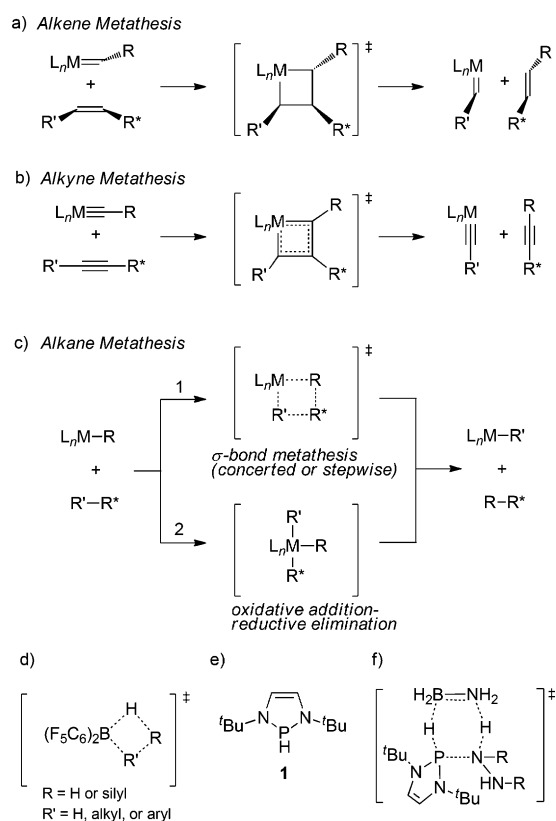# Metal-Free σ-Bond Metathesis in 1,3,2-Diazaphospholene-Catalyzed Hydroboration of Carbonyl Compounds**

Che Chang Chong, Hajime Hirao,* and Rei Kinjo*

Abstract: *The first metal-free catalytic hydroboration of carbonyl derivatives has been developed in which a catalytic amount of 1,3,2-diazaphospholene effectively promotes a hydroboration reaction of aliphatic and aromatic aldehydes and ketones. The reaction mechanism involves the cleavage of both the P−O bond of the alkoxyphosphine intermediate and the B−H bond of pinacolborane as well as the formation of P−H and B−O bonds. Thus, the reaction proceeds through a non-metal σ-bond metathesis. Kinetic and computational studies suggest that the σ-bond metathesis occurred in a step-wise but nearly concerted manner.*

Metathesis has been broadly used as a preferred method for the formation of new bonds in organic synthesis, material science, and biochemistry, as a consequence of the development of robust and convenient metal catalysts.[1,2] In particular, the development of well-defined metathesis systems as well as the utilization of computational approaches enabled comprehensive mechanistic studies, which revealed that alkene and alkyne metathesis reactions have their own preferred pathways: alkene metathesis occurs via a metallocyclobutane transition state, whereas alkyne metathesis undergoes a sequence of cycloaddition-cycloreversion steps via a metallacyclobutadiene transition state (Scheme 1 a, b).[3,4] Meanwhile, it has been proposed that alkane metathesis, the simplest bonding exchange between two molecules, may proceed via either a σ-bond metathesis transition state (Scheme 1 c, path 1) or a two-step process consisting of oxidative addition and subsequent reductive elimination (Scheme 1 c, path 2), depending on the property of the metal and the environment around the metal center.[5] Irrespective of the reaction pathway, however, the same products will be obtained from either process. Significantly, the common feature of the transition states in these metathesis reactions is a four-membered ring framework formed by a [2+2] cycloaddition, which is normally orbital

Scheme 1. General reaction pathways for a) alkene metathesis, b) alkyne metathesis, and c) alkane metathesis. d) Proposed transition state for σ-bond metathesis involving strongly Lewis acidic boranes. e) Structure of 2-*H*-1,3,2-diazaphospholene **1**. f) Transition state for transfer hydrogenation of azobenzene with ammonia-borane catalyzed by **1**.

symmetry forbidden. Nevertheless, such a mechanism can be rationalized by the fact that vacant d or f orbitals of the metal centers address the symmetry limitation, allowing for the [2+2] interaction.[6] Thus, these vacant orbitals of metal centers in the catalysts are essential to achieve the metathesis process. Only a few metal-free σ-metathesis reactions have recently been found in bond-exchange processes between boranes and hydrogen or silanes, for which concerted and stepwise metathesis mechanisms were proposed.[7,8] In these reactions, formation of a four-membered-ring transition state relies on the low-lying unoccupied 2p orbital of the boron atom in boranes bearing at least two C_6F_5 groups (Scheme 1 d). Although these results indicate that even non-metal p block elements may provide a low-energy means for a formal [2+2] interaction, the reaction is still limited to

