ChemPubSoc Europe

DOI: 10.1002/chem.201406585

CHEMISTRY
A European Journal
Full Paper

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Mechanism of Phosphine Borane Deprotection with Amines: The Effects of Phosphine, Solvent and Amine on Rate and Efficiency

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Abstract: The kinetics of borane transfer from simple tertiary phosphine borane adducts to a wide range of amines have been determined. All data obtained, including second-order kinetics, lack of cross-over, and negative entropies of activation for reaction of triphenylphosphine borane with quinuclidine and triethylamine, are consistent with a direct (S_N2-like) transfer process, rather than a dissociative (S_N1-like) process. The identities of the amine, phosphine, and solvent all impact substantially on the rate (*k*) and equilibrium (*K*) of the transfer, which in some cases vary by many orders of magnitude. P-to-N transfer is more efficient with cyclic amines in apolar solvents due to reduced entropic costs and ground-state destabilisation. Taken as a whole, the data allow informed optimisation of the deprotection step from the stand-point of rate, or synthetic convenience. In all cases, both reactants should be present at high initial concentration to gain kinetic benefit from the bimolecularity of the process. Ultimately, the choice of amine is dictated by the identity of the phosphine borane complex. Aryl-rich phosphine boranes are sufficiently reactive to allow use of diethylamine or pyrrolidine as a volatile low polarity solvent and reactant, whereas more alkyl-rich phosphines benefit from the use of more reactive amines, such as 1,4-diaza[2.2.2]bicyclooctane (DABCO), in apolar solvents at higher temperatures.

Introduction

The central role of phosphines (R_3P) in coordination chemistry, catalysis and materials chemistry has resulted in a diverse range of methods being developed for their synthesis. Synthetic intermediates are frequently complexed by borane (BH_3) to modify the reactivity at phosphorus,[1] and to provide the advantage of air and moisture stability.[2] Accordingly, removal of the BH_3 is usually left to a late or final stage in the synthesis. This "protection-deprotection" strategy was pioneered in 1985 by Imamoto, who reported that, at elevated temperatures, a large excess of diethylamine smoothly decomplexed a P-stereogenic phosphine borane with retention of P configuration.[3] The utility of such BH_3-complexation was quickly recognised and has become a routine methodology in phosphine synthesis, especially for systems containing stereogenic phosphorus centres.[4] Protection is readily achieved by reaction with commercially available $BH_3{\cdot}SMe_2$ or $BH_3{\cdot}THF$, or by using $NaBH_4$ as an in situ source of BH_3.[5] However, the deprotection step can be more problematic, and a number of alternative strategies to achieve this have been reported.[6–9] Nonetheless, the most commonly applied procedure is still the use of an amine,[3,10–15] which acts as a competing Lewis base to generate the free phosphine R_3P, and the corresponding amine–borane ($R_3N{\cdot}BH_3$) species. A large variety of amines, stoichiometry, solvent, and reaction temperatures have been reported, with some conditions taking several days to reach acceptable levels of conversion.[16,17]

Despite the synthetic importance of the deprotection process, very little information has been published regarding the mechanism of transfer of the borane from P-to-N. There have been tentative suggestions that the process is dissociative (Scheme 1, S_N1-like; top pathway),[18] although detailed studies of related reactions involving substituted boron species, for example, $Me_3N{\cdot}BH_2R$,[19] and $Ph_3P{\cdot}BH(CN)(R)$[17] have shown that S_N2 mechanisms can also operate.[20] Herein we report on the kinetics and equilibria for borane (BH_3) transfer from tertiary phosphine adducts ($R_3P{\cdot}BH_3$, R = aryl and alkyl) to a wide range of amines under synthetically relevant conditions. We also probe for cross-over between free and complexed triarylphosphine, and explore the effect of solvent polarity on the kinetics of transfer. The data allow an informed choice of amine and reaction conditions for the efficient deprotection of various types of tertiary phosphine borane adducts.

