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New active-iron based reducing system for carbonyl compounds and imines. Stereoselective reduction of cyclic ketones

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Abstract—The reaction of different carbonyl compounds and imines with a mixture of iron(II) chloride tetrahydrate, an excess of lithium powder, and a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB, 5 mol%) in THF at room temperature, led to the formation of the corresponding alcohols and amines, respectively. The process was also applied to the transformation of α,β-unsaturated carbonyl compounds into the corresponding saturated alcohols. The new reducing system exhibited good to excellent diastereoselectivity toward the reduction of different monocyclic and polycyclic ketones.

1. Introduction

From the fundamental point of view, reduction reactions of unsaturated organic substrates represent one of the most widely used and valuable functional group transformations in synthetic organic chemistry. Metal-mediated reductions of unsaturated organic substrates by hydrogen- or electron-transfer, are currently considered as interesting alternatives to the widely used catalytic hydrogenation, because of their both considerable practical and fundamental importance. Their practical meaning arise from the fact that such reactions are convenient both in large- or lab-scale synthesis, since there is no need to employ a high hydrogen pressure or to use hazardous reducing agents.

Among the various reducible substrates, aldehydes, ketones, α,β-unsaturated carbonyl compounds and imines, are of great relevance in order to obtain the corresponding alcohols and amines, respectively. Different valuable methods have been reported to perform these reactions, from which four important general procedures can be highlighted involving the use of (a) metal hydrides; (b) dissolving metals; (c) catalytic hydrogenation, mainly under heterogeneous reaction conditions and (d) transfer hydrogenation.[1] Some other methods, such as electrochemical or enzymatic methods are of less general application.

On the other hand, the stereoselective reduction of cyclic ketones is an extremely important reaction in organic synthesis. Most of the published results in this area consist in using metal hydrides or complex reducing agents, for which correlations of the stereochemical outcome have been proposed by numerous investigators.[2] In general, bulky reducing agents favour the approach to the carbonyl group via an equatorial trajectory, giving the thermodynamically less stable axial alcohol. Among the known methods to achieve this transformation, those involving the Selectride reagents developed by Brown are the most notable,[3] although many other interesting methods have been reported.[4] Concerning the synthesis of the more stable equatorial alcohols from cyclic ketones, although several valuable methods have been devised,[5] generally acceptable reagents for this transformation are not as well developed.

In recent years, we have worked with new reducing systems based on the use of activated transition metals, mainly active nickel, generated from the system $NiCl_2 \cdot 2H_2O$–Li–arene (cat.), which demonstrated to be very efficient in the reduction of a wide variety of organic functionalities.[6] More recently, and taking into account the periodic table proximity and the little work published regarding copper-mediated reduction reactions, we focused on the copper-based $CuCl_2 \cdot 2H_2O$–Li–arene (cat.) combination, which

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was found to be very efficient in the reduction of carbonyl compounds and imines,[7] as well as in the hydrodehalogenation[8a] of aryl and alkyl halides.[8b]

The results obtained thereof together with our ongoing interest in the field above described, encouraged us to explore new metal alternatives to these active-metal based reducing systems, now focusing on iron, as a possible candidate to be used in the reduction or carbonyl compounds and imines. Iron salts are cheap when compared with other transition metal salts. Other main advantages are, however, the fact that its environmental impact is virtually nil and that there is no exposure limit to humans, as stated by the OSHA (United States Occupational Safety and Health Administration).

In this sense, most of the literature revised deals with the reduction of α,β-unsaturated carbonyl compounds. Conjugate reduction can be accomplished either by using hydridoiron complexes, prepared in situ from iron pentacarbonyl $Fe(CO)_5$ and a small amount of NaOH in methanol,[9] or by the binuclear cluster hydride $NaHFe_2(CO)_2$ with both excellent yields and mild reaction conditions.[10] On the other hand, the *cis*-hydride η^2-dihydrogen iron complex, $[P(CH_2CH_2PPh_2)_3Fe(H)(H_2)]BPh_4$, has been used as homogeneous catalyst in the hydrogen transfer reduction of α,β-unsaturated ketones to give either the saturated ketones, or the saturated or unsaturated alcohols, depending on the substrate, with fairly good results.[11] In another case, the iron(II) or (III) chloride–sodium hydride system has demonstrated to be an effective reducing agent for the reduction of ketones and aldehydes to the corresponding alcohols but with long reaction times.[12]

Finally, to the best of our knowledge, no published results appear in the literature regarding the iron-mediated stereoselective reduction of cyclic ketones (a fundamental subject in the synthesis of organic biomolecules) or the reduction of imines.