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considerably strongly Lewis acidic boranes. In fact, less Lewis acidic 9-borabicyclo-[3.3.1]nonane (9-BBN) cannot undergo the bond exchange under similar reaction conditions.[7]

Recently, we reported that 1,3,2-diazaphospholene **1** (Scheme 1e) effectively catalyzes transfer hydrogenation of a N=N bond with ammonia–borane.[9] The rate-determining step involves a concerted double-hydrogen transfer where the electrophilic P atom accepts a hydride ion (H⁻) via a six-membered-ring transition state (Scheme 1 f).[10] We reasoned that, similar to the cases of highly Lewis acidic boranes,[7,8] the strong electron-accepting ability of the P atom of **1** may allow for interaction with a σ-bond of other substrates, presumably leading to the formation of a four-membered-ring transition state followed by σ-bond metathesis, if the pathway is favored thermodynamically. To examine our hypothesis, we employed a hydroboration reaction[11] so as to let an interaction between boron and oxygen atoms in the transition state be involved, expecting the subsequent formation of the strong B−O bond which could be a driving force to induce the desired metathesis. Herein, we report a stepwise σ-bond metathesis in 1,3,2-diazaphospholene-catalyzed hydroboration of aldehydes and ketones under metal-free conditions.

In their pioneering work, Gudat and co-workers revealed the hydride-type reactivity of the P−H bond in 2-*H*-1,3,2-diazaphospholenes.[12,13] Following this procedure, we first synthesized alkoxyphosphine **2** from **1**. Treatment of 2-*H*-1,3,2-diazaphospholenes **1** with benzaldehyde provided **2** quantitatively (Scheme 2). Compound **2** was subsequently
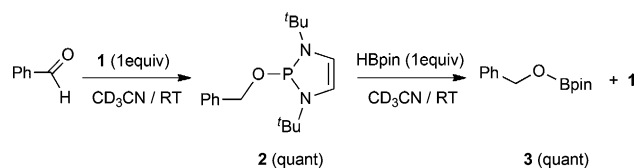
Scheme 2. Synthesis of N-heterocyclic alkoxyphosphine **2**, and stoichiometric reaction between **2** and pinacolborane (HBpin).

reacted with a stoichiometric amount of pinacolborane (HBpin) at room temperature in a deuterated acetonitrile solution. The reaction was monitored by ¹¹B and ³¹P NMR spectroscopy. The formation of the desired molecule PhCH₂OBpin (**3**) and molecule **1** was confirmed, demonstrating σ-bond exchange between the exocyclic P−O bond of **2** and the B−H bond of pinacolborane (Scheme 2). To our knowledge, this is the first report of a metal-free σ-bond metathesis involving cleavage of a P^{III}−O bond. Note that the metathesis occurred selectively at only the exocyclic P−O bond in **2** and no P−N bond cleavage was found, probably as a result of the high polarity of the P−O bond and the kinetic stability of the endocyclic P−N bonds.

We next attempted to apply these stoichiometric transformations of benzaldehyde into **3** via **2** in a catalytic process. Without catalysts, little formation of **3** was detected (Table 1, entry 1). Neither diphenylphosphine nor di-*tert*-butyl-phosphine promoted the reaction, even when stoichiometric amounts were employed (Table 1, entries 2 and 3). To our delight, **1** showed remarkable catalytic activity for the hydroboration. With 1 mol% of **1**, quantitative formation of **3** was

Table 1: Optimization of the reaction conditions.[a]

Entry	cat. [mol%]	Solvent	Time [h]	3 Yield [%][b]
1	None (0 mol%)	CD₃CN	1	6
2	Ph₂PH (100 mol%)	CD₃CN	1	6
3	ᵗBu₂PH (100 mol%)	CD₃CN	1	6
4	**1** (1 mol%)	CD₃CN	1	>99
5	**1** (1 mol%)	C₆D₆	1	79
6	**1** (1 mol%)	[D₈]THF	1	57
7	**1** (1 mol%)	CDCl₃	1	93
8	**1** (1 mol%)	CD₂Cl₂	1	>99
9	**1** (1 mol%)	CD₃CN	0.25	>99
10	**1** (0.5 mol%)	CD₃CN	0.75	>99

[a] Reaction conditions: benzaldehyde (1.50 mmol), HBpin (1.50 mmol), solvent (0.3 mL). Catalyst loading relative to benzaldehyde. [b] Yields were determined by ¹H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard.

