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Tandem Reactions Involving 1-Silyl-3-Boryl-2-Alkenes. New Access to (*Z*)-1-Fluoro-1-Alkenes, Allyl Fluorides, and Diversely α-Substituted Allylboronates

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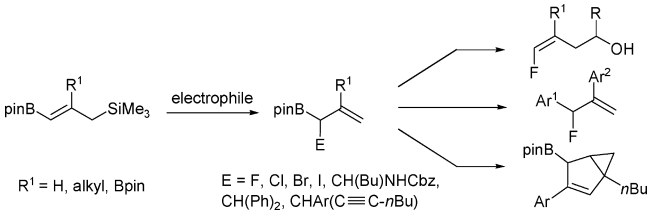
ABSTRACT



The reactions of 1-silyl-3-boryl-2-alkenes with various electrophilic reagents (Selectfluor, *N*-halosuccinimides, benzhydryl, and propargylic alcohols in the presence of a Lewis acid, *N*-alkoxycarbonyliminium ion) have been investigated as new routes to α-substituted allylboronates. Further functional transformations, including allylboration, Suzuki coupling, protodeboronation, and cycloisomerization, have been carried out to illustrate the synthetic potential of these γ-borylallylsilanes.

Allylboronic esters and allylsilanes have been proven to be highly versatile carbon nucleophiles, usually showing very good levels of chemo-, regio-, and stereocontrol in various reactions with electrophiles. Both of them can add to carbonyl derivatives in the presence, or absence, of a Lewis acid activator.[1] In addition, allylboronic acids can also be engaged in palladium-catalyzed cross-couplings[2] and conjugate allylation of electron-deficient alkynes.[3] Regarding allylsilanes, they are prone to halogen addition, dihydroxylation, epoxidation, cyclopropanation, and Lewis acid mediated [2 + 2]- and [3 + 2]-annulation or free radical additions.[4]

Reagents **1**–**5** possessing both trialkylsilyl and boronic ester groups have enhanced synthetic potential when one of them is in an allylic position (Figure 1).[5–9]

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(1) For reviews on allylboronic esters, see: (a) Kennedy, J. W.; Hall, D. G. In *Boronic Acids*; Hall, D. G., Ed.; Wiley-VCH: Weinheim, 2005; pp 241–277. (b) Lachance, H.; Hall, D. G. *Org. React.* **2008**, *73*, 1. (c) Hall, D. G *Pure Appl. Chem.* **2008**, *80*, 913. For reviews on allylsilanes, see: (d) Masse, C. E.; Panek, J. S. *Chem. Rev.* **1995**, *95*, 1293. (e) Jacques, T.; Markó, I. E.; Pospíšil, J. In *Multicomponent Reactions*; Zhu, J., Bienaymé, H., Eds.; Wiley-VCH: Weinheim, 2005; pp 398–452.

(2) (a) Zhang, P.; Le, H.; Kyne, R. E.; Morken, J. P. *J. Am. Chem. Soc.* **2011**, *133*, 9716. (b) Gerbino, D. C.; Mandolesi, S. D.; Schmalz, H-G; Podesta, J. C. *Eur. J. Org. Chem.* **2009**, 3964. (c) Flegeau, E. F.; Schneider, U.; Kobayashi, S. *Chem.—Eur. J.* **2009**, *15*, 12247. (d) Yamamoto, Y.; Takada, S.; Miyaura, N.; Iyama, T.; Tachikawa, H. *Organometallics* **2009**, *28*, 152. (e) Sebelius, S.; Olsson, V. J.; Wallner, O. A.; Szabo, K. J. *J. Am. Chem. Soc.* **2006**, *128*, 8150.

(3) Yamamoto, Y.; Yamada, S.; Nishiyama, H. *Chem.—Eur. J.* **2012**, *18*, 3153.

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(5) For α-silylallylboronate **1**, see: (a) Tsai, D. J.; Matteson, D. S. *Organometallics* **1983**, *2*, 236. (b) Shimizu, M.; Kitagawa, H.; Kurahashi, T.; Hiyama, T. *Angew. Chem., Int. Ed.* **2001**, *40*, 4283.

