



Cite this: RSC Adv., 2019, 9, 18013

 Received 2nd May 2019
 Accepted 29th May 2019

 DOI: 10.1039/c9ra03277k
rsc.li/rsc-advances

Lewis acidic FeCl_3 promoted 2-aza-Cope rearrangement to afford α -substituted homoallylamines in dimethyl carbonate†

Karthik Gadge, Jonas Daelemans, Bert U. W. Maes and Kourosh Abbaspour Tehrani *

The iron(III)-catalyzed efficient strategy for the synthesis of α -substituted homoallylamines was accomplished *via* a cationic 2-aza-Cope rearrangement of aldimines, generated *in situ* by condensation of commercially available aldehydes and easily synthesizable 1,1-diphenylhomoallylamines. This reaction features a broad substrate scope with high yields and is conducted in an eco-friendly solvent, *i.e.* dimethyl carbonate.

The use of sustainable catalysts and green solvents are the most influential factors to reduce the environmental impact of chemical synthesis. In this context, abundant base-metal catalysis, especially the field of iron catalysis has gained significant attention in organic synthesis.¹ Iron has many advantages over other transition metals, such as low cost, low toxicity, its natural abundance, environmentally benign nature and often straightforward protocols for conversion to its corresponding salts and complexes. During the last three decades, there has been a growing interest in using green solvents in chemical processes. In recent solvent selection guidelines, dimethyl carbonate (DMC) has been classified as a “recommended” solvent.² The green merits of dimethyl carbonate are fast biodegradability, low toxicity, mild odor, low evaporation rate, low density and good environmental compatibility.³ The latter can be explained by its low photochemical ozone creation potential (POCP) in comparison to common volatile organic compounds (VOCs) (2.5; *e.g.* ethylene = 100) and its recent production methods using CO_2 as a raw material.^{3f,g}

Homoallylamines are valuable intermediates and important structural motifs in organic chemistry for the synthesis of heterocycles, natural products and pharmaceutical compounds.⁴ The most common approach for α -substituted homoallylamine synthesis is the direct nucleophilic addition of allylic organometal or metalloid derivatives to imines (Scheme 1A).⁵ However, the addition of allyl Grignard reagents to imines are limited and mainly restricted to non-enolizable imines.⁶ Aldimines which contain α -hydrogens generally fail to give acceptable yields of secondary amines due to the poor electrophilicity of the imine carbon and competing α -deprotonation.^{6a–e} In this regard, less

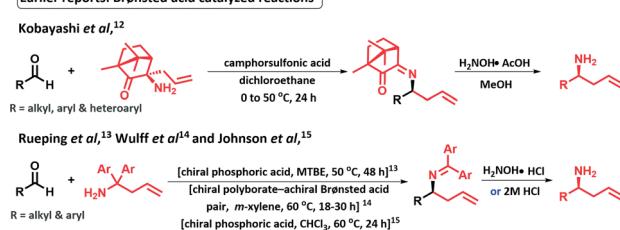
basic reagents such as allyl stannanes, allyl silanes, allyl boronates and allyl boranes have been used. Despite significant utility of these reported methods, many of these procedures still show drawbacks, including generation of stoichiometric amounts of metal-containing (toxic) waste. Furthermore, often harsh deprotection conditions are required to obtain N-unprotected homoallylamines, also generating extra waste, which in most of the cases cannot be recovered and reused for reagent synthesis.^{5–7}

[A] The most common approach: Nucleophilic addition to imines and iminium ions

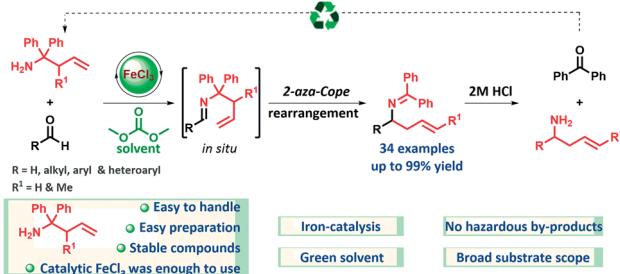


[B] 2-Aza-Cope rearrangement approach

Earlier reports: Brønsted acid catalyzed reactions



This work: Iron Lewis acid catalyzed reaction in dimethyl carbonate



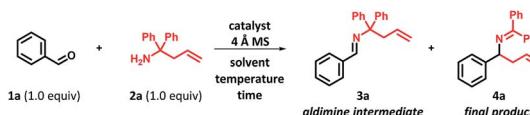
Organic Synthesis, Department of Chemistry, University of Antwerp, Groenenborgerlaan 171, 2020 Antwerp, Belgium. E-mail: kourosh.abbaspourtehrani@uantwerpen.be; Fax: +32 32653233; Tel: +32 32653226

† Electronic supplementary information (ESI) available. See DOI: 10.1039/c9ra03277k

Scheme 1 Synthesis of α -substituted homoallylamines.

