_3)_2$ " appear to show that this mono-amide bis-alkyl species is in equilibrium with a bis-amide mono-alkyl compound (and a tris-alkyl lithium magnesiate). When a genuine bis-amide lithium magnesiate solution is used, the deprotonation results were essentially identical to those obtained for " $\text{LiMg}(\mathbf{2})(\text{CH}_2\text{SiMe}_3)_2$ ". By adding LiCl to " $\text{LiMg}(\mathbf{2})(\text{CH}_2\text{SiMe}_3)_2$ " the er at 0 °C improved to 81 : 19. At −78 °C good yields and an er of 93 : 7 were obtained. This LiCl-containing base was used to successfully deprotonate other 4-alkylcyclohexanones.

Received 18th September 2013,
Accepted 1st November 2013

DOI: 10.1039/c3dt52577e

www.rsc.org/dalton

Introduction

One of the most fundamentally important reactions in modern day synthesis is metallation, that is the replacement of a relatively unreactive C–H bond with a more reactive (more useful) C–metal one.¹ Over the past 60 years, the reagents of choice to carry out such reactions have generally been from the organolithium family, primarily due to their high Brønsted basicity. However, these reagents have their drawbacks including that their carbanions are often so basic that they attack common solvents (particularly ethers such as THF) and they are frequently nucleophilic; hence they generally exhibit poor functional group tolerance. To counteract these pitfalls, lithiations are mostly performed at sub-ambient temperatures (often approaching −100 °C), proving a massive financial burden for the chemical industry. Kerr has recently stated that by carrying out metallations at temperatures below −40 °C, the additional energetic cost to industry is in the region of

£250 000 per year per batch tonne process.² Therefore one priority in modern day synthesis is to provide solutions to this problem by designing new metallating reagents that are capable of producing excellent results akin to their lithium counterparts but at temperatures closer to ambient. Over the past decade the concept of *ate chemistry* in synthesis has come to the fore.³ When an alkali metal organometallic reagent is combined with a magnesium one, the new 'synergic' bi-metallic entity (an alkali metal magnesiate) has often been shown to function as a highly efficient base at temperatures approaching ambient temperature. By combining LiCl with conventional Grignard (RMgX) or Hauser (R_2NMgX) reagents, Knochel has demonstrated the tremendous scope achievable when these new *turbo* reagents are used in a multitude of deprotonations.^{3c,4} Mongin has utilised lithium tri(*n*-butyl)-magnesiate to regioselectively metallate an array of substrates, including thiophenes, fluoroaromatics, oxazoles, chloropyridines at temperatures close to ambient temperature.⁵ The subsequent metallo-intermediate can undergo electrophilic quenching to generate substituted derivatives. In special cases, unique reactivity, including multideprotonations and unprecedented regiochemistries with respect to 'normal' lithium reagents can also be achieved.⁶ Until recently, the domain of *ate* reagents has been essentially confined to achiral anions.

WestCHEM, University of Strathclyde, Department of Pure and Applied Chemistry,
295 Cathedral Street, Glasgow, G1 1XL, UK. E-mail: charlie.ohara@strath.ac.uk;
Tel: +44 (0)141 548 2667

† Electronic supplementary information (ESI) available: Full experimental procedures, and NMR data. See DOI: 10.1039/c3dt52577e

Gros has shown that the use of chiral magnesiate specifically heteroleptic lithium magnesium alkyl TADDOLates, can induce good levels of enantioselection, most recently in the enantioselective addition of chiral pyrazyl magnesiate intermediates across aldehydes.⁷

