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CO₂ Hydroboration: Impact of the Boryl Moieties on the Reactivity of Four Bis(boryl)acetal Compounds toward 2,6-Diisopropylaniline

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Abstract: The hydroboration of CO₂ into bis(boryl)acetal (BBA) compounds is an important transformation, since it enabled to selectively reduce CO₂ by 4e⁻ and to subsequently use the BBA compounds as C₁ and C_n sources. However, the influence of the nature of the boryl moieties on the reactivity of BBA compounds has not been evaluated so far. In the present study, four BBA compounds – including two new ones – were reacted with 2,6-diisopropylaniline to afford the expected imine. Significant differences in the rate of the reaction from minutes to weeks have been observed depending on the BBA used, showing the importance of the nature of the boryl moieties. Theoretical investigations enabled to propose a mechanism involving the addition of the aniline to the BBA as the rate-determining step and to determine that the steric hindrance of the BBA compounds is the main factor driving the rate of this condensation reaction.

Introduction

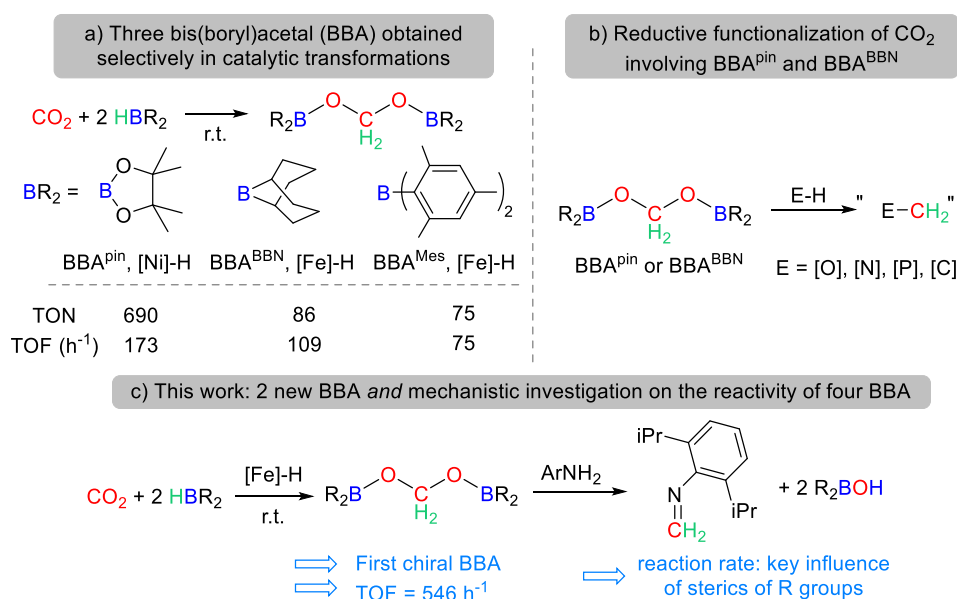
Bis(boryl)acetal (BBA) compounds are strongly associated with 4e⁻ reduction of CO₂ (Scheme 1).^[1] The first BBA was reported in 2012 and was obtained from the Ru-catalyzed reduction of CO₂ with pinacolborane (HBpin).^[2] Most of the reported BBA were indeed obtained from double CO₂ hydroboration reactions. The observation of BBA compounds served initially at understanding this reduction stage and at optimizing the catalytic conditions leading to their efficient and selective production under mild conditions. They were subsequently shown to be reactive C₁^[3] and C_n^[4] sources highlighting the importance of the 4e⁻ reduction level in complex transformations of CO₂.^[5]

In more details, BBA^{BBN} and BBA^{pin} – deriving from CO₂ hydroboration with 9-BBN and HBpin, respectively – were obtained with several catalytic systems until eventually generated selectively.^[1] BBA^{BBN} was obtained with the highest TON and TOF

of 86 and 109 h⁻¹, respectively with an iron hydride catalyst,^[3a] while BBA^{pin} was obtained with highest TON and TOF of 690 and 173 h⁻¹, respectively with a nickel hydride catalyst (Scheme 1a).^[6] While the two other common commercially available hydroboranes, catecholborane (HBCat) and BH₃, were employed in CO₂ hydroboration, BBA^{Cat} was only observed *in situ* in small amount by ¹H NMR analysis at low temperature,^[6] and no acetal characterization was reported when using BH₃. More recently, we reported the selective hydroboration of CO₂ with dimesitylborane (HBMe₂) affording BBA^{Mes}, which was isolated and structurally characterized in solution and in solid state.^[4b] Overall, only three BBA have been obtained selectively from catalytic CO₂ hydroboration and no chiral BBA has been reported.

BBA^{BBN} and BBA^{pin} were used as formaldehyde surrogates in condensation or Wittig reactions, formally transferring a methylene fragment from BBA to various organic co-reactants and generating H₂C-O, H₂C-N, H₂C-P and H₂C-C bonds (Scheme 1b).^[3] To date, the mechanism of these transformations has not been investigated. In particular, the importance of the nature of the boryl moieties (BR₂) on the reactivity of BBA compounds has not been assessed.

In the present publication, we report the synthesis of two new BBA from CO₂ hydroboration catalyzed by [Fe(H)₂(dmpe)₂], previously used to prepare BBA^{BBN} and BBA^{Mes}.^[3a, 4b] One of these species is the first reported chiral BBA, while the second one has been generated with a record TOF of 546 h⁻¹ (Scheme 1c). The generation of these two additional BBA with the same [Fe]-based catalyst gave us access to four BBA in similar conditions to explore their reactivity toward 2,6-diisopropylaniline (Scheme 1c). A very strong impact of the boryl moiety on the rate of the reaction from minutes to weeks was observed. With such significant variation, the mechanism was explored by DFT and the impact of the electronic and steric factor of the BR₂ moieties assessed.



