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Tetrahedron Letters
Tetrahedron Letters 46 (2005) 6945–6948

Regioselective synthesis of 1,2- and 1,3-diols from ω-hydroxy allyl acetates and carbonates via Pd complexes using boric acid and trialkyl borates

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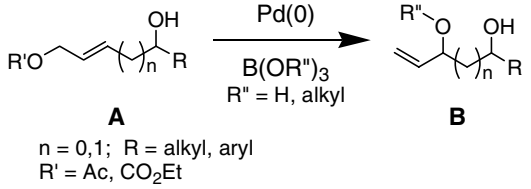
Received 8 June 2005; revised 25 July 2005; accepted 26 July 2005

Abstract—The synthesis of 1,2- and 1,3-diols and derivatives has been achieved from ω-hydroxy π-allyl palladium complexes by using boric acid and trialkyl borates.

1,2- and 1,3-Diols and derivatives are present in a great variety of natural products and/or biologically active compounds.[1] The most widely used method to prepare 1,2- and 1,3-diols is the nucleophilic attack of 2- or 3-hydroxy ketones or aldehydes by organometallic species. An alternative approach is the formation of C–O bond using transition metal-catalyzed allylic substitution. However, if the formation of C–C bonds through palladium-catalyzed nucleophilic substitution of allylic substrates has been found to be a useful tool in organic synthesis, in contrast, the formation of C–O bonds by the introduction of a hydroxyl group is less common, although intra- and intermolecular substitutions using alcohols, phenols,[2] or carboxylic acids[3] have been reported recently. For example, carboxylic acids were used in a palladium-catalyzed reaction of 2-allylic trichloroacetimidate to produce allylic esters.[3]

Boric acid and alcohols with trialkyl boranes have been employed in the palladium-catalyzed ring opening of vinyl epoxide to produce 1,2-diols and derivatives.[4–6] Here, we would like to report that the use of boric acid and trialkyl borates can produce 1,2- and 1,3-diols and derivatives of type **B** from compounds of type **A**, via π-allyl palladium complexes (Scheme 1).



Scheme 1. Formation of 1,2- and 1,3-diols and derivatives.

Compounds of type **A** were prepared using a cross-metathesis reaction between homoallylic alcohols **1a–c** and 1,4-diacetoxybut-2-ene **2** or 1,4-diethylcarbonyloxybut-2-ene **3** in the presence of Grubbs catalyst[7] **Ru1** or Grubbs–Hoveyda catalyst[8] **Ru2** (3–6 mol %) for 24 h. Compounds **4a–e** were obtained in 56–91% yield as a 5/1–10/1 *E*/*Z* ratio. The results are reported in Table 1.

Initially, the reaction of **4a** with boric acid (3 equiv) was examined in the presence of Pd(0) in THF at rt and at 50 °C (Table 2, entries 1 and 2). When **4a** was treated with $Pd_2(dba)_3{\cdot}CHCl_3$ (0.05 equiv) in the presence of dppb (0.25 equiv) at rt or at 50 °C, the expected 1,3-diol **5a** was not formed. On the contrary, when $Pd(PPh_3)_4$ (0.1 equiv) in the presence of PPh_3 (0.25 equiv) was used in THF at 50 °C, **4a** was transformed to 1,3-diol **5a** in 83% yield as a 1/1 mixture of *syn* and *anti* isomers (Table 2, entry 3). It is worth noting that the reaction did not occur in acetonitrile or in dichloromethane (Table 2, entries 4 and 5) as well as without Pd(0). The best conditions for obtaining 1,3-diol **5a** from compound **4a** seem to be $Pd(PPh_3)_4$ (10 mol %), PPh_3 (25 mol %), $B(OH)_3$ (3 equiv), and Na_2CO_3 (1.5 equiv) in THF at

Keywords: Allyl alcohols; Diols; Borates; Boric acid; π-Allyl palladium complexes.
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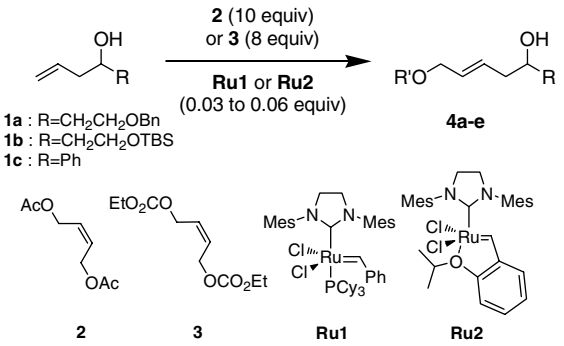
doi:10.1016/j.tetlet.2005.07.135

