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Improved dimethylzinc-promoted vinylation of nitrones with vinylboronic esters

Nageswaran PraveenGanesh [a], Cristina de Candia [a], Antony Memboeuf [b], György Lendvay [b], Yves Gimbert [a], Pierre Y. Chavant [a,*]

[a] Département de Chimie Moléculaire, UMR 5250-ICMG FR2607, CNRS-Université Joseph Fourier BP 53, 38041 Grenoble cedex 9, France
[b] Institute of Chemistry, Chemical Research Center, Hungarian Academy of Sciences, P.O. Box 17, H-1525, Budapest, Hungary

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ABSTRACT

Vinylboronic esters derived from 4,4,6-trimethyl-[1,3,2]dioxaborinane react with nitrones in the presence of dimethylzinc; nucleophilic addition of the vinyl group onto nitrones produces *N*-allylic hydroxylamines in fair yields. The sequence is compatible with various functional groups on the vinylic moiety. The mechanism and kinetic aspects are discussed on the basis of DFT calculations.

1. Introduction

In the course of our study on the reactivity of nitrones with functionalized organometallics, we have shown [1] that vinylboronic esters of pinacol (4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane) **1** could, in the presence of dimethylzinc, transfer their vinyl substituent to nitrones **2** to yield *N*-hydroxy-allylamines **3** in fair yields. The starting pinacol esters were conveniently prepared in pure *trans* form by hydroboration of alkynes with pinacolborane [2] (4,4,5,5-tetramethyl-1,3,2-dioxaborolane). The hydroboration step was compatible with functional groups in propargylic position [3], thus highly functional vinylboronic esters like **1b** (Scheme 1) were readily accessible. However, in the addition step the pinacolboronate esters **1** reacted sluggishly and our process required rather harsh conditions. When α-substituted boronic esters were used in these conditions, they decomposed and very poor yields were attained [1] (Scheme 1).

We assumed that the poor reactivity of the pinacolborane derivatives was due to steric hindrance around the boron. Thus, we considered using unhindered vinylboronic esters. Our first choice was 5,5-dimethyl-2-vinyl-1,3,2-dioxaborinanes **4** [4]. The protection of boronic acids with 2,2-dimethylpropane-1,3-diol is a well-known, convenient procedure [5]. The corresponding esters can be easily handled and stored. In order to prepare samples of these vinylboronic esters, we used the one-pot sequence proposed by Hoffmann et al. [6] starting from dicyclohexylborane (Scheme 2). The 4,4-dimethyl-2-vinyl-1,3,2-dioxaborinanes **4a**,**b** were purified by flash chromatography. They can be stored in neat form at room temperature.

2. Reaction of 4,4-dimethyl-2-vinyl-1,3,2-dioxaborinanes 4a,b with dimethylzinc and nitrone 2a

Very interestingly, the esters **4a**,**b** reacted with nitrones and dimethylzinc (3 M equiv.) to yield *N*-allyl-hydroxylamines **3** in 3 h at 20 °C (Scheme 3). The best solvents were toluene and dichloromethane; the reactions were slower in THF.

Chai et al. [7] described the transmetallation of unhindered 2-vinyl-1,3-dioxaborinanes with diethylzinc at 20 °C. A related preparation of vinylzinc species from vinylboronic acids and diethylzinc should also be noted [8].

The enhanced reactivity of the unhindered boronic esters **4** compared to pinacol esters **1** allowed much milder conditions, which were compatible with more functionalized molecules. Reaction of the ether-substituted pinacol vinylboronate **1b** required 60 °C in DMF and led mainly to degradation products

* Corresponding author. Tel.: +33 476635796.
E-mail address: Pierre-Yves.Chavant@ujf-grenoble.fr (P.Y. Chavant).

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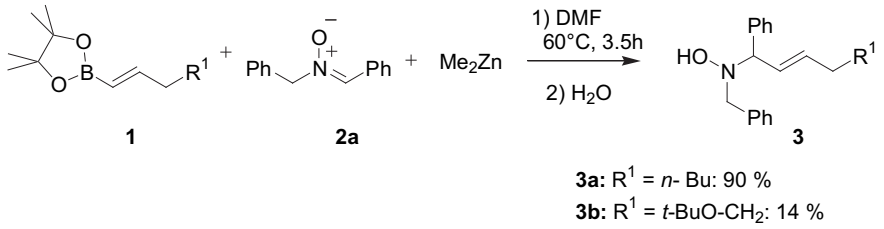
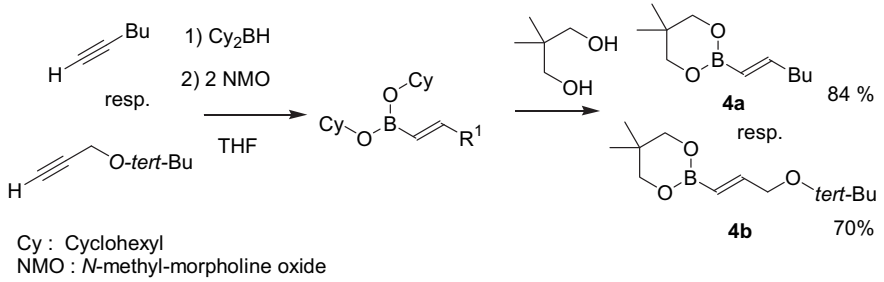


Scheme 1. Reaction of pinacol esters **1** with nitrones.



Scheme 2. Preparation of **4a**,**b**.

