B-Alkylcatecholboranes as a Source of Radicals for Efficient Conjugate Additions and Allylations

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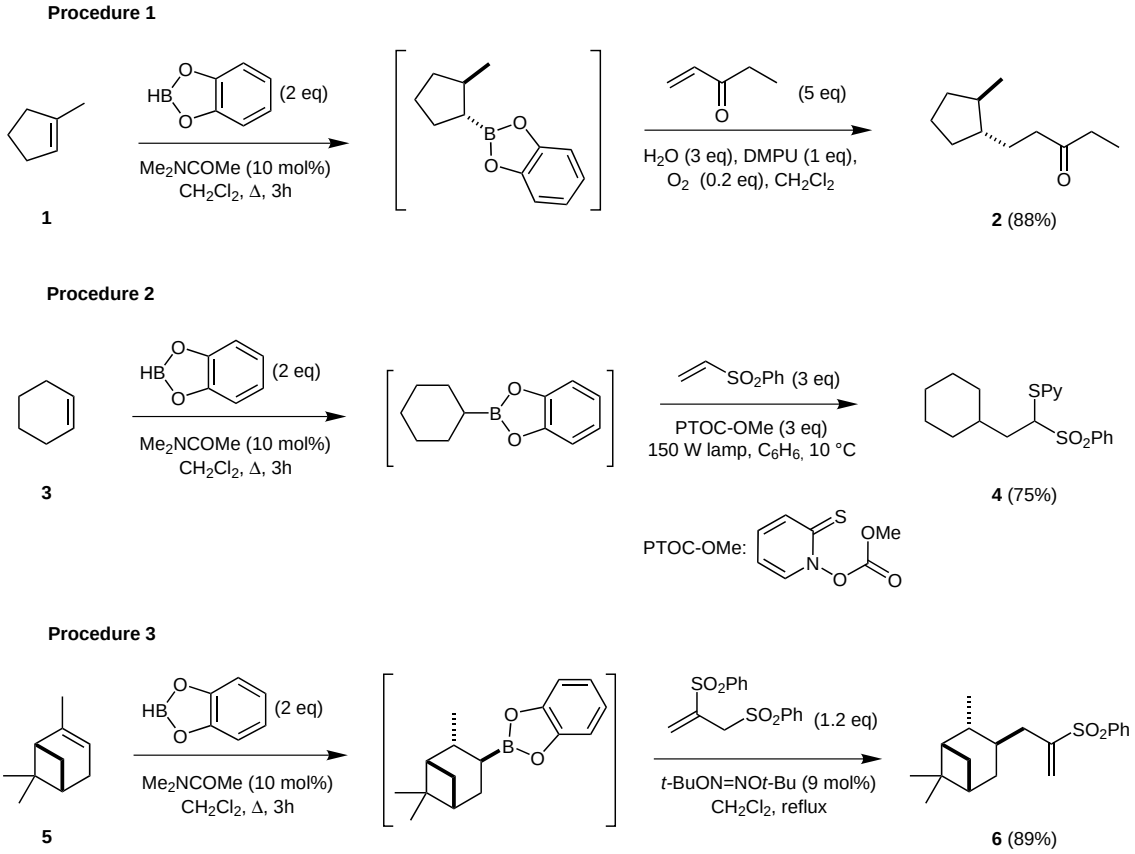
Received 11 September 2003

PSP No 12

Abstract: *B*-Alkylcatecholboranes, easily prepared in situ by hydroboration of alkenes, are powerful radical precursors that can be used for carbon–carbon bond formation. Typical procedures for (a) conjugate addition to enones, (b) conjugate addition to activated alkenes such as vinyl sulfones, and (c) direct allylation are described. Experimentally, these three one-pot reactions are easy to perform. No slow addition of a reagent, a procedure frequently encountered in intermolecular radical additions, is required.

