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Facile metal free regioselective transfer hydrogenation of polarized olefins with ammonia borane $\dagger \ddagger$

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Transfer hydrogenation of polarized olefins bearing strongly electron-withdrawing groups on one side of the double bond was achieved with ammonia borane under mild conditions without using a catalyst. Mechanistic studies proved the character of the direct H transfers proceeding stepwise with a unique hydroboration intermediate and hydride before proton transfer.

Transfer hydrogenation is a broadly applied method for hydrogenation of unsaturated compounds using a source other than gaseous H_2 .¹ Concerning the mechanism for transfer hydrogenations, they are commonly classified into two groups:² (a) direct hydrogen transfers from the hydrogen donor to the acceptor species, and (b) an indirect mechanism, by which the H atoms are transferred from the hydrogen donor to the acceptor through mediation by catalytic or non-catalytic centers.

A typical example for the first route is the aluminium complex catalyzed Meerwein–Ponndorf–Verley reduction of carbonyl substrates to alcohols, which was proposed to occur through a six-membered transition state including the Lewis acidic centers.³ The second type, often also called bifunctional catalysis, is the preferred mechanism for metal catalyzed hydrogen transfers, where a metal hydride intermediate and a protic site are formed prior to the double H transfer to the hydrogen acceptor. The widely applied Noyori and Shvo type transfer hydrogenations are of this type.⁴ However, double H transfers via the elementary process of direct transfer without the presence of a metal center are rare.⁵

We recently approached metal free transfer hydrogenation of imines with ammonia borane (BH_3NH_3 , AB) as the hydrogen donor.⁶ By various mechanistic studies it was proven to involve a concerted double H transfer. Herein, we will report another direct H transfer reaction with AB as the hydrogen donor, applying polarized olefins as hydrogen acceptors and study the H transfer mechanism in detail.

2-Cyclohexylidenemalononitrile (1a) was used first to test the reaction conditions. It was surprising to see that the 1:1 hydrogen transfer from AB to 1a can be completed within 10 min in THF at room temperature and at 10 °C in less than 1 h, with 2a as the only hydrogenated product and borazine ((BHNH)₃, **BZ**) as the by far predominant dehydrocoupling product (a small amount of polyborazine and cyclotriborazane were also observed).⁷ When the solvent was changed to acetonitrile, 1 h was required to complete the hydrogenation at room temperature. Benzene and chloroform were also tried: in both cases, the reactions were slow presumably due to poor solubility of AB in these solvents, but the rate was much faster in the less polar solvent benzene (20 h) than in chloroform (more than 3 days). Considering that 10 min is too fast for proper pursuit of the reaction course at room temperature, acetonitrile was selected for the model studies.

To test the chemical scope of this reaction, a series of polarized olefins with two electron-withdrawing (EWD) groups on one side of the double bond and on the other side with H, alkyl or aryl substituents (1a-1k) were applied in the reaction with AB in acetonitrile at room temperature. High yields in the hydrogenated products were achieved (Table 1).

The required time for completion of the reactions varied from several minutes to several days. Comparing the reaction times of different olefins, it was found that alkyl groups accelerate the hydrogen transfers, since the required times for the olefins **1a–1e** were less than those for **1f–1h** (Table 1, entries 1–8). Comparing the effect of the ester substituent with the stronger EWD group CN, the latter seemed to activate the olefin more (entries 1 to 2 and 9 to 11). Hydrogen substituents also accelerated the reaction rates presumably imposing less steric hindrance on the reactants (entries 6, 7 and 9).

To ensure the transfer hydrogenation to proceed with 'polarity-match' of the hydrogen donor and the acceptor, reactions of three different olefins (1a, 1h and 1i) with selectively deuterated AB adducts (BD₃NH₃ (AB(D)) and BH₃ND₃ (A(D)B)) were carried out. The reactions were pursued by *in situ* ¹H, ²H and ¹³C NMR spectroscopies, and only the expected regio-orientation of the deuterated products was observed. This confirmed regiospecificity in the hydrogen transfer processes. The possibility of radical involvement in the reaction course seemed less probable.

