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Boron Carboxylate Catalysis of Homoallylboration

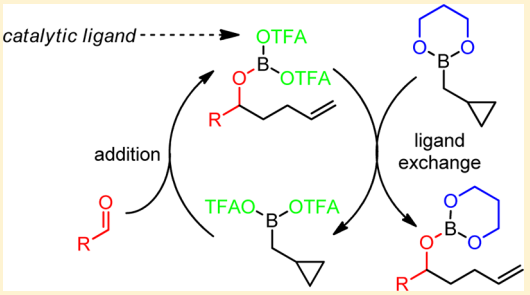
Gabrielle J. Dugas,[†] Yu-hong Lam,[‡] K. N. Houk,*[,‡] and Isaac J. Krauss*[,†]

[†]Department of Chemistry, Brandeis University, Waltham, Massachusetts 02454-9110, United States

[‡]Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90095-1569, United States

Supporting Information

ABSTRACT: Boron tris(trifluoroacetate) is identified as the first effective catalyst for the homoallyl- and homocrotylboration of aldehydes by cyclopropylcarbinylboronates. NMR spectroscopic studies and theoretical calculations of key intermediates and transition states both suggest that a ligand-exchange mechanism, akin to our previously reported $PhBCl_2$-promoted homoallylations, is operative. Our experimental and theoretical results also suggest that the catalytic activity of boron tris(trifluoroacetate) might originate from more facile catalytic turnover of the trifluoroacetate ligands (in agreement with DFT calculations) or from a lower propensity for formation of off-pathway reservoir intermediates (as observed by ^1H NMR). This work shows that carboxylates are viable catalytic ligands for homoallyl- and homocrotylations of carbonyl compounds and opens the door to the development of catalytic asymmetric versions of this transformation.



INTRODUCTION

Allylboration of carbonyl compounds is an extensively studied transformation whose regio- and stereochemical outcomes are readily predicted from reagent structure via Zimmerman–Traxler transition-state models.[1] We have recently shown that *cyclopropanated* allyl- and crotylboron reagents (**1**–**3**) are also capable of reacting through Zimmerman–Traxler transition states, affording *homo*allylation products (**5**–**7**) with complete regio-, diastereo-, and enantioselectivity (Scheme 1).[2]

We previously established $PhBCl_2$ as an effective promoter for this reaction.[2a] Theoretical calculations and NMR studies support the involvement of (cyclopropylcarbinyl)-dichloroboranes (**8**) as the homoallylating species, generated in situ by ligand exchange between **1**–**3** and $PhBCl_2$. However, the $PhBCl_2$ promoter must be used in excess and is strongly Lewis acidic. For greater substrate compatibility, it would be desirable to develop milder promoters which could be used catalytically. Moreover, in the case of achiral unsubstituted cyclopropylcarbinyl reagent **1**, asymmetric homoallylation

Scheme 1. Homoallylation via the Allylation Paradigm

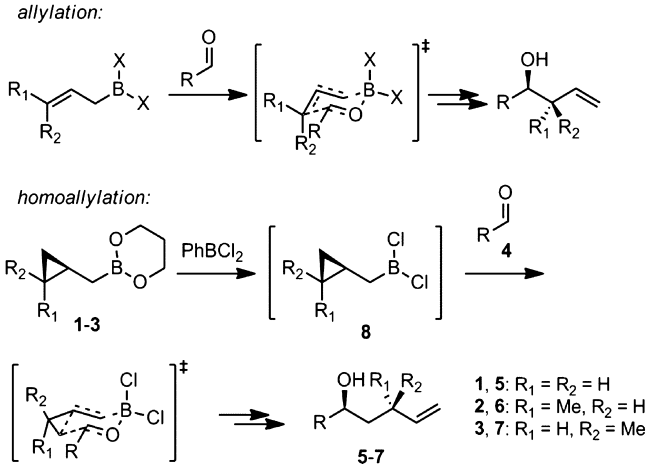
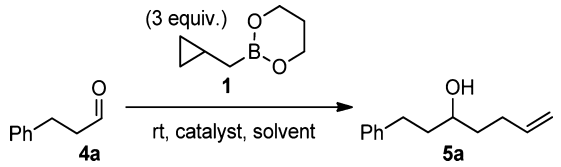


Table 1. Selected Preliminary Experiments



entry	catalyst	amount (mol %)	solvent	time (h)	yield[a] (%)
1	$PhBCl_2$	15	DCM	3	0[b]
2	$Sc(OTf)_3$	5	$CDCl_3$	2	0[b]
3	$Sc(OTf)_3$	10	$CDCl_3$	20	0[b]
4	$AlCl_3$	10	$CDCl_3$	24	0[b]
5	$Cu(OTf)_2$	10	$CDCl_3$	168	0[b]
6	$B(OTFA)_3$	15	DCM	0.5	74[c]
7	$B(OTFA)_3$	15	Et_2O	18	3
8	$B(OTFA)_3$	15	THF	18	1
9	$B(OTFA)_3$	15	pentane	4	1
10	$B(OTFA)_3$	15	toluene	1.5	26

[a]NMR yield, except entry 6. [b]Forcing the reaction with higher temperatures resulted in self-aldol products from **4a** and/or ring opening of reagent **1**. [c]Isolated yield.

