Ring opening reactions of NHC-boriranes with in situ generated HCl: Synthesis of a new class of NHC-boralactones

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Abstract: The first ring-opening reactions of ligated boriranes (boracyclopropanes) are described. Treatment of readily available NHC-boriranes bearing ester substituents on the borirane ring with HCl provides stable γ-NHC-bora-γ-lactones in isolated yields ranging from 40–73%. The reactions occur through 1,3-addition of HCl across a B–C bond of the NHC-borirane to form a ring-opened NHC-boryl chloride, followed by lactonization with chloride displacement. Experimental evidence suggests that both the borirane ring opening reaction and the boralactonization reaction occur with inversion at boron.

Introduction

Boriranes (boracyclopropanes) are rare and therefore little is known about their chemistry.[1] Borirane itself is isoelectronic with the cyclopropyl cation (Figure 1a). The archetypical transformation of this cation is disrotatory ring opening to the allyl cation,[2] but experimental studies by Denmark[3] (on 1,2,3-triphenylborirane) and calculations by Bettinger[1] (on borirane) show that boriranes do not undergo this reaction.

Ligated boriranes (borirane–Lewis base complexes) are isoelectronic with cyclopropane, aziridine and oxirane (Figure 1a), but again little is known about their chemistry.[3] One of the most common reactions of three-membered rings is ring opening with nucleophiles, either directly or with assistance of Brønsted or Lewis acids.[4] To the best of our knowledge, there are no such ring opening reactions of ligated boriranes and it is not clear that they are viable. Most ligated boriranes have no good site for acid activation, and direct nucleophilic opening would produce an unstable borenium ion.[5]

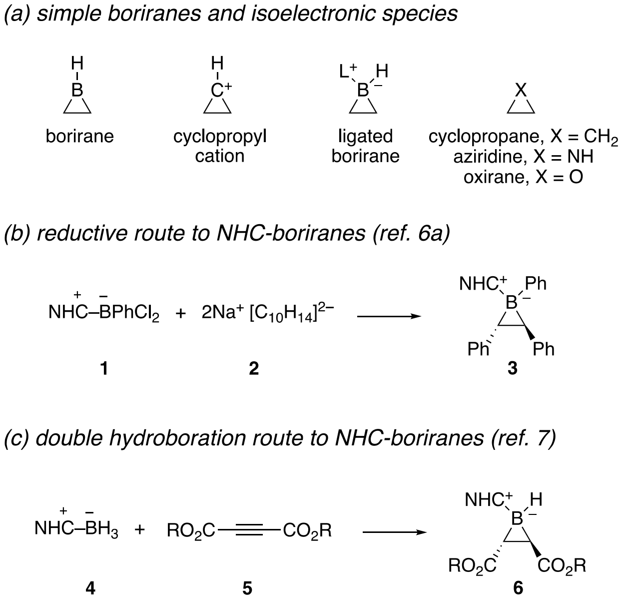


Figure 1. Borirane structures and recent routes to NHC-boriranes (L = Lewis base; NHC = N-heterocyclic carbene)

Recently, Braunschweig[6] and later our group[7] provided access to various N-heterocyclic carbene complexes of boriranes (hereafter, NHC-boriranes).[8] For example, Braunschweig reduced NHC-*B*-phenyl-*B,B*-dichloroboranes **1** with disodium stilbene dianion **2** ($2Na^+$ $[C_{10}H_{14}]^{2-}$) to provide *trans*-1,2,3-triphenyl NHC-boriranes **3** (Figure 1b).[6a] And we discovered a convenient double hydroboration of acetylenedicarboxylates **5** with NHC-boranes **4** to provide various *trans* diester-substituted NHC-boriranes **6** (Figure 1c).[7] A theme cutting across this early work is the robustness of the NHC-boriranes that emerged. Most of the compounds are high-melting solids that survive flash chromatography and are stable to ambient lab conditions.

We hypothesized that diester-substituted NHC-boriranes of the general structure **6** might be loosely analogous to donor-acceptor substituted cyclopropanes[4b,9] and undergo ring opening promoted by acids or Lewis acids. The acceptor substituent of **6** is the ester. In contrast, the donor is not a substituent but the boron atom itself. Here we report that facile ring opening reactions of **6** with HCl produce stable NHC-boralactones. Like boriranes, boralactones are also rare species,[10] and examples of ligated derivatives of boralactones of any kind are sparse.[11] Ring-opened chloroboranes are key intermediates on the way to the NHC-boralactones.

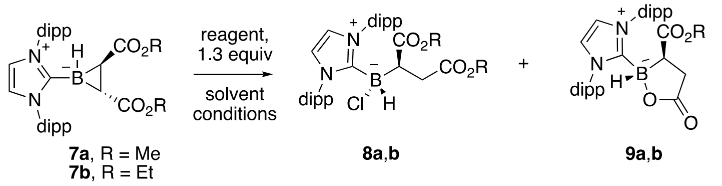
Results and Discussion

We selected bis-2,6-diisopropylphenyl (dipp) substituted NHC-borane **7a** for initial screening of reaction conditions both because it is readily available and because most dipp-substituted NHC-boranes are stable and crystalline.[12] Selected results from a larger group of preliminary experiments are summarized in Table 1.

In an initial experiment, trimethylsilyl chloride (TMSCl, 1.3 equiv) was added to a solution of **7a** in DCM. The mixture was heated at 40 ˚C and reaction progress was followed by ^{11}B NMR spectroscopy. After 12 h, the peak for **7a** was gone, being replaced by a broad resonance at –11.6 ppm (no discernable multiplicity) and a doublet at –4.1 ppm (J_{BH} = 120 Hz) in a ratio of 51/49 (entry 1). After concentration, the resulting product mixture was purified by flash chromatography to give NHC-boryl chloride **8a** (–11.6 ppm) in 40% yield along with the novel γ-NHC-bora-γ-lactone **9a** (–4.1 ppm) in 37% yield (combined isolated yield, 77%). Boralactone **9a** is formally a complex between bis-2,6-diisopropylphenylimidazol-2-ylidene (an

N-heterocyclic carbene Lewis base) and methyl 5-oxo-1,2-oxaborolane-3-carboxylate (a γ-bora-γ-lactone Lewis acid).