Table 1. Preparation of compounds **4a**–**e** using a cross-metathesis reaction



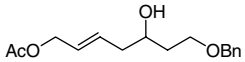
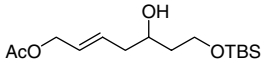
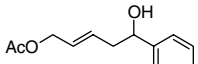
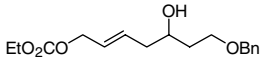
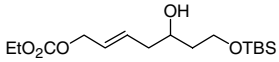
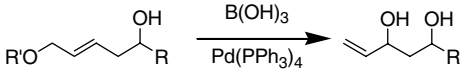
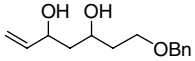
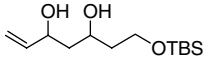
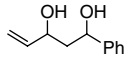
Entry	1	Solvent, t (°C)	2 or 3	Ru (equiv)	4 (yield, E/Z ratio)
1	**1a**	CH_2Cl_2, rt	**2**	**Ru2** (0.03)	 **4a** (89%, 8/1)
2	**1b**	CH_2Cl_2, rt	**2**	**Ru2** (0.03)	 **4b** (86%, 10/1)
3	**1c**	CH_2Cl_2, rt	**2**	**Ru2** (0.03)	 **4c** (91%, 8/1)
4	**1a**	CH_2Cl_2, 40	**3**	**Ru1** (0.06)	 **4d** (56%, 9/1)
5	**1b**	Toluene, 80	**3**	**Ru1** (0.06)	 **4e** (81%, 5/1)

Table 2. Reaction of palladium π-allyl complexes with $B(OH)_3$



Entry	4	Solvent	t (°C)	Time (h)	5 (yield, *syn*/*anti*)
1[a]	**4a** (OAc)	THF	rt	3	—
2[a]	**4a** (OAc)	THF	50	3	—
3[b]	**4a** (OAc)	THF	50	1	 **5a** (83% , 1/1)
4[b]	**4a** (OAc)	CH_3CN	50	3	—
5[b]	**4a** (OAc)	CH_2Cl_2	40	3	—
6[b]	**4b** (OCO_2Et)	THF	50	1	 **5b** (56%, 1/1)
7[b]	**4c** (OCO_2Et)	THF	50	1	 **5c** (40%, 1/1)
8[b]	**4d** (OCO_2Et)	THF	50	1	**5a** (63%, 1/1)
9[b]	**4d** (OCO_2Et)	THF	rt	18	**5a** (51%, 2/1)
10[b]	**4d** (OCO_2Et)	CH_2Cl_2	rt	18	**5a** (57%, 4/1)

[a] $Pd_2(dba)_3{\cdot}CHCl_3$ (5 mol %)/dppb (25 mol %).
[b] $Pd(PPh_3)_4$ (10 mol %)/PPh_3 (25 mol %).

50 °C for 1 h. Under these conditions, compounds **4b** and **4c** were transformed into diols **5b** and **5c** in 56% yield and 40% yield, respectively, in a 1/1 *syn*/*anti* ratio (Table 2, entries 6 and 7). Furthermore, 1,3-diol **5a** can be obtained from allylic carbonate **4d** in 63% yield in a 1/1 *syn*/*anti* ratio when the reaction was achieved in

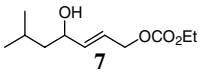
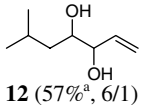
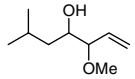
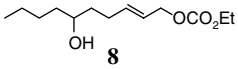
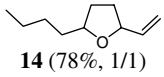
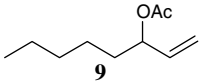
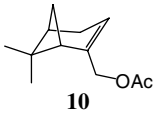
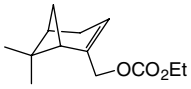
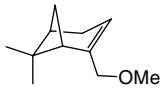
THF at 50 °C (Table 2, entry 8). As carbonates are more reactive than acetates and in order to improve the diastereoselectivity, the reaction was performed on carbonate **4d** at rt in the presence of $Pd(PPh_3)_4$. Diol **5a** was isolated in 51% yield and the *syn*/*anti* ratio was slightly increased to 2/1 in favor of the *syn* isomer (Table 2, entry 9). Furthermore, the *syn*/*anti* ratio was increased to 4/1 when the reaction was performed in CH_2Cl_2 at rt (Table 2, entry 10).[9,10]

Monoprotected 1,3-diols can be useful in the synthesis of various natural products. In order to produce these diols, allylic acetate **4a** was treated with trimethyl borate (3 equiv) or tribenzyl borate (3 equiv) in the presence of $Pd(PPh_3)_4$ (0.1 equiv) and PPh_3 (0.25 equiv) in THF at 50 °C. Unfortunately, the desired products **6a** and **6b** were not obtained. However, treatment of the allylic carbonate **4d**, under the conditions used to transform **4a** in **5a**, provided the monoprotected 1,3-diols. The reaction is general as methyl ether **6a**[11] and benzyl ether **6b** were isolated in 93% and 74% yield when **4d** was treated with trimethyl borate and tribenzyl borate, respectively (Table 3, entries 3 and 4). When **4d** and **4e** were treated at rt in CH_2Cl_2 with trimethyl borate, **6a** (76%) and **6c** (70%) were isolated in a 2/1 *syn*/*anti* ratio (Table 3, entries 5 and 6).