On the other hand, the [3,3]-sigmatropic rearrangement approach for homoallylamine synthesis is much less developed. In 1950, Horowitz and Geissman first reported a 2-aza-Cope rearrangement.⁸ This reaction has rarely been utilized in organic synthesis due to the inherent problem of the reversibility of the process.⁹ In pioneering studies, Overman and co-workers devised an aza-Cope–Mannich reaction sequence to overcome this problem and have applied this development successfully in numerous alkaloid syntheses.¹⁰ Recently, an aza-Cope rearrangement strategy has been utilized in fluorescent probes for imaging formaldehyde in biological systems.¹¹ In literature, very few reports of 2-aza-Cope rearrangements are known for the synthesis of homoallylamines from aldehydes (Scheme 1B).^{12–15} In 2006, Kobayashi and co-workers developed a Brønsted acid catalyzed method for the synthesis of chiral homoallylamines from aldehyde and chiral camphorquinone derived homoallylamine.¹² Unfortunately, highly hazardous dichloroethane was employed as solvent. In 2008, Rueping and Antonchick reported the first chiral phosphoric acid catalyzed aza-Cope rearrangement for the synthesis of chiral homoallylamines.¹³ Although the α -substituted homoallylamines were isolated in moderate to good yield (up to 87%), in good to high enantiomeric excesses (up to 94% ee) at 50 °C in methyl *tert*-butyl ether, this method limited to aromatic aldehydes and requires longer reaction times (48 h), which is a drawback. In 2011, Wulff *et al.*, developed chiral polyborate – achiral Brønsted acid pair catalyzed reaction at 60 °C in *m*-xylene to improve the enantioselection with broader substrate scope for homoallylamines.¹⁴ Most recently, Johnson and co-workers reported an enantioconvergent method for the synthesis of chiral β -amino amides from racemic β -formyl amides and diphenylhomoallylamines at 60 °C in chloroform.¹⁵ To the best of our knowledge, no examples of Lewis acid catalyzed 2-aza-Cope rearrangement for the synthesis of homoallylamines from aldehydes in green solvent have been reported. Inspired by above catalytic methodologies and as a continuation of our efforts in imine activation reactions,¹⁶ herein we report an efficient and eco-friendly synthesis of homoallylamines *via* an iron(III)-catalyzed 2-aza-Cope rearrangement of *in situ* generated aldimines from readily accessible 1,1-diphenylhomoallylamines and aldehyde feedstocks. In this developed protocol, non-toxic and inexpensive iron(III) chloride has been used as a catalyst and the reaction has been carried out in dimethyl carbonate.

We commenced the optimization studies using benzaldehyde (**1a**) and 1,1-diphenylhomoallylamine (**2a**) as the model substrates. In the light of the recent advances in the field, the choice of sterically hindered 1,1-diphenylhomoallylamine was crucial to drive the reaction from the aldimine intermediate to the ketimine product.^{13–15} Our preliminary experiments with screening of various Lewis acids revealed that, the aza-Cope rearrangement on intermediate **3a** can be achieved by using 10 mol% of $\text{Fe}(\text{OTf})_3$ (see the ESI Section-2† for details). Further, we continued our study from benzaldehyde (**1a**, 1.0 equiv.) and 1,1-diphenylhomoallylamine (**2a**, 1.0 equiv.) using iron salts as catalysts in standardly used dichloromethane in a sealed vial at 50 °C (Table 1). Screening of a number of iron salts revealed that FeCl_3 was the best catalyst in terms of higher yield and relative cost (entries 1–5). Interestingly from solvent screening studies, dimethyl carbonate was found to

