Transfer Hydrogenation

Transfer Hydrogenation of Azo Compounds with Ammonia Borane Using a Simple Acyclic Phosphite Precatalyst

Miguel A. Chacón-Terán,[a] Rafael E. Rodríguez-Lugo,*[b] Robert Wolf,*[c] and Vanessa R. Landaeta*[a]

Abstract: Tris(quinolin-8-yl)phosphite, P(Oquin)$_3$, promotes the dehydrogenation of H$_3$N·BH$_3$ (**AB**) and the transfer hydrogenation of azoarenes using ammonia borane (**AB**) as H$_2$ source. The metal-free reduction of azoarenes proceeds under mild reaction conditions upon which several diphenylhydrazine derivatives are obtained in high yields. The reactivity of P(Oquin)$_3$ toward **AB** was evaluated through NMR in situ tests. The rate of the reaction, activation parameters, deuterium kinetic isotope effect (DKIE) and linear-free energy relationship were investigated. Such mechanistic and kinetic studies suggest that P(Oquin)$_3$ is a precatalyst and that **AB** is likely involved in more than one stage of the reaction pathway. Furthermore, the kinetic data indicate that the reaction proceeds through an ordered transition state, possibly associative.

Introduction

Hydrogenation is one of the most fundamental transformations in organic synthesis, and its industrial applications are broad, particularly in the production of fine chemicals to pharmaceuticals.[1] Considering that using H$_2$(g) requires special reaction (pressure) vessels and particular safety measures, researchers have dedicated substantial effort to develop simpler and safer alternatives for the reduction of unsaturated moieties. In this sense, transfer hydrogenation (TH) has become a practical and useful tool in reduction chemistry in the last decade.[2] TH-reactions using precious-metal catalysts have been intensively investigated.[3] However, for these, abundance, cost, and toxicity are significant issues. Furthermore, considering that for large-scale applications a catalyst for the release/transfer of hydrogen must be cheap and based on abundant materials, the use of platinum-group metals should be avoided. In this respect, organocatalytic-TH using main-group compounds is currently undergoing great development.[4]

Among the broad variety of potential hydrogen storage materials, ammonia borane (**AB**) has attracted particular interest due to its high weight percent of available hydrogen (19.6 %), high stability in air, high portability and the fact that its dehydrogenation is thermodynamically favorable (ΔH= –5.1 kcal/

mol).[5] Although rapid H$_2$-release from **AB** has been widely demonstrated by metal-based catalysts,[6,7] latest focus on the hydrogen transfer from **AB** (or amine-boranes in general) has been directed to organocatalyzed dehydrogenation using, for example, p-block-based systems.[8a–8f,9] have addressed the use of pnictogen-based compounds for TH reactions from **AB**, e.g. a bismuth-[10] and several phosphorus-based catalysts.[11–19] DFT calculations have revealed an energetically feasible pathway for a concerted double hydrogen transfer (concerted metathesis) from **AB**, using a phosphorus catalyst.[11]

Studies by Radosevich and co-workers[12] have shown that the highly-strained T-shaped phosphorus(III) compound **A** (Scheme 1a) promotes the TH of azobenzene (**2a**) with yields up to 98 % of 1,2-diphenylhydrazine (**3a**). Reduction of **2a** with quantitative yields was also achieved by Kinjo and co-workers[13,14] using diazaphospholene **B** (Scheme 1b).[15] In addition, these authors also investigated the potential of such compounds as transfer hydrogenation/hydroboration catalysts for the reduction of unsaturated bonds using **AB** and HB(pin) respectively, through a hydrophosphination/metathesis mechanism.[14] Similarly, Speed et al. described the reduction of imines and conjugated C=C bonds using HB(pin) and diazaphospholene **C** as precatalyst (Scheme 1c).[15,16] Treatment of **C** with HB(pin) (1 equiv.) resulted in the formation of **B**. The authors remarked that, after the hydrophosphination reaction, the initial metathesis occurred only at the exocyclic P–N or P–O bond (whichever the case). Prolonged exposure of **B** to **AB** or HB(pin) initiates further P–N bond cleavage, and the generation of PH$_3$ was observed.[17,18] Lately, reports by the groups of Radosevich,[17] Kinjo[18] and Speed[19] proved that it is possible to extend this application to challenging reduction reactions such as stereoselective reduction of imines and α,β-unsaturated aldehydes, chemoselective reduction of C=C bonds in α,β-unsaturated esters and hydroboration of pyridines. Additionally, diazaphospholene **B** catalyzes C-C coupling reactions,[18b] and an

[a] Departamento de Química, Universidad Simón Bolívar,
Valle de Sartenejas, Apartado 89000, Caracas 1020-A, Venezuela
E-mail: vlandaeta@usb.ve
[b] Laboratorio de Química Bioinorgánica, Centro de Química,
Instituto Venezolano de Investigaciones Científicas (IVIC),
Carretera Panamericana Km. 11. Caracas 1020-A, Venezuela
E-mail: rrodriguez@ivic.gob.ve
[c] Institute of Inorganic Chemistry, University of Regensburg,
93040 Regensburg, Germany
E-mail: robert.wolf@ur.de
Supporting information and ORCID(s) from the author(s) for this article are available on the WWW under https://doi.org/10.1002/ejic.201900572.

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analog of **C** has been used to promote reductive Claisen rearrangement in the presence of boranes.[20] These investigations suggest the possibility to further expand the scope of phosphorus compounds and their catalytic reactivity.