Results and Discussion

Molecularity and kinetics of deprotection of $Ph_3P{\cdot}BH_3$

Our initial studies focused on borane transfer from triphenylphosphine borane (**1**, 0.02 M in toluene)—a simple system that provides a homogeneous reaction mixture amenable to in situ analysis by $^{11}B\{^1H\}$ NMR spectroscopy. Addition of quinuclidine (**2**) led to clean conversion to quinuclidine borane (**3**) and Ph_3P

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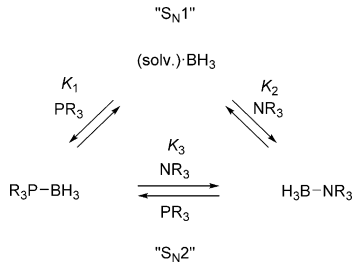
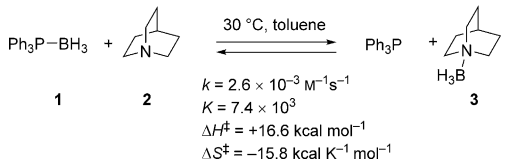
Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201406585.



Scheme 1. Generic mechanisms for dissociative (S_N1-like, K_1K_2) and associative (S_N2-like, K_3) BH_3 transfer between a phosphine (R_3P) and an amine (R_3N), R = aryl, alkyl, etc.

(Scheme 2). At concentrations of amine (**2**) ranging from 0.01 to 0.73 M, a standard bimolecular equilibrium, $-d[\mathbf{1}]/dt = k([\mathbf{1}][\mathbf{2}]-[Ph_3P][\mathbf{3}]/K)$, albeit with pseudo-first-order irreversible character ($-d[\mathbf{1}]/dt = k_{obs}[\mathbf{1}]$) under most conditions studied,[21] correlated fully with all data and no intermediate species were detected ($\leq 1\%$).[22]



Scheme 2. Kinetic and thermodynamic parameters for the deprotection of $PPh_3·BH_3$ with quinuclidine (**1**, 0.02 M; **2**, 0.01–0.73 M).

Second-order kinetics exclude a dissociative mechanism in which P–B scission (k_1, Scheme 1) is rate-limiting, but not fully one in which dissociative pre-equilibrium (K_1) precedes rate-limiting capture (k_2) of a low steady-state concentration of a "free" or solvated BH_3 intermediate. However, this possibility was eliminated by $^{31}P\{^1H\}$ NMR analysis of the same process conducted in the presence of 0.030 M $[D_{15}]Ph_3P$; no significant generation of $[D_{15}]$**1** occurred in competition with the generation of **3**. Transfer of BH_3 between $[D_{15}]Ph_3P$ and **1** does proceed in the absence of **2**, but is around two orders of magnitude slower. Activation parameters for reaction of **1** with **2**, determined from second-order rate constants obtained between 30 and 70 °C,[21] indicate a significant negative entropy of activation ($\Delta S^{\ddagger} = -15.8$ cal K^{-1} mol^{-1}) and overall, the data are best accounted for by an associative (S_N2-like) mechanism.

Effect of phosphine substituents

The effect of the phosphine substituents on the kinetics of deprotection was studied by reaction of a series of aryl/alkyl phosphine borane complexes ($Ph_{(3-n)}(alkyl)_nP·BH_3$) with quinuclidine (**2**) in toluene at 30 °C. For the cyclohexyl (Cy) series (**1**, **4**, **5**, **6**; $n = 0$, 1, 2, 3 respectively; Figure 1) the equilibrium constants were also determined by $^{11}B\{^1H\}$ NMR analysis of the kinetics of the reverse reaction in which borane is transferred from the quinuclidine adduct **3** to the phosphine (Table 1). The effect of sequentially replacing the phenyl groups by cyclohexyl groups is a strong and progressive attenuation of both the rate (k) and favourability (K) of borane transfer from P-to-N.

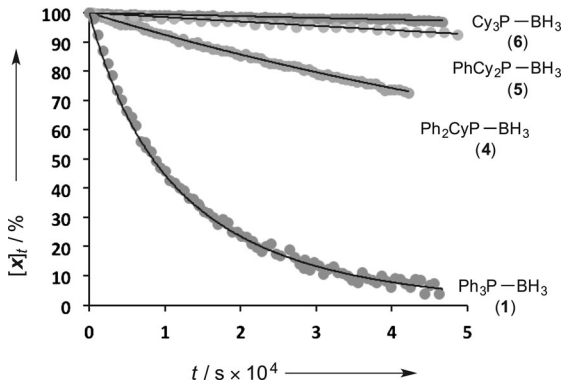


Figure 1. Temporal conversion data (in situ $^{11}B\{^1H\}$ NMR analysis) for transfer of BH_3 from phosphine boranes **1**, **4**, **5** and **6** to quinuclidine (**2**). Solid lines through data are simulations for bimolecular equilibration using the rate and equilibrium constants given in Table 1. For direct visual comparison of initial rates the data should be bimolecularly normalised by initial concentrations: (**1**, 0.02 M + **2** 0.04 M), (**4**, 0.02 M + **2** 0.04 M), (**5**, 0.02 M + **2** 0.08 M), and (**6**, 0.05 M + **2** 0.40 M).