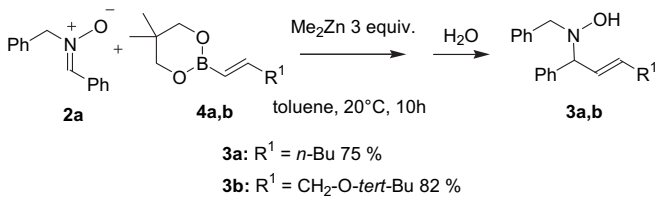
(14% yield of **3b**, Scheme 1). The corresponding unhindered boronic ester **4b** reacted at 20 °C with the same nitrone **2a** in 82% yield (Scheme 3). Thus, unhindered boronic esters **4** would clearly enlarge the scope of the method, without losing the practical advantages of using air- and chromatography-stable reagents, if they could be readily accessible by hydroboration [9]. But unlike hydroboration with pinacolborane, reaction of alkynes with 5,5-dimethyl-1,3,2-dioxaborinane leads to mixtures. We [10] and others [11] observed that 5,5-dimethyl-1,3,2-dioxaborinane is prone to a fast disproportionation, releasing *in situ* BH_3 which reacts with more than one alkyne.

Thus the readily prepared, hindered pinacol esters **1** are not reactive enough and the unhindered, reactive esters **4** are not easily prepared. We looked for a compromise.

3. 4,4,6-Trimethyl-2-vinyl-1,3,2-dioxaborinanes 6

We demonstrated earlier [10] that the use of 4,4,6-trimethyl-1,3,2-dioxaborinane **5** (Methyl Pentanediol Borane, MPBH) [12] for the hydroboration of 1-alkynes [13] provided a convenient and efficient method to 4,4,6-trimethyl-2-vinyl-1,3,2-dioxaborinanes **6** (Scheme 4). This hydroboration is easy, robust, and gives access to a large array of highly functionalized vinylboronic esters. Moreover, the hydroborating agent MPBH is inexpensive, very stable, easily prepared and stored [14].

In the expectation that compounds **6** could be a compromise between unreactive **1** and poorly accessible **4**, we submitted the boronic esters **6** to the same conditions as **4**.



Scheme 3. Reaction of **4a**,**b**, dimethylzinc and **2a**.

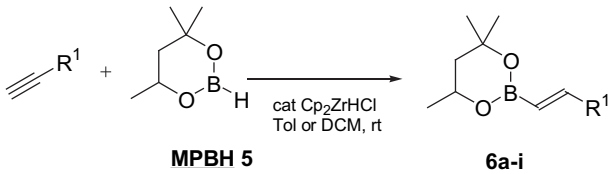
The initial experiments clearly showed that the reactions with **6** could be run at lower temperatures and with less dimethylzinc than with pinacol boronic esters **1**. The reaction proceeded to completion in 36 h at room temperature. Nevertheless, we found that slightly higher temperatures (40 °C) led to faster reaction and cleaner products. The reaction was best performed in toluene. For better yields, a rather large excess (3 M equiv.) of dimethylzinc is necessary.

Thus, we submitted a variety of vinylboronic esters to reaction with selected nitrones, in the presence of 3 M equiv. of dimethylzinc in toluene at 40 °C. We were particularly interested in testing the α-functionalized vinylboronic esters made easily available by our former work [10]. The results are illustrated in Table 1.

The reaction proceeds generally in good isolated yields. α-oxygenated vinylboronic esters can be used successfully, giving access to highly functional derivatives.

The use of MPB-derived boronic esters **6** is a clear improvement over our precedent use of pinacol-protected boronic esters, both in terms of accessibility [10] of the reagents **6** and their reactivity.

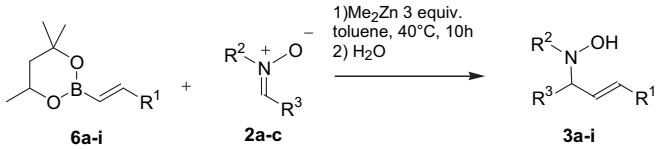
To compare more accurately the reactivity of **1a**, **4a** and **6a**, we submitted them to competition experiments. Equal amounts of two different 2-hex-1-enyl-boronic esters were put in the same reaction mixture in the presence of excess dimethylzinc and excess nitrone. The conversion of the boronic esters was monitored by gas chromatography and the ratio of initial rates was estimated. At 40 °C pinacol ester **1a** reacted 5 times slower than the MPB ester **6a**.



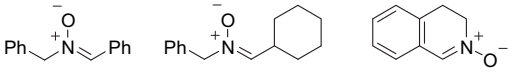
a: R^1 = Ph b: R^1 = H c: R^1 = 1-cyclohexenyl
d: R^1 = *n*-Bu e: R^1 = CH_2O-*tert*-Bu f: R^1 = CH_2OMe
g: R^1 = CH_2OAc h: R^1 = $Si(Me)_3$ i: R^1 = CH_2-Cl

Scheme 4. Hydroboration of alkynes with MPBH **5** [14].

Table 1
Reaction of MPB esters **6a**–**I** with nitrones **2a**–**c**.