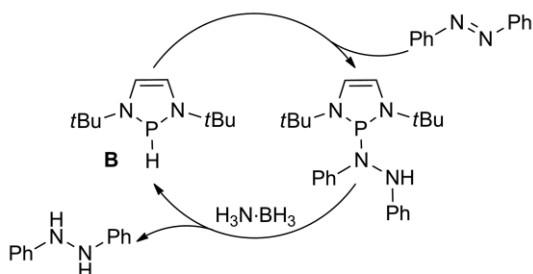**Phosphorus-based catalysts used in transfer hydrogenation**

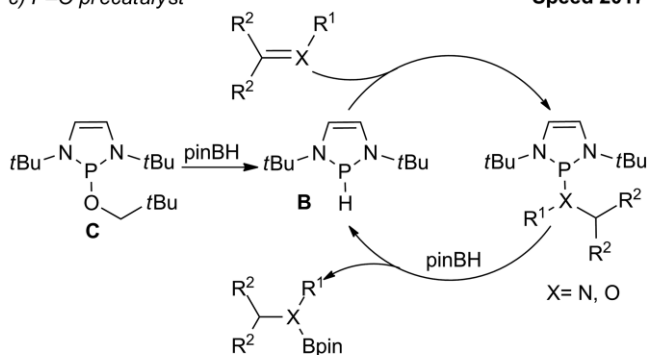*a) P–O catalyst*   **Radosevich 2012**
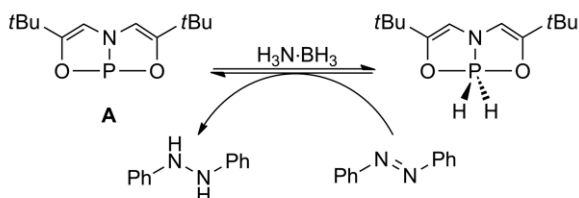
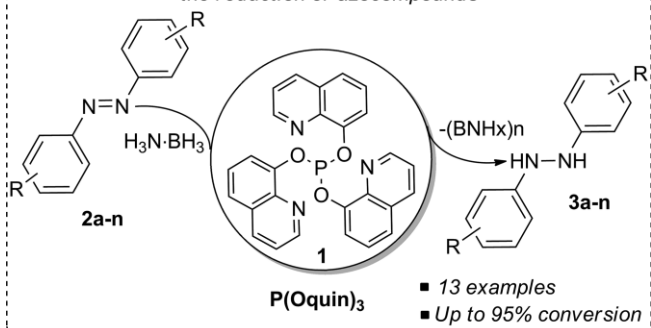*b) P–H activation / P–N hydrogenolysis catalyst*   **Kinjo 2014**

c) P–O precatalyst   **Speed 2017**

This work: P–O precatalyst
Acyclic phosphite precatalyst for the reduction of azocompounds

P(Oquin)₃
- *13 examples*
- *Up to 95% conversion*

Scheme 1. Cyclic phosphorus compounds and the acyclic phosphite P(Oquin)₃ used in catalytic transfer hydrogenation (TH) from different H₂ sources to unsaturated bonds.

Recently, some of us described the synthesis of the phosphorus(III) compound P(Oquin)₃ (**1**), as well as its coordination

chemistry toward Pd^{II} and an application of such a complex as a catalyst for the solvent-free, mild oxidative coupling of primary amines to imines using air as an oxidant.[21] Unlike **A–C**, which require several synthetic steps, **1** is quickly prepared in a one-pot reaction from commercial products on a gram scale, rendering it convenient for catalytic applications. Furthermore, in the solid-state, **1** presents intramolecular interactions that restrain the structure and originate a distorted geometry around the P-atom (with an average O-P–O bond angle of 93.5 degrees)[21] which, being *acyclic*, could somehow be similar to the strained or cyclic P^{III} compounds previously mentioned.

Herein, we report that **1** promotes the reduction of azoarenes using **AB** as H₂ source, a reaction that has attracted considerable interest recently.[10,12–14] Furthermore, we describe the results of spectroscopic and kinetic investigations, which give insight into the mechanistic features of this reaction. To the best of our knowledge, there is no precedent on the use of an *acyclic* tricoordinate phosphorus(III) compound for the TH of aromatic azo compounds into arylhydrazines.

Results and Discussion

In a recent report,[21] the preparation of P(Oquin)₃ (**1**) was described. According to the reported protocol, the phosphite can be obtained by treating phosphorus trichloride with 8-hydroxyquinoline (HOquin) in the presence of a base (NEt₃ or *n*BuLi). Following this reported procedure, **1** is sufficiently pure to perform coordination chemistry toward Pd^{II}, but not appropriate for organocatalytic applications. The problem lies in the difficulties to eliminate the formed NEt₃·HCl or LiCl in an efficient way. For this reason, an alternative preparation of **1**, depicted in Scheme 2, has been now developed in our group. The new methodology consists in the in situ preparation of the 8-quinolinol sodium salt followed by its reaction with PCl₃ (for further details see the supporting information). The NaCl can be separated more easily than NEt₃·HCl or LiCl. An analytically pure batch of phosphite was obtained in 90 % yield after recrystallization from dichloromethane and diethyl ether.
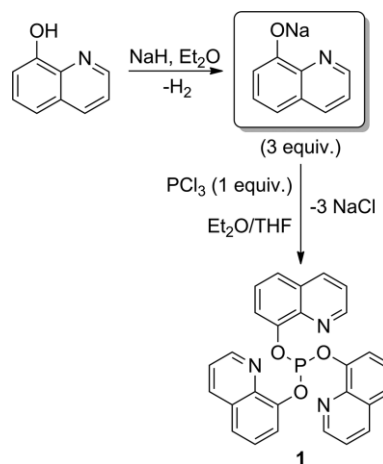
Scheme 2. Alternative synthesis of P(Oquin)₃ (**1**).