Table 1. Selected ring opening reactions of **7a** with silyl chlorides and HCl (dipp = 2,6-diisopropylphenyl)



entry	borirane	reagent	solvent	conditions	yield **8**[a]	yield **9**[a]
1	**7a**	TMSCl	DCM	40 ˚C, 12 h	51% (40%[b])	49% (37%[b])
2	**7a**	TMSCl	THF	70 ˚C, 12 h	>99% (68%[b])	–[c]
3	**7b**	TMSCl	DCM	40 ˚C, 12 h	(40%[b])	(43%[b])
4	**7b**	TMSCl	THF	70 ˚C, 12 h	(70%[b])	–[c]
5	**7a**	TMSCl, EtN(iPr)	DCM	40 ˚C, 12 h	–[c]	–[c]
6	**7a**	TMSCl, EtN(iPr)$_2$	THF	70 ˚C, 12 h	–[c]	–[c]
7	**7a**	HCl	DCM	40 ˚C, 12 h	49% (40%[b])	51% (36%[b])
8	**7a**	HCl	THF	70 ˚C, 12 h	>99% (70%[b])	
9	**7a**	LiCl	THF	70 ˚C, 12 h	–[c]	–[c]

a) yield estimated from ^{11}B NMR spectrum of the reaction mixture; b) isolated yield, c) not detected

The two-dimensional structures of both **8a** and **9a** were apparent from the set of NMR spectra (^{1}H, ^{11}B and ^{13}C) on the isolated samples, and both compounds exhibited satisfactory HRMS data (see Supporting Information). In addition, both compounds are single diastereomers whose configurations were assigned by X-ray crystallography (see below).

Next we conducted a reaction of **7a** with TMSCl in THF (70 ˚C, 12 h). This produced only the boryl chloride **8a**, which was isolated in 68% yield after flash chromatography (entry 2). Similar results were obtained in preparative reactions with the diethyl ester **7b**. A reaction with

TMSCl in DCM provided boryl chloride **8b** in 40% yield along with *trans*-boralactone **9b** in 43% yield (entry 3). The corresponding reaction in THF provided only boryl chloride **8b** in 70% yield (entry 4).

We next conducted two reactions of **7a** with TMSCl in THF and DCM with added diisopropyl ethyl amine (1.3 equiv). We chose this amine because it reacts with HCl but not TMSCl. No conversion of borirane **7a** was observed in either of these experiments (entries 5 and 6), suggesting that HCl might be the active reagent. Indeed, reactions of **7a** with HCl (1.3 equiv) gave about the same results as with the TMSCl. The reaction in DCM gave **8a**/**9a** in a ratio of 49/51 and the products were isolated in 40% and 36% yields, respectively (entry 7, compare to entry 1). The reaction in THF gave only **8a**, which was isolated in 70% yield (entry 8, compare to entry 2). Finally, we conducted a reaction with lithium chloride in THF, but **7a** was not converted to products (entry 9). Taken together, the results suggest that in situ generated HCl is the active reagent in these borirane opening reactions.

Scouting reactions in THF at 70 ˚C were also conducted with trimethylsilyl azide ($TMSN_3$), cyanide (TMSCN), acetate ($TMSO_2CCH_3$) and acetamide ($TMSNHCOCH_3$), but **7a** remained unreacted in all these experiments. Borirane **7a** also did not react with acetic acid under these conditions.

To assign the configurations of **8a** and **9a**, crystals of each sample were grown and ORTEP diagrams of the resulting X-ray structures are shown in Figure 2. NHC-boryl chloride **8a** is the *anti*-diastereomer when the longest chain is drawn in an extended manner (as shown in the Table 1 structure). By CIP nomenclature, **8a** is the *S**R** diastereomer. The NHC ring and the ester group of boralactone **9a** are *trans*-oriented, and this is also the *S**R** diastereomer. Since the CIP priorities are the same in the two compounds, this probably means that **9a** does not arise from **8a**. (More precisely, if it did then retention of the configuration at boron would be required.) Indeed, in a control experiment, **8a** did not convert to **9a** under the reaction conditions.

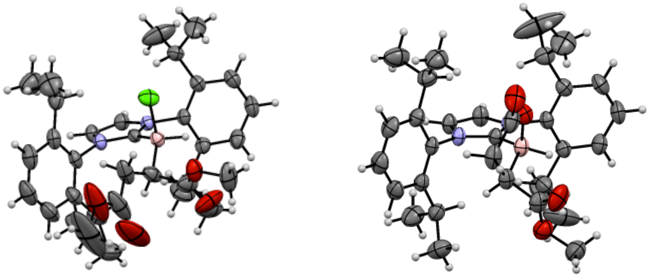
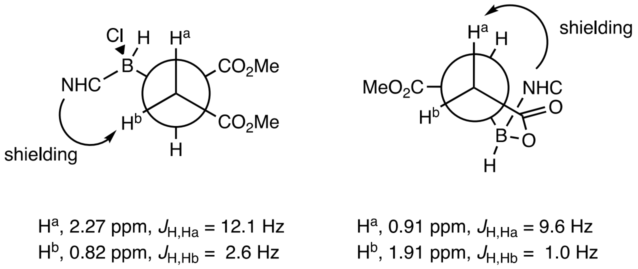


Figure 2. ORTEP representations of X-ray structures of chloroborane **8a** (left) and *trans*-lactone **9a** (right) at 50% probability level

In preparation for an isotope labeling experiment with DCl, we used these X-ray crystal structures to assign the two diastereotopic protons on the CH_2CO_2 group, which is an ester in the case of **8a** and a lactone in the case of **9a**. These assignments are shown in the Newman projections of the CH_2–CH bonds in Figure 3. In the boryl chloride **8a**, one of the diastereotopic methylene protons (H^a) has a normal chemical shift (2.27 ppm). It is roughly *anti* to the adjacent methyne proton (H), and these two protons have a large coupling constant. ($J_{H,Ha}$ = 12.1 Hz). Resonating at 0.82 ppm, the other diastereotopic proton (H^b) is shielded by one of diisopropylphenyl groups on the NHC ring. And H^b is roughly gauche to the adjacent methyne proton, $J_{H,Hb}$ = 2.6 Hz.