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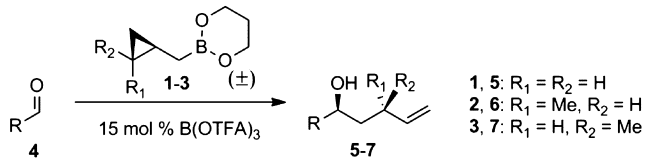
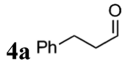
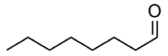
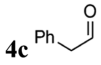
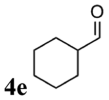
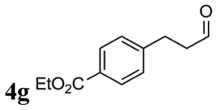
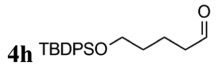
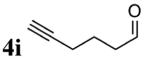
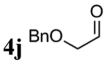
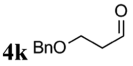
Table 2. Catalytic Homoallylation Scope[a]



entry	boronate	RCHO	time	product	yield[c]
1	**1**	**4a** 	30	**5a**	74 83[d]
2	**1**	**4b** 	45	**5b**	70
3	**1**	**4c** 	3.5h	**5c**	38
4	**1**	**4d** 	3h	**5d**	25 (56)
5	**1**	**4e** 	30	**5e**	49
6	**1**	**4f** 	5h	**5f**	50 (64)
7	**1**	**4g** 	1.5h	**5g**	74
8	**1**	**4h** 	60	**5h**	42
9	**2**	**4a**	30	**6a**	78
10	**2**	**4b**	30	**6b**	86
11	**2**	**4c**	25	**6c**	62
12	**2**	**4d**	30	**6d**	47 (77)
13	**2**	**4e**	30	**6e**	62
14	**2**	**4f**	60	**6f**	58 (78)
15	**2**	**4g**	30	**6g**	77
16	**2**	**4h**	30	**6h**	83
17	**2**	**4i** 	30	**6i**	76
18	**2**	**4j** 	45	**6j**	69
19	**2**	**4k** 	45	**6k**	60
20	**3**	**4a**	20	**7a**	87
21	**3**	**4b**	30	**7b**	69
22	**3**	**4c**	45	**7c**	54
23	**3**	**4d**	30	**7d**	39 (67)
24	**3**	**4e**	30	**7e**	75
25	**3**	**4f**	60	**7f**	53 (70)
26	**3**	**4g**	30	**7g**	81
27	**3**	**4h**	15	**7h**	87
28	**3**	**4i**	15	**7i**	93
29	**3**	**4j**	15	**7j**	56
30	**3**	**4k**	30	**7k**	52

[a]Reagents **2** and **3** were used in racemic form. [b]All reactions were performed with 3.0 equiv f boronates **1**−**3**, except where indicated. Entries 3−8 are reactions run at 45 °C, and all others were run at rt. [c]Isolated yields for reactions on 0.1−0.3 mmol scale, except where indicated. For volatile substrates, NMR yields are listed in parentheses. The diastereomeric ratios, as determined by ^{1}H NMR integration, were >20:1 for **6a**−**k** and >12:1 for **7a**−**k**. [d]Isolated yield for reaction run on 1 mmol scale and with 2.0 equiv of **1**.

would only be possible with a chiral promoter, in which case it would also be preferable to use catalytic amounts.

RESULTS AND DISCUSSION

For these reasons, we tested several promoters under catalytic conditions (Table 1). When a catalytic amount (15 mol %) of $PhBCl_2$ was used, no homoallylation product was observed at all. Other Lewis acids previously reported to catalyze allylation, such as $Sc(OTf)_3$,[3] $AlCl_3$,[4] and $Cu(OTf)_2$,[3b] also failed to produce any homoallylation product, although aldehyde self-aldol products were observed in most cases after extended reaction times. On the other hand, we found that 15 mol % of boron tris(trifluoroacetate) ($B(OTFA)_3$)[5] effectively promoted the homoallylation in 74% yield. As we had previously seen with the stoichiometric $PhBCl_2$-promoted homoallylation,[2a] coordinating solvents such as Et_2O and THF hindered the reaction, and another noncoordinating solvent, toluene, effected a slower, lower yielding reaction.

We thus investigated the scope of the $B(OTFA)_3$ catalyst with a panel of aldehydes and cyclopropylcarbinylboronates **1**−**3** (Table 2). In parallel with what we had observed for stoichiometric $PhBCl_2$-promoted reactions, under $B(OTFA)_3$

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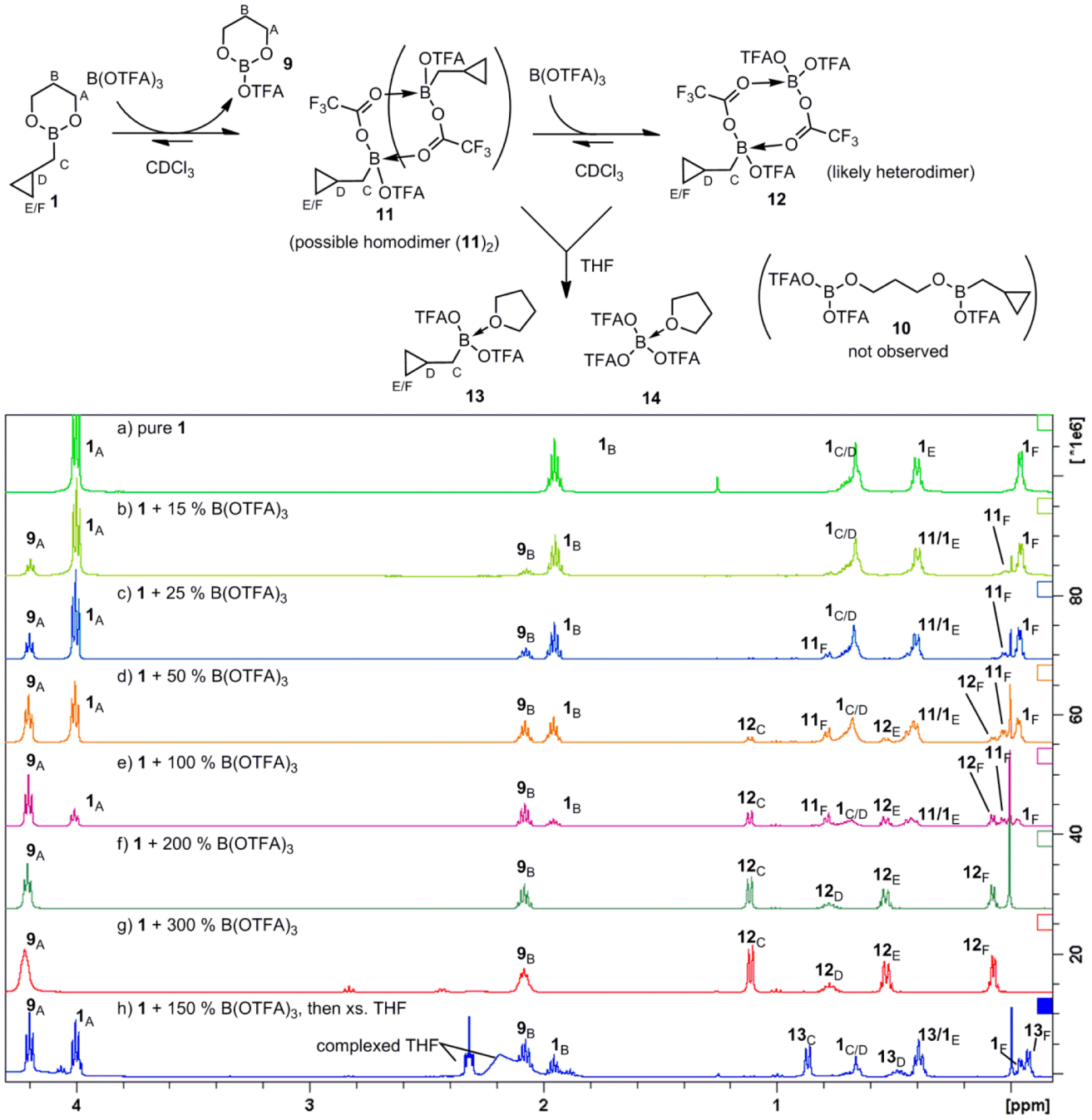