Considering the studies by Radosevich,[17] Kinjo[18] and Speed,[19] our group became interested in exploring the poten-

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tial of the *p*-block compound P(Oquin)$_3$ (**1**) as an organocatalyst in similar transformations. Thus, initially, it was important to study the reactivity of **1** toward **AB**. To this end, a test using a twenty-fold excess of **AB** was carried out. The quantitative formation of PH$_3$ (^{31}P = δ = –242 ppm, $^1J_{PH}$ = 180 Hz), along with dehydrogenated ammonia borane species, such as borazine and polyborazylene[7] was observed by ^{31}P and ^{11}B NMR spectroscopy (Figures S8 and S9, supporting information). These findings evidence the dehydrogenation of ammonia borane along with a chemical transformation of **1**. To evaluate the effect of the amount of **AB** complex on the reaction with **1**, the ratio **1/AB** was reduced to 1:5 and 1:1 (pseudo-stoichiometric or stoichiometric reaction, respectively) in independent tests. Although in such cases the reaction is less selective, producing several phosphorus- and boron-containing species (identified by ^{31}P or ^{11}B NMR, respectively), it was possible to observe products of the interaction of **1** with **AB** and to confirm that **1** is a hydrogen acceptor, which is transformed into other compounds. In particular, the presence of quinoline-based boron compounds, such as the corresponding borinate ester BH$_2$(Oquin) (^{11}B = δ = 5.9 ppm, $^1J_{BH}$ = 122 Hz) and the boronate ester BH(Oquin)$_2$ (^{11}B = δ = 8.8 ppm, $^1J_{BH}$ = 135 Hz), was determined (Figure S14, supporting information). Also, another (major) signal at 14 ppm in ^{11}B NMR, attributed to the in situ formation of B(Oquin)$_3$ (Figure S3), was identified, along with the common **AB** dehydrogenation product polyborazylene.[7]

Regardless of such lack of selectivity, after determining the reactivity of **1** as hydrogen acceptor from **AB**, it was important than to study its potential to promote transfer hydrogenation reactions or, more specifically, to determine whether the phosphite or its products after dehydrogenation of **AB** could engage in the transfer of hydrogen to an unsaturated substrate. Thus, the hydrogenation of azobenzene (**2a**) in the presence of **1** to yield 1,2-diphenylhydrazine (**3a**), was tested as a model reaction (Table 1). For the sake of comparison, other analogous phosphite compounds were also tested as catalyst precursors.

The reduction of **2a** in THF at 60 °C produces **3a** in high yields (>95 % after 16 h, entry 1). By using stoichiometric amounts of **AB** (1.1 equiv. relative to azobenzene) at the highest catalyst loading studied (i.e. 30 mol-%), the reaction proceeded without significant loss in yield, but a longer reaction time was required (>95 % after 24 h, entry 2). However, when stoichiometric amounts of **AB** were used at catalysts loadings between 20 mol-% and 5 mol-%, the catalytic activity dropped significantly (entries 4, 6, 9 and 11 compared to entries 3, 5, 8 and 10, respectively). The observed effect is more pronounced for lower catalyst loadings. Good conversion was achieved using 10 mol-% of **1** and a four-fold excess of **AB** (80 % after 24 h, entry 8). Moderate activity was observed for loadings below 5 mol-% of P(Oquin)$_3$ (57 %, entry 10). Lowering the (pre)catalyst loading to 12.5 mol-% still gave high conversions of **2a** when compared to higher catalysts loadings (ca. 90 %, entries 3 or 5 vs. entry 7). Compounds similar to **1**, e.g. ((R)-binapthol)-P(8-Oquin) (((R)-binapthol)P(8-Oquin) = 8-(dinaphtho-[2,1-d:1′,2′-f][1,3,2]dioxaphosphepin-4-yloxy)quinoline)[22] and P(1-O-Naphthyl)$_3$,[23] or the aromatic phosphite P(OPh)$_3$, were

Table 1. Metal-free transfer hydrogenation of **2a** using phosphite **1** as precatalyst. Screening of catalyst precursors.[a]

Entry	Catalyst precursor P(OR)$_3$	Time (h)	Catalyst loading (mol%)	Conversion (%)[c]
1	**1**[b]	16	30	>95
2	**1**[b]	24	30	>95
3	**1**[b]	24	20	>95
4	**1**[b]	24	20	78
5	**1**[b]	24	15	94 ± 1 (91)[d]
6	**1**[b]	24	15	75 ± 3
7	**1**[b]	24	12.5	87 ± 3
8	**1**[b]	24	10	80 ± 2
9	**1**[b]	24	10	57 ± 2
10	**1**[b]	24	5	57 ± 2
11	**1**[b]	24	5	20 ± 1
12	(structure)	64	30	40
13	(structure)	64	30	63
14	(structure)	64	30	17
15	None	64	0	<5

[a] **2a** (54.7 mg, 0.300 mmol), **AB** (37.0 mg, 1.200 mmol, 4 equivalents), 1,3,5-trimethoxybenzene (16.7 mg, 0.099 mmol, internal standard), THF (1.25 mL), argon atmosphere, 60 °C, 24 h. [b] **AB** (10.2 mg, 0.330 mmol, 1.1 equivalents). [c] Conversions determined by ^{1}H NMR using the internal standard. Values with errors are the result of at least two independent experiments. Triplicates were performed when the deviation of two experiments was larger than ±5. [d] Values in parenthesis correspond to isolated yield.

inefficient catalyst precursors under the studied conditions, yielding **3a** in only 63 %, 17 % or 40 %, respectively (entries 13 and 14). In the absence of a catalyst precursor, a very poor conversion was observed, thus highlighting the catalytic nature of the transformation (entry 15). In a screening of solvents (see the supporting information), high activity was also obtained in acetonitrile, benzene, and toluene. In particular, the latter two apolar hydrocarbons gave a quantitative reduction of **2a** after 24 h. However, THF was selected as the solvent for the rest of the studies to avoid interference with aromatic signals at quantifying steps on the ^{1}H NMR spectra.

