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Hydroxylation of olefins using molecular oxygen via alkylboronic esters

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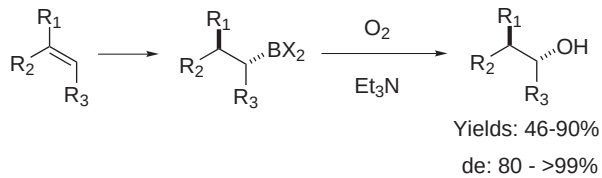
Abstract—Alkylboronic esters derived from olefins undergo a hydroxylation in the presence of triethylamine and molecular oxygen. Alcohols were obtained in good to excellent yields without alkaline treatment of the boronate ester intermediates. Radical-clock experiments allowed the comparison between radical and polar reaction paths.

Hydroxylation of olefins by hydroboration followed by oxidation is one of the most general reactions in organic chemistry.[1] Due to the pivotal role of this reaction, a variety of hydroborating agents as well as oxidation conditions were elaborated allowing milder and more selective reactions. Although treatment of organoboranes with hydrogen peroxide in alkaline media[2] is widely appreciated, other reagents such as sodium perborate,[3] amine *N*-oxides,[4] perbenzoic acid,[5] sodium percarbonate,[6] sodium hypochlorite,[7] oxone[8] or electrochemical oxidation[9] were developed and represent alternatives for this transformation. Despite the general interest in the use of molecular oxygen in fields spanning from biochemistry[10] to homogeneous catalysis,[11] the use of oxygen for the transformation of organoboranes to alcohols was seldom considered.[12]

The oxidation of trialkylboranes by molecular oxygen is often limited as only two of the three-alkyl groups on boron are converted to the desired oxidized products. The reaction stops at the monoalkylboronic ester stage due to a weak propensity of this intermediate to oxidize further to the corresponding borate.[12c] Other hydroboration intermediates such as catechol-esters afford, in turn, low yield in molecular oxygen promoted hydroxylation due to the extensive polycondensation and other free-radical side-reactions.[13] We report here that the oxidation of trialkylboranes by oxygen in the presence of triethylamine decreases the formation of the free-radical by-products and allows to prepare the corresponding hydroxylated compounds in synthetically appreciable stereoselectivity and yields (Scheme 1).



Scheme 1.

Hydroboration with $BH_3{\cdot}SMe_2$ in THF followed by addition of catechol resulted in the formation of the requisite alkylboronic esters.[14–16] Triethylamine (1.5–2.5 equiv.) was introduced prior to oxidation and the reaction mixture was flushed with a gentle stream of oxygen. It is noteworthy that the hydrolysis of the boronate ester intermediates occurred spontaneously during the aqueous work-up. The isolated yields and observed selectivity of the hydroxylation reactions are summarized in Table 1. A control experiment without triethylamine was performed and noted in Table 1.

Oxidation of alkylboronic ester derived from 2-methylindene **1a** with molecular oxygen in the presence of triethylamine (1.5 equiv.) afforded a mixture of *trans*/*cis* diastereomers **1b** and **1c** in a 10:1 ratio[17] (yield 85%)[17b] with a small amount of ketone (<5%). In a parallel experiment, when triethylamine was omitted, only traces of hydroxylated products were formed beside the corresponding ketone (12%). Under identical conditions, as used for the conversion of **1a**, the