Table 1 Optimization of the reaction conditions^a

Entry	Catalyst (10 mol%)	Solvent	Temp (°C)	Time (h)	Yield [%]	
					3a	4a
1	$\text{Fe}(\text{OTf})_3$	CH_2Cl_2	50	18	17	78
2	$\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$	CH_2Cl_2	50	18	22	76
3	$\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$	CH_2Cl_2	50	18	54	29
4	FeCl_2	CH_2Cl_2	50	18	38	44
5	FeCl_3	CH_2Cl_2	50	18	13	85
6	FeCl_3	$\text{ClCH}_2\text{CH}_2\text{Cl}$	85	18	0	98
7 ^c	FeCl_3	H_2O	50	18	65	0
8	FeCl_3	DMSO	50	18	58	0
9	FeCl_3	DMF	50	18	47	0
10	FeCl_3	MeCN	82	18	0	94
11	FeCl_3	MeOH	65	18	84	14
12	FeCl_3	1,4-Dioxane	101	18	0	94
13	FeCl_3	EtOAc	78	18	0	89
14	FeCl_3	2-MeTHF	80	18	0	94
15	FeCl_3	<i>n</i> -BuOAc	126	18	0	94
16	FeCl_3	Toluene	110	18	0	91
17 ^c	FeCl_3	Neat	50	18	48	0
18	FeCl_3	DMC	25	18	9	71
19	FeCl_3	DMC	50	18	3	90
20	FeCl₃	DMC	90	6	0	99
21 ^c	FeCl_3	DMC	90	18	1	59
22 ^d	FeCl_3	DMC	90	18	64	24
23	No catalyst	DMC	90	18	91	6
24	$\text{Fe}(\text{OTf})_3$	DMC	90	18	0	91
25	InCl_3	DMC	90	18	0	94
26	AlCl_3	DMC	90	18	70	11
27 ^e	$\text{BF}_3 \cdot \text{Et}_2\text{O}$	DMC	90	18	0	81

^a Reaction conditions: **1a** (0.25 mmol, 1.0 equiv.), **2a** (0.25 mmol, 1.0 equiv.), catalyst (10 mol%), 4 Å MS (100 mg) and solvent (0.5 mL).

^b Yields were determined by ¹H NMR analysis with 1,3,5-trimethoxybenzene as internal standard. ^c Without MS. ^d 5 mol% of FeCl_3 was used. ^e 100 mol% of $\text{BF}_3 \cdot \text{Et}_2\text{O}$ was used. DMC = dimethyl carbonate. MS = molecular sieves.

be the best alternative for dichloromethane and the most of the solvents were compatible solvents for the reaction except polar solvents such as water, DMSO, DMF and MeOH (entries 5–20). Further, elevating the reaction temperature increased the reaction rate with complete conversion (entries 18–20). The FeCl_3 catalyst furnished a complete and clean conversion within 6 h at 90 °C in dimethyl carbonate (99%, entry 20) and no traces of aldimine intermediate **3a** were found in the reaction mixture.

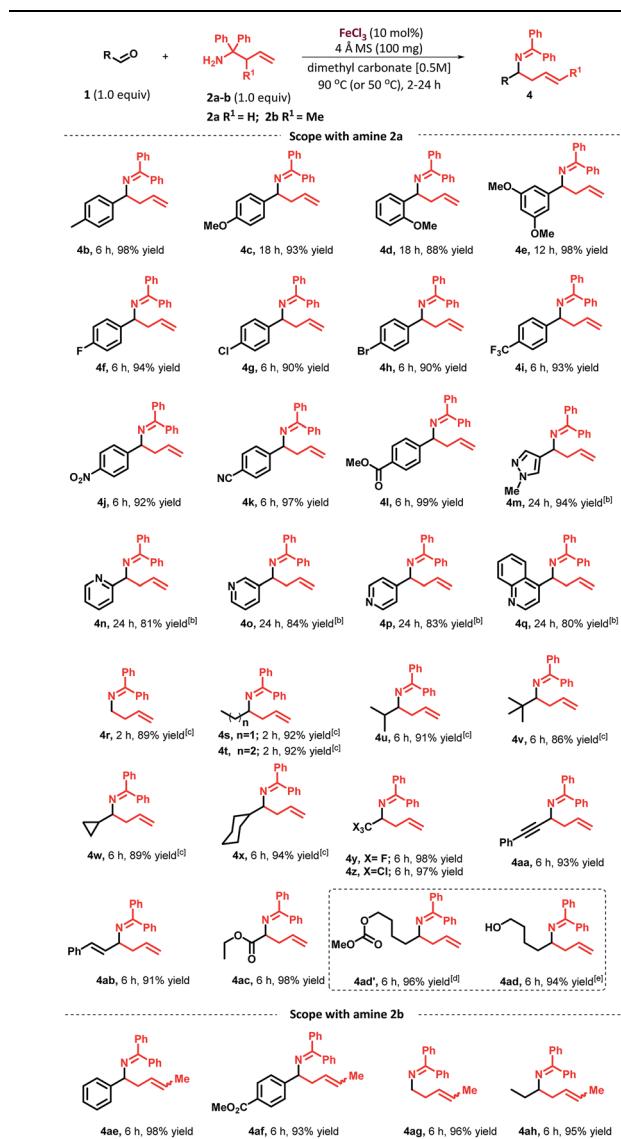
The formation of the product **4a** was reduced when the reaction was carried out in the absence of molecular sieves (entry 21). Further, upon decreasing the amount of FeCl_3 to 5 mol%, the yield of the product **4a** was reduced and unsurprisingly, **3a** was observed as major product without catalyst (entries 22–23). Under the optimized condition, similar yields were achieved with $\text{Fe}(\text{OTf})_3$ and InCl_3 (entries 24–25), while other Lewis acids such as AlCl_3 and $\text{BF}_3 \cdot \text{Et}_2\text{O}$ afforded the product in lower yield (entries 26–27). Based