Key words: radicals, tin-free, hydroboration, allylation, conjugate addition



Scheme 1

For many years, organoboron chemistry has been a privileged field of research for synthetic organic chemists. Following the spectacular development of radical chemistry in organic synthesis, the use of organoboranes has recently led to many novel and useful synthetic applications,[1,2] particularly for the formation of carbon–carbon bonds in intra- and intermolecular processes. In this context, we have recently reported several procedures involving the hydroboration of alkenes with catecholborane, followed by treatment with a catalytic amount of a radical initiator [O_2, di-*tert*-butyl hyponitrite or PTOC-OMe (PTOC = pyridine-2-thione-*N*-oxycarbonyl)] in the presence of a radical trap.[3–9] We have demonstrated that these *B*-alkylcatecholboranes are excellent radical precursors and can be used for highly efficient radical additions to α,β-unsaturated ketones (Procedure 1),[3] for conjugate ad-

SYNTHESIS 2003, No. 17, pp 2740–2742
Advanced online publication: 14.10.2003
DOI: 10.1055/s-2003-42430; Art ID: Z13303SS.pdf

ditions to various activated olefins using a Barton's carbonate as chain transfer reagent (Procedure 2)[5,10] and finally for allylation with allyl sulfones (Procedure 3)[9] (Scheme 1).

Procedures

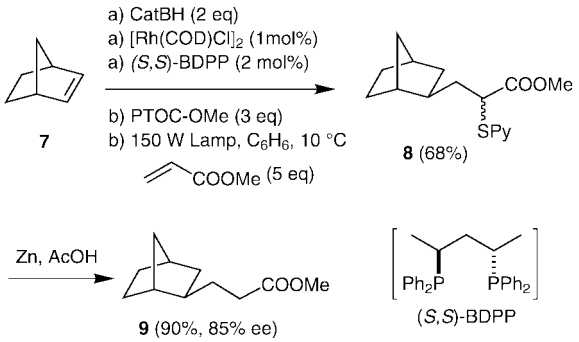
Procedure 1 depicts a radical-mediated conjugate addition of organoboranes to enones.[3] 1-Methylcyclopent-1-ene (**1**) is hydroborated with commercially available catecholborane using *N*,*N*-dimethylacetamide as catalyst.[11] Water (3 equiv), ethyl vinyl ketone (5 equiv), DMPU (1 equiv) are added successively to the solution of the intermediate *B*-alkylcatecholborane. Traces of air are sufficient to initiate the chain process, after treatment and purification by flash chromatography, 1-(2-methylcyclopentyl)pentan-3-one (**2**) is obtained in 88% yield. This reaction is presumably occurring via formation of a transient boron enolate. DMPU is essential to obtain good yield, however, its exact role is still obscure. The oxygen initiated procedure is suitable for a wide range of α,β-unsaturated ketones and aldehydes. Other radical traps such as unsaturated esters and amides as well as vinyl sulfones do not react under these conditions.

Procedure 2 represents the conjugate addition of the cyclohexyl radical to phenyl vinyl sulfone.[5] This reaction requires the use of PTOC-OMe (Barton carbonate) as chain transfer reagent. The Barton carbonate acts also as an initiator by providing a methoxycarbonyloxyl radical upon irradiation with a standard 150 W tungsten lamp. This oxyl radical reacts rapidly with the *B*-alkylcatecholborane to afford a nucleoplilic cyclohexyl radical that adds to phenyl vinyl sulfone. The radical adduct has some electrophilic character due to its substitution by an electron-withdrawing group and therefore reacts rapidly with the electron-rich thiocarbonyl group of the PTOC-OMe to afford the α-*S*-pyridyl sulfone **4** together with the methoxycarbonyloxyl radical necessary to sustain the chain reaction. The remarkable reactivity difference between the three radicals involved is the key point for the success of this reaction. The reaction can be run in a one-pot procedure without any slow addition of the chain transfer reagent. This represent a clear advantage relative to the tin hydride-mediated conjugate addition. Moreover, the process is nonreductive and furnishes products bearing a *S*-pyridyl group than can be removed or transformed into a variety of functional groups. This procedure can be extended to a wide range of radical traps such as methyl acrylate, dimethyl fumarate, *N*-phenylmaleimide, phenyl vinyl sulfone and phenyl vinyl sulfoxide.

Procedure 3 illustrates the radical allylation of organoboranes with allylsulfones.[9] In situ hydroboration of (–)-α-pinene **5** with catecholborane, followed directly by treatment with 1.2 equivalents of 2,3-bis(phenylsulfonyl)propene affords the allylated product in 89% yield. The efficiency of this intermolecular allylation reaction using only 1.2 equivalents of the allylating agent is unique. A large variety of allylsulfones have been reported to react satisfactorily under these conditions.

