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Reductive Openings of Acetals: Explanation of Regioselectivity in Borane Reductions by Mechanistic Studies

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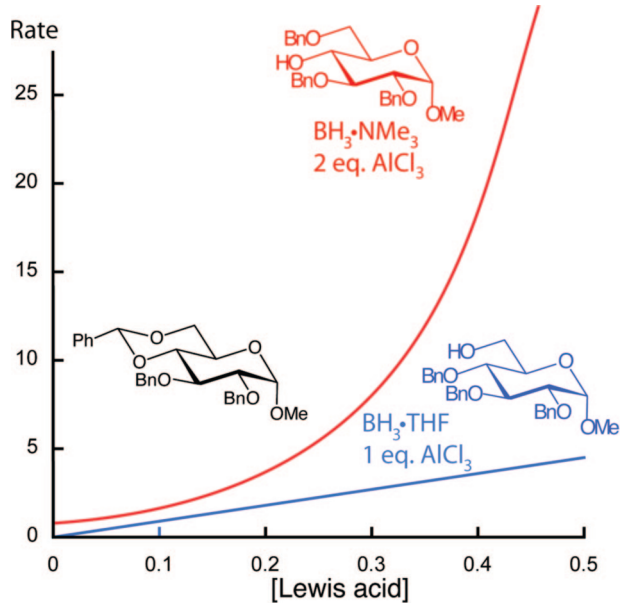

The mechanisms of regioselective reductive openings of acetals were investigated in several model systems by a combination of Hammett plots, kinetic experiments, density functional calculations, and ^{11}B NMR. The regioselectivity of borane reductions of cyclic acetals can be controlled by the choice of borane. Lewis acid activation of $BH_3 \cdot NMe_3$ increases the reaction rate and renders the borane the most electrophilic species, which associates to the more electron-rich oxygen of the acetal. In contrary, without activation, the regioselectivity is instead directed by the Lewis acid, as exemplified by the reaction with $BH_3 \cdot THF$.

Introduction

In 1951, Doukas and Fontaine opened the acetal diosgenin using $LiAlH_4$ and HCl, to give dihydrodiosgenin.[1] Later investigations established the active reagent in the reduction as $LiAlH_4-AlCl_3$ and the chemo-, stereo-, and regioselectivity of reductive openings of cyclic acetals were intensively explored.[2] The methodology turned out to be especially fruitful in carbohydrate chemistry, where reductive openings of acetals facilitated protective group manipulation.[3]

The harsh conditions, that made the use of many functionalities impossible, turned out a major problem. Thus, Garegg and Hultberg introduced the reagent combination $NaCNBH_3-HCl-THF$ which, interestingly, gave the opposite regioselectivity compared to the original method.[4] In order to get back to the original regioselectivity the Garegg group turned

(1) Doukas, H. M.; Fontaine, T. D. *J. Am. Chem. Soc.* **1951**, *73*, 5917–5918.
(2) (a) Eliel, E. L.; Rerick, M. *J. Org. Chem.* **1958**, *23*, 1088. (b) Eliel, E. L.; Badding, V. G.; Rerick, M. N. *J. Am. Chem. Soc.* **1962**, *84*, 2371–2377.
(3) (a) Bhattacharjee, S. S.; Gorin, P. A. J. *Can. J. Chem.* **1969**, *47*, 1195–1206. (b) Lipták, A.; Jodál, I.; Nánási, P. *Carbohydr. Res.* **1975**, *44*, 1–11.

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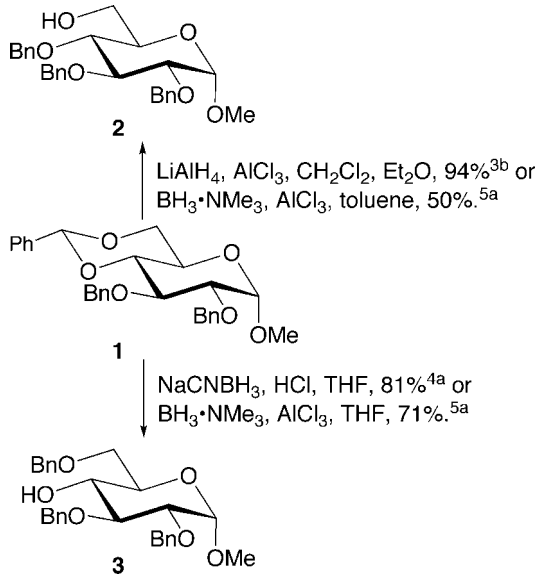
SCHEME 1. Examples of Regioselective Openings of Benzylidene Acetals



their attention to boranes. They found that the reagent combination $BH_3 \cdot NMe_3-AlCl_3$ gave different regioselectivity in different solvents, i.e., 6-*O*-benzyl ethers in THF and 4-*O*-benzyl ethers in toluene or dichloromethane/ether mixtures. Due to degradation, reactions in toluene usually gave low yields. The methods are summarized in Scheme 1.

