EurJOC
European Journal of Organic Chemistry

Chemistry Europe
European Chemical Societies Publishing

Accepted Article

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To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.202000977

Link to VoR: https://doi.org/10.1002/ejoc.202000977

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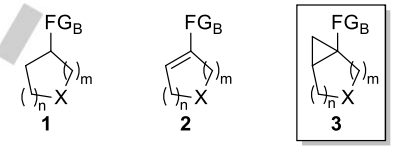
Multigram synthesis of heterabicyclo[n.1.0]alkan-1-yl trifluoroborates

Ihor Kleban,[a,b] Yevhen Krokhmaliuk,[a,c] Sofiia Reut,[a,c] Serhii Shuvakin,[a,c] Vyacheslav V. Pendyukh,[a] Oleksandr I. Khyzhan,[a] Dmytro S. Yarmoliuk,[a] Dr. Andriy V. Tymtsunik,*[a,d] Dr. Yuliya V. Rassukana,[b,d] Dr. Oleksandr O. Grygorenko[a,c]

Abstract: An approach to the synthesis of oxa- and azabicyclo[n.1.0]alkan-1-yl trifluoroborates on a multigram scale was developed. Two synthetic schemes were evaluated: the first one based on the lithiation – borylation of the corresponding 2-bromoallyl derivatives, and another one relying on regioselective hydroboration of the appropriate hetera-substituted enynes. The second method appeared to be more efficient in terms of scalability and substrate scope. Further steps included ring closing-metathesis, mild palladium-catalyzed cyclopropanation with diazomethane, and reaction with KHF_2 and furnished the title compounds on up to *ca.* 50 g scale in a single run (10–41% overall yield, 4–5 steps).

Introduction

Saturated heterocycles have always been considered as attractive structural motifs for early drug discovery;[1–3] interest to these compounds has even increased in recent years when concepts like "escape from flatland"[4,5] and "lead-likeness"[6–8] have been established in medicinal chemistry. While synthetic methodologies allowing for the construction of the saturated heterocyclic rings are of immense value to synthetic chemistry, alternative approach relying on the use of building blocks[9] already including heteroaliphatic moieties is also worth attention. In most cases, common reactions of such compounds include C–N bond formation.[10,11] Building blocks providing new C–C bonds are relatively rarer; typically, they are organoboron derivatives which have gained momentum with recent advances in sp^2-sp^3 couplings.[12–15] Molander's photoredox and related methodologies are excellent examples of introducing building blocks of type **1** (X = $BF_3^-K^+$) into such transformations (Figure 1);[16–21] however, building blocks **1** have low reactivity under other commonly used C–C coupling conditions. An alternative approach that steps back to classical palladium-catalyzed couplings involves partially unsaturated reagents of general structure **2**, which are highly effective in *e.g.* Suzuki – Miyaura reaction and are hence widely used for that reason.[22–28] Nevertheless, introducing the double bond alters significantly chemical properties of the products obtained, as well as results in increasing sp^2 carbon atom fraction and "flattening" of their molecules, which is not compatible with the spirit of "thinking in 3D"-type concepts of medicinal chemistry mentioned above.



X = O, NPG, S; FG_B = Bpin, $BF_3^-K^+$ etc.
m = 1, 2; n = 1, 2, 3

Figure 1. Heteroaliphatic organoboron derivatives – potential reagents for the C–C coupling reactions

A possible idea to solve this issue includes the use of a cyclopropane ring as an isostere of the double bond.[29,30] It should be noted that cyclopropylboronic acids and their derivatives have attracted increasing attention in recent years.[31,32,41,42,33–40] Having partially unsaturated nature, cyclopropyl boronates possess sufficient reactivity towards the Suzuki – Miyaura reaction conditions, while keeping some important structural features of the parent saturated analogues (*e.g.* chirality). Application of this design concept to heteroaliphatic organoboron derivatives **1** leads to hetera-substituted bicyclo[n.1.0]alkan-1-yl boronates **3**, which are the key compounds in this study.

It should be noted that in 2017, Harris and co-workers published a communication describing synthesis and coupling reactions of trifluoroborates **4a–c** (Figure 2).[43] The published approach to the preparation of these compounds relied on the Simmons – Smith reaction of the corresponding cyclic vinyl boronates as the key step; it had moderate yield (46–51%) and was performed at up to 3 g scale of the final product. Meanwhile, the utility of the building blocks of type **4** for medicinal chemistry has been approved by successful C–C couplings since 1-aryl-3-azabicyc-lo[3.1.0]hexane motif and similar bicyclic cores are widespread among biologically active compounds, clinical candidates bicifadine (for pain treatment), centanafadine (for attention deficit hyperactivity disorder), and amitifadine (for the treatment of addiction) being among the most prominent examples.[43] The ultimate goal of our current work was the development of the

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general and efficient method for the preparation of aza-, oxa- and thia-substituted bicyclo[n.1.0]alkan-1-yl boronates of type **3**, which could be used at the multigram scale. Specifically, we were interested in the synthesis of trifluoroborates **4a–j** (Figure 3).

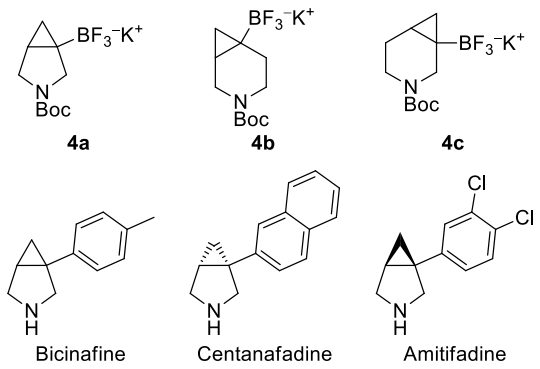


Figure 2. Some useful azabicyclo[n.1.0]alkanes reported in the literature

Results and Discussion

Our strategy for the preparation of the building blocks **4a–j** was quite straightforward and relied on cyclopropanation of the appropriate cyclic vinyl boronates **5a–j**. The most accessible substrates in these series were pinacol esters **5b** and **5g** since they could be prepared from the corresponding symmetric ketones **6b** and **6g** *via* the palladium-catalyzed reaction of the corresponding triflates **7b** and **7g** with bis(pinacolato)diboron (Scheme 1). This approach has been reported in the literature for both *O*- and *N*-derived compounds **5b**[44] and **5g**.[27]

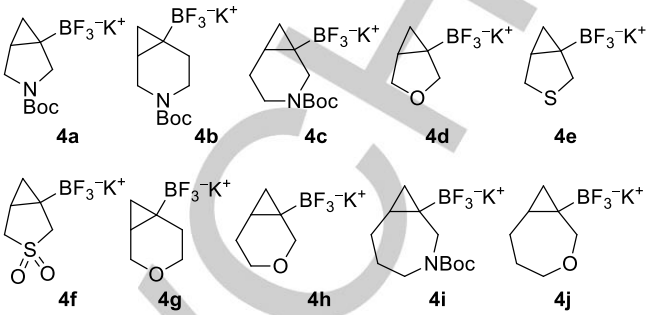
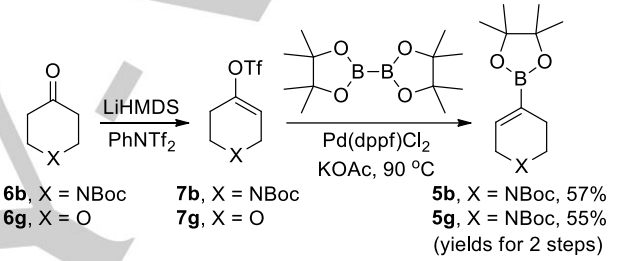
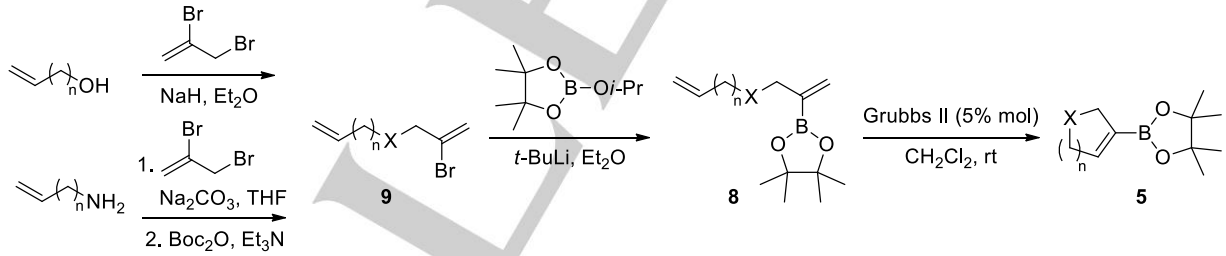


Figure 3. Target molecules of this study



Scheme 1. Known synthesis of heteroaliphatic vinyl boronates **5b** and **5g**

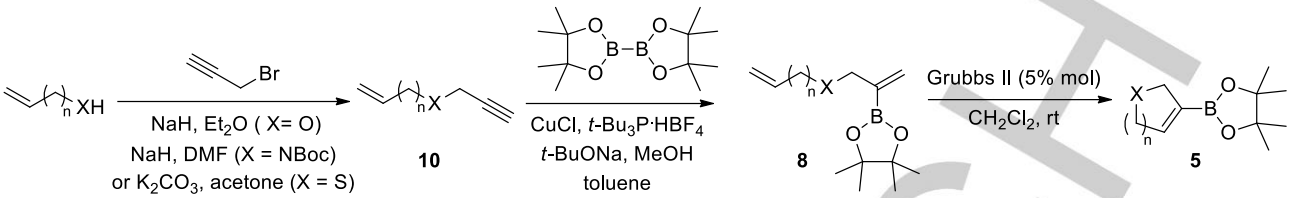
Table 1. Synthesis of boronates **5a**, **5c**, **5d**, and **5i–k** using the modified method of Renaud and Ouellet



#	X	n	Vinyl bromide **9** (yield, %)	Acyclic boronate **8** (yield, %)	Cyclic boronate **5** (yield, %)	Overall yield of **5**
1	NBoc	1	**9a** (44)	**8a** (45)	**5a** (84)	7.6 g, 16%
2	NBoc	2	**9c** (48)	**8c** (52)	**5c** (72)	7.2 g, 18%
3	O	1	**9d** (76)	**8d** (65)	**5d** (85)	16.3 g, 42%
4	O	2	**9h** (60)	**8h** (75)	**5h** (81)	17.6 g, 36%
5	NBoc	3	**9i** (52)	**8i** (58)	**5i** (70)[a]	7.7 g, 21%
6	O	3	**9j** (80)	**8j** (55)	**5j** (60)[a]	14.9 g, 26%

[a] The reaction was performed in toluene at reflux.

