

# Deoxygenative Divergent Synthesis: En Route to Quinic Acid Chirons

Suvi Holmstedt,\* Lijo George, Alisa Koivuporras, Arto Valkonen, and Nuno R. Candeias\*



Cite This: <https://dx.doi.org/10.1021/acs.orglett.0c02995>



Read Online

ACCESS |



Metrics & More

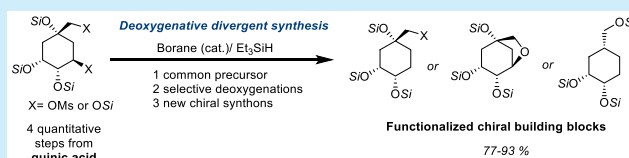


Article Recommendations



Supporting Information

**ABSTRACT:** The installation of vicinal mesylate and silyl ether groups in a quinic acid derivative generates a system prone for stereoselective borane-catalyzed hydrosilylation through a siloxonium intermediate. The diversification of the reaction conditions allowed the construction of different defunctionalized fragments foreseen as useful synthetic fragments. The selectivity of the hydrosilylation was rationalized on the basis of deuteration experiments and computational studies.



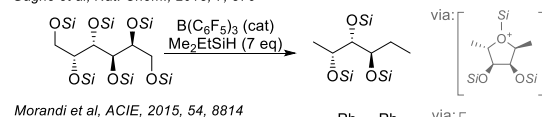
Synthetic strategies remain critically dependent on hemi-synthesis or chiral pool synthesis despite the plethora of currently available catalytic asymmetric transformations.<sup>1</sup> The contemporary mandatory transition from fossil to biobased carbon resources calls for the development of synthetic transformations that maximize the full potential of chemical entities or fragments created by nature. Saccharides are the main components of biomass, and the efforts done for their integration in biorefineries have augmented the development of methods for removal of their oxygen functionalities.<sup>2</sup> Dehydration<sup>3</sup> and selective cleavage of C–O bonds<sup>4</sup> of saccharides have been explored in the expansion of the biomass-derived chemical space.<sup>5</sup> Yamamoto's seminal B-(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>-catalyzed hydrosilylation of C–O bonds<sup>6</sup> has been used in the extensive deoxygenation of saccharides<sup>7</sup> and recently in the regioselective deoxygenation of saccharides<sup>8</sup> and polyols<sup>8c</sup> to provide new chiral entities (Scheme 1a). Alternative boron catalysts such as Piers' borane (HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>)<sup>9</sup> and more recently B((3,5-CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>)<sub>3</sub><sup>10</sup> have been demonstrated to catalyze the silylative deoxygenation of biomass-derived sugars.<sup>11</sup> The outcome of this deoxygenation method depends on several stereochemical and electronic parameters: first and foremost is the structure of the oxygenated substrate,<sup>8a</sup> as vicinal groups can assist the C–O bond cleavage.<sup>8c</sup> The second parameter is the hydrosilane employed,<sup>8b,c</sup> and the third is the fluoroarylborane catalyst.<sup>12</sup> Gagné and co-workers have recently progressed the field by replacing hydrosilanes by hydroboranes as precursors of H–B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub><sup>–</sup>hydride in the C–O bond cleavage with different selectivities than the ones observed in the hydrosilylation.<sup>13</sup>

Morandi<sup>14</sup> and Oestreich<sup>15</sup> have expanded the B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>-catalyzed hydrosilylation of C(sp<sup>3</sup>)–O bonds to 1,2-diols and primary tosylates, respectively. Both methods are effective in cleaving the terminal C–O bond, the former due to the formation of a cyclic siloxane intermediate and the latter due to the higher reactivity of the tosylate compared with the silyl

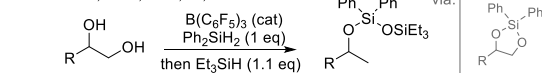
## Scheme 1. B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>-Catalyzed Selective Deoxygenation of 1,2-Diols and Primary Alkyl Tosylates

Previous work:

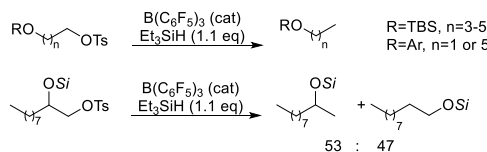
a) Regio- and chemoselective C(sp<sup>3</sup>)–O bond hydrosilylative cleavage of diols  
Gagné et al, Nat. Chem., 2015, 7, 576



Morandi et al, ACIE, 2015, 54, 8814

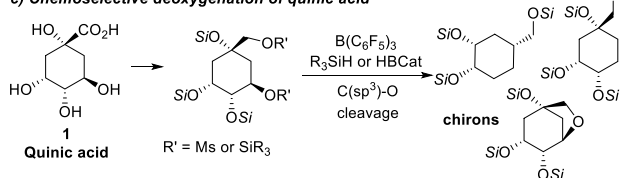


b) Chemoselective C(sp<sup>3</sup>)–O bond hydrosilylative cleavage of primary tosylates  
Oestreich et al, ACIE, 2017, 56, 3389



This work:

c) Chemoselective deoxygenation of quinic acid



Received: September 8, 2020

ether. Although suitable for the cleavage of primary tosylates containing a primary silyl ether (Scheme 1b, R = TBDMS,  $n = 3-5$ ), or an aryl ether (Scheme 1b, R = Ar,  $n = 1$  or 5), rearranged products from anchimeric assistance were observed for 1,2-diols (Scheme 1b, bottom). Indeed, the nonselective opening of a three-membered silyloxonium ion leads to the indiscriminate formation of a primary and secondary silyl ether. Substituents' migration competing with direct deoxygenation processes was further explored by Morandi, providing a reductive pinacol-type rearrangement of vicinal diols.<sup>16</sup> On a related note, the  $B(C_6F_5)_3$ -catalyzed hydrosilylation of tetrasubstituted epoxides leads to a migratory ring-opening process after the formation of a silyloxonium ion intermediate.<sup>17</sup> While the  $B(C_6F_5)_3$ -catalyzed hydrosilylation of C–O bonds has been rapidly expanding the accessibility to saccharides-derived chiral fragments for synthesis,<sup>8c,10,11,13,18</sup> we envisioned that different chiral synthons<sup>19</sup> could be reached by focusing on natural cyclitols.