In this paper, we want to present a simple and effective methodolgy to accomplish the reduction of carbonyl compounds and imines under very mild reaction conditions, based on the use of active iron, generated from commercially available iron(II) chloride tetrahydrate, lithium and a catalytic amount of DTBB (4,4′-di-*tert*-butylbiphenyl) as electron carrier.[13] The results obtained are encouraging since aldehydes, ketones (including saturated, cyclic, and α,β-unsaturated substrates) and imines are reduced to the corresponding alcohols and amines in good yields, the reduction of cyclic ketones showing good to excellent diastereoselectivity.

2. Results and discussion

2.1. Reduction of carbonyl compounds

The reaction of different ketones and aldehydes with a mixture of iron(II) chloride tetrahydrate (1.0–2.5 mmol), an excess of lithium powder (1/8 molar ratio, referred to the iron salt), and a catalytic amount of DTBB (0.1 mmol/mmol of iron salt, 5 mol%) in tetrahydrofuran at room temperature, led to the corresponding secondary and primary alcohols, respectively, in good yields (Table 1).

Two blank experiments with nonan-5-one demonstrated the necessity of using the hydrated iron salt: either without the mentioned salt or using the corresponding anhydrous one, the starting material was recovered accompanied by traces of the pinacol coupling products after stirring overnight at room temperature.

The reducing system found application in the reduction of linear acyclic (Table 1, entry 1), dicycloalkyl (Table 1, entry 2), polycyclic (Table 1, entry 3), and aromatic ketones (Table 1, entries 4 and 5). For instance, the reduction of 2-adamantan-2-one (Table 1, entry 3) using 2 equiv of the reducing system rendered the corresponding 2-adamantan-2-ol in excellent yield. Lower conversion of the highly hindered ketone dicyclohexylketone (Table 1, entry 2), was, however, obtained and proved to be difficult to improve even with long reaction times, higher reaction temperature, or using an excess of the reducing system. More intriguing was the mediocre conversion achieved with acetophenone (Table 1, entry 4), above all taking into account that the related compound benzophenone (Table 1, entry 5) gave the corresponding alcohol in good yield after a reasonable reaction time.

On the other hand, the mentioned reducing system showed a remarkable behaviour in the reduction of cyclic ketones prone to yield diastereomeric alcohol products (Table 1, entries 6–10). In general, good to excellent diastereoselectivity was obtained, which was, however, difficult to rationalise in terms of a general mechanism, due to the different factors affecting the reduction pathway of cyclic ketones, namely: the nature of the metal, the structure of the ketone, the size of the reducing agent, the solvent, and the possibility of conformational equilibrium and of electrophilic assistance. Nonetheless, some comparison can be established on the basis of the examples available in the literature and of the steric approach control and product development control applied by Dauben and co-workers,[14] and redefined later by Brown and Deck[15] as steric strain control and product stability control, for the reduction of relatively hindered or unhindered cyclic ketones, respectively.

In the case of 4-*tert*-butylcyclohexanone (Table 1, entry 6), in which the bulky *tert*-butyl group is far from the carbonyl group, the resulting product was the thermodynamically more stable equatorial alcohol (eq/ax 99:1), *trans*-4-*tert*-butylcyclohexanol, the reduction seemingly being product stability controlled. Taking into account that the ratio of the alcohols formed remained constant after complete disappearance of the starting material, and considering that in an equilibrium mixture the more stable equatorial alcohol predominates by only 2.4:1, we discarded any isomerizing process.[2e] On one hand, the result obtained resembles those with the most common metal hydrides ($LiAlH_4$, $NaBH_4$, or $LiBH_4$, up to eq/ax 94:6)[16] or the complex reducing agents of Caubère's group (up to eq/ax 90:10).[17] In both cases, it was demonstrated that a maximum selectivity towards the axial attack was achieved by the addition of alkaline salts (like the LiCl in situ generated in our reaction). On the other