Table 2. Synthesis of boronates **5a**–**k** using an alternative method developed in this work



#	X	n	Enyne **10** (yield, %)	Acyclic boronate **8** (yield, %)	Cyclic boronate **5** (yield, %)	Overall yield of **5**
1	NBoc	1	**10a** (87)	**8a** (82)	**5a** (85)	74.8 g, 60%
2	NBoc	2	**10c** (92)	**8c** (86)	**5c** (72)	61.3 g, 57%
3	O	1	**10d**[a]	**8d** (48)[b]	**5d** (85)	82.2 g, 40%
4	S	1	**10e**[a]	**8e** (46)[b]	**5e** (86)[c]	9.66 g, 40%
5	SO_2	2	**10f** (91)[c]	**8f** (71)	**5f** (88)	32.0 g, 57%
6	O	2	**10h** (74)	**8h** (73)	**5h** (81)	188 g, 44%
7	NBoc	3	**10i** (94)	**8i** (77)	**5i** (72)[d]	11.3 g, 52%
8	O	3	**10j** (80)	**8j** (60)	**5j** (60)[d]	32.0 g, 29%

[a] Used in the next step without isolation or purification [b] Yield for two steps [c] 2nd generation Hoveyda – Grubbs catalyst (5% mol) was used. [d] The reaction was performed in toluene at reflux. [c] Compound **10f** was obtained by oxidation of **10e** with MCPBA (2 eq, CH_2Cl_2, rt)

The method was not effective for other substrates of type **5** due to the regioselectivity problem at the first step of the reaction sequence. Therefore, synthesis of *N*- and *O*-substituted cyclic vinyl boronates **5a**, **5c**, **5d**, and **5h**–**j** relied on an alternative method by Renaud and Ouellet[23] including ring-closing metathesis as the key transformation (Table 1), which was used by the previous authors for the preparation of **5a**, **5d**, and **5h** on *ca.* 100 mg scale. We have found that intermediate **8d** could be obtained using the reported procedure in 65% overall yield on up to 22.4 g scale. For the ring-closing metathesis of **8d**, the original protocol was modified to ensure its scalability. In particular, the benzene solvent was replaced with less toxic CH_2Cl_2, the more stable 2nd generation Grubbs catalyst was used, and the concentration of the substrate was increased from 0.004–0.05 M to 0.33 M to minimize the solvent consumption. As a result, the target product **5d** was obtained in 85% yield (16.3 g scale).

Using these optimized conditions, the substrates **5a**, **5c**, and **5i** were obtained in 72–84% yield on a 7.2–17.6 g scale (Table 1). In the case of **5i** and **5j**, the metathesis step was performed at elevated temperature (toluene, reflux; 70% and 60% yield, respectively).

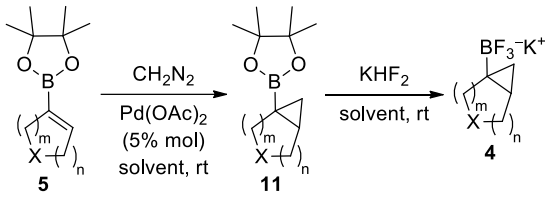
Unfortunately, the synthesis was not amendable to further scale-up. The lithiation – borylation step appeared to be the bottleneck of the method. Thus, a considerable drop of the yield (to 16%) occurred upon attempted preparation of **8h** from 80 g of **9h** in a single run using the procedures developed. Moreover, the method did not work for the preparation of sulfur-containing boronates **5e** and **5f** since the corresponding synthetic intermediates **8e** or **8f** could not be obtained according to the proposed scheme.

Therefore, an alternative approach was considered which relied on copper-catalyzed hydroboration of enynes **10**, in turn, obtained by alkylation of the corresponding *O*-, *N*-, or *S*-nucleophiles with propargyl bromide (Table 2). Using the conditions similar to those reported for other propargylic derivatives (bis(pinacolato)diboron, CuCl, *t*-$Bu_3P{\cdot}HBF_4$, *t*-BuONa, MeOH in toluene),[45] the target product **8h** was obtained from **10h** in 73% yield with good regioselectivity: less than 3% of the corresponding terminal boronate was observed in the crude product by ^1H NMR. The method worked well for all the substrates **10** and appeared to be very efficient upon scale up so that up to 236 g of the target products **8** (for the case of **8h**) could be obtained. Ring-closing metathesis of these dienes using the optimized protocol described above also showed good scalability (up to 188 g for the case of **5h**).

For the preparation of the remaining cyclic vinyl boronate **5f**, chemoselective oxidation of **5e** with MCPBA was envisaged initially. Unfortunately, the target product could not be obtained in all attempts. Therefore, oxidation of **10e** was performed

instead (MCPBA (2 eq), CH_2Cl_2, rt), and the resulting product **10f** (91% yield) was transformed into target sulfolene derivative **5f** using the common reaction sequence described above (62% yield over 2 steps).

Table 3. Synthesis of trifluoroborates **4a–k**



#	X	n	m	Starting material **5**	Product **11** (yield, %)	Product **4** (yield, %)	Overall yield of **4**[a]
1	NBoc	1	1	**5a**	**11a** (64)	**4a** (94)	11.2 g, 36%
2	NBoc	1	2	**5b**	**11b** (73)	**4b** (99)	53.5 g 41%
3	NBoc	2	1	**5c**	**11c** (63)	**4c** (92)	35.1 g, 33%
4	O	1	1	**5d**	**11d** (51)[b]	**4d** (98)	12.3 g, 20%
5	S	1	1	**5e**	**11e** (0)	–	–
6	SO_2	1	1	**5f**	**11f** (0)	–	–
7	O	1	2	**5g**	**11g** (58)	**4g** (96)	20.5 g, 31%
6	O	2	1	**5h**	**11h** (50)	**4h** (95)	26.4 g 21%
7	NBoc	3	1	**5i**	**11i** (40)	**4i** (94)	6.81 g, 20%
8	O	3	1	**5j**	**11j** (38)[a]	**4j** (95)[a]	5.48 g 10%

[a] Including synthesis of **5** according to Scheme 1 or Table 2 [b] After the two consecutive runs with the same sample

The final part of this study was related to the cyclopropanation of the substrates **5a–j**. Initially, the reported method (i.e. the Simmons – Smith reaction)[43] was checked for scalability with substrate **5b**; unfortunately, the yield of the target product **11b** was not satisfactory. Therefore, we have switched our efforts to the elaboration of an alternative cyclopropanation procedure. A recent publication by AbbVie chemists attracted our attention; they described flow reactor-based cyclopropanation of various styrylboronic esters with diazomethane on up to 2.4 mmol scale.[35] Although we had some concerns about using this dangerous reagent, recent procedures for safe generation and handling of diazoalkane solutions[46–48] prompted us to consider this approach for the cyclopropanation of **5**. It was found that a reaction of **5b** with CH_2N_2 in *t*-BuOMe in the presence of $Pd(OAc)_2$ (5% mol) proceeded with high efficiency already at 0 °C and gave target cyclopropane derivative **11b** in 73% yield (58.9 g scale) (Table 3). The method was also efficient for the preparation of other bicyclic boronates **11a**, **11c**, **11d**, and **11g–j** (but not **11e** and **11f**); the products were obtained in 38–64% yield on 6.87–39.5 g scale. In the case of **5d**, a repetition of the procedure with the crude product obtained after the first run (i.e. using larger excess of the diazomethane) was required.

It should be noted that high reactivity of vinyl boronates **5** bearing a trisubstituted double bond towards diazomethane is not usual since, in our experience, trisubstituted alkenes typically do not react under such conditions.[35,49,50] A more detailed study of this phenomenon will be reported in another publication. A possible explanation of the fact that **5e** and **5f** did not react with the carbenoid under the aforementioned conditions might include catalyst poisoning and electron-withdrawing effects of the sulfone moiety, respectively. The latter statement is also partially confirmed by the fact that compound **5d** also demonstrated lowered reactivity.