Somewhat counter-intuitively, the rate of borane transfer is rather insensitive to differences in steric factors across a series of alkyl groups (Me, *n*Bu, *t*Bu, Cy) with each sequential alkyl for Ph replacement in **1** reducing the rate by the same factor: approximately one order of magnitude. This phenomenon is consistent with an associative S_N2-like transition state in which the phosphine substituents are shielded from the amine by the borane moiety, and there is no significant change in the steric interaction between the R substituents in R_3P on progress from the ground state to the transition state. The change in the rate through the series $Ph_n(alkyl)_{3-n}P·BH_3$ then predominantly arises from the difference in the (inductive) electron donating ability of the alkyl versus phenyl substituents; the more alkyl groups, the poorer the R_3P functions as a "leaving group" from BH_3 as the amine attacks. The cumulative effect is so pronounced that $Cy_3P·BH_3$ (**6**) undergoes decomplexation (k) nearly four orders of magnitude more slowly than **1**, Table 1.

In terms of general synthetic application, it is not just the rate (k) but also the equilibrium constant (K) that is important. For example, to achieve 99% deprotection of the trialkyl phosphine complex $Cy_3P·BH_3$ (**6**) more than 70 equivalents of quinuclidine **2** are required (Table 1, entry 4). In stark contrast, the

Table 1. Second-order rate (k) and equilibrium (K) constants for BH_3 transfer to quinuclidine (**2**) from $R_3P·BH_3$ complexes **1**, **4**, **5** and **6** in toluene at 30 °C.

Entry	$R_3P·BH_3$	k [$M^{-1}s^{-1}$][a]	K[a]	equiv. **2** for > 99% R_3P[b]
1	$Ph_3P·BH_3$ (**1**)	2.6×10^{-3}	7.4×10^{3}	1.003
2	$Ph_2(Cy)P·BH_3$ (**4**)	2.1×10^{-4}	5.0×10^{2}	1.19
3	$Ph(Cy)_2P·BH_3$ (**5**)	1.9×10^{-5}	2.4×10^{1}	5.1
4	$Cy_3P·BH_3$ (**6**)	1.5×10^{-6}	1.4×10^{0}	71

[a] For associated errors see the Supporting Information. [b] Equivalents of **2** (relative to $R_3P·BH_3$) required to generate > 99% R_3P at equilibrium.

triarylphosphine complex $Ph_3P{\cdot}BH_3$ (**1**) requires just a 0.3% excess (Table 1, entry 1).[23]

Impact of amine identity on deprotection kinetics

Using the reaction of triphenylphosphine complex **1** with quinuclidine (**2**) in toluene at 30 °C as a benchmark, second-order rate (k) and equilibrium (K) constants were then determined for reaction of **1** with a wide range of amines. This included those commonly reported for phosphine borane deprotection: diethylamine,[3,10] morpholine,[11] 1,4-diazabicyclo[2.2.2]octane (DABCO, **7**),[12] pyrrolidine,[13] triethylamine,[14,16] and *N*-methylpyrrolidine,[15] as well as diisopropylamine, piperidine, and *N*,*N*-dimethylaminopyridine (DMAP), to more broadly explore structure–activity relationships (Figures 2 and 3).

