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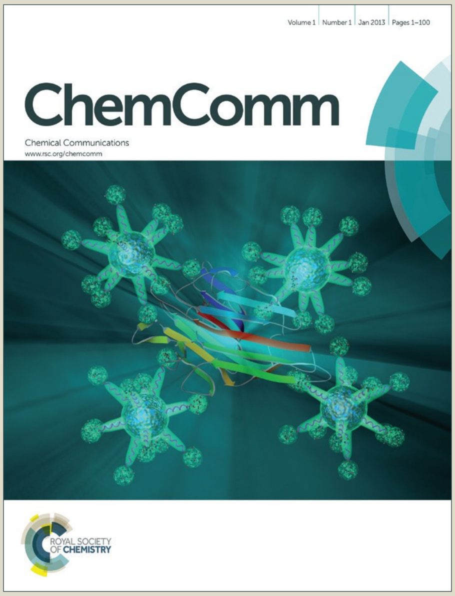

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Synergistic Effects in Ambiphilic Phosphino-Borane Catalysts for the Hydroboration of CO_2

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The benefit of combining both a Lewis acid and a Lewis base in a catalytic system has been established for the hydroboration of CO_2, using ferrocene-based phosphine, borane and phosphino-borane derivatives.

Featuring a carbon atom at the +IV oxidation state, CO_2 is a stable molecule and its conversion to either fuels or chemicals necessitates the use of a mild reductant and an efficient catalyst, to promote the cleavage of C–O bonds and the formation of novel C–H and/or C–C bonds.[1] In this respect, hydroboranes (R_2BH) have a mild reduction potential (ca. –0.5 V *vs* NHE) well-suited for the reduction of CO_2 to the methanol level.[2] In contrast to borohydrides, the reduction of CO_2 with hydroboranes requires a catalyst.[3] In fact, the catalytic hydroboration of CO_2 has first been reported in 2010 by Guan and coworkers who showed that nickel(II) pincer complexes were able to catalyze the reduction of CO_2 to methoxyboranes in the presence of 9-BBN, catBH and pinBH.[4] Shortly after, Sabo-Etienne and Bontemps described efficient ruthenium catalysts for this transformation and a variety of inorganic and organometallic catalysts have been reported since then.[5] Notably, the polarized B−H bond in hydroboranes can also be activated by simple organic compounds: the organocatalyzed hydroboration of CO_2 has been unveiled in 2013 by Fontaine and coworkers with P/B Frustrated Lewis Pairs (FLPs), and by our group with guanidines and amidines bases as well as using an isolated FLP-CO_2 adduct.[6] This collection of catalysts has been completed with several bases among which phosphines proved to be potent catalysts for this reduction process.[7]
In this context, we have also shown recently that proazaphosphatranes enable the first catalytic methylation of amines involving CO_2 reduction with hydroboranes.[7a]

Thus, since the hydroboration of CO_2 is a reaction of fundamental importance, it becomes crucial now to better apprehend the role of the organocatalysts in these reduction processes. In particular, the possible positive influence of combining a Lewis base with a Lewis acid in the same catalytic system is still to be established.

To address this question, we report herein the synthesis of simple phosphine, borane and phosphino-borane compounds based on the same ferrocene backbone (Chart 1). Comparing the catalytic performances of the separated Lewis acids and bases and their combination as intermolecular or intramolecular systems demonstrates the benefits of the ambiphilic systems, for the first time.

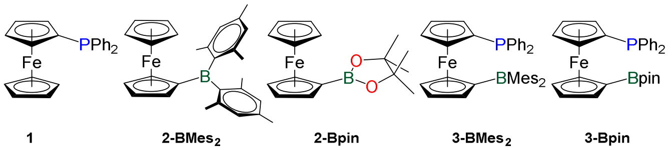
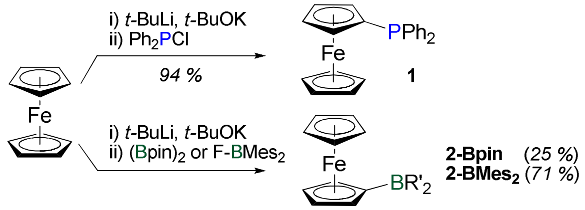