Results and discussion

Previous foundation work from our group has focused on determining the structures (both in solution and as solids) of magnesiates (and zincates) that incorporate chiral donor ligands [such as (–)-sparteine and (*R,R*)-TMCD] or the chiral amide [(*R*)-*N*-benzyl- α -methylbenzylamide].⁸ Building on this foundation, here we systematically study the use of lithium magnesiate in the enantioselective deprotonation of a class of yardstick reagents, namely some prochiral 4-alkylcyclohexanones.⁹ We decided to thoroughly investigate whether lithium magnesiate are feasible candidates for performing these metallations. The approach we chose was to co-complex a chiral lithium amide with another additive, ultimately an organomagnesium reagent. Firstly, we compared the performance of two commercially available chiral amines (Scheme 1) [(*R*)-*N*-benzyl- α -methylbenzylamine (1-H) and (+)-bis[(*R*)-1-phenylethyl]amine (2-H)] to generate the desired chiral lithium amide (1-Li or 2-Li). When the respective lithium amides were utilised in the deprotonation of 4-*tert*-butylcyclohexanone at ambient temperature in THF solution, the quenched silylenol ether was obtained in moderate yields (32 and 76% respectively) and in poor enantiomeric ratios (er) [(*S*:*R*); 50:50 and 60:40 respectively] (entries 1 and 3, Table 1). On adding ⁿBu₂Mg to the lithium amides, encouragingly gave vastly improved yields (95 and 83%) and most significantly enhanced er [(*S*:*R*); 65:35 and 70:30] (entries 2 and 4, Table 1). As the latter experiment showed most promise in terms of enantioselection,

Scheme 1 Reaction of lithium chiral amides and amido (bis)alkyl lithium magnesiate with 4-*tert*-butylcyclohexanone.

Table 1 Outcome of reacting 1-Li and 2-Li with (or without) Bu₂Mg in the deprotonation of 4-*tert*-butylcyclohexanone at 20 °C

Entry	Base	Yield ^a (%)	er (<i>S</i> : <i>R</i>) ^a
1	1-Li	32	50:50
2	1-Li + ⁿ Bu ₂ Mg	95	65:35
3	2-Li	76	60:40
4	2-Li + ⁿ Bu ₂ Mg	83	70:30

^a Determined by GC analysis.

Table 2 Outcome of adding different metal reagents to chiral lithium amides in the asymmetric deprotonation of 4-*tert*-butylcyclohexanone at 0 °C for 1 hour^a

Entry	Metal reagent added to 2-Li	Yield ^b (%)	er (<i>S</i> : <i>R</i>) ^b
1	—	76	60:40
2	MgBr ₂	0	—
3 ^a	CoBr ₂	4	—
4 ^a	ZnCl ₂	25	65:35
5	ⁿ Bu ₂ Mg	83	70:30
6	(Me ₃ SiCH ₂) ₂ Mg	96	74:26
7	Me ₂ Zn	99	58:42
8	^t Bu ₂ Zn	98	60:40
9	Me ₃ Al	89	64:36
10	ⁱ Bu ₃ Al	78	60:40
11	(Me ₃ SiCH ₂) ₂ Mn	99	72:28

^a CoBr₂ and ZnCl₂; reaction time was 16 h. ^b Determined by GC analysis.

we decided to use 2-Li in our subsequent reactions but altering the second metal.

At 0 °C, the additive-free reaction produced an enantiomeric ratio (*S*:*R*) of 60:40 in a yield of 76%. Inorganic salts are known to have an effect – advantageous or detrimental – on the course of reactions.¹⁰ When simple inorganic salts such as MgBr₂ and CoBr₂ were utilised (entries 2–4, Table 2), essentially none of the desired product was formed, although addition of ZnCl₂ produced a yield of 25% with a *S*:*R* ratio of 65:35. If an organometallic reagent was added instead of the salt, the main trend observed was that the yields improved (in excess of 78%) although enantiomeric ratios were variable.