Considering the spectroscopic evidence obtained from the reactivity tests (i.e. the formation of PH$_3$, BH$_2$(Oquin), BH(Oquin)$_2$ and HOquin) it was important then to determine the influence of such compounds on the model reaction (Table S2, Section D.5, Supporting Information) and, thus, to shed some light into the possible mechanism and/or catalytic species involved in the transformation. In this sense, initially, the catalytic activity of 8-quinolinol (HOquin) was tested. 70 % conversion was achieved with 30 mol-% of 8-quinolinol after 24 h. Longer reaction time (64 h) did not increase the conversion in this case. Also, NaPH$_2$ was independently examined as a PH$_3$ source. No conversion of **2a** to **3a** was observed, using either

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NaPH$_2$ or combining NaPH$_2$ with HCl (10 mol-%, 1.0 M in Et$_2$O) to produce PH$_3$ in situ. Subsequently, the catalytic performance of a 1:3 mixture of NaPH$_2$ and 8-quinolinol was investigated. This mixture yielded a conversion to **3a** of >95 % after 24 h, thus reproducing the performance (in terms of product yield) achieved by **1**. The substrate to **AB** ratio could be lowered to 2:1 and the reduction of **2a** still occurred effectively (>95 %).

Finally, to investigate the possible role of the boron-containing species generated in situ from the system **1** + **AB**, separate TH reactions were performed using some of the boron-esters observed in the reactivity tests. In fact, BH$_2$Oquin and BH(Oquin)$_2$ were among such boron compounds detected on the NMR scale experiments. These were also independently synthesized[24] to be used on the catalytic tests (see the Supporting Information), yielding 70 % and >95 % conversion of **2a** to **3a**, respectively. The use of BH$_2$(Oquin) as catalyst[24] in the reaction

led to a yield of the diphenylhydrazine product **3a** lower than with the system **1** + **AB**. This seems to indicate that BH$_2$(Oquin) is not the (sole) species responsible for the catalysis in this case. Unfortunately, it was impossible to assess the role of B(Oquin)$_3$ on the reaction. Attempts to isolate pure B(Oquin)$_3$ (which was assigned to a signal at 14 ppm in the ^{11}B NMR spectra, vide supra) yielded a mixture of BH$_x$(Oquin)$_{3-x}$ (x = 0,1,2) that could not be separated. Steric crowding on the boron atom, due to the presence of the three "Oquin" moieties, could be responsible for the impossibility to isolate such compound.

The findings from the reactivity tests strongly suggest that **1** is indeed a catalyst precursor, which serves as an appropriate source of the actual catalyst(s). While the identity of the true catalyst(s) presently remains unknown, both the phosphorus source and the "Oquin" moiety are required for the catalytic TH of **2a** from **AB**. Furthermore, although NaPH$_2$/8-quinolinol and

Table 2. Metal-free transfer hydrogenation of azo compounds using phosphite **1** as precatalyst. Screening of substrates.[a]
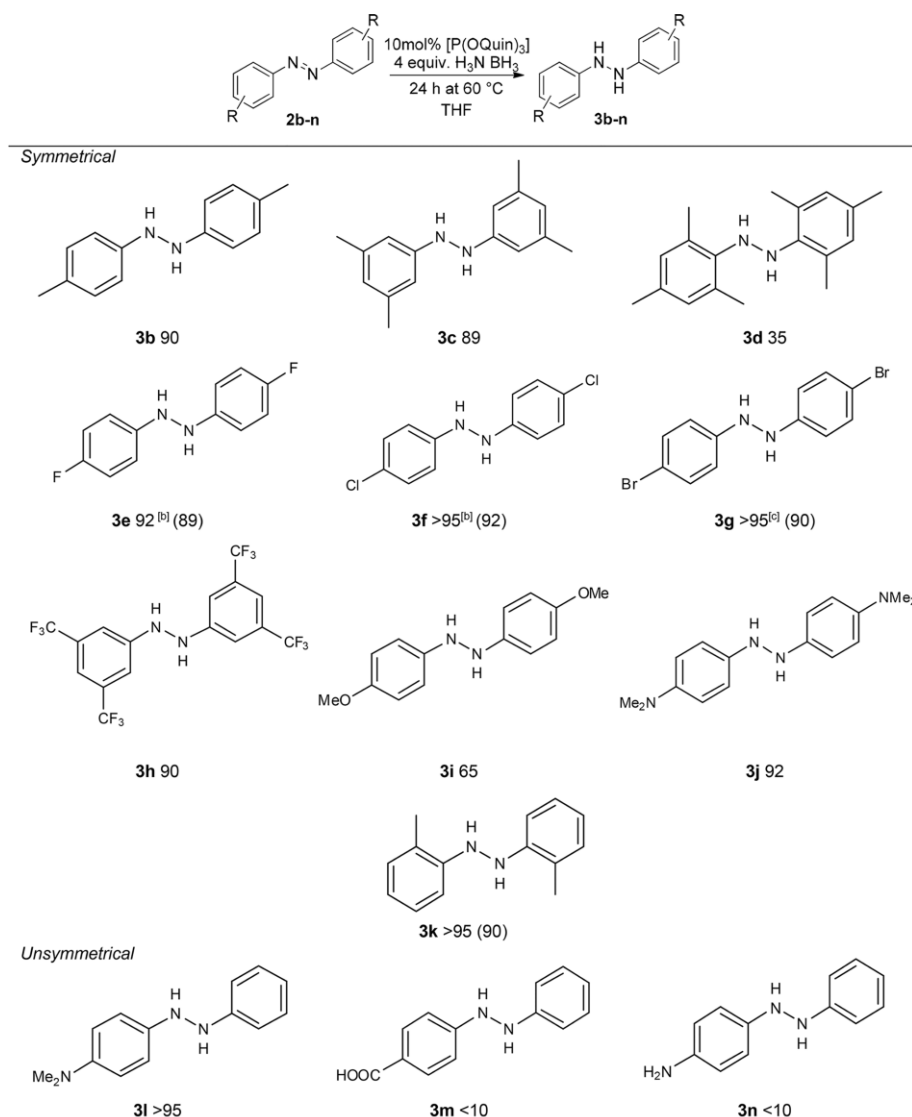
[a] **2b–n** (0.300 mmol), **1** (13.9 mg, 0.030 mmol), AB (37.0 mg, 1.200 mmol), 1,3,5-trimethoxybenzene (16.7 mg, 0.099 mmol, internal standard) THF (1.25 mL), Argon atmosphere, 60 °C, 24 h. [b] 16 h. [c] 12 h. Given conversions (%) determined by ^{1}H NMR spectroscopy. Values in parentheses (%) correspond to isolated yields.