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$ \begin{array}{c} R \\ \hline \\ R' \\ E' \end{array} \begin{array}{c} E \\ + \end{array} \begin{array}{c} 1/2 \\ BH_3NH_3 \\ \hline \\ BH_3NH_3 \end{array} \begin{array}{c} CH_3CN \\ \hline \\ R' \\ H \\ E' \end{array} \begin{array}{c} R \\ + \end{array} \begin{array}{c} H \\ E' \\ H \\ E' \end{array} \begin{array}{c} 2 \\ + \end{array} \begin{array}{c} 1/6 \\ (BHNH)_3 \end{array} $					
Entry	Olefin		Temperature	Time	Yield ^{b} (%)
1		1a	rt	1 h	>99 (86)
2		1b	rt	2 h	>99
3		1c	rt	5 h	>99
4	Me CN Me CN	1d	rt	4 h	>99
5	Me ⁷ Bu CN	1e	rt	1 h	>99
6	Et Ph CN	1f	rt	6 h	>99
	Ph, CN		rt	5 d	92
7	Ph CN	1g	60 °C	6 h	>99
	\square		rt	2 d	98
8	CN	1h	60 °C	0.5 h	>99 (93)
9		1i	rt	10 min	>99 (90)
10	H CO ₂ Me	1j	rt	0.5 h	>99
11		1k	rt	3 d	98

Table 1Transferhydrogenationreactionsofvariouspolarizedolefins with AB^a

^{*a*} Reactions in acetonitrile with a 1 : 1 molar ratio of 0.1 mmol olefin to **AB**. ^{*b*} Reactions pursued by ¹H NMR and the yields were established by GC-MS based on the amount of olefins, in brackets were the isolated yields with a 1 mmol scale, all reactions were carried out at least twice to ensure the results as reported.

In addition to these deuterium labelling studies, the primary deuterium kinetic isotope effect (DKIE) was also investigated in reactions with **1a**. According to the kinetic conversion chart of Fig. 1, which is based on ¹¹B NMR experiments, the rate constants (k) were simulated with a first order equation to obtain the DKIE values. In our former study on the hydrogen transfer from **AB** to imines, an inverse DKIE was observed with **AB(D)** and a normal DKIE with **A(D)B** indicating that in this case the cleavage of both H_B and H_N is involved in the rate determining step (RDS).⁶ However, using the push–pull olefin **1a** as the hydrogen-acceptor, a DKIE could not be observed

with **AB(D)** (see Fig. 1, $k_{AB}/k_{AB(D)} = 1$). Assuming that any H_B transfer in the RDS would cause some kind of DKIE $\neq 1$, a DKIE of 1 is expected to indicate that the double H transfer is stepwise and the H_B transfer being fast occurring before or after the RDS.⁸

For the reaction of **1a** with A(D)B, a normal DKIE of 1.55 was obtained, indicating the participation of the breakage of the N–H bond in the RDS. For BD₃ND₃ (A(D)B(D)), the DKIE value was 1.61. This further addresses the fact that the H_N transfer is rate determining regardless of H_B or D_B in the neighborhood.

Since the reaction of a 1 : 1 molar mixture of **AB** and **1a** in THF was very fast at room temperature, a NMR sample with **1a** in excess (**AB** to **1a** 1 : 3) was prepared at low temperature in THF-D₈ and kept at -40 °C. A set of new signals appeared in the NMR (Fig. 2, spectrum c), which apparently belong to a reaction intermediate (**3a**), since they disappeared with increasing temperature and prolonged reaction times.

Based on ¹H, ¹³C NMR and DEPT (THF-D₈, -40 °C), the intermediate 3a is a hydrogenation product formed via 1,2-addition of a B-H bond across the olefinic double bond, while the boron substituent went to the cyano substituted side; the C_{CN} atom is thus characterized by a very broad signal at ¹³C NMR due to the quadrapolar broadening influence of the ¹¹B nucleus (Fig. 2). The newly formed –BH₂NH₃ unit with a 4-coordinate boron showing a broad triplet at -14 ppm in the ¹¹B NMR (different from cyclotriborazane which should be a sharp triplet at -11 ppm in the ¹¹B NMR). A new broad signal also developed at 5.15 ppm in the ¹H NMR, having no ¹¹B correlation, no (or invisible) NOE nor long range correlations to other ¹H or ¹³C NMR signals indicating that this signal belongs to the H_N nuclei of 3a. Given enough time at low temperature, the intensities of the signals for 3a will increase until the signal of AB had completely disappeared from the ¹¹B NMR spectrum, while the signals of 2a also