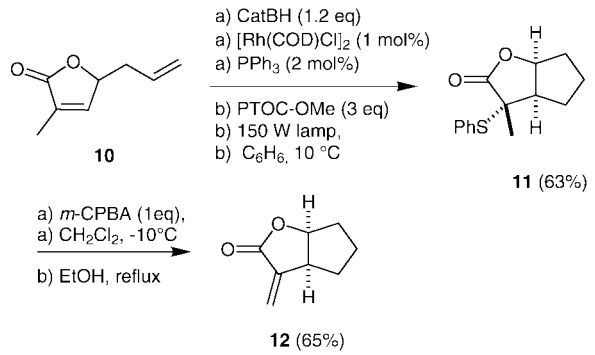
Applications

We have recently demonstrated that rhodium(I)-catalyzed hydroboration is perfectly compatible with radical reactions. For instance, enantioselective hydroboration of norbornene (**7**) with $[Rh(COD)Cl]_2$/(*S*,*S*)-BDPP as catalyst furnished the α-*S*-pyridyl ester **8** after conjugate addition of the intermediate boronate to methyl acrylate in the presence of PTOC-OMe (Scheme 2).[8] Desulfurization with zinc in acetic acid afforded the ester **9** in 85% ee.



Scheme 2

Cyclization reactions starting from dienyl systems are also possible. A typical example is shown in Scheme 3. The regioselective hydroboration of the α,β-unsaturated lactone **10** followed by treatment with PTOC-OMe affords the bicyclic lactone **11**. The versatility of the thiopyridyl group is demonstrated by the efficient conversion of **11** to the α-methylenelactone **12**.[7]



Scheme 3

1-(2-Methylcyclopentyl)pentan-3-one (2)

Freshly distilled catecholborane (0.64 mL, 6.0 mmol) was added dropwise at 0 °C to a solution of 1-methylcyclopent-1-ene (**1**; 0.247 g, 3.0 mmol) and *N*,*N*-dimethylacetamide (28.0 μL, 0.3 mmol) in CH_2Cl_2 (2.0 mL) under N_2. The reaction mixture was heated under reflux for 3 h. H_2O (0.16 mL, 9 mmol) was added at 0 °C and the solution was stirred for 15 min at r.t. CH_2Cl_2 (8 mL), 1,3-dimethylhexahydro-2-pyrimidone (DMPU; 0.36 mL, 3 mmol), and pent-1-en-3-one (1.26 g, 15 mmol) were successively added to this solution. Air (60 mL, 0.5 mmol O_2) was introduced over 2 h with a syringe (needle placed just above the reaction surface). After stirring for 2 h at r.t., the mixture was treated with aq sat. solution of NH_4Cl (10 mL) and extracted with Et_2O (3 × 20 mL). The combined organic layers were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Purification by flash chromatography over silica gel (Et_2O–hexane, 5:95) afforded **2** (443 mg, 88%) as a colorless oil.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 2.41 (m, 4 H), 1.80 (m, 3 H), 1.54 (m, 2 H), 1.40 (m, 1 H), 1.32 (m, 1 H), 1.23 (m, 2 H), 1.23–1.13 (m, 3 H), 1.05 (t, *J* = 7.3 Hz, 3 H), 0.96 (d, *J* = 7 Hz, 3 H).

^{13}C NMR (90.5 MHz, $CDCl_3$): δ = 212.2, 47.2, 41.5, 40.5, 35.8, 34.7, 32.1, 28.7, 23.3, 19.3, 7.8.

MS (EI): *m*/*z*: 169 [M^+ + 1], 151, 139, 121, 95, 93, 81, 69, 57.

Anal. Calcd for $C_{11}H_{20}O$ (168.15): C, 78.51; H, 11.98. Found: C, 78.45, H, 11.94.

2-{[2-Cyclohexyl-1-(phenylsulfonyl)ethyl]sulfanyl}pyridine (4)

Freshly distilled catecholborane (0.64 mL, 6.0 mmol) was added dropwise at 0 °C to a solution of cyclohexene (0.247 g, 3.0 mmol) and *N*,*N*-dimethylacetamide (28.0 μL, 0.3 mmol) in CH_2Cl_2 (2.0 mL) under N_2. The reaction mixture was heated under reflux for 3 h. MeOH (0.15 mL, 3.6 mmol) was added at 0 °C and the solution was stirred for 15 min at r.t. CH_2Cl_2 was evaporated under vacuum with strict exclusion of O_2. A yellow solution of PTOC-OMe (9 mmol) [freshly prepared by stirring the sodium salt of *N*-hydroxypyridine-2-thione (1.41 g, 9.45 mmol) and methyl chloroformate (0.7 mL, 9 mmol) in benzene (15 mL) for 1 h in the dark] was added to the solution followed by phenyl vinyl sulfone (2.52 g, 15 mmol) and DMPU (0.36 mL, 3 mmol). The mixture was irradiated at 10 °C with a 150 W tungsten lamp for 14 h, and treated with aq 1 N NaOH (20 mL). The aqueous layer was extracted with CH_2Cl_2 and the combined organic phases were washed with brine (30 mL), dried ($MgSO_4$), and concentrated under reduced pressure. The crude product was purified by flash chromatography over silica gel (hexane–EtOAc, 4:1) to afford **4** (0.892 g, 88%) as a white solid. For analytical purpose, a sample was recrystallized from EtOH; mp 80–81 °C.