6a-i **2a-c** **3a-i**



2a **2b** **2c**

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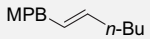
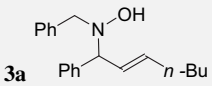
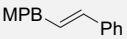
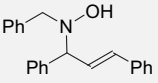
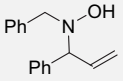
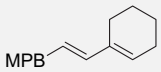
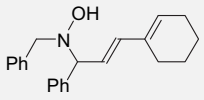
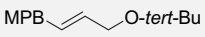
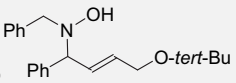
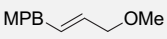
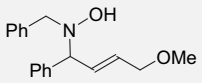
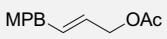
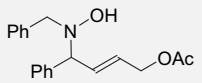
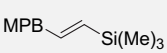
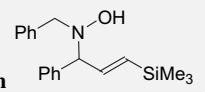
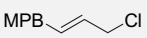
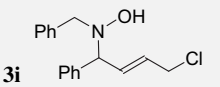
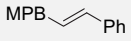
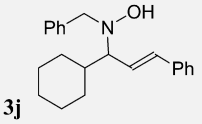
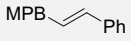
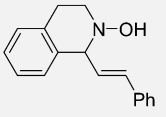
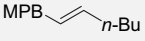
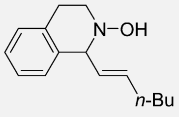
Entry	Vinylboronate **6**	Nitrone **2**	Product **3**	%Yield
1		**2a**	 **3a**	76
2		**2a**	 **3c**	84
3		**2a**	 **3d**	77
4		**2a**	 **3e**	60
5		**2a**	 **3b**	80
6		**2a**	 **3f**	75
7		**2a**	 **3g**	63
8		**2a**	 **3h**	60
9		**2a**	 **3i**	31

(*continued on next page*)

Table 1 (*continued*)

Entry	Vinylboronate **6**	Nitrone **2**	Product **3**	%Yield
10		**2b**	 **3j**	64
11		**2c**	 **3k**	61
12		**2c**	 **3l**	66

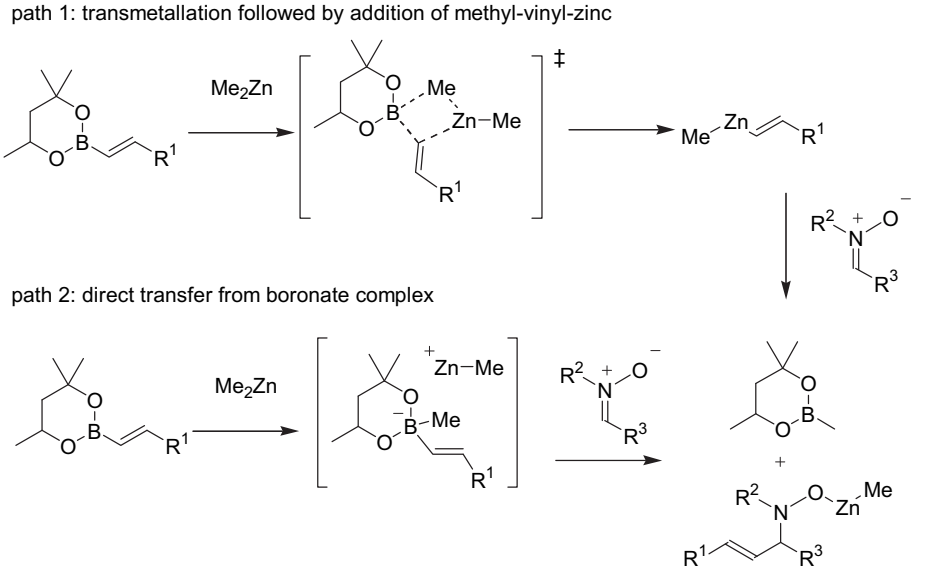
In turn, **6a** reacted 4 times slower than the unhindered **4a** at 40 °C, and more than 9 times at 60 °C. So, a strong influence of steric factors appeared clearly.

4. Mechanism

Two mechanisms can be considered for this reaction (Scheme 5). According to the first hypothesis, the reacting species is vinylmethylzinc issued from a boron-to-zinc exchange. Analogous transmetallations are largely documented: Srebnik [15,16] and Oppolzer [9b,c] found than vinylboranes can be transmetallated to vinylzinc species by the action of diethylzinc. Then, addition onto aldehydes can be achieved in the presence of various amino-alcohol catalysts [8]. Also related is the aryl transfer from a "Ph_3BEt_2Zn" entity proposed by Tamaru [17], and the formation of arylzinc [18] and vinylzinc [8] reagents from boronic acids described by Bolm et al. The studies on the transmetallation of alkylboranes by Knochel's group [19] should also be mentioned. This vinylmethylzinc would react in a separate step with the nitrone to produce the allylic hydroxylamine (Scheme 5, pathway 1). Such an organozinc species can transfer selectively the vinyl group to various electrophiles [9]. With vinylboronic esters of the **1**, **4**, and **6** families, we attempted to obtain boron-to-zinc transmetallation in the absence of electrophile. It turned out that the reaction products were never stable in the reaction conditions, and degradation always occurred.

According to the second mechanistic hypothesis, the reactive species is a tetracoordinate boronate complex formed from the boronic ester and dimethylzinc. This anionic boronate complex would coordinate with the nitrone and transfer the vinyl group (Scheme 5, pathway 2) directly from the boron atom. Such an "ate" complex has been postulated [4,20] in other analogous reactions.

As we are interested in designing a strategy towards an enantioselective version of the reaction, it is very important to identify which is the actual mechanism of the reaction. If it goes through



Scheme 5. Possible mechanisms for the reaction sequence.

pathway **1**, transmetallation and the C–C bond formation are two separate bimolecular steps. In this case, we are dealing with the question of making the addition of a nitrone and an alkylvinylzinc enantioselective. Such a question has been extensively studied and solved with aldehydes as the ultimate electrophiles and amino-alcohols as catalysts [21]. Alternatively, if the reaction takes place according to pathway **2** through an "ate" complex, chirality on the starting vinylboronate would still be present in the reactive intermediate, and therefore influence the stereochemistry of the final adduct. In this case, the application of chiral enantiopure vinylboronates from chiral diols could ensure the enantioselectivity of the reaction.