(6) For β-silylallylboronates **2**, see: (a) Wu, J. Y.; Moreau, B.; Ritter, T. *J. Am. Chem. Soc.* **2009**, *131*, 12915–12917. (b) Chang, K-J; Rayabarapu, D. K.; Yang, F. Y.; Cheng, C.-H. *J. Am. Chem. Soc.* **2005**, *127*, 126.

(7) For β-borylallylsilanes **3**, see: (a) Endo, K.; Sakamoto, A.; Ohkubo, T.; Shibata, T. *Chem. Lett.* **2011**, *40*, 1440. (b) Ohmura, T.; Oshima, K.; Suginome, M. *Angew. Chem., Int. Ed.* **2011**, *50*, 12501. (c) Ohmura, T.; Suginome, M. *Bull. Chem. Soc. Jpn.* **2009**, *82*, 29.

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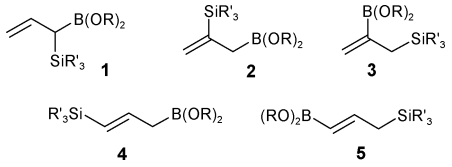


Figure 1. Allylic reagents containing a trimethylsilyl and a boronic ester group in an allylic position.

The reactions of these bifunctional reagents with carbonyl compounds have been well documented, with some specificity according to the location of the boron and silicon atoms. For example, an interesting switch of selectivity was observed when allylic compounds **1** were added to aldehydes upon use of an acidic catalyst,[10] while the rhodium-catalyzed conjugate addition of **5** to enones provided an efficient access to functionalized allylsilanes.[9e] In natural product synthesis, allylboronic esters **4** have found remarkable applications as building blocks for amphidinoline E,[11] hemibrevetoxin B,[12]mycalamine,[13] dictyostatin,[14] and bullatacin.[15]

Our interest in three-component reactions involving organoboron reagents[16] prompted us to explore the reactivity of configurationally stable γ-borylallylsilanes **5** toward various electrophilic species. This could open efficient new routes to α-substituted allylboronates **6**, complementary to that usually employed involving S_N2 (or S_N2') reactions on allyl (or vinyl)boranes possessing a leaving group X α (or γ) to the boron (Scheme 1).[10,17] The resulting products could further react with aldehydes or be involved in a cyclization process.

(8) For γ-silylallylboronates **4**, see: (a) Zhang, P.; Roundtree, I. A.; Morken, J. P. *Org. Lett.* **2012**, *14*, 1416. (b) Selander, N.; Szabó, K. J.; Aggarwal, V. K. *Synthesis* **2008**, 2293. (c) Lira, R.; Roush, W. R. *Org. Lett.* **2007**, *9*, 4315. (d) Jankowska, M.; Pietraszuk, C.; Marciniec, B.; Zaidlewicz, M. *Synlett* **2006**, 1695. (e) Dutheuil, G.; Hoffmann, R. W.; Brinkmann, H.; Frenking, G. *Chem. Ber.* **1990**, *123*, 2387.

(9) For γ-borylallylsilanes **5**, see: (a) Takaya, J.; Kirai, N.; Iwasawa, N. *J. Am. Chem. Soc.* **2011**, *133*, 12980. (b) Selander, N.; Willy, B.; Szabo, K. J. *Angew Chem Int. Ed.* **2010**, *49*, 4051. (c) Jankowska, M.; Pietraszuk, C.; Marciniec, B.; Zaidlewicz, M. *Synlett* **2006**, 1695. (d) Morill, C.; Funk, T. W.; Grubbs, R. H. *Tetrahedron Lett.* **2004**, *45*, 7733. (e) Yamamoto, Y.; Fujita, M.; Miyaura, N. *Synlett* **2002**, 767. (f) Pereira, S.; Srebnik, M. *Organometallics* **1995**, *14*, 3127.

(10) Carosi, L.; Lachance, H.; Hall, D. G. *Tetrahedron Lett.* **2005**, *46*, 8981.

(11) Va, P.; Roush, W. R. *J. Am. Chem. Soc.* **2006**, *128*, 15960.

