Pergamon

Tetrahedron Letters, Vol. 36, No. 11, pp. 1805-1808, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)00148-4

Conjugate Addition of gem-Borazirconocene Alkanes to Michael Acceptors

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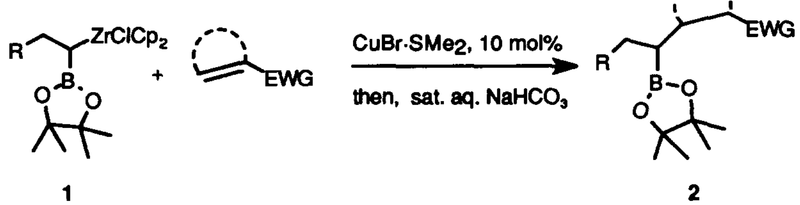
Summary: *gem-Borazirconocenes, 1, readily add across Michael acceptors in the presence of Cu(I)Br·SMe2, to afford 1,4-addition products in good to excellent yields. In the case of cycloalkenones diastereomers are produced, with the anti product favored. The selectivity with cyclopentenone is high (9:1), while with cyclohexenone it is less (3:1). In the present context, gem-borazirconocene alkanes can be regarded as α-hydroxyl anion equivalents.*

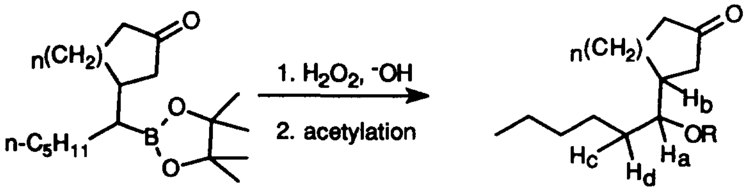
The conjugate addition of zirconocene alkenes to enones in the presence of Cu or Ni salts was first reported by Schwartz.[1] Lipshutz subsequently extended the transmetalation to higher order cuprates.[2] The reaction was however restricted to the transfer of alkenyl groups. More recently Wipf has shown that alkyl groups transfer from zirconocenes in the presence of catalytic amounts of thermally stable Cu(I) salts and add to α,β-unsaturated systems in a 1,4-manner.[3] While these and other reactions have extended the original scope of alkylzirconocene chemistry, only one transformation with the organometallic reagent is possible. Bimetallics offer the possibility of multiple transformations. Specifically, bimetallics in which the reactivities of the carbon-metal bonds are sufficiently different make possible two sequential transformations, thereby greatly extending the utility of these kinds of reagents. In the case of zirconocenes, Lipshutz has prepared *gem*-stannazirconocene alkenes and reacted them with α,β-unsaturated enones.[4] We have recently prepared and characterized various *gem*-borazirconocene alkanes and alkenes and have shown that the latter readily undergo 1,4-addition with enones.[5] In the present case we were interested in exploring whether compounds 1 would behave similarly and in examining their selectivity with cycloalkenones.

Reaction of 1 (R= Me, n-Bu, 3-chloropropyl) with various Michael acceptors in the presence of CuBr·SMe$_2$ (10 mol %) gave exclusively products of 1,4 addition, 2 (eq 1). Results are summarized in Table 1.



(1)

In each case it is the C-Zr bond that reacts to give, after aqueous workup, the 1,4-addition product. The C-B bond is stable under the conditions of the reaction. Suitable substrates are α,β-unsaturated aldehydes, esters, ketones, and nitriles. In general the yields are excellent. The somewhat lower yields with acrylonitrile and methyl acrylate are possibly due to competing polymerization reactions. Many of these boron-containing adducts would be very difficult or impossible to synthesize by other methods. We also briefly investigated the selectivity in the addition of **1** to cycloalkenones. The *syn:anti* ratio could not be determined directly on the boronates. Instead, adducts **2g** and **2h** were oxidized and then acetylated to give products **3** and **4** respectively (eq 2).



