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ROMPgel supported allylboronate: a purification-free method for the preparation of homoallylic alcohols

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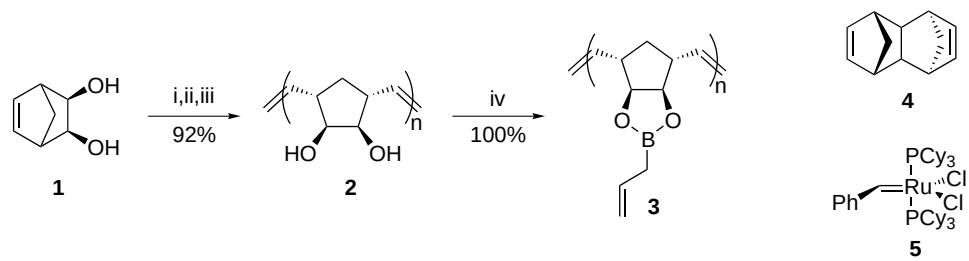
Abstract—Allylboration of various aldehydes was carried out by a ROMPgel supported allylboronate. Filtration and evaporation gave the corresponding homoallylic alcohols in high yield and purity (>95%).

The reaction of allylboranes[1] and allylboronates[2] with aldehydes is an outstanding procedure for the elaboration of 4-hydroxy-1-alkene derivatives.[3] Since these products can be easily converted into β-hydroxy aldehydes by oxidative cleavage of the terminal alkene,[4] the process is of considerable value in the construction of polyfunctional carbon frameworks. Additionally, both allylboranes and allylboronates containing chiral auxiliaries are especially valuable in enantioselective synthesis. Of particular note are the seminal contributions to asymmetric synthesis by Brown,[1] Roush[5] and Hoffmann.[6] Recently, the use of polymer supported reagents and scavengers for parallel synthesis in the solution phase have gained significantly in popularity.[7] Ideally, a polymer supported reagent should allow for the formation of all products in quantitative yield in a parallel array. Additionally, filtration and evaporation should provide all products significantly pure (>90%) without recourse to crystallization, distillation, chromatography or other classical methods of purification. Recently, we introduced Ring Opening Metathesis Polymer gels, ROMPgels, as support for parallel synthesis.[8] These polymers are readily prepared from polyfunctional monomers, are high loading gels which are insoluble yet swell in common organic solvents and undergo reaction at acceptable rates. Herein, we report the development of a ROMPgel for the conversion of aldehydes into (±)-4-hydroxy-1-alkenes.

The ROMPgel **2** was prepared by the silylation of *exo*-5-norbornene-2,3-diol **1**,[9] polymerization using the Grubbs' catalyst **5** (1.5 mol%) with tetracyclo [6.2.1.1^{3,6}.0^{2,7}]dodeca-4,9-diene[10] **4** (15 mol%) as a crosslinker, and desilylation using hydrogen fluoride triethylamine.[11] Subsequent reaction of polymer **2** with freshly prepared allylboronic acid[5] gave the ROMPgel boronate **3** (100%) (Scheme 1). The ROMPgel **3** displayed excellent swelling properties in most solvents and high boronate loading (5.8 mmol g^{-1}). Polymerization without the crosslinker **4** provided inferior polymers with significant solubility in dichloromethane.

Allylboration reactions were carried out using aliphatic and aromatic aldehydes, affording in a few hours the



Scheme 1. *Reagents and conditions*: (i) Me_3SiCl, Et_3N, CH_2Cl_2; (ii) **4** (15 mol%), **5** (1.5 mol%), CH_2Cl_2; (iii) $Et_3N{\cdot}3HF$, CH_2Cl_2; (iv) $CH_2{=}CHCH_2B(OH)_2$, CH_2Cl_2.

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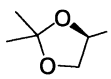
corresponding homoallylic alcohols (Table 1). The mix-filter-evaporate procedure was applied and the expected products were isolated in high yield and excellent purity in all cases. The filtration itself was performed through a short plug of silica gel, collecting a single fraction. A three fold excess of supported allylboronate was necessary to allow for a quantitative conversion in a reasonable time frame (≤ 7 h). It must also be noted that the reaction as well as the hydrolysis of the boronate ester were performed under very mild conditions of temperature and pH.[12] A small amount of water was added at the start to accelerate the rate of the reaction from 24 to 6 h in the case of benzaldehyde and to eliminate the formation of the side product 1-phenyl-1,3-butadiene **7**. Formation of this side product probably arose by elimination from the boronate intermediate **6** (Scheme 2).

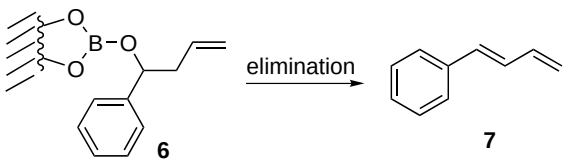
Table 1. Allylboration of aldehydes **9** with ROMPgel supported allylboronate to provide **10**[a]

Entry	R	R'	Time	Yield[b]
1	H	*n*-Bu	3	82
2	H	*c*-C_6H_{11}	3	92
3	H	*t*-Bu	4	49
4	H	$CH_3CH=CH$	3	70
5	H	Ph	6	87
6	H	4-MeO-C_6H_5	7	93
7	H	4-Cl-C_6H_5	4	85
8	H	4-NO_2-C_6H_5	3	90
9	H	4-MeO_2C-C_6H_5	4	95
10	H		3	79
11	H		6	88
12	H		14	95
13[c]	H		5	81
14	CH_3	*n*-Bu	1	68
15	CH_3	Ph	2	87
16	CH_3	4-MeO-C_6H_5	5	95
17	CH_3	4-NO_2-C_6H_5	3	96
18	CH_3		2	87

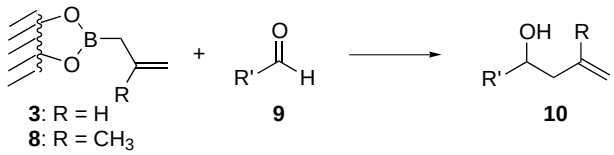
[a]Reactions monitored by GC/MS. All products were obtained with >95% purity (NMR).