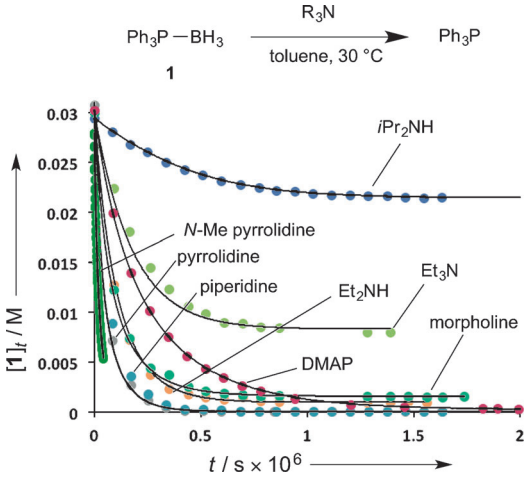


Figure 2. Temporal concentration data for conversion of **1** to Ph_3P with a series of amines. Data shown are for all amines in Table 2, except quinuclidine (**2**) and DABCO (**7**). Initial concentrations: iPr_2NH 0.049 M; *N*-methylpyrrolidine 0.074 M + 0.098 M Ph_3P; pyrrolidine 0.048 M; piperidine 0.049 M; Et_2NH 0.095 M, Et_3N 0.082 M; morpholine 0.045 M; DMAP 0.06 M. Solid lines are simulations where $-d[\mathbf{1}]/dt = k([\mathbf{1}][\mathbf{2}] - [Ph_3P][R_3N]/K)$.

As with structural variation in the phosphine (Table 1), a wide range of reactivity was observed. Indeed the rates ranged about three orders of magnitude between the most and least reactive amines (DABCO and diisopropylamine, Table 2). Unsurprisingly, there is neither a simple correlation between the aqueous Brønsted basicity (pK_{aH}) of the amine and the second-order rate constant for decomplexation (k), nor is there a simple correlation with the amines for which Mayr's nucleophilicity parameters[24] are available. Nonetheless, some general trends do emerge in Table 2. Cyclic amines, most especially those that feature nitrogen at a bridgehead, are faster and more effective than similar acyclic amines, consistent with a reduced entropic cost on generation of the B–N bond, both on approach to the transition state (k) and in the product (K). This is fully reflected in the difference in activation parameters for triethylamine versus quinuclidine: the enthalpies of activation are very similar ($\Delta H^{\neq} = +16.1$ and $+16.6$ kcal mol^{-1}, respectively), but the entropy of activation is substantially more negative for triethylamine ($\Delta S^{\neq} = -25.6$ vs. -15.8 cal K^{-1} mol^{-1}).

Table 2. Second-order rate (k_{rel}) and equilibrium (K_{rel}) constants for borane transfer from **1** to a variety of amines (Figure 2), relative to diisopropylamine.

Amine	k_{rel}[a]	K_{rel}[a]	equiv. R_3N for > 99% Ph_3P[b]
diisopropylamine	1	1	~4000
triethylamine	13	41	~100
DMAP[c]	24	~4700[d]	~2.0
diethylamine	28	560	8.5
morpholine	84	1400	4.2
piperidine	121	~29000[d]	~1.2
pyrrolidine	152	~43000[d]	~1.1
N-methylpyrrolidine	186	~2100[d]	~3.0
quinuclidine (**2**)	691	322000	~1.01
DABCO (**7**)	1250[e]	17400[e]	~1.2

[a] Data shown are second-order rate and equilibrium constants relative to diisopropylamine (k_{rel} and K_{rel}). Absolute values, together with associated errors, are given in the Supporting Information. [b] Equivalents of amine (relative to $Ph_3P{\cdot}BH_3$) required to generate > 99% Ph_3P at equilibrium. [c] DMAP = 4-*N*,*N*-dimethylaminopyridine. [d] Approximate values see supporting information for independent determinations. [e] Values refer to first complexation (k_{1B} and K_{1B}, Figure 3) to generate $DABCO{\cdot}BH_3$.

Analogous factors account for more subtle structural differences, for example diethylamine being faster (k) and more effective (K) than triethylamine.

Overall, and in full agreement with work of Le Corre,[12i] DABCO (**7**) affords the greatest decomplexation rates, reacting almost 50-times faster than the other most commonly employed amine, diethylamine, and is reactive enough to mediate transfer (K_{2B}, Figure 3) of a second borane from **1**.