As the *n*-butyl ligand contains β -hydrogen atoms, and is therefore prone to decomposition *via* a β -hydride elimination pathway we switched our attention to the trimethylsilylmethyl anion (Me₃SiCH₂[–]). The best *S*:*R* enantiomeric ratio (74:26) was obtained when the dialkylmagnesium (Me₃SiCH₂)₂Mg was used (entry 6, Table 2). When Zn or Al organometallics were used (entries 7–10, Table 2) the er observed were essentially identical to those obtained when 2-Li was utilised without an additional metal (entry 1, Table 2). Interestingly, on adding the transition metal alkyl (Me₃SiCH₂)₂Mn to the lithium reagent, essentially quantitative conversion to the silyl enol ether was observed with a high degree of enantioselection (*S*:*R*, 72:28; entry 11, Table 3). Thus far our best enantioselection was achieved using 2-Li and (Me₃SiCH₂)₂Mg (entry 6, Table 3).

Table 3 Outcome of altering the 2-Li to dialkylmagnesium ratio in the asymmetric deprotonation of 4-*tert*-butylcyclohexanone at 0 °C

Entry	Metal reagent added to 2-Li	Yield ^a (%)	er (<i>S</i> : <i>R</i>) ^a
1	—	76	60:40
2	1 equivalent ⁿ Bu ₂ Mg	83	70:30
3	2 equivalents ⁿ Bu ₂ Mg	52	62:38
4	0.5 equivalent ⁿ Bu ₂ Mg	99	62:38
5	1 equivalent (Me ₃ SiCH ₂) ₂ Mg	96	74:26
6	2 equivalents (Me ₃ SiCH ₂) ₂ Mg	89	78:22
7	0.5 equivalent (Me ₃ SiCH ₂) ₂ Mg	99	72:28

^a Determined by GC analysis.

Therefore we focused our attention on trying to optimise this reaction (and that involving commercially available $^n\text{Bu}_2\text{Mg}$) further. By adding a deficit (0.5 equivalents) or an excess (two equivalents) of $^n\text{Bu}_2\text{Mg}$ to 2-Li we discovered that the yield of product increased for the former, but decreased for the latter, and the enantiomeric ratio in both cases dropped to 62:38 (entries 2–4, Table 3). When 1:1, 1:2 and 2:1 ratios of 2-Li and $(\text{Me}_3\text{SiCH}_2)_2\text{Mg}$ are utilised, the product yields are excellent (>89%) and all the er are improved from the optimum $^n\text{Bu}_2\text{Mg}$ case, the best obtained was for the magnesium-rich reaction (pro the *S* enantiomer, 78:22) although it was modestly better than the 1:1 case (74:26) (entries 5–7, Table 3).

The next variable to be considered was ascertaining what effect changing the solvent medium from THF would have on the results. In carrying out the reaction of 2-Li and $(\text{Me}_3\text{SiCH}_2)_2\text{Mg}$ in neat toluene, only a trace of the desired product formed. In diethyl ether, the GC-yield was 40% and the er was only 67:33 in favour of the *S* enantiomer. To aid solubility in hexane, one molar equivalent of THF was added; however, the product yield was low (23%) and the er was 65:35; hence it appears that for the systems tested THF remains the optimum solvent choice.