Finally, the synthesized boronates **11a–j** were transformed into the corresponding trifluoroborates **4a–j** (which are more suitable substrates for the C–C and C–N coupling reactions[41,43] using the standard protocol (94–98% yield, up to *ca.* 50 g scale).[51]

Conclusions

Two approaches to the synthesis of heterabicyclo[n.1.0]alkan-1-yl trifluoroborates **4** were evaluated for the multigram preparation of the title compounds. One synthetic scheme was based on the lithiation – borylation of the corresponding 2-bromoallyl derivatives **9**; it could be used to obtain up to *ca.* 10–15 g of the target products but was not amendable to further scale-up. Moreover, it could not be applied to the sulfur-containing derivatives. An alternative approach that relied on copper-catalyzed chemo- and regioselective hydroboration of enynes **10** was more convenient and worked well on up to 236 g scale of acyclic boronates **8**. Further ring-closing metathesis of **8** was also optimized for a hundred-gram scale; special conditions were required for the sulfur (II)-containing diene (i.e. the use of Hoveyda – Grubbs 2nd generation catalyst), as well as for the reactions leading to the formation of seven-membered rings (elevated temperatures). To construct the bicyclic system of the title compounds, palladium-catalyzed cyclopropanation of resulting heterocyclic alkenyl boronates **5** with diazomethane appeared to be very efficient. The reaction proceeded very smoothly already at 0 °C, which is not common for the trisubstituted alkenes. Therefore, despite the use of the potentially dangerous reagent, a safe protocol for the key cyclopropanation step could be developed. The method worked well for oxa- and aza-, but not for sulfa-substituted derivatives. Finally, pinacolates **11** were transformed into target oxa- and azabicyclo[n.1.0]alkan-1-yl trifluoroborates **4** on up to *ca.* 50 g scale in a single run (10–41% yield over 4–5 steps).

Experimental Section

General. The solvents were purified according to the standard methods.[52] Compounds **5b**[44] and **5g**[27] were obtained using the reported procedures. All other starting materials were purchased from commercial sources. Melting points were measured on MPA100 OptiMelt automated melting point system. Analytical TLC was performed using Polychrom SI F254 plates. Column chromatography was performed using Kieselgel Merck 60 (230–400 mesh) as the stationary phase. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 170 Avance 500 spectrometer (at 499.9 MHz for Protons and 124.9 MHz for Carbon-13) and Varian Unity Plus 400 spectrometer (at 400.4 MHz for protons and 100.7 MHz for Carbon-13). Chemical shifts are reported in ppm downfield from TMS as an internal standard. Mass spectra were recorded on an Agilent 1100 LCMSD SL instrument (chemical ionization (APCI), electrospray ionization (ESI)) and Agilent 5890 Series II 5972 GCMS instrument (electron impact ionization (EI)). High-resolution mass spectra (HRMS) were recorded on Agilent Infinity 1260 UHPLC system coupled to 6224 Accurate Mass TOF LC/MS system.

General procedure for the synthesis of 9a, 9c, and 9i. To a solution of the corresponding amine (0.350 mol) in THF (700 mL), 2,3-dibromopropene (63.0 g, 0.315 mol) was added dropwise, and the resulting mixture was stirred for 2 h at rt. Then Et_3N (88 mL, 0.630 mol) and Boc_2O (75.5 g, 0.345 mol) were added, and the reaction mixture was left overnight at rt. The solvent was removed in vacuo, the residue was dissolved in EtOAc (700 mL), washed with 1 M aq KH_2PO_4 (500 mL), H_2O (500 mL), and brine (500 mL). The organic phase was dried over Na_2SO_4 and evaporated in vacuo.

***tert*-Butyl allyl(2-bromoallyl)carbamate (9a).** Yield 42.5 g (44%) from allyl amine (20.0 g, 0.350 mol). Colorless liquid; the compound existed as a mixture of rotamers; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.84–5.61 (m, 2H), 5.56 (s, 1H), 5.22–5.02 (m, 2H), 4.07 (s, 1H), 4.01 (s, 1H), 3.89 (s, 1H), 3.82 (s, 1H), 1.53 (s, 2H) and 1.46 (s, 7H) ppm; MS (EI): *m/z* = 220/222 $[M–C_4H_8]^+$; HRMS (ESI) *m/z* calcd. for $C_{11}H_{18}BrNO_2Na$ $[M+Na]^+$ 298.0418; found: 298.0414. Other spectral and physical data were in accordance with the literature.[53]

***tert*-Butyl (2-bromoallyl)(but-3-en-1-yl)carbamate (9c).** Yield 18.2 g (48%) from homoallylamine (9.28 g, 0.131 mol). Reddish liquid; the compound existed as a mixture of rotamers; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.86–5.74 (m, 1H), 5.71 (d, *J* = 11.0 Hz, 1H), 5.56 (s, 1H), 5.08 (d, *J* = 18.2 Hz, 1H), 5.04 (d, *J* = 11.0Hz, 1H), 4.09 and 4.02 (s, 2H), 3.32 and 3.27 (t, *J* = 7.8Hz, 2H), 2.30 (t, *J* = 7.8Hz, 2H), 1.48 and 1.46 (s, 9H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 155.3 and 155.0, 135.2, 129.9 and 129.7, 117.0 and 116.7, 116.3, 80.1, 55.0 and 54.5, 46.5 and 46.4, 33.0 and 32.5, 28.3 ppm; MS (CI): *m/z* = 234/236 $[M–C_4H_8+H]^+$; HRMS (ESI) *m/z* calcd. for $C_{12}H_{20}BrNO_2Na$ $[M+Na]^+$ 312.0575; found: 312.0570.

***tert*-Butyl (2-bromoallyl)(pent-4-en-1-yl)carbamate (9i).** The product was purified by flash chromatography (hexanes – EtOAc (12:1) as eluent). Yield 21.3 g (52%) from pent-4-en-1-amine (11.4 g, 0.135 mol). Yellowish liquid; the compound existed as a mixture of rotamers; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.77 (ddt, *J* = 17.2, 10.3, 6.6 Hz, 1H), 5.70–5.60 (m, 1H), 5.52 (s, 1H), 5.00 (d, *J* = 17.2 Hz, 2H), 4.95 (d, *J* = 10.6 Hz, 1H), 4.05 and 3.98 (s, 2H), 3.21 (dd, *J* = 17.2, 7.5 Hz, 2H), 2.02 (q, *J* = 7.5 Hz, 2H), 1.60 (quint, *J* = 7.5 Hz, 2H), 1.43 (s, 9H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 155.4 and 155.0, 137.8, 129.9, 116.9 and 116.3, 115.0, 80.0, 54.8 and 54.3, 46.4, 31.0, 28.3, 27.4 and 27.2 ppm; HRMS (ESI) m/z calcd. for $C_{13}H_{22}BrNO_2Na$ $[M+Na]^+$ 326.0732; found: 326.0729.

General procedure for the synthesis of 9d, 9h, and 9j. NaH (27.7 g, 60% in mineral oil, 0.692 mol) was washed with hexanes (3×250 mL) under an argon flow. Et_2O (700 mL) was added, followed by dropwise addition of the corresponding alkenol (0.694 mol) upon stirring (CAUTION! Vigorous gas evolution and reaction mixture thickening was observed). After the addition was complete, the reaction mixture was heated at 30 °C for 1 h, and 2,3-dibromopropene (124.7 g, 0.624 mol) was added dropwise at rt. The reaction mixture was refluxed overnight (monitored by ^{1}H NMR spectra), then cooled, and H_2O (400 mL) was added carefully dropwise. The organic phase was separated, dried over Na_2SO_4, and evaporated in vacuo.

3-(Allyloxy)-2-bromoprop-1-ene (9d). Yield 35.3 g (76%) from allyl alcohol (15.2 g, 0.262 mol). Brownish liquid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.99–5.86 (m, 2H), 5.63 (s, 1H), 5.32 (dt, *J* = 17.2, 1.9 Hz, 1H), 5.23 (dt, *J* = 10.9, 1.9 Hz, 1H), 4.11 (d, *J* = 1.9 Hz, 2H), 4.05 (dt, *J* = 5.5, 1.9 Hz, 2H) ppm. Other spectral and physical data were in accordance with the literature.[53]

4-((2-Bromoallyl)oxy)but-1-ene (9h). Yield 79.5 g (60%) from but-3-en-1-ol (50.0 g, 0.624 mol). Brownish liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.92 (s, 1H), 5.90–5.78 (m, 1H), 5.61 (s, 1H), 5.12 (d, *J* = 17.3 Hz, 1H), 5.07 (d, *J* = 10.3 Hz, 1H), 4.11 (s, 2H), 3.54 (t, *J* = 6.7 Hz, 2H), 2.38 (q, *J* = 6.7 Hz, 2H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 134.9, 129.6, 117.3, 116.6, 74.9, 69.8, 34.1 ppm; HRMS (ESI) *m/z* calcd. for $C_7H_{11}BrONa$ $[M+Na]^+$ 212.9891; found: 212.9894.

5-((2-Bromoallyl)oxy)pent-1-ene (9j). Yield 75.8 g (80%) from pent-4-en-1-ol (39.7 g, 0.462 mol). Brownish liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.90 (q, *J* = 1.7 Hz, 1H), 5.87–5.75 (m, 1H), 5.60 (d, *J* = 1.7 Hz, 1H), 5.03 (dq, *J* = 17.1, 1.7 Hz, 1H), 4.97 (dd, *J* = 10.4, 1.7 Hz, 1H), 4.07 (s, 2H), 3.48 (t, *J* = 6.7 Hz, 2H), 2.15 (q, *J* = 6.7 Hz, 2H), 1.70 (quint, *J* = 6.7 Hz, 2H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 138.1, 129.9, 117.2, 114.9, 74.9, 69.8, 30.2, 28.8 ppm; HRMS (ESI) *m/z* calcd. for $C_8H_{13}BrONa$ $[M+Na]^+$ 227.0047; found: 227.0041.