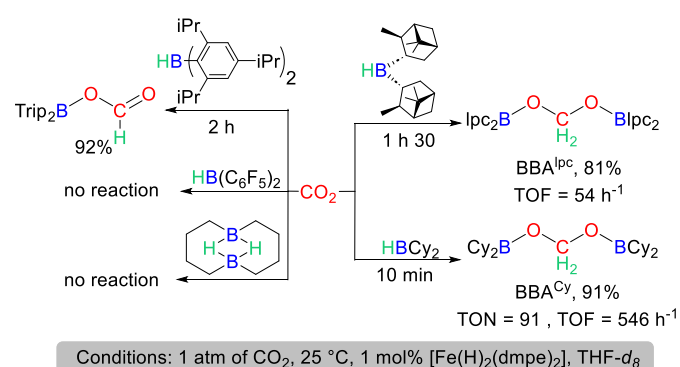
Scheme 1. Nature of the three reported BBA generated selectively from previous studies and catalytic performances.

Results and Discussion

Generation of new BBA compounds from CO₂ double hydroboration reactions. [Fe(H)₂(dmpe)₂] complex was shown previously to selectively generate BBA^{BBN} and BBA^{Mes} from CO₂ hydroboration with *in situ* yields of 85% and 75%, respectively.^[3a, 4b] Using the same catalytic system, the hydroboration of CO₂ was probed with Piers' borane (HB(C₆F₅)₂), 1,6-diboracyclodecane, di(2,4,6-triisopropylphenyl)borane (HBTrip₂), dicyclohexylborane (HBCy₂) and diisopinocampheylborane (HBIPC₂) (Scheme 2). The former two boranes do not react at room temperature with CO₂ in the presence of 1 mol% of [Fe(H)₂(dmpe)₂] over several hours. In both cases, increasing the temperature to 80 °C led mostly to decomposition products, small amount of methoxy signals were detected but no acetal signals were observed. HBTrip₂ afforded the corresponding formoxyborane (*i.e.* 2e⁻ reduction product) in high 92% yield measured *in situ* after 2 h of reaction. Prolonged reaction time or temperature increase did not modify this result. We hypothesized that the absence of reactivity of the former two borane reactants is explained by the low hydricity of Piers' borane^[7] and the inaccessible monomeric form for 1,6-diboracyclodecane. In the case of HBTrip₂, the steric hindrance might be the reason why no further reduction is observed beyond the 2e⁻ reduction level.^[6]

Satisfyingly, the latter two hydroborane reductants led to the selective formation of BBA^{Cy} and BBA^{IPC} as major products of the reaction, obtained in 91% and 81% yields, respectively. Noticeably, BBA^{Cy} was obtained within 10 min. The performance of the catalytic system is thus noticeable as the calculated TOF of 546 h⁻¹, is three time higher than the best TOF reported in CO₂ hydroboration to BBA^{pin} (173 h⁻¹).^[6] Several attempts to isolate these compounds by crystallization failed in our hands, eventually leading to the isolation of Cy₂BOBCy₂ probably from BBA^{Cy} decomposition (see ESI for details on the crystal structure). BBA^{IPC} is the first chiral BBA reported. As for BBA^{Cy}, attempts to isolate BBA^{IPC} failed. The measurement of the optical properties of pure

sample of BBA^{IPC} was thus not possible. The mixture was composed of 78% BBA^{IPC}, 8% (+)- α -pinene ([α]_D = +47.1, neat) and 2% MeOBlpc ([α]_D = (-11.2, 65 g/L in THF-*d*₆). The optical [α]_D parameter of the mixture was measured at -7.3 (11 g/L, THF-*d*₆).



Scheme 2. Fe-catalyzed hydroboration of CO₂ with HBTrip₂, HB(C₆F₅)₂, 1,6-diboracyclodecane, HBIPC₂ and HBCy₂.

Reactivity of four BBA compounds toward 2,6-diisopropylaniline. The reactivity of the newly generated BBA^{Cy} and BBA^{IPC}, as well as of BBA^{Mes} and BBA^{BBN} toward 2,6-diisopropylaniline was probed (Figure 1 and Table 1). It must be noted that besides BBA^{Mes}, the three other BBA could not be isolated. This first part of the study was thus conducted with *in situ* generated BBA compounds which were used without isolation in subsequent reaction with 2,6-diisopropylaniline. While in each case, the expected condensation reaction occurred to afford the methylene aniline in 63% to 89% yields at total consumption of the BBA compounds, Figure 1 shows that the rates of reaction are very different. BBA^{BBN} and BBA^{Cy} reacted within 20 min, while the full conversion of BBA^{Mes} took 11 days. In between these limits stand BBA^{IPC} with a complete transformation within 425 min. Table 1 shows the yields obtained and the comparison with the condensation reaction with formaldehyde. BBA^{Cy} and BBA^{BBN}

reacted within 20 min with 1 or 10 equivalents of aniline with yields ranging from 76 and 89% (entries 1-4, Table 1). BBA^{lpc} and BBA^{Mes} afforded the imine with 63% and 88% yield, respectively (entry 5 and 6, Table 1). When formaldehyde was used in the same conditions, it took 10 and 2 days for full conversion at 25 °C (1 eq of aniline) and 80 °C (10 eq of aniline, entry 7, Table 1), respectively. Free formaldehyde was generated in-situ from cracking para-formaldehyde at 130°C before conducting the reaction at 25 or 80 °C (see ESI). We also probed the reactivity of three bis(silyl)acetal (BSA) compounds (BSA^{Et} , BSA^{Me_2Ph} , BSA^{Ph_2Me}) and did not observe any reaction even under prolonged reaction time and increased temperature to 100 °C. It was shown earlier that BSA^{Ph_3} releases formaldehyde at the same temperature when reacted with 5 equivalents of H_2O in DMSO. The generated formaldehyde was then subsequently used in various condensation reaction.^[8] In our case, no formaldehyde was observed. We thus assume that BSA compound do not react with aniline if formaldehyde is not released.