(12) Zakarian, A.; Batch, A.; Holton, R. A. *J. Am. Chem. Soc.* **2003**, *125*, 7822.

(13) Marron, T.; Roush, W. R. *Tetrahedron Lett.* **1995**, *36*, 1581.

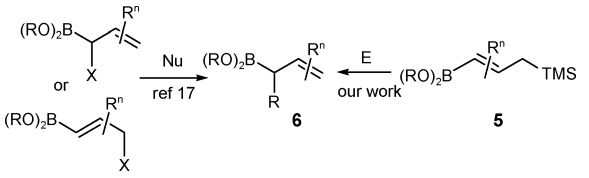
(14) Shimp, H. L.; Micalizio, G. C. *Tetrahedron* **2009**, *65*, 5908.

(15) Tinsley, J. M.; Mertz, E.; Chong, P. Y.; Rarig, R. A; Roush, W. R. *Org. Lett.* **2005**, *7*, 4245.

(16) (a) Tripoteau, F.; Verdelet, T.; Hercouet, A.; Carreaux, F.; Carboni, B. *Chem.—Eur. J.* **2011**, *17*, 13670. (b) Berrée, F.; Gernigon, N.; Hercouet, A.; Lin, C. H.; Carboni, B. *Eur. J. Org. Chem.* **2009**, 329. (c) Hercouet, A.; Berrée, F.; Lin, C. H.; Toupet, L.; Carboni, B. *Org. Lett.* **2007**, *9*, 1717. (d) Gao, X.; Hall, D. G.; Deligny, M.; Favre, A.; Carreaux, F.; Carboni, B. *Chem.—Eur. J.* **2006**, *12*, 3132.

(17) For selected examples, see: (a) Carosi, L.; Hall, D. G. *Angew. Chem., Int. Ed.* **2007**, *46*, 5913. (b) Lombardo, M.; Morganti, S.; Tozzi, M.; Trombini, C. *Eur. J. Org. Chem.* **2002**, 2823. (c) Schlapbach, A.; Hoffmann, R. W. *Eur. J. Org. Chem.* **2001**, 323. (d) Hoffmann, R. W.; Wolff, J. *Chem. Ber.* **1991**, *124*, 563. (e) Hoffmann, R. W.; Landmann, B. *Chem. Ber.* **1986**, *119*, 1039. (f) Matteson, D. S.; Majumdar, D. *J. Am. Chem. Soc.* **1980**, *102*, 7588.

Scheme 1. Access to α-Substituted Allylboronates



We started by studying the stereocontrolled synthesis of (*Z*)-1-fluoro-1-alkenes **8** from **5** (Scheme 1, R = F, Table 1). Fluorinated molecules have essential applications in the life sciences, medicine, medical imaging, agrochemicals, and materials.[18] A literature survey revealed several methods for the synthesis of 1-fluoro-1-alkenes, including Wittig type olefination, elimination reactions, addition to alkynes, electrophilic addition, or metathesis.[19] S_N2' Displacement of an allylic fluoride atom of 3,3-difluoropropenes with organolithium reagents was also reported recently.[20] Herein, we disclose an alternative approach based on a tandem electrophilic fluoration/allylation sequence from compounds **5** (Table 1).

The synthesis of starting allylsilanes featuring a boronic ester group at the extremity of the double bond was first carried out according to literature procedures: **5a** by Zr-catalyzed hydroboration of propargyltrimethylsilane with pinacolborane (57%);[21] **5b** by hydrogenation of [3-(trimethylsilyl)-1-propyn-1-yl] boronic ester in the presence of the Lindlar catalyst in combination with quinoline (77%);[22] **5c** by bromoboration of 1-hexyne followed by Pd-catalyzed cross-coupling with trimethylsilylmethylzinc bromide (28%);[23] and **5d** by Pt-catalyzed diboration of propargyltrimethylsilane (81%).[24]

Electrophilic fluorodesilylation of **5** was carried out using Selectfluor in acetonitrile in the presence of sodium bicarbonate (Table 1).[25] Due to the moderate stability of the expected allyl fluoride **7**,[26] we decided to perform a one-pot fluorodesilylation/allyboration sequence from **5**.