BH(Oquin)$_2$ also worked effectively in converting **2a** into **3a** in the presence of **AB**, the use of these catalytic systems would be more inconvenient. NaPH$_2$ is hard to prepare, difficult to handle and pyrophoric.[25] BH(Oquin)$_2$ (as well as BH$_2$(Oquin)[24]) is thermally unstable and needs to be stored cold under inert atmosphere. For all the above, **1** was chosen as catalyst precursor for the rest of the study.

The following were selected as optimized conditions to examine the scope of the catalytic system with a series of symmetrical and unsymmetrical (*E*)-diazenes (Table 2): 10 mol-% of catalyst precursor **1**, 4 equivalents of **AB**, 60 °C, 24 h (unless otherwise stated). Although the best conversion for substrate **2a** was achieved using 15 mol-% of phosphite **1** as catalyst, for the rest of the azoarenes studied the use of catalytic loadings of 10 mol-%, 12.5 mol-% or 15 mol-% did not significantly affect the conversion obtained. Thus, the catalyst loading was kept to the lowest possible to achieve the observed yields (Table 2). Symmetrical azoarenes bearing electron-donating groups (EDG) such as methyl in different relative positions (*p*-, *m*- and/or *o*-, **2b**-**d**, **k**), were converted into the corresponding phenyl-hydrazine compounds with good yields. The bulky compound **2d** is the only exception, for which 35 % of the corresponding product was achieved after 24 h. Steric hindrance around the N=N bond might explain the low yield for such a compound. In the case of *p*-dimethylamino derivatives (**2j** and **2l**, symmetrical and unsymmetrical, respectively) a quantitative conversion was achieved. For *p*-methoxy (**2i**) a moderate conversion was obtained. Additionally, symmetrical and unsymmetrical azoarenes bearing electron-withdrawing groups (EWG) in the *para*-position, such as fluoro (**2e**), chloro (**2f**), and bromo (**2g**) derivatives, were reduced with good to excellent yields. In addition, a derivative substituted with trifluoromethyl groups (**2h**) in the *m*-position was tested, and a conversion of 90 % was achieved. (*E*)-diazenes bearing a *p*-NH$_2$ (**2n**) or *p*-COOH (**2m**) gave very poor yields of the corresponding hydrazine after 24 h. Increasing the reaction time up to 64 h in these cases did not improve the conversion, suggesting that the system does not tolerate groups that have acidic protons.

The kinetics for the catalytic TH of **2a** to yield **3a** were examined. The progress of the reaction as a function of time was monitored by ^{1}H NMR spectroscopy (Figure S15, supporting information). Plotting ln ([AZB]/[AZB]$_o$) vs. time (h) produced a straight line (Figure S16, supporting information). Here, [AZB] is the molar concentration of azobenzene at each given time and [AZB]$_o$ is the initial molar concentration of azobenzene. This simple experiment suggested a pseudo-first-order rate equation with respect to the azobenzene concentration in the presence of an excess of **AB**. Additionally, an induction period was observed, which needed to be considered for the analysis of the kinetic data. This period might be related to the time required for the activation of the precatalyst **1**, thus forming the actual active species, as evidenced by the reactivity (mechanistic) tests (vide supra).