General procedure for the synthesis of 10a, 10c, and 10i. To a suspension of NaH (54.0 g, 60% in mineral oil, 1.35 mol) in DMF (1.3 L), a solution of the corresponding *N*-Boc-amine (0.900 mol) in DMF (200 mL) was added dropwise at –10 °C. The reaction mixture was stirred at 0 °C for 30 min, and propargyl bromide (215 g, 1.80 mol) was added dropwise at 0 °C. The reaction mixture was left at rt overnight (monitored by ^{1}H NMR spectra). H_2O (200 mL) was added carefully dropwise to the reaction mixture, followed by an additional amount of H_2O (2.5 L). The resulting mixture was extracted with *t*-BuOMe (3×700 mL). The combined organic phases were washed with brine (1 L), dried over Na_2SO_4, and evaporated in vacuo.

***tert*-Butyl allyl(prop-2-yn-1-yl)carbamate (10a).** Yield 153 g (87%) from *tert*-butyl allylcarbamate (141 g, 0.900 mol). Physical state; the compound existed as a mixture of rotamers; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 5.75 (ddq, *J* = 16.6, 11.3, 5.9 Hz, 1H), 5.22–5.09 (m, 2H), 4.15–3.93 (m, 2H), 3.91 (s, 2H), 2.16 (s, 1H), 1.44 (s, 9H) ppm. Other spectral and physical data were in accordance with the literature.[54]

***tert*-Butyl but-3-en-1-yl(prop-2-yn-1-yl)carbamate (10c).** Yield 65.0 g (92%) from *tert*-butyl but-3-en-1-ylcarbamate (53.2 g, 0.311 mol). Brownish liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.04–5.88 (m, 1H), 5.58 (d, *J* = 7.6 Hz, 1H), 5.56 (d, *J* = 2.8 Hz, 1H), 3.93 (dd, *J* = 7.6, 2.8Hz, 2H), 3.84 (d, *J* = 3.3Hz, 2H), 2.54 (d, *J* = 3.3 Hz, 1H) ppm. Other spectral and physical data were in accordance with the literature.[55]

***tert*-Butyl pent-4-en-1-yl(prop-2-yn-1-yl)carbamate (10i).** The product was purified by flash chromatography (hexanes – EtOAc (15:1) as eluent). Yield 59.6 g (94%) from *tert*-butyl pent-4-en-1-ylcarbamate (52.6 g, 0.284 mol). Brownish liquid; the compound existed as a mixture of rotamers; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.91–5.67 (m, 1H), 5.08–4.87

(m, 2H), 4.14–3.85 (m, 2H), 3.29 (q, *J* = 7.0 Hz, 2H), 2.17 and 2.15 (t, *J* = 2.6 Hz, 1H), 2.03 (quint, *J* = 7.0 Hz, 2H), 1.64 (sept, *J* = 7.0Hz, 2H), 1.45 and 1.43 (s, 9H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ = 155.1, 137.9, 114.9, 80.1 and 79.9, 76.0, 71.2, 46.1, 36.5 and 36.0, 30.9, 28.4, 27.2 ppm; HRMS (ESI) *m*/*z* calcd. for $C_{13}H_{21}NO_2Na$ $[M+Na]^+$ 246.1470; found: 246.1462.

General procedure for the preparation of 10d, 10h, and 10j. NaH (80.0 g, 60% in mineral oil, 1.99 mol) was washed with hexanes (3×500 mL) under an argon flow. Et_2O (1.5 L) was added, followed by dropwise addition of the corresponding alkenol (1.66 mol) (CAUTION! Vigorous gas evolution and reaction mixture thickening was observed). After the addition was complete, the reaction mixture was heated at 30 °C for 1 h, and propargyl bromide (237 g, 1.99 mol) was added dropwise at rt. The reaction mixture was refluxed overnight (monitored by ^1H NMR spectra), then cooled, and H_2O (700 mL) was added carefully dropwise. The organic phase was separated, dried over Na_2SO_4, and evaporated in vacuo.

3-(Prop-2-yn-1-yloxy)prop-1-ene (10d), from allyl alcohol (42.1 g, 0.726 mol). The compound was not isolated in pure form but used in the next step as an Et_2O solution. The spectral data were in accordance with the literature.[56]

4-(Prop-2-yn-1-yloxy)but-1-ene (10h). Yield 136 g (74%) from but-3-en-1-ol (120 g, 1.67 mol). Brownish liquid; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.90–5.70 (m, 1H), 5.09 (d, *J* = 17.2 Hz, 1H), 5.04 (d, *J* = 10.2 Hz, 1H), 4.14 (d, *J* = 2.5Hz, 2H), 3.57 (t, *J* = 6.6Hz, 2H), 2.40 (t, *J* = 2.5Hz, 1H), 2.35 (q, *J* = 6.6 Hz, 2H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ = 134.9, 116.5, 79.8, 74.2, 69.3, 58.1, 33.9 ppm. Other spectral and physical data were in accordance with the literature.[56]

5-(Prop-2-yn-1-yloxy)pent-1-ene (10j). Yield 87.7 g (80%) from pent-4-en-1-ol (76.0 g, 0.884 mol). Colorless liquid; ^1H NMR (500 MHz, $CDCl_3$): δ = 5.90–5.75 (m, 1H), 5.12–4.90 (m, 2H), 4.14 (dd, *J* = 7.1, 2.5 Hz, 2H), 3.53 (q, *J* = 7.1 Hz, 2H), 2.46–2.39 (m, 1H), 2.14 (quint, *J* = 7.1 Hz, 2H), 1.78–1.62 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ = 138.1, 114.9, 80.0, 74.1, 69.5, 58.0, 30.2, 28.7 ppm. Other spectral and physical data were in accordance with the literature.[57]

Allyl(prop-2-yn-1-yl)sulfane (10e). To a solution of allyl mercaptan (50.0 g, 0.674 mol) in acetone (750 mL), K_2CO_3 (186 g, 1.35 mol) was added, followed by dropwise addition of propargyl bromide (57.0 mL, 0.741 mol) at rt. The reaction mixture was refluxed overnight (monitored by ^1H NMR spectra), then filtered. The precipitate was washed with acetone (500 mL), and the solvent was distilled off from the combined filtrates at atmospheric pressure to *ca.* 40% of its volume. The residue was diluted with H_2O (500 mL) and extracted with pentane (3×300 mL). The combined organic extracts were dried over Na_2SO_4 and evaporated at atmospheric pressure. Yield 46.9 g. Brownish liquid; used in the next step without additional purification. The spectral and physical data were in accordance with the literature.[58]

4-(Prop-2-yn-1-ylsulfonyl)but-1-ene (10f).[59] To a solution of **10e** (45.4 g, 0.405 mol) in CH_2Cl_2 (800 mL), MCPBA (140 g, 0.810 mol) was added in portions at 0 °C. The resulting mixture was left stirring at rt overnight. Then 10% aq K_2CO_3 (500 mL) was added, the organic phase was separated, washed with H_2O (500 mL), dried over Na_2SO_4, and evaporated in vacuo. Yield 53.0 g (91%). Brownish liquid. The spectral and physical data were in accordance with the literature.[59,60]

General procedure for the synthesis of boronates 8 from dienes 9. To a solution of **9** (82.0 mmol) in Et_2O (200 mL), a solution of *t*-BuLi (104 mL, 1.7 M in pentane, 0.177 mol) was added dropwise at –78 °C. The reaction mixture was stirred at –78 °C for 1 h, and then 2-isopropoxy-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (31.2 g, 0.167 mol) was added dropwise at the same temperature. The reaction mixture was allowed to warm to rt and then stirred for an additional 1.5 h. 4 M aq HCl was added dropwise to pH = 6–7, followed by H_2O (300 mL) was. A precipitate that formed was filtered and washed with Et_2O (100 mL). An organic phase was separated from the filtrate, dried over Na_2SO_4, and evaporated in vacuo.

General procedure for the synthesis of boronates 8 from enynes 10. To a solution of compound **10** (1.36 mol) in toluene (4 L), CuCl (13.5 g, 0.136 mol), B_2Pin_2 (380 g, 1.50 mol), $(t\text{-Bu})_3P{\cdot}HBF_4$ (47.4 g, 0.163 mol), NaO*t*-Bu (39.2 g, 0.408 mol) were added at rt under argon atmosphere. Then MeOH (110 mL, 2.69 mol) was added in portions at rt (CAUTION! Vigorous reaction: in several minutes, the internal temperature increased to *ca.* 80 °C). The resulting mixture was stirred at ambient temperature for 2 h (monitored by ^1H NMR). Then the mixture was filtered through SiO_2 (500 g), the pad was washed with EtOAc (1 L), and the combined extracts were evaporated in vacuo.

***tert*-Butyl allyl(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)-carbamate (8a).**[23] The product was purified by flash chromatography (hexanes – EtOAc (20:1) as eluent). Yield 103 g (82%) from compound **10a** (74.4 g, 0.381 mol). Yellowish liquid; the compound existed as a mixture of rotamers; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.87 (s, 1H), 5.77 (br. s, 1H), 5.63 (s, 1H), 5.09 (d, *J* = 12.7 Hz, 2H), 3.96 and 3.95 (s, 2H), 3.84 and 3.75 (s, 2H), 1.44 (s, 9H), 1.26 (s, 12H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ = 155.7 and 155.4, 148.5, 134.1 and 133.8, 128.7 and 128.4, 116.2 and 115.7, 83.5 and 83.2, 79.6 and 79.2, 49.5 and 48.8, 28.3, 24.7, 24.6 (br. s) ppm; HRMS (ESI) *m*/*z* calcd. for $C_{17}H_{31}BNO_4$ $[M+H]^+$ 324.2346; found: 324.2347.