In order to explore the scope and limitation of the method, the reaction was tested on compounds **7**–**11** in the presence of $Pd(PPh_3)_4$ in THF at 50 °C. 1,2-Diols **12** can be obtained in 57% yield (*syn*/*anti* = 6/1) when **7** was treated with boric acid and the corresponding monomethyl ether derivative **13** was isolated in 64% yield (*syn*/*anti* = 6/1) when trimethyl borate was used.[12] On the contrary, 1,4-diol was not formed when **8** was treated with trimethyl borate as the intramolecular reaction was faster than the intermolecular reaction and the disubstituted tetrahydrofuran **14**[13] was isolated in 78% yield as an equimolecular mixture of *cis*/*trans* isomers.

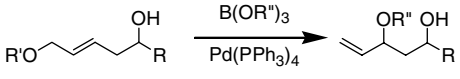
It is worth noting that for allylic acetates **9** and **10**, the presence of a hydroxy group is necessary to produce the corresponding allylic alcohol or ether (Table 4, entries 4 and 5). In contrast, with allylic carbonates, the hydroxy group does not seem necessary as allylic carbonate **11** was transformed to ether **15** (60%), which corresponds to the substitution of the carbonate on the less hindered carbon, whereas the presence of a hydroxyl group directs the attack of the OR group on the π-allyl palladium complex at the more substituted carbon.

Table 4. Formation of 1,2-diols and derivatives

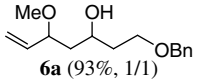
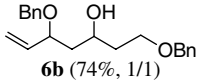
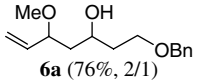
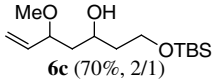
Entry	Substrate	$B(OR)_3$	Product (yield, *syn*/*anti*)
1	 **7**	$B(OH)_3$	 **12** (57%[a], 6/1)
2	**7**	$B(OMe)_3$	 **13** (64%, 6/1)
3	 **8**	$B(OMe)_3$	 **14** (78%, 1/1)
4	 **9**	$B(OH)_3$	—[b]
5	 **10**	$B(OMe)_3$	—[b]
6	 **11**	$B(OMe)_3$	 **15** (60%)

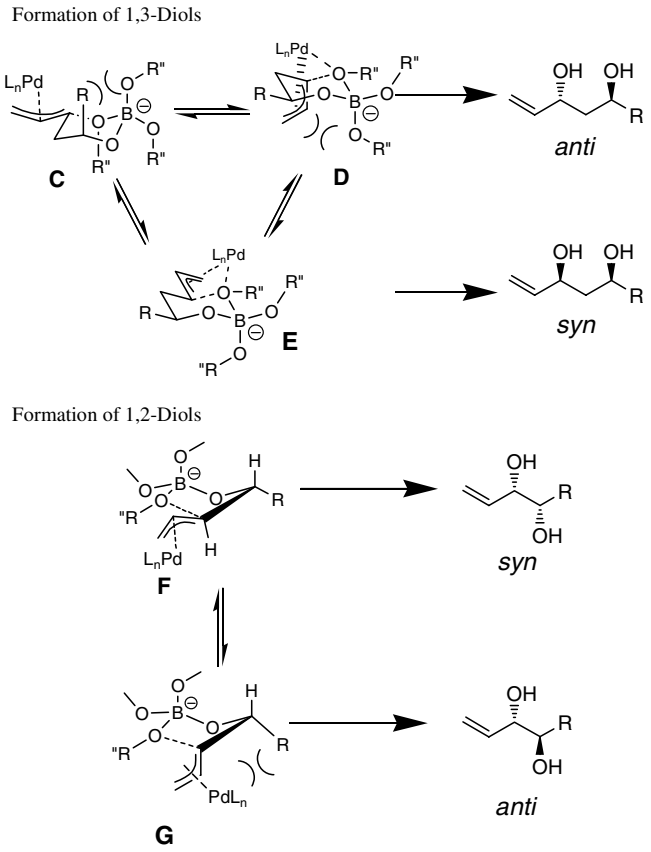
[a] 29% of starting material was recovered.
[b] 100% of starting material was recovered.