on our Lewis acid catalyst screening (see the ESI Section-2† for details), FeCl_3 , InCl_3 , BiCl_3 , $\text{Fe}(\text{OTf})_3$, $\text{In}(\text{OTf})_3$, $\text{Sc}(\text{OTf})_3$ and $\text{Yb}(\text{OTf})_3$ were found to be effective catalysts and furnished the expected rearranged product in above 75% yield, while FeCl_2 , CuCl_2 , AlCl_3 , $\text{Ni}(\text{OTf})_2$ and other Lewis acids did not lead to good yields. These results seems to be in good agreement with literature¹⁷ data on classification of Lewis acids with respect to their activities in aldimine reactions. The low-toxic and inexpensive FeCl_3 catalyst was selected for further investigation of the scope of the reaction.

As depicted in Table 2, the scope of aldehydes was first investigated with 1,1-diphenyl homoallylamine (2a). To our

Table 2 Substrate scope^a

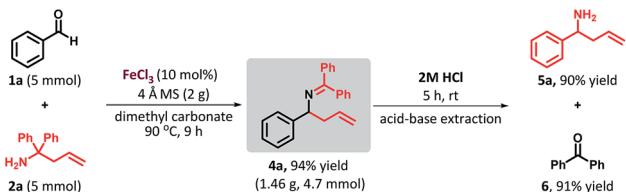


^a Reaction conditions: **1** (0.25 mmol, 1 equiv.), **2a** or **2b** (0.25 mmol, 1 equiv.), FeCl_3 (10 mol%), 4 Å molecular sieves (100 mg) in dimethyl carbonate (0.5 mL, 0.5 M), 90 °C, isolated yield. ^b 25 mol% of FeCl_3 was used. ^c Reactions were carried out at 50 °C. ^d 96% yield of methoxycarbonylation of alcohol product was obtained. ^e In place of dimethyl carbonate, propylene carbonate was used as solvent at 90 °C.