The analogous bond in **9a** is close to eclipsed due to the lactone ring, and clear assignments again emerge. Now it is H^a that is shielded by the dipp ring (0.91 ppm), but this time $J_{H,Ha}$ is large (9.6 Hz) because these two protons are nearly eclipsed. And H^b has a more normal chemical shift (1.91 ppm), but now $J_{H,Hb}$ is small (1.0 Hz) because these protons are close to orthogonal. The consistency between the X-ray structures and the NMR data suggests that the crystal conformations are also the low energy conformations in solution for both molecules.



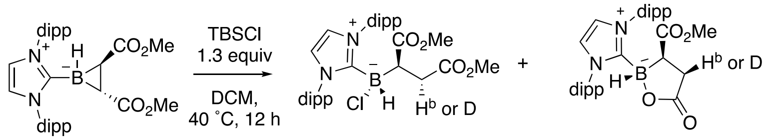
H^a, 2.27 ppm, $J_{H,Ha}$ = 12.1 Hz
H^b, 0.82 ppm, $J_{H,Hb}$ = 2.6 Hz

H^a, 0.91 ppm, $J_{H,Ha}$ = 9.6 Hz
H^b, 1.91 ppm, $J_{H,Hb}$ = 1.0 Hz

Figure 3. Newman projections of the CH_2–CH bond of boryl chloride **8a** (left) and lactone **9a** (right) illustrate the assignment of the resonances of the diastereotopic methylene protons H^a and H^b

Table 2 shows the results of the DCl labeling experiment and two associated controls. These experiments were conducted with a freshly unsealed sample of solid *tert*-butyldimethylsilyl chloride (TBSCl) to ensure high reagent quality. First we conducted an experiment with **7a** in DCM and that paralleled the TMSCl experiment and gave similar results. Boryl chloride **8a** and boralactone **9a** were each formed in about 50% yield according to ^{11}B NMR analysis (Table 2, entry 1; compare to Table 1, entry 1). Because high quality TBSCl was used, this result suggests that the source of HCl is water from either the solvent or the ambient air atmosphere.

Table 2. Control and labeling experiments with TBSCl



7a **8a** or **8a**-d_1 **9a** or **9a**-d_1

entry	solvent dry	atmosphere	D_2O added	yield **8a**[a]	yield **9a**[a]
1	no	air	no	50%	50%
2	yes[b]	argon	no	–[c]	–[c]
3	yes[b]	argon	yes	54% (40%[d])	42% (33%[d])

a) yield estimated from ^{11}B NMR spectrum of the reaction mixture; b) the solvent source was a sealed bottle of dry CD_2Cl_2; c) not detected; d) isolated yield

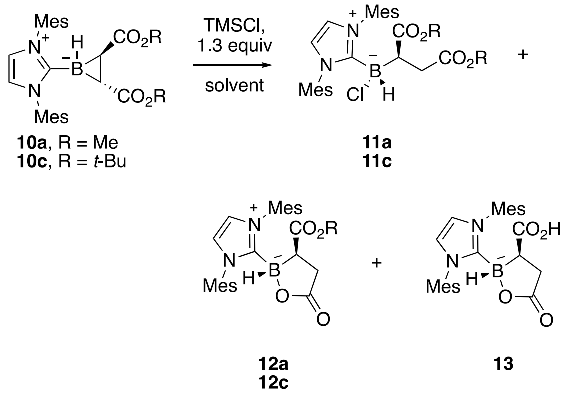
Next we conducted a control experiment with **7a** and TBSCl, this time in dry solvent and under argon. As expected, neither product was formed and the starting material remained (entry 2). Clearly **7a** does not react directly with TBSCl or (by implication) TMSCl.

A similar experiment was conducted with TBSCl (dry solvent, argon atmosphere), but this time D_2O (1.3 equiv) was added at the start. Products **8a**-d_1 and **9a**-d_1 were formed in 54% and 42% yield according to ^{11}B NMR analysis, and were isolated in 40% and 33% yield (entry 3). MS analysis of both products showed that deuterium incorporation was very high (>95% d_1). In both cases, the deuterium resided at the position H^b to the extent of 90% or more as assessed by integration of the ^1H NMR spectrum of each product. These results show that this reaction is a net 1,3-addition of in situ generated HCl and that the protonation step is highly stereoselective.

Next we studied opening reactions of two boriranes **10a**,**c** with *N,N*-dimesityl (2,4,6-trimethylphenyl) substituents, with results shown in Table 3. These preparative experiments were conducted on small scale (0.1 mmol), and we found it expedient to continue to use TMSCl as a source of HCl. Reaction of the dimethyl ester **10a** with TMSCl in DCM gave boryl chloride **11a** in 42% yield and *trans*-lactone **12a** in 35% yield (entry 1). The structures of both **11a** and **12a** were again solved by X-ray crystallography, see Supporting Information. Reaction of **10a** with

TMSCl in DCM produced a 71% isolated yield of boryl chloride **11a** (entry 2). In contrast, a reaction of the di-*t*-butyl ester **10c** with TMSCl in DCM gave no boryl chloride **11c**, producing instead 46% of *trans*-lactone **12c** and 8% of a new product that was soon identified as *trans*-NHC-boralactone **13** with a carboxylic acid substituent rather than an ester (entry 3).

