Dalton Transactions

ROYAL SOCIETY OF CHEMISTRY

COMMUNICATION

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Cite this: *Dalton Trans.*, 2021, **50**, 10696

Received 23rd June 2021,
Accepted 15th July 2021

DOI: 10.1039/d1dt02092g

rsc.li/dalton

Hydroboration of aldehydes, ketones and CO_2 under mild conditions mediated by iron(III) salen complexes†

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The hydroboration of aldehydes, ketones and CO_2 is demonstrated using a cheap and air stable [Fe(salen)]$_2$-μ-oxo pre-catalyst with pinacolborane (HBpin) as the reductant under mild conditions. This catalyst system chemoselectively hydroborates aldehydes over ketones and ketones over alkenes. In addition, the [Fe(salen)$_2$]-μ-oxo pre-catalyst shows good efficacy at reducing "wet" CO_2 with HBpin at room temperature.

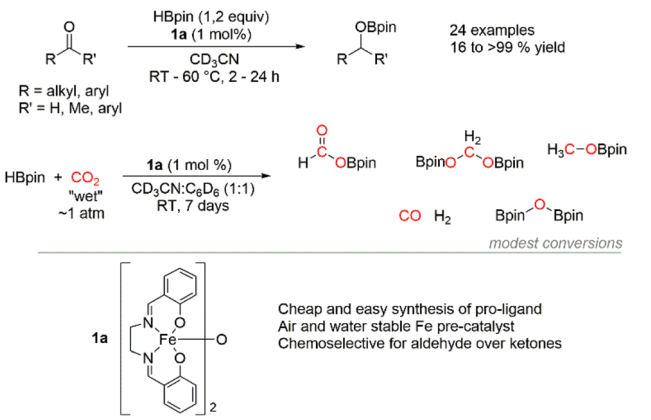
Introduction

Hydroboration (HB) of aldehydes and ketones is an efficient route to access primary and secondary alcohols respectively through the facile hydrolysis of organoborate intermediates formed in these reactions.[1–3] In recent years there has been a focus on using earth abundant base metals, such as iron, to catalyse hydrofunctionalisation reactions of unsaturated moieties (alkenes, alkynes, nitriles)[4–10] which have historically been dominated by late transition metal complexes.[11–17]

Relative to noble metals, there are significantly fewer reports on using iron complexes to mediate hydroboration of aldehydes and ketones.[18–24] Notably in 2017, Findlater and co-workers reported the simple use of a Fe(acac)$_3$/NaHBEt$_3$ system to hydroborate a range of aldehydes and ketones in moderate to excellent yields in the presence of 10 mol% catalyst.[25] Following on, Baker, Hein and co-workers demonstrated the use of a [Fe(N$_2$S$_2$)]$_2$ complex at 0.1 mol% catalyst loading to hydroborate aldehydes selectively with TON *ca.* 5200 easily achieved in one instance.[26] In addition, the first case of an iron(II) coordination polymer and heterogeneous Fe_2O_3 nanoparticles mediated hydroboration of these carbonyl moieties have been reported by Zhang and co-workers[27,28] and Geetharani, Bose and co-workers[29] respectively. A more difficult but highly desired transformation is the asymmetric hydroboration of ketones to achieve optically active secondary alcohols,[1] with only a handful of examples using iron complexes reported to date.[23,30]

Beyond HB of carbonyl functionality of simple molecules, there has been a paucity in reports of HB of CO_2 mediated by iron complexes.[31] In 2015, Sabo-Etienne, Bontemps and co-workers[32] reported high conversion and selectivity for the formation of bis(boryl)acetal using 9-borabicyclo[3.3.1]-nonane (9-BBN) as the borane source and [Fe(H)$_2$(dmpe)$_2$] (dmpe = 1,2-bis(dimethylphosphino)ethane) as the catalyst.

Continuing from our previous studies using a simple iron salen complex (**1a**) to effect the hydrophosphination of alkenes[33,34] and the cyclotrimerization of alkynes,[35] here we report the hydroboration of both aldehydes and ketones with good chemoselectivity observed for aldehydes over ketones. Furthermore, we disclose modest rate of reduction of CO_2 with HBpin (Scheme 1).