Table 1. Reduction of carbonyl compounds

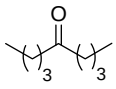
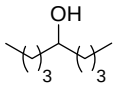
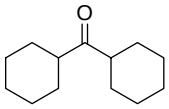
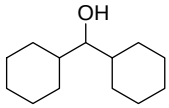
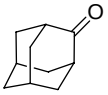
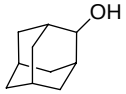
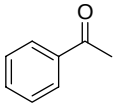
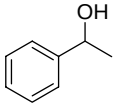
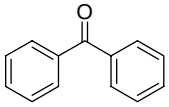
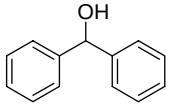
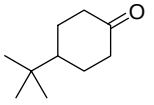
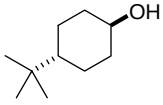
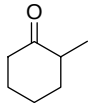
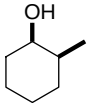
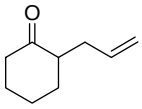
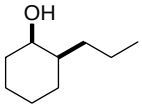
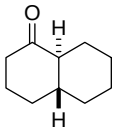
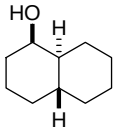
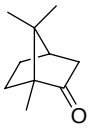
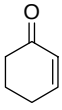
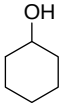
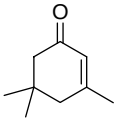
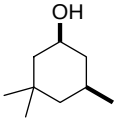
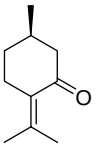
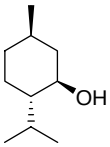
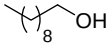
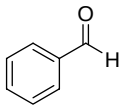
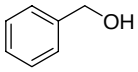
Entry	Carbonyl compound	Reaction conditions		Product[a]	
		$FeCl_2 \cdot 4H_2O$ (equiv)	t (h)	Structure	Yield (%)[b]
1		1.0	4		85
2		2.0	24		53[c]
3		2.0	3		90
4		2.0	24		50[d]
5		2.0	5		77
6		1.0	4		70[e]
7		1.5	3		82[f]
8		2.0	12		74[g]
9		1.5	3		91[h]
10		2.0	24		62[i]
11		2.5	4		82[j]
12		2.5	5		78[k]
13		2.5	5		75[l]
14		1.0	6		82

Table 1 (*continued*)

Entry	Carbonyl compound	Reaction conditions		Product[a]	
		$FeCl_2 \cdot 4H_2O$ (equiv)	*t* (h)	Structure	Yield (%)[b]
15		1.0	8		60[m]

[a] All isolated products were >95% pure (GLC).
[b] Isolated yield after column chromatography (silica gel, hexane/EtOAc) based on the starting material, unless otherwise stated.
[c] 60% Conversion; 40% recovered starting material.
[d] 55% Conversion; 45% recovered starting material.
[e] Diastereoisomeric ratio: trans/cis 99:1.
[f] Diastereoisomeric ratio: cis/trans 95:5.
[g] Diastereoisomeric ratio: cis/trans 95:5.
[h] Diastereoisomeric ratio: cis/trans 99:1.
[i] Diastereoisomeric ratio: *endo*/*exo* 90:10.
[j] GLC yield based on the starting material (cyclohexanol as external standard).
[k] 86% Conversion; diastereoisomeric ratio: cis/trans 99:1.
[l] Diastereoisomeric ratio: menthol/neoisomenthol/neomenthol 75:6:19.
[m] 70% Conversion; 25% recovered starting material.

hand, lithium in liquid ammonia afforded only the trans isomer, although in moderate yield (57%) and accompanied with unreacted ketone (25%) and the corresponding pinacol (18%).[18]