Fig. 1 Conversion chart of the reaction of 0.5 mmol **1a** with 0.1 mmol **AB**, **AB(D)**, **A(D)B** or **A(D)B(D)** pursued by ¹¹B NMR in CH₃CN at rt, derived from the intensities of **AB** of the ¹¹B NMR spectra with 2 min intervals. The black squares stand for reactions with **AB**, red circles for **AB(D)**, blue triangles for **A(D)B** and orange triangles for **A(D)B(D)**. Simulated reaction half-life times were: $t_{1/2}(AB) = 309$ s, $t_{1/2}(AB(D)) = 308$ s, $t_{1/2}(A(D)B) = 480$ s, $t_{1/2}(A(D)B(D)) = 499$ s. For first order reactions, the reaction constant $k = 0.693/t_{1/2}$,⁹ thus $k_{AB}/k_{A(D)B} = t_{1/2}(AB(D))/t_{1/2}(AB) = 1.00$, $k_{AB}/k_{A(D)B} = 1.55$, $k_{AB}/k_{A(D)B(D)} = 1.61$.



Fig. 2 Selected ¹³C NMR spectra (range of 24 to 45 ppm) in THF-D₈: (a) pure **1a**, labeled with circles ●; (b) pure **2a**, labeled with triangles ▼; (c) *in situ* spectrum for the reaction of **1a** with **AB** (2 to 1 molar ratio) at -40 °C: five new resonances from **3a** appeared (labeled with squares ■)—including a broad signal; (d) *in situ* spectrum for the reaction of **1a** with **AB(D)** at -40 °C: two triplets belonging to C_D (¹J_{DC} = 20 Hz) appeared as labeled with arrows ↓, and the broad resonance became sharper; (e) *in situ* spectrum for the reaction of **1a** with **A(D)B** at -40 °C: only one triplet of **2a** appeared.

started to grow in. The same experiment was also carried out in acetonitrile leading to similar observations but at lower rate.

From the related reactions of **1a** with **AB(D)** and **A(D)B** at $-40 \,^{\circ}$ C, ¹H, ¹³C and ¹¹B NMR spectra were taken. Comparing the ¹³C NMR spectra with that of the reaction of **1a** with **AB**, it can clearly be seen that the H_B (or D_B) atom was in the intermediate already transferred, while the H_N (or D_N) atom was not, since a triplet due to C–D coupling (¹J_{DC} = 20 Hz) was exclusively observed for the intermediate only when **AB(D)** was used (Fig. 2, spectrum d).

Based on all these mechanistic facts, a two-step hydrogen transfer mechanism is proposed with fast initial hydroboration forming intermediate 3 (Scheme 1).⁹ There are two possible routes to 3, the ionic pathway A and the concerted pathway B. Considering the solvent effect and comparing THF with acetonitrile, the ionic pathway A is expected to work better in the more polar solvent acetonitrile, while the concerted route B seems to be in operation in the less polar solvent THF. Since the reaction proceeds much faster in THF than in acetonitrile, route B seems more reasonable. The RDS is the transfer of the H_N atom of AB, which could be transferred *via* an intra-molecular mode as shown in 4 of Scheme 1, followed by the elimination of the very reactive [BH₂NH₂], which will be rapidly further dehydrogenated to BZ presumably in a similar manner as the reaction of 1 with AB.

In summary, we have demonstrated a very efficient metal free transfer hydrogenation of polarized olefins substituted with EWD groups on one side of the double bond with AB at room temperature. Deuterium labelling studies confirmed the regiospecificity in the H transfer processes. The DKIE demonstrated that only the H_N transfers get involved in the



Scheme 1 Proposed reaction mechanism.

RDS, and the structure of the hydroboration intermediate clearly indicated that H_B transfer occurs before the H_N transfer. Thus, this double-H transfer can be defined as stepwise and in a polar terminology with hydride before proton transfer.

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