Figure 1. 400 MHz ^{1}H NMR spectra of **1** in the presence of 0−300 mol % of $B(OTFA)_3$.

catalysis, the *cis* (**2**) and *trans* boronates (**3**) reacted faster and gave higher yields than the unsubstituted reagent **1**. Interestingly, 15 mol % of $B(OTFA)_3$ also promoted a faster reaction than did stoichiometric $PhBCl_2$. As seen in entry 1, the reaction of dihydrocinnamaldehyde (**4a**) was complete after 30 min at room temperature, as compared with 14 h with our previous $PhBCl_2$-promoted conditions.[2a] Similarly, pivaldehyde (**4f**) reacted completely with **2** in about 60 min under $B(OTFA)_3$ catalysis (entry 14), as compared with 7 days under $PhBCl_2$ conditions.[2b] The ester (**4g**), the silyl ether (**4h**), and the terminal alkyne (**4i**) were all well tolerated. The compatibility of the $B(OTFA)_3$ catalyst with the benzyl ether (**4j** and **4k**) is also noteworthy, as attempted $PhBCl_2$-mediated reactions with these substrates result in immediate debenzylation.[6]

In order to investigate the possible structure of the active homoallylating species, we conducted ^{1}H and ^{11}B NMR spectroscopic studies. To begin, $B(OTFA)_3$ showed a ^{11}B NMR resonance at δ 3.4, consistent with tetracoordinate boron, suggesting a bridged dimer structure, $[B(OTFA)_3]_2$ (although, for simplicity, we will continue to refer to this compound as a monomer).[7] The dimeric nature of boron trifluoroacetates was further evident from the ^{1}H NMR spectrum (Figure 1) upon mixing boronate **1** (spectrum a)[2a] with various amounts of $B(OTFA)_3$ (spectra b−g). As $B(OTFA)_3$ was titrated in, an intermediate set of cyclopropylcarbinyl resonances ($\mathbf{11}_{C-F}$), and later a final set ($\mathbf{12}_{C-F}$), became visible, simultaneous with

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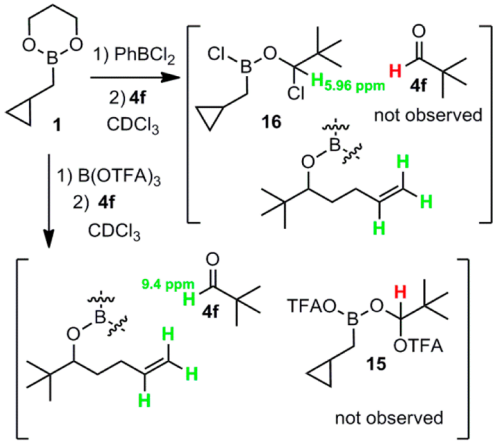
the conversion of propanediol derived peaks from $\mathbf{1}_{A,B}$ to just *one* new set of peaks, $\mathbf{9}_{A,B}$. Conversion of **1** entirely to **12** and **9** was complete only upon addition of two full equivalents of $B(OTFA)_3$ (spectrum f) and could be driven backward again by adding more **1**. Furthermore, no peak corresponding to unreacted $B(OTFA)_3$ could be seen in the ^{19}F NMR spectra when **1** was combined with 1−2 equiv of $B(OTFA)_3$. Together, these observations strongly support a picture in which cyclopropylcarbinyl$B(OTFA)_2$ (**11**) initially generated from **1** + $B(OTFA)_3$ is ultimately captured as a heterodimeric complex $RB(OTFA)_2{\cdot}B(OTFA)_3$ (**12**). Because only two sets of propanediol CH_2−O peaks were ever observed at around δ 4, we rule out the possibility that the peaks $\mathbf{11}_{C-F}$ could correspond to a partial ligand transfer product **10**, and we speculate that **11** is either the monomeric or dimeric $RB(OTFA)_2$ species. Consistent with this overall picture, the mixture of **11**/**12** is converted to a single cyclopropylcarbinyl species ($\mathbf{13}_{C-F}$, spectrum h) upon addition of THF, which we have assigned as the THF complex **13**.