Despite the numerous reports on acid-mediated nucleophilic addition to acetals,[6] and the immense importance of regioselective reductive openings of acetals for organic chemistry in general and for carbohydrate chemistry in particular, the underlying principles for the regioselectivity are still not understood.[7] However, one mechanism, proposed by Garegg (Scheme 2),[8] explain the regioselective outcome by the difference in steric bulk between $AlCl_3$ and a proton. This means that in the original method, $AlCl_3$ is supposedly first coordinated to the sterically less demanding oxygen at position 6 (path A). In contrary, in the $NaCNBH_3-HCl$ method the proton, which is not restricted by steric effects, coordinates to *O*-4 to give the more stable oxocarbenium ion at *C*-6 (path B).

There are several problems associated with this mechanistic explanation. The major issue is the problem to explain the regiochemical outcome of the reaction with $BH_3 \cdot NMe_3-AlCl_3$ in THF, which follows path B, despite the obvious conclusion that the strongly solvated $AlCl_3 \cdot THF$ would preferably associate with the less sterically hindered *O*-6 to give the 4-*O*-benzyl ether.[5] This mechanism also fails to rationalize why $Cu(OTf)_2$ gives the 4-*O*-benzyl ether in combination with $BH_3 \cdot THF$ and the 6-*O*-benzyl ether with $BH_3 \cdot NMe_3$.[9]

Results

In our investigations of reductive openings of compound **1** we found that, irrespective of the Lewis acid used ($AlCl_3$, $BF_3 \cdot OEt_2$, $In(OTf)_3$, $Cu(OTf)_2$, AgOTf), the 4-*O*-benzyl ether **2** was formed using $BH_3 \cdot THF$, and the 6-*O*-benzyl ether **3** was isolated using $BH_3 \cdot NMe_3$ as reducing agent, in THF as solvent. To our surprise, reductions using $BH_3 \cdot NMe_3$ were generally faster compared to reactions using $BH_3 \cdot THF$, despite the general belief that $BH_3 \cdot THF$ is the more reactive reagent.[10]

A. Lewis Acid Activation of $BH_3 \cdot NMe_3$. We have previously introduced benzylic−phenolic acetals for the synthesis of fluorescently labeled probes.[11] These acetals were opened under reductive conditions to yield double benzylic ethers, and we realized that these compounds form an excellent model system to investigate regioselective reductive openings of cyclic acetals. Compounds **4a**−**i** (Scheme 3) were thus synthesized from the corresponding dimethyl acetals and opened using $BH_3 \cdot NMe_3-AlCl_3$ in THF at 0 °C.[12] In all cases, double benzylic ethers (compounds **5a**−**i**) were isolated as the single products.

The proposed mechanism for reductive opening of acetals presumes coordination of the Lewis acid to one of the oxygen atoms, according to path A in Scheme 4, followed by reduction of either the unopened acetal or the oxocarbenium ion. Irrespective of mechanistic pathway, the Lewis acid must associate with the oxygen that will become a free hydroxyl group. Since only compounds **5a**−**i** were isolated, the Lewis acid must have coordinated to the phenolic oxygen.

The electrostatic potentials of the oxygen atoms in compounds **4a**−**i** were calculated using density functional theory at the B3LYP/6-31G* level.[13] Throughout the series, the benzylic oxygen showed the highest electrostatic potential. Interestingly, the benzylic oxygen is thus both the more basic and also the less sterically hindered oxygen atom, but not the one chosen by the Lewis acid. With respect to these calculations, there are two alternative explanations: (i) the relative energies of the two oxocarbenium ions direct the regiochemistry or (ii) the outcome is instead directed by initial coordination of the borane, followed by coordination of the Lewis acid and subsequent reduction (Scheme 4, path B).

To investigate these two options, we calculated the energy of BH_3 associated to the oxygen atoms of compound **4a**, generating structures **7a** and **7b**, as well as the relative energies of two analogous oxocarbenium ions, i.e., structures **8a** and **8b** (Chart 1).[14] From the energy differences, the ratios were calculated using the Boltzmann distribution and showed exclusive preference for **7a** and **8a**. This means that the most stable oxocarbenium ion and the most stable boron complex would lead to the same product (i.e., compound **5a**). As a control, we calculated the energy of $AlCl_3$ associated to the two oxygen

(4) (a) Garegg, P. J.; Hultberg, H. *Carbohydr. Res.* **1981**, *93*, C10–C11. (b) Garegg, P. J.; Hultberg, H.; Wallin, S. *Carbohydr. Res.* **1982**, *108*, 97–101.

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(6) (a) Sammakia, T.; Smith, R. S. *J. Am. Chem. Soc.* **1992**, *114*, 10998–10999. (b) Bartels, B.; Hunter, R. *J. Org. Chem.* **1993**, *58*, 6756–6765. (c) Denmark, S. E.; Almstead, N. G. *J. Am. Chem. Soc.* **1991**, *113*, 8089–8110. (d) Mori, I.; Ishihara, K.; Flippin, L. A.; Nozaki, K.; Yamamoto, H.; Bartlett, P. A.; Heathcock, C. H. *J. Org. Chem.* **1990**, *55*, 6107–6115.

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(8) Garegg, P. J. In *Preparative Carbohydrate Chemistry*; Hanessian, S., Ed.; Marcel Dekker: New York, 1996; pp 53−67..