Scheme 1 This work using [Fe(salen)]$_2$-μ-oxo pre-catalyst in HB of aldehydes, ketones and CO_2.

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† Electronic supplementary information (ESI) available: Synthetic methods, analysis data and NMR spectra. See DOI: 10.1039/d1dt02092g

Results and discussion

Optimisation of reaction conditions using 4-methylbenzaldehyde as the model substrate shows proficiency of the catalyst system to hydroborate the substrate using aromatic solvents (benzene, toluene) and polar solvents (dimethylformamide, methylene chloride, tetrahydrofuran). Acetonitrile was chosen due to higher solubility of **1a** and ease of monitoring the reactions in CD_3CN. Furthermore, HBpin was found to be much more active than catecholborane (HBcat) under comparable conditions (see ESI†). The reactions are carried out with 1 mol% catalyst loading at room temperature and 60 °C for aldehyde and ketone substrates respectively. Control reactions without any **1a** show lower conversion for benzaldehyde (58%) and acetophenone (<5%) under similar reaction conditions (Fig. 1 and Fig. 2).

Excellent yields are achieved across all the aldehydes tested with almost full conversion to the organoborate product observed spectroscopically. Electronic effects *para* to the benzaldehyde do not influence yields and the system is proficient for both aryl and alkyl aldehydes. 4-Hydroxybenzaldehyde requires a second equivalent of HBpin due to competing reactivity of the hydroxyl group with the reducing reagent (**2f**). Chemoselectivity is demonstrated with the alkene functionality left intact for cinnamaldehyde and only the mono hydroboration product observed (**2h**) by NMR spectroscopy. The organoborate products can be converted to their primary alcohol by quenching the reaction with minimal MeOH and then removal of the iron through a silica plug with methylene chloride as the eluent.

The homogeneity of the HB of aldehydes was tested. Complementary results from parallel PMe_3 and Hg dropping test suggest the reaction is homogenous in nature (see ESI†).

Hydroboration of ketones requires a higher temperature and longer reaction time. Standard substrate, acetophenone, gives **3a** in good spectroscopic yield on 0.25 mmol scale and 58% (0.59 g) isolated yield of 1-phenyl ethan-1-ol when the reaction is scaled by over 30 times (to 8.3 mmol). Good yields are obtained with electron withdrawing groups (**3d–f**) in the *para* position with lower conversions found for electron donating groups (**3b**, **3g**) in the same position. The conversions of the ketones are comparable to the recent literature on iron mediated HB of ketones (*vide supra*). Aliphatic products **3i** and **3j** are formed in excellent spectroscopic yield. Competitive alkene HB is not observed, for example **3k** is produced in low spectroscopic yield but the alkene is unreacted, while we attribute the modest yield of **3m** to the volatility of the starting material. Unfortunately, our catalyst system is unable to hydroborate esters or tertiary amides, with less than 5% conversion of starting material observed for the ester substrates; ethyl benzoate, vinyl benzoate, methyl 2-bromobenzoate, methyl formate, and the amide substrates; *N*,*N*-diisopropylbenzamide, *N*-(*tert*-butyl)-*N*-isopropyl-3,5-bis(trifluoromethyl)benzamide and, *N*-(*tert*-butyl)-*N*-ethyl-4-methylbenzamide respectively, even at 80 °C with higher equivalents of HBpin used (Fig. 2).