Chart 1. Candidates for the catalytic hydroboration of CO_2

The ferrocene backbone is a well-suited platform to assemble Lewis acids and bases by substituting the cyclopentadienyl ligands on iron. This approach has been exemplified over the last years by the groups of Bourissou, Aldridge and Erker to access novel FLPs and ambiphilic ligands.[8] Additionally, rotation around the ferrocene axis provides some flexibility that can adapt the catalyst to the geometric constraints associated with the catalytic pathway. In this respect, ferrocene based FLPs differ from the system used by Fontaine *et al.* for the hydroboration of CO_2, where a benzene ring maintains a rigid structure between the P and B centres.[6a]

In this study, diphenylphosphinoferrocene, **1**,[9a] was isolated by quenching the lithiated ferrocene[9b] with chlorodiphenylphosphine (Scheme 1). Similarly, the corresponding ferrocenyl-pinacolborane **2-Bpin** was obtained in a moderate 25% yield by reacting bis(pinacolato)diboron with lithiated ferrocene. Crystals of **2-Bpin** were obtained by recrystallization from dichloromethane (see ESI). When dimesitylboron fluoride was used as an electrophile, **2-BMes$_2$** was obtained in a significantly better yield of 71% (Scheme 1).



Scheme 1. Synthesis of **1**, **2-Bpin** and **2-BMes$_2$**

The phosphino-borane derivatives **3-Bpin** and **3-BMes$_2$** were prepared using an established procedure based on a sequential

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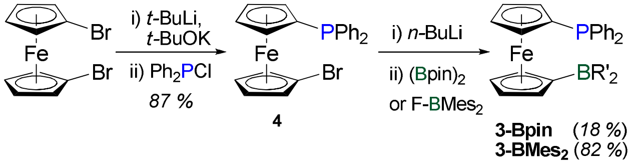
halogen/lithium exchange starting from 1,1'-dibromoferrocene (Scheme 2).[8a] Thus, 1-bromo-1'-(diphenylphosphino)ferrocene **4** was obtained in 87% isolated yield. Subsequently, a second bromine/lithium exchange was conducted and the lithiated ferrocene was quenched with bis(pinacolato)diboron, yielding the desired product **3-Bpin** in a low 18 % yield. Other pinacol-boron electrophiles including 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane, were also tested, without success. Alternative routes were explored to improve the yields of **3-Bpin**. Unfortunately, inverting the reaction sequence by quenching 1-bromo-1'-lithio-ferrocene with bis(pinacolato)diboron first proved unproductive. Also, quenching **4** with trimethyl borate and subsequent reaction with pinacol failed.



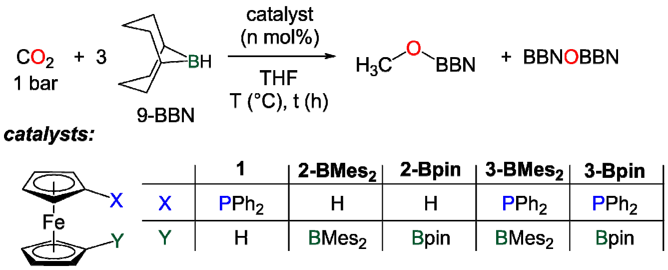
Scheme 2. Synthesis of **3-Bpin** and **3-BMes₂**

As reported by Bourissou *et al.*, replacing bis(pinacolato)diboron with dimesitylboron fluoride yielded **3-BMes$_2$** in 82% yield.[8a] It is noteworthy that the P/B derivatives **3-BMes$_2$** and **3-Bpin** display ^{31}P NMR chemical shifts similar to those of (diphenylphosphino)ferrocene (**1**: δ = -16.2; **3-Bpin**: δ = -17.4; **3-BMes$_2$**: δ = -19.3 ppm). This suggests the absence of any interaction between the two heteroatoms, as noted previously by Bourissou *et al.* Moreover, no interaction with CO_2 has been observed either by ^{31}P or ^{1}H NMR, when a solution of **3-BMes$_2$** is exposed to an atmosphere of CO_2.[10]