Table 3. Isolated yield of products from preparative reactions of *bis*-dimesityl NHC-boriranes



entry	borirane	solvent[a]	**11**	**12**	**13**
1	**10a**	DCM	42%	35%	–[b]
2	**10a**	THF	71%	–[b]	–[b]
3[c]	**10c**	DCM	–[b]	46%	8%

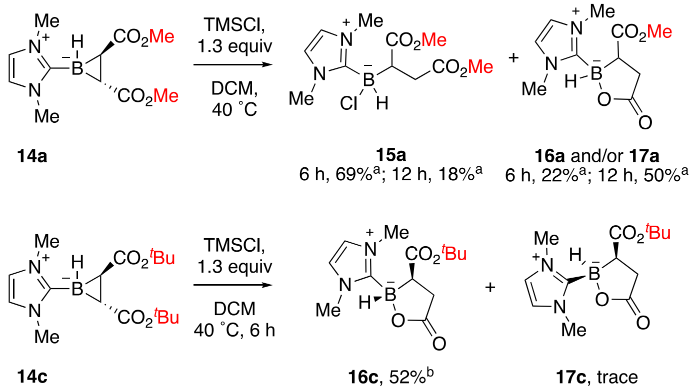
a) conditions: THF, 70 ˚C, 6 h; or DCM, 40 ˚C, 12 h; b) not isolated; c) reaction time, 6 h

We then conducted reactions with several *N,N*-dialkyl NHC-boriranes. Previous work has shown that boryl chlorides of the type NHC-BH_2Cl with *N,N*-dialkyl groups are not stable to water and therefore cannot be easily isolated.[13] Accordingly, we used DCM as the reaction solvent for these studies because it provided more of the stable boralactone products in the preceding experiments.

Reactions of two boriranes **14a**,**c** with *N,N*-dimethyl substituents are summarized in Scheme 1. The progress of a preliminary reaction of borirane **14a** with methyl esters was followed by ^{11}B NMR spectroscopy. After 6 h, the borirane was consumed and resonances for a boryl chloride **15a** (–10.1 ppm) and a boralactone **16a** and/or **17a** (–3.7 ppm) appeared in yields of 69% and 18% respectively. The configurations of these products were not assigned because the pairs of stereoisomers likely exhibit similar or identical ^{11}B NMR resonances. Another spectrum was recorded at 12 h, and the two products were now present in yields of 22% and 50%. Although the total yield declined somewhat on extended reaction time (from 87% to 72%), these results clearly show that the boralactone is a secondary product that arises from the boryl chloride (because its yield increased from 18% to 50%).

After 12 h, the reaction was stopped and automated flash chromatography was conducted, but no pure products were isolated. We expected that boryl chloride **15a** would be subject to hydrolysis on silica gel, and it may be that the boralactones **16a**/**17a** are also. However, these are also the most polar boralactones of the study and it may be that are too polar to emerge from the column. Whatever the case, this is the only reaction in this study where boralactones were produced but could not be isolated.

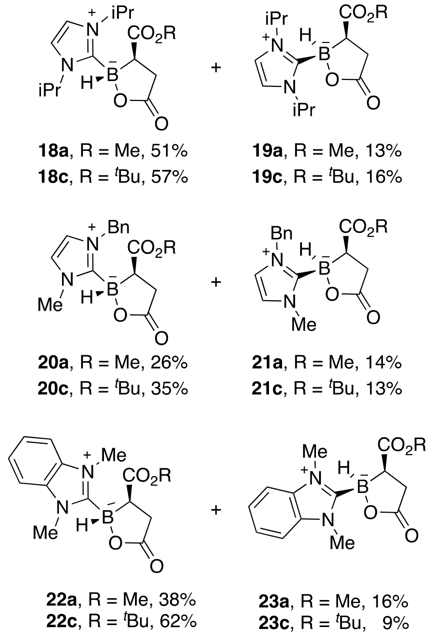
Scheme 1. Ring opening reactions of N,N-dimethyl NHC-boriranes



a) yield from ^{11}B NMR integration; b) isolated yield

Better preparative results were obtained with the *tert*-butyl ester analog **14c**. This reaction was already complete at 6 h (no starting material or boryl chloride detected by ^{11}B NMR analysis), and flash chromatography provided 52% yield of *trans*-boralactone **16c**. A small amount of what we suspect to be *cis*-boralactone **17c** (see below) was detected by TLC, but this could not be isolated in pure form.

Six other *N,N*-dialkyl NHC-boriranes were reacted under the standard conditions (1.3 equiv TMSCl, DCM, rt, 0.1 mmol scale), and the structures and isolated yields of the NHC-boralactone products from these reactions are shown in Figure 4. Mimicking the experiments in Scheme 1, the reactions of methyl esters ("**a**" series) and *t*-butyl esters ("**c**" series) were run for 12 h and 6 h, respectively, followed by flash chromatographic purification.



18a, R = Me, 51%
18c, R = ^{t}Bu, 57%

19a, R = Me, 13%
19c, R = ^{t}Bu, 16%

20a, R = Me, 26%
20c, R = ^{t}Bu, 35%

21a, R = Me, 14%
21c, R = ^{t}Bu, 13%

22a, R = Me, 38%
22c, R = ^{t}Bu, 62%

23a, R = Me, 16%
23c, R = ^{t}Bu, 9%

Figure 4. Structures and isolated yields of boralactone products in reactions of *N,N*-dialkyl NHC-boriranes

The pair of esters from the *N,N*-diisopropyl NHC-borirane gave similar results. The dimethyl ester gave 51% of *trans*-lactone **18a** and 13% of *cis*-lactone **19a**, while the di-*t*-butyl ester gave 57% and 16% of the corresponding products **18c** and **19c**. Reaction of the *N*-benzyl-*N*-methyl borirane methyl ester gave **20a** and **20c** in 26% and 14% yield, respectively, while the corresponding di-*t*-butyl ester **17c** gave **20c** and **21c** in 35% and 13% yield.