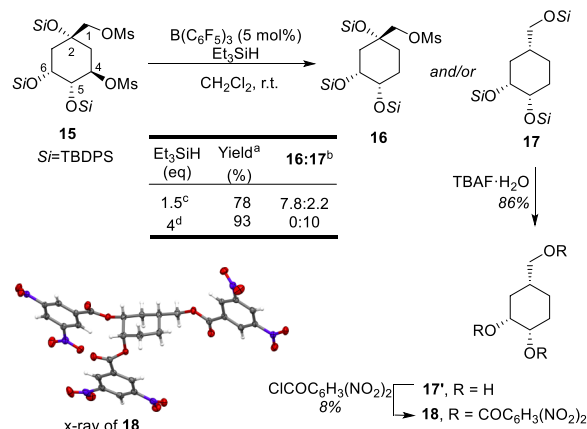
Quinic acid **1** was provisionally considered as one suitable feedstock for the biobased benzoic acid production<sup>20</sup> or other aromatics.<sup>21</sup> However, high cost associated with the use of glucose as feedstock for bacterial production of quinic acid<sup>22</sup> has again relegated this cyclitol to the chiral pool.<sup>23</sup> Nevertheless, quinic acid and its acyl-derivatives are widespread secondary metabolites of the shikimic acid pathway<sup>24</sup> in plants and can be obtained for instance from coffee beans, plants, fruits, and even food wastes.<sup>25</sup> Herein we present our efforts toward the selective cleavage of  $C(sp^3)$ –O bonds of a common quinic acid-derived precursor with judiciously selected O-substituents, into diverse chiral fragments (Scheme 1c).

Aware of putative effects imposed by the diverse conformations of cyclitols on the regioselectivity of deoxygenation using the  $B(C_6F_5)_3$ /SiH system, the vicinal *cis* diol moiety of quinide **2** was derivatized to several functional groups. Besides conferring the desired conformational effect, further deprotection after deoxygenation would provide substrates prone to typical C–C oxidative cleavage and subsequently give chiral linear  $C_7$  fragments. Attempts on the hydrosilylation of cyclitol derivatives **3–13** (Scheme 2) failed in providing any deoxygenated products (see Supporting Information section 1 for complete rationale).

The discouraging lack of reactivity of the silylated quinic acid derivatives prompted us to explore the anchimeric assistance by silyl ethers in the C–O bond cleavage of tosylates, as previously reported by Oestreich and co-workers.<sup>15</sup> Excellent chemoselectivity was reported for the deoxygenation of primary alkyl tosylates from nonvicinal diol

derivatives. However, the formation of a three-membered silyloxonium ion intermediate resulted in rearranged products, and a lack of regioselectivity was observed when considering aliphatic 1,2-vicinal diol systems. Gratifyingly, treatment of **15** with different catalyst loadings and amounts of triethylsilane resulted in formation of **16** and/or **17** in different ratios (Scheme 3 and Table S1 in SI for further experiments). Silyl