At this juncture it is appropriate to detail some of the NMR spectroscopic work that was performed in an attempt to shed light on the active species that is likely to carry out the deprotonation. Full details and spectroscopic data can be found in the ESI.† The ^1H (and where appropriate ^7Li) NMR spectra of: (a) 2-H; (b) 2-Li; (c) $(2)_2\text{Mg}$; (d) 1:1 2-Li and $(\text{Me}_3\text{SiCH}_2)_2\text{Mg}$; and, (e) $\text{Me}_3\text{SiCH}_2\text{Li}$ in $\text{D}_8\text{-THF}$ were compared. The NCH methylene H-atom proved an important handle for comparing the spectra of (a)–(d). For (a)–(c) the respective ^1H NMR shifts were 3.50, 3.64 and 3.84 ppm. For (d) – the active base system – two distinct resonances in approximately equal proportions were observed (3.53 and 3.69 ppm). It was initially envisaged that these two resonances belonged to the diastereotopic *H* atoms present in the organometallic complex. However, a DOSY NMR experiment on a $\text{D}_8\text{-THF}$ solution of (d) revealed that the solution contained two distinct amido-containing species.† Thus we believe that the *expected* mono(amido)-bis(alkyl) species “ $\text{LiMg}(2)(\text{CH}_2\text{SiMe}_3)_2$ ” undergoes ligand reorganisation and is in equilibrium with a bis(amido)-mono(alkyl) relative “ $\text{LiMg}(2)_2(\text{CH}_2\text{SiMe}_3)$ ” and the tris(alkyl) “ $\text{LiMg}(\text{CH}_2\text{SiMe}_3)_3$ ” (Scheme 2 and Fig. 1). To provide evidence of this equilibrium, we prepared genuine $\text{D}_8\text{-THF}$ solutions of “ $\text{LiMg}(2)_2(\text{CH}_2\text{SiMe}_3)$ ” and “ $\text{LiMg}(\text{CH}_2\text{SiMe}_3)_3$ ” and obtained their respective ^1H NMR spectra corroborating that these species were present in the initial 1:1 2-Li and $(\text{Me}_3\text{SiCH}_2)_2\text{Mg}$ reaction (Fig. 2).

Interestingly, when the bis(amido) magnesiate “ $\text{LiMg}(2)_2(\text{CH}_2\text{SiMe}_3)$ ” was utilised in the enantioselective

Table 4 Outcome of introducing an additive to a 1:1 mixture of 2-Li and (Me₃SiCH₂)₂Mg in the asymmetric deprotonation of 4-*tert*-butylcyclohexanone at 0 °C

Entry	Additive	Yield ^a (%)	er (<i>S</i> : <i>R</i>) ^a
1	—	96	74:26
2	TMEDA	90	71:29
3	LiCl	98	81:19
4	DMPU	94	78:22

^a Determined by GC analysis.

(Table 4). Focusing on the reactions involving 2-Li and (Me₃SiCH₂)₂Mg, it was discovered that high yields were maintained using additives; however, TMEDA (*N,N,N',N'*-tetramethylethylenediamine) addition caused a slight drop-off in er (from 74:26 to 71:29), but DMPU [1,3-dimethyl-3,4,5,6-tetrahydro-2-(1*H*)-pyrimidinone] and LiCl both enhanced selectivity (to 78:22 and 81:19 respectively). The same 81:19 ratio was obtained when the LiCl was generated *in situ* by reaction of 2-HCl with two equivalents of ⁿBuLi.

Although the primary purpose of this work was to find an optimum system to operate at close to ambient temperature, for completeness we also investigated the reaction at various temperatures down to −78 °C (Table 5). As expected the optimum er was obtained at the lowest temperature (93:7) with an isolated yield of 87%. When compared with literature work² which utilised the chiral magnesium bis(amide) (2)₂Mg, it was noted that an identical er was obtained; however, using the magnesiate system gave an increased isolated yield (87% *versus* 66%). As alluded to earlier, in the monometallic magnesium system two equivalents of chiral amide are required, as one equivalent would produce an alkylmagnesium amide that has an inherently different reactivity and is also subject to Schlenk-type equilibria and perhaps oligomerisation in solution. In our magnesiate system, only one equivalent of chiral amine is required and our sole additive is LiCl *i.e.*, there is no need for DMPU. A final advantage is that the magnesiate reaction time is 3 hours; whereas for the magnesium bis(amide) it is 16 hours.