The evaluation of the reaction order respect to the other individual components of the system was also carried out. A generic rate law for the TH of azobenzene is shown in (Equation (1)). From this, the values α, β, and γ were determined by measuring the influence of the concentration for each respective component on the reaction rate.

$$r = k \cdot [AZB]^\alpha \cdot [cat]^\beta \cdot [AB]^\gamma \tag{1}$$

The rate of the reaction was measured as a function of the concentration of azobenzene, ranging between 0.044 M and 0.220 M, while the concentration of precatalyst and **AB**, temperature and time were kept constant. The representation of ln *r* vs. ln [AZB] (Figure S17, supporting information) returned a straight line with a slope of 1.02, indicating a first-order dependence on the concentration of azobenzene. This confirmed the result from the monitoring of the reaction as a function of time (vide supra). Likewise, the rate of reaction was measured depending on the catalyst concentration, ranging from 0.004 M to 0.025 M, while the concentration of azobenzene, concentration of **AB**, temperature and reaction time were kept constant. A fractional order (1/2) dependence on catalyst concentration can be observed from the plot of ln *r* vs. ln [cat] with a slope value of 0.48 (Figure S18, supporting information). The kinetic data were also analyzed using the graphical method described by Burés,[26] thus confirming our findings for catalyst loadings higher than 10 mol-% (see supporting information). This result suggests that there is a complex relationship between the catalyst concentration and the reaction rate and confirms that **1** acts as a precatalyst. The fractional order could be a consequence of the induction time required to form the actual catalyst or could also be related to the fact that more than one catalytically active species is involved. Given the fact that an excess of **AB** (4 equivalents respect AZB, formally up to 8 eq. H$_2$) has been used, its concentration is higher than needed at any time and, thus, it can be considered constant. Consequently, **AB** concentration disappears from the rate law equation (Equation 1) and it is integrated into the rate constant *k*, leading to an apparent rate constant $k_{app} = k[AB]^\gamma$. Once the order of reaction with respect [AZB] and [**1**] were determined, the magnitude of k_{app} could be calculated (0.029 ± 0.005 s^{-1}·L$^{0.5}$·mol$^{-0.5}$). These kinetic experiments indicate that the rate law can be represented as in (Equation (2)) at constant temperature (60 °C) and using a four-fold excess of **AB** (formally 8 equivalents of H$_2$).

$$r = k_{app} \cdot [AZB] \cdot [\mathbf{1}]^{1/2} \tag{2}$$

The temperature dependence on the rate of reaction was evaluated using temperature ranges between 40 °C and 80 °C, at 10 °C intervals. The representation of the ln [AZB] vs. time gave a straight line (Figure S19, supporting information). An induction time caused by precatalyst activation was observed, which was inversely proportional to the temperature and the substrate concentration. Points representing the induction time were discarded from the graph, to obtain a better fit on linearity.

After determination of the temperature influence on the reaction rate, an Eyring and Arrhenius analysis was performed (see Figure 1). The ln (*r*/T) was plotted against the inverse of the temperature (1/T) (Figure 1a) yielding a straight line. From the slope and the intercept, values of ΔH‡=17.1 ± 2.6 kcal/mol, ΔS‡=-31 ± 7 e.u and ΔG$^\ddagger_{(298.15)}$= 26.4 ± 5.7 kcal/mol were calcu-

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lated. The sign and magnitude of the entropy of activation are consistent with a reaction step involving a transition structure typical of a bimolecular reaction. This might be in agreement with an associative mechanism, in which at least two reaction partners form a single activated complex.[8b,8c,17,27] The ln r was plotted against $1/T$ (Figure 1b) and from the Arrhenius analysis, an activation energy of 17.8 ± 4.1 kcal/mol was obtained.
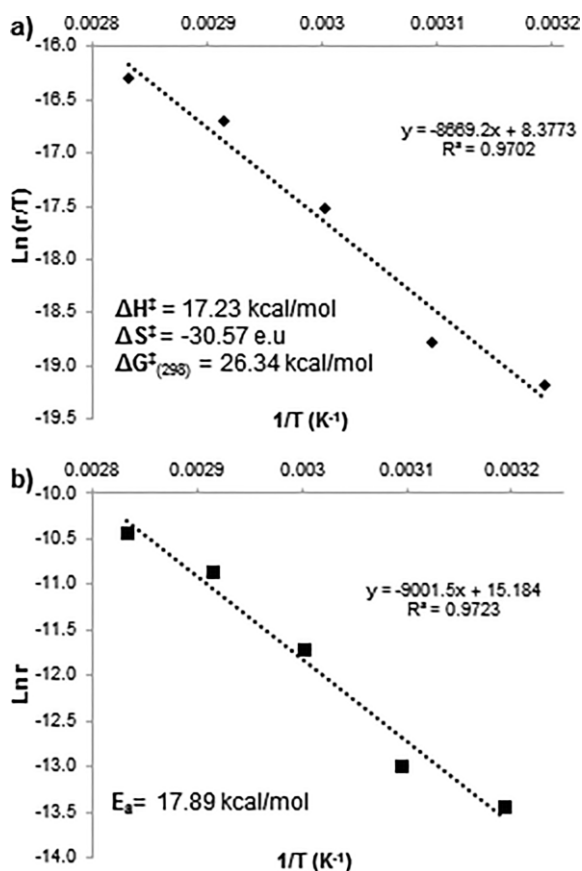
Figure 1. Eyring (a) and Arrhenius (b) plot for TH of azobenzene catalyzed by P(Oquin)$_3$. Based on respective equations, activation thermodynamic parameters and activation energy were determined.