**Scheme 3. Deoxygenation of Quinic Acid Derivative 15**

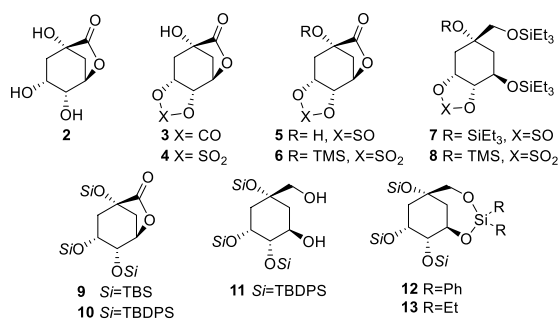


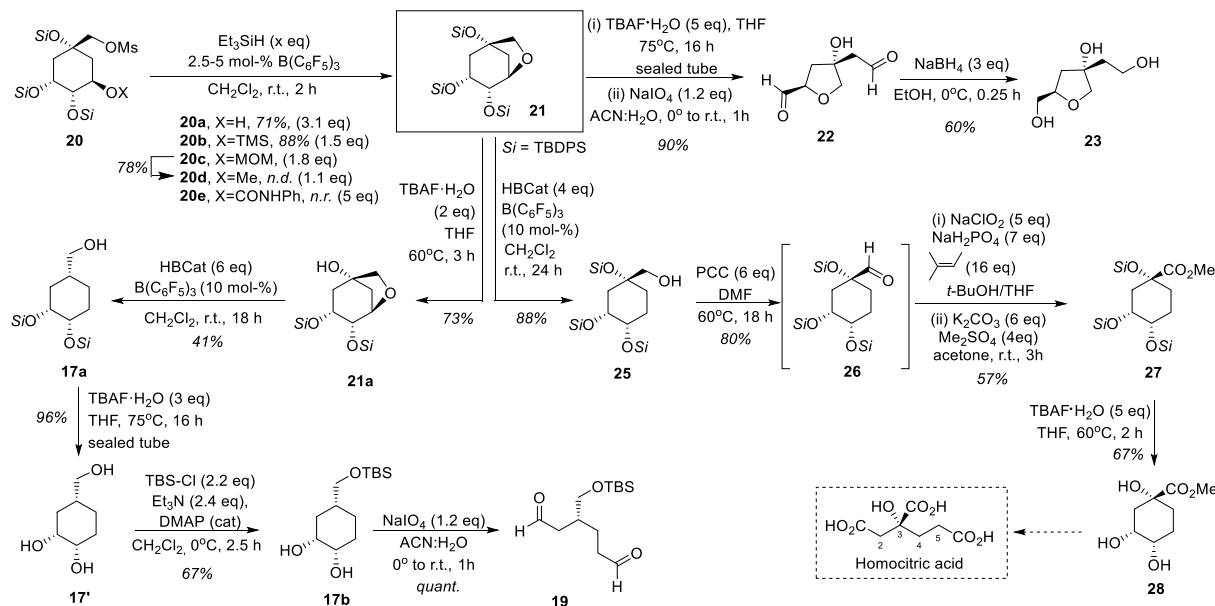
<sup>a</sup> **15** (0.14 mmol) and  $B(C_6F_5)_3$  in  $CH_2Cl_2$ , at r.t. followed by addition of  $Et_3SiH$ . <sup>b</sup> Ratio determined from isolated yields. <sup>c</sup>  $[15] = 0.05$  M. <sup>d</sup>  $[15] = 0.3$  M.

ethers derived from primary and secondary alcohols have been reported to be more reactive toward  $B(C_6F_5)_3$ -catalyzed reduction with hydrosilanes than the ones derived from tertiary homologues.<sup>6c,d</sup> On the other hand, the neighboring group assistance can deeply impact the regioselectivity. Notably, cleavage of the primary mesylate in **15** was accompanied by stereospecific migration of the silyloxy group from the vicinal tertiary carbon to provide **17** (Scheme 3). The absolute configuration of the deoxygenated product was determined through X-ray diffraction analysis of the 3,5-dinitrobenzoyl derivative **18**, obtained after desilylation of **17** and benzylation of the triol **17**.

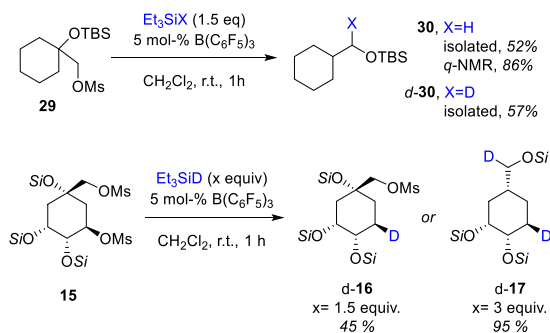
Attempts to overcome the higher propensity of C4 toward deoxygenation by replacing the mesylate with protecting groups proved futile. Instead,  $B(C_6F_5)_3$ /SiH treatment of **20** having the secondary hydroxyl protected as silyl ether (**20b**) resulted in fast intramolecular cyclization to bicyclic compound **21** in up to 88% yield (Scheme 4). Exposure of MOM-ether **20c** to the same conditions resulted in the formation of compound **20d** in 78% yield (Scheme 5). Treatment of methyl ether **20d** with additional triethylsilane (1.1 equiv) in the presence of  $B(C_6F_5)_3$  led to formation of cyclic ether **21**, as deduced from crude NMR. Carbamoyl protected **20e** was unreactive toward  $B(C_6F_5)_3$ -catalyzed hydrosilylation, and only starting material was recovered, despite the harsh reaction conditions used (20 mol % catalyst, excess of silane and refluxing toluene). The structural complexity of compound **21**<sup>26</sup> was broken down through oxidative cleavage of the C–C bond upon desilylation and oxidation of the *cis* glycol moiety via Malaprade oxidation to provide dialdehyde **22** in excellent yield. The cyclic ethers **22** and **23** are envisioned as interesting synthetic intermediates due to the presence of oxygen functionality-containing substituents at C1 and C3 positions of the tetrahydrofuran core.<sup>27</sup> The selective deprotection of the

**Scheme 2. Quinic Acid Derivatives Explored in  $B(C_6F_5)_3$ -Catalyzed Hydrosilylation**



Scheme 4. Formation and Controlled Cleavage of Bicyclic Tetrahydrofuran **21**<sup>a</sup>

<sup>a</sup>n.d. = yield not determined; n.r. = no reaction.

Scheme 5.  $\text{B(C}_6\text{F}_5)_3$ -Catalyzed Siloxonium Opening with  $\text{Et}_3\text{SiD}$ 