Table 5 The effect of temperature on the enantioselective deprotonation of 4-*tert*-butylcyclohexanone using a 1:1:1 mixture of 2-Li, (Me₃SiCH₂)₂Mg and LiCl (reaction time 1 hour)

Entry	Temperature (°C)	Yield ^a (%)	er (<i>S</i> : <i>R</i>) ^a
1	0	98 (87) ^b	81:19
2	−10	97	83:17
3	−20	96	85:15
4	−30	96	85:15
5	−40	94	86:14
6	−50	94	86:14
7	−60	81	88:12
8	−70	78	88:12
9	−78	72	93:7
10 ^c	−78	87	93:7

^a Determined by GC analysis. ^b Value in parenthesis is an isolated yield. ^c Reaction time 3 hours.**Table 6** Investigating the enantioselective deprotonation of several 4-substituted-cyclohexanones using a 1:1:1 mixture of 4-Li, (Me₃SiCH₂)₂Mg and LiCl at 0 °C

Entry	R	Isolated yield (%)	er ^a (<i>S</i> : <i>R</i>)
1	^t Bu	87	81:19
2	ⁱ Pr	75	82:18
3	ⁿ Pr	52	78:22
4	Me	57	75:25
5	Ph	89	77:23
6 ^b	^t Bu	75	18:82

^a Determined by GC analysis. ^b Enantiomer of 4 used in this reaction.

To summarise, the optimal results that we have obtained thus far are when we utilise a 1:1:1 mixture of 2-Li, (Me₃SiCH₂)₂Mg and LiCl. As such we tested this reaction mixture with other 4-alkylcyclohexanones (Table 6). In all cases attempted, moderate to good yields were obtained (52–89%). The best er obtained was when the alkyl group's steric bulk was reduced to isopropyl, producing an er of 82:18. Good enantioselection was also obtained for ⁿPr, Ph and Me which were 78:22, 77:23 and 75:25 respectively (Table S1†). Finally, to ascertain whether the opposite enantioselection is possible we employed (−)-bis[(*S*)-1-phenylethyl]amine in our optimum reaction instead of its enantiomer 2. We obtained 75% isolated yield of the compound with an *S*:*R* er of 18:82 at 0 °C (Table 6).

Experimental

General methods

¹H, ¹³C NMR and ⁷Li NMR spectra were recorded on a Bruker DPX 400 MHz spectrometer. All ¹³C NMR spectra were proton decoupled. Reagents were obtained from commercial suppliers and were used without further purification unless stated below. Purification was carried out according to standard laboratory methods. Diethyl ether, tetrahydrofuran, hexane and toluene were distilled from sodium-benzophenone. (CH₂SiMe₃)₂Mg was prepared from the Grignard reagent (Me₃SiCH₂)MgCl by manipulation of the Schlenk equilibrium *via* the dioxane precipitation method. The resultant off-white solid was purified *via* sublimation at 175 °C (10^{−2} Torr) to furnish pure (CH₂SiMe₃)₂Mg. ^tBu₂Zn¹¹ and (CH₂SiMe₃)₂Mn¹² were prepared according to literature methods and all synthetic work was carried out under an inert argon atmosphere. Gas chromatography was carried out using a Perkin Elmer Clarus 500 Gas Chromatograph.

Achiral G.C. analysis: (i) CP Chirasil-DEX CB column; (ii) carrier gas, H₂ (45 cm s^{−1}); (i) injector/detector temperature, 250 °C; (ii) initial oven temperature, 90 °C; (iii) temperature gradient, 45 °C min^{−1}; (iv) final oven temperature, 220 °C; and (v) detection method, FID.

Chiral G.C. analysis: (i) CP Chirasil-DEX CB column; (ii) carrier gas, H₂ (45 cm s^{−1}); (i) injector/detector temperature, 250 °C; (ii) initial oven temperature, 70 °C; (iii) temperature

gradient, 1.7 °C min⁻¹; (iv) final oven temperature, 120 °C; and (v) detection method, FID.