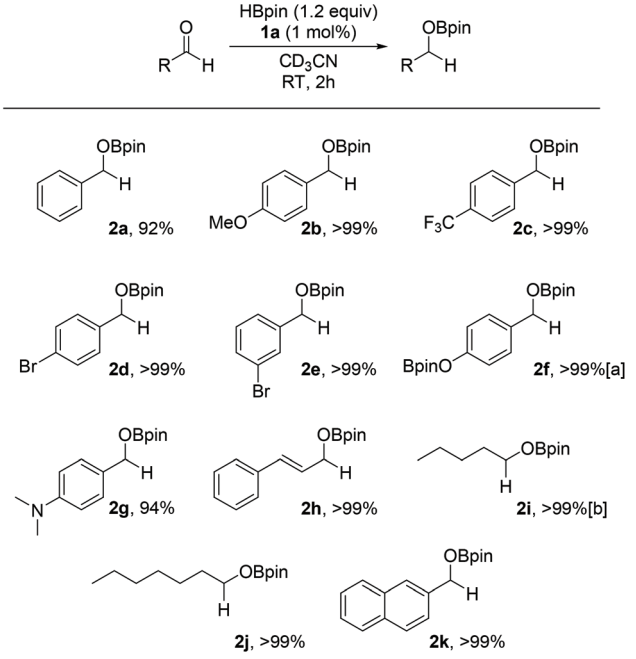


Fig. 1 Substrate scope for HB of aldehydes. All reactions were performed using 0.25 mmol aldehyde and 0.30 mmol HBpin in CD_3CN (500 μL) unless stated otherwise. Spectroscopic yields reported using 1,2-dichloroethane as the internal standard. [a]2.4 equiv. of HBpin required for doubly reduced product. [b]Percentage conversion determined by loss of C*H*O signal due to 1,2-dichloroethane signal overlapping with characteristic methylene peak from reduction.

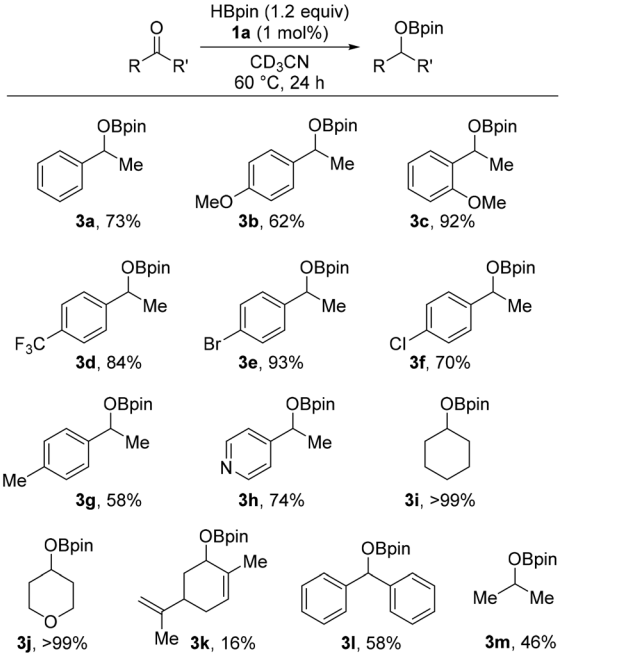


Fig. 2 Substrate scope for HB of ketones. All reactions were performed using 0.25 mmol ketone and 0.30 mmol HBpin in CD_3CN (500 μL) unless stated otherwise. Spectroscopic yields reported using 1,2-dichloroethane as the internal standard.

The chemoselectivity of the catalyst system was further investigated; intermolecular competition reactions show the catalytic system selectively hydroborates aldehydes over ketones and ketones over alkenes (Scheme 2a–c). Due to the high conversions across all benzaldehyde derivatives with different electronic properties in the *para* position, a qualitative intermolecular competition reaction using 4-bromobenzaldehyde, benzaldehyde and 4-methoxybenzaldehyde was set up (Scheme 2d). The calculated spectroscopic conversions show faster reaction with electron withdrawing substituent –Br at the *para* position relative to electron donating substituent –OMe.

To further interrogate the limits of this catalytic system, the HB of acetophenone derivatives using the chiral iron salen complex **1b** under the same reaction conditions was carried out to probe if enantioinduction[36] can be conferred to the product (Fig. 3, top). The reactions of the substrates are visibly faster; good to excellent conversions are achieved within 2 h at 60 °C compared to 24 h using **1a**. Unfortunately, no enantioinduction is observed in the organoborate products after work-up to the secondary alcohols and reacting these with the chiral auxiliary (*R*)-Mosher's acid[37] to form the corresponding diastereoisomeric ester product.[38]