Having in hand a homogeneous series of P-, B- and P/B-based catalysts, their reactivity has been investigated in the catalytic hydroboration of CO_2. At room temperature, phosphine **1** (1 mol%) exhibits a negligible catalytic activity in the conversion of CO_2 and 9-borabicyclo[3.3.1]nonane (9-BBN) to methoxyborane MeO-BBN (Table 1, Entry 1). Indeed a Turn Over Number (TON) lower than 5 was observed after 28 h at 25 °C. Increasing the reaction temperature to 70 °C did not improve the catalytic performances of **1** (Entry 11 in Table 1). These results are in line with the results of Stephan *et al.* on the phosphine catalysed hydroboration of CO_2.[7b] Similarly, the borane **2-BMes$_2$** is inefficient both at 25 and 70 °C (Entries 2 and 12 in Table 1). In stark contrast, a mixture of **1** and **2-BMes$_2$** provides a competent catalytic system, enabling the reduction of CO_2 to MeOBBN with a TON of 41 after 28 h at 25 °C (TOF = 1.5 h^{-1}). This result demonstrates for the first time the synergistic and positive influence of combining a Lewis base and a Lewis acid in the reduction of CO_2 with hydroboranes. Replacing **2-BMes$_2$** with the less acidic **2-Bpin** borane somewhat deactivates the catalytic system and a TON of 36 (TOF = 1.3 h^{-1}) is measured under the same conditions. To further establish the benefit of an ambiphilic structure, the catalytic potential of the intramolecular Lewis pairs **3-BMes$_2$** and **3-Bpin** has been determined. **3-BMes$_2$** presents a better activity than the mixture of **1** and **2-BMes$_2$** and a TON of 100 was reached after 28 hours at 25 °C (TOF = 3.6 h^{-1}).

It is worth noting here, that the reaction course follows a profile similar to the one observed previously for guanidines and N/B FLPs.[6f] Indeed, monitoring the product distribution over time, using ^{1}H and ^{13}C NMR spectroscopy, reveals that CO_2 is first reduced to the boryl formate HCOO–BBN which is present in only a very low concentration and does not accumulate (Fig. S1). This intermediate is subsequently reduced to the acetal form $H_2C(OBBN)_2$, with a conversion rate of 90% after just 1 hour. Finally, reduction of the acetal provides MeO–BBN. This step is slow and requires 27 hours at 25 °C to yield the methoxyborane species quantitatively. The kinetics of the reaction improved at 70 °C. These conditions revealed a remarkable catalytic activity of **3-BMes$_2$**, allowing the full conversion of CO_2 to the corresponding methoxyborane with a TON of 100, in only 2 hours (Table 1, entry 7). Reducing the loading of catalyst **3-BMes$_2$** to 0.1 and 0.05 mol%, afforded an excellent TON of 1980, after 20 h at 70 °C, and a TOF of 250 h^{-1}, while the isolated components of the catalytic system, namely **1** and **2-BMes$_2$**, are unreactive (Table 1, Entries 9-12).

Table 1. Catalytic reduction of CO_2 to methoxyborane CH_3OBBN



	1	2-BMes$_2$	2-Bpin	3-BMes$_2$	3-Bpin
X	PPh$_2$	H	H	PPh$_2$	PPh$_2$
Y	H	BMes$_2$	Bpin	BMes$_2$	Bpin