Table 3. Synthesis of monoprotected 1,3-diols



4 **6a-c**

Entry	**4**	$B(OR'')_3$	Solvent, *t* (°C)	Time (h)	**6** (yield, *syn*/*anti*)
1	**4a** (OAc)	$B(OMe)_3$	THF, 50	3	—
2	**4a** (OAc)	$B(OBn)_3$	THF, 50	3	—
3	**4d** (OCO_2Et)	$B(OMe)_3$	THF, 50	1	 **6a** (93%, 1/1)
4	**4d** (OCO_2Et)	$B(OBn)_3$	THF, 50	1	 **6b** (74%, 1/1)
5	**4d** (OCO_2Et)	$B(OMe)_3$	CH_2Cl_2, rt	2	 **6a** (76%, 2/1)
6	**4e** (OCO_2Et)	$B(OMe)_3$	CH_2Cl_2, rt	2	 **6c** (70%, 2/1)



Scheme 2. Proposed transition states for the *syn*/*anti* selectivity.

The poor diastereoselectivity in the synthesis of 1,3-diols can be explained by a six-membered chair transition state where the borate is complexed by the free hydroxy group (Scheme 2). In the **C**, **D**, and **E** transition states, 1,3-diaxial interactions and/or interactions with the palladium complex are present and the stability of all the intermediates should be similar, leading to a low *syn*/*anti* ratio.

For the formation of 1,2-diols, the five-membered ring transition state **G** is disfavored by a $A_{1,3}$-strain or a 1,2-diaxial interaction, favoring the transition state **F**, which is responsible for the formation of the *syn* isomers.

In conclusion, we have developed a new palladium-catalyzed formation of 1,2- and 1,3-diols as well as the formation of monoprotected diols from ω-hydroxy allylic acetates and carbonates using boric acid and trialkyl borates.

Acknowledgments

One of us (J. Cluzeau) thanks the CNRS for a postdoctoral grant.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2005.07.135.

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9. The *syn* relationship was proved by the chemical shift of $(CH_3)_2C$ in the diol acetonide by ^{13}C NMR. (a) Evans, D. A.; Rieger, D. L.; Gage, J. R. *Tetrahedron Lett.* **1990**, *31*, 7099–7100; (b) Rychnovsky, S. D.; Rogers, B.; Yang, G. *J. Org. Chem.* **1993**, *58*, 3511–3515.
10. General procedure for the reaction using $B(OR)_3$: Compound of type **4** (1 equiv) was dissolved in THF or CH_2Cl_2 (0.05 M). Trialkyl borate or boric acid (3 equiv) and Na_2CO_3 (1.5 equiv) were added and the mixture was stirred for 1 h. $Pd(PPh_3)_4$ (0.1 equiv) and PPh_3 (0.25 equiv) were then added and the mixture was stirred until completion of the reaction (monitoring by TLC). The reaction was then diluted with Et_2O and washed with a saturated aqueous $NaHCO_3$ solution, 0.1 M aqueous HCl solution, and brine. The organic phase was dried over anhydrous Na_2SO_4, filtered, and concentrated. The reaction mixture was purified by flash chromatography.
11. 1-Benzyloxy-5-methoxy-hept-6-en-3-ol (**6a**): Compound **4d** (50 mg, 0.15 mmol, 1 equiv) was treated with $B(OMe)_3$ (52 μL, 0.46 mmol, 3 equiv) in THF (3 mL) at 50 °C. Product **6a** was obtained as a 1/1 mixture of diastereomers (93%). $R_f = 0.31$ (70/30 hexane/EtOAc); ^1H NMR δ ($CDCl_3$) 7.32 (m, 5H), 5.70 (m, 1H), 5.26–5.18 (m, 2H), 4.51 (s, 3H), 4.00 and 3.98 (2br s, 1H), 3.90–3.76 (m, 1H), 3.68 (m, 2H), 3.29 and 3.28 (2s, 3H), 1.81–1.54 (m, 4H); ^{13}C NMR δ ($CDCl_3$) 138.3 (×2), 138.1, 138.0, 128.4 (×2), 127.7, 127.6, 117.6, 116.9, 83.1, 80.1, 73.3, 73.2, 69.0, 68.8, 67.9, 67.5, 56.4, 56.1, 42.7, 42.6, 37.3, 36.9. IR (cm^{-1}) 3447, 2923, 2856, 1496, 1453, 1420, 1362, 1205, 1092, 1027, 992, 925, 808, 735, 696. MS (IE) *m*/*z* 218 (M^+-CH_3O-H).
12. The relative stereochemistry of the diols was determined by comparison with the reported ^1H and ^{13}C NMR data. Lombardo, M.; Morganti, S.; Trombini, C. *J. Org. Chem.* **2003**, *68*, 997–1006.
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