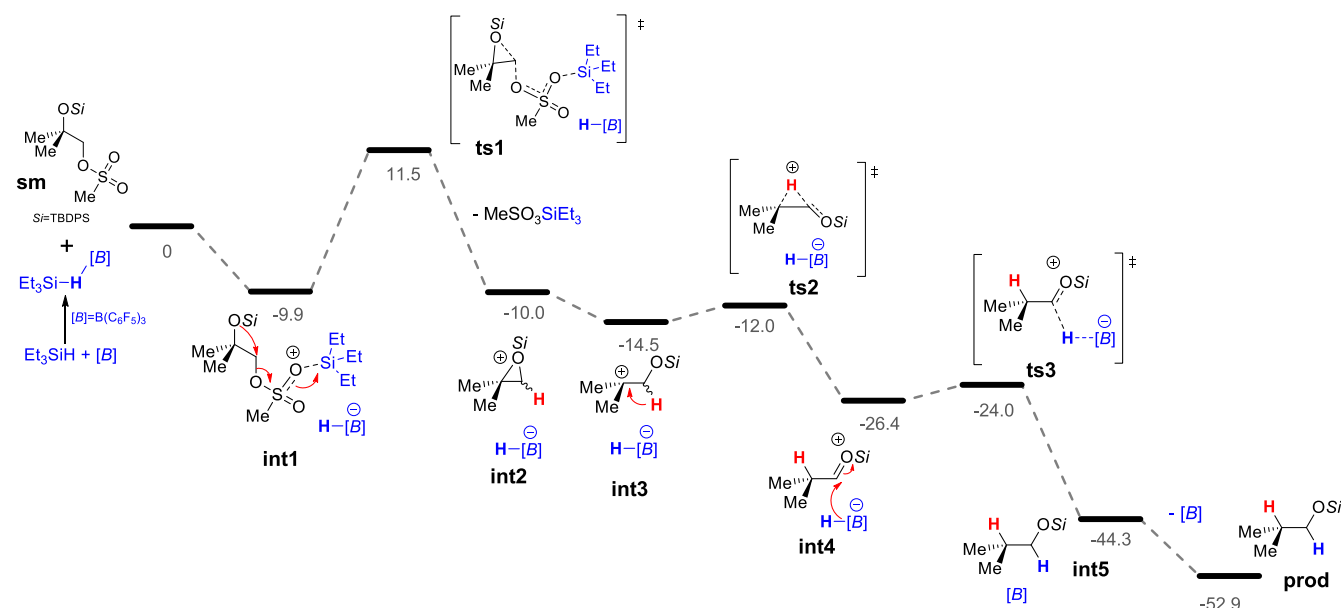
tertiary silyl ether of **21** followed by similar cleavage with catechol borane and desilylation also provided compound **17a**. A sequence of silyl ethers' cleavage and primary alcohol protection resulted in **17b** that was submitted to Malaprade oxidation providing dialdehyde **19**, envisioned as a rich fragment for stereoselective synthesis due to the three functionalities and structural similarities with Perlin aldehydes.<sup>28</sup> Impelled by the bicyclic skeleton of **21**, the controlled modification of its stereogenic carbons was attempted. The lack of reactivity of **21** toward cleavage of the O–Si bond by  $\text{B(C}_6\text{F}_5)_3$ -catalyzed hydrosilylation was overcome by reduction with catechol borane, as recently developed by Gagné,<sup>13</sup> resulting in the selective cleavage of the C–O bond from the secondary carbon to provide **25** in 88% yield.

Selective oxidation of primary alcohol moiety of **25** followed by one-pot esterification and desilylation led to **28**, a known intermediate in the synthesis of homocitric acid.<sup>29</sup> Even though not attempted, it is worth noticing that the use of deuteriocatecholborane in the manipulation of **21** would provide an entry for the preparation of labeled homocitrate. Although of potential interest for biological studies, deuterium labeling at position 5 remains unveiled.<sup>29a,30</sup>

The observed preferred chemoselectivity for C–O bond cleavage of the secondary carbon over the primary mesylate in **15** suggests the formation of the three-membered siloxonium ion as proposed previously by Oestreich. The higher propensity of C4 for deoxygenation compared to C1 is justified by the easier formation of the strained three-membered siloxonium ion in C4–C5 than in C1–C2, as the later will turn C2 into a spiro carbon. Such events should become less energy demanding after removal of one of the carbocycle substituents. Additionally, the easier access of the hydride to C4 over C5 renders this process highly regioselective in the opening of the siloxonium. Motivated by the excellent regioselectivity in opening of the putative three-membered siloxonium ion with hydrosilanes, compound **29**, an analogue of **15**, was submitted to similar deoxygenation protocol. The treatment of cyclohexanol derivative **29** with  $\text{B(C}_6\text{F}_5)_3$  and silyl hydrides resulted in cleavage of the C–O bond and migration of the silyl ether moiety to the primary carbon (Scheme 5), contrasting with the previously reported lack of selectivity for deoxygenation of primary tosylates vicinal to a secondary silyl ether.<sup>15</sup> While no alkyl migration was observed in the deoxygenations of quinic acid derivatives, which was expected given the precedents on the hydrosilylation of epoxides in acyclic systems<sup>17</sup> the migration of hydride from the primary to tertiary carbon was considered.<sup>31</sup> When using  $\text{Et}_3\text{SiD}$  as a reducing agent, the deuteration occurred selectively at the primary carbon, affording *d*-**30** in 57% after isolation. Similar behavior was observed in the hydrosilylation of **15** with  $\text{Et}_3\text{SiD}$ . The delivery of the deuteride to the opposite face of the silyl ethers of the cyclohexane derivative (absolute configuration determined from inspection of vicinal coupling constants) seems to indicate a different mechanism when comparing with the tertiary silyl ether/primary mesylate counterpart.

In order to get further insight on the formation of the siloxonium intermediate and its regioselective opening, a simplified system was studied by means of Density Functional Theory<sup>32</sup> (Scheme 6), and geometries of the transition states

Scheme 6. Free Energy Profile (M06-2X/6-311++G\*\*//M06-2X/6-31G\*\*) and Mechanistic Representation for Deoxygenation of Model Substrate **sm**, via Siloxonium and 1,2-Hydride Shift<sup>a</sup>



<sup>a</sup>Values are presented in kcal/mol, referring to the initial pair of **sm** and Et<sub>3</sub>Si-H-B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>.