Both pathways were investigated computationally at DFT level for the model system where $R^1 = H$, and the methyl substituents in the pinacol–ester part of vinylboronate are also replaced by H atoms. The Gibbs free energies for both reaction pathways are presented in Fig. 1. Using Gibbs energies in lieu of conventional electronic energies is useful mainly because entropic contributions are accounted for and are naturally included in the discussion.

The mechanism corresponding to pathway **1** consists in two major steps. The first is the transmetallation reaction between boronate ester **C** and dimethylzinc **A**. When **A**, $Zn(CH_3)_2$ and **C** (vinylboronate ester) interact, they initially form a compound **AC**. From that, intermediate **I** is formed, featuring a tetracoordinated boron atom carrying both a vinyl and a methyl group. Formation of **I** from **A** and **C** occurs via the transition state **H**, requiring an activation free energy of 28.7 kcal/mol with respect to the reactants. This step is endothermic by 17.7 kcal/mol. The B–C ($-CH{=}CH_2$) bond in **I** (1.660 Å) is much longer than the same bond in boronate ester **C** (1.550 Å). Transformation of **I** to form vinylmethylzinc **E** requires a low activation energy (3.9 kcal/mol). This step is exothermic by 17.7 kcal/mol with respect to **I**, and as a whole the transmetallation is essentially thermoneutral referring to starting reagents **A**, **B** and **C** (0.9 kcal/mol is necessary to form separated **E** and **F**).

The second step of pathway **1** is a bimolecular reaction of the vinylmethylzinc **E** produced in the first step, and nitrone **B**. **E** and **B** give a complex (**EB**) via a barrierless process, exothermic by 4.1 kcal/mol with respect to reactants.

The formation of the C–C bond, yielding **W**, requires 7.3 kcal/mol (through transition state **X**) and is strongly exothermic ($\Delta G_r = -24.8$ kcal/mol). In conclusion, the rate-determining step of pathway **1** would be the formation of **I**, corresponding to the methyl transfer from zinc to the boron atom. It is worth noting that, although not surprisingly, the zinc atom is always anchored to an O atom of the boronate ester.

According to the mechanism of pathway **2**, dimethylzinc **A** and nitrone **B** form, without any barrier, the adduct **G**. Reaction of **G** with the vinylboronate ester **C** leads through transition state **K** to intermediate **L**, where a methyl group has moved from zinc to boron. This methyl transfer requires here only 24.5 kcal/mol (against 28.7 kcal/mol in the absence of nitrone) and is endothermic by 13.8 kcal/mol referring to energies of separated starting reagents **G** and **C**. We can conclude that the methyl transfer from zinc to boron is facilitated when dimethylzinc is initially coordinated by nitrone: the Gibbs free energy is lower and the transformation is not endothermic.

The next step corresponds to the formation of the C–C bond to yield adduct **N** exothermically (16.5 kcal/mol). The free energy of the transition state **M** is 18.5 kcal/mol above intermediate **L** (31.9 kcal/mol above the reactants). We can conclude that the formation of the C–C bond is more difficult in pathway **2**: the reaction has to go through a free energy barrier of 18.5 kcal/mol instead of 7.3 kcal/mol in the absence of the boronate as in the (**E** + **B**)⇒**W** step of pathway **1**. Overall, in pathway **2** nitrone catalyses the Zn-to-B methyl transfer but direct transfer of the vinyl group from the boronate to the nitrone is not favored.

In summary, the expected rate-determining steps, according to the energetics presented in Fig. 1, are for pathway **1** the transfer of vinyl from B to Zn (to **I** through **H**) and for pathway 2 the formation of the C–C bond (to **N** through **M**; **N** is a van der Waals complex of **F** and **W**).

The two reaction pathways, however, do not take place separately. Because the initial barriers in both channels are high, the reaction proceeds slowly and does not disturb the thermodynamical equilibrium significantly. Barrier **K** is lower than barrier **H**, but much lower than barrier **M**. This means that the initial reactants, complexes **AC**, **G**, **GC** and complex **L** are in equilibrium. The relative concentration of these intermediate species is determined by their relative free energy according to the van't Hoff equation:

$$K_{eq}(T) = \frac{[\text{product}]}{[\text{reactant}]} = e^{-\Delta G^0(T)/RT}$$

The key is the balance between the relative concentration of the reactant of the rate-determining step of each pathway (**AC** and **L**, respectively) and the rate coefficient of their removal by the same process (via **H** and **M**, resp.). Complex **L** has 6.6 kcal/mol higher free

