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HYDROBORATION OF METHOXYENYNES. A NOVEL SYNTHESIS OF *(E)*-METHOXYENONES

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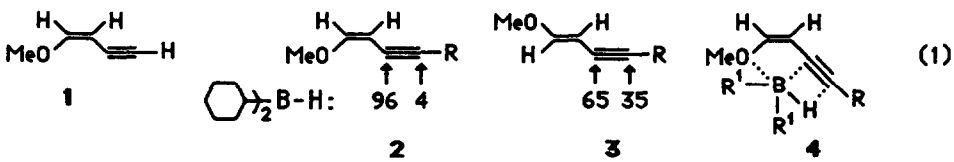
Abstract: Chemo- and regioselective hydroboration of *(Z)*-methoxyenynes with dialkylboranes furnishes organoboranes which produce on oxidation the synthetically valuable *(E)*-methoxyenones

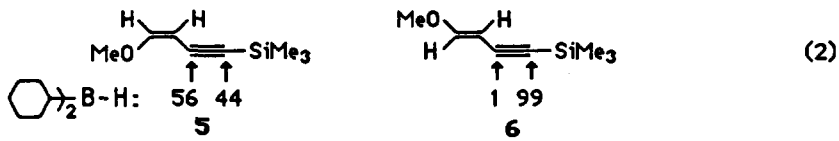
Recently we have shown that the commercially available (*Z*)-1-methoxybut-1-en-3-yne **1** is a versatile synthon for a variety of synthetic transformations.[1] The possibility of being able to prepare chemo- and regiodefined organoboranes containing the synthetically useful enol ether moiety led us to explore the hydroboration of 4-substituted 1-methoxybut-1-en-3-ynes **2**[2] (Table) . Monohydroboration of **2** (R=*n*-C_3H_7) with one equiv. of dicyclohexylborane was highly chemo-and regioselective, placing the boron preferentially (96%) at the internal acetylenic carbon of the enyne, as evidenced by ^{1}H-NMR examination of the reaction mixture. On the other hand, hydroboration of the corresponding (*E*)-methoxyenyne **3**[5] with dicyclohexylborane was chemoselective, but not regioselective, furnishing a 65 to 35 mixture of dienylboranes (eq. 1).



1 **2** **3** **4** (1)

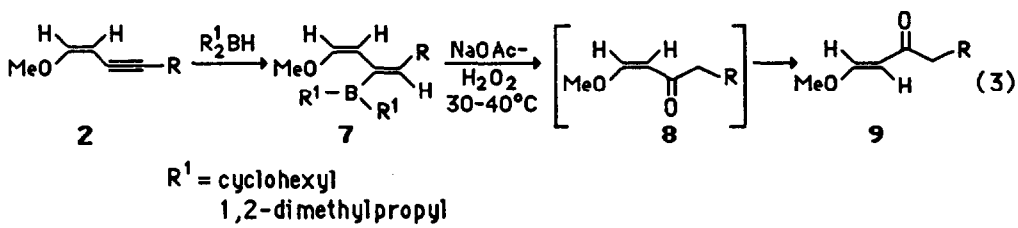
The observed directive effects in the hydroboration of the enynes **2** and **3** may be rationalized as follows. With the alkyl substituted *(Z)*-methoxyenyne **2**, the trigonal boron of the dialkylborane coordinates with the oxygen of the methoxy group, directing the boron to the internal acetylenic carbon of the enynyl moiety as in **4** (R^1=cyclohexyl). For the alkyl substituted *(E)*-methoxyenyne **3**, where coordination of the boron with the methoxy group is precluded, the electron withdrawing effect of the methoxyvinyl group could account for the observed direction of addition of the B-H bond to the triple bond.[6] In this connection it is interesting to note that a completely opposite regiochemical behavior is

observed when the alkyl group of the methoxyenyne is substituted by a trimethylsilyl group. Whereas the hydroboration of the (Z)-isomer **5** is non-regioselective (eq. 2), the (*E*)-isomer **6** reacts with dicyclohexylborane in a highly regioselective manner. In **6**, the trimethylsilyl group directs the boron regioselectively to the silicon bearing carbon of the triple bond.[7] However, in the case of the (Z)-silylmethoxyenyne **5**, the coordinative directive effect of the methoxy group opposes the effect of the trimethyl silyl group, thereby resulting in a diminished regioselectivity.