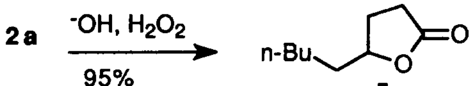
2

R= H, **3 a**; R=Ac, **3b**, n=1
R= H, **4 a**; R=Ac, **4b**, n=2

(2)

The ratio of diastereomers was determined from the ^1H NMR spectra of either **3** or **4** by examining the peak ratios of the carbinyl protons. However, the carbinyl protons in **3a** were not sufficiently separated to determine the diastereomeric ratio directly. Even decoupling of H_c and H_d in **3a** did not separate the carbinyl multiplet. However the diastereomeric ratio could be determined by decoupling of H_c and H_d in **3b** at 1.55 ppm, collapsing the H_a multiplet into two sets of doublets in a 9:1 ratio. On the other hand, the diastereomeric ratios of either **4a** or **4b** could be determined directly from the ^1H NMR. After appropriate decoupling experiments, the vicinal coupling constants, $^3J_{Ha...Hb}$ were assigned, with the smaller of the two coupling constants in each case being assigned to the major *anti* isomer. This is consistent with assignments of similar compounds in the literature.[6]

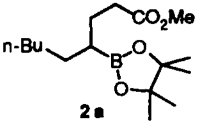
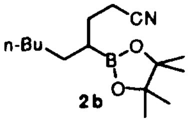
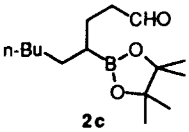
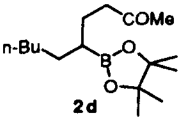
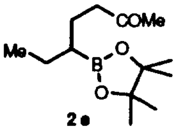
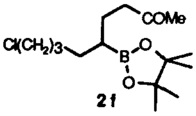
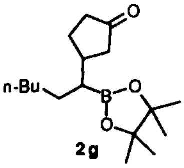
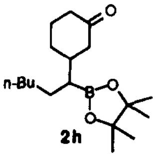
In the case of the addition to methyl acrylate, (Entry 1), oxidation of **2a** followed by cyclization gave lactone **5** (eq 3).



5

(3)

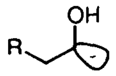
Table 1. Results of 1,4-Addition Reactions.

Entry	R in Eq 1	Michael Acceptor	Product[a]	% Yield[b]	syn:anti[c]
1	n-Butyl	Methyl Acrylate	 2a	62	
2	n-Butyl	Acrylonitrile	 2b	65	
3	n-Butyl	Acrolein	 2c	78	
4	n-Butyl	Methyl Vinyl Ketone	 2d	84	
5	Methyl	Methyl Vinyl Ketone	 2e	94	
6	3-Chloropropyl	Methyl Vinyl ketone	 2f	87	
7	n-Butyl	2-Cyclopentenone	 2g	94	1:9
8	n-Butyl	2-Cyclohexenone	 2h	90	1:3

[a]Compounds 2-5 gave satisfactory ^1H NMR, ^{13}C NMR and mass spectra and are consistent with the assigned structures. [b]Isolated yield. [c]*Syn;anti* ratio was determined by ^1H-NMR analysis of the acetates, 3b and 4b.

Thus 1,4-addition of borazirconocenes followed by oxidation of the C-B bond makes compound **1** the equivalent of the as yet unknown α–hydroxy carbanion **6**.

1 =



6

General procedure for the preparation of 2. Hydrozirconation of the pinacol 1-alkenyl boronate (1.0 mmol) with Schwartz's reagent[7] ($HZrCp_2Cl$, 0.283 g, 1.1 mmol) at 25 ^oC in 10 ml of THF, under an atmosphere of argon, gave a clear yellow solution after 25 minutes.[8] Addition of 1 equiv. of the α,β–unsaturated compounds, 8-10 mol% of $CuBr{\cdot}SMe_2$, followed by quenching with a saturated solution of aqueous $NaHCO_3$ (1 ml) after 20 minutes afforded the corresponding addition products. The reaction mixture was washed with water (3 X 5 ml), dried with Na_2SO_4 (2.0 g) and analyzed by GC. The products were isolated by silica gel column chromatography.

Acknowledgment: SP thanks the University of Toledo for a teaching fellowship. We thank Dr. Craig Blankenship of Boulder Scientific for a generous supply of zirconocene dichloride.

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(*Received in USA* 6 *December* 1994; *revised* 16 *January* 1995; *accepted* 19 *January* 1995)