In the reduction of more hindered ketones (Table 1, entries 7–9), the reaction apparently proceeded through the approach of the reducing species from the less hindered side of the substrate, rendering the less stable axial alcohol, the reduction apparently being steric strain controlled. In particular, the diastereoselectivity observed in the reduction of 2-methylcyclohexanone (Table 1, entry 7, ax/eq 95:5) was comparable to that obtained with the more hindered lithium and potassium Selectrides (up to ax/eq 99:1) or with dicyclohexylborane (ax/eq 94:6)[19] in contrast with the major equatorial alcohol obtained with other common reducing systems such as $LiAlH_4$, $NaBH_4$, 9-BBN,[19] $BH_3 \cdot THF$[20] or with Li/NH_3.[21] The reduction of *trans*-decalone was highly effective (Table 1, entry 9), providing both high yield (91%) and diastereoselectivity (ax/eq 99:1), therefore being much superior to that reported with $NaBH_4$/MeOH (ax/eq ~35:65).[22]

Interestingly, the reduction of (±)-camphor (Table 1, entry 10) leading to the more stable of the two possible isomers, *endo*-borneol (*endo*/*exo* 90:10), required long reaction times (24 h) and an excess of the reducing system for a 70% conversion of the starting material. In this case, the stereochemistry of the alcohol product obtained was more consistent with a dissolving metal-type mechanism.[23] Thus, *endo*-borneol was the major product (*endo*/*exo* 82:18) in the reduction of (±)-camphor by alkali-metal/NH_3,[24] whereas M/NH_3 in the presence of MBr (M=Li, K) reduced (+)-camphor in a 53:47–80:20 *endo*/*exo* ratio of the corresponding alcohols.[25] According to Huffman and Charles,[21] for a hindered ketone, or one reacting sluggishly at the carbonyl carbon atom, the principal pathway for the reduction using dissolving metals would be that through the corresponding dianion, leading to a near-equilibrium distribution of product alcohols, which is quite consistent with our experimental observations.

When the above described methodology was applied to α,β-unsaturated carbonyl compounds (Table 1, entries 11–13), the use of an equimolecular amount of the metal salt afforded different mixtures of both possible partially reduced products (saturated ketones and α,β-unsaturated alcohols) together with the unreacted starting material. Unfortunately, all our efforts to drive the reaction pathway towards only one of these semireduction products were unsuccessful, even at low temperature (−10 to −78 °C) or at shorter reaction times. By using a 1:2.5 ketone to iron salt molar ratio, the process afforded the corresponding saturated alcohols in good yields. Regarding the stereochemistry of the reaction products, isophorone (Table 1, entry 12) was reduced to the more stable 1,5-diequatorial 3,3,5-trimethylcyclohexanol with excellent diastereoselectivity (see Table 1, footnote k). On the other hand, the reduction of (+)-pulegone also rendered the most stable of the four possible diastereomers, (−)-menthol, as the major product accompanied by minor amounts of neomenthol and neoisomenthol (see Table 1, footnote 1). Similar selectivity towards the axial attack on the carbonyl group of (+)-pulegone was also reported with $NaBH_4$–MeOH[26] or with lithium pyrrolidinoborohydride.[5d] On the other hand, the dissolving-metal reduction (both in the presence or absence of proton donors) of 3,3,5-trimethylcyclohexanone[21] and menthone[27] afforded high ratios of equatorial to axial alcohols, whereas the reduction of the former by either $LiAlH_4$ or $NaBH_4$ gave the axial alcohol as the major product.[28]

Finally, the reducing system described herein also found application in the reduction of aldehydes to the corresponding primary alcohols (Table 1, entries 14 and 15). Decanal was transformed into decan-1-ol in good yield (Table 1, entry 14), whereas benzaldehyde could not be completely reduced, exhibiting a similar behaviour to that of acetophenone (Table 1, entry 4).