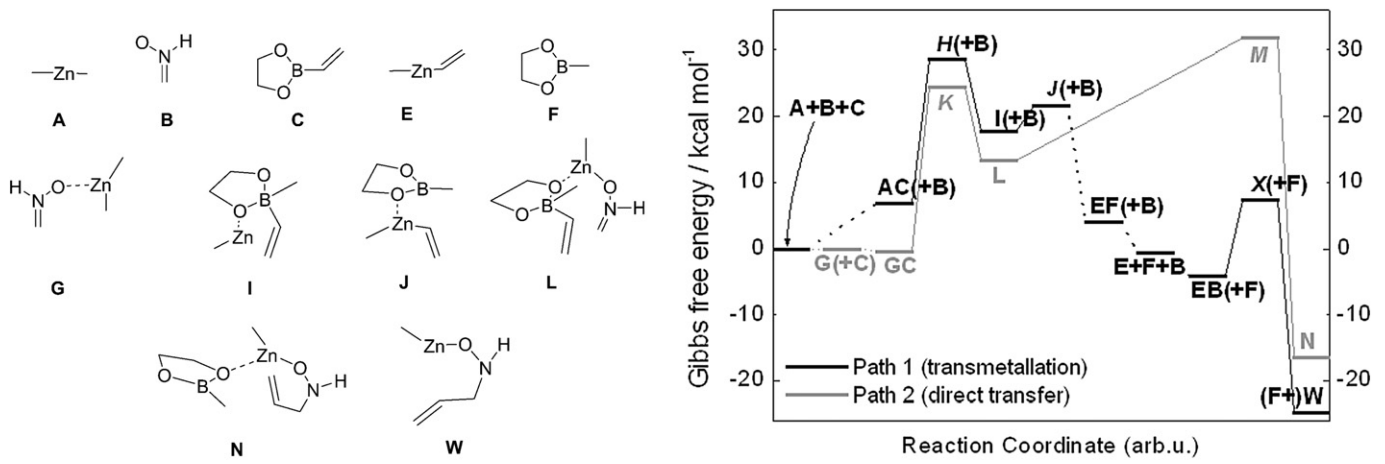


Fig. 1. Gibbs free energies for both reaction pathways. The reference energy is the sum of energies of the separated reactants. TS are shown in italics, spectators are in parenthesis and bimolecular steps indicated using dotted lines.

energy than **AC**, thus the concentration of **AC** will be higher. On the other hand, the activation free energy for reaction **AC** → **I** is 21.9 kcal/mol and that for reaction L → M is 18.5 kcal/mol, i.e. the latter reaction is faster. Both the relative concentrations and the rate coefficients depend on the temperature (T). At a given T, numerical values of the relative rate of the two processes, $r_1/r_2 = k_H[AC]/k_M[L]$ can be used to decide which channel dominates. At 40 °C, the optimal experimental temperature for the reaction, the relative concentration [AC]/[L] = 42200, i.e. the key intermediate of pathway **1** is much more abundant than that of pathway **2**. On the other hand, the ratio of the respective rate coefficients, calculated according to the thermodynamic formulation of the transition-state-theory: $k = k_B T/he^{-\Delta G^{\neq}/RT}$ is $k_H/k_M = 0.00414$, which is clearly too small to counterbalance the concentration ratio. Really, the ratio of the rates of the rate-determining steps is $r_1/r_2 = 174$, which means that pathway **1** dominates. Increasing the temperature would change this ratio, but even at 100 °C it is 70, so the dominant channel remains pathway **1**.

5. Conclusion

We have shown here that vinylboronic esters issued from the easy hydroboration of 1-alkynes with 4,4,6-trimethyl-[1,3,2]dioxaborinane, can be readily activated by the reaction of dimethylzinc in the presence of nitrones as electrophiles. An important advantage of the method is that the vinylboronate can carry functional groups in allylic position. This chemoselective addition provides highly functionalized *N*-hydroxy-allylamines in good yields. The DFT study coupled with a kinetic analysis indicates that the mechanism of this reaction is an *in situ* Boron-to-Zinc transmetallation, possibly favored by the nitrone itself acting as a ligand. It is followed by a separate step, addition of the vinylzinc species to the nitrone.

6. Experimental

6.1. Computational methods

DFT calculations were carried out with the G98 system of programs [22]. Stationary points (reactants, transition structures, pre-reaction complexes and products) were located at the B3LYP/6-31G(d) level [23] and identified as minima or first-order saddle points by diagonalizing the Hessian matrices. Transition structures were found to have only one negative eigenvalue with the corresponding eigenvector involving the formation of the newly created bonds and elongation of the breaking ones. The minimum energy reaction path was also calculated starting from each transition structure (IRC analysis [24]) to make sure that they correspond to the elementary step. Gibbs free energies were derived using the conventional rigid rotor – harmonic oscillator approximation based on the calculated vibrational frequencies.

6.2. Reaction of 4,4-dimethyl-2-vinyl-1,3,2-dioxaborinanes ***4a***,***b***, nitrone ***2a*** and dimethylzinc

In a 10 mL Schlenk vessel under nitrogen, vinylboronate **4** [6] (1.5 mmol) and nitrone **2** (1 mmol, 210 mg) were dissolved in 4 mL toluene. At room temperature, a solution of dimethylzinc was added (2 M in toluene, 1.5 mL, 3 mmol) and the mixture was stirred for at 20 °C for 10 h. Hydrolysis was performed at 20 °C by addition of a saturated NaHCO solution (2 ml) and the mixture was extracted with DCM (3 × 5 ml). The gathered organic phases dried over sodium sulphate and concentrated under reduced pressure, the hydroxylamines **3a**,**b** were purified by chromatography on silica gel (cyclohexane 80/ethyl acetate 20).

6.3. General procedure for the reaction of 3,3,5-trimethyl-2-vinyl-1,3,2-dioxaborinanes ***6***, nitrone ***2*** and dimethylzinc

In a 10 mL Schlenk vessel under nitrogen, dimethylzinc (2 M solution in toluene, 0.5 ml, 1.0 mmol, 2.0 equiv.) was added to a mixture of nitrone **2** (0.5 mmol) and vinylborane **6** [1] (0.6 mmol) in anhydrous toluene (0.5 mL). The mixture was stirred at 40 °C for 16 h. Hydrolysis was performed at 20 °C by addition of a saturated ammonium chloride solution (2 ml) and the mixture was extracted with DCM (3 × 5 ml). The collected organic phases were dried over sodium sulphate and concentrated under reduced pressure. The crude material was purified by column chromatography (cyclohexane/EtOAc).