Representative experimental procedure

To a flame-dried and Ar-purged Schlenk flask, (CH₂SiMe₃)₂Mg (0.19 g, 1.0 mmol) was added and dissolved in anhydrous THF (5 mL) and the solution stirred for 5 min. BuLi (1.6 M in hexanes, 1.0 mmol) was added and then the solution was cooled to 0 °C. Bis[(R)-1-phenylethyl]amine (0.22 mL, 1.0 mmol) was added and the cold solution is stirred for 1 hour. After that, 4-*tert*-butylcyclohexanone (**1a**) (152 mg, 1.0 mmol) was added to the mixture, and the resulting suspension was allowed to stir for 1 hour. TMSCl (0.256 mL, 2.0 mmol) was added and regular sampling and analysis by gas chromatography monitored the progress of the reaction. After that the reaction is quenched with aq. NH₄Cl solution (10 mL) and extracted with AcOEt (3 × 15 mL). The combined organic layers were dried over Na₂SO₄ and concentrated *in vacuo* to give a residue that was purified by combi-flash chromatography [hexanes–Et₂O = 99 : 1] to afford (4-*tert*-butylcyclohexen-1-enyloxy)trimethylsilane as a colourless oil (195 mg, 87%).

Conclusions

Our 'optimised' lithium magnesiate appears to have the high activity of a lithium reagent, good selectivity of a magnesium one. This promising outcome is in keeping with the previously expressed view that mixed-metal formulations can often operate synergically.¹³ Future studies will focus on transforming this stoichiometric reaction to a catalytic one.

We gratefully acknowledge the support of the EPSRC (J001872/1 and L001497/1) for the award of a Career Acceleration Fellowship to CTOH.