were calculated (please consult Figure S1 and full computational account in the SI). The energetically favorable interaction of the mesylate group of **sm** with silylium ion in **int1** increases the electrophilic character of the primary carbon, triggering the formation of the siloxonium ion **int2** through a 21.4 kcal/mol energy barrier. C–O bond lengths in the siloxonium **int2** differ by 0.05 Å, with the most substituted bond being elongated. The equilibration of the siloxonium to **int3**, where the above-mentioned C–O bond is clearly broken (*d*<sub>C–O</sub> = 2.385 Å), is energetically more favorable by 4.5 kcal/mol. The 1,2-hydride shift for neutralization of the positive charge on the tertiary carbon is a favorable process with **int4** being 11.9 kcal/mol more stable than **int3**. Additionally, the energy barrier for the 1,2-hydride migration through **ts2** is only 2.5 kcal/mol. The hydride delivery from the hydridoborate anion to the electrophilic carbon of the oxocarbenium is almost spontaneous and **int4** can simply overcome the barely existent energy barrier of 2.4 kcal/mol for **ts3** to ultimately form the very stable silyl ether **int5**. The overall process is energetically favored as demonstrated by the Δ*G*<sub>f</sub> of **prod** (52.9 kcal/mol) with the rate limiting step being the formation of the siloxonium **int2**.

In conclusion, we have described the B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>-catalyzed defunctionalization of a cyclitol through hydride delivery to three-membered siloxonium ions. The success of the deoxygenation of quinide and derivatives using this hydrosilylation depends on the protecting groups. Nevertheless, the achieved deoxygenations proved highly stereoselective and allowed the diversification of chiral fragments that can be obtained from quinic acid. The expansion of this transition-metal-free deoxygenation protocol to cyclitols has diversified the array of molecules and fragments that can be obtained from biorenewables.

## ■ ASSOCIATED CONTENT

### SI Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.orglett.0c02995>.

Experimental details, preliminary studies on hydrosilylation and characterization data of all synthetic intermediates, full accounts on computational calculations, and <sup>1</sup>H and <sup>13</sup>C NMR copies of spectra for all reported compounds (PDF)

## Accession Codes

CCDC 2005907 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif), or by emailing [data\\_request@ccdc.cam.ac.uk](mailto:data_request@ccdc.cam.ac.uk), or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

## ■ AUTHOR INFORMATION

### Corresponding Authors

**Suvi Holmstedt** – Faculty of Engineering and Natural Sciences, Tampere University, 33101 Tampere, Finland;  
Email: [suvi.holmstedt@tuni.fi](mailto:suvi.holmstedt@tuni.fi)

**Nuno R. Candeias** – Faculty of Engineering and Natural Sciences, Tampere University, 33101 Tampere, Finland;  
LAQV-REQUIMTE, Department of Chemistry, University of Aveiro, 3810-193 Aveiro, Portugal; [orcid.org/0000-0003-2414-9064](https://orcid.org/0000-0003-2414-9064); Email: [ncandeias@ua.pt](mailto:ncandeias@ua.pt)

### Authors

**Lijo George** – Faculty of Engineering and Natural Sciences, Tampere University, 33101 Tampere, Finland  
**Alisa Koivuporras** – Faculty of Engineering and Natural Sciences, Tampere University, 33101 Tampere, Finland



Arto Valkonen – Department of Chemistry, University of Jyväskylä, 40014 Jyväskylä, Finland; [orcid.org/0000-0003-2806-3807](https://orcid.org/0000-0003-2806-3807)

Complete contact information is available at:  
<https://pubs.acs.org/10.1021/acs.orglett.0c02995>

## Notes

The authors declare no competing financial interest.

## ACKNOWLEDGMENTS

The Academy of Finland is duly acknowledged for financial support to N.R.C. (Decisions No. 326487 and 326486) and to A. V. (No. 314343). Finnish Cultural Foundation is acknowledged for financial support to S.H. (00190336). CSC–IT Center for Science Ltd., Finland is acknowledged for the allocation of computational resources. Professor Luis F. Veiros (Centro de Química Estrutural, Instituto Superior Técnico, Universidade de Lisboa, Portugal) is acknowledged for fruitful discussions on the computational section.