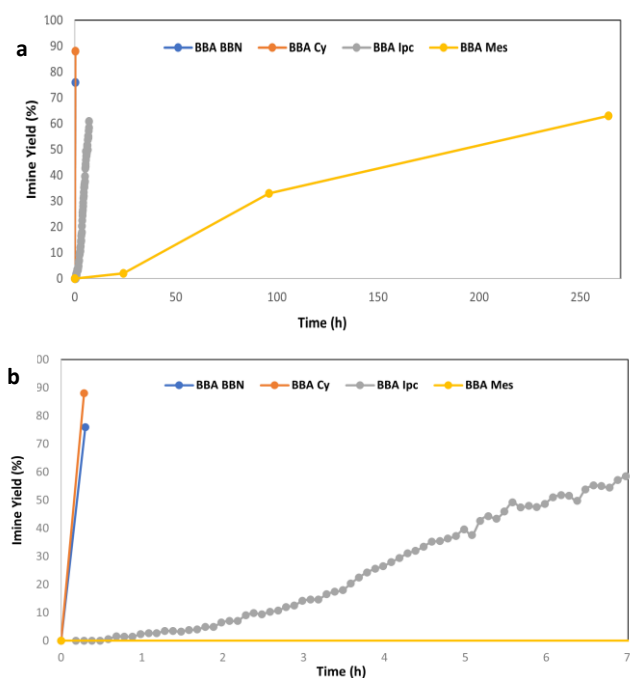
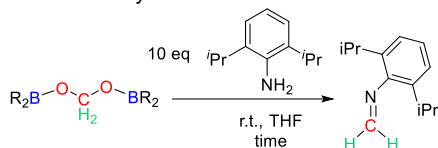


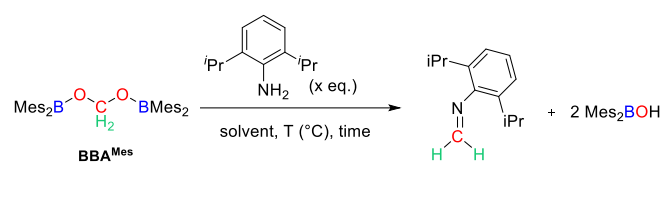
Figure 1. Evolution of the yield of formation of the imine from the reaction of 10 equivalent of BBA^{BBN} , BBA^{Mes} , BBA^{Cy} , and BBA^{lpc} with 2,6-diisopropylaniline in THF-*d*₆ at 25 °C. **1a:** full diagram, **1b:** zoom over 7h

Table 1. Reaction of BBA^{BBN} , BBA^{Mes} , BBA^{Cy} , BBA^{lpc} and HCHO with 2,6-diisopropylaniline.

Entry	BBA	Aniline (equiv.)	Time	Imine yield (%)
1 ^[a]	BBA^{BBN}	1	20 min	83
2	BBA^{BBN}	10	18 min	76
3	BBA^{Cy}	1	19 min	89
4	BBA^{Cy}	10	17 min	88
5	BBA^{lpc}	10	425 min	63
6	BBA^{Mes}	10	11 days	88
7 ^[b]	HCHO	10	2 days	> 99

[a] previous work, [b] the reaction was performed at 80 °C.

In order to get insights into the reaction mechanism, we further explored the reaction with BBA^{Mes} , because i) the condensation of BBA^{Mes} with the aniline is the slowest reaction, thus increasing the possibilities to observe intermediates and variation in the rate of the reaction depending on the conditions and ii) BBA^{Mes} is isolable which enables a better control of the stoichiometry and to observe the reaction in the absence of the mixture of products and catalyst from the reduction step. The solvent, temperature and quantity of aniline were varied (Table 2). While similar excellent yields ranging from 85% to 98% were obtained, the reaction time for complete consumption of BBA^{Mes} varied from 3 to 118 days. In general, the reaction is much faster with a 10-fold excess of aniline (96% yield in 21 days, entry 2, Table 2) compared to a stoichiometric quantity (93% yield in 118 days, entry 1, Table 2). Increasing the temperature to 80 °C in the presence of 1 or 10 equivalent(s) of aniline also led to a faster reaction (entries 3 and 4, Table 2, respectively). In both cases, the reaction is faster than at 25 °C (118 vs 27 days, entries 1 vs 3, respectively, and 21 vs 7 days, entries 2 vs 4, respectively). It is interesting to compare entries 2 (Y = 96% in 21 days) and 5 (Y = 88% in 11 days) of Table 2, differing only by the fact that the engaged BBA^{Mes} is isolated in entry 2 and generated *in situ* from CO_2 hydroboration in entry 5 (this entry corresponds to entry 6 of Table 1). While the better yield obtained with the isolated BBA^{Mes} is somewhat expected because less competitive side reactions may occur, the higher rate from the *in situ* generated BBA^{Mes} was more surprising. The replacement of THF-*d*₈ by C_6D_6 led to faster or similar reaction rate as indicated in entries 6-9 to be compared to entries 1-4 in Table 2.