detected after one hour at room temperature (Table 1, entry 4). A brief screening of solvents showed that dichloromethane and acetonitrile are suitable for the reaction (Table 1, entries 4–8). We also confirmed near completion of the reaction only after 15 minutes (Table 1, entry 9). Even when the catalyst loading was decreased to 0.5 mol%, **3** was formed in excellent yield after 45 minutes (Table 1, entry 10). It is noteworthy to mention that this result shows the first example of hydroboration of carbonyl derivatives catalyzed by a non-metal main-group compound.[14–16]

With the optimized reaction conditions in hand, the scope of the catalytic reaction was briefly examined with a variety of aldehydes **4** (Table 2). Aliphatic aldehydes (**4a,b**) afforded the corresponding borate esters in good to high yields (**5a**: 92%, **5b**: 88%). Electron-withdrawing (**4c–g**) as well as electron-donating (**4h–k**) aromatic groups were well tolerated (**5c–k**: 70–>99%). For the analogous reactions with substrates including heterocycles (**4l,m**), the desired products were obtained in excellent yields (**5l**: 99%, **5m**: 99%). Importantly, dearomatization products were obtained in the previous report,[16b] but not in the current study, which underscores the catalyst selectivity for carbonyl groups. With two equivalents of HBpin, terephthalaldehyde (**4n**) was cleanly converted into the bis(hydroborated) derivative (**5n**: 99% yield). Significantly, when 4-acetylbenzaldehyde (**4o**) was used, a selective hydroboration only at the aldehyde functional group was found (**5o**: >99%), which has never been achieved thus far.[14,15] To expand the scope of the catalytic hydroboration, next we examined ketones as substrates. Although higher catalyst loading as well as longer reaction time were required than the cases of the less sterically hindered aldehyde substrates, nearly quantitative formation of the corresponding borate ester derivatives were confirmed after the completion of all reactions (Table 3). Both acyclic and cyclic ketones bearing electron-donating or electron-withdrawing groups were well tolerated (**7a–j**: >98%).

To gain insight into the hydroboration mechanism, we carried out further analysis of the catalytic reactions using

Table 2: Scope of hydroboration of aldehyde substrates.

4	Time [h]	4 Yield [%][a]	TON	TOF [hr^{-1}][b]
4a	9	92	184	20.4
4b	9	88	176	19.6
4c	< 0.25	> 99	> 198	> 792[c]
4d	< 0.25	> 99	> 198	> 792[c]
4e	0.25	99	198	792
4f	< 0.25	> 99	> 198	> 792[c]
4g	< 0.25	> 99	> 198	> 792[c]
4h	3	99	198	66
4i	1	> 99	> 198	396
4j	4	70	140	35
4k	2	> 99	> 198	99
4l	< 0.25	> 99	> 198	> 792[c]
4m	< 0.25	99	198	> 792[c]
4n[d]	0.50	> 99	> 198	396
4o	< 0.25	> 99	> 198	> 792[c]

[a] Yields were determined by ^{1}H NMR spectroscopy using 1,3,5-trimethoxybenzene as an internal standard. [b] Turnover frequency (TOF) = turnover number (TON)/average reaction time. [c] TOF lower limit. [d] HBpin (2 equiv) were employed in this reaction.

Table 3: Scope of hydroboration of ketone substrates.

| 6	Time [h]	7 yield [%][b]	TON	TOF [hr^{-1}][c]
6a	12	99	9.9	0.83
6b	4	> 99	9.9	2.48
6c	6	> 99	9.9	1.65
6d	5.5	> 99	9.9	1.8
6e[a]	6	99	9.9	1.65
6f[a]	9	> 99	9.9	1.1
6g	0.5	> 99	9.9	19.8
6h	0.75	> 99	9.9	13.2
6i[d]	3.5	> 99	9.9	2.8
6j	6	98	9.8	1.63

[a] Reaction conducted using C_6D_6 as solvent. [b] Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard. [c] Turnover frequency (TOF) = turnover number (TON)/average reaction time. [d] Reaction was conducted at room temperature.

deuterated pinacolborane (DBpin) to examine deuterated kinetic isotope effects (DKIEs) on the reactions with benzophenone. A CD$_3$CN solution of (HCN^{t}Bu)$_2$P-OCHPh$_2$ (**8**) and excess deuterated pinacolborane (13.5 equiv) in a sealed NMR tube was heated at 50°C, and the reaction was monitored by NMR at 3 minute intervals. The DKIE value was determined based on the rate constants simulated from the kinetic conversion chart,[17] and a normal DKIE of 2.69 was determined for the reactions. We also performed the same reaction employing ^{18}O-labelled benzophenone **6d**(^{18}O), which provided a ^{16}O/^{18}O KIE value of 1.05.[18] The double KIE reaction with DBpin and **6d**(^{18}O) showed the largest KIE value of 2.96. These results indicate that the bond

exchange between the P−O bond and the B−H bond is involved in the rate-determining transition state.