Some additional experiments were carried out in order to disclose the main reaction mechanism operating in the above reactions. For instance, when 2-methylcyclohexanone was subjected to reduction with anhydrous $FeCl_2$–Li–DTBB (cat.)

under a molecular hydrogen atmosphere for 24 h, 2-methylcyclohexanol was obtained in 23% yield but with opposite diastereoselectivity to that shown in Table 1 (entry 7). The 75:25 trans/cis ratio obtained for 2-methylcyclohexanol might discard a catalytic hydrogenation-type reaction, in which iron would catalyse the addition to the carbonyl group of the molecular hydrogen resulting from the reaction of the excess of lithium with the hydration water of the iron salt. Despite the platinum-catalysed hydrogenation of 2-methylcyclohexanone in protic solvents furnished mainly the cis product, it is well known that several factors such as the structure of the substrate, the catalyst, the solvent, the reaction temperature, the pressure of hydrogen and other reaction conditions, can vary the stereochemistry of the catalytic hydrogenation of cyclic ketones.[29]

A preliminary mechanistic proposal can be made according to all the data showed above. A metal-dissolving reaction mechanism could be very plausible, which would directly explain the formation of the most stable *trans*-4-*tert*-butylcyclohexanol (Table 1, entry 6) and *endo*-borneol (Table 1, entry 10) by protonation of the most stable carbanion intermediate.[23b] In these two cases, a fast equilibrium between the two epimeric carbanions, followed by a slow protonation step through the lower axial and exo protonation transition states, respectively, would account for the formation of the thermodynamically more stable products. In contrast, due to the presence of acidic protons in the reaction medium, a kinetically controlled protonation of the intermediate carbanion can take place prior to equilibration,[23a] to furnish the less thermodynamically stable axial alcohols in the case of the structurally related 2-methylcyclohexanone, 2-allylcyclohexanone, and *trans*-decalone (Table 1, entries 7–9).

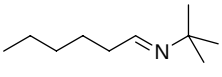
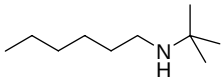
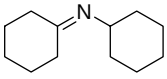
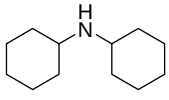
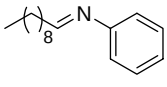
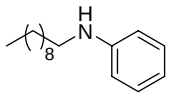
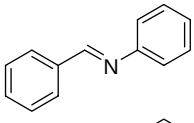
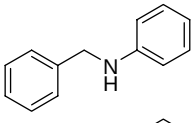
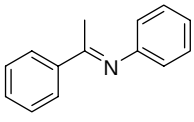
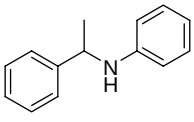
The reduction of α,β-unsaturated cyclic ketones (Table 1, entries 11–13) could be also explained in terms of a dissolving-metal mechanism. Assuming that two steps are involved in this process, reduction of the carbon–carbon double bond and reduction of the carbonyl group, enolate formation in the first step may lead to equilibration before reduction of the carbonyl group in (+)-pulegone, leaving the isopropyl group mainly trans to the methyl group (94:6). The high ratios in favour of the equatorial alcohols could be also explained by an equilibration pathway in the second step and are in agreement with those reported in the literature.[21,27]

Nonetheless, even with the assumption that a dissolving-metal mechanism is operating in the reduction of cyclic ketones, it must be pointed out the controversy arisen about whether these reductions are kinetically or thermodynamically controlled. As stated by Huffman, the different explanations proposed to account for the stereoselectivity of these reductions are of dubious predictive value.[30]

2.2. Reduction of imines

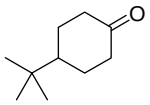
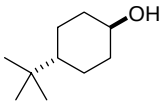
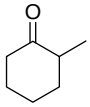
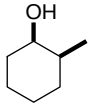
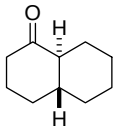
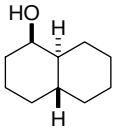
Table 2 lists the results obtained in the reduction of a series of aldimines and ketimines by applying the same above mentioned protocol for the reduction of carbonyl compounds. The corresponding secondary amines were obtained in good yields using a 1:2.0–2.5 imine to iron salt molar ratio. The lower yield observed in the case of the aldimine derived from benzaldehyde and aniline can be attributed to an overreduction, to some extent, at the benzylic position (Table 2, entry 4). On the contrary, this side reaction was not observed in the reduction of the ketimine derived from acetophenone and benzylamine, probably due to the shorter reaction time required (Table 2, entry 5).