Table 2. Formation of the imine from the condensation reaction between BBA^{Mes} and 2,6-diisopropylaniline under various conditions.

Entry	Aniline (equiv.)	Solvent	T (°C)	Time (days)	Imine yield (%)
1	1	THF- <i>d</i> ₈	25	118	93
2	10	THF- <i>d</i> ₈	25	21	96
3	1	THF- <i>d</i> ₈	80	27	87
4	10	THF- <i>d</i> ₈	80	7	95
5 ^{[a],[b]}	10	THF- <i>d</i> ₈	25	11	88
6	1	C ₆ D ₆	25	50	98
7	10	C ₆ D ₆	25	23	85
8	1	C ₆ D ₆	80	14	90
9	10	C ₆ D ₆	80	3	94

[a] BBA^{Mes} was generated in situ, [b] entry 6 of Table 1.

The condensation reactions of BBA^{Mes} with the aniline presented in Table 2 were conducted in NMR tube for *in situ* study. We were particularly interested in detecting possible intermediates and co-product(s) of the reaction to get experimental insights in the mechanism. The main question regarding the reactivity of BBA - and of related BSA compounds - as formaldehyde surrogate is whether or not formaldehyde is released alongside the boroxane R₂BOBR₂ or siloxane R₃SiOSiR₃ prior to the condensation reaction. Formaldehyde or Mes₂BOBMe₂ were never detected in any of the entries of Table 2 and only a minimal amount of H₂O was observed in some cases (see ESI). However, borinic acid (Mes₂BOH) was detected in ¹H NMR analysis at 9.09 ppm in THF-*d*₈^[4b] and at 5.26 ppm in C₆D₆^[9] in a 2:1 ratio versus imine along the kinetic profile of the reaction (see Figure 2 for entry 1 and ESI for entry 2-9, Table 2). This feature strongly suggests that Mes₂BOH is directly associated with the reactivity of BBA^{Mes} with the aniline and do not derive from the hydrolysis of unobserved boroxane Mes₂BOBMe₂.

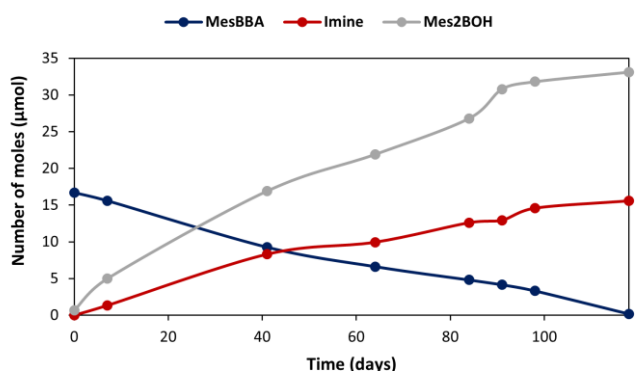


Figure 2. Evolution of the quantities of BBA^{Mes} (blue curve), imine (red curve) and Mes₂BOH (green curve) overtime in the presence of 1 equivalent of aniline in THF-*d*₈ at 25 °C (entry 1, Table 2).

Theoretical investigations. With these experimental data showing very significant differences between BBA's reactivity toward 2,6-diisopropylaniline in various reaction conditions, we explored the reaction computationally. DFT investigations were conducted at the M06-2X/6-311+G(d,p)(THF, SMD)//M06-2X/6-31G(d) level. The energy profile of a first mechanism (**M1**) of the condensation reaction of BBA^{BBN} with the aniline is presented in Figure 3. The first step goes through transition state **TS1** with a barrier of 36.6 kcal/mol to intermediate **B** uphill by 5.8 kcal/mol compared to BBA^{BBN}. **TS1** implicates the concomitant addition of the amine to the methylene of BBA and the migration of an O-BR₂ fragment to the other boron atom (Figure 3). The formation of intermediate **B** via a S_N2 type transition state is similar to the reaction of BBA^{BBN} with *N*-Heterocyclic Carbene.^[4d] We have indeed reported the isolation and characterization of a compound analogous to **B** with a NHC fragment in place of the ammonium fragment and a similar transition state was found from DFT investigations. The analogy is only on this first elementary step as the subsequent reactivities of **B** and the analogous NHC intermediates differs. The intermediate **B** evolves with a small barrier of 4.3 kcal/mol (*via* **TS2**) into the *O*-borylated hemiaminal intermediate **C** by the release of one equivalent of borinic acid R₂BOH. An alternative mechanism leading to the release of boroxane R₂BOBR₂ and the formation of the hemiaminal intermediate **C'** was also explored without additive (**TS2A**) or catalyzed by borinic acid or water in **TS2B** and **TS2C**, respectively. As shown in Figure 3, **TS2A**, **TS2B** and **TS2C** are higher in energy compared to **TS2** (+ 11.7 to + 22.7 kcal/mol higher).

The methylene aniline end product is then formed in one step from **C** by proton shift from the amino group to the O-BR₂ fragment to release a second equivalent of borinic acid. Three transition states in red (**TS3**, **TS3E** and **TS3F**) were explored. The uncatalyzed unimolecular **TS3E** is the highest in energy with a barrier of 39.8 kcal/mol relative to intermediate **C**. We found that the catalytic activation of **C** by 1 equivalent of borinic acid is the most accessible transition state. It serves as a proton relay in the 6 membered-ring **TS3** (29.0 kcal/mol). A similar 6 membered-ring **TS3F** was also found with H₂O as the catalytic proton relay with a slightly higher barrier of 30.3 kcal/mol. Although the formation of intermediate **C'** was ruled out, we nonetheless explored the mechanism leading to the imine from **C'**. The resulting **TS3A**, **TS3B**, **TS3C** and **TS3D** are all higher in energy compared to **TS3** and **TS3F**.