## REFERENCES

- (1) (a) Brill, Z. G.; Condakes, M. L.; Ting, C. P.; Maimone, T. J. Navigating the Chiral Pool in the Total Synthesis of Complex Terpene Natural Products. *Chem. Rev.* **2017**, *117*, 11753–11795. (b) Pfaffenbach, M.; Bakanas, I.; O'Connor, N. R.; Herrick, J. L.; Sarpong, R. Total Syntheses of Xiamycins A, C, F, H and Oridamycin A and Preliminary Evaluation of their Anti-Fungal Properties. *Angew. Chem., Int. Ed.* **2019**, *58*, 15304. (c) Hu, N.; Dong, C.; Zhang, C.; Liang, G. Total Synthesis of (–)-Indoxamycins A and B. *Angew. Chem., Int. Ed.* **2019**, *58*, 6659–6662. (d) Hung, K.; Condakes, M. L.; Novaes, L. F. T.; Harwood, S. J.; Morikawa, T.; Yang, Z.; Maimone, T. J. Development of a Terpene Feedstock-Based Oxidative Synthetic Approach to the Illicium Sesquiterpenes. *J. Am. Chem. Soc.* **2019**, *141*, 3083–3099.
- (2) (a) Sheldon, R. A. The Road to Biorenewables: Carbohydrates to Commodity Chemicals. *ACS Sustainable Chem. Eng.* **2018**, *6*, 4464–4480. (b) Mika, L. T.; Csefalvay, E.; Nemeth, A. Catalytic Conversion of Carbohydrates to Initial Platform Chemicals: Chemistry and Sustainability. *Chem. Rev.* **2018**, *118*, 505–613.
- (3) (a) Zhang, X.; Wilson, K.; Lee, A. F. Heterogeneously Catalyzed Hydrothermal Processing of C<sub>5</sub>–C<sub>6</sub> Sugars. *Chem. Rev.* **2016**, *116*, 12328–12368. (b) Gómez Millán, G.; Hellsten, S.; Llorca, J.; Luque, R.; Sixta, H.; Balu, A. M. Recent Advances in the Catalytic Production of Platform Chemicals from Holocellulosic Biomass. *ChemCatChem* **2019**, *11*, 2022–2042.
- (4) Kühne, B.; Vogel, H.; Meusinger, R.; Kunz, S.; Kunz, M. Mechanistic study on –C–O– and –C–C– hydrogenolysis over Cu catalysts: identification of reaction pathways and key intermediates. *Catal. Sci. Technol.* **2018**, *8*, 755–767.
- (5) (a) Brun, N.; Hesemann, P.; Esposito, D. Expanding the biomass derived chemical space. *Chem. Sci.* **2017**, *8*, 4724–4738. (b) Bender, T. A.; Dabrowski, J. A.; Gagné, M. R. Homogeneous Catalysis for the Production of Low-volume, High-value Chemicals from Biomass. *Nat. Rev. Chem.* **2018**, *2*, 35–46.
- (6) (a) Yamamoto, Y.; Bajracharya, G. B.; Nogami, T.; Jin, T.; Matsuda, K.; Gevorgyan, V. Reduction of Carbonyl Function to a Methyl Group. *Synthesis* **2004**, 308–311. (b) Gevorgyan, V.; Liu, J.-X.; Rubin, M.; Benson, S.; Yamamoto, Y. A novel reduction of alcohols and ethers with a HSiEt<sub>3</sub> catalytic B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub> system. *Tetrahedron Lett.* **1999**, *40*, 8919–8922. (c) Gevorgyan, V. V.; Rubin, M.; Benson, S.; Liu, J.-X.; Yamamoto, Y. A novel B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>-catalyzed reduction of alcohols and cleavage of aryl and alkyl ethers with hydrosilanes. *J. Org. Chem.* **2000**, *65*, 6179–6186. (d) Gevorgyan, V.; Rubin, M.; Liu, J.-X.; Yamamoto, Y. A Direct Reduction of Aliphatic Aldehyde, Acyl Chloride, Ester, and Carboxylic Functions into a Methyl Group. *J. Org. Chem.* **2001**, *66*, 1672–1675.
- (7) Adduci, L. L.; McLaughlin, M. P.; Bender, T. A.; Becker, J. J.; Gagné, M. R. Metal-Free Deoxygenation of Carbohydrates. *Angew. Chem., Int. Ed.* **2014**, *53*, 1646–1649.
- (8) (a) Seo, Y.; Gagné, M. R. Positional Selectivity in the Hydrosilylative Partial Deoxygenation of Disaccharides by Boron Catalysts. *ACS Catal.* **2018**, *8*, 81–85. (b) Hein, N. M.; Seo, Y.; Lee, S. J.; Gagné, M. R. Harnessing the reactivity of poly(methylhydrosiloxane) for the reduction and cyclization of biomass to high-value products. *Green Chem.* **2019**, *21*, 2662–2669. (c) Adduci, L. L.; Bender, T. A.; Dabrowski, J. A.; Gagné, M. R. Chemoselective Conversion of Biologically Sourced Polyols into Chiral Synthons. *Nat. Chem.* **2015**, *7*, 576–581.