Notes and references

- (a) M. Schlosser, in *Organometallics in Synthesis*, ed. M. Schlosser, Wiley, Chichester, UK, 2002; (b) M. Schlosser, *Angew. Chem., Int. Ed.*, 2005, **44**, 376; (c) N. S. Simpkins, *Top. Stereochem.*, 2010, **26**, 1.
- L. S. Bennie, W. J. Kerr, M. Middleditch and A. J. B. Watson, *Chem. Commun.*, 2011, **47**, 2264.
- (a) R. E. Mulvey, F. Mongin, M. Uchiyama and Y. Kondo, *Angew. Chem., Int. Ed.*, 2007, **46**, 3802; (b) R. E. Mulvey, *Acc. Chem. Res.*, 2009, **42**, 743; (c) B. Haag, M. Mosrin, H. Ila, V. Malakhov and P. Knochel, *Angew. Chem., Int. Ed.*, 2011, **50**, 9794.
- C. T. O'Hara, in *Specialist Periodical Reports: Organometallic Chemistry*, ed. I. J. S. Fairlamb and J. M. Lynam, The Royal Society of Chemistry, Cambridge, UK, 2011, vol. 37, p. 1.
- (a) S. Dumouchel, F. Mongin, F. Trecourt and G. Queguiner, *Tetrahedron*, 2003, **59**, 8629; (b) F. Mongin, A. Bucher, J. P. Bazureau, O. Bayh, H. Awad and F. Trecourt, *Tetrahedron Lett.*, 2005, **46**, 7989; (c) D. Catel, F. Chevallier, F. Mongin and P. C. Gros, *Eur. J. Inorg. Chem.*, 2012, 53.
- W. Clegg, K. W. Henderson, A. R. Kennedy, R. E. Mulvey, C. T. O'Hara, R. B. Rowlings and D. M. Tooke, *Angew. Chem., Int. Ed.*, 2001, **40**, 3902.
- (a) G. Dayaker, D. Tilly, F. Chevallier, G. Hilmersson, P. C. Gros and F. Mongin, *Eur. J. Inorg. Chem.*, 2012, 6051; (b) O. Payen, F. Chevallier, F. Mongin and P. C. Gros, *Tetrahedron: Asymmetry*, 2012, **23**, 1678; (c) D. Tilly, K. Snegaroff, G. Dayaker, F. Chevallier, P. C. Gros and F. Mongin, *Tetrahedron*, 2012, **68**, 8761.
- (a) A. R. Kennedy and C. T. O'Hara, *Dalton Trans.*, 2008, 4975; (b) D. R. Armstrong, W. Clegg, S. H. Dale, J. Garcia-Alvarez, R. W. Harrington, E. Hevia, G. W. Honeyman, A. R. Kennedy, R. E. Mulvey and C. T. O'Hara, *Chem. Commun.*, 2008, 187.
- (a) K. Aoki, H. Noguchi, K. Tomioka and K. Koga, *Tetrahedron Lett.*, 1993, **34**, 5105; (b) K. Aoki and K. Koga, *Chem. Pharm. Bull.*, 2000, **48**, 571; (c) M. J. Bassindale, J. J. Crawford, K. W. Henderson and W. J. Kerr, *Tetrahedron Lett.*, 2004, **45**, 4175; (d) M. Majewski, A. Ulaczyk-Lesanko and F. Wang, *Can. J. Chem.*, 2006, **84**, 257; (e) M. Majewski and F. Wang, *Tetrahedron*, 2002, **58**, 4567; (f) M. Majewski, A. Ulaczyk and F. Wang, *Tetrahedron Lett.*, 1999, **40**, 8755; (g) M. Majewski and P. Nowak, *Tetrahedron Lett.*, 1998, **39**, 1661; (h) M. Majewski, R. Lazny and P. Nowak, *Tetrahedron Lett.*, 1995, **36**, 5465; (i) C. D. Graf, C. Mulan and P. Knochel, *Angew. Chem., Int. Ed.*, 1998, **37**, 3014.
- (a) D. Seebach, *Angew. Chem., Int. Ed. Engl.*, 1988, **27**, 1624; (b) B. Tchoubar and A. Loupy, *Salt Effects in Organic and Organometallic Chemistry*, VCH, New York, 1992; (c) P. Caubère, *Chem. Rev.*, 1993, **93**, 2317; (d) G. T. Achonduh, N. Hadei, C. Valente, S. Avola, C. J. O'Brien and M. G. Organ, *Chem. Commun.*, 2010, **46**, 4109; (e) M. Hatano, O. Ito, S. Suzuki and K. Ishihara, *Chem. Commun.*, 2010, **46**, 2674; (f) M. Hatano, O. Ito, S. Suzuki and K. Ishihara, *J. Org. Chem.*, 2010, **75**, 5008; (g) H. Ochiai, M. Jang, K. Hirano, H. Yorimitsu and K. Oshima, *Org. Lett.*, 2008, **10**, 2681; (h) H. Ren, G. Dunet, P. Mayer and P. Knochel, *J. Am. Chem. Soc.*, 2007, **129**, 5376; (i) A. Krasovskiy, V. Malakhov, A. Gavryushin and P. Knochel, *Angew. Chem., Int. Ed.*, 2006, **45**, 6040; (j) E. Hevia and R. E. Mulvey, *Angew. Chem., Int. Ed.*, 2011, **50**, 6448.
- P. C. Andrikopoulos, D. R. Armstrong, H. R. L. Barley, W. Clegg, S. H. Dale, E. Hevia, G. W. Honeyman, A. R. Kennedy and R. E. Mulvey, *J. Am. Chem. Soc.*, 2005, **127**, 6184.
- A. Alberola, V. L. Blair, L. M. Carrella, W. Clegg, A. R. Kennedy, J. Klett, R. E. Mulvey, S. Newton, E. Rentschler and L. Russo, *Organometallics*, 2009, **28**, 2112.
- (a) A. R. Kennedy, J. Klett, R. E. Mulvey and D. S. Wright, *Science*, 2009, **326**, 706; (b) R. E. Mulvey, V. L. Blair, W. Clegg, A. R. Kennedy, J. Klett and L. Russo, *Nat. Chem.*, 2010, **2**, 588.