The corresponding homoallylic alcohols **8**–**16** were obtained in moderate to good yields (35–71%, two steps) with high stereocontrol. The structures of the major

(18) (a) *Fluorine in Medicinal. Chemistry and Chemical Biology*; Ojima, I., Ed.; Wiley-Blackwell: United Kingdom, 2009. (b) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320. (c) O'Hagan, D. *Chem. Soc. Rev.* **2008**, *37*, 309. (d) *Modern Fluoroorganic Chemistry: Synthesis, Reactivity, Applications*; Kirsch, P., Ed.; Wiley-VCH; Weinheim, 2005.

(19) For a recent pertinent review, see: Landelle, G.; Bergeron, M.; Turcotte-Savard, M. O.; Paquin, J.-F. *Chem. Soc. Rev.* **2011**, *40*, 2867.

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(22) Srebnik, M.; Bhat, N. G.; Brown, H. C. *Tetrahedron Lett.* **1988**, *29*, 2635.

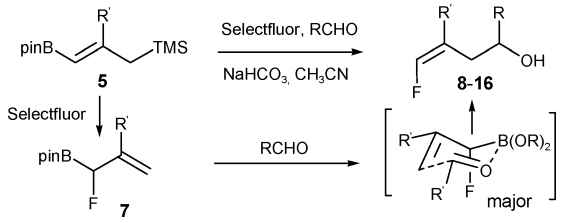
(23) Wang, C.; Tobrman, T.; Xu, Z.; Negishi, E-I *Org. Lett.* **2009**, *11*, 4092.

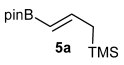
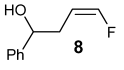
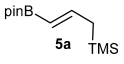
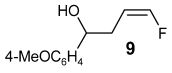
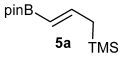
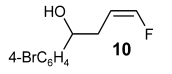
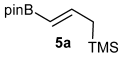
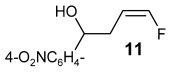
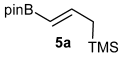
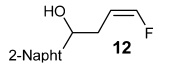
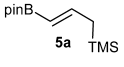
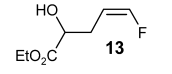
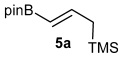
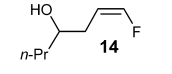
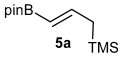
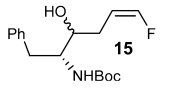
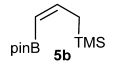
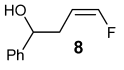
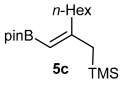
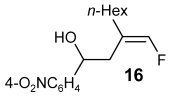
(24) Ishiyama, T.; Matsuda, N.; Miyaura, N.; Suzuki, A. *J. Am. Chem. Soc.* **1993**, *115*, 11018.

(25) Pacheco, M. C.; Purser, S.; Gouverneur, V. *Chem. Rev.* **2008**, *108*, 1943 and references therein.

(26) Although **7a** was identified in the crude ^1H NMR spectrum, we were unable to isolate it with satisfactory yield and purity.

Table 1. Electrophilic One-Pot Fluorodesilylation/Allylboration



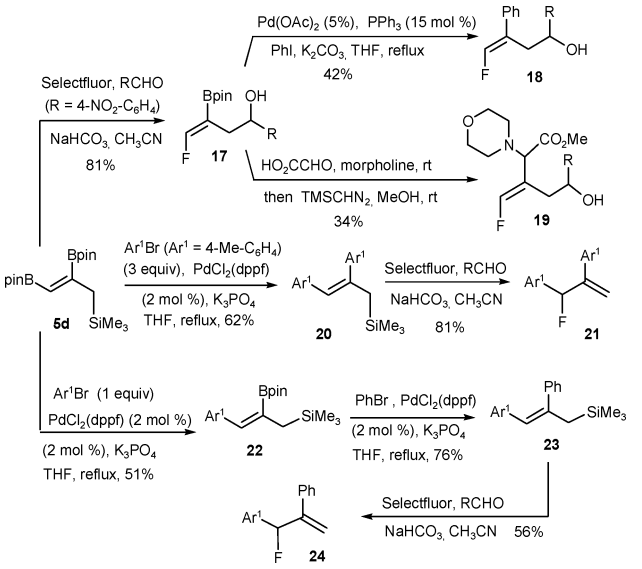
entry	allylsilane	R	product	yield(%)[a] (Z/E)[b]
1		Ph		51(95:5)
2		4-MeOC$_6$H$_4$-		43(93:7)
3		4-Br-C$_6$H$_4$-		49(95:5)
4		4-NO$_2$C$_6$H$_4$-		71(97:3)
5		2-Napht-		46(93:7)
6		EtO$_2$C		63(98:2)
7		*n*-Pr		35(95:5)
8				66(97:3)[c]
9		Ph		55(94:6)
10		4-NO$_2$C$_6$H$_4$-		54(93:7)[d]