Finally, we studied preparative reactions of two esters of the *N,N*-dimethylbenzimidazole boriranes. The usual reaction of dimethyl ester provided the pair of *trans*- and *cis*-lactones **22a** and **23a** in 38% and 16% yield, respectively. The structure of **23a** was confirmed by X-ray crystallography, see Supporting Information. The reaction with di-*t*-butyl ester provided *trans*-lactone **22c** in 62% yield along with *cis*-lactone **23c** in 9% yield. In all the examples in Figure 4, the *trans*-NHC-boralactone is major product and the *cis*-isomer is minor.

The crystal structures of both isomers of the *N,N*-diisopropyl boralactones **18a** and **19a** were solved, and the corresponding ORTEP diagrams are shown in Figure 5. These structures confirmed the NMR assignments of the *trans* and *cis* isomers, and reliable trends in the ^{1}H NMR spectra of the boralactones in Figure 4 (see Supporting Information) allowed secure stereochemical assignments of all these products.

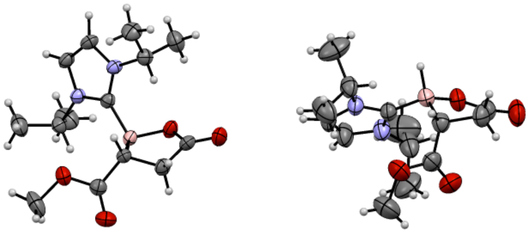
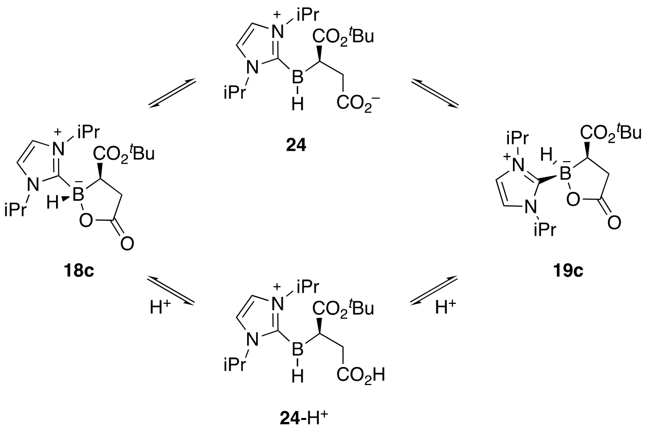


Figure 5. ORTEP representations of X-ray structures in the *N,N*-diisopropyl series of *trans*-boralactone **18a** (left) and *cis*-boralactone **19a** (right) at 50% probability level

We also used the pure samples of **18c** and **19c** to assess whether the lactone isomers can equilibrate during the reaction. This equilibrium could potentially occur thermally by reversible cleavage of the lactone B–O bond to give a borenium/carboxylate zwitterion **24**. The B–O cleavage reaction could also be subject to acid catalysis via protonated borenium ion **24**-H$^+$, and both pathways are summarized in Scheme 2.



Scheme 2. Potential paths to *cis/trans* equilibration involve planar, sp^2-hydrbidized borenium ions

Because the isomers have overlapping resonances in the ^{11}B NMR spectra, these control experiments were conducted in CD_2Cl_2 (DCM-d_2) and followed by ^{1}H NMR spectroscopy. Both **18c** and **19c** were thermally stable when heated alone in DCM-d_2 (40 ˚C, 6 h). In addition, addition *trans*-boralactone **18c** was also stable under the standard reaction conditions (TMSCl, DCM-d_2, 40 ˚C, 6 h). In contrast, exposure of *cis*-boralactone **19c** to the same conditions returned mostly **19c** (95%) alongside a small amount of *trans*-boralactone **18c** (5%). These experiments suggest that *cis/trans* isomerization is inefficient at best under the reaction conditions.

The small scale (0.1 mmol) procedure did not prove to be amenable to scale up, undoubtedly because the reliance on ambient water to generate HCl is ill-advised. This problem was solved simply by adding water to the reaction mixture. For example, in a 1 mmol (392 mg) scale reaction in the *N,N*-diisopropyl series, water (1.3 equiv) was added immediately after TMSCl (1.3 equiv), then the usual reaction and purification process was followed to provide *trans*-boralactone **18a** in 52% yield (175 mg) and *cis*-boralactone **19a** in 8% yield (27 mg). These yields are similar to the small scale yields in Figure 4.

A plausible mechanistic pathway to understand these results is shown in Figures 6 and 7. Figure 6 shows the stepwise mechanism with a focus on the various intermediates and on the stereochemistry of proton transfer. Figure 7 in turn focuses on the stereochemistry of the displacements at boron.

The process in Figure 6 starts with protonation (here illustrated with D^+) of one of the esters of NHC-borirane **6**. This provides activated cationic intermediate **25**, which in turn undergoes nucleophilic attack at boron by chloride to provide transient enol **26**. This enol could in principle adopt several conformers about the now rotatable CH–CH bond (formerly constrained by the borirane ring); however, inspection of the various open chain conformers of this bond did not readily account for the high degree of stereoselectivity that is observed in the tautomerization. It may be that this enol is constrained by an intramolecular hydrogen bond (as shown in **26**), and that proton transfer then occurs *trans* to the large NHC-BHCl group. This also explains the high stereoselectivity in the same direction for both deuterated products (because the boron substituent is large regardless of its relative configuration).

In any event, the experiments show that tautomerization largely forms **27**-*anti*, which in turn is in equilibrium with its conformer **27**-*eclipsed* (a transition state rather than an intermediate) by σ-bond rotation. Lactonization of **27**-*eclipsed* to give **29** is the second nucleophilic displacement at boron, this time with chloride as the leaving group.

Nucleophilic dealkylation of **28** by chloride is shown as the final step in Figure 6, and this is probably the way that boralactone **29** forms when R = Me or Et (S_N2 reaction). In contrast, when R = *t*-Bu, **29** is more likely formed by direct loss of *t*-butyl cation from **28** (S_N1 reaction). In addition, we can understand why the minor acid product **13** (9%) is isolated in the from the *t*-Bu ester **10c** but not from the methyl ester **10a** (see Table 3). This is a secondary product formed by acid-induced loss of the *t*-butyl group from the primary product **12c**.