(9) Shie, C.-R.; Tzeng, Z.-H.; Kulkarni, S. S.; Uang, B.-J.; Hsu, C.-Y.; Hung, S.-C. *Angew. Chem., Int. Ed.* **2005**, *44*, 1665–1668.

(10) Smith, K.; Pelter, A. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Vol. 8, p 708

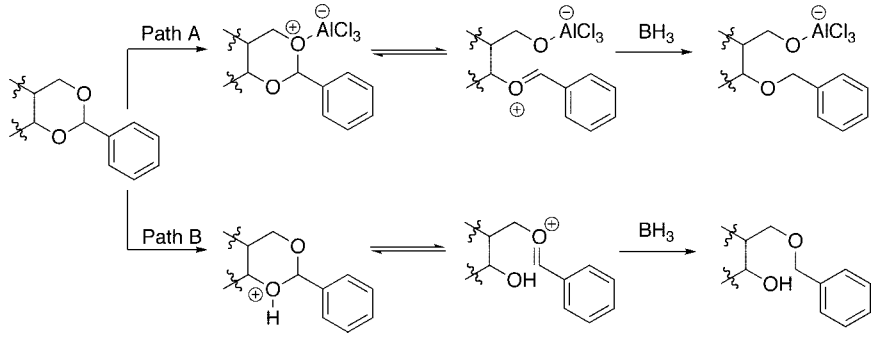
(11) Johnsson, R.; Mani, K.; Cheng, F.; Ellervik, U. *J. Org. Chem.* **2006**, *71*, 3444–3451.

(12) Experimental details can be found in the Supporting Information.

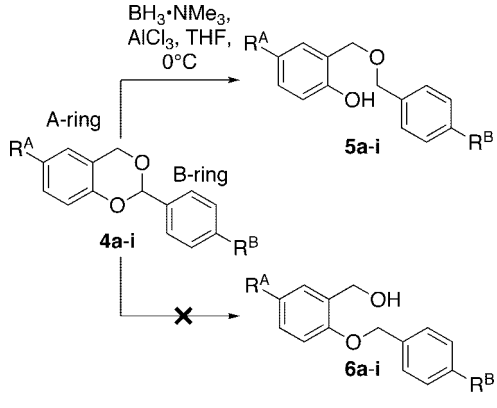
(13) Spartan '02 for Macintosh, Wavefunction, Inc., Irvine, CA.

(14) Jaguar, version 7.0, Schrödinger, LLC, New York, NY, 2007.

SCHEME 2. Mechanistic Pathways Proposed for Regioselective Reductive Opening of Cyclic Acetals



SCHEME 3. Reductive Opening of Phenolic−Benzylic Acetals



a: $R^A = R^B = H$ **f**: $R^A = H$, $R^B = NO_2$
b: $R^A = NO_2$, $R^B = H$ **g**: $R^A = H$, $R^B = Br$
c: $R^A = Br$, $R^B = H$ **h**: $R^A = H$, $R^B = Me$
d: $R^A = Me$, $R^B = H$ **i**: $R^A = H$, $R^B = OMe$
e: $R^A = OMe$, $R^B = H$

atoms of compound **4a**. Not surprisingly, we found a 100:0 distribution of the Lewis acid associated with the benzylic oxygen.

To distinguish between the two mechanistic possibilities, we turned to Hammett plots. Compounds **4a**−**i** were subjected to $BH_3 \cdot NMe_3$−$AlCl_3$ in THF, and the rate constants were determined by initial-rate analysis over the linear part of the plots (Figure 1).

The Hammett correlation for the A ring was best fitted to normal σ_{para}-parameters, while the correlation for the B ring best fitted to σ^+-parameter. Both Hammett plots resulted in negative ρ values with a more pronounced effect for the B ring compared to the A ring. This indicates that the buildup of a positive charge of the acetal carbon is more important than the charge of the phenolic oxygen, which in turn implies a diminished importance of the oxocarbenium ion pathway.

To gain further insight in the reaction mechanism, the concentrations of **4a**, $BH_3 \cdot NMe_3$, and $AlCl_3$ were systematically varied and the initial-rate kinetics determined (Figure 2).

From these data, we conclude that the reaction is first order with respect to **4a**. Interestingly, the kinetic data for variation of $[AlCl_3]_0$ show that the reaction is of higher order (Figure 2b, dotted line indicates first order kinetics). One possible explanation is activation of the borane by the Lewis acid, a concept suggested, but not further investigated by Brown.[15] To investigate this option, we estimated the energies for formation of different complexes as shown in Scheme 5. The dissociation energies for known complexes (Table 1), in combination with calculated data for formation of complexes of **4a** with the electrophiles (i.e., BH_3 and $AlCl_3$), indicate that reactions a and b are thermodynamically unfavorable (by 32 and 45 kJ/mol, respectively), whereas reaction c is thermoneutral.[12,14] The driving force is the formation of the highly stabilized $AlCl_3 \cdot NMe_3$.