[b]Isolated yields.

[c]Ratio 2**R**,3**R** : 2**R**,3**S** : 67 : 33.



Scheme 2.



Scheme 3.

We limited our study to the two different ROMPgel supported allylboronate moieties **3** and **8** (Scheme 3) that were allowed to react with a range of aromatic and aliphatic aldehydes. The progress of the reaction was monitored by GC/MS. The results are consistent throughout the Table 1, with high purities (>95% NMR) and yields (79–96%). Only in the case of starting materials of low molecular weight were the yields found to be slightly lower. This was observed with valeraldehyde (entries 1 and 14), pivaldehyde (entry 3) and crotonaldehyde (entry 4), which have low boiling points. A reaction time of 7 h was adequate for most substrates, although several aldehydes underwent reaction at a faster rate. However, the preparation of 1-(2-thienyl)-3-buten-1-ol (95%) required prolonged reaction time (14 h, entry 12). (*R*)-(+)-Glyceraldehyde acetonide (entry 13) provided the corresponding diastereoisomeric homoallylic alcohols (**ds** 2:1).

In conclusion, we describe a purification-free method, based on ROMPgel chemistry, which allows for the simplified parallel synthesis of a range of homoallylic alcohols in high yield and excellent purity.

Itsuno[13] and co-workers have reported the use of DVB crosslinked polystyrene supported chiral boronates in enantioselective synthesis of homoallylic alcohols. These reagents needed an acidic work up and chromatography for isolation of the homoallylic alcohols.

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References

1. See for example: (a) Racherla, U. S.; Brown, H. C. *J. Org. Chem.* **1991**, *56*, 401–404; (b) Chen, G. M.; Brown, H. C.; Ramachandran, P. V. *J. Org. Chem.* **1999**, *64*, 721–725.

2. See for example: (a) Pace, R. D.; Kabalka, G. W. *J. Org. Chem.* **1995**, *60*, 4838–4844; (b) Kabalka, G. W.; Narayana, C.; Reddy, N. K. *Tetrahedron Lett.* **1996**, *37*, 2181–2184.
3. Yamamoto, Y.; Asao, N. *Chem. Rev.* **1993**, *93*, 2207–2293.
4. Schreiber, S. L.; Goulet, M. T. *J. Am. Chem. Soc.* **1987**, *109*, 8120–8122.
5. Roush, W. R.; Hoong, L. K.; Palmer, M. A. J.; Park, J. C. *J. Org. Chem.* **1990**, *55*, 4109–4117.
6. Herold, T.; Schrott, U.; Hoffmann, R. W. *Chem. Ber.* **1981**, 359–374.
7. (a) Kirshning, A.; Monenschein, H.; Wittenberg, R. *Angew. Chem., Int. Ed.* **2001**, *40*, 650–679; (b) Ley, S. V.; Baxendale, I. R.; Bream, R. N.; Jackson, P. S.; Leach, A. G.; Longbottom, D. A.; Nesi, M.; Scott, J. S.; Storer, I.; Taylor, S. T. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3815–4195; (c) Bhattacharyya, S. *Comb. Chem. High T. Scr.* **2000**, *3* (2), 65–92.
8. See for example: (a) Barrett, A. G. M.; Cramp, S. M.; Hennessy, A. J.; Procopiou, P. A.; Roberts, R. S. *Org. Lett.* **2001** *3*, 271–273; (b) Arnauld, T.; Barrett, A. G. M.; Cramp, S. M.; Roberts, R. S.; Zecri, F. J. *Org. Lett.* **2000** *2*, 2663–2666.
9. (a) Balo, C.; Fernandez, F.; Lens, E.; Lopez, C. *Chem. Pharm. Bull.* **1998**, 687–689; (b) Sano, H.; Sugai, S. *Tetrahedron* **1995**, *51*, 4635–4646.
10. Stille, J.; Frey, D. A. *J. Am. Chem. Soc.* **1959**, *81*, 4273–4275.
11. Weinstein, L. B.; Earnshaw, D. J.; Cosstick, R.; Cech, T. R. *J. Am. Chem. Soc.* **1996**, *118*, 10341–10350.
12. Typical procedure (entry 5): To a suspension of ROMPgel supported allylboronate ester **3** (520 mg, 4 mmol) in CH_2Cl_2 (20 mL) was added PhCHO (106 mg, 1 mmol) and H_2O (50 μL). The reaction mixture was stirred at room temperature and the conversion was monitored by GC/MS. The solution was filtered, concentrated, taken up in Et_2O (3 mL) and filtered through silica gel (2 cm in a Pasteur pipette). The silica gel was washed with Et_2O (15 ml) and the solution was evaporated and dried under vacuum at 25°C to yield 1-phenyl-3-buten-1-ol (129 mg, 0.87 mmol, 87%, purity (NMR)>95%).
13. Itsuno, S.; El-Shehawy, A.; Sarhan, A. A. *React. Funct. Polym.* **1997**, *37*, 283–287.