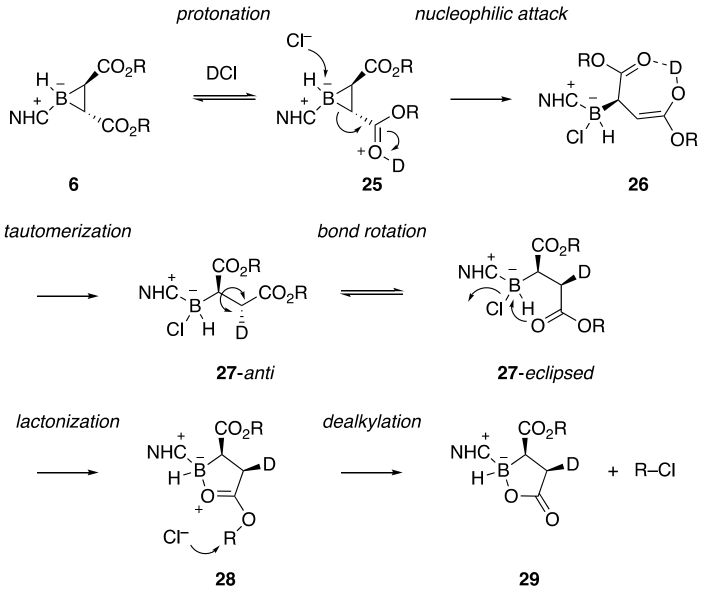


Figure 6. Stepwise mechanism for NHC-boralactone formation, illustrated with DCl to show stereoselective tautomerization

With respect to the configuration at boron, the two key steps in this multistep process are opening of the borirane and closure to form the boralactone, and stereochemical consequences of these steps are illustrated with Newman projections in Figure 7. The two esters in **6** are related by what is often called pseudo C2-symmetry, and are therefore diastereotopic. In Path A, protonation of one ester to give **30A** followed by nucleophilic scission of the adjacent borirane B–C bond by backside attack of chloride provides the *R*,R** isomer of boryl chloride **31** after tautomerization of the resulting ester enol. Next, intramolecular displacement of the chloride of *R*,R**-**31** by the same ester that departed provides the *trans*-isomer of lactone **32** after dealkylation. In Path B, the other ester is protonated to give **30B**, and chloride opening provides the *S*,R** isomer of the boryl chloride **31** in conformer "**a**". In turn, *S*,R**-**31a** engenders the *cis*-lactone isomer of **32** after chloride displacement and ester dealkylation.

Notice that the protonated precursor **30A** leads immediately to what is probably the low energy conformer of *R*,R**-**31** because this conformer has two gauche interactions (the other two staggered conformers have three), whereas the immediate boryl chloride product *S*,R**-**31a** from **30B** has three gauche interactions. The modest selectivity in favor of the *trans*-lactones in the *N,N*-dialkyl series can be understood because this difference is reflected to some extent in the energies of the transition states leading to the two diastereomers of **31**.

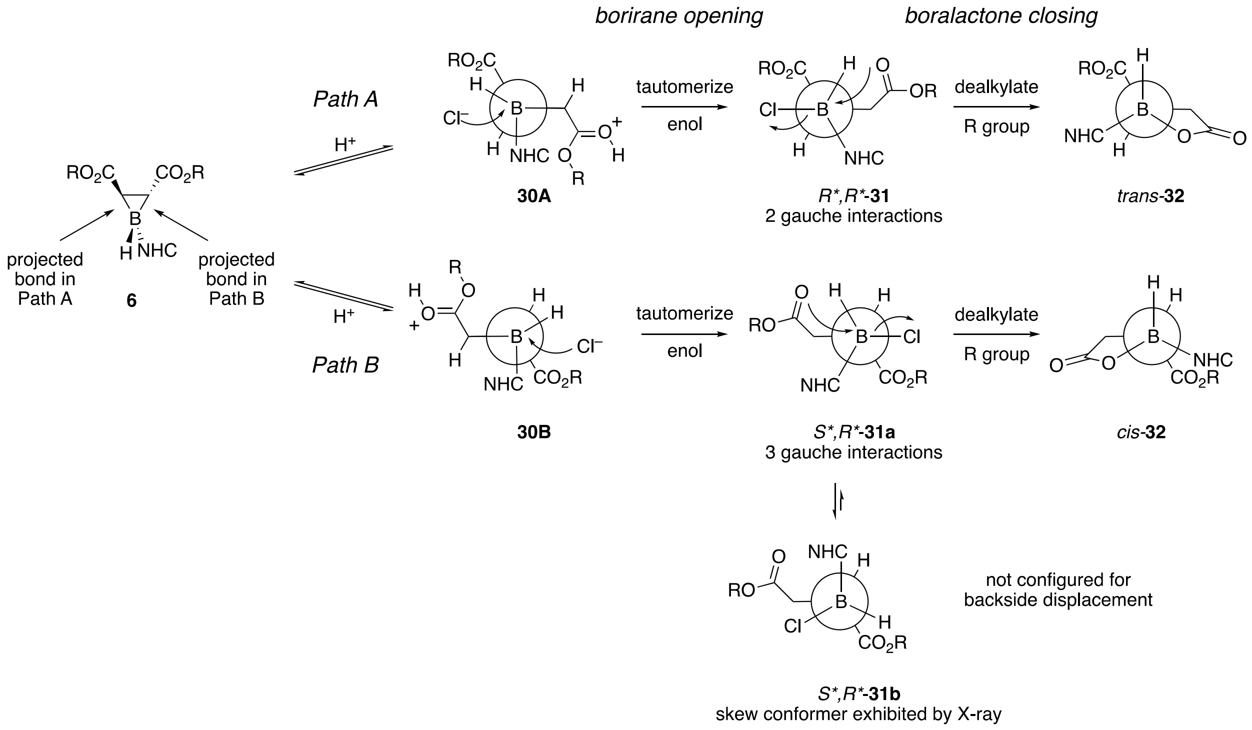


Figure 7. Newman projections of key intermediates in the substitution reactions at boron. Results suggest that both steps occur with inversion.