Scheme 2. −OTFA/RCHO Adducts Not Observed by ^1H NMR



Upon addition of the aldehyde to **11**/**12**, we also looked for possible formation of OTFA adducts to the aldehyde carbon (**15**), analogous to chloride adduct **16**, which we had observed as reservoir species when $PhBCl_2$ was used as promotor (Scheme 2).[2b] When aldehyde is added to the $PhBCl_2$-promoted reaction, it is immediately converted entirely to **16**, which then slowly converts to product. After **1** was mixed with 15% $B(OTFA)_3$, we added aldehyde **4f** and observed only product peaks and unconsumed aldehyde in the ^1H NMR. No peaks corresponding to putative OTFA adduct **15** were observed in the ∼4.6−7 ppm δ region, suggesting that **15** is most likely absent.

We performed density functional theory (DFT) calculations to investigate the possible intermediates implicated in these homoallylations. As shown in Scheme 3, the ligand-exchange reaction between **1** and $B(OTFA)_3$ to form **11** and **9** is exergonic, with $\Delta G_{rxn} = -7.7$ kcal/mol (eq 1). The Lewis acid−base reaction between **1** and $B(OTFA)_3$ forming adduct **17** is less exergonic and has a ΔG_{rxn} value of only −6.2 kcal/mol (eq 2). The Zimmerman−Traxler transition structures for the homoallylation of acetaldehyde involving **11** and **17** were also computed (Figure 2). The free energy of activation ($\Delta G^{‡}$) is

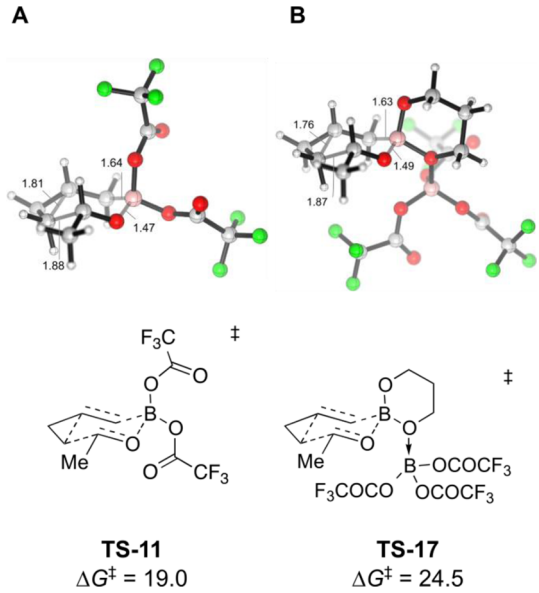
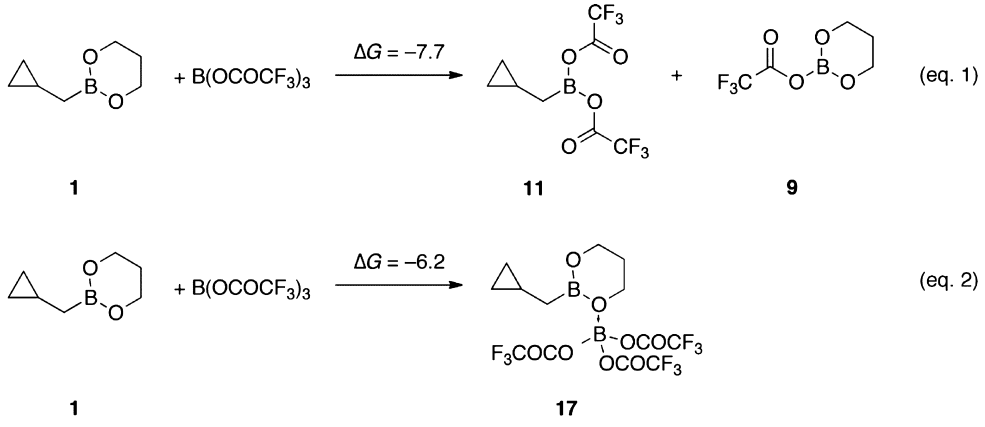


Figure 2. Zimmerman−Traxler transition structures (B3LYP-D3/TZVP, $\Delta G^{‡}$ values in kcal/mol) for homoallylborations of acetaldehyde by **11** (A) and **17** (B).

19.0 kcal/mol involving **11** (TS-**11**), but 24.5 kcal/mol starting from **17** (TS-**17**). Thus, the DFT calculations suggest that the homoallylating species is the spectroscopically observable species **11** generated in situ from **1** and $B(OTFA)_3$.

Scheme 3. Energetics of Formation of Intermediates 11 and 17 (B3LYP-D3/TZVP, in kcal/mol).



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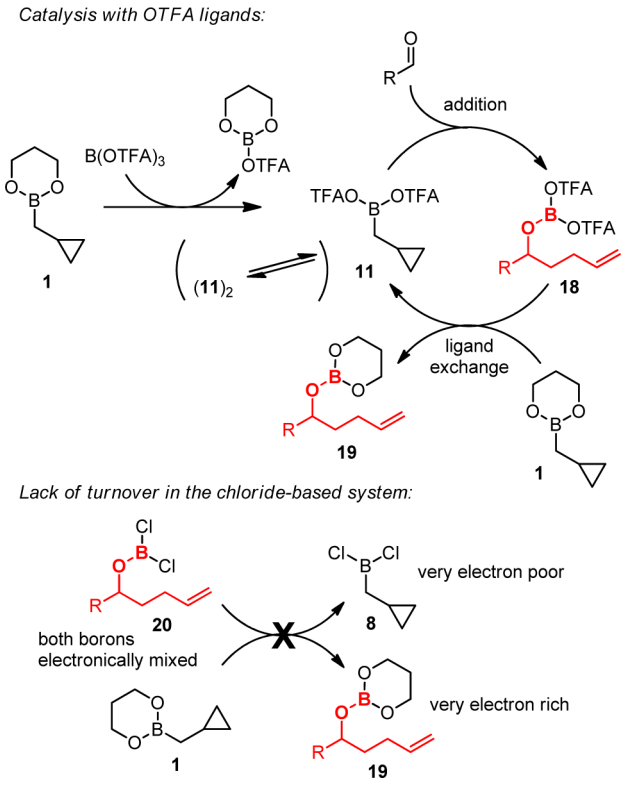
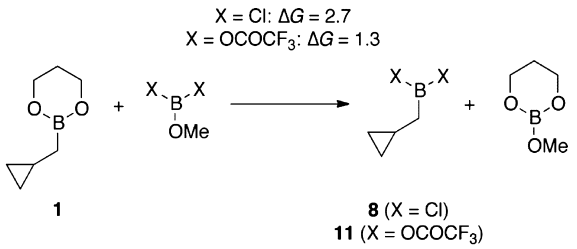
The proposed mechanism of catalysis is depicted in Scheme 4. Exchange of diol and OTFA ligands between **1** and