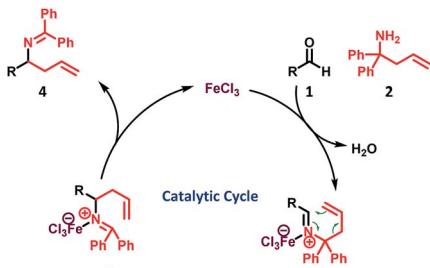
delight, the scope of aldehydes was broad, providing high yields and showcasing the generality of this method. Aryl aldehydes bearing *ortho*-, *meta*- and *para*-substituents at the arene ring were all well tolerated under the optimized reaction conditions. As tabulated, *p*-tolualdehyde furnished the desired product **4b** in 98% yield. In the case where the aryl ring contains an electron-donating methoxy group at the *para*-position (**4c**) and *ortho*-position (**4d**), it took 18 h to drive the reaction to completion. In general, we observed that electron rich aromatic aldehydes require longer reaction time than electron-poor aromatic aldehydes. The reaction of 3,5-dimethoxybenzaldehyde furnished the desired product **4e** in 98% yield. Similarly, benzaldehyde with fluoro-, chloro-, bromo- or trifluoromethyl substituents at the *para*-position afforded the desired products **4f-i** in excellent yields (94%, 90%, 90% and 93% respectively). In addition, substituted benzaldehydes containing a variety of functional groups such as nitro (**4j**), nitrile (**4k**) and ester (**4l**) were compatible with the reaction conditions. Interestingly, heteroaromatic aldehydes containing a pyrazole, pyridine and quinoline ring were also successful and provided the desired products **4m-q** in good yields, although a higher catalyst loading (25 mol%) was required. The use of a higher catalyst loading and slow progress of the reaction can be explained by the strong coordination between the nitrogen from the heterocyclic aldehyde with the metal catalyst, rendering the metal catalyst unavailable for participation in the catalytic cycle. As expected, the reaction of paraformaldehyde afforded **4r** in 89% yield. Furthermore, linear, branched, and cyclic aliphatic aldehydes such as propionaldehyde, butyraldehyde, isobutyraldehyde, pivalaldehyde, cyclopropane- and cyclohexanecarboxaldehyde furnished the corresponding homoallylamines **4s-x**, at 50 °C in 92%, 92%, 91%, 86%, 89% and 94% yields, respectively. Interestingly, transformation with trifluoroacetaldehyde hydrate and chloral hydrate provided the desired products **4y** and **4z** in excellent yields. In addition, it is worth noting that a variety of functional groups such as phenylpropargyl (**4aa**), *trans*-cinnamyl (**4ab**) and ester (**4ac**) were all well tolerated in the transformation, which would offer the potential for increasing molecular complexity *via* further functionalization. In the case of aldehyde substrate containing a hydroxy group, under the optimized reaction conditions, the methoxycarbonylated product **4ad'** was obtained in 96% yield instead of the expected product **4ad**.¹⁸ To overcome this particular substrate issue, switching solvent system to propylene carbonate afforded the desired product **4ad** in 94% yield. Next, we examined the scope of aldehydes with 2-methyl-1,1-diphenyl homoallylamine (**2b**). Under the optimized conditions, these reactions furnished *E/Z* mixtures of the corresponding homoallylamines **4ae-ah** in good to excellent yields. The most of the examples in Table 2 did not require column chromatography purification.

To further demonstrate the potential of this method, a gram-scale reaction was performed. The reaction of benzaldehyde (**1a**, 5 mmol) and 1,1-diphenyl homoallylamine (**2a**, 5 mmol) under standard reaction conditions furnished the desired product **4a** in 94% yield (Scheme 2). Further, the ketimine **4a** was easily hydrolyzed under mild acidic conditions to obtain free amine **5a**





Scheme 2 Scale-up reaction, hydrolysis of the ketimine and recovery of benzophenone.



Scheme 3 Plausible catalytic cycle.

in 90% yield and recovered benzophenone in 91% yield after simple acid–base extraction (Scheme 2).

Based on our observations (see the ESI Section-3† for details) and in light of recent reports,^{13–15,16} the following reaction mechanism is proposed (Scheme 3). The reaction of the 1,1-diphenylhomoallylamine and an aldehyde promoted by iron(III) chloride generates iminium species A first, and further subsequent a cationic 2-aza-Cope rearrangement of A affords intermediate B through a cyclic transition state, which is less sterically hindered than the starting sigmatropic isomer A. Further, the intermediate B results in the formation of the corresponding α -substituted homoallylamine 4 with concomitant regeneration of the active iron(III) chloride.

In summary, this study demonstrate the first example of iron catalyzed 2-aza-Cope rearrangement for the synthesis of a wide variety of α -substituted homoallylamines from readily accessible starting materials in a green solvent, producing water as the sole by-product. By this protocol, the synthesis of α -alkyl-, alkenyl-, aryl- and heteroaryl homoallylamines are achieved with high yields. Notably, N-unprotected (free NH_2) α -substituted homoallylamines can be easily generated by mild acidic treatment of the rearranged benzophenone imines.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This research was financially supported by the University of Antwerp (BOF) and the Hercules Foundation. The authors

thank Prof. Filip Lemière (University of Antwerp) for HRMS measurements.