In addition, the conformer of *R*,R**-**31** with two gauche interactions is well oriented for ester displacement to give *trans*-**32**, which may explain why this diastereomer of the boryl chloride has not been observed. In contrast, the X-ray structures of **8a** and **11a** suggest that the epimeric boryl chlorides with *N,N*-diaryl groups favor a skew conformer *S*,R**-**31b** that is not properly oriented for backside displacement (because the chloride is roughly eclipsed to the C–C bond to connecting the displacing ester). Thus, the skew conformer of *S*,R**-**31b** has to go back uphill to the conformer *S*,R**-**31a** with three gauche interactions in order to form *cis*-**32**. In turn, *cis*-**32** is probably higher in energy than its *trans*-isomer. Together, these two effects may explain why the *S*R** diastereomer of **31** can be observed in some cases but the *R*,R**-isomer cannot. Indeed, the methyl and ethyl esters of the boryl chlorides **8a** and **11a** are analogs of *S*,R**-**31** with large N-aryl substituents (dipp and mesityl); they resist lactonization entirely and are stable to isolation.

Figure 7 shows a "double inversion" mechanism, which is rather common when carbon is the element undergoing the substitutions. The twist in this reaction is that a boron atom undergoes the two displacements with inversion. We deduce this from two different observations. First, we learned that boryl chlorides are precursors to boralactones from the ^{11}B NMR experiment in Scheme 1. However, this experiment does not directly confirm inversion since the configurations of the chloride and lactone intermediates cannot be confidently assigned by ^{11}B NMR chemical shifts alone. However, from the results in Tables 1 and 2, we know that the *S*,R**-boryl chloride **8a** is *not* the precursor of the *trans*-lactone **9a**. Further, the *S*,R**-boryl chloride **11a** is *not* the precursor of *trans*-boralactone **12a** (Table 3). This rules out boralactone formation by displacement with retention at boron, and in turn rules out both inversion/retention and double retention mechanisms. Displacements of some phosphine-boranes are known to occur with inversion,[14] but to the best of our knowledge this is the first evidence that NHC-borane displacements also occur with inversion.

Conclusions

We have described the first ring-opening reactions of ligated boriranes (boracyclopropanes). Treatment of readily available NHC-boriranes bearing ester substituents on the borirane ring with in situ generated HCl in CH_2Cl_2 provides stable γ-NHC-bora-γ-lactones in isolated yields ranging from 40–73%. α,β-Unsaturated-γ-NHC-bora-γ-lactones have recently been made by 5-

endo radical cyclizations of ester substituted alkenyl NHC-boranes,[11c] and the ionic reactions of the NHC-boriranes reported herein now provide saturated NHC-boralactone products.

The borirane opening reactions occur through 1,3-addition of HCl across a B–C bond of the NHC-borirane followed by tautomerization a transient ester enol to form a ring-opened NHC-boryl chloride. This is followed by lactonization with chloride displacement and finally dealkylation of the ester substituent.

In the *N,N*-diaryl series, one of the two isomeric NHC-boryl chlorides resists lactonization and can be isolated by flash chromatography. The other isomer in *N,N*-diaryl series and both isomers in the *N,N*-dialkyl series are thought to be intermediates on the way to stable *trans*- and *cis*-NHC-boralactones. Experimental evidence suggests that both the borirane ring opening reaction and the boralactonization reaction occur with inversion at boron.

The reaction products have been well characterized by seven X-ray crystal structures, with four featured in the paper (Figures 2 and 5) and the other three in the Supporting Information. These include two boryl chlorides, three *trans*-boralactones, and two *cis*-boralactones. The crystal structures of the boryl chlorides in particular help to understand why the enol tautomerization step is highly stereoselective, as shown by a DCl labeling experiment (Table 2).

Finally, ring opening reactions of cyclopropanes, aziridines and oxiranes have long been a staple of organic chemistry. Taken together, the recent discoveries of stable ligated boriranes[6,7] and this report on ring-opening reactions to give stable products suggest that ring opening reactions of boriranes may be poised to take a place alongside the reactions of their three-membered ring nuclear analogs. In particular, while the analogy is admittedly distant and therefore limited, ring opening reactions of donor-acceptor cyclopropanes might serve as starting points for discovering new reactions of NHC-boriranes that bear at least one electron withdrawing group.

ASSOCIATED CONTENT

Supporting Information. Contains experimental procedures and compound characterization data for all new compounds along with copies of NMR spectra and cif files of all crystal structures. This material is available free of charge via the Internet at http://pubs.acs.org.

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References and Notes

1. The following paper has a nice summary of known boriranes: Krasowska, M.; Bettinger, H. F., Computational Study of the Isomerization Reactions of Borirane. *J. Org. Chem.* **2018**, *83*, 1804-1809.

2. Dewar, M. J. S.; Kirschner, S., Mindo [Modified Intermediate Neglect of Differential Overlap]/2 Study of Aromatic ("Allowed") Electrocyclic Reactions of Cyclopropyl and Cyclobutene. *J. Am. Chem. Soc.* **1971**, *93*, 4290-4291.

3. Denmark, S. E.; Nishide, K.; Faucher, A. M., On the Generation and Configurational Stability of (2*S*,3*S*)-1,2,3-Triphenylborirane. *J. Am. Chem. Soc.* **1991**, *113*, 6675-6676.

4. (a) Murphree, S. S., Three-Membered Heterocycles. Structure and Reactivity. In *Modern Heterocyclic Chemistry*, Alvarez-Builla, J.; Vaquero, J. J.; Barluenga, J., Eds. Wiley-VCH: Weinheim, 2011; pp 11-162; (b) Schneider, T. F.; Kaschel, J.; Werz, D. B., A New Golden Age for Donor-Acceptor Cyclopropanes. *Angew. Chem., Int. Ed.* **2014**, *53*, 5504-5523.