To the best of our knowledge, only two examples of kinetic experiments have been reported for the TH of azobenzene involving **AB** as the hydrogen source. Kinjo and co-workers. studied the kinetics for the TH of azobenzene using the diazaphospholene catalyst **B**.[13,14] Their results also suggest a first-order rate equation with respect to the substrate. Radosevich and co-workers[12] carried out kinetic experiments for the TH of azobenzene catalyzed by species **A**. Also, in this case, in the presence of an excess of azobenzene, the reaction follows a pseudo-first-order kinetics. Furthermore, Eyring analyses were performed obtaining the following activation thermodynamics parameters: $\Delta H^\ddagger = 21.8$ kcal/mol, $\Delta S^\ddagger = -11.6$ e.u and $\Delta G^\ddagger_{(298.15)} = 25.2$ kcal/mol, for Kinjo's system; $\Delta H^\ddagger = 12.4$ kcal/mol, $\Delta S^\ddagger = -36$ e.u and $\Delta G^\ddagger_{(298.15)} = 23.13$ kcal/mol, for Radosevich's system. The sign of the enthalpy of activation ($+\Delta H^\ddagger$) and the sign and magnitude of the entropy of activation ($-\Delta S^\ddagger$) in the present work agree with the results cited before. Moreover, the magnitudes of the free-energy of activation ($+\Delta G^\ddagger$) are very similar in all cases. This might suggest that the nature of the

transition state of the rate-determining step is related in these cases.

Further kinetic analysis using deuterated ammonia boranes was carried out to examine deuterium kinetic isotope effects (DKIEs, Figure 2). The DKIEs values were determined based on the ratio of the reaction constants ($k\textbf{AB}/k_{DAB}$), where $k\textbf{AB}$ corresponds to the reaction constant with the protiated ammonia borane and k_{DAB} is the reaction constant of each of the respective deuterated ammonia boranes.
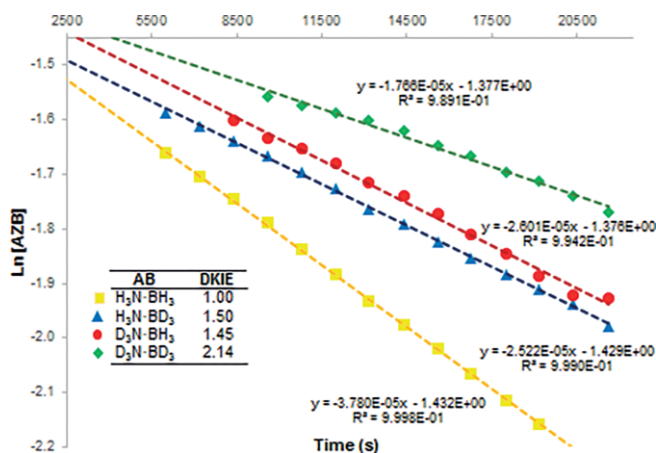

Figure 2. Deuterated kinetic isotopic effect (DKIE's) on reaction rate for the TH of azobenzene with deuterated ammonia boranes.

Normal DKIEs values of 1.45 and 1.50 were observed for the reaction of azobenzene with D$_3$N·BH$_3$ and H$_3$N·BD$_3$, respectively, and a DKIE of 2.14 in the case of the fully-deuterated compound. The group of Kinjo reported a trend similar to the one found in this investigation for the kinetic isotope effect (KIE) in their system, i.e. $k\textbf{AB} > k_{AB(D)} > k_{A(D)B} > k_{A(D)B(D)}$ (AB(D) = H$_3$N·BD$_3$; A(D)B = D$_3$N·BH$_3$; A(D)B(D) = D$_3$N·BD$_3$), determined by experimental and theoretical means. The overall KIE was associated with the cleavage of both B–H and N-H bonds in the rate-determining step of the reaction, in a double-hydrogen-transfer concerted mechanism.[13,14] For the TH of azobenzene catalyzed by **1**, as expected, the DKIE obtained with perdeuterated **AB** (D$_3$N·BD$_3$, $k\textbf{AB}/k_{A(D)B(D)} = 2.14$), corresponds to the product of the individual KIEs (within the experimental error, $k\textbf{AB}/k_{A(D)B} = 1.45$, $k\textbf{AB}/k_{AB(D)} = 1.50$, $k\textbf{AB}/k_{A(D)B} \times k\textbf{AB}/k_{AB(D)} = 2.18$). This suggests that B–H and N-H bonds are simultaneously broken and are probably relevant to the rate-determining step (RDS). Similar observations have been previously made for other homogeneous catalytic systems of **AB** dehydrogenation.[10,28] In the literature,[6d,10,13,14,27–29] $k\textbf{AB}/k_{A(D)B(D)}$ values ranging from 1.39[27] to 7.05[10] have been considered as significant and a clear indication of both B–H/N-H bond breaking as the rate-determining step.

Finally, a Hammett study was performed to investigate the effect of different substituents in p-position on the aryl ring. THF solutions (0.132 M) of different p-substituted azobenzene compounds were chosen as follow: two of them bearing electron-donating groups (Me and OMe), and two with electron-withdrawing groups (Cl and F). The reaction rate (r) for each substrate (**2a–b**, **e–f**, **i**) was obtained from the slope of the plot

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of the natural logarithm of the substrate concentration ln ([*p*-FG-AZB]) against time. Once the reaction rate for the *p*-substituted azobenzene series was known, a Hammett analysis was carried out. Log *k* was plotted against the substituted constant (σ) as depicted in Figure 3.
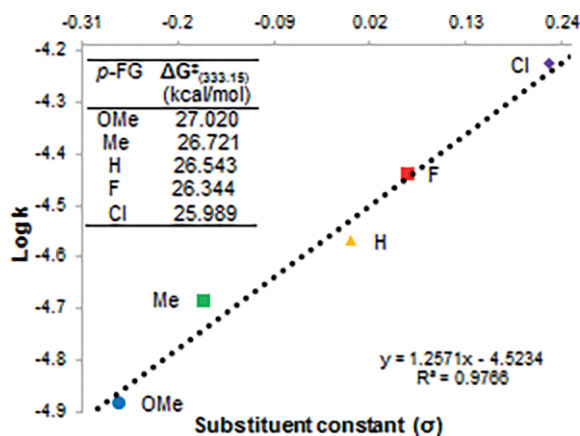

Figure 3. Hammett plot for the TH of *p*-substituted azobenzene compounds with **AB** catalyzed by P(Oquin)$_3$.