Scheme 4. Proposed Catalytic Cycle



$B(OTFA)_3$ produces **11** (possibly dimeric), which reacts with aldehyde to afford product **18**.[8] Trifluoroacetates then exchange with the propanediol ligand on the next catalytic equivalent of **1** to regenerate **11**. In the analogous $PhBCl_2$-promoted reaction, chlorides may fail to turn over for multiple reasons. We computed the reaction energies for the ligand exchange step involved in catalytic turnover, using a methyl group to represent the alkyl chain in the homoallylated products **18**–**20** (Scheme 5). With ΔG = 2.7 kcal/mol, the ligand exchange

Scheme 5. Energetics of Ligand Exchange Implicated in Catalytic Turnover (B3LYP-D3/TZVP, in kcal/mol)



in the chloride system (X = Cl) is calculated to be thermodynamically less favorable than the system employing the trifluoroacetate ligand (X = $OCOCF_3$), for which we calculated a ΔG value of 1.3 kcal/mol. The uphill nature of this turnover step is intuitive because of the electronic properties of the ligands. In the formation of **11** and **19** from **1** and **18**, all resonance electron-donating ligands (3 alkoxides) must be collected together on the boron atom of **19**, and all electron-withdrawing ligands ($OCOCF_3$ and alkyl) must be collected on the boron of **11**. By contrast, prior to turnover, species **1** and **18** both contain mixtures of electron-donating and -withdrawing ligands, intuitively a lower energy arrangement. By this reasoning, the analogous turnover step ought to be even more uphill in the case of the more electronegative X = Cl, and this notion is consistent with the computational result. Apart from the increased difficulty of the turnover step, an alternative explanation for the difference in catalytic activity for X = Cl vs $OCOCF_3$ is the fact that the chlorides from $PhBCl_2$ are largely sequestered as aldehyde adduct **16** (Scheme 2), whereas the less nucleophilic trifluoroacetates seem not to form analogous adduct **15** and thus remain mobile between boron atoms.

CONCLUSION

In conclusion, we have identified boron tris(trifluoroacetate) as an effective catalyst for the homoallylation of aldehydes. Spectroscopic studies and DFT calculations suggest that the active homoallylating species is the ligand-exchange product **11** rather than the Lewis adduct **17**. The problem of aldehyde sequestration by nucleophilic addition of a ligand on the boron Lewis acid, which was previously observed under $PhBCl_2$-promoted conditions,[2b] is circumvented as the trifluoroacetate ligand in the active catalyst is less nucleophilic than chloride. Studies with structurally related chiral boron catalysts are under way and will be reported in due course.

EXPERIMENTAL SECTION

General Information and Methods. All solvents for routine isolation of products and chromatography were reagent grade. Aldehydes were purchased from commercial sources and freshly distilled, except for aldehydes **4g**,[9] **4h**,[10] **4i**,[11] and **4k**,[12] which were synthesized based on literature procedures. Flash chromatography was performed using Silicycle R10030B F60 SiliaFlash silica gel (230–400 mesh) with the indicated solvents. All reactions were monitored by thin-layer chromatography on 0.25 mm silica plates (F-254), except for the reactions with isobutryaldehyde (**4d**) and pivaldehyde (**4f**), which were monitored by GC/MS (see below). TLC plates were stained with vanillin or $KMnO_4$. Reactions with volatile products were monitored by GC/MS with a triple-axis detector. NMR spectra were recorded with 400 MHz spectrometers (proton frequency) for ^1H, ^{11}B, ^{13}C, and ^{19}F NMR. The ^1H NMR data are reported as the chemical shift in parts per million, multiplicity (s, singlet; d, doublet; dd, doublet of doublets; t, triplet; q, quartet; m, multiplet), and number of protons. ^{11}B spectra are reported as ppm relative to $BF_3{\cdot}OEt_2$. ^{13}C spectra are referenced to the central peak of $CDCl_3$ as 77.0 ppm. ^{19}F spectra are reported as ppm relative to $CFCl_3$. HRMS was performed using electrospray (ES) or electron-impact (EI) ionization, as needed.

Synthesis of Boronates. Starting boronates **1**, **2**, and **3** were prepared according to our previous literature procedure, and characterization data were reported previously, with the *trans* reagent (**2**) containing ~5% *cis* isomer by ^1H NMR.[2] The catalyst $B(OTFA)_3$ was prepared according to a literature procedure.[5] Thus, a solution of trifluoroacetic acid in pentane (3.0 equiv, or 3.0 mL in 100 mL pentane) was transferred by cannulation to a solution of BBr_3 in pentane (1.0 equiv, or 1.3 mL in 100 mL pentane), followed by 50 mL of pentane rinse. After 1 h of stirring, the solvent was distilled off in vacuo (using manifold vacuum, not a rotary evaporator), and the resulting material was subjected to ~1 mmHg vacuum overnight to yield a white powder in 64% yield (3 g). NMR spectroscopic data for this compound have not previously been reported: ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.2 (q, J_{CF} = 46 Hz), 113.7 (q, J_{CF} = 284 Hz); ^{11}B NMR (128 MHz, $CDCl_3$) δ 3.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ 75.7.