Entry[a]	Catalyst (mol%)	T°C	Time (h)	TON[b]	TOF (h^{-1})[b]
1	**1** (1 mol%)	25 °C	28h	<5	<0.2
2	**2-BMes$_2$** (1 mol%)	25 °C	28h	0	0
3	**3-Bpin** (1 mol%)	25 °C	28h	84	3.0
4	**3-BMes$_2$** (1 mol%)	25 °C	28h	100	3.6
5	**1** (1 mol%) + **2-Bpin** (1 mol%)	25 °C	28h	36	1.3
6	**1** (1 mol%) + **2-BMes$_2$** (1 mol%)	25 °C	28h	41	1.5
7	**3-BMes$_2$** (1 mol%)	70 °C	2h	100	50
8	**3-Bpin** (1 mol%)	70 °C	2h	57	29
9	**3-BMes$_2$** (0.1 mol%)	70 °C	4h	1000	250
10	**3-BMes$_2$** (0.05 mol%)	70 °C	20h	1980	99
11	**1** (1 mol%)	70 °C	2h	<2	<1
12	**2-BMes$_2$** (1 mol%)	70 °C	2h	0	0

[a] reactions performed in J-Young tubes; monitored by NMR spectroscopy with 0.0048 mmol of catalyst, 0.48 mmol of 9-BBN in d_8-THF (0.40 mL) and exposed to an atmosphere of CO_2 (1 bar), [b] The TON is obtained by ^{1}H NMR monitoring (CH_3O-BBN formation), with mesitylene as internal standard.

Dialkylboranes, other than 9-BBN, were also tested as potential reductants. As expected, the hydroboration of CO_2 with catecholborane is slower than with 9-BBN because of the lower Lewis acidity of the borane. In fact, under the optimized reaction conditions (48 h at 70 °C), **3-BMes$_2$** promotes the reduction of CO_2 to MeOBcat with a modest TOF of 23. Replacing catecholborane with $BH_3{\cdot}SMe_2$ did not lead to any significant product formation.

Again, replacing the BMes$_2$ unit with a Bpin fragment somewhat slows down the catalytic reaction and a TOF of 3.0 h^{-1} is measured with **3-Bpin**, at 25 °C (vs 3.6 h^{-1} for BMes$_2$). The difference of reactivity between **3-BMes$_2$** and **3-Bpin** is more pronounced at 70 °C, with TOFs values of 50 and 29 h^{-1}, respectively (Entries 7-8

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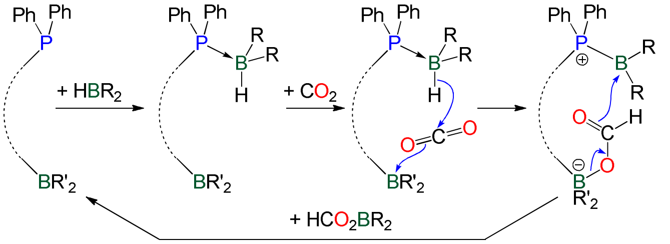
in Table 1). This behaviour directly follows from the Arrhenius rate law.

Previous studies by the groups of Stephan and Cantat have established that basic guanidines, N-heterocyclic carbenes and phosphines can promote the hydroboration of CO_2.[6f, 11] Mechanistic and computational investigations have shown that basic catalysts proceed through the activation of the B–H bond, by coordination of the Lewis base to the hydroborane.[6f] Therefore we propose here that the benefit of combining a trivalent phosphorus function with a remote Lewis acid, as in **3-BMes$_2$**, results from a concomitant H-transfer / borane-formate adduct formation, in the first step of the CO_2 reduction process (Scheme 3). In this approach, linking together the Lewis acid and the Lewis base functions should reduce the volume of the non-productive region of the conformational space between the catalysts and the substrates and thus increase further the reaction rates.[12] In fact, experimentally, catalysts **3-BMes$_2$** and **3-Bpin** are about twice as reactive as the corresponding bimolecular systems at 25 °C. This difference of reactivity corresponds roughly to a decrease of ca. 1 kcal/mol in activation energy, consistent with an entropic effect.



Scheme 3. Proposed synergistic effect of phosphino-borane catalysts in the hydroboration of CO_2

Overall, we have demonstrated for the first time that the combination of phosphines and boranes offers a synergistic effect in the catalytic reduction of CO_2 with hydroboranes. While the phosphine and the borane fragments, taken separately, do not catalyse the reduction of CO_2, the P/B derivatives **3**, combining the two functions, display high catalytic activity.

Notes and references

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† Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.
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