When statistically normalised, quinuclidine (**2**) is slightly more reactive (k, per nitrogen) than DABCO (**7**), consistent with an attenuating inductive effect of one nitrogen on the other in **7**. Nonetheless, **2** is substantially more expensive, and overall **7** remains an ideal reagent for rapid deprotection.[12]

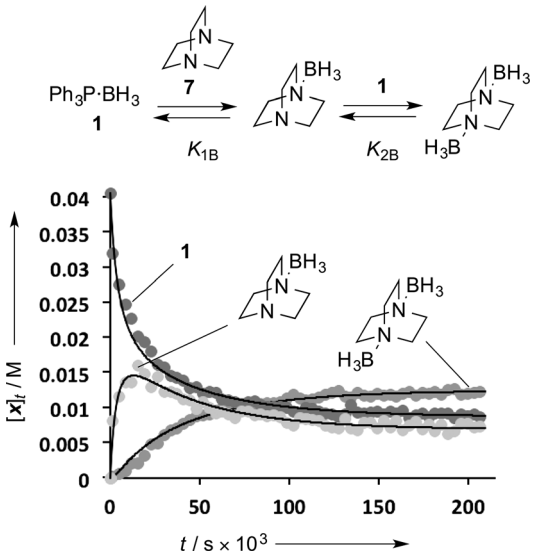


Figure 3. Temporal concentration data (in situ $^{13}C\{^1H\}$ NMR spectroscopy)[25] for sequential twofold transfer of BH_3 from **1** (0.04 M) to DABCO (**7**, 0.02 M). Solid line: simulation, $k_{1B} = 4.6 \times 10^{-3}$ M^{-1} s^{-1}; $K_{1B} \geq 400$; $k_{2B} = 8.6 \times 10^{-4}$ M^{-1} s^{-1}; $K_{2B} = 7$.

The effect of solvent on the deprotection kinetics

The impact of the solvent on the rate of reaction was also explored. Our studies were initially constrained by the limited solubility of triphenylphosphine complex **1** in a suitable range of solvents at 30 °C. However, the 4-chloro analogue **8**[26] was found to be much more soluble and this allowed the second-order rate constant for reaction of **8** with quinuclidine (**2**) to be correlated with the normalised Dimroth–Reichardt polarisation parameter (E_T^N)[27] across a wide range of solvents (Figure 4).

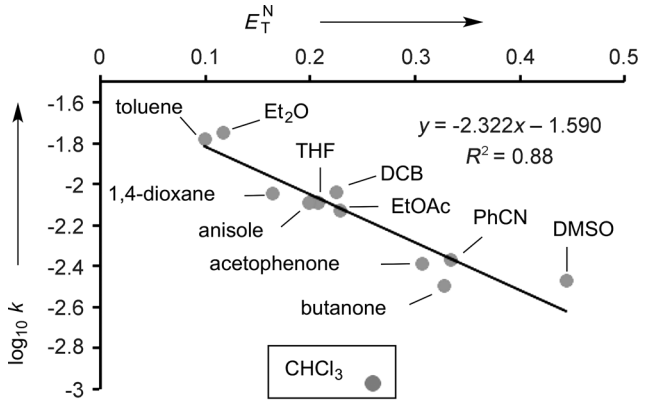


Figure 4. Correlation between $\log k$ (k = second-order rate constant for borane transfer from $(4\text{-Cl-}C_6H_4)_3P{\cdot}BH_3$ (**8**) to quinuclidine (**2**) and the normalised Dimroth–Reichardt solvent polarity/polarisation parameter E_T^N.[26,27] DCB = 1,2-dichlorobenzene.

Notable in Figure 4 is chloroform, an outlier from the reasonably good correlation of $\log k$ versus E_T^N obtained with all other solvents tested. Indeed, reaction of **8** with **2** in $CHCl_3$ is approximately fivefold lower than would be predicted by the solvent ionising power (E_T^N) alone. The origin of this rate-suppression lies in the strong dynamic H bonding of chloroform with quinuclidine, to generate [**2**·$HCCl_3$].[28] This sequestration of **2** causes a net reduction in the equilibrium concentration of amine available for borane transfer, and the apparent rate constant is substantially lower than the true rate constant for the bimolecular decomplexation reaction.[29]

Compared to the effect of changes in amine and phosphine substituents, the influence of solvent is less marked. Nonetheless, moving to a less ion-stabilising solvent, for example, from DMSO to diethyl ether, increases the rate, by up to an order of magnitude. The effect is too small to be investigated quantitatively by PCM variation in DFT studies (Figure 5). Nonetheless, the influence of the ion-stabilising ability of the solvent can be qualitatively rationalised by consideration of the charge dispersion in the ground state versus the transition state (Figure 5).