The different reactivity observed between **1a** and **1b** on the HB of ketones may allude to the mechanism involved in these reactions. The varying modes of activation that **1a** can undergo have been investigated previously by our group showing potential to form a twisted Fe salen complex containing 'Bpin' fragment, or alternatively can simply be reduced down to **1c**, an Fe(II) air and moisture sensitive analogue of **1a**.[34,35] Reacting benzaldehyde with 2 mol% **1c**, results in 92% conversion to **2a** at room temperature after 2 h which is comparable to the efficacy of **1a** (Fig. 3, bottom). This data would suggest the mechanism of the HB of carbonyls is likely to undergo a reduction with HBpin to generate the active species **1c** that participates in the catalytic cycle. The empirical observation that **1b** is a more active pre-catalyst than **1a** could be due to the greater electron density on the iron centre from the *tert*-butyl groups on the phenolate arms as well as the cyclohexyl backbone of the ligand for a faster reduction to the active Fe(II) species. Further detailed study is necessary to determine whether **1c** undergoes further activation (*i.e.* twisting) to generate an on-cycle species, or whether **1c** is a discrete on-cycle catalyst in its own right.

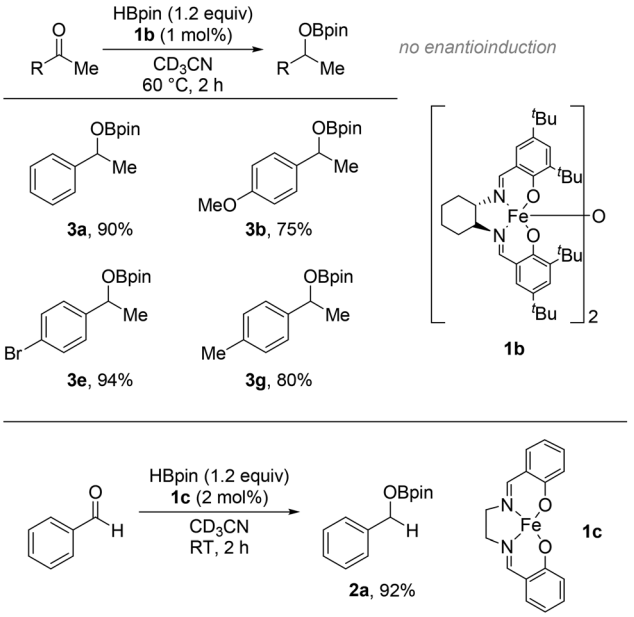
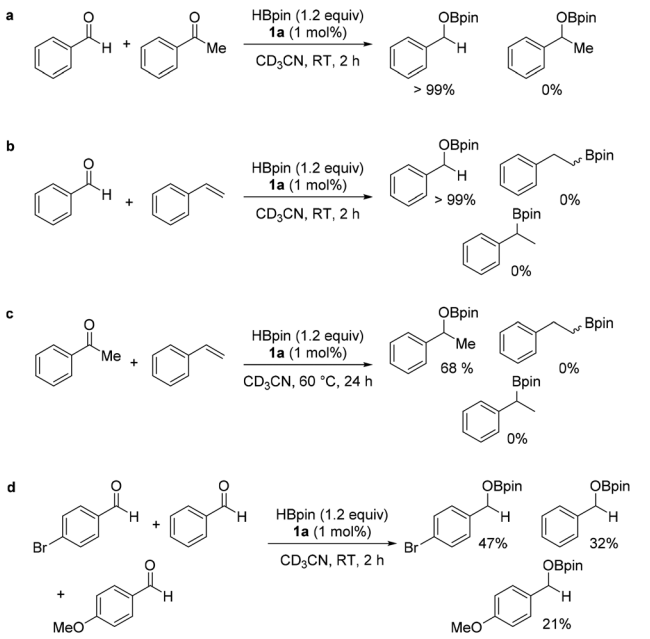


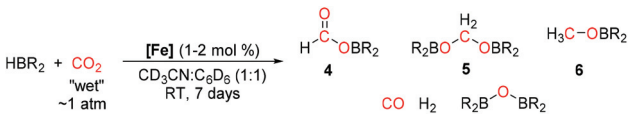
Fig. 3 (Top) HB of acetophenone derivatives mediated by **1b**, unfortunately no enantioinduction was induced to the organoborate product. (Bottom) HB of benzaldehyde (0.25 mmol) and HBpin (0.30 mmol) in CD_3CN (500 μL) mediated by **1c**.