^{1}H NMR (360 MHz, $CDCl_3$): δ = 8.20 (d, *J* = 5.0 Hz, 1 H), 7.88 (d, *J* = 7.3 Hz, 2 H), 7.43–7.26 (m, 4 H), 6.95 (d, *J* = 7.7 Hz, 1 H), 6.89 (dd, *J* = 7.3, 5.4 Hz, 1 H), 5.80 (dd, *J* = 12.2, 3.1 Hz, 1 H), 2.19 (ddd, *J* = 14.5, 9.5, 2.7 Hz, 1 H), 1.86–1.77 (m, 2 H), 1.74–1.56 (m, 5 H), 1.31–1.00 (m, 4 H), 0.96–0.83 (m, 1 H).

^{13}C NMR (90 MHz, $CDCl_3$): δ = 122.7, 120.7, 63.6, 34.5, 33.9, 33.8, 31.6, 26.3, 26.1, 25.7.

MS (CI, CH_4): *m*/*z* = 361 [M^+], 253, 220, 143, 112, 79, 55.

Anal. Calcd for $C_{19}H_{23}NO_2S_2$ (361.52): C, 63.13; H, 6.41. Found: C, 63.20, H, 6.47.

Phenyl 1-{[(1*S*,2*R*,3*R*,5*S*)-2,6,6-Trimethylbicyclo[3.1.1]hept-3-yl]methyl}vinyl Sulfone (6)

Freshly distilled catecholborane (0.64 mL, 6 mmol) was added dropwise at 0 °C to a solution of (–)-α-pinene (**5**; 409 mg, 3.0 mmol) and *N*,*N*-dimethylacetamide (28.0 μL, 0.3 mmol) in CH_2Cl_2 (2.0 mL) under N_2. The reaction mixture was heated under reflux for 3 h. MeOH (0.15 mL, 3.6 mmol) was added at 0 °C and the solution was stirred for 15 min at r.t. 2,3-Bis(phenylsulfonyl)propene (1.160 g, 3.6 mmol) and di-*tert*-butyl hyponitrite (15 mg, 3 mol%) were added, and the solution was heated at reflux, while adding di-*tert*-butyl hyponitrite (15 mg, 3 mol%) every 1 h. After 3 h, the reaction mixture became black and the reaction was stopped. Evaporation of the solvent under reduced pressure followed by purification of the residue by flash chromatography over silica gel (hexane–EtOAc, 4:1) afforded **6** (0.848 g, 89%) as a colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.93–7.83 (m, 2 H), 7.64–7.45 (m, 3 H), 6.41 (s, 1 H), 5.80 (s, 1 H), 2.52 (dd, *J* = 15.1, 3.7 Hz, 1 H), 2.24 (m, 1 H), 2.06 (m, 1 H), 1.95–1.69 (m, 3 H), 1.54 (m, 1 H), 1.23 (m, 2 H), 1.13 (s, 3 H), 0.93 (m, 3 H), 0.86 (s, 3 H), 0.61 (d, *J* = 9.6 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 149.3, 139.2, 133.4, 129.1, 128.2, 124.6, 47.9, 43.7, 41.6, 38.6, 34.2, 34.1, 33.9, 27.9, 22.8, 21.2.

MS (EI): *m*/*z* = 319 [M^+ + 1], 246, 218, 177, 137, 81, 55, 41.

HRMS (ESI-MS): *m*/*z* calcd for $C_{19}H_{27}O_2S$ ([M + 1]$^+$): 319.1731; found: 319.1729.

Acknowledgment

This work was supported by the Swiss National Science Foundation (grant 21-67106.01 and 7SUPJ062348). We thank Callery Chemical Company (Pittsburgh) and Z & S Handel AG (Kloten) for the generous gift of catecholborane.

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