General Experimental Procedure for the Synthesis of Bishomoallyl alcohols. To a solution of $B(OTFA)_3$ (7.5 mol %) in anhydrous DCM (enough to produce a 0.2 M solution of aldehyde) in an oven-dried Schlenk tube was added boronate (3.0 equiv). The

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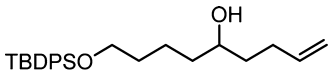
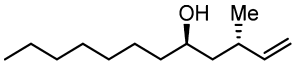
solution was stirred under nitrogen for 1 min. Aldehyde (1.0 equiv) was added, and the reaction mixture was stirred at 45 °C (for products **5c−h**) or room temperature (all other products). After TLC analysis showed consumption of aldehyde, the reaction was quenched with 3 M sodium hydroxide, and the mixture was extracted with EtOAc three times. The organic layers were then dried over $MgSO_4$, combined, and concentrated on a rotary evaporator, and the crude reaction mixture was purified by flash chromatography (EtOAc/hexane) to yield the desired product. For reactions with benzyl-protected products (employing **4j** and **4k**), flash chromatography was performed with 5% EtOAc/toluene. For volatile substrates (**4d**,**f**), reactions were monitored by GC/MS, extraction was done with DCM, and solvent was removed with no lower than 200 Torr vacuum, until a small amount of solvent remained, at which point the remaining solvent was blown off under a gentle stream of nitrogen. For these substrates, chromatography was performed with Et_2O/pentane solvent mixtures.

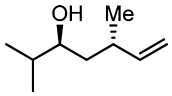
Characterization Data of New Compounds.



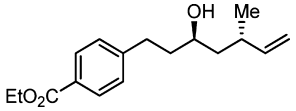
5h: colorless oil (0.130 mmol scale, 21.2 mg, 41%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71−7.61 (m, 4H), 7.45−7.32 (m, 6H), 5.90−5.77 (m, 1H), 5.04 (app d, J = 17.3 Hz, 1H), 4.97 (app d, J = 10.2 Hz, 1H), 3.67 (t, J = 6.3 Hz, 2H), 3.64−3.53 (m, 1H), 2.26−2.05 (m, 2H), 1.70−1.30 (m, 9H + H_2O), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 138.6, 135.6, 134.1, 129.5, 127.6, 114.7, 71.4, 63.8, 37.1, 36.4, 32.5, 30.0, 26.9, 21.9, 19.2; IR (neat) 3356 (br), 3070, 2931, 2858, 1724, 1466, 1427, 1109, 702; HRMS (ES-TOF) (m/z) calcd for $C_{25}H_{37}O_2Si$ (M + H)$^+$ 397.2568, found 397.2563.



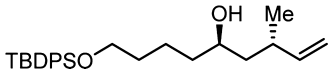
6b: colorless oil (0.324 mmol scale, 55.5 mg, 86%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (ddd, 1H, J = 17.3, 10.2, 7.8), 5.03 (br d, 1H, J = 17.2), 4.93 (br d, 1H, J = 10.2), 3.72−3.63 (m, 1H), 2.33 (app sept, 1H, J = 7.1), 1.53−1.19 (m, 15H), 1.02 (d, 3H, J = 6.7), 0.88 (t, 3H, J = 6.8); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 112.7, 70.4, 44.4, 37.7, 35.5, 31.8, 29.6, 29.3, 25.5, 22.6, 20.2, 14.1; IR (neat) 3341 (br), 3070, 2958, 2923, 2856, 1641, 1557, 1459, 994, 909, 725; HRMS (EI-TOF) calcd for $C_{13}H_{26}O$ (M$^+$) 198.1984, found 198.1982.



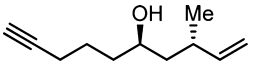
6d: colorless oil (0.250 mmol scale, 16.8 mg, 47%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (ddd, 1H, J = 17.2, 10.2, 7.7), 5.04 (ddd, 1H, J = 17.2, 1.4, 1.4), 4.94 (br d, 1H, J = 10.3), 3.52−3.44 (m, 1H), 2.34 (app sept, 1H, J = 7.0), 1.71−1.58 (m, 1H), 1.50 (br d, 1H, J = 4.4), 1.48−1.33 (m, 2H), 1.02 (d, 3H, J = 6.6), 0.92 (d, 3H, J = 6.8), 0.90 (d, 3H, J = 6.8); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 112.6, 75.0, 41.1, 35.5, 33.7, 19.9, 18.7, 16.9; IR (neat) 3359 (br), 3072, 2961, 2883, 1638, 1461, 1374, 988, 910; HRMS (EI-TOF) calcd for $C_6H_{11}O$ (M − iPr$^-$)$^+$ 99.0810, found 99.0812, calcd for C_4H_9O (M − homocrotyl$^-$) 73.0753, found 73.0654.



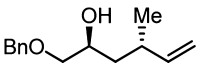
6g: colorless oil (0.124 mmol scale, 38.6 mg, 77%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 (app d, 2H, J = 8.2), 7.26 (app d, 2H, J = 8.1), 5.76 (ddd, 1H, J = 17.2, 10.2, 8.0), 5.01 (br d, 1H, J = 17.2), 4.93 (br dd, 1H, J = 10.3, 1.3), 4.36 (q, 2H, J = 7.1), 3.77−3.62 (m, 1H), 2.93−2.79 (m, 1H), 2.79−2.64 (m, 1H), 2.32 (app sept, 1H, J = 7.1), 1.96−1.65 (m, 3H), 1.54 (app dt, 1H, J = 13.9, 8.1), 1.44 (app td, 1H, J = 6.8, 4.2), 1.38 (t, 3H, J = 7.1), 1.00 (d, 3H, J = 6.8); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 147.7, 144.9, 129.6, 128.4, 128.1, 113.0, 69.8, 60.8, 44.5, 38.9, 35.7, 31.9, 20.4, 14.3; IR (neat) 3402 (br), 3071, 2970, 2929, 2869, 1712, 1610, 1452, 1274, 1176, 1104, 1021, 912, 856, 763; HRMS (ES-TOF) calcd for $C_{17}H_{25}O_3$ (M + H)$^+$ 277.1804, found 277.1802.