***tert*-Butyl but-3-en-1-yl(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)carbamate (8c).** The product was purified by flash chromatography (hexanes – EtOAc (18:1) as eluent). Yield 54.3 g (86%) from compound **10c** (39.1 g, 0.187 mol). Yellowish liquid; the compound existed as a mixture of rotamers; ^1H NMR (400 MHz, $CDCl_3$): δ = 5.87 (d, *J* = 2.8 Hz, 1H), 5.83–5.66 (m, 1H), 5.61 (s, 1H), 5.05(d, *J* = 18.0Hz, 1H), 5.00 (d, *J* = 10.7 Hz, 1H), 3.96 and 3.90 (s, 2H), 3.26 and 3.19 (t, *J* = 7.4 Hz, 2H), 2.26 (q, *J* = 7.4Hz, 2H), 1.46 and 1.44 and 1.41 (m, 9H), 1.26 (s, 12H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ = 155.7 and 155.5, 135.7, 128.5 and 128.3, 116.3, 83.5, 79.1, 50.4 and 50.1, 46.6 and 46.5, 33.2 and 32.6, 28.4, 24.8, 24.6 (br. s) ppm; MS (EI): *m*/*z* = 237 $[M–C_4H_8–CO_2]^+$; HRMS (ESI) *m*/*z* calcd. for $C_{18}H_{33}BNO_4$ $[M+H]^+$ 338.2503; found: 338.2506.

2-(3-(Allyloxy)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (8d). Yield 78.1 g (48%, over two steps) from allyl alcohol (42.1 g, 0.726 mol). Yellowish liquid; ^1H NMR (400 MHz, $CDCl_3$): δ = 6.00–5.82 (m, 3H), 5.28 (d, *J* = 17.3 Hz, 1H), 5.15 (d, *J* = 10.3 Hz, 1H), 4.09 (s, 2H), 4.00 (d, *J* = 5.6 Hz, 2H), 1.25 (s, 12H) ppm. Other spectral and physical data were in accordance with the literature.[23]

2-(3-(Allylthio)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (8e). The product was purified by flash chromatography (hexanes – EtOAc (40:1) as eluent). Yield 74.4 g (46%, over two steps) from allyl mercaptan (50.0 g, 0.674 mol). Purified by column chromatography (hexanes – EtOAc (40:1) as eluent). Colorless liquid; %); ^1H NMR (500 MHz, $CDCl_3$): δ = 5.84 (d, *J* = 2.7 Hz, 1H), 5.82–5.72 (m, 1H), 5.63 (d, *J* = 2.7Hz, 1H), 5.10 (d, *J* = 3.7 Hz, 1H), 5.08 (s, 1H), 3.20 (s, 2H), 3.06 (d, *J* = 7.2 Hz, 2H), 1.29 (s, 12H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$): δ = 134.6, 130.1, 116.9, 83.7, 34.7, 33.5, 24.7, 24.5 (br. s) ppm; HRMS (ESI) *m*/*z* calcd. for $C_{12}H_{22}BO_2S$ $[M+H]^+$ 241.1434; found: 241.1434.

2-(3-(Allylsulfonyl)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (8f). The product was purified by flash chromatography (hexanes – EtOAc (4:1) as eluent). Yield 75.2 g (71%) from compound **10f** (61.5 g, 0.389 mol). Brownish liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.21 (d, *J* = 2.5 Hz, 1H), 6.00 (s, 1H), 5.92 (dq, *J* = 17.3, 7.5 Hz, 1H), 5.47 (d, *J* = 10.2 Hz, 1H), 5.42 (d, *J* = 17.3 Hz, 1H), 3.79 (s, 2H), 3.67 (d, *J* = 7.5 Hz, 2H), 1.26 (s, 12H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 138.5, 125.0, 124.6, 84.4, 56.7, 56.2, 24.7, 24.4 (br. s) ppm; HRMS (ESI) *m*/*z* calcd. for $C_{12}H_{25}BNO_4S$ $[M+NH_4]^+$ 290.1597; found: 290.1598.

2-(3-(But-3-en-1-yloxy)prop-1-en-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (8h). Yield 236 g (73%) from compound **10h** (149 g, 1.36 mol). Yellowish liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.97–5.73 (m, 3H), 5.06 (d, *J* = 17.2 Hz, 1H), 4.99 (d, *J* = 10.2 Hz, 1H), 4.09–4.04 (m, 2H), 3.46 (q, *J* = 6.7 Hz, 2H), 2.33 (q, *J* = 6.7 Hz, 2H), 1.24 (s, 12H) ppm. Other spectral and physical data were in accordance with the literature.[23]

***tert*-Butyl pent-4-en-1-yl(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)carbamate (8i).** The product was purified by flash chromatography (hexanes – EtOAc (6:1) as eluent). Yield 57.6 g (77%) from compound **10i** (47.5 g, 0.213 mol). Yellowish liquid; %); the compound existed as a mixture of rotamers; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 5.87 (d, *J* = 3.0 Hz, 1H), 5.81 (dq, *J* = 16.9, 7.4 Hz, 1H), 5.61 (s, 1H), 5.02 (d, *J* = 16.9 Hz, 1H), 4.95 (d, *J* = 10.2 Hz, 1H), 3.96 and 3.90 (s, 2H), 3.20 and 3.13 (t, 7.4 Hz, 2H), 2.03 (q, *J* = 7.4 Hz, 2H), 1.61 (quint, *J* = 7.4 Hz, 2H), 1.47 and 1.42 (s, 9H), 1.27 (s, 12H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 155.8, 138.2, 128.4 and 128.2, 114.6, 83.5, 79.0, 50.2 and 49.9, 46.5, 31.1, 28.4, 27.7 and 27.3, 24.8, 24.0 (br. s) ppm; HRMS (ESI) *m*/*z* calcd. for $C_{19}H_{35}BNO_4$ $[M+H]^+$ 352.2659; found: 352.2669; *m*/*z* calcd. for $C_{19}H_{34}BNO_4Na$ $[M+Na]^+$ 374.2478; found: 374.2482.

4,4,5,5-Tetramethyl-2-(3-(pent-4-en-1-yloxy)prop-1-en-2-yl)-1,3,2-dioxaborolane (8j). The product was purified by flash chromatography (hexanes – EtOAc (10:1) as eluent). Yield 63.7 g (60%) from compound **10j** (52.2 g, 0.421 mol). Yellowish liquid; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.88 (s, 2H), 5.80 (ddt, *J* = 17.0, 10.2, 6.9 Hz, 1H), 4.99 (dt, *J* = 17.0, 2.1 Hz, 1H), 4.92 (dd, *J* = 10.2, 2.1 Hz, 1H), 4.04 (s, 2H), 3.43 (t, *J* = 6.9 Hz, 2H), 2.11 (q, *J* = 6.9 Hz, 2H), 1.66 (quint, *J* = 6.9 Hz, 2H), 1.24 (s, 12H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 138.5, 129.1, 114.5, 83.5, 72.3, 69.8, 30.4, 29.0, 24.8, 24.3 (br. s) ppm; HRMS (ESI) *m*/*z* calcd. for $C_{14}H_{26}BO_3$ $[M+H]^+$ 253.1975; found: 253.1975.

General procedure for the large-scale synthesis of boronates 5a–h. A solution of compound **8** (1.00 mol) in CH_2Cl_2 (3 L) was refluxed under argon flow for 1 h, then cooled to rt, and Grubbs 2nd generation catalyst (41.1 g, 0.05 mol) was added carefully. The reaction mixture was stirred at rt overnight (monitored by ^{1}H NMR spectra). After the reaction was complete, the mixture was filtered through SiO_2 (500 g), the pad was washed with EtOAc (1 L), and the combined filtrates were evaporated in vacuo.

***tert*-Butyl 3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,5-dihydro-1*H*-pyrrole-1-carboxylate (5a).**[23] The product was purified by flash chromatography (hexanes – EtOAc (5:1) as eluent). Yield 74.8 g (85%) from compound **8a** (96.4 g, 0.298 mol). Yellowish oil; the compound existed as a mixture of rotamers; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.46 and 6.41 (s, 1H), 4.31–4.02 (m, 4H), 1.45 (s, 9H), 1.26 (s, 12H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 153.6, 141.6 and 141.1, 130.0 and 123.3, 83.9, 79.6 and 78.9, 55.6 and 55.3, 54.9 and 54.8, 28.6, 25.0 ppm; MS (EI): *m*/*z* = 239 $[M–C_4H_8]^+$; HRMS (ESI) *m*/*z* calcd. for $C_{15}H_{26}BNO_4Na$ $[M+Na]^+$ 318.1852; found: 318.1848.