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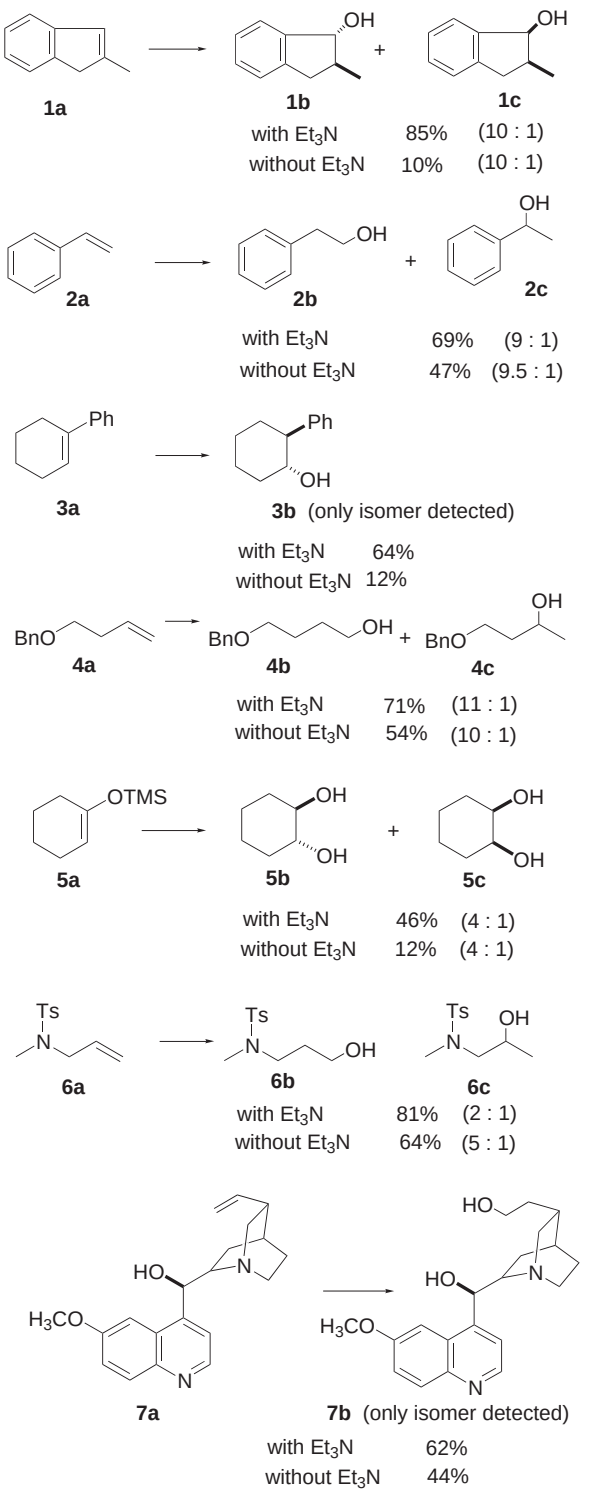
Table 1. Hydroxylation of olefins via alkylboronic esters



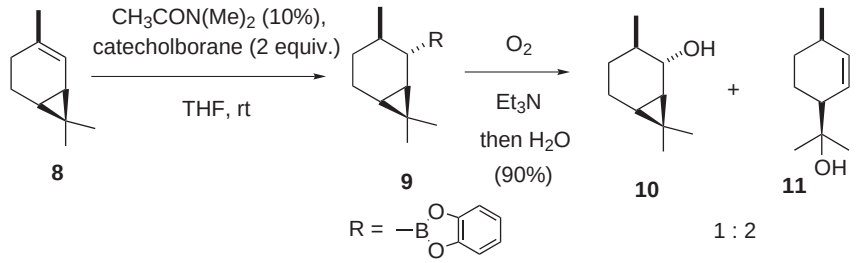
Reaction conditions: (i) $BH_3{\cdot}SMe_2$ in THF (1.2 equiv.), 0–5°C, then rt, 4 h; (ii) Et_3N (1.5 equiv.), then catechol (1.2 equiv.), THF, 0–5°C then rt, 2.5 h; (iii) O_2, rt, 12 h.