The Hammett plot returns a straight line and reveals a linear free-energy relationship ($\Delta G^\ddagger$) between the *p*-substituted azobenzene compounds. In other words, $\Delta H^\ddagger$ is constant for the series whereas $\Delta S^\ddagger$ is proportional to the substituent constant σ. The azocompound series studied followed the linear-free energy relationship (LFER) equation with a reaction constant (ρ) of 1.294. The sign of the reaction constant indicates that the transition state of the rate-determining step presumably carries a negative charge, while the magnitude means that this system is less sensitive to functional groups around the aryl ring than related systems.[13,14]

The experimental evidence and results obtained, along with the kinetic data (rate of reaction, activation thermodynamics parameters, DKIE, and LFER) confirm that **AB** suffers dehydrogenation initiated by the acyclic phosphite P(Oquin)$_3$ (**1**), thus generating catalytically active species which perform the transfer hydrogenation of azobenzenes. The system is very efficient, and a variety of substituted phenylhydrazines were obtained. However, it is not possible to make a mechanistic outline or to propose a catalytic cycle for the system since the identity of the active species (catalyst) could not be unequivocally determined. Regardless of that, it becomes clear that: 1) P(Oquin)$_3$ is a pre-catalyst, and its use is more convenient than the generation of the catalytic system in situ since it can be more easily handled, 2) the mechanism is probably associative, as reflected in the $\Delta S^\ddagger$ which indicates a more ordered (concerted TH) transition state, and 3) deuteration of **AB** significantly affects the reaction rate and suggests a simultaneous N-H and B-H bond cleavage that (directly or indirectly) influences the rate-determining step.

Conclusions

The phosphorus(III) compound **1** reacts with **AB** generating a catalytically active system which was exploited to perform the transfer hydrogenation of apolar N=N bonds in azoarenes. The

corresponding hydrazines were obtained in high yields. The reaction conditions were studied for a model reaction (azobenzene as substrate) and the hydrazine formation proceeds under mild conditions: 10 mol-% **1** as catalyst precursor, 60 °C, 24 h and 4 equivalents of **AB**. Kinetic measurements indicate that the best approximation for the rate law is $r = 0.029\pm0.005 \text{ s}^{-1}\cdot\text{L}^{0.5}\cdot\text{mol}^{-0.5}.[\text{AZB}].[\textbf{1}]^{1/2}$ at a constant concentration of **AB** and temperature (60 °C). The analysis of KIEs indicated that the cleavage of B–H and N-H bonds of **AB** is either part of the rate-determining step or at least has a significant indirect effect in the reaction rate. Activation thermodynamic parameters were obtained from both Eyring and Arrhenius analysis, and suggest that the reaction proceeds through an organized transition state, consistent with an associative mechanism. A Hammett plot showed a linear free-energy relationship ($\Delta G^\ddagger$) among the *p*-substituted azobenzene compounds studied. The kinetic and mechanistic investigations do not provide enough evidence on the identity of the catalytically active species, formed from **1**, but suggest that **AB** is involved in more than one reaction step (at least in the reaction with phosphite **1** and in the hydrogen transfer to the substrates). The potential of **1** to promote novel transformations via bond activation in small molecules will certainly be an ongoing area of interest in our group. Additional efforts are also being directed to the synthesis of alternative σ^3-P compounds for the reduction of even less reactive, nonpolar covalent bonds.

Experimental Section

General Information: A full description of the general experimental methods, including preparation and purification of starting materials for the catalytic and kinetic studies can be found in the Supporting Information. The synthesis of P(Oquin)$_3$, following an alternative method to the one reported in the literature,[21] is described in the electronic supplementary information (ESI) file.

Catalytic TH of azo compounds. Compound **1** (13.9 mg, 0.030 mmol), the corresponding azocompound **2a–n** (0.300 mmol), ammonia borane (37.0 mg, 1.20 mmol), the internal standard 1,3,5-trimethoxybenzene (16.7 mg, 0.099 mmol) and THF (1.25 mL) were loaded in a Schlenk tube under argon atmosphere. The Schlenk tube was sealed, placed in an oil bath, and heated at 60 °C. The reaction was monitored by ^{1}H NMR spectroscopy. Products **3a–n** were purified by flash column chromatography on silica gel (9:1 = petroleum ether/ethyl acetate) or simply extracted from the reaction mixture with *n*-hexane when quantitative conversion was achieved.

Kinetic study. In a dry 25 mL Schlenk tube with a silicone septa-screw cap and under argon atmosphere a THF solution of azobenzene (0.500 mmol, 0.132 M), **1** (23.2 mg, 0.050 mmol), ammonia borane (72.1 mg, 2.00 mmol), and 1,3,5-trimethoxybenzene (28.0 mg, 0.165 mmol) was loaded and heated at 60 °C. Aliquots (0.2 mL) for NMR sample were transferred with a syringe and the NMR tubes were filled with dry THF and a C$_6$D$_6$ capillary. Reaction progress was monitored as consumption of azobenzene, by ^{1}H NMR, every 30 minutes for 14 h.

Rate of reaction as a function of substrate or precatalyst concentration.

Dependence on the Concentration of Substrate: The general procedure was applied using the following concentration (mol.L^{-1}) of azo-

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