Scheme 2 Competition HB reactions: a – intermolecular chemoselectivity between benzaldehyde and acetophenone, b – intermolecular chemoselectivity between benzaldehyde and styrene, c – intermolecular chemoselectivity between acetophenone and styrene and d – intermolecular competition of electronic effects *para* to benzaldehyde.

We next examined the reduction of CO_2 using **1a** as the pre-catalyst.‡ The advantage of using boranes for CO_2 reduction circumvents harsher reaction conditions normally associated when using dihydrogen gas as the reductant by exploiting the more reactive B–H bond.[39–43] Due to the insolubility of bis(pinacolato)diborane (BOB) formed during the reaction in CD_3CN, a 1 : 1 mixture of $CD_3CN : C_6D_6$ is used for the following studies. Furthermore, "wet" CO_2 generated from dry ice/toluene mixture, and without passing through a drying column, is added directly to the reaction vessel. Modest consumption of HBpin is achieved after 7 days at room temperature, with formation of the formoxy (**4**), acetal (**5**), methoxy (**6**) derivatives of HBpin, and undesired BOB confirmed by ^1H and ^{11}B NMR spectroscopy.[44] Repeating the reaction at 60 °C

Table 1 Reduction of CO_2 with boranes



[Fe]	Borane	4	5	6	$CO^a + H_2 + R_2BOBR_2$
1a (1 mol%)	HBpin	5%	1%	1%	8%
1a (1 mol%)	HBcat	—	—	12%	44%
1a (1 mol%)	9-BBN	6%	—	—	—
1b (1 mol%)	HBpin	—	—	—	20%
1c (2 mol%)	HBpin	8%	2%	7%	22%

[a] $^{13}CO_2$ reaction performed to try and detect free ^{13}CO or Fe–^{13}CO species. However, these were not observed, potentially due to the small scale of the reaction and paramagnetic nature of any Fe–CO complex formed.

shows similar conversions to **4**, **5**, and **6** but with a higher yield of BOB (see ESI†). Although the rate of the reaction is slow and conversions modest, the use of "wet" CO_2 demonstrates the air and moisture stability of **1a** in this catalytic transformation and the accessibility of this chemistry without the need of specialist equipment. Reaction with "dry" CO_2 from gas cylinder shows similar reactivity and confirmed no detrimental effect in using "wet" CO_2.

Alternative borane sources 9-BBN and HBcat were also tested but perform poorly in the reaction; differing from trends observed in the reported literature.[31,32,45] Furthermore, no advantageous improvement to reduction of CO_2 is observed using **1b** as the pre-catalyst. However, the potential to optimise the ligand design of these [Fe(salen)]$_2$-μ-oxo complexes provides an attractive opportunity to improve the rate of CO_2 reduction but is beyond the scope of this study (Table 1).

Conclusions

The hydroboration of aldehydes and ketones was achieved using an air and moisture stable [Fe(salen)]$_2$-μ-oxo (**1a**) pre-catalyst. The catalyst system was chemoselective for aldehyde over ketone substrates. Unfortunately, the chemistry could not be expanded to induce enantioinduction using a chiral pre-catalyst, **1b**. However, the reduction of CO_2 using boranes was investigated with **1a** tolerating "wet" CO_2, formed from a dry ice/toluene mixture. Although the rate of conversion was slow and conversions modest for the reduction of CO_2, future work on ligand design provides an attractive opportunity to improve the reaction whilst still benefitting from the air and moisture stability of these [Fe(salen)]$_2$-μ-oxo complexes.

Conflicts of interest

There are no conflicts to declare.

Notes and references

‡ CO_2 reactions performed in a standard J. Young NMR tube. Estimated theoretical maximum amount of CO_2 in reaction vessel at 1 atm and 25 °C was calculated to be 0.08 mmol.

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