- (9) (a) Parks, D. J.; Piers, W. E.; Yap, G. P. A. Synthesis, Properties, and Hydroboration Activity of the Highly Electrophilic Borane Bis(pentafluorophenyl)borane, HB(C<sub>6</sub>F<sub>5</sub>)<sub>2</sub>. *Organometallics* **1998**, *17*, 5492–5503. (b) Parks, D. J.; von H. Spence, R. E.; Piers, W. E. Bis(pentafluorophenyl)borane: Synthesis, Properties, and Hydroboration Chemistry of a Highly Electrophilic Borane Reagent. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 809–811. (c) Zhang, J.; Park, S.; Chang, S. Selective C–O Bond Cleavage of Sugars with Hydrosilanes Catalyzed by Piers' Borane Generated In Situ. *Angew. Chem., Int. Ed.* **2017**, *56*, 13757–13761.
- (10) Seo, Y.; Lowe, J. M.; Gagné, M. R. Controlling Sugar Deoxygenation Products from Biomass by Choice of Fluoroarylborane Catalyst. *ACS Catal.* **2019**, *9*, 6648–6652.
- (11) Seo, Y.; Gagné, M. R. Silylium (R<sub>3</sub>Si<sup>+</sup>) Catalyzed Condensative Cyclization for Anhydrosugar Synthesis. *ACS Catal.* **2018**, *8*, 6993–6999.
- (12) Patrick, E. A.; Piers, W. E. Twenty-five years of bis-pentafluorophenyl borane: a versatile reagent for catalyst and materials synthesis. *Chem. Commun.* **2020**, *56*, 841–853.
- (13) Lowe, J. M.; Seo, Y.; Gagné, M. R. Boron-Catalyzed Site-Selective Reduction of Carbohydrate Derivatives with Catecholborane. *ACS Catal.* **2018**, *8*, 8192–8198.
- (14) Drosos, N.; Morandi, B. Boron-Catalyzed Regioselective Deoxygenation of Terminal 1,2-Diols to 2-Alkanols Enabled by the Strategic Formation of a Cyclic Siloxane Intermediate. *Angew. Chem., Int. Ed.* **2015**, *54*, 8814–8818.
- (15) Chatterjee, I.; Porwal, D.; Oestreich, M. B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>-Catalyzed Chemoselective Defunctionalization of Ether-Containing Primary Alkyl Tosylates with Hydrosilanes. *Angew. Chem., Int. Ed.* **2017**, *56*, 3389–3391.
- (16) Drosos, N.; Cheng, G. J.; Ozkal, E.; Cachera, B.; Thiel, W.; Morandi, B. Catalytic Reductive Pinacol-Type Rearrangement of Unactivated 1,2-Diols through a Concerted, Stereoinvertive Mechanism. *Angew. Chem., Int. Ed.* **2017**, *56*, 13377–13381.
- (17) The regioselective silyloxonium opening was reported to occur when using Piers borane: Zhang, J.; Park, S.; Chang, S. Piers' Borane-Mediated Hydrosilylation of Epoxides and Cyclic Ethers. *Chem. Commun.* **2018**, *54*, 7243–7246.
- (18) Bender, T. A.; Dabrowski, J. A.; Zhong, H.; Gagné, M. R. Diastereoselective B(C<sub>6</sub>F<sub>5</sub>)<sub>3</sub>-Catalyzed Reductive Carbocyclization of Unsaturated Carbohydrates. *Org. Lett.* **2016**, *18*, 4120–4123.
- (19) For selected examples on the use of chiral synthons, from carbohydrates: (a) Lin, S.; Guo, X.; Qin, K.; Feng, L.; Zhang, Y.; Tang, Y. Efficient Production of Biomass-Derived C<sub>4</sub> Chiral Synthons in Aqueous Solution. *ChemCatChem* **2017**, *9*, 4179–4184. (b) Hollingsworth, R. I.; Wang, G. Toward a Carbohydrate-Based Chemistry: Progress in the Development of General-Purpose Chiral Synthons from Carbohydrates. *Chem. Rev.* **2000**, *100*, 4267–4282. (c) Ramesh, N. G.; Balasubramanian, K. K. 2-C-Formyl Glycals: Emerging Chiral Synthons in Organic Synthesis. *Eur. J. Org. Chem.* **2003**, *2003*, 4477–4487. (d) Cairns, R.; Gomm, A.; Ryan, J.; Clarke, T.; Kulcinskaja, E.; Butler, K.; O'Reilly, E. Conversion of Aldoses to Valuable ω-Amino Alcohols Using Amine Transaminase Biocatalysts. *ACS Catal.* **2019**, *9*, 1220–1223. From noncarbohydrates: (e) Hoffmann, R. W. meso Compounds: stepchildren or favored children of stereoselective synthesis? *Angew. Chem., Int. Ed.* **2003**, *42*, 1096–1109. (f) Guo, C.; Saifuddin, M.; Saravanan, T.; Sharifi, M.; Poelarends, G. J.