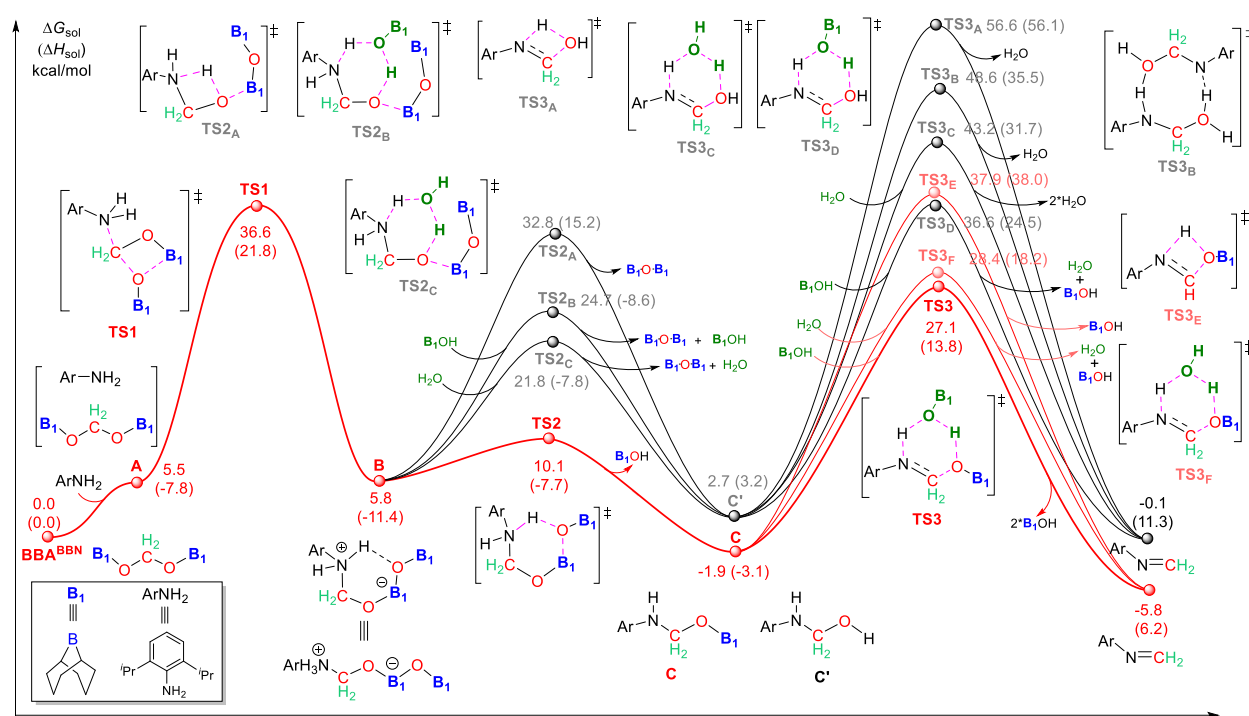


Figure 3. Energy profile of M1 for the condensation reaction of BBA^{BBN} with 2,6-diisopropylaniline. Relative Gibbs free energies and enthalpies (in parentheses) are calculated at the M06-2X/6-311+G(d,p) (THF, SMD)/M06-2X/6-31G(d) level. The grey and red pathways both leads to the formation of the same imine along with B₁OB₁ and 2eq. of B₁OH, respectively. The indicated energies thus correspond to the sum of imine + B₁OB₁ for the grey pathway and the sum of imine + 2B₁OH for the red pathway, which explain the difference in the final energies.

Next, we wondered if the boryl moieties of the BBA could play a role as a Lewis acid in a first elementary step with the incoming aniline. This would explain why, in our conditions, BBA compounds react with the aniline while the related BSA compounds tested do not. An alternative mechanism **M2** was thus found to afford the borylated hemiacetal compound **C** (Figure 4). It involves the initial coordination of the basic amine fragment on a boryl moiety and the proton transfer from the amine to the second boryl in a six membered-ring **TS1'** (31.4 kcal/mol). Three molecules are released from **TS1'**: formaldehyde, borinic acid and borylated aniline for a slightly exothermic reaction (-1.1 kcal/mol). No pathway could be found to directly link **TS1'** to **C** and one equivalent of borinic acid. The second step is then higher in energy than the first step. The addition of formaldehyde to the borylated amine *via* **TS2'** (35.8 kcal/mol) leads to intermediate **C**. The possible involvement of HCHO and R₂BOH in **TS2b'** (37.2 kcal/mol, grey path, Figure 4) would lead to a hemiaminal compound featuring a borylated amine fragment that would need to be rearranged (37.4 kcal/mol) to afford the final imine product. This last possibility was ruled out because of the two additional higher energy barriers. The initial coordination of a THF molecule on a boryl moiety to give a THF-BBA^{BBN} adduct was also examined. The result shows that the relative free energy and enthalpy of THF-BBA^{BBN} are 6.1 and -10.4 kcal/mol, respectively, which is comparable with the energies of ArNH₂...BBA^{BBN} (**A'**, 6.1 and -11.3 kcal/mol). Therefore, the THF solvent coordination to boron would be in competition with the aniline coordination.