Notes and references

- For selected reviews on iron catalysis, see: (a) C. Bolm, J. Legros, J. Le Pailh and L. Zani, *Chem. Rev.*, 2004, **104**, 6217; (b) B. Plietker, in *Iron Catalysis in Organic Chemistry*, ed. B. Plietker, WILEY-VCH Verlag, Weinheim, 2008; (c) S. Enthaler, K. Junge and M. Beller, *Angew. Chem., Int. Ed.*, 2008, **47**, 3317; (d) A. Correa, O. Garcia Mancheño and C. Bolm, *Chem. Soc. Rev.*, 2008, **37**, 1108; (e) B. D. Sherry and A. Fürstner, *Acc. Chem. Res.*, 2008, **41**, 1500; (f) W. M. Czaplik, M. Mayer, J. Cvengroš and A. Jacobi von Wangelin, *ChemSusChem*, 2009, **2**, 396; (g) R. H. Morris, *Chem. Soc. Rev.*, 2009, **38**, 2282; (h) C.-L. Sun, B.-J. Li and Z.-J. Shi, *Chem. Rev.*, 2011, **111**, 1293; (i) K. Gopalaiah, *Chem. Rev.*, 2013, **113**, 3248; (j) I. Bauer and H.-J. Knölker, *Chem. Rev.*, 2015, **115**, 3170; (k) A. Fürstner, *ACS Cent. Sci.*, 2016, **2**, 778; (l) A. Guérinot and J. Cossy, *Top. Curr. Chem.*, 2016, **374**, 49; (m) R. Shang, L. Ilies and E. Nakamura, *Chem. Rev.*, 2017, **117**, 9086.
- (a) D. Prat, A. Wells, J. Hayler, H. Sneddon, C. R. McElroy, S. Abou-Shehada and P. J. Dunn, *Green Chem.*, 2016, **18**, 288; (b) H. E. Gottlieb, G. Graczyk-Millbrandt, G. G. A. Inglis, A. Nudelman, D. Perez, Y. Qian, L. E. Shuster, H. F. Sneddon and R. J. Upton, *Green Chem.*, 2016, **18**, 3867; (c) C. M. Alder, J. D. Hayler, R. K. Henderson, A. M. Redman, L. Shukla, L. E. Shuster and H. F. Sneddon, *Green Chem.*, 2016, **18**, 3879; (d) N. R. Babij, E. O. McCusker, G. T. Whiteker, B. Canturk, N. Choy, L. C. Creemer, C. V. De Amicis, N. M. Hewlett, P. L. Johnson, J. A. Knobelsdorf, F. Li, B. A. Lorsbach, B. M. Nugent, S. J. Ryan, M. R. Smith and Q. Yang, *Org. Process Res. Dev.*, 2016, **20**, 661.
- (a) P. Tundo and M. Selva, *Acc. Chem. Res.*, 2002, **35**, 706; (b) B. Schäffner, F. Schäffner, S. P. Verevkin and A. Börner, *Chem. Rev.*, 2010, **110**, 4554; (c) F. Aricò and P. Tundo, *Russ. Chem. Rev.*, 2010, **79**, 479; (d) S.-H. Pyo, J. H. Park, T.-S. Chang and R. Hatti-Kaula, *Curr. Opin. Green Sustain. Chem.*, 2017, **5**, 61; (e) G. Fiorani, A. Perosa and M. Selva, *Green Chem.*, 2018, **20**, 288; (f) F. Rivetti, *Green Chemistry: Challenging Perspectives*, ed. P. T. Anastas and P. Tundo, Oxford University Press, 2000, p. 201; (g) M. E. Jenkin and G. D. Hayman, *Atmos. Environ.*, 1999, **33**, 1275.
- Representative examples, see: (a) C. O. Puentes and V. Kouznetsov, *J. Heterocycl. Chem.*, 2002, **39**, 595; (b) T. Saloranta and R. Leino, *Tetrahedron Lett.*, 2011, **52**, 4619; (c) I. Bosque, J. C. González-Gómez, A. Guijarro, F. Foubelo and M. Yus, *J. Org. Chem.*, 2012, **77**, 10340; (d) S. Zhao, G. Sirasani, S. Vaddypally, M. J. Zdilla and R. B. Andrade, *Angew. Chem., Int. Ed.*, 2013, **52**, 8309; (e) A. Feula, S. S. Dhillon, R. Byravan, M. Sangha, R. Ebanks, M. A. H. Salih, N. Spencer, L. Male, I. Magary, W. P. Deng, F. Müller and J. S. Fossey, *Org. Biomol. Chem.*, 2013, **11**, 5083; (f) B. Su, H. Zhang, M. Deng and Q. Wang, *Org. Biomol. Chem.*, 2014, **12**, 3616; (g) S. Munagala, G. Sirasani,