Activation of the borane by $AlCl_3$ can also explain the complex kinetics shown by variation of $[BH_3 \cdot NMe_3]_0$. At low amounts of borane, the relative amount of $AlCl_3$ is high (7:1), resulting in unusually high reaction rates.

Finally, to examine the fate of the borane in the reaction we performed a ^{11}B NMR study. Compound **4a** was dissolved in THF-d_8 and subjected to the reductive conditions. At the beginning of the reaction, only $BH_3 \cdot NMe_3$ (quartet at −7.5 ppm) can be seen (Figure 3). Over the course of the reaction, a new peak (triplet at 8 ppm) appears, which corresponds to a BH_2 group, probably associated with oxygen.[17] The species Me_3NBH_2 would have appeared at 38 ppm, where no peak was observed. This clearly shows that the borane is cleaved from the amine, possibly by interaction with the Lewis acid.

SCHEME 4. Possible Mechanistic Pathways for Regioselective Reductive Opening of Phenolic−Benzylic Acetals

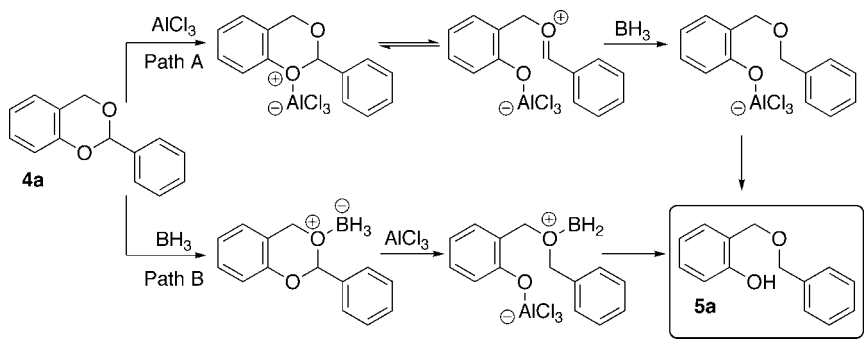
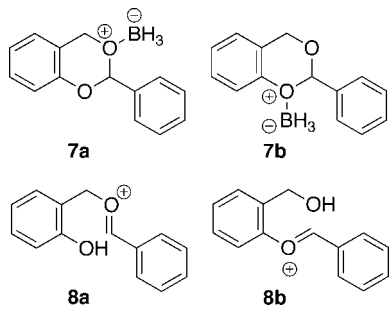


CHART 1. Energies for Compounds 7 and 8 Calculated Using Density Functional Theory at the B3LYP/6-31G Level**



B. Regioselectivity by Choice of Borane. Due to unfavorable thermodynamics, it is reasonable to assume that $BH_3 \cdot THF$ is not activated by the Lewis acid. Thus, in order to evaluate the differences between $BH_3 \cdot NMe_3$ and $BH_3 \cdot THF$, we turned to catechols, where it is possible to fine tune the stereoelectronics without interference of steric effects. We therefore synthesized catechol acetals and subjected these to the reductive conditions (Scheme 6). Generally, these acetals were more difficult to open, compared to the six-membered rings, and the analogous nitro compound was inert under these conditions.

Compound **9a** was opened using $BH_3 \cdot NMe_3$ to give a mixture of **10a**:**11a** in a 34:66 ratio. A similar opening of **9b**, carrying a less electron-donating methyl group, gave a 47:53 distribution of **10b**:**11b** (duplicate reactions). Interestingly, opening of **9a** and **9b** using $BH_3 \cdot THF$ gave a 65:35 mixture of **10a**:**11a** and a 53:47 mixture of **10b**:**11b**, i.e., the opposite results compared to $BH_3 \cdot NMe_3$.

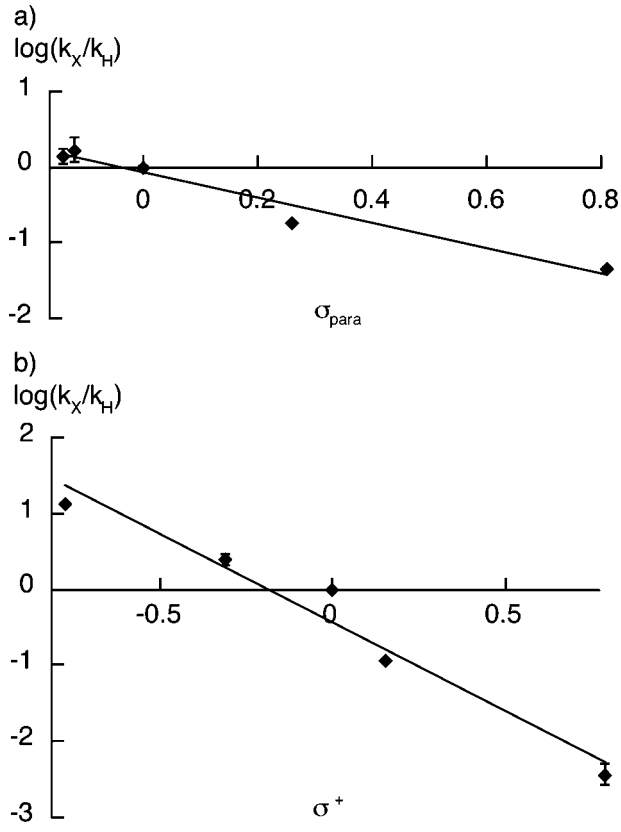


FIGURE 1. Hammett plots of (a) substituent variation in the A ring and (b) substituent variation in the B ring. Error bars show standard deviation.