This alternative mechanism **M2** thus proposes two barriers of 31.4 kcal/mol (**TS1'**) and 35.8 kcal/mol (**TS2'**) to produce intermediate **C**, when the first mechanism **M1** proposes two barriers of 36.6 kcal/mol (**TS1**) and 29.0 kcal/mol (**TS3**) to afford the same intermediate **C**. At this stage, it is difficult to differentiate the two proposed mechanisms featuring similar highest Gibbs free energy of activation ΔG^\ddagger of 36.6 and 35.8 kcal/mol corresponding to **TS1** and **TS2'**, respectively. In addition, these free energy barriers are too high for the observed reaction that takes place at 25 °C. On one hand, DFT method can affect the energy barriers. **TS1**, and **TS2'** were recalculated by using B3LYP-D3 method which includes the empirical dispersion term. The B3LYP-D3 result show that the trend of energy barrier is the same as that of M06-2X method. However, it is worth pointing out that the overall barrier is lowered by 5-6 kcal/mol for B3LYP-D3 for **TS1** (**M1**) but not for **TS2'** (**M2**) (Table S2 and Fig. S47). On the other hand, DFT calculations are known to present difficulties to estimate entropy of reaction and thus of free energy when the number of components varies between reactants and products which is the case in the different steps. A correction of 4.3 kcal/mol per component variation was proposed by Martin *et al.*,^[10] which would afford slightly more acceptable barriers. In order to avoid combining different errors,^[11] the enthalpies are alternatively considered. In this case, the highest barrier in **M1** is of 29.6 kcal/mol for **TS1** (since the formation of the adduct **A** between BBA^{BBN} and 2,6-diisopropylaniline is exothermic by 7.8 kcal/mol), while it is of 42.3 kcal/mol for **TS2'** in the alternative mechanism **M2** (from **A'**). This last comparison argues in favor of the first

mechanism **M1** on a theoretical point of view. Moreover, a compound related to intermediate **B** was isolated and

characterized in a previous work involving a carbene in place of the aniline and BBA^{BBN} which also support **M1** over **M2**.^[4d]

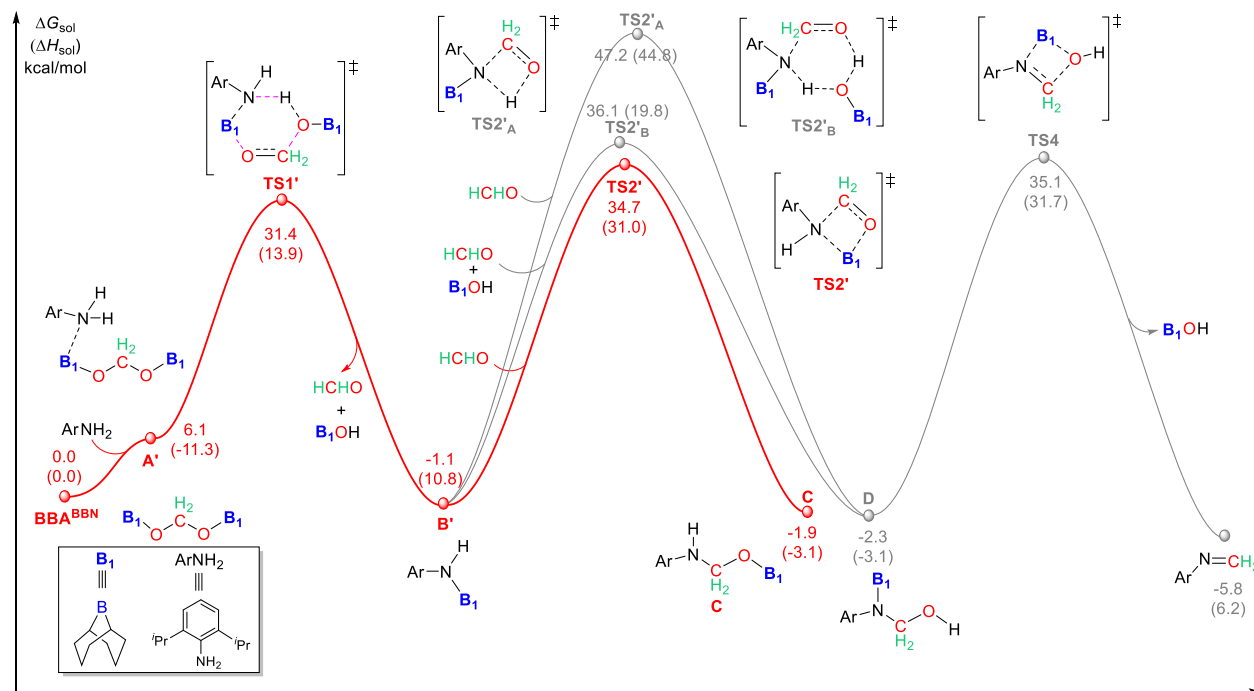


Figure 4. Energy profile of alternative mechanism **M2** for the condensation reaction of BBA^{BBN} with 2,6-diisopropylaniline. Relative Gibbs free energies and enthalpies (in parentheses) are calculated at the M06-2X/6-311+G(d,p) (THF, SMD)//M06-2X/6-31G(d) level.