6.3.1. *N*-Benzyl-*N*-(1-phenyl-hept-2-enyl)-hydroxylamine ***3a*** [1]

Prepared according to the General Procedure from *N*-benzylidene-benzylamine *N*-oxide **2a** (0.5 mmol, 105 mg) and dioxaborolane **6d** (0.6 mmol, 126 mg) in 76% yield (112 mg). Colorless oil. TLC: $R_f = 0.52$ (cyclohexane/ethyl acetate, 50:50); **^{1}H NMR** (200 MHz, $CDCl_3$/TMS): $\delta = 0.87$ (t, $J = 6.8$ Hz, 3H), 1.20–1.45 (m, 4H), 2.05 (q, $J = 6.4$ Hz, 2H), 3.68 (d, $J = 13.5$ Hz, 1H), 3.83 (d, $J = 13.5$ Hz, 1H), 4.17 (d, $J = 7.6$ Hz, 1H), 5.19 (s, 1H), 5.64 (dt, $J = 6.4$, 15.6 Hz, 1H), 5.80 (dd, $J = 7.6$, 15.6 Hz, 1H), 7.15–7.40 (m, 10H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$/TMS): $\delta = 14.4$, 22.7, 29.3, 31.8, 61.5, 75.1, 127.5, 127.6, 128.4, 128.6, 128.9, 129.5(br.), 129.8, 135.2, 138.7, 142.4 ppm; **LRMS** (EI, 70 eV): *m*/*z* (%) = 295 (2) [M^+], 213 (7), 212 (9), 173 (30), 91 (100); **HRMS** calcd. for $C_{20}H_{26}NO$ 296.2014, found 296.2001.

6.3.2. *N*-Benzyl-*N*-(4-tert-butoxy-1-phenyl-but-2-enyl)-hydroxylamine ***3b***

Prepared according to the General Procedure from *N*-benzylidene-benzylamine *N*-oxide **2a** (0.5 mmol, 105 mg) and dioxaborolane **6e** (0.6 mmol, 144 mg) in 80% yield (130 mg). Colorless oil. $R_f = 0.3$ (Cyclohexane/ethyl acetate 70:30); **^{1}H NMR** (400 MHz, $CDCl_3$/TMS): $\delta = 1.18$ (s, 9H), 3.70–3.90 (m, 2H), 3.91 (dd, $J = 5.5$ Hz, $^4J = 1.3$ Hz, 2H), 4.28 (d, $J = 8.4$ Hz, 1H), 5.78 (dt, $J = 15.5$ Hz, $J = 5.5$ Hz, 1H), 5.52 (s, 1H), 6.00 (ddt, $J = 15.5$ Hz, $J = 8.4$ Hz, $^4J = 1.3$ Hz, 1H), 7.21–7.42 (m, 10H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$/TMS): $\delta = 27.0$, 61.3, 62.3, 73.2, 74.7, 127.0, 127.3, 128.1, 128.2, 128.5, 129.2., 130.8, 131.8, 138.4, 141.3 ppm; **MS** (DCI, NH_3/isobutane): *m*/*z* 326 $(M + H)^+$; **HRMS**: calcd. for $C_{21}H_{27}O_2N_1Na$ 348.1934, found 348.1933.

6.3.3. *N*-Benzyl-*N*-(1,3-diphenyl-allyl)-hydroxylamine ***3c*** [1]

Prepared according to the General Procedure from *N*-benzylidene-benzylamine *N*-oxide **2a** (0.5 mmol, 105 mg) and dioxaborolane **6a** (0.6 mmol, 139 mg) in 84% yield (133 mg). Pale yellow solid. $R_f = 0.5$ (Cyclohexane/ethylacetate, 60:40); **^{1}H NMR** (300 MHz, $CDCl_3$/TMS) δ ppm 1.50 (1H), 3.84 (d, $J = 13.1$ Hz, 1H), 3.99 (d, $J = 13.1$ Hz, 1H), 4.47 (d, $J = 7.9$ Hz, 1H), 6.53 (dd, $J = 15.9$, 7.9 Hz, 1H), 6.63 (d, $J = 15.9$ Hz, 1H), 7.5–7.0 (m, 15H); **^{13}C NMR** (75 MHz, $CDCl_3$/TMS) δ ppm: 62.1, 75.7, 126.5, 127.2, 127.5, 127.7, 128.06, 128.3, 128.5, 128.7, 128.7, 129.3; **HRMS** calcd. for $C_{22}H_{22}NO$: 315.1623, found 316.1695.

6.3.4. *N*-Benzyl-*N*-(1-phenyl-allyl)-hydroxylamine ***3d***

Prepared according to the General Procedure from *N*-benzylidene-benzylamine *N*-oxide **2a** (0.5 mmol, 105 mg) and dioxaborolane **6c** (0.6 mmol, 92 mg) in 77% yield (92 mg). Oil. **^{1}H NMR** (300 MHz, $CDCl_3$/TMS) δ ppm: 3.70 (d, $J = 13.4$ Hz, 1H), 3.74 (d, $J = 13.4$ Hz, 1H), 4.21 (d, $J = 8.4$ Hz, 1H), 5.17–5.25 (m, 2H), 5.75 (s, 1H), 6.12 (ddd, $J = 8.4$ Hz, $J = 17.2$ Hz, $J = 10.2$ Hz, 1H), 7.19–7.39 (m, 10 H); **^{13}C NMR** (75 MHz, $CDCl_3$/TMS) δ ppm: 61.0, 75.3, 117.7, 172.2, 127.4, 128.1, 128.2, 128.6, 129.4, 137.7, 138.0, 141.0; **MS** (DCI, NH_3/isobutane) *m*/*z* = 240 $(M + H)^+$; **HRMS** calcd. for $C_{16}H_{18}NO$ 240.1382, found 240.1381.