The pathway for the reaction between **1**, benzophenone **6d**, and pinacolborane (HBpin) was explored theoretically using DFT calculations.[19] An energetically feasible pathway for stepwise σ-bond metathesis was obtained (Figure 1),[20] which is similar to the proposed mechanism in the stepwise σ-bond metathesis between Et$_3$SiH and HB(C$_6$F$_5$)$_2$.[8] The
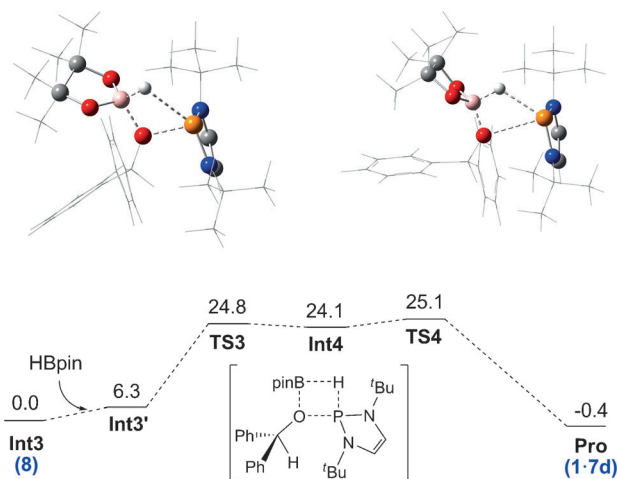

Figure 1. DFT-calculated free energy profiles (kcal mol^{-1}) in CH$_3$CN at 298 K for the reaction between (HCNtBu)$_2$P-OCHPh$_2$ (**8**) and HBpin, as determined at the B3LYP-D3(SCRF)/B2//B3LYP-D3/B1 level. Int3 and Pro correspond to **8** and **1·7d**, respectively [Ref. [20]]. Atom sphere colors: C = gray; N = blue; P = orange; H = white; O = red; B = pink.

four-membered cyclic transition states (TS3 and TS4) involved a H-bonding interaction between the B and P atoms, which is consistent with the polarized natural bond orbital (NBO) atomic-charge distributions (P = +1.39, O = −0.86) on the exocyclic P−O bond in (HCN^{t}Bu)$_2$P-OCHPh$_2$ (**8**). In the first transition state (TS3) of the metathesis process, the P−O bond and the B−H bond are still relatively strong whereas they are elongated in the second transition state (TS4). In contrast, stronger P−H and B−O interactions were found in TS4 than those in TS3. Charge transfer among the four bonding interactions (P−O, B−H, P−H, and B−O) was also confirmed by Wiberg bond index (WBI) values obtained in NBO analysis (see the Supporting Information, Table S3-1). The computationally estimated activation parameters for the σ-bond metathesis process ($\Delta H^{\pm} = 9.5$ kcal mol^{-1}, $\Delta G^{\pm}_{(298)} = 25.1$ kcal mol^{-1}, $\Delta S^{\pm} = -52.3$ e.u.) agreed reasonably well with the experimental results ($\Delta H^{\pm} = 13.0 \pm 0.6$ kcal mol^{-1}, $\Delta G^{\pm}_{(298)} = 23.4 \pm 1.2$ kcal mol^{-1}, $\Delta S^{\pm} = -34.9 \pm 2.0$ e.u.).

In summary, we have developed the first metal-free hydroboration of various aldehydes and ketones, catalyzed by diazaphospholene **1**. The kinetic study and DFT calculations revealed that the bond dissociation and recombination between the P−O bond and the B−H bond are involved in the rate-determining transition state, and the results suggest that this process proceeds in a stepwise but nearly concerted manner. As σ-bond metathesis is formally equivalent to an oxidative addition–reductive elimination sequence which has to date been exclusive for metal complexes in many catalytic reactions, this result paves the way for the design of novel main-group catalysts as mimics for metal catalysts.[21] We are currently investigating reactions with substrates featuring other unsaturated bonds.[22]

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