While the experimental and theoretical investigations are in favor of **M1** in case of BBA^{BBN}, the mechanism was then explored with BBA^{Cy}, BBA^{lpc} and BBA^{Mes} to see whether **M1** is consolidated. In these three cases, the same two pathways (**M1** and **M2**) were found. The Gibbs free energies (ΔG^\ddagger) and enthalpies (ΔH^\ddagger) of **TS1** and **TS2'** of the rate-determining steps in **M1** and **M2**, respectively, are given in Table 3. Again, the Gibbs free energies appear overestimated in both pathways. Considering enthalpies, the values for the alternative pathway **M2** do not reproduce the experimental observations. Very satisfyingly, the enthalpy barriers reproduce well the tendencies observed in the rate of reaction in case of **TS1** of **M1**. BBA^{Cy}, which reacted within 17 min, exhibits a 27.4 kcal/mol barrier of activation (ΔH^\ddagger), in the same range as BBA^{BBN}, while BBA^{lpc} and BBA^{Mes} feature barriers of 37.4 and 43.4 kcal/mol, respectively, in line with 7 h and 11 days of reaction times required to consumed the BBA reactants. In addition, the calculated enthalpy barrier of activation for BSA^{Et} was found at 49.9 kcal/mol, while it was found at 31.7 kcal/mol for HCHO *via* **TS3c** (Figure 3). Moreover, the experimental investigations on BBA^{Mes} do not show any formaldehyde nor borylated amine build up, contrarily to what the alternative mechanism **M2** suggests. Finally, the rate increase with an excess of aniline indicates that the aniline plays a role in the rate-determining step (rds), which is the case in **TS1** (**M1**) but not in **TS2'** (**M2**). The array of experimental and theoretical data thus points toward **M1** as the most valid envisioned mechanism.

Table 3. Comparisons of the energy barriers (ΔG^\ddagger (ΔH^\ddagger)) of the rate-determining steps **TS1** and **TS2'** for **M1** and **M2**, respectively, for BBA^{BBN}, BBA^{Mes}, BBA^{Cy}, BBA^{lpc}, BSA^{Et} and HCHO calculated at the M06-2X/6-311+G(d,p) (THF, SMD)//M06-2X/6-31G(d) level.

BBA ^R	Reaction time	rds M1 [ΔG^\ddagger (ΔH^\ddagger)] TS1	rds M2 [ΔG^\ddagger (ΔH^\ddagger)] ^a TS2'
BBA ^{BBN}	18 min	36.6 (29.6)	35.8 (42.3)
BBA ^{Cy}	17 min	34.8 (27.4)	39.1 (42.3)
BBA ^{lpc}	7 h	47.7 (37.4)	45.7 (48.2)
BBA ^{Mes}	11 days	54.9 (43.4)	53.2 (43.6)
BSA ^{Et}	-	59.3 (49.9)	
HCHO	2 days	43.2 (31.7) <i>via</i> TS3c ^b	

[a] ΔH^\ddagger in **M2** should relate to the first adduct (with lowest enthalpy), [b] the reaction of HCHO with 2,6-diisopropylaniline first goes through **TS1**-like transition state ($\Delta G^\ddagger = 37.3$ and $\Delta H^\ddagger = 27.2$ kcal/mol, Figure S38) to give intermediate **C'** and then undergoes the rate-determining step **TS3c** to give the final product

Although the condensation reaction of the four BBA compounds with 2,6-diisopropylaniline likely follows the same pathway **M1**, the differences of rate of reaction are significant, in line with the relative stability of the BBA: it is indeed possible to isolate and even crystallize BBA^{Mes}, when the three other BBA could not be isolated in our hands. We then sought to disclose the origin of

these differences by probing both electronic and steric factors. The natural population analysis (NPA) charge distribution and frontier orbitals were evaluated to probe electronic factors (Figures S43 and S44). We first looked at the NPA charges of the methylene fragment since **TS1** involves the nucleophilic attack of the amino group of the aniline to the methylene fragment of BBA. The NPA charges of the methylene fragment do not vary with charges of 0.31 for the carbon atom of the four BBA compounds. While the NPA charges on the O and B atoms vary slightly, the values for BBA^{Mes} are intermediates between the ones for BBA^{BBN} and BBA^{Cy}, which could not explain the experimental observations of fast reaction for BBA^{BBN} and BBA^{Cy} and very slow reaction for BBA^{Mes}. Similarly, no significant differences are observed in the NPA charges in **TS1** of the four BBA compounds. The level of energy of the frontier orbital was then evaluated (Figure S44). In line with the NPA charges, no trend could explain the experimental findings, since the LUMO of the BBA exhibit energy levels of 1.26, 1.23, 1.07 and 0.04 eV for BBA^{BBN}, BBA^{Cy}, BBA^{lpc} and BBA^{Mes}, respectively. It thus appears that the most accessible LUMO is for BBA^{Mes} which is the less reactive compound.

The importance of distortion in **TS1** was then explored, by means of distortion-interaction analyses (DIA).^[12] This analysis determines the energy cost of distortion for the aniline (Fragment-N) and the BBA (Fragment-B), as exemplified in Figure 5 for **TS1**

with BBA^{BBN}. The energies of the two parts are evaluated through single-point calculations in the geometry adopted in the transition state and compared to their initial energy in adduct **A**, affording the variation of energy for each fragment: $\Delta E_{\text{dist}}(\text{N})$ and $\Delta E_{\text{dist}}(\text{B})$. The difference in the interaction energies between the Fragment-N and Fragment-B in the adduct **A** and the transition state **TS1** is denoted ΔE_{int} . The activation energy ΔE^\ddagger is defined as $\Delta E^\ddagger = \Delta E_{\text{dist}}(\text{N}) + \Delta E_{\text{dist}}(\text{B}) + \Delta E_{\text{int}}$. Although DIA at single point might be taken with care, this analysis reveals that the activation energies (ΔE^\ddagger) of the five **TS1** transition states (including BSA^{Et}) are consistent with the trends in their corresponding free-energy or enthalpy barriers (ΔG^\ddagger or ΔH^\ddagger , respectively). Moreover, the distortion energy $\Delta E_{\text{dist}}(\text{B})$ of BBA reactants strongly dominates ΔE^\ddagger with very small variations in $\Delta E_{\text{dist}}(\text{N})$ (-0.1 to +0.5 kcal/mol) and limited energy of interaction ΔE_{int} gain (Figure 5). It thus appears that the steric factor associated with BBA compounds (Fragment-B) is the main factor to explain the rate of the reaction of BBA with 2,6-diisopropylaniline. The percent of buried volumes (%V_{Bur}) of the boron atom in the four BBA compounds were then evaluated to estimate the steric hindrance associated with each boryl moiety.^[13] While the difference between BBA^{BBN} (%V_{Bur} = 72.8) and BBA^{Cy} (%V_{Bur} = 83.4) could not be explained, the %V_{Bur} of the boron atom in these compounds remain smaller than the bulkier BBA^{lpc} (%V_{Bur} = 87.3) and BBA^{Mes} (%V_{Bur} = 90.2).