[a] Isolated yields after column chromatography. [b] Measured by ^{19}F NMR on the crude product. [c] Mixture of *anti*/*syn* isomers (55:45). [d] The *Z*/*E* ratio was determined by ^{1}H NMR on the crude product.

(*Z*)-isomers were determined by ^{1}H NMR analysis: $J_{HC=CH}$ = 4.5–4.7 Hz for **8**–**15**, ^{1}H–^{1}H NOESY and ^{19}F–^{1}H HOESY experiments for **16**. The stereochemical course of the allylation step resulted from a preferred transition state where the F-atom adopts a pseudoaxial position, as mentioned in the literature for polar α-substituents.[27] Best results in terms of yield and isomeric purity were obtained with electron-deficient aldehydes, such as 4-nitrobenzaldehyde or ethyl glyoxylate (entries 4 and 6). All attempts to extend these results to the enantioenriched homoallylic alcohols failed, either from an (*S*,*S*)-1,2-dicyclohexylethanediol boronate **5a**′ or by carrying out the fluorination in the presence of hydroquinidine-2,5-diphenyl-4,6-pyrimidinediyldiether as a chiral additive.[28]

The presence of two boronic ester groups significantly increases the synthetic potential of 1-silyl-3-boryl-2-alkenes. In the case of **5d**, the fluorodesilylation/allyboration sequence can be followed by a Suzuki coupling or a borono-Mannich condensation to afford the alcohol **18** or the aminoester **19**. The coupling can also be directly carried out regio- and stereoselectively at the terminal over the internal B-pin.[29] A second coupling with another aryl bromide then provided the allylsilane **23**, a precursor of the allylic fluoride **24**. The same groups were directly introduced if 2 equiv of aryl bromide were engaged in the first step (Scheme 2).

Scheme 2. Access to Vinylic and Allylic Fluorides from **5e**



In a similar way, other halosuccinimides can be used to achieve electrophilic halogenations of **5a**. The reaction with *N*-iodosuccinimide was completed within 30 min to give **25** which slowly isomerized to the rearranged allylic iodide **26** (X = I) (20% after 1 h at rt) (Scheme 3). In the presence of an aldehyde, the homoallylic alcohol **27** was obtained in a low yield due to this competitive isomerization phenomenon. With *N*-bromosuccinimide, due to a slower 1,3-bromine migration, 1-bromoalkene **28** was produced in a better yield (43%, two steps, *Z*/*E*: 92/8). With the chloro derivative, the reaction proceeded to completion for 5 d at 60 °C without any trace of the corresponding allylic chloride **26** (X = Cl).[30]

Regarding carbon electrophiles, these can also be used in similar desilylation processes. With benzhydryl alcohol or propargylic alcohols, in the presence of 10 mol % of iron trichloride in methylene chloride, **5a** afforded the

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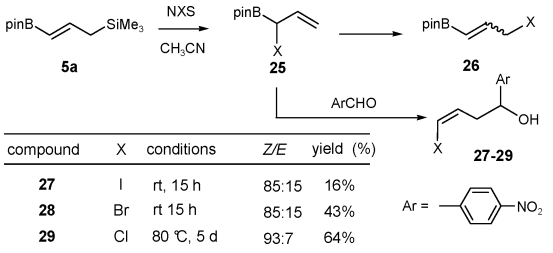
(30) The chloro derivative **24** was stable on storage, whereas the corresponding bromide deteriorated rapidly. Hoffmann, R. W.; Landmann, B. *Tetrahedron Lett.* **1983**, *24*, 3209.