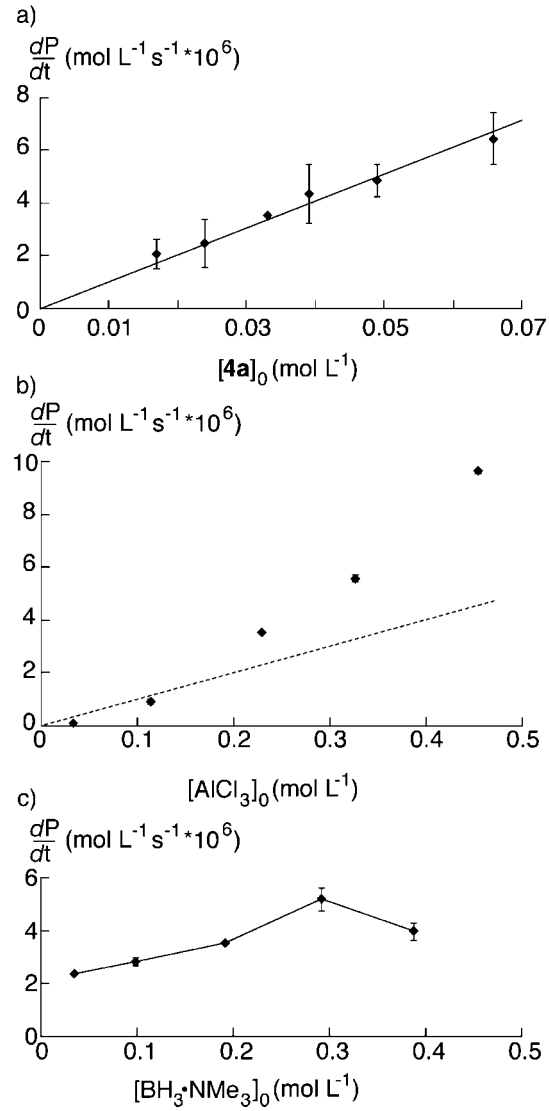


FIGURE 2. Initial rate analysis of the formation of product (P). Variation of (a) $[\mathbf{4a}]_0$, (b) $[AlCl_3]_0$, (c) $[BH_3 \cdot NMe_3]_0$. When constant $[\mathbf{4a}] = 0.033$ mol L^{-1}, $[AlCl_3] = 0.23$ mol L^{-1}, $[BH_3 \cdot NMe_3] = 0.20$ mol L^{-1}. Error bars show standard deviation.

SCHEME 5. Possible Reactions between Reactive Species in the Mixture[a]

a) **4a** + $BH_3 \cdot NMe_3$ ⇌ **4a**$\cdot BH_3$ + NMe_3

b) **4a** + $AlCl_3 \cdot THF$ ⇌ **4a**$\cdot AlCl_3$ + THF

c) **4a** + $BH_3 \cdot NMe_3$ + $AlCl_3 \cdot THF$ ⇌

⇌ **4a**$\cdot BH_3$ + THF + $AlCl_3 \cdot NMe_3$

[a] While reactions a and b are thermodynamically unfavorable, reaction c is thermoneutral.

The energies of possible reactive intermediates (Chart 2) were calculated using density functional theory at the B3LYP/6-31G** level, and ratios (leading to **10** and **11**) were estimated using the Boltzmann distribution. The data are summarized in Table 2.[14]

These data show a remarkable agreement with initial coordination of the borane in the case of $BH_3 \cdot NMe_3$ as reducing agent (i.e., **12**:**13**) and association of the Lewis acid in the case

TABLE 1. Dissociation Energies for Lewis Acid−base Complexes[16]

complex	dissociation energy (kJ/mol)
$BH_3 \cdot NMe_3$	160
$AlCl_3 \cdot NMe_3$	199
$AlCl_3 \cdot THF$	90
$AlCl_3 \cdot 2THF$	132

of $BH_3 \cdot THF$ (i.e., **15**:**14**). It seems less likely that the outcome is directed by the oxocarbenium ions (i.e., **17**:**16**).

The results can be explained by $BH_3 \cdot NMe_3$ being activated by $AlCl_3$, and that this activation results in both higher reaction rates and also, somewhat surprising, that the borane is the most electrophilic species and thus directs the reactivity. It is also reasonable to assume that no such activation would occur in the reaction with $BH_3 \cdot THF$ and that the selectivity instead depends on the Lewis acid, similar to the earlier proposed mechanism.