hydroxylation of terminal olefins such as **2a**, **4a** and **6a** followed similar trends. Accordingly, hydroboration using $BH_3{\cdot}SMe_2$ in THF followed by addition of catechol and oxidation by molecular oxygen in the presence of Et_3N afforded, respectively, a mixture of regioisomers **2b–2c**, **4b–4c** and **6b–6c** with a marked preference for the less substituted alcohols. When 1-phenylcyclohexene **3a** was oxidized, the *trans* hydroxy compound **3b** was obtained exclusively. The hydroboration of enol ether **5a** produced, after oxidation and an aqueous workup, the corresponding 1,2-diols **5b** and **5c** in modest yield (46%). Basic nitrogen-containing products do not change the reactivity of the system. Hydroxylation of quinine **7a** using excess of borane reagent[18] followed by oxidation and decomplexation of the aminoborane intermediate in refluxing ethanol produced the desired alcohol **7b**.

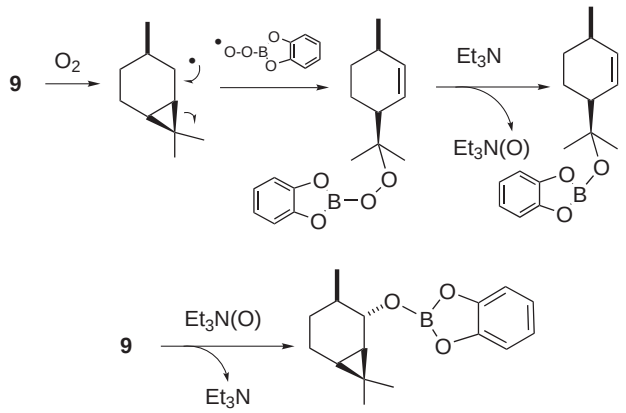
The mechanism of the reaction and in particular the role of the Et_3N was intriguing. According to the general consensus, the initial oxidation produces a peroxide which may evolve to the alcohol by intermolecular redox reactions.[12] The parallel polar and radical mechanisms operating in this transformation were probed by a radical-clock experiment[19] (Scheme 2).

Hydroboration of carene **8** under Fu's condition[20] followed by oxidation with O_2/Et_3N afforded a 1:2 mixture of alcohols **10** and **11** (yield 90%). The presence of the two isomers confirms the supposed concurrent radical and polar paths (Scheme 3). Although the parallel mechanisms match the classical free-radical fragmentation and intermolecular redox reaction established earlier,[12] it does not explain the effect of the additive. The trialkylamine intervenes probably in more than one process. It may serve to quench the perborate ester intermediates forming the corresponding alkyl borates and amine *N*-oxide (Scheme 3).[21] This mild decomposition depletes the ketone-forming and polycondensation free-radical paths increasing the yield of the hydroxylation products. On the other hand, the amine-oxide formed in this reaction oxidizes the alkylboronic ester (such as **9**) according to the earlier proposed mechanism.[4] The product distribution reflects the relative rates of the competing reactions.

Typical procedure: To a solution of borane–dimethylsulfide complex (1.2 mmol, 600 μL, 2.0 M in THF), the olefin **1a** (neat, 1.0 mmol) was added in one portion at 0–5°C under an inert atmosphere. The mixture was stirred for 4 h at rt and triethylamine (210 μL, 1.5 mmol) was added in one portion at 0°C. After 5 min at 0–5°C a solution of catechol (132 mg, 1.2 mmol) in THF (400 μL) was introduced, the reaction mixture was stirred for 2.5 h and a gentle stream of dry oxygen was bubbled through the reaction mixture for 1 h. The mixture was stirred vigorously for an additional 11 h by maintaining the oxygen atmosphere over the reaction mixture. The slightly rose colored solution was diluted with CH_2Cl_2 (10 mL), washed with a saturated solution of $NaHCO_3$ (2×20 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (pentane/ethyl acetate: 4/1) to afford the desired alcohols.



Scheme 2.



Scheme 3.

Acknowledgements

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15. ^{1}H NMR analyses in selected cases of the crude mixtures showed the presence of minor amounts of isomers alongside with the desired product.
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