On progression from **1** + **2** to the S_N2 transition state, there is a reduction in the formal dipole in **1**, resulting in less sensitivity to solvation than the ground state. Use of a low polarity solvent, for example, toluene, for deprotection is thus beneficial in terms of reaction rate.[30] Interestingly, the Dimroth–Reichardt parameter (E_T^N) for many amines is low (e.g., E_T^N = 0.145 for Et_2NH, a value similar to that of 1,4-dioxane, E_T^N = 0.164)[27] and thus the use of an amine as both solvent and reactant can be of benefit in terms of the effect of a lower polarity reaction medium and a high concentration of the amine component in the bimolecular rate-limiting process.

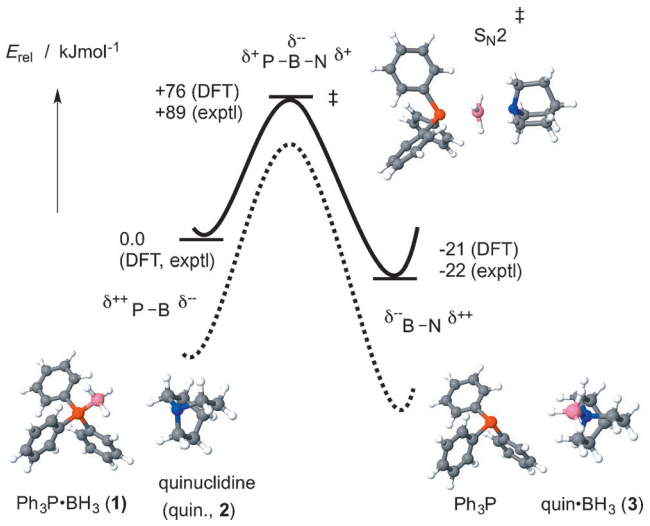


Figure 5. Upper (solid) curve: comparison of the calculated (DFT) versus experimentally determined (exptl) activation barrier and overall driving force for deprotection of **1** with quinuclidine (**2**) in toluene. Lower (dashed) curve: schematic energies for reaction in a solvent of greater polarity or ion-stabilising ability than toluene, resulting in a greater relative stabilisation of the ground state reactants than the more charge dispersed transition state. Reference relative energies relate to DFT (B3LYP, 6-31G(d)) in a toluene PCM at 298.15 K (see Figure S12 in Supporting Information for full details).

Conclusions

The above data, including kinetics ($-d[\mathbf{1}]/dt = k([\mathbf{1}][\mathbf{2}] - [\mathbf{3}][PPh_3]/K)$), thermodynamics (negative $\Delta S^{\neq}$) and cross-over experiments (negative), for borane transfer from **1** to **2** eliminate a dissociative (S_N1-like) mechanism, but are fully consistent with an associative (S_N2-like) process in which triphenylphosphine (**1**) is displaced by nucleophilic attack of the quinuclidine (**2**) at boron. This conclusion is supported by DFT studies (Figure 5) and by the impact of solvent on the rate, where solvents with low polarity or ion-stabilising ability (E_T^N) accelerate the process through differential stabilisation of the ground state relative to the transition state.

For the series $Ar_n(alkyl)_{3-n}P{\cdot}BH_3$, n = 3 to 0, reactions become progressively slower (k) and less efficient (K) as alkyl groups sequentially replace aryl substituents on the phosphine. Each substitution reduces the rate by approximately one order of magnitude. Cyclic amines, for predominantly entropic factors, perform more efficiently in terms of both rate (k) and equilibrium (K), and taken together, Tables 1 and 2 provide guidelines for the appropriate choice of amine for a particular type of phosphine borane adduct. Phosphine–borane complexes that are aryl-rich ($Ar_n(alkyl)_{3-n}P{\cdot}BH_3$, n = 3, 2) require less reactive amines to allow deprotection to proceed to completion. For these systems, diethylamine can be used as both solvent and reactant. These conditions are convenient as diethylamine and

its borane adduct are both volatile and, unless the phosphine is also volatile, are readily separated from the product at the end of reaction by evaporation. Notably, pyrrolidine is similarly volatile and inexpensive, but significantly more reactive than diethylamine (Table 2) and should be considered as an advantageous alternative. In contrast, for the more alkyl-rich phosphines ($n=0$, 1) the decomplexation reaction is much less efficient. For these systems, there is considerable advantage to use cyclic non-hindered or bridgehead amines, such as DABCO (**7**),[12] in an apolar solvent. If thermally labile phosphine P-stereogenicity is not an issue, then the solvent should ideally be of a suitable boiling point to allow reaction at higher temperature, for example toluene, xylene or mesitylene. Crucially, to gain kinetic benefit from the bimolecularity of the process, both reactants ($R_3P{\cdot}BH_3$ and **7**) should be present at as high an initial concentration as is practical.