Table 2. Reduction of imines

Entry	Imine	Reaction conditions		Product[a]	
		$FeCl_2 \cdot 4H_2O$	*t* (h)	Structure	Yield (%)[b]
1		2.0	8		78
2		2.0	12		74
3		2.5	14		82
4		2.5	14		65
5		2.5	8		77

[a] All isolated products were >95% pure (GLC).
[b] Isolated yield after column chromatography (silica gel, hexane/EtOAc) based on the starting material.

Table 3. Comparative stereoselective reduction of ketones with different metal salts

Entry	Ketone	Product[a]			
		Structure[b]	$NiCl_2 \cdot 2H_2O$[c]	$CuCl_2 \cdot 2H_2O$[c]	$FeCl_2 \cdot 4H_2O$[c]
1			95:5 (73)	95:5 (70)	99:1 (70)
2			90:10 (85)	85:15 (73)	95:5 (82)
3			99:1 (88)	99:1 (84)	99:1 (91)
4			80:20 (65)	85:15 (55)	90:10 (62)

[a] The reducing system was composed of the hydrated metal salt (1–2 mmol), an excess of lithium powder (1/8 molar ratio, referred to the metal salt), and a catalytic amount of DTBB (0.1 mmol/mmol of metal salt) in THF at room temperature.
[b] The structure of the major diastereoisomer is shown.
[c] Diastereomeric ratio determined by GLC/MS; isolated yields after column chromatography (silica gel, hexane/EtOAc) in parentheses.

Taking into account the previous reduction studies on carbonyl compounds and imines carried out with other transition-metal salts, we also want to compare herein the reactivity and selectivity of the present reducing system with those of the closely related nickel and copper salts, $NiCl_2 \cdot 2H_2O$[31] and $CuCl_2 \cdot 2H_2O$,[7] respectively. Concerning the reactivity, in general, similar results were obtained both in the reduction of carbonyl compounds and imines irrespective of the reducing system used, in all cases with moderate to good yields.[7,31] As regards the selectivity, however, the $NiCl_2 \cdot 2H_2O$-based system showed to be more selective in the reduction of α,β-unsaturated ketones, several examples of which could be transformed into the corresponding saturated ketones or saturated alcohols depending on the amount of salt used. In order to compare the stereoselectivity, 4-*tert*-butylcyclohexanone, 2-methylcyclohexanone, *trans*-decalone, and (±)-camphor were used as substrates and subjected to reduction with $NiCl_2 \cdot 2H_2O$, $CuCl_2 \cdot 2H_2O$, and $FeCl_2 \cdot 4H_2O$, under the same reaction conditions (Table 3). Comparable isolated yields of the products were obtained for any of the substrates studied. It is worthy of note that the highest diastereoselectivities were reached with the present reducing system, $FeCl_2 \cdot 4H_2O$. Despite in most of the cases the values are relatively high and not very different, it can be concluded that the efficiency in diastereoselectivity follows the trend: $FeCl_2 \cdot 4H_2O > NiCl_2 \cdot 2H_2O \approx CuCl_2 \cdot 2H_2O$, which is the same order found for the atomic radii of the corresponding metals. The importance of the structure of the starting ketone in the final result is exemplified by the reduction of *trans*-decalone, which is reduced with equal diastereoselectivity by any of the reducing systems (Table 3, entry 3). The fact that the selectivities observed work in the same direction for any of the metal salts tested, indicate that a similar type of reaction mechanism may be operating in all these reductions (see above).