***tert*-Butyl but-3-en-1-yl(2-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)allyl)carbamate (5c).** The product was purified by flash chromatography (hexanes – EtOAc (5:1) as eluent). Yield 61.3 g (72%) from compound **8c** (92.8 g, 0.276 mol). Colorless crystals, m.p. 104–106°C; the compound existed as a mixture of rotamers; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.61 (s, 1H), 3.96 (s, 2H), 3.44 (t, *J* = 5.8 Hz, 2H), 2.17 (s, 2H), 1.45 (s, 9H), 1.23 (s, 12H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 154.9, 140.5 and 139.8, 127.8 and 127.1, 83.3, 79.3, 44.5, 40.1 and 39.0, 28.5, 26.4, 24.7 ppm; MS (EI): *m*/*z* = 252 $[M–C_4H_8]^+$; HRMS (ESI) *m*/*z* calcd. for $C_{16}H_{28}BNO_4Na$ $[M+H]^+$ 332.2009; found: 332.2005.

2-(2,5-Dihydrofuran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5d).[23] The product was purified by flash chromatography (hexanes – EtOAc (10:1) as eluent). Yield 82.2 g (85%) from compound **8d** (110 g, 0.493 mol). Yellowish oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.52 (t, *J* = 2.6 Hz, 1H), 4.77–4.69 (m, 2H), 4.69–4.61 (m, 2H), 1.25 (s, 12H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 141.1, 83.5, 78.0, 76.4, 24.7, 24.5 (br. s) ppm; MS (EI): *m*/*z* = 196 $[M]^+$; HRMS (ESI) *m*/*z* calcd. for $C_{10}H_{18}BO_3$ $[M+H]^+$ 197.1349; found: 197.1343.

2-(2,5-Dihydrothiophen-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5e). Yield 9.66 g (86%) from compound **8e** (12.7 g, 53.0 mmol); Hoveyda – Grubbs 2nd generation catalyst (1.33 g, 2.12 mmol) was used instead of Grubbs 2nd generation catalyst. Beige powder, m.p. 78–80°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.60–6.42 (m, 1H), 3.92–3.73 (m, 4H), 1.25 (s, 12H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 143.5, 83.7, 41.6, 41.5, 24.8. 22.2 (br. s) ppm; MS (EI): *m*/*z* = 212 $[M]^+$; HRMS (ESI) *m*/*z* calcd. for $C_{10}H_{18}BO_2S$ $[M+H]^+$ 213.1120; found: 213.1119.

3-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)-2,5-dihydrothiophene 1,1-dioxide (5f). The product was purified by flash chromatography (hexanes – EtOAc (2:1) as eluent). Yield 32.0 g (88%) from compound **8f** (40.5 g, 0.149 mol). Brownish crystals, m.p. 115–117°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.77–6.65 (m, 1H), 3.87–3.82 (m, 2H), 3.82–3.78 (m, 2H), 1.28 (s, 12H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 137.2, 84.5, 57.4, 56.9, 24.7, 24.6 ppm; MS (EI): *m*/*z* = 180 $[M–SO_2]^+$; HRMS (ESI) *m*/*z* calcd. for $C_{10}H_{17}BO_4SNa$ $[M+Na]^+$ 267.0838; found: 267.0847.

2-(5,6-Dihydro-2*H*-pyran-3-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (5h).[23] The product was purified by flash chromatography (hexanes – EtOAc (8:1) as eluent). Yield 188 g (81%) from compound **8h** (263 g, 1.10 mol). Brownish crystals; m.p. 115–117°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.77–6.65 (m, 1H), 3.87–3.82 (m, 2H), 3.82–3.78 (m, 2H), 1.28 (s, 12H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 137.2, 84.5, 57.4, 56.9, 24.7, 24.6 ppm; MS (EI): *m*/*z* = 180 $[M–SO_2]^+$; HRMS (ESI) *m*/*z* calcd. for $C_{11}H_{20}BO_3$ $[M+H]^+$ 211.1506; found: 211.1500.

General procedure for the large-scale synthesis of boronates 5i and 5j. A solution of compound **8** (0.238 mol) in toluene (715 mL) was refluxed under argon flow for 1 h, then cooled to rt, and Grubbs 2nd generation catalyst (9.78 g, 11.9 mmol) was added carefully. The reaction mixture was refluxed overnight (monitored by ^{1}H NMR spectra). After the reaction was complete, the mixture was filtered through SiO_2 (200 g), the pad was washed with EtOAc (250 L), and the combined filtrates were evaporated in vacuo.

***tert*-Butyl 6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-2,3,4,7-tetrahydro-1*H*-azepine-1-carboxylate (5i** The product was purified by flash chromatography (hexanes – EtOAc (4:1) as eluent). Yield 11.3 g (72%) from compound **8i** (17.0 g, 48.6 mmol). Brownish oil; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.60 (s, 1H), 3.95 (s, 2H), 3.51 (s, 2H), 2.27 (q, *J* = 6.0 Hz, 2H), 1.78 (q, *J* = 6.0 Hz, 2H), 1.40 (s, 9H), 1.23 (s, 12H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ = 155.7, 147.6, 83.3, 78.9, 47.6, 45.7, 28.9,

28.4, 25.8, 24.8, 24.7 ppm; MS (EI): *m/z* = 267 [M–C_4H_8]$^+$; HRMS (ESI) *m/z* calcd. for $C_{17}H_{31}BNO_4$ [M+H]$^+$ 324.2346; found: 324.2347; *m/z* calcd. for $C_{17}H_{30}BNO_4Na$ [M+Na]$^+$ 346.2166; found: 346.2167.

4,4,5,5-Tetramethyl-2-(2,5,6,7-tetrahydrooxepin-3-yl)-1,3,2-dioxaborolane (5j). The product was purified by flash chromatography (hexanes – EtOAc (11:1) as eluent). Yield 32.0 g (60%) from compound **8j** (60.0 g, 0.238 mol). Colorless liquid; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.80–6.68 (m, 1H), 4.27 (s, 2H), 3.83 (td, *J* = 5.7, 2.4Hz, 2H), 2.46–2.33 (m, 2H), 1.80 (td, *J* = 5.7, 2.4 Hz, 2H), 1.22 (s, 12H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 148.2, 83.3, 72.6, 69.4, 29.0, 28.6, 24.7, 24.5 ppm; MS (EI): *m/z* = 224 [M]$^+$; HRMS (ESI) *m/z* calcd. for $C_{12}H_{22}BO_3$ [M+H]$^+$ 225.1662; found: 225.1662.

General procedure for the synthesis of cyclopropanes 11. A solution of boronate **5** (0.250 mol) in *t*-BuOMe (500 mL) was cooled to –10 °C, and $Pd(OAc)_2$ (2.81 g, 12.5 mmol) was added. Then a freshly prepared solution of diazomethane in *t*-BuOMe (0.8 mol/L, 600 mL, 0.75 mol) was added slowly upon stirring so that the temperature remained below 0 °C. (**CAUTION!** Diazomethane solutions are potentially explosive and should be handled with great care. The glassware used should contain no smallest defects, and direct contact of the solution or its vapors with ground-glass joints should be avoided, e.g. by applying a polytetrafluoroethylene (fum) tape. It is also not recommended to further increase the scale of this procedure in common (non-flow) reactors; several runs should be performed to obtain larger quantities of the product). After the addition was complete, the reaction mixture was stirred at the same temperature for an additional 1 h, then filtered through SiO_2 (20 g) and evaporated in vacuo.

Preparation of the diazomethane solution:[61] 50% aq KOH (330 mL) and *t*-BuOMe (700 mL) were placed into a 3-L round-bottomed reactor. The mixture was cooled to 5 °C, and 113 g (1.10 mol) of nitrosomethylurea was added portionwise upon stirring. The aqueous phase was separated; the organic phase was dried over solid NaOH and decanted. The resulting solution contained 0.8 M of diazomethane (determined as described in the literature[61]) and was used immediately in the next step.

***tert*-Butyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-azabicyclo[3.1.0]hexane-3-carboxylate (11a).**[43] The product was purified by flash chromatography (gradient hexanes to hexanes – *t*-BuOMe (9:1) as eluent). Yield 14.2 g (64%) from compound **5a** (21.2 g, 71.8 mmol). Yellowish crystals, m.p. 66–69 °C; the compound existed as a mixture of rotamers; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.58 (d, *J* = 10.8 Hz, 1H), 3.44 (d, *J* = 10.8 Hz, 1H), 3.38 (d, *J* = 10.8 Hz, 1H), 3.31 (dd, *J* = 10.8, 4.2 Hz, 1H), 1.60 (dt, *J* = 7.8, 4.2 Hz, 1H), 1.40 (s, 9H), 1.20 (s, 12H), 0.93 (dd, *J* = 7.8, 4.2 Hz, 1H), 0.39 (t, *J* = 4.2 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 155.2 and 155.1, 83.4, 79.0 and 78.9, 49.5 and 49.3, 48.1 and 47.8, 28.5, 24.6, 23.7 and 23.1, 15.2 and 15.1, 11.2 (br. s) ppm; MS (EI): *m/z* = 253 [M–C_4H_8]$^+$; HRMS (ESI) *m/z* calcd. for $C_{16}H_{28}BNO_4Na$ [M+Na]$^+$ 332.2009; found: 332.2007.