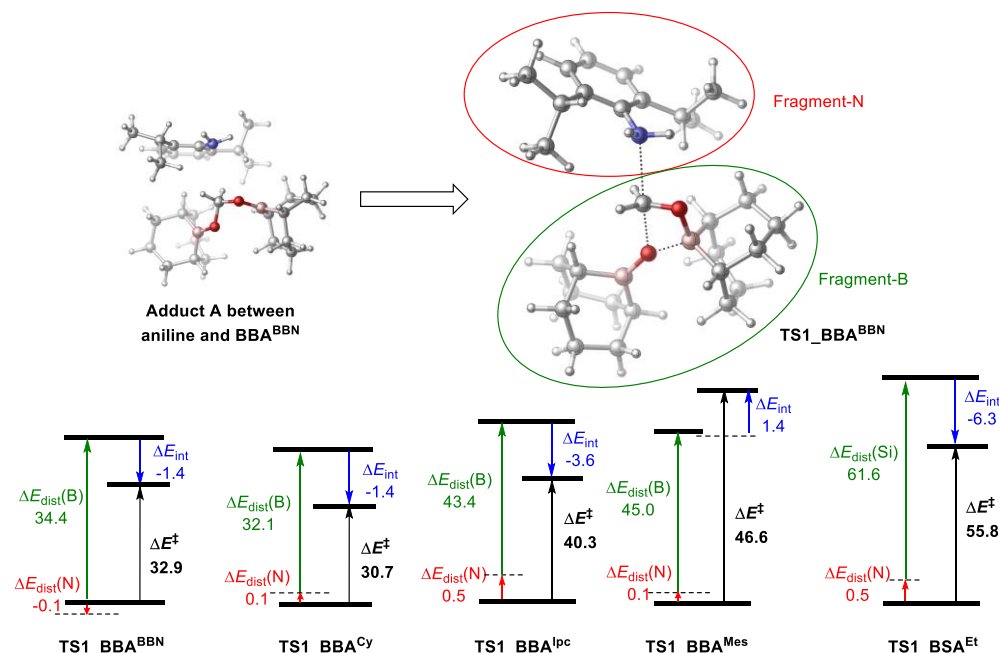


Figure 5. Distortion-interaction analysis (DIA) for BBA^{BBN}, BBA^{Mes}, BBA^{Cy}, BBA^{lpc} and BSA^{Et}.

Conclusion

In most of the report describing the reduction of CO₂ with hydroborane reductants, the level of reduction depends on the nature of hydroborane. Several studies have indeed shown that with the same catalyst, the variation of the hydroborane led to 2, 4 or 6e- reduction stage.^[6, 12, 14] In the present publication, we showed that the [Fe(H)₂(dmpe)₂] complex is able to consistently catalyze the 4e- reduction of CO₂ to some extent. Two new BBA compounds, BBA^{lpc} and BBA^{Cy}, have been selectively generated and characterized *in situ*. BBA^{lpc} is the first reported chiral BBA

compound, while BBA^{Cy} was generated with a particularly high TOF value of 546 h⁻¹.

Furthermore, the ability of [Fe(H)₂(dmpe)₂] to catalyze the generation of four different BBA compounds in the same conditions was exploited to assess the impact of the boryl moieties on the reactivity of BBA compounds toward 2,6-diisopropylaniline. The reaction rate of this condensation reaction was shown to strongly depend on the nature of the BBA, and thus on the nature of the boryl moieties, with reaction time ranging from minutes to weeks. Theoretical investigations enabled to propose a mechanism in which formaldehyde is never released during the

reaction. Moreover, the rate-determining step was shown to involve both BBA and the aniline and to prove that the steric factors are the predominant ones to explain the difference in reactivity while the electronic factors were found to be negligible. While the difference of stability between the reported BBA compounds was a clear sign of the influence of the boryl moieties on BBA compounds on their stability and thus reactivity, the present study offers a clear assessment of the extent of this influence and disclose the main reason for such differences. BBA compounds have been used as C_1 and C_n sources in complex transformations. The findings presented herein might be of interest to guide future research exploring the reactivity of BBA compounds obtained from CO_2 hydroboration.

Experimental Section

The supporting information includes experimental details, compounds synthesis and characterization and description of the optimization procedure.

Acknowledgements

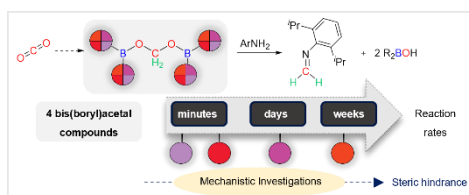
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Keywords: Bis(boryl)acetal • CO_2 • hydroboration • reductive functionalization • DFT

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Entry for the Table of Contents



Four bis(boryl)acetal compounds – including two new ones - were synthesized under identical conditions. Mechanistic investigations proved that their condensation toward 2,6-diisopropylaniline is very sensitive to the steric hindrance of the boryl moieties.

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