*6.3.5. N-Benzyl-N-(3-cyclohex-1-enyl-1-phenyl-allyl)-hydroxylamine **3e** [1]*

Prepared according to the General Procedure from *N*-benzylidene-benzylamine *N*-oxide **2a** (0.5 mmol, 105 mg) and dioxaborolane **6c** (0.6 mmol, 141 mg) in 60% yield (96 mg). Colorless oil. $R_f = 0.60$ (cyclohexane/ethyl acetate, 50:50). **^{1}H NMR**: (300 MHz, $CDCl_3$/TMS): δ ppm = 1.45–1.55 (m, 4H), 1.95–2.15 (m, 4H), 3.60 (d, $J = 13.8$ Hz, 1H), 3.86 (d, $J = 13.8$ Hz, 1H), 4.22 (d, $J = 8.7$ Hz, 1H), 4.49 (s, 1H), 5.65–5.80 (m, 2 H), 6.17 (d, $J = 15.8$ Hz, 1 H), 7.10–7.44 (m, 10 H); **^{13}C NMR**: (75 MHz, $CDCl_3$/TMS): δ ppm = 22.5, 22.6, 24.7, 26.0, 61.5, 75.6, 125.2, 127.2, 127.4, 128.0, 128.4, 129.3, 130.2, 135.4, 136.7, 138.7, 142.2 ppm; **MS** (CI): m/z (%) = 320 ($M + H^+$, 3), 302 (7), 214 (8), 197 (100). **HRMS** calcd. for $C_{22}H_{26}NO$ 320.2014, found 320.2070.

*6.3.6. N-Benzyl-N-(4-methoxy-1-phenyl-but-2-enyl)-hydroxylamine **3f***

Prepared according to the General Procedure from *N*-benzylidene-benzylamine *N*-oxide (0.5 mmol, 105 mg) and dioxaborolane **6f** (0.6 mmol, 119 mg) in 75% yield (106 mg). Colorless oil. TLC: R_f = 0.4 (cyclohexane/ethyl acetate, 60:40); **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 3.24 (s, 3H), 3.58 (s, 1H), 3.70 (d, $J = 13.2$ Hz, 1H), 3.79 (d, $J = 13.2$ Hz, 1H), 3.86 (d, $J = 5.6$ Hz, 2H), 4.24 (d, $J = 8.4$ Hz, 1H), 5.71 (dt, $J = 15.4$, 5.6 Hz, 1H), 6.03 (dd, $J = 15.4$, 8.4 Hz, 1H), 7.40–7.16 (m, 10H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ = 27.6, 58.5, 61.9, 73.2, 74.7, 127.8, 128, 128.9, 129.2, 130.1, 130.4, 130.5, 133.3, 138.8, 141.8 ppm; **HRMS**: calcd. for $C_{18}H_{22}NO_2$ 284.1651, found 284.1659.

*6.3.7. Acetic acid 4-(benzyl-hydroxy-amino)-4-phenyl-but-2-enyl ester **3g***

Prepared according to the General Procedure from *N*-benzylidene-benzylamine *N*-oxide (0.5 mmol, 105 mg) and dioxaborolane **6g** (0.6 mmol, 136 mg) in 63% yield (98 mg). Colorless oil. $R_f = 0.6$ (Cyclohexane/EtOAc 60:40); **^{1}H NMR** (300 MHz, $CDCl_3$) δ ppm: 2.06 (s, 3H), 3.82 (d, $J = 13.5$ Hz, 1H), 3.96 (d, $J = 13.5$ Hz, 1H), 4.51 (d, $J = 8.0$ Hz, 1H), 4.55 (dt, $J = 16.0$ Hz, $J = 8.0$ Hz, 2H), 4.65 (br s, 1H), 5.85 (d, $J = 16.0$ Hz, 1H), 5.88 (m, 1H), 7.0–7.3 (m, 10H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ ppm 21.0, 61.3, 65.2, 71.8, 124.9, 128.4, 128.5, 128.8, 128.9, 135.64, 138.2, 141.2, 170.6; **HRMS:** calcd. for $C_{19}H_{21}NO_3Na$ 334.1419; found 334.1405.

*6.3.8. N-Benzyl-N-(1-phenyl-3-trimethylsilanyl-allyl)-hydroxylamine **3h***

Prepared according to the General Procedure from *N*-benzylidene-benzylamine *N*-oxide (0.5 mmol, 105 mg) and dioxaborolane **6h** (0.6 mmol, 138 mg) in 60% yield (94 mg). Colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$/TMS): δ = 0.05 (s, 9H), 3.72 (d, $J = 13.5$ Hz, 1H), 3.85 (d, $J = 13.5$ Hz, 1H), 4.26 (d, $J = 7.7$ Hz, 1H), 5.3 (Br s, 1H), 5.92 (d, $J = 18.6$ Hz, 1H), 6.30 (dd, $J = 18.6$ Hz, $J = 7.7$ Hz, 1H), 7.23–7.42 (m, 11H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$/TMS): δ = −1.1, 61.4, 77.4, 127.3, 127.5, 128.3, 128.4, 128.7, 129.5, 134.1, 138.3, 141.2, 145.0 ppm; **MS** (**ESI**): 312 (100) $(M + H)^+$, 310 (29), 350 (16), $(M + K)^+$, 334 (14) $(M + Na)^+$; **HRMS** calcd. for $C_{19}H_{26}O_1N_1Si_1$ 312.1778, found 312.1775.