***tert*-Butyl 4-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3,6-dihydropyridine-1(2*H*)-carboxylate (11b).**[43] The product was purified by flash chromatography (gradient hexanes to hexanes – *t*-BuOMe (9:1) as eluent). Yield 58.9 g (73%) from compound **5b** (77.2 g, 0.250 mol). White powder, m.p. 72–74 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.83 (d, *J* = 14.1 Hz, 1H), 3.58–3.25 (m, 3H), 2.84 (s, 1H), 2.13–1.98 (m, 1H), 1.62–1.52 (m, 1H), 1.43 (s, 9H), 1.20 (s, 12H), 0.88 (s, 1H), 0.41 (t, *J* = 4.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 155.2, 83.2, 79.1, 42.1, 41.3, 40.3, 28.4, 24.7, 23.9, 16.6, 15.9 ppm; MS (EI): *m/z* = 267 [M–C_4H_8]$^+$; HRMS (ESI) *m/z* calcd. for $C_{17}H_{30}BNO_4Na$ [M+Na]$^+$ 346.2166; found: 346.2165.

***tert*-Butyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-azabicyclo[4.1.0]heptane-3-carboxylate (11c).**[43] The product was purified by flash chromatography (gradient hexanes to hexanes – *t*-BuOMe (9:1) as eluent). Yield 39.5 g (63%) from compound **5c** (60.0 g, 0.194 mol). White powder, m.p. 78–81 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.73 (d, *J* = 13.6 Hz, 1H), 3.55 (d, *J* = 13.6 Hz, 1H), 3.37 (dt, *J* = 12.4, 5.7 Hz, 1H), 2.91 (ddd, *J* = 13.6, 8.8, 5.7 Hz, 1H), 1.91 (dq, *J* = 12.4, 5.7 Hz, 1H), 1.82–1.69 (m, 2H), 1.43 (s, 9H), 1.20 (s, 12H), 0.84 (dd, *J* = 8.8, 4.2 Hz, 1H), 0.40 (t, *J* = 4.2 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 155.2, 83.1, 79.0, 43.6, 40.3, 39.7, 28.5, 24.7, 22.1, 14.8, 4.0 (br. s) ppm; MS (EI): *m/z* = 267 [M–C_4H_8]$^+$; HRMS (ESI) *m/z* calcd. for $C_{17}H_{31}BNO_4$ [M+H]$^+$ 324.2346; found: 324.2344; *m/z* calcd. for $C_{17}H_{30}BNO_4Na$ [M+Na]$^+$ 346.2166; found: 346.2165.

2-(3-Oxabicyclo[3.1.0]hexan-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (11d). The general procedure was repeated with the crude product obtained after the first run (so that two repetitive runs were required to complete the transformation). The product was purified by flash chromatography (gradient hexanes to hexanes – *t*-BuOMe (4:1) as eluent). Yield 15.9 g (51%) from compound **5d** (29.1 g, 0.148 mol). Brownish solid, m.p. 57–58°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.83 (d, *J* = 8.3 Hz, 1H), 3.78 (d, *J* = 8.3 Hz, 1H), 3.72 (d, *J* = 8.3 Hz, 1H), 3.62 (dd, *J* = 8.3, 3.4 Hz, 1H), 1.71 (dt, *J* = 7.0, 3.4 Hz, 1H), 1.22 (s, 12H), 0.80 (dd, *J* = 7.0, 3.4 Hz, 1H), 0.56 (t, *J* = 3.4 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 83.2, 71.1, 69.0, 25.0, 24.7, 24.6, 12.2 ppm; HRMS (ESI) *m/z* calcd. for $C_{11}H_{20}BO_3$ [M+H]$^+$ 211.1506; found: 211.1505.

2-(3-Oxabicyclo[4.1.0]heptan-6-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (11g). The product was purified by flash chromatography (gradient hexanes to hexanes – *t*-BuOMe (4:1) as eluent). Yield 22.7 g (58%) from compound **5g** (36.7 g, 0.174 mol). White powder, m.p. 81–83°C; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.99 (d, *J* = 11.3 Hz, 1H), 3.82 (dd, *J* = 11.3, 3.1 Hz, 1H), 3.58 (ddd, *J* = 11.3, 5.8, 3.1 Hz, 1H), 3.14 (td, *J* = 11.3, 5.8 Hz, 1H), 2.01 (ddd, *J* = 14.3, 5.8, 3.1 Hz, 1H), 1.64 (ddd, *J* = 14.3, 11.3, 5.8 Hz, 1H), 1.21 (s, 12H), 1.11–1.02 (m, 1H), 0.93 (dd, *J* = 8.3, 3.1 Hz, 1H), 0.63 (dd, *J* = 5.8, 3.1 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 83.1, 65.5, 64.7, 24.7, 24.5, 17.1, 16.1, 1.6 (br. s) ppm; MS (EI): *m/z* = 224 [M]$^+$; HRMS (ESI) *m/z* calcd. for $C_{12}H_{22}BO_3$ [M+H]$^+$ 225.1662; found: 225.1661.

2-(3-Oxabicyclo[4.1.0]heptan-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (11h). The product was purified by flash chromatography (gradient hexanes to hexanes – *t*-BuOMe (4:1) as eluent). Yield 28.0 g (50%) from compound **5h** (52.5 g, 0.250 mol). Yellowish oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.00 (d, *J* = 11.4 Hz, 1H), 3.81 (d, *J* = 11.4 Hz, 1H), 3.46 (ddd, *J* = 11.4, 5.6, 3.8 Hz, 1H), 3.23 (ddd, *J* = 11.4, 9.2, 5.6 Hz, 1H), 1.94–1.77 (m, 1H), 1.25–1.22 (m, 1H), 1.20 (s, 12H), 0.94–0.82 (m, 2H), 0.64 (dd, *J* = 5.6, 3.8 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 83.1, 67.6, 63.5, 24.6, 22.8, 16.5, 14.2, 11.2 (br. s) ppm; HRMS (ESI) *m/z* calcd. for $C_{12}H_{22}BO_3$ [M+H]$^+$ 225.1662; found: 225.1661.

***tert*-Butyl 1-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-3-azabicyclo[5.1.0]octane-3-carboxylate (11i).** The product was purified by flash chromatography (gradient hexanes to hexanes – *t*-BuOMe (4:1) as eluent). Yield 8.57 g (40%) from compound **5i** (20.5 g, 63.6 mmol). White powder, m.p. 85–87°C; the compound existed as a mixture of rotamers; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.79 (d, *J* = 14.5 Hz, 1H), 3.75–3.72 (m, 1H), 3.41 (d, *J* = 14.5 Hz, 1H), 2.80–2.56 (m, 1H), 2.04–1.89 (m, 1H), 1.89–1.74 (m, 1H), 1.67–1.49 (m, 3H), 1.46 (s, 9H), 1.22 (s, 12H), 0.72 (dd, *J* = 8.9, 4.0 Hz, 1H), 0.41 (t, *J* = 5.1 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$): δ = 155.4 and 155.0, 83.0, 78.8, 49.1, 48.4 and 48.0, 28.4, 27.5 and 26.7, 27.1 and 26.4, 24.7 and 24.4, 20.7 and 20.6, 13.1 and 12.6, 8.8 (br. s) ppm; MS (EI): *m/z* = 281 [M–C_4H_8]$^+$; HRMS (ESI) *m/z* calcd. for $C_{18}H_{33}BNO_4$ [M+H]$^+$ 338.2503; found: 338.2496.

2-(3-Oxabicyclo[5.1.0]octan-1-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane (11j). The product was purified by flash chromatography (gradient hexanes to hexanes – *t*-BuOMe (4:1) as eluent). Yield 6.87 g (38%) from compound **5j** (18.2 g, 76.0 mmol). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.19 (d, *J* = 12.2 Hz, 1H), 3.75–3.59 (m, 1H), 3.48 (t, *J* = 12.2 Hz, 1H), 3.31 (d, *J* = 12.2 Hz, 1H), 2.26–2.09 (m, 1H), 1.72–1.65 (m, 1H), 1.63–1.48 (m, 2H), 1.36–1.27 (m, 1H), 1.22 (s, 12H), 0.85 (dd, *J* = 8.1, 3.7 Hz, 1H), 0.72 (dd, *J* = 5.7, 3.7 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$): δ = 83.0, 75.1, 74.0, 30.8, 29.4, 24.6, 22.4, 17.5, 12.4 (br. s) ppm; MS (EI): *m/z* = 238 $[M]^+$; HRMS (ESI) *m/z* calcd. for $C_{13}H_{24}BO_3$ $[M+H]^+$ 239.1818; found: 239.1817.

General procedure for the preparation of trifluoroborates 4. To a solution of compound **11** (0.232 mol) in MeOH (930 mL) and MeCN (930 mL), a solution of KF (53.9 g, 0.928 mol) in H_2O (93 mL), followed by a suspension of tartaric acid (66.3 g, 0.475 mol) in THF (350 mL). The reaction mixture was stirred at rt for 2 h; the precipitate was filtered and washed with MeCN (300 mL). The combined filtrates were evaporated in vacuo to dryness, and the residue was triturated with *t*-BuOMe or Et_2O.

Potassium (*tert*-butyl 3-azabicyclo[3.1.0]hexane-3-carboxylate-1-yl)-trifluoroborate (4a).[43] Yield 11.2 g (94%) from compound **11a** (12.7 g, 41.2 mmol). White powder, m.p. >200 °C; the compound existed as a mixture of rotamers; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.31 (s, 1H), 3.20–3.02 (m, 3H), 1.35 (s, 9H), 0.94 (s, 1H), 0.34 (dd, *J* = 7.2, 2.9 Hz, 1H), –0.41 (s, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, [D$_6$]DMSO): δ = 155.1 and 154.9, 78.1 and 78.1, 52.3 and 51.9, 49.7 and 49.4, 28.6, 19.6, 18.8, 13.0 ppm; ^{19}F{^{1}H} NMR (376 MHz, [D$_6$]DMSO): δ = –142.9 ppm; HRMS (ESI) *m/z* calcd. for $C_{10}H_{16}BF_3NO_2$ $[M–K]^–$ 250.1226; found: 250.1239.