To shed further light on the mechanism of reductive opening of carbohydrate benzylidene acetals, we investigated the reaction kinetics with respect to $[AlCl_3]_0$, in the openings of compound **1**, using $BH_3 \cdot NMe_3$ (to give **3**) and $BH_3 \cdot THF$ (to give **2**). The reactions were monitored by quantitative TLC, and the initial rate kinetics were determined (Figure 4).[18]

We conclude that reductive opening of compound **1** follows first order kinetics using $BH_3 \cdot THF$, but higher order kinetics using $BH_3 \cdot NMe_3$. This is in full agreement with our mechanistic proposal, where the activation of $BH_3 \cdot NMe_3$ requires a second equivalent of Lewis acid compared to the reaction using $BH_3 \cdot THF$. The regioselectivity is directed by association of the most electrophilic species (i.e., BH_3 or $AlCl_3$ depending on activation) to the most electron-rich oxygen.

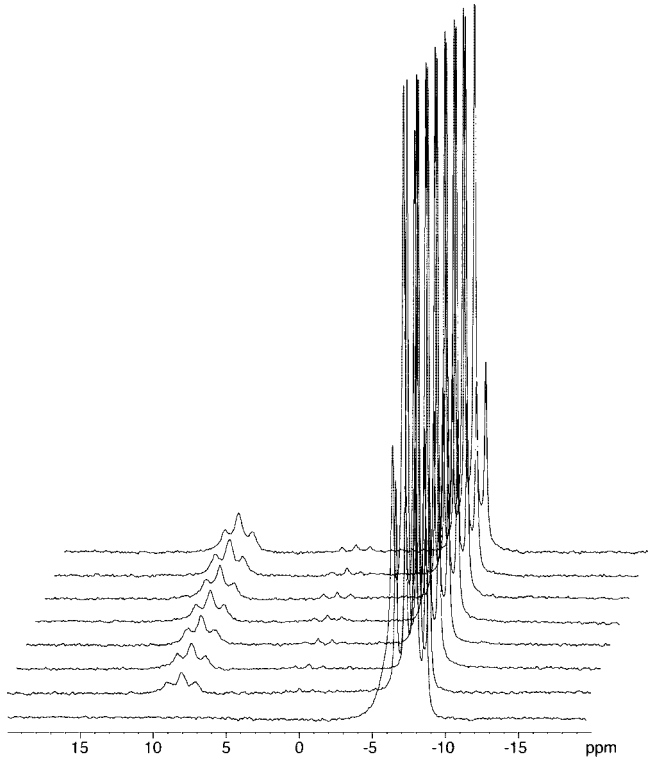


FIGURE 3. Stacked ^{11}B NMR spectra of the reductive opening of compound **4a** (0−45 min).

SCHEME 6. Reductive Opening of Catechol Acetals

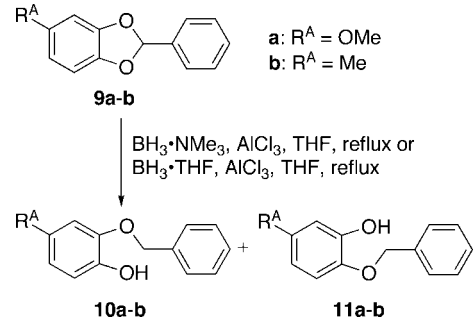


CHART 2. Possible Reactive Intermediates

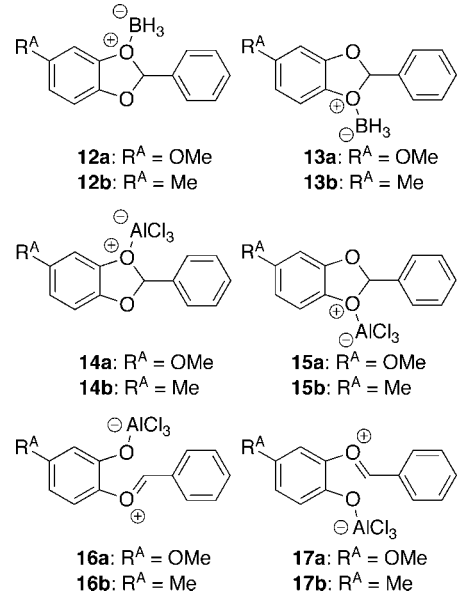


TABLE 2. Experimental and Calculated Ratios for Reductive Opening of Compounds 12−17

	acetal **9a**	acetal **9b**
experimental ratio[a] ($BH_3 \cdot NMe_3$)	34:66	47:53
experimental ratio[a] ($BH_3 \cdot THF$)	65:35	53:47
calculated ratio (**12**:**13**)[b]	35:65	46:54
calculated ratio (**15**:**14**)[b]	70:30	52:48
calculated ratio (**17**:**16**)[b]	2:98	22:78

[a] **10**:**11**. [b] The ratios are calculated to indicate the formation of **10**:**11**.

Discussion

With these observations, we propose a mechanism for reductive openings of acetals using $BH_3 \cdot NMe_3$ in THF, where the Lewis acid activates the borane complex and the more electron-rich oxygen of the acetal associate with the borane (Scheme 7). The reduction takes place by activation of the other oxygen by a second molecule of $AlCl_3$, which explains the higher reaction order.

Since the introduction of reductive openings of benzylidene acetals, a plethora of reagent combinations have been developed. The methods are summarized in Table 3.