We are currently exploring the use of the borane transfer reaction for the parameterisation of reactant descriptors for linear free energy relationships, across a series of amines and phosphines. We will report on this, as well as a predictive model for P-to-N borane transfer kinetics, in due course.

Experimental Section

Kinetics of reaction of triphenylphosphine borane (1) with quinuclidine (2)

The following procedure is typical. Complex **1** (14.0 mg, 0.05 mmol) was added to an oven-dried Schlenk tube under an atmosphere of nitrogen. Dry toluene was added. The mixture was stirred and heated to 30 °C until complete dissolution was achieved, to give a 0.02 M solution of **1**. A known mass of **2** was then added to the solution, ($t=0$) and after dissolution (normally occurring within a matter of seconds), a sample was transferred via pipette to an NMR tube. This was placed in a preheated (30 °C) spectrometer for $^{11}B\{^1H\}$ NMR reaction monitoring. Kinetic data were obtained with $[\mathbf{2}]_0$ in the range 0.01–0.73 M; an additional set of reactions were performed at a higher initial concentration of **1** ($[\mathbf{1}]_0=0.04$ M), using $[\mathbf{2}]_0=0.1$ M in toluene at 30 °C. Full data are presented in the Supporting Information, Figure S1. In all cases, kinetic simulations, performed using Dynochem 2011 v4, using the following bimolecular equilibrium rate law: $-d[\mathbf{1}]/dt=k([\mathbf{1}][\mathbf{2}]-[Ph_3P][\mathbf{3}]/K)$ gave excellent correlations with experimental data with $k=2.6\times10^{-3}\,M^{-1}s^{-1}$, when K is large; that is, $-d[\mathbf{1}]/dt\approx k([\mathbf{1}][\mathbf{2}])$. The kinetics of bimolecular equilibrium reaction of a large excess of Ph_3P with **3** (i.e., the reverse reaction) was then employed to determine K.

Determination of activation parameters

Variable temperature analysis was carried out using the same procedure as above with $[\mathbf{1}]_0=0.02$ M and $[\mathbf{2}]_0=0.04$ M in toluene, to obtain the second-order rate constants (k [$M^{-1}s^{-1}$]) for BH_3 transfer. Reactions were performed every 10 °C from 30–70 °C inclusive. Analysis by linear least-squares fitting of a standard Eyring plot (see Supporting Information, Figures S3 and S10) gave $\ln(k/T)=15.8–8.3\times10^3/T$ ($R^2=0.996$) and thus $\Delta H^{\neq}=16.6$ kcal mol^{-1} and $\Delta S^{\neq}=-15.8$ cal K^{-1} mol^{-1}. Reactions between **1** and triethylamine were also performed every 10 °C from 30–70 °C inclusive. Stock solutions of triethylamine in dry toluene were prepared, and a set volume transferred to a J. Youngs NMR tube. This was then placed into an NMR spectrometer preheated (to 40, 50, 60 or 70 °C) for 10 min to allow thermal equilibration. The NMR tube was removed from the spectrometer and **1** was added. The tube was shaken to ensure dissolution, and then returned to the spectrometer (still at temperature) for $^{11}B\{^1H\}$ analysis. Analysis by linear least-squares fitting of a standard Eyring plot (see Supporting Information, Figure S10) gave $\ln(k/T)=10.9–8.1\times10^3/T$ ($R^2=0.996$) and thus $\Delta H^{\neq}=16.1$ kcal mol^{-1} and $\Delta S^{\neq}=-25.6$ cal K^{-1} mol^{-1}.