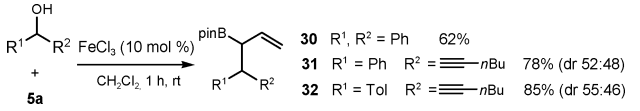
Scheme 3. Electrophilic Halogenations of **5a**



compound	X	conditions	*Z*/*E*	yield (%)
27	I	rt, 15 h	85:15	16%
28	Br	rt 15 h	85:15	43%
29	Cl	80 °C, 5 d	93:7	64%

corresponding allylboronates **30**–**32** in 62–85% yields (Scheme 4).[31,32]

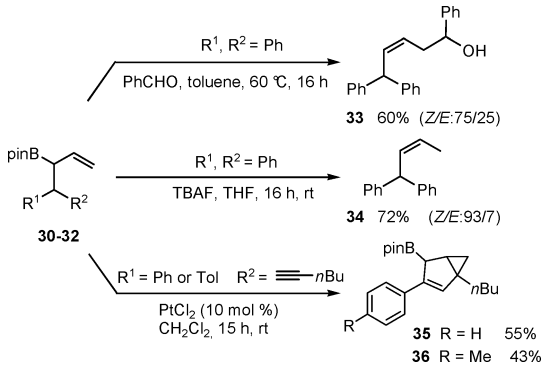
Scheme 4. $FeCl_3$-Catalyzed Allylation of Benzyhydrol and Propargylic Alcohols with **5a**



These compounds can be used in further functional transformations. The addition of benzaldehyde to **30** afforded the homoallylic alcohol **33** as a 25/75 mixture of *E*/*Z* isomers in 60% yield, while **34** was obtained with high *Z*-selectivity (93/7) following the protodeboronation procedure recently reported by V. K. Aggarwal (Scheme 5).[33] Since 1,5-enynes constitute an interesting class of substrate, where cycloisomerization under transition metal catalysis leads to highly functionalized carbocyclic structures,[34] we also investigated the behavior of **31**–**32** in the presence of metal catalysts.[35] Complex mixtures were produced with $(Ph_3P)AuCl$, $Au(OAc)_3$, $NaAuCl_4 \cdot 2H_2O$, and Na_2PdCl_4. By contrast, upon moving to $PtCl_2$, the boronated bicyclic products **35**–**36** were isolated in moderate yields (Scheme 5).

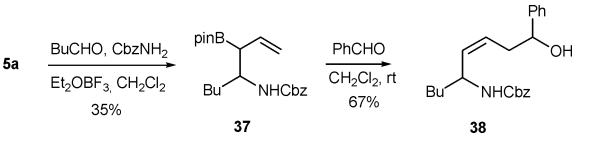
Other carbon electrophiles can also be involved in similar desilylation processes. Thus, acyliminium, formed *in situ* by mixing butyraldehyde and benzylcarbamate in the presence of boron trifluoride etherate,[36,37] led to a

Scheme 5. Transformations of Allylboronates **30**–**32**



mixture of diastereoisomeric *N*-protected allylamine **37** in a modest unoptimized 35% yield, a *N*-protected boron analogue of β-amino carboxylic ester[38] (Scheme 6). Addition to benzaldehyde afforded the *N*-protected amino alcohol **38** as a mixture of four stereomers.

Scheme 6. Lewis Acid Catalyzed Allylation of Iminium Species with **5a**



In summary, we have shown that 1-silyl-3-boryl-2-alkenes **5** are valuable precursors of diversely α-substituted allylboronates. Electrophilic fluorodesilylation can be applied as an efficient entry to (*Z*)-1-fluoro-1-alkenes and allyl fluorides, while their addition to activated alcohols in the presence of a Lewis acid afforded bicyclic compounds after platinum dichloride cyloisomerization. Studies are underway to expand this chemistry to enantioselective allylation reactions of other differently substituted γ-borylallylsilanes.

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Supporting Information Available. Experimental details and characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.