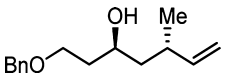
6h: colorless oil (0.202 mmol scale, 67.1 mg, 81%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.62 (m, 4H), 7.44−7.32 (m, 6H), 5.77 (ddd, J = 17.4, 10.2, 7.8 Hz, 1H), 5.01 (app d, J = 17.4 Hz, 1H), 4.93 (app d, J = 10.2 Hz, 1H), 3.67 (t, 6.4 Hz, 2H), 3.69−3.60 (m, 1H), 2.32 (app sept, J = 7 Hz, 1H), 1.69−1.30 (m, 9 H + H_2O), 1.05 (s, 9H), 1.01 (d, 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 135.6, 134.1, 129.5, 127.6, 112.7, 70.3, 63.8, 44.4, 37.4, 35.4, 32.5, 26.9, 21.7, 20.2, 19.2; IR (neat) 3374 (br), 3071, 2930, 2858, 1960, 1890, 1822, 1725, 1460, 1427, 1108, 701; HRMS (ES-TOF) (m/z) calcd for $C_{26}H_{38}O_2NaSi$ (M + Na)$^+$ 433.2539, found 433.2537.



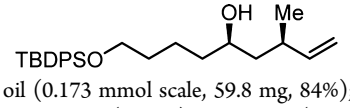
6i: colorless oil (0.191 mmol scale, 24.1 mg, 76%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.78 (ddd, 1H, J = 17.2, 10.3, 8.0), 5.04 (ddd, 1H, J = 17.2, 1.6, 1.0), 4.95 (ddd, 1H, J = 10.2, 1.6, 0.6), 3.76−3.66 (m, 1H), 2.33 (app sept, 1H, J = 7.1), 2.23 (td, 2H, J = 6.6, 2.7), 1.95 (t, 1H, J = 2.7), 1.76−1.36 (m, 7H + water), 1.02 (d, 3H, J = 6.6); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 113.0, 84.4, 70.0, 68.4, 44.5, 36.5, 35.6, 24.5, 20.3, 18.4; IR (neat) 3388 (br), 3299, 3075, 2924, 2118 (weak), 1839, 1818, 1638, 1454, 1092, 994, 912; HRMS (EI-TOF) calcd for $C_{11}H_{18}O$ (M$^+$) 166.1358, found 166.1358.



6j: colorless oil (0.151 mmol scale, 23.2 mg, 69%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29−7.39 (m, 5H), 5.73−5.81 (m, 1H), 4.99 (d, J = 17 Hz, 1H), 4.93 (d, J = 10 Hz, 1H), 4.57 (s, 2H), 3.86−3.94 (m, 1H), 3.52 (dd, J = 3, 9 Hz, 1H), 3.34 (dd, J = 8, 10 Hz, 1H), 2.31−2.36 (m, 2H), 1.56−1.60 (m, 1H + H_2O), 1.31−1.38 (m, 1H) 1.03 (d, J = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 138.0, 128.4, 127.8, 127.7, 112.7, 74.5, 73.3, 68.6, 39.7, 34.3, 19.8; IR (neat) 3468, 3064, 3028, 2963, 2924, 2866, 1638, 1453, 1099, 912, 749 cm^{-1}; HRMS (ES-TOF) (m/z) [M + Na]$^+$ calcd for $C_{14}H_{20}O_2Na$ 243.1361, found 243.1362.



6k: colorless oil (0.173 mmol scale, 24.3 mg, 60%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.38 (m, 5H), 5.72−5.81 (m, 1H), 5.00 (d, J = 17 Hz, 1H), 4.93 (d, J = 10 Hz, 1H), 4.53 (s, 2H), 3.85−3.93 (m, 1H), 3.70−3.75 (m, 1H), 3.63−3.68 (m, 1H), 2.85 (s, 1H), 2.29−2.39 (m, 1H), 1.72−1.79 (m, 2H), 1.55−1.62 (m, 2H), 1.31−1.38 (m, 1H), 1.03 (d, J = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 137.9, 128.4, 127.7, 127.6, 112.5, 73.3, 69.4, 69.1, 44.2, 36.6, 34.7, 19.9; IR (neat) 3425, 3065, 3031, 2960, 2930, 2866, 1638, 1458, 1098, 911, 748 cm^{-1}; HRMS (ES-TOF) (m/z) [M + Na]$^+$ calcd for $C_{15}H_{22}O_2Na$ 257.1517, found 257.1519.



7h: colorless oil (0.173 mmol scale, 59.8 mg, 84%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70−7.63 (m, 4H), 7.44−7.32 (m, 6H), 5.67 (ddd, J = 17.3, 10.2, 8.3 Hz, 1H), 5.02 (app d, 17.3 Hz, 1H), 4.95 (app d, 10.2 Hz, 1H), 3.67 (t, J = 6.3 Hz, 2H), 3.63−3.55 (m, 1H), 2.46−2.35 (m, 1H), 1.65−1.30 (m, 9H + H_2O); 1.05 (s, 9H), 1.01 (d, 6.7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.2, 135.5, 134.1, 129.5, 127.6, 113.4, 69.6, 63.8, 44.2, 37.6, 34.7, 32.5, 26.9, 21.8, 21.2, 19.2; IR (neat) 3356 (br), 3070, 2930, 2858, 1960, 1890, 1820, 1724, 1460, 1427, 1108, 700; HRMS (ES-TOF) (m/z) calcd for $C_{26}H_{38}O_2NaSi$ (M + Na)$^+$ 433.2539, found 433.2538.