Test for cross-over during reaction of triphenylphosphine borane (1) with quinuclidine (2)

Complex **1** (5.8 mg, 0.021 mmol), amine **2** (3.1 mg, 0.028 mmol), and $[D_{15}]Ph_3P$ (5.8 mg, 0.021 mmol) were added to a vacuum-dried NMR tube. Dry toluene was then added to give a total volume of 0.7 mL. The NMR tube was placed in a preheated (30 °C) NMR spectrometer for $^{31}P\{^1H\}$ reaction monitoring. No significant loss of the absolute intensity of the $[D_{15}]Ph_3P$ peak was observed over the course of 8 h, during which >80% of **1** had been converted to Ph_3P. Simulation of the temporal concentration of **1**, using Dynochem 2011 v4, with the following bimolecular equilibrium rate law: $-d[\mathbf{1}]/dt=(k([\mathbf{1}][\mathbf{2}]-[[D_n]Ph_3P][\mathbf{3}]K)$; $n=0,15$), gave a second-order rate constant $k=2.4\times10^{-3}\,M^{-1}s^{-1}$, consistent with that determined in the absence of $[D_{15}]Ph_3P$.

Acknowledgements

University of Edinburgh and the Bristol Chemical Synthesis DTC (EPSRC grant EP/G036764/1) provided financial support to N.P.T. We also thank Dr. Oren Sherman (Cambridge, UK), Dr. David Fox (Warwick, UK), and Prof. Jeremy Harvey (Leuven, Belgium) for valuable discussion and preliminary DFT studies.

Keywords: boranes · phosphane ligands · phosphine boranes · protecting groups · reaction mechanisms

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[20] The switch between mechanisms is dependent on the identities of the B-substituents (see refs. [17] and [19]) and the solvent, with inversion of configuration at the stereogenic B centre providing evidence for an S_N2-like process.

[21] For full details see Supporting Information.

[22] The minimum threshold of detection was defined by a signal-to-noise ratio of 1.5 (maximum height of signal versus noise).

[23] At the same initial concentrations of phosphine borane, reaction of **1** would also proceed at $>$23-fold initial relative rate compared to **6**, despite a 70-fold lower concentration of amine **2**. However, rates of approach to bimolecular equilibrium under pseudo-first order (70 equiv **2**) versus second order (1.003 equiv **2**) conditions are different, and use of a slight excess of **2** over **1** does provide considerable advantage.

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[25] DABCO (**7**) only forms significant quantities of DABCO·$(BH_3)_2$ when **7** is the limiting reagent, or in small excess relative to **1**. The extent of this second displacement could not be accurately quantified by $^{11}B\{^1H\}$ NMR as the ^{11}B signal in DABCO·$(BH_3)_2$ was almost isochronous with the signal of DABCO·BH_3. Quantification was instead achieved using $^{13}C\{^1H\}$ NMR spectroscopy; see Supporting Information for full details.

[26] Consistent with the effect of induction on reactivity (Table 1), **8** was more reactive than **1**, by a factor corresponding to an approximate doubling of the rate per chlorine substituent. This phenomenon is being explored in depth and will be reported in full in due course.

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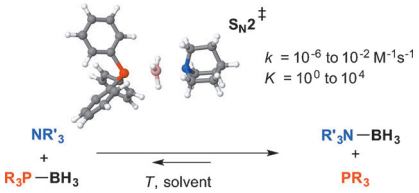
[29] Normalisation of the rate by the effective concentration of quinuclidine $[\mathbf{2}]_{eff}$ in cyclohexane/chloroform mixtures (for *K*, see ref. [28]) moves the data point towards, but not fully into, correlation. Data are not available for the equilibrium constant for association of $CHCl_3$ with **2** in pure $CHCl_3$.

[30] Analogy may be drawn to Ingold's classification of S_N2 reactions, and the impact of solvent on their reaction rates; the reactions in question fit into both class I and IV. C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, 2nd ed., Cornell University Press, Ithaca, **1969**, pp. 457 – 463.

Received: December 21, 2014
Published online on ■■ ■■, 0000

FULL PAPER

Efficient deprotection: Kinetic and thermodynamic data for amine-mediated deprotection of phosphine boranes under synthetically relevant conditions is consistent with an S_N2-like rather than S_N1-like mechanism. The amine, solvent, and phosphine substituents all strongly influence the reaction efficiency (see scheme). The data allow informed selection of optimal reaction conditions.



Reaction Mechanisms

G. C. Lloyd-Jones, N. P. Taylor*

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Mechanism of Phosphine Borane Deprotection with Amines: The Effects of Phosphine, Solvent and Amine on Rate and Efficiency