*6.3.9. N-Benzyl-N-(4-chloro-1-phenyl-but-2-enyl)-hydroxylamine **3i***

Prepared according to the General Procedure from *N*-benzylidene-benzylamine *N*-oxide (0.5 mmol, 105 mg) and dioxaborolane **6i** (0.6 mmol, 122 mg) in 31% yield (44 mg). Colorless oil. **^{1}H NMR** (300 MHz, $CDCl_3$/TMS): δ = 3.71 (d, $J = 13.4$ Hz, 1H), 3.75 (d, $J = 13.4$ Hz, 1H), 4.00 (d, $J = 6.9$ Hz, 2H), 4.25 (d, $J = 8.4$ Hz, 1H), 5.79 (dt, $J = 15.2$ Hz, $J = 6.9$, 1H), 6.09 (dd, $J = 15.2$ Hz, $J = 8.4$ Hz, 1H), 7.20–7.36 (m, 10H) ppm; **^{13}C NMR** (75 MHz, $CDCl_3$/TMS): δ = 44.4, 61.3, 73.6, 127.3, 127.7, 128.1, 128.3, 128.7, 129.1, 129.3, 134.1, 137.9, 140.4 ppm; **IR** (film) υ = 3530, 3060, 3027, 2920, 2847, 1495, 1454, 1028, 969, 745, 697 cm^1; **MS** (DCI, NH_3/isobutane) $m/z = 288$ $(M + H)^+$; **HRMS** calcd. for $C_{17}H_{19}ClNO$ 288.1155; found 288.1137.

*6.3.10. N-Benzyl-N-(1-cyclohexyl-3-phenyl-allyl)-hydroxylamine **3j***

Prepared according to the General Procedure from *N*-cyclohexylidene-benzylamine *N*-oxide (0.5 mmol, 109 mg) and dioxaborolane **6a** (0.6 mmol, 139 mg) in 64% yield (103 mg); colorless oil.1.25–1.35 (m, 1H), 1.45–1.68 (m, 7H), 1.77–2.0 (m, 3H), 3.68 (d, $J = 13.0$ Hz, 1H), 3.71 (d, $J = 13.0$ Hz, 1H), 4.27 (d, 1H, $J = 6.8$ Hz), 3.14 (dd, 1H, $J = 6.4$, 8.3 Hz), 4.27 (d, 1H, $J = 6.8$ Hz), 5.94 (dd, 1H, $J = 15.2$, 8.3 Hz), 6.63 (d, 1H, 15.2 Hz), 7.20–7.36 (m, 10H); **^{13}C NMR** (75 MHz, $CDCl_3$/TMS): δ = 136.7, 135.9, 135.2, 132.1, 129.2, 129.1, 128.8, 128.5, 127.6, 69.8, 64.3, 40.57, 29.7, 25.9, 25.6, 2.5 ppm; **HRMS** calcd. for $C_{22}H_{28}NO$: 322.2171, found 322.2166.

*6.3.11. 1-Styryl-3,4-dihydro-1H-isoquinolin-2-ol **3k***

Prepared according to the General Procedure from 1,2,3,4-Tetrahydroisoquinoline-*N*-oxide (0.5 mmol, 66 mg) and dioxaborinane **6a** (0.6 mmol, 139 mg) in 61% yield (77 mg). Colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ = 2.87–2.92 (m, 1H), 3.08–3.17 (m, 2H), 3.51–3.54 (m, 1H), 4.49 (d, 1H, $J = 8.0$ Hz), 6.30 (dd, 1H, $J = 15.6$, 8.0 Hz), 6.72 (d, 1H, $J = 15.6$ Hz), 7.1–7.2 (m, 4H), 7.3–7.4 (m, 3H), 7.4–7.45 (m, 2H); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 28.6, 53.9, 71.9, 126.2, 126.7, 127.0, 127.9, 128.1, 128.4, 128.7, 133.4, 135.3, 135.5, 136.7, 129.5 ppm; **HRMS** calcd. for $C_{17}H_{17}NONa$: 274.1208; found 274.1223.

*6.3.12. 1-Hex-1-enyl-3,4-dihydro-1H-isoquinolin-2-ol **3l** [1]*

Prepared according to the General Procedure from 1,2,3,4-Tetrahydroisoquinoline-*N*-oxide (0.5 mmol, 66 mg) and dioxaborinane **6d** (0.6 mmol, 126 mg) in 66% yield (77 mg). Colorless oil. $R_f = 0.4$ ($CHCl_3$/MeOH, 80:20); **^{1}H NMR** (300 MHz, $CDCl_3$) δ ppm: 0.94 (t, 3H, $J = 7.1$ Hz), 1.3–1.5 (m, 4H), 2.15–2.21 (m, 2H), 2.90–2.96 (m, 1H), 3.03–3.18 (m, 2H), 3.49–3.53 (m, 1H), 4.27 (d, 1H, $J = 6.8$ Hz), 5.52 (dd, 1H, $J = 15.2$, 8.3 Hz), 5.87–5.78 (m, 1H), 7.19–7.10 (m, 4H); **^{13}C NMR** (75 MHz, $CDCl_3$) δ ppm: 13.9, 22.3, 28.3, 31.4, 32.1, 53.5, 71.4, 125.9, 126.6, 127.9, 128.1, 129.7, 133.3, 135.9, 137.0 ppm; **LRMS** (CI): m/z (%) = 232 (6), 231 (19), 214 (12), 172 (25), 148(80), 129 (100).

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