3. Conclusion

In conclusion, we have described herein a new procedure to reduce carbonyl compounds and imines to the corresponding alcohols and secondary amines, respectively, under very mild reaction conditions, using the active iron-based reducing combination $FeCl_2 \cdot 4H_2O$–Li–DTBB (cat.). The most prominent feature of this system is the high diastereoselectivity achieved in the reduction of cyclic ketones, higher than that achieved with the $NiCl_2 \cdot 2H_2O$ and $CuCl_2 \cdot 2H_2O$ salts. In addition, the simplicity, together with the commercial availability ($NiCl_2 \cdot 2H_2O$ is not commercially available) and low toxicity of the iron salt (much lower than the analogous nickel or copper salts previously studied), makes this new system a very attractive alternative to other reducing agents. We are actively exploring new applications of this reagent to the reduction of other organic functional groups.

4. Experimental

4.1. General

All moisture sensitive reactions were carried out under a nitrogen atmosphere. Anhydrous tetrahydrofuran was freshly distilled from sodium/benzophenone ketyl. Other solvents used were treated prior to use by standard methods.[32] Iron(II) chloride tetrahydrate was commercially available (Aldrich). Column chromatography was performed with Merck silica gel 60 (0.040–0.063 μm, 240–400 mesh). Thin-layer chromatography (TLC) was performed on precoated silica gel plates (Merck 60, F254, 0.25 mm). Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker ARX-300 spectrophotometer using $CDCl_3$ as solvent and tetramethylsilane (TMS) as internal

reference. Mass spectra (EI) were obtained at 70 eV on a Hewlett Packard HP-5890 GC/MS instrument equipped with a HP-5972 selective mass detector. Infrared (FT-IR) spectra were obtained on a Nicolet-Nexus spectrophotometer. The purity of volatile compounds and the chromatographic analyses (GC) were determined with a Shimadzu GC-9A instrument equipped with a flame-ionization detector and a 2 m column (1.5% OV17 9_A SUS Chrom 103 80/1000), using nitrogen as carrier gas.

All starting carbonyl compounds (Table 1) were commercially available (Merck, Aldrich, Fluka) of the best grade and were used without further purification. Imines showed in entries 1,[33] 2,[34] 3,[33] 4,[35] and 5[33] (Table 2) were prepared according to the corresponding literature procedures. In all cases, except for benzylideneaniline, the crude imine was used for the reduction step without further purification.

4.2. Reduction of carbonyl compounds and imines using the $FeCl_2 \cdot 4H_2O$–Li–DTBB (cat.) combination. General procedure

A solution of the corresponding carbonyl compound (1.0 mmol) in THF (10 mL) was added to a mixture of iron(II) chloride tetrahydrate (198 mg, 1.0 mmol), lithium powder (56 mg, 8.0 mmol) and DTBB (27 mg, 0.1 mmol), at room temperature under a nitrogen atmosphere. The reaction mixture, which was initially dark green, changed to black, indicating that iron(0) was formed. The reaction time was monitored by GLC. After a total conversion of the starting material, the resulting suspension was diluted with ether (10 mL) and carefully hydrolysed with water (15 mL, for imines), or with 10% hydrochloric acid solution (15 mL, for carbonyl compounds). The organic layer was dried over anhydrous magnesium sulfate and evaporated (15 Torr) to give a residue, which after purification by column chromatography (silica gel, hexane/EtOAc) yielded the corresponding pure compound. For volatile products, the dried organic layer was analysed by GLC using octan-1-ol as an internal standard. Nonan-5-ol, dicyclohexylmethanol, adamantan-2-ol, *sec*-phenethyl alcohol, diphenylmethanol, *cis*- and *trans*-4-*tert*-butylcyclohexanol, *cis*-2-methylcyclohexanol, *endo*-borneol, cyclohexanol, (−)-menthol, *n*-decanol, and benzyl alcohol, as well as *N*-dicyclohexylamine and phenylbenzylamine, were characterised by comparison of their chromatographic and spectral data with those of the corresponding commercially available pure samples. ($1R^*$,$4aR^*$,$8aS^*$)-decahydronaphthalen-1-ol,[36] *cis*-2-propylcyclohexanol,[37] *cis*-3,3,5-trimethylcyclohexanol,[38] *N*-*tert*-butylhexylamine,[31,39] *N*-decylaniline,[40] and *N*-benzyl-1-phenethylamine,[31,41] were characterised by comparison of their chromatographic and spectral data with those described in the literature.

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