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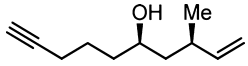
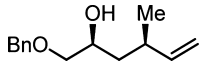
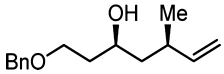


7i: colorless oil (0.242 mmol scale, 37.5 mg, 93%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.57 (ddd, J = 8.2, 10.3, 17.7 Hz, 1H) 5.03 (d, 17.7 Hz, 1H), 4.97 (d, 10.3 Hz, 1H), 3.71−3.61 (m, 1H), 2.46−2.34 (m, 1H), 2.26−2.17 (m, 2H) 1.95 (t, 2.6 Hz, 1H), 1.78−1.63 (m, 1H), 1.63−1.33 (m, 6H + H_2O), 1.02 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.0, 113.5, 83.3, 69.2, 68.4, 44.3, 36.8, 34.7, 24.6, 21.1, 18.4 IR (neat) 3400 (br), 3301, 3078, 2950, 2115 (weak), 1639, 1454, 995, 912; HRMS (EI-TOF) calcd for $C_{11}H_{18}O$ (M^+) 166.1358, found 166.1359.



7j: colorless oil (0.191 mmol, 23.6 mg, 56%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.38 (m, 5H), 5.60−5.69 (m, 1H), 5.03 (d, J = 17 Hz, 1H), 4.96 (d, J = 10 Hz, 1H), 4.55 (s, 2H), 3.84−3.90 (m, 1H), 3.48 (dd, J = 3, 9 Hz, 1H), 3.32 (dd, J = 8, 10 Hz, 1H), 2.37−2.49 (m, 1H), 2.25−2.33 (m, 1H), 1.44−1.52 (m, 1H), 1.26−1.33 (m, 1H), 1.03 (d, J = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 138.0, 128.4, 127.7, 127.6, 113.6, 74.9, 73.3, 68.4, 39.9, 34.4, 21.2; IR (neat) 3463, 3065, 2961, 2928, 2865,1640, 1495, 1275, 1260, 1104, 913, 750 cm^{-1}; HRMS (ES-TOF) (m/z) [M + Na]$^+$ calcd for $C_{14}H_{20}O_2Na$ 243.1361, found 243.1359.



7k: colorless oil (0.101 mmol, 12.5 mg, 52%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27−7.37 (m, 5H), 5.64−5.73 (m, 1H), 5.04 (d, J = 17 Hz, 1H), 4.97 (d, J = 10 Hz, 1H), 4.52 (s, 2H), 3.82−3.90 (m, 1H), 3.62−3.74 (m, 2H), 2.76 (s, 1H), 2.38−2.47 (m, 1H), 1.72−1.78 (m, 2H), 1.48−1.55 (m, 2H), 1.31−1.37 (m, 1H), 1.02 (d, J = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.1, 138.0, 128.4, 127.7, 127.6, 113.3, 73.3, 69.1, 69.0, 44.4, 37.0, 34.5, 21.1; IR (neat) 3411, 3065, 3031, 2959, 2923, 2865, 1639, 1453, 1275, 1097, 913, 749 cm^{-1}; HRMS (ES-TOF) (m/z) [M + Na]$^+$ calcd for $C_{15}H_{22}O_2Na$ 257.1517, found 257.1513.

Scale, weights, yields, and references listing spectral data for reactions producing known compounds: **5a**[13] (1.00 mmol scale, 158 mg, 83%); **5b**[14] (0.215 mmol scale, 28 mg, 70%); **5c**[15] (0.200 mmol scale, 13 mg, 38%); **5d**[16] (0.120 mmol scale, 3.8 mg, 25% (56% NMR)); **5e**[17] (0.139 mmol scale, 12 mg, 49%); **5f**[18] (0.116 mmol scale, 8.3 mg, 50% (64% NMR)); **5g**[2a] (0.156 mmol scale, 30 mg, 74%); **6a**[19] (0.255 mmol scale, 41 mg, 78%); **6c**[20] (0.192 mmol scale, 23 mg, 62%); **6e**[21] (0.238 mmol scale, 27 mg, 62%); **6f**[21] (0.217 mmol scale, 20 mg, 58% (78% NMR)); **7a**[19] (0.246 mmol scale, 44 mg, 87%); **7b**[2b] (0.179 mmol scale, 25 mg, 69%); **7c**[2b] (0.122 mmol scale, 13 mg, 54%); **7d**[2b] (0.135 mmol scale, 7.5 mg, 39% (67% NMR)); **7e**[2b] (0.168 mmol scale, 23 mg, 75%); **7f**[2b] (0.141 mmol scale, 12 mg, 53% (70% NMR)); **7g**[2b] (0.204 mmol scale, 46 mg, 81%).

COMPUTATIONAL METHODS

The geometry optimizations and frequency computations were performed in the gas phase using the dispersion-corrected density functional B3LYP[22−25]-D3[26] (with Becke−Johnson damping[27−30]) in conjunction with the triple-ζ TZVP[31] basis set. The errors in the computed entropies introduced by the treatment of low-frequency modes as harmonic oscillators were corrected for by a quasiharmonic approximation described by Cramer and Truhlar,[32] in which the vibrational frequencies lower than 100 cm^{-1} were raised to 100 cm^{-1} when computing the vibrational partition functions using the usual harmonic oscillator approximation.

All of the quantum chemical computations were performed using Gaussian 09.[33] All structural representations were generated with CYLview.[34]

ASSOCIATED CONTENT

Supporting Information

^{1}H NMR and ^{13}C NMR spectra. Full citation of ref 33. Computational details and energies and Cartesian coordinates of all computed structures. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding Authors

*E-mail: houk@chem.ucla.edu.
*E-mail: kraussi@brandeis.edu.

Notes

The authors declare no competing financial interest.

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