- Biocatalytic Asymmetric Michael Additions of Nitromethane to  $\alpha,\beta$ -Unsaturated Aldehydes via Enzyme-bound Iminium Ion Intermediates. *ACS Catal.* **2019**, 9, 4369–4373. (g) Brenna, E.; Crotti, M.; Gatti, F. G.; Monti, D.; Parmeggiani, F.; Santangelo, S. Asymmetric Bioreduction of  $\beta$ -Acylaminonitroalkenes: Easy Access to Chiral Building Blocks with Two Vicinal Nitrogen-Containing Functional Groups. *ChemCatChem* **2017**, 9, 2480–2487. (h) Chen, Y. H.; McDonald, F. E. New chiral synthons for efficient introduction of bispropionates via stereospecific oxonia-cope rearrangements. *J. Am. Chem. Soc.* **2006**, 128, 4568–4569. (i) Hudlicky, T.; Thorpe, A. J. Current status and future perspectives of cyclohexadiene-*cis*-diols in organic synthesis: versatile intermediates in the concise design of natural products. *Chem. Commun.* **1996**, 1993–2000. (j) Padarti, A.; Han, H. Rationally Designed Chiral Synthons Enabling Asymmetric Z- and E-Selective Vinylogous Aldol Reactions of Aldehydes. *Org. Lett.* **2018**, 20, 1448–1452.
- (20) Arceo, E.; Ellman, J. A.; Bergman, R. G. A direct, biomass-based synthesis of benzoic acid: formic acid-mediated deoxygenation of the glucose-derived materials quinic acid and shikimic acid. *ChemSusChem* **2010**, 3, 811–813.
- (21) (a) Assoah, B.; Veiros, L. F.; Afonso, C. A. M.; Candeias, N. R. Biomass-Based and Oxidant-Free Preparation of Hydroquinone from Quinic Acid. *Eur. J. Org. Chem.* **2016**, 2016, 3856–3861. (b) Ran, N.; Knop, D. R.; Draths, K. M.; Frost, J. W. Benzene-Free Synthesis of Hydroquinone. *J. Am. Chem. Soc.* **2001**, 123, 10927–10934.
- (22) Pfennig, T.; Carraher, J. M.; Chemburkar, A.; Johnson, R. L.; Anderson, A. T.; Tessonnier, J.-P.; Neurock, M.; Shanks, B. H. A new selective route towards benzoic acid and derivatives from biomass-derived coumalic acid. *Green Chem.* **2017**, 19, 4879–4888.
- (23) (a) Enev, V. 2.11 Chiral Pool Synthesis: Chiral Pool Synthesis from Quinic Acid In *Comprehensive Chirality*; Carreira, E. M., Yamamoto, H., Eds.; Elsevier: Amsterdam, 2012; pp 325–345. (b) Barco, A.; Benetti, S.; Risi, C. D.; Marchetti, P.; Pollini, G. P.; Zanirato, V. D-(–)-Quinic acid: a chiron store for natural product synthesis. *Tetrahedron: Asymmetry* **1997**, 8, 3515–3545. (c) Mulzer, J.; Drescher, M.; Enev, V. S. Quinic Acid as Versatile Chiral Scaffold in Organic Synthesis. *Curr. Org. Chem.* **2008**, 12, 1613–1630.
- (24) Candeias, N. R.; Assoah, B.; Simeonov, S. P. Production and Synthetic Modifications of Shikimic Acid. *Chem. Rev.* **2018**, 118, 10458–10550.
- (25) (a) Wianowska, D.; Gil, M. Recent advances in extraction and analysis procedures of natural chlorogenic acids. *Phytochem. Rev.* **2019**, 18, 273–302. (b) Clifford, M. N.; Jaganath, I. B.; Ludwig, I. A.; Crozier, A. Chlorogenic acids and the acyl-quinic acids: discovery, biosynthesis, bioavailability and bioactivity. *Nat. Prod. Rep.* **2017**, 34, 1391–1421. (c) Yuda, N.; Tanaka, M.; Suzuki, M.; Asano, Y.; Ochi, H.; Iwatsuki, K. Polyphenols extracted from black tea (*Camellia sinensis*) residue by hot-compressed water and their inhibitory effect on pancreatic lipase in vitro. *J. Food Sci.* **2012**, 77, H254–261. (d) Grunovaitė, L.; Pukalskienė, M.; Pukalskas, A.; Venskutonis, P. R. Fractionation of black chokeberry pomace into functional ingredients using high pressure extraction methods and evaluation of their antioxidant capacity and chemical composition. *J. Funct. Foods* **2016**, 24, 85–96. (e) Wang, J.; Lu, D.; Sun, Q.; Zhao, H.; Ling, X.; Ouyang, P. Reactive extraction and recovery of mono-caffeoylquinic acids from tobacco wastes by trialkylphosphine oxide. *Chem. Eng. Sci.* **2012**, 78, 53–62. (f) Santana-Méridas, O.; González-Coloma, A.; Sánchez-Vioque, R. Agricultural residues as a source of bioactive natural products. *Phytochem. Rev.* **2012**, 11, 447–466.
- (26) For the synthesis of unprotected derivative, see: Gorin, P. A. J. Replacement Reactions in the Quinic Acid Series. *Can. J. Chem.* **1963**, 41, 2417–2423.
- (27) (a) Benhamou, L.; Foster, R. W.; Ward, D. P.; Wheelhouse, K.; Sloan, L.; Tame, C. J.; Bučar, D.-K.; Lye, G. J.; Hailes, H. C.; Sheppard, T. D. Functionalised tetrahydrofuran fragments from carbohydrates or sugar beet pulp biomass. *Green Chem.* **2019**, 21, 2035–2042. (b) Foster, R. W.; Tame, C. J.; Bucar, D. K.; Hailes, H. C.; Sheppard, T. D. Sustainable Synthesis of Chiral Tetrahydrofurans through the Selective Dehydration of Pentoses. *Chem. - Eur. J.* **2015**, 21, 15947–15950. (c) Monasterolo, C.; Muller-Bunz, H.; Gilheany, D. G. Very short highly enantioselective Grignard synthesis of 2,2-disubstituted tetrahydrofurans and tetrahydropyrans. *Chem. Sci.* **2019**, 10, 6531–6538.
- (28) Reddy, L. V.; Kumar, V.; Sagar, R.; Shaw, A. K. Glycal-derived D-hydroxy  $\alpha,\beta$ -unsaturated aldehydes (Perlin aldehydes): versatile building blocks in organic synthesis. *Chem. Rev.* **2013**, 113, 3605–3631.
- (29) (a) Tavassoli, A.; Duffy, J. E.; Young, D. W. Synthesis of trimethyl (2S,3R)- and (2R,3R)-[2- $^2\text{H}_1$ ]-homocitrates and dimethyl (2S,3R)- and (2R,3R)-[2- $^2\text{H}_1$ ]-homocitrate lactones—an assay for the stereochemical outcome of the reaction catalysed both by homocitrate synthase and by the Nif-V protein. *Org. Biomol. Chem.* **2006**, 4, 569–580. (b) Tavassoli, A.; Duffy, J. E. S.; Young, D. W. Synthesis of trimethyl (2S,3R)- and (2R,3R)-[2- $^2\text{H}_1$ ]-homocitrates and the corresponding dimethyl ester lactones—towards elucidating the stereochemistry of the reaction catalysed by homocitrate synthase and by the Nif-V protein. *Tetrahedron Lett.* **2005**, 46, 2093–2096.
- (30) Pansare, S. V.; Adsool, V. A. Enantioselective synthesis of (R)-homocitric acid lactone. *Tetrahedron Lett.* **2007**, 48, 7099–7101.
- (31) 1,2-Hydride shifts triggered by boron Lewis acids have been explored in 1,1-carboborations: (a) Chen, C.; Voss, T.; Frohlich, R.; Kehr, G.; Erker, G. 1,1-carboboration of 1-alkynes: a conceptual alternative to the hydroboration reaction. *Org. Lett.* **2011**, 13, 62–65. (b) Kehr, G.; Erker, G. 1,1-Carboration. *Chem. Commun.* **2012**, 48, 1839–1850. (c) Hansmann, M. M.; Melen, R. L.; Rudolph, M.; Rominger, F.; Wade, H.; Stephan, D. W.; Hashmi, A. S. Cyclopropanation/Carboboration Reactions of Enynes with B-( $\text{C}_6\text{F}_5$ )<sub>3</sub>. *J. Am. Chem. Soc.* **2015**, 137, 15469–15477.
- (32) Parr, R. G.; Yang, W. *Density Functional Theory of Atoms and Molecules*; Oxford University Press: New York, 1989.