(2)

Oxidation of the regiodefined organoboranes derived from (Z)-methoxyenynes should provide access to 1-methoxyalken-3-ones. These are valuable precursors for a number of synthetic transformations such as for the preparation of *trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (Danishefsky's diene),[8a] in cycloaromatization reactions,[8b] for the synthesis of γ-pyrones,[8c] and for the preparation of enynones and dienones.[8d] Preliminary experiments revealed that hydroboration of **2** (R=C_3H_7) with dicyclohexylborane followed by oxidation of the intermediate organoborane **7** with aqueous sodium acetate-hydrogen peroxide (30%)[9] afforded the corresponding methoxyenone **9** in 85% yield (eq. 3).[10]



(3)

Unfortunately, isolation of **9** from the cyclohexanol by-product by distillation was not successful, and attempted separation of the compounds on a silica gel column resulted in the polymerization of **9**. This problem was circumvented by using disiamylborane [bis(1,2-dimethylpropyl)borane] instead of dicyclohexylborane as the hydroborating agent. Thus, treatment of **2** with 1.5 equiv. of disiamylborane[11] at -15°C and oxidation of the resultant organoborane with aqueous sodium acetate-hydrogen peroxide afforded, after workup and distillation, the methoxyenone **9** free from 3-methyl-2-butanol. It should be noted that under the conditions employed for the oxidation of the organoboranes, the (Z)-methoxyenones **8** initially formed isomerize to the corresponding *trans*-enones **9**.[12] A summary of the yields of methoxyenyne starting materials and *(E)*-methoxyenone products obtained in this study is shown in the Table.

Table. Yields of Methoxyenynes 2 and *(E)*-Methoxyenones 9

Entry	R=	%Yield 2[a,b,c]	% Yield 9[a,b,c]
1	*n*-C_3H_7	86 (97)	70 (96)
2	*n*-C_6H_{13}	76 (98)	76 (98)
3	*c*-C_6H_{11}	43 (91)	73 (98)
4	$CH(OSiMe_3)C_2H_5$	80 (98)	70 (98)

[a] Isolated yields. [b] ^{1}H-NMR, IR, and mass spectral data were obtained for all compounds. [c] Isomeric purities are in parentheses.

The following procedure for the preparation of methoxyenones is representative. Into a dry, nitrogen flushed 25-ml flask, kept under a static pressure of nitrogen were placed THF (15 ml) and neat $BH_3{\cdot}SMe_2$ (1.5 ml, 15 mmol). To this solution was added dropwise a 4 M solution of 2-methyl-2-butene (8.3 ml, 33 mmol) in THF while maintaining the temperature during the addition at -10°C. The disiamylborane formed was stirred for an additional 2 h at 0°C, then was added slowly by means of a double ended needle into a second flask containing the freshly distilled (over CaH_2) methoxyenyne 2 (R=*n*-C_3H_7; 1.2 g, 10 mmol) while maintaining the temperature during the addition between -15 and -20°C (Dry ice-$CaCl_2$ bath). The reaction mixture was stirred at -15°C for 5 h, excess hydride was decomposed with H_2O (4 ml), the organoborane was oxidized by adding a 3 M solution of sodium acetate (30 mmol) followed by dropwise addition of H_2O_2 (30%, 7 ml) so as to maintain the temperature between 40-50°C. The mixture was vigorously stirred for an additional 1 h at 40-50°C, then was diluted with brine (20 ml) and the layers formed were separated. The aqueous layer was extracted with pentane and the combined organic extracts were dried ($MgSO_4$). The solvents and the 3-methyl-2-butanol (bp 112°C) by-product were removed by distillation (50°C, 100 mm Hg). Distillation (short path column) of the residue furnished 1.0 g (70%) of the methoxyenone 9 (R=*n*-C_3H_7); bp 82°C (4 mm Hg); n^{22}_D 1.4594; IR (neat) 1680, 1620, 1600 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.90 (t, J= 7.5 Hz, 3H), 1.35 (m, 2H), 1.60 (m, 2H), 2.40 (t, J=8.0 Hz, 2H), 3.75 (s, 3H), 5.60 (d, J=12.9 Hz, 1H, OC=CH), 7.60 (d, J=12.9 Hz, 1H, OCH=C).

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References and Notes

1. Zweifel, G.; Rajagopalan, S. *J. Am. Chem. Soc.*, **1985**, *107*, 700.
2. The enynes 2 (Table, entries 1 and 2,) were prepared by treatment of *(Z)*-MeOCH=CHC≡CLi (A)[1] with the appropriate alkyl halides (1.1 equiv., -40°C, then at 0°C /2 h) in HMPA (1.5 equiv.). The