5. De Vries, T. S.; Prokofjevs, A.; Vedejs, E., Cationic Tricoordinate Boron Intermediates: Borenium Chemistry from the Organic Perspective. *Chem. Rev.* **2012**, *112*, 4246-4282.

6. (a) Braunschweig, H.; Claes, C.; Damme, A.; Dei; Dewhurst, R. D.; Horl, C.; Kramer, T., A Facile and Selective Route to Remarkably Inert Monocyclic NHC-Stabilized Boriranes. *Chem. Commun.* **2015**, *51*, 1627-1630; (b) Bissinger, P.; Braunschweig, H.; Kraft, K.; Kupfer, T., Trapping the Elusive Parent Borylene. *Angew. Chem. Int. Ed.* **2011**, *50*, 4704-4707; (c) Curran, D. P.; Boussonnière, A.; Geib, S. J.; Lacôte, E., The Parent Borylene: Betwixt and Between. *Angew. Chem. Int. Ed.* **2012**, *51*, 1602-1605.

7. (a) Walton, J. C.; McFadden, T. R.; Curran, D. P., Generation and Structure of Unique Boriranyl Radicals. *J. Am. Chem. Soc.* **2017**, *139*, 16514-16517; (b) McFadden, T. R.; Fang, C.; Geib, S. J.; Merling, E.; Liu, P.; Curran, D. P., Synthesis of Boriranes by Double Hydroboration Reactions of N-Heterocyclic Carbene Boranes and Dimethyl Acetylenedicarboxylate. *J. Am. Chem. Soc.* **2017**, *139*, 1726-1729.

8. (a) Nesterov, V.; Reiter, D.; Bag, P.; Frisch, P.; Holzner, R.; Porzelt, A.; Inoue, S., NHCs in Main Group Chemistry. *Chem. Rev.* **2018**, *118*, 9678-9842; (b) Curran, D. P.; Solovyev, A.; Makhlouf Brahmi, M.; Fensterbank, L.; Malacria, M.; Lacôte, E., Synthesis and Reactions of N-Heterocyclic Carbene Boranes. *Angew. Chem. Int. Ed.* **2011**, *50*, 10294-10317.

9. Yu, M.; Pagenkopf, B. L., Recent Advances in Donor-Acceptor (DA) Cyclopropanes. *Tetrahedron* **2005**, *61*, 321-347.

10. (a) Zhang, L.; Cheng, J.; Carry, B.; Hou, Z., Catalytic Boracarboxylation of Alkynes with Diborane and Carbon Dioxide by an N-Heterocyclic Carbene Copper Catalyst. *J. Am. Chem. Soc.* **2012**, *134*, 14314-14317; (b) Barnett, B. R.; Moore, C. E.; Rheingold, A. L.; Figueroa, J. S., Frustrated Lewis Pair Behavior of Monomeric (Boryl)Iminomethanes Accessed from Isocyanide 1,1-Hydroboration. *Chem. Commun.* **2015**, *51*, 541-544.

11. (a) Bohnke, J.; Braunschweig, H.; Dellermann, T.; Ewing, W. C.; Hammond, K.; Jimenez-Halla, J. O.; Kramer, T.; Mies, J., The Synthesis of $B_2(Sidip)_2$ and Its Reactivity between the Diboracumulenic and Diborynic Extremes. *Angew. Chem. Int. Ed.* **2015**, *54*, 13801-13805; (b) Braunschweig, H.; Dellermann, T.; Dewhurst, R. D.; Ewing, W. C.; Hammond, K.; Jimenez-Halla, J. O. C.; Kramer, T.; Krummenacher, I.; Mies, J.; Phukan, A. K.; Vargas, A., Metal-Free Binding and Coupling of Carbon Monoxide at a Boron–Boron Triple Bond. *Nat. Chem.* **2013**, *5*, 1025-1028; (c) Dai, W.; McFadden, T. R.; Curran, D. P.; Fruchtl, H. A.; Walton, J. C., 5-Endo Cyclizations of NHC-Boraallyl Radicals Bearing Ester Substituents. Characterization of Derived 1,2-Oxaborole Radicals and Boralactones. *J. Am. Chem. Soc.* **2018**, *140*, 15868-15875.

12. Solovyev, A.; Chu, Q.; Geib, S. J.; Fensterbank, L.; Malacria, M.; Lacôte, E.; Curran, D. P., Substitution Reactions at Tetracoordinate Boron: Synthesis of N-Heterocyclic Carbene Boranes with Boron-Heteroatom Bonds. *J. Am. Chem. Soc.* **2010**, *132*, 15072-15080.

13. (a) Merling, E., Halogen Exchanges with Carbene Boranes. *Ph.D. Thesis, University of Pittsburgh* **2015**, 19-36 (download at http://d-scholarship.pitt.edu/24858/); (b) Pak, Y. L.; Park, S. J.; Wu, D.; Cheon, B.; Kim, H. M.; Bouffard, J.; Yoon, J., N-Heterocyclic Carbene Boranes as Reactive Oxygen Species-Responsive Materials: Application to the Two-Photon Imaging of Hypochlorous Acid in Living Cells and Tissues. *Angew. Chem. Int. Ed.* **2018**, *57*, 1567-1571.

14. (a) Vedrenne, P.; Le Guen, V.; Toupet, L.; Le Gall, T.; Mioskowski, C., Synthesis of Diastereomerically Pure Monoisopinocampheylcyanoborane Adducts of Phosphines. Direct Evidence of an S_N2 Substitution at a Boron Atom. *J. Am. Chem. Soc.* **1999**, *121*, 1090-1091; (b) Imamoto, T.; Morishita, H., An Enantiomerically Pure Tetracoordinate Boron Compound: Stereochemistry of Substitution Reactions at the Chirogenic Boron Atom. *J. Am. Chem. Soc.* **2000**, *122*, 6329-6330.

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