From the data in Table 3 we conclude that $BH_3 \cdot THF$ generally gives reductive openings to the free 6-hydroxyl (i.e.,

(15) Brown, H. C.; Murray, L. T. *Inorg. Chem.* **1984**, *23*, 2746–2753.

(16) (a) Jonas, V.; Frenking, G.; Reetz, M. T. *J. Am. Chem. Soc.* **1994**, *116*, 8741–8753. (b) Richards, R. L.; Thompson, A. *J. Chem. Soc. A* **1967**, 1244–1248. (c) Rablen, P. R. *J. Am. Chem. Soc.* **1997**, *119*, 8350–8360.

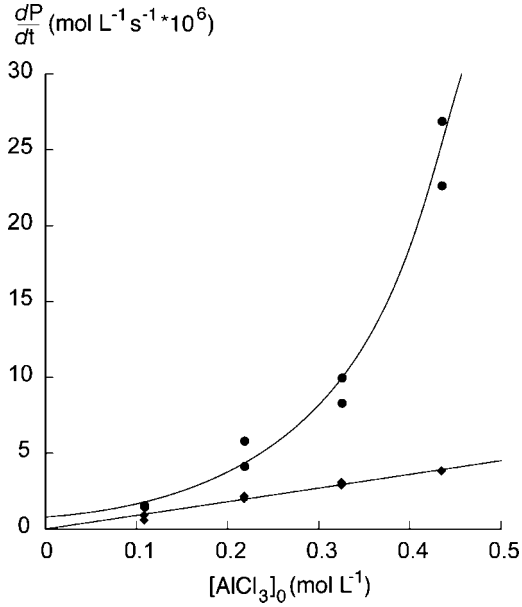
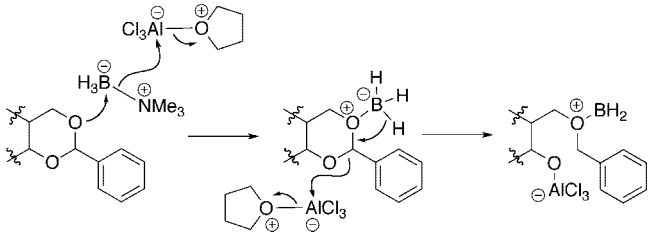


FIGURE 4. Initial rate analysis for the formation of compound **2** using $BH_3 \cdot THF$ (diamonds) or **3** using $BH_3 \cdot NMe_3$ (circles). $[\mathbf{1}]_0 = 0.054$ mol L^{-1}, $[BH_3 \cdot NMe_3]_0 = [BH_3 \cdot THF]_0 = 0.217$ mol L^{-1}. All reactions were performed in duplicate.

SCHEME 7. Proposed Mechanism for Lewis Acid Activation of Borane Acetal Openings Using $BH_3 \cdot NMe_3$



compound **2**). $BH_3 \cdot Me_2S$ seems to be a borderline case, while $BH_3 \cdot NMe_3$ (Table 3 and our data) gives the free 4-hydroxyl (**3**) in THF. When the reactions are performed in nonpolar solvents, such as toluene or CH_2Cl_2, the selectivities are probably directed exclusively by the Lewis acid, but the higher reactivity of the unsolvated electrophiles results in degradation and unselective reactions.[5]

It is reasonable to assume that the active borane in other methods actually is a borane−solvent complex. For example, a solution of $BH_3 \cdot THF$ can be formed by reaction of $NaBH_4$ with $AlCl_3$ in THF or by addition of $BF_3 \cdot OEt_2$ to $LiAlH_4$. In a similar way HCl would activate $NaCNBH_3$. Interestingly, $LiAlH_4$ reacts with $AlCl_3$ in ether solvents to give AlH_3, which reacts similarly to BH_3, to explain the selectivity in the original method for reductive openings. Finally, DIBAL can act as both Lewis acid and reducing agent in these reactions.

TABLE 3. Examples of Reagents for Reductive Opening of 1

conditions	yield **2**:**3** (%)	ref
$BH_3 \cdot THF$, Bu_2BOTf, THF/CH_2Cl_2, 0 °C, 1 h	87:0	19
$BH_3 \cdot THF$, $Cu(OTf)_2$, THF/CH_2Cl_2, rt, 45 min	94:0	9
$BH_3 \cdot THF$, $CoCl_2$, THF, rt, 10 min	100:0	20
$BH_3 \cdot THF$, M(OTf)n,[a] CH_2Cl_2, rt, 3−5 h	87−94:0	21
$BH_3 \cdot Me_2S$, $Cu(OTf)_2$, THF, rt, 10 h	78:3	9
$BH_3 \cdot Me_2S$, $BF_3 \cdot Et_2O$, CH_2Cl_2, 0 °C	62:20	22
$BH_3 \cdot Me_3N$, $Cu(OTf)_2$, THF/CH_2Cl_2, rt, 25 h	0:40	9
$BH_3 \cdot Me_2NH$, $BF_3 \cdot Et_2O$, CH_2Cl_2, 0 °C	73:3	23
$BH_3 \cdot Me_2NH$, $BF_3 \cdot Et_2O$, CH_3CN, 0 °C	55:30	23
9-BBN, $Cu(OTf)_2$, THF, rt, 27	40:0	9
Me_2EtSiH, $Cu(OTf)_2$, CH_3CN, 0 °C, 30 min	0:84	9
PMHS,[b] $AlCl_3$, Et_2O/CH_2Cl_2, rt, 12 h	80:0	24
DIBAL, CH_2Cl_2, 0 °C, 6 h	75:8	25

[a] M = V(O), Sc, Pr, Nd, Sm, Eu, Gd. [b] Polymethylhydrosiloxane.