P. Kokkonda, M. Phadke, N. Krynetskaia, P. Lu, F. J. Sharom, S. Chaudhury, M. D. M. Abdulhameed, G. Tawa, A. Wallqvist, R. Martinez, W. Childers, M. Abou-Gharbia, E. Krynetskiy and R. B. Andrade, *Bioorg. Med. Chem.*, 2014, **22**, 1148; (h) P.-F. Chiang, W.-S. Li, J.-H. Jian, T.-S. Kuo, P.-Y. Wu and H.-L. Wu, *Org. Lett.*, 2018, **20**, 158; (i) T. Druzhenko, Y. Skalenko, M. Samoilenko, A. Denisenko, S. Zozulya, P. O. Borysko, M. I. Sokolenko, A. Tarasov and P. K. Mykhailiuk, *J. Org. Chem.*, 2018, **83**, 1394; (j) T. Guo, B.-H. Yuan and W.-J. Liu, *Org. Biomol. Chem.*, 2018, **16**, 57.

5 For selected reviews, see: (a) Y. Yamamoto and N. Asao, *Chem. Rev.*, 1993, **93**, 2207; (b) D. Enders and U. Reinhold, *Tetrahedron: Asymmetry*, 1997, **8**, 1895; (c) R. Bloch, *Chem. Rev.*, 1998, **98**, 1407; (d) S. Kobayashi and H. Ishitani, *Chem. Rev.*, 1999, **99**, 1069; (e) G. Alvaro and D. Savoia, *Synlett*, 2002, **2002**, 651; (f) S. Kobayashi, Y. Mori, J. S. Fossey and M. M. Salter, *Chem. Rev.*, 2011, **111**, 2626; (g) M. Yus, J. C. González-Gómez and F. Foubelo, *Chem. Rev.*, 2011, **111**, 7774.

6 (a) H. Thies and H. Schonenberger, *Chem. Ber.*, 1956, **89**, 1918; (b) H. Gilman and J. Eisch, *J. Am. Chem. Soc.*, 1957, **79**, 2150; (c) G. Stork and S. R. Dowd, *J. Am. Chem. Soc.*, 1963, **85**, 2178; (d) R. W. Layer, *Chem. Rev.*, 1963, **63**, 489; (e) A. R. Katritzky, Q. Hong and Z. Yang, *J. Org. Chem.*, 1994, **59**, 7947; (f) A. Desmarchelier, P. Ortiz and S. R. Harutyunyan, *Chem. Commun.*, 2015, **51**, 703.

7 P. G. M. Wuts, *Greene's Protective Groups in Organic Synthesis*, John Wiley & Sons, Hoboken, 5th edn, 2014.

8 R. M. Horowitz and T. A. Geissman, *J. Am. Chem. Soc.*, 1950, **72**, 1518.

9 (a) D. J. Hart and Y. M. Tsai, *Tetrahedron Lett.*, 1981, **22**, 1567; (b) P. M. M. Nossin, J. A. M. Hamersma and W. N. Speckamp, *Tetrahedron Lett.*, 1982, **23**, 3807; (c) H. Ent, H. de Koning and W. N. Speckamp, *Tetrahedron Lett.*, 1983, **24**, 2109; (d) H. Ent, H. de Koning and W. N. Speckamp, *Tetrahedron Lett.*, 1985, **26**, 5105; (e) E. Vedejs, S. C. Fields, R. Hayashi, S. R. Hitchcock, D. R. Powell and M. R. Schrimpf, *J. Am. Chem. Soc.*, 1999, **121**, 2460; (f) P. Müller, J.-L. Toujas and G. Bernardinelli, *Helv. Chim. Acta*, 2000, **83**, 1525; (g) Z. D. Aron and L. E. Overman, *Org. Lett.*, 2005, **7**, 913; (h) P. Merino, T. Tejero and V. Mannucci, *Tetrahedron Lett.*, 2007, **48**, 3385; (i) E. Marca, I. Delso, T. Tejero, J. T. Vazquez, R. L. Dorta and P. Merino, *Tetrahedron Lett.*, 2009, **50**, 7152; (j) M. P. McCormack, T. Shalumova, J. M. Tanski and S. P. Waters, *Org. Lett.*, 2010, **12**, 3906; (k) I. Delso, T. Tejero, A. Goti and P. Merino, *J. Org. Chem.*, 2011, **76**, 4139; (l) I. Delso, A. Melicchio, A. Isasi, T. Tejero and P. Merino, *Eur. J. Org. Chem.*, 2013, **2013**, 5721; (m) M. P. McCormack and S. P. Waters, *J. Org. Chem.*, 2013, **78**, 1176; (n) S. Toulot, Q. Bonnin, V. Comte, L. Adriaenssens, P. Richard and P. Le Gendre, *Eur. J. Org. Chem.*, 2013, **2013**, 736; (o) I. Bosque, F. Foubelo and J. C. Gonzalez-Gomez, *Org. Biomol. Chem.*, 2013, **11**, 7507; (p) J. Liu, C. G. Cao, H. B. Sun, X. Zhang and D. Niu, *J. Am. Chem. Soc.*, 2016, **138**, 13103.