Potassium (*tert*-butyl 3-azabicyclo[4.1.0]heptane-3-carboxylate-6-yl)-trifluoroborate (4b).[43] Yield 53.5 g (99%) from compound **11b** (57.5 g, 0.178 mol). White powder, m.p. 241–243 °C; the compound existed as a mixture of rotamers; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 3.56–3.36 (m, 3H), 3.07 (dt, *J* = 12.0, 5.7 Hz, 1H), 2.87 (s, 1H), 1.74 (s, 1H), 1.36 (s, 9H), 1.31–1.17 (m, 1H), 0.58 (s, 1H), 0.22 (dd, *J* = 7.6, 2.8 Hz, 1H), –0.28 (s, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, [D$_6$]DMSO): δ = 154.7, 78.1, 43.3 and 42.6, 41.7, 28.6, 26.1 and 25.6, 25.4, 13.2 and 13.0, 8.7 ppm; ^{19}F{^{1}H} NMR (376 MHz, [D$_6$]DMSO): δ = –147.2 ppm; HRMS (ESI) *m/z* calcd. for $C_{11}H_{18}BF_3KNO_2$ $[M–K]^–$ 264.1383; found: 264.1397.

Potassium (*tert*-butyl 3-azabicyclo[4.1.0]heptane-3-carboxylate-1-yl)-trifluoroborate (4c).[43] Yield 35.1 g (92%) from compound **11c** (40.7 g, 0.126 mol). White powder, m.p. >200 °C; the compound existed as a mixture of rotamers; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 3.58 (s, 1H), 3.28–3.03 (m, 2H), 2.70 (s, 1H), 1.68 (s, 1H), 1.58 (s, 1H), 1.35 (s, 9H), 0.60 (s, 1H), 0.20 (d, *J* = 7.8 Hz, 1H), –0.34 (s, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, [D$_6$]DMSO): δ = 155.1 and 154.7, 77.9, 45.7, 44.9, 41.5, 28.7, 23.4 and 23.1, 12.1, 11.1 ppm; ^{19}F{^{1}H} NMR (376 MHz, [D$_6$]DMSO): δ = –146.2 ppm; HRMS (ESI) *m/z* calcd. for $C_{11}H_{18}BF_3NO_2$ $[M–K]^–$ 264.1383; found: 263.1382.

Potassium (3-oxabicyclo[3.1.0]hexan-1-yl) trifluoroborate (4d). Yield 12.3 g (98%) from compound **11d** (13.9 g, 66.0 mmol). White powder, m.p. >200 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 3.57 (d, *J* = 7.6Hz, 1H), 3.45 (qd, *J* = 7.6, 2.0 Hz, 2H), 3.40 (dd, *J* = 7.6, 2.9 Hz, 1H), 1.02 (dd, *J* = 6.8, 2.9 Hz, 1H), 0.20 (dd, *J* = 6.8, 2.0 Hz, 1H), –0.23 (s, 1H) ppm; ^{13}C{^{1}H} NMR (101 MHz, [D$_6$]DMSO): δ = 73.5, 69.8, 21.1, 18.4 (br. s), 10.4 ppm; ^{19}F{^{1}H} NMR (470 MHz, [D$_6$]DMSO): δ = –140.5 ppm; HRMS (ESI) *m/z* calcd. for $C_5H_7BF_3O$ $[M–K]^–$ 151.0542; found: 151.0551.

Potassium (3-oxabicyclo[4.1.0]heptan-6-yl)trifluoroborate (4g). Yield 20.5 g (96%) from compound **11g** (23.7 g, 0.106 mol). White powder, m.p. >200 °C; ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 3.73 (d, *J* = 10.7Hz, 1H), 3.65 (dd, *J* = 10.7, 4.5Hz, 1H), 3.33–3.27 (m, 1H), 2.97 (td, *J* = 10.7, 4.5Hz, 1H), 1.69 (dt, *J* = 14.2, 4.5Hz, 1H), 1.30 (ddd, *J* = 14.2, 10.0, 5.8 Hz, 1H), 0.48 (dt, *J* = 8.7, 4.5Hz, 1H), 0.31–0.22 (m, 1H), –0.10– –0.18 (m, 1H) ppm; ^{13}C{^{1}H} NMR (151 MHz, [D$_6$]DMSO): δ = 66.8, 64.5, 26.7, 14.5, 13.0, 8.1 (br. s) ppm; ^{19}F{^{1}H} NMR (376 MHz, [D$_6$]DMSO): δ = –147.6 ppm; HRMS (ESI) *m/z* calcd. for $C_6H_9BF_3O$ $[M–K]^–$ 165.0698; found: 165.0705.

Potassium (3-oxabicyclo[4.1.0]heptan-1-yl)trifluoroborate (4h). Yield 26.4 g (95%) from compound **11h** (30.5 g, 0.136 mol). White powder, m.p. >200 °C; ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ = 3.65–3.56 (m, 2H), 3.36 (s, 1H), 2.94 (td, *J* = 10.6, 5.4 Hz, 1H), 1.68–1.51 (m, 2H), 0.67–0.59 (m, 1H), 0.28 (dd, *J* = 7.8, 1.9 Hz, 1H), –0.12 (d, *J* = 4.3 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, [D$_6$]DMSO): δ = 69.9, 64.0, 24.5, 14.4, 10.9 (br. s), 10.5 ppm; ^{19}F{^{1}H} NMR (470 MHz, [D$_6$]DMSO): δ = –144.9 ppm; HRMS (ESI) *m/z* calcd. for $C_6H_9BF_3O$ $[M–K]^–$ 165.0698; found: 165.0710.

Potassium (*tert*-butyl 3-azabicyclo[5.1.0]octane-3-carboxylate-1-yl)-trifluoroborate (4i). Yield 6.81 g (94%) from compound **11i** (7.68 g, 22.8 mmol). White powder, m.p. >200 °C; the compound existed as a mixture of rotamers; ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 3.67–3.46 (m, 2H), 3.17 and 3.07 (d, *J* = 13.5 Hz, 1H), 2.81–2.63 (m, 1H), 1.76 (td, *J* = 9.5, 4.5 Hz, 1H), 1.56–1.45 (m, 1H), 1.45–1.29 (m, 2H), 1.36 (s, 9H), 0.68–0.58 (m, 1H), 0.12–0.04 (m, 1H), –0.35 (s, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, [D$_6$]DMSO): δ = 155.5 and 154.8, 77.8, 51.0 and 50.7, 47.5 and 46.5, 28.7, 27.8 and 27.6, 27.4 and 27.0, 25.3, 17.2 and 16.9, 10.9 and 10.6 ppm; ^{19}F{^{1}H} NMR (376 MHz, [D$_6$]DMSO): δ = –145.8 ppm; HRMS (ESI) *m/z* calcd. for $C_{12}H_{20}BF_3NO_2$ $[M–K]^–$ 278.1539; found: 278.1553.

Potassium (3-oxabicyclo[5.1.0]octan-1-yl)trifluoroborate (4j). Yield 5.48 g (95%) from compound **11j** (6.31 g, 26.5 mmol). White powder, m.p. >200 °C; ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 3.66 (d, *J* = 13.0 Hz, 1H), 3.59–3.48 (m, 2H), 2.92 (t, *J* = 10.8 Hz, 1H), 1.83–1.69 (m, 2H), 1.43 (dd, *J* = 13.0, 5.5 Hz, 1H), 1.36–1.25 (m, 0H), 0.71 (dd, *J* = 8.0, 4.4 Hz, 1H), 0.13–0.03 (m, 1H), –0.03 (d, *J* = 8.0 Hz, 1H) ppm; ^{13}C{^{1}H} NMR (126 MHz, [D$_6$]DMSO): δ = 75.5, 73.9, 30.4, 29.1, 25.3, 18.4, 10.7 ppm; ^{19}F{^{1}H} NMR (376 MHz, [D$_6$]DMSO): δ = –144.7 ppm; HRMS (ESI) *m/z* calcd. for $C_7H_{11}BF_3O$ $[M–K]^–$ 179.08550; found: 179.0866.

Acknowledgements

The work was funded by Enamine Ltd. O.O.G. also received funding from Ministry of Education and Science of Ukraine (grant No. 19BF037-03). The authors thank Prof. Andrey A. Tolmachev for his encouragement and support, Dr. Alexey V. Dobrydnev for his help with manuscript preparation, Dr. Andriy Kozytskyi and Mr. Artur Breslavskyi for NMR experiments, and Mr. Denys Bylina for HRMS measurements.

Keywords: Organoboron compounds • Cyclopropanes • Heteroaliphatic compounds • Bicyclic compounds • Suzuki–Miyaura reaction

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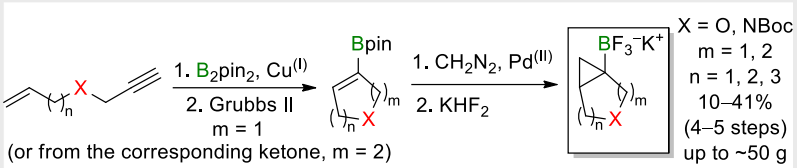

Multigram synthesis of oxa- and azabicyclo[n.1.0]alkan-1-yl trifluoroborates relying on efficient 4–5-step reaction sequences is described.

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Heteroaliphatic trifluoroborates

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