Conclusions

To summarize, Lewis acid activation of the borane complex renders the borane the most electrophilic species, which associates to the more electron-rich oxygen of the acetal (Scheme 8, path B). In contrary, without activation, the regioselectivity is instead directed by the Lewis acid (path A).

Experimental Section

For general experimental details, synthesis of all starting materials, and kinetic data see the Supporting Information.

General Procedure for Hammett Plots. Compounds **4a**−**i** (0.146 mmol) and $BH_3 \cdot NMe_3$ (0.874 mmol) were dissolved in THF (3 mL), and an ice-cold solution of $AlCl_3$ (1.019 mmol) in THF (1.5 mL) was then added at 0 °C. Samples (0.450 mL) were taken at different times and quenched by addition of $NaHCO_3$ (aq satd, 0.500 mL). The samples were then extracted twice with Et_2O (0.450 mL) and concentrated in vacuum. The residues were dissolved in $CDCl_3$ and analyzed by ^1H NMR. All reactions were run in triplicate. The molar concentration of product was determined from NMR peak ratios and plotted versus time. Linear regression over the linear part of the curves (determined by *f* values) gave the reaction rates.

General Procedure for Rate Determination of Reductive Opening of 4a. The amounts of $AlCl_3$, $BH_3 \cdot NMe_3$, and **4a** were varied according to Figure 2. Compound **4a** and $BH_3 \cdot NMe_3$ were dissolved in THF (3 mL), and an ice-cold solution of $AlCl_3$ in THF (1.5 mL) was then added at 0 °C. Samples (0.450 mL) were taken at different times and quenched by addition of $NaHCO_3$ (aq satd, 0.500 mL). The samples were then extracted twice with Et_2O (0.450 mL) and concentrated in vacuum. The residues were dissolved in $CDCl_3$ and analyzed by ^1H NMR. All reactions were run in duplicate. The molar concentration of product was determined from NMR peak ratios and plotted versus time. Linear regression over the linear part of the curves (determined by *f* values) gave the reaction rates.

General Procedure for Rate Determination of Reductive Opening of 1. The amounts of $AlCl_3$ were varied according to

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SCHEME 8. Regiochemical Outcome Is Directed by the Relative Nucleophilicity of the Acetal Oxygens toward the Lewis Acid (Path A) or the Activated Borane (Path B)

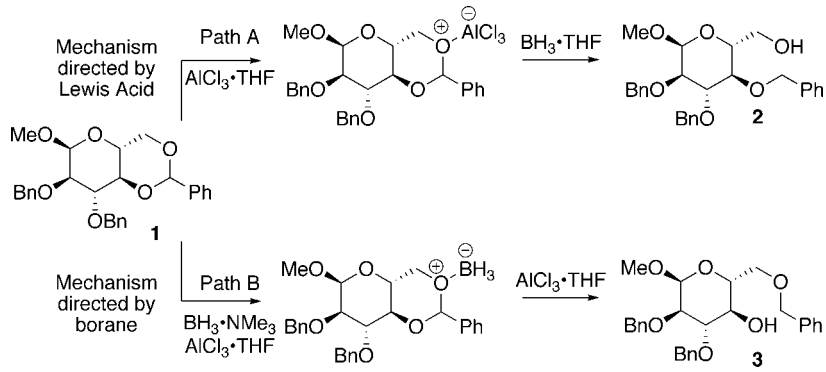

Figure 4. To a solution of **1** in THF (0.250 mL, 0.216 M) were added BH_3•THF (0.215 mL, 1 M in THF) *or* BH_3•NMe_3 (0.250 mL, 0.088 M in THF), THF (0.100−0.435 mL), and finally $AlCl_3$ (0.100−0.400 mL, 1.09 M in THF). Samples (0.050 mL) were taken at different times, quenched by addition of $NaHCO_3$ (0.250 mL, satd aq), and extracted with ether (0.100 mL). All reactions were run in duplicate. The molar concentration of product was determined from quantitative TLC ratios and plotted versus time. Linear regression over the linear part of the curves (determined by *f* values) gave the reaction rates.

^{11}B NMR Experiments. Compound **4a** (4 mg, 0.02 mmol) and BH_3•NMe_3 (8 mg, 0.11 mmol) were dissolved in THF-d_8(0.75 mL). $AlCl_3$ (18 mg, 0.13 mmol) was added, and the reaction was followed by ^{11}B NMR.

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Supporting Information Available: Complete experimental procedures, product characterization, spectral data, kinetic data, and computational data. This material is available free of charge via the Internet at http://pubs.acs.org

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