10 (a) L. E. Overman and M.-A. Kakimoto, *J. Am. Chem. Soc.*, 1979, **101**, 1310; (b) L. E. Overman and L. T. Mendelson, *J. Am. Chem. Soc.*, 1981, **103**, 5579; (c) L. E. Overman, L. T. Mendelson and L. A. Flippin, *Tetrahedron Lett.*, 1982, **23**, 2733; (d) L. E. Overman, M. Kakimoto, M. E. Okazaki and G. P. Meier, *J. Am. Chem. Soc.*, 1983, **105**, 6622; (e) M. Brüggemann, A. I. McDonald, L. E. Overman, M. D. Rosen, L. Schwink and J. P. Scott, *J. Am. Chem. Soc.*, 2003, **125**, 15284; (f) W. G. Earley, J. E. Jacobsen, A. Madin, G. P. Meier, C. J. O'Donnell, T. Oh, D. W. Old, L. E. Overman and M. J. Sharp, *J. Am. Chem. Soc.*, 2005, **127**, 18046; (g) C. L. Martin, L. E. Overman and J. M. Rohde, *J. Am. Chem. Soc.*, 2008, **130**, 7568; (h) T. B. Dunn, J. M. Ellis, C. C. Kofink, J. R. Manning and L. E. Overman, *Org. Lett.*, 2009, **11**, 5658; (i) C. L. Martin, L. E. Overman and J. M. Rohde, *J. Am. Chem. Soc.*, 2010, **132**, 4894.

11 (a) T. F. Brewer and C. J. Chang, *J. Am. Chem. Soc.*, 2015, **137**, 10886; (b) A. Roth, H. Li, C. Anorma and J. Chan, *J. Am. Chem. Soc.*, 2015, **137**, 10890.

12 M. Sugiura, C. Mori and S. Kobayashi, *J. Am. Chem. Soc.*, 2006, **128**, 11038.

13 M. Rueping and A. P. Antonchick, *Angew. Chem., Int. Ed.*, 2008, **47**, 10090.

14 (a) H. Ren and W. D. Wulff, *J. Am. Chem. Soc.*, 2011, **133**, 5656; (b) H. Ren and W. D. Wulff, *Org. Lett.*, 2013, **15**, 242.

15 C. G. Goodman and J. S. Johnson, *J. Am. Chem. Soc.*, 2015, **137**, 14574.

16 (a) S. Stas, K. Abbaspour Tehrani and G. Laus, *Tetrahedron*, 2008, **64**, 3457; (b) C. C. Malakar, B. U. W. Maes and K. Abbaspour Tehrani, *Adv. Synth. Catal.*, 2012, **354**, 3461; (c) C. C. Malakar, S. Stas, W. Herrebout and K. Abbaspour Tehrani, *Chem.-Eur. J.*, 2013, **19**, 14263; (d) W. E. Van Beek, J. Van Stappen, P. Franck and K. Abbaspour Tehrani, *Org. Lett.*, 2016, **18**, 4782.

17 S. Kobayashi, T. Busujima and S. Nagayama, *Chem.-Eur. J.*, 2000, **6**, 3491.

18 S. Jin, A. J. Hunt, J. H. Clark and C. R. McElroy, *Green Chem.*, 2016, **18**, 5839.

