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# A NEW REGIO- AND STEREOCONTROLLED SYNTHESIS OF ENOL SILYL ETHERS

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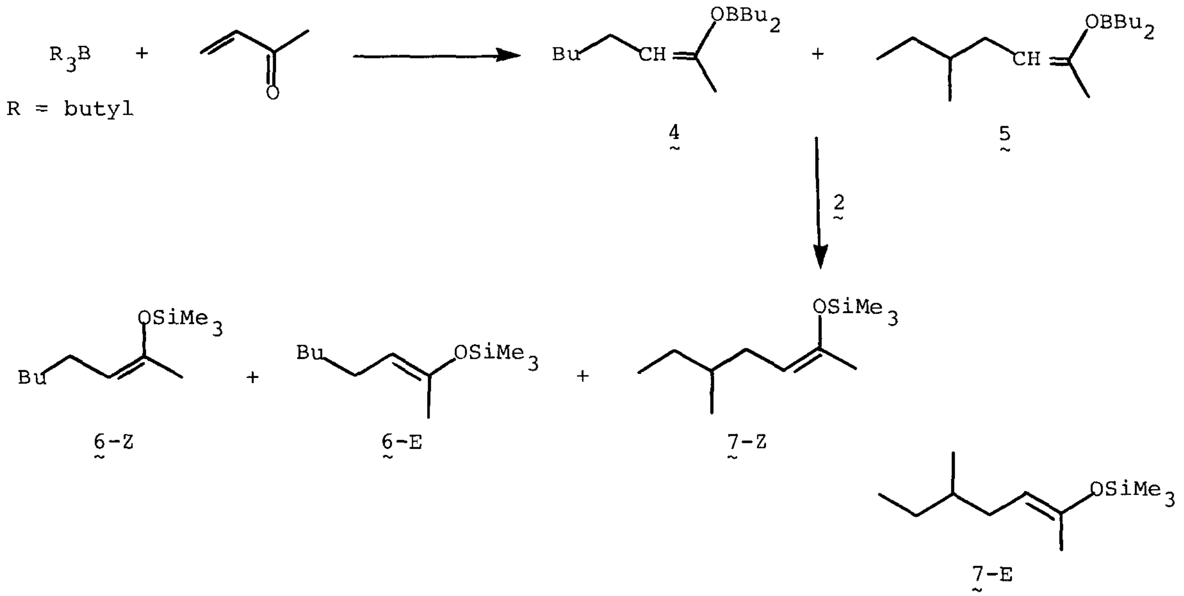
Summary: Enol boranes, 1, undergo efficient exchange with N-trimethylsilylimidazole, 2, to afford the corresponding trimethylsilyl enol ethers, 3, in good yield under mild conditions.

Synthetic routes to enol silyl ethers and enol boranes have received considerable attention recently because of their importance as synthetic intermediates.[1] In particular, reactions of enol boranes, 1, with various electrophiles have served as a means of controlling regio- and stereochemical problems (enolate scrambling) normally associated with enolate alkylations, en route to several important classes of compounds (α,β-enones,[2] α-alkylated ketones,[2] β-diketones,[2] β-hydroxyketones[3]).

During the course of these studies, an efficient mild exchange process has been discovered which enlarges the applications of reagents 1, and provides a novel route to regio- and stereodefined trimethylsilyl enol ethers 3,[4] according to eq. 1.

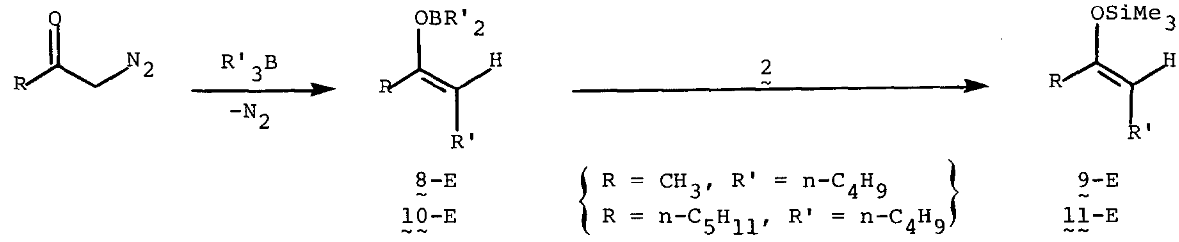
1 2 3 (1)

The conjugate addition of tributylborane to methyl vinyl ketone is known[6] to produce (after hydrolysis) an *ca* 85:15 mixture of 2-octanone and 5-methyl-2-heptanone, *via* enol borane intermediates 4 and 5 (undefined stereochemistry). Hydrolytic instability precluded direct glpc analysis of the intermediates, but the $^1$H NMR spectrum of the distilled (90°C, 0.01 Torr) mixture indicated modest Z-stereoselectivity (total Z:E vinylic hydrogen ratio of *ca*. 3.5 : 2, appearing at δ 4.55 and 4.67, respectively).[7] Addition of N-trimethylsilylimidazole, 2, in tetrahydrofuran at room temperature was *exothermic* and afforded after distillation (87%, 85°C / 20 Torr) a mixture whose $^1$H NMR spectrum displayed the virtually identical 3.5 : 2 ratio of Z:E vinylic protons. Analysis of the resulting, and less hydrolytically-sensitive, enol trimethylsilyl ethers indicated (glc mass spectrometry, nmr) the presence of two sets of diastereomers, 6-Z, 6-E, 7-Z, 7-E (57%, 31%, 6%, 6%, respectively). The total 6 : 7 ratio is in good accord with hydrolysis results,[6] and, importantly, the identical Z:E vinyl proton ratio before and after treatment with reagent 2 suggested that the $—OBR_2 \longrightarrow —OSiMe_3$ exchange had occurred stereoselectively.

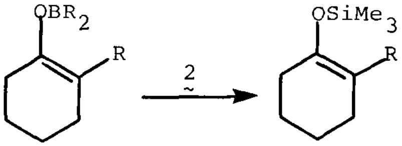


In accord with this expectation, the reaction of an isomerically homogeneous enol borane, **8**-E, (from diazoacetone and tributylborane)[8] with **2** afforded **9**-E, 80% isolated; ir (neat) 1665 $cm^{-1}$; $^1H$ NMR: $\delta$ 4.50 (t, J = 7.5 Hz, 1 H) $C\underline{H}=$; 1.8—2.0 (m, 2 H) $C\underline{H}_2C=$; 1.67 (s, 3 H) $C\underline{H}_3C=$; 1.1—1.4 (m, 4 H) $C\underline{H}_2$; 0.8—1.1 (m, 3 H) $C\underline{H}_3$; 0.13 (s, 9 H) $(C\underline{H}_3)_3Si$. Similarly, enol trimethylsilyl ether **11**-E was isolated (85%) upon treatment of pure **10**-E with reagent **2**.

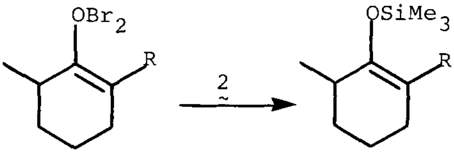
Each enol borane was readily prepared *via* the $R_3B$-$\underline{\alpha}$-diazoketone route,[9] and the entire sequence was conducted as a single-flask operation, by sequential addition of reagents.



Several cyclic enol boranes also underwent smooth exchange with **2**, illustrated by the conversions **12** ⟶ **13**, and **14** ⟶ **15**. In all cases, there was no indication of loss of either positional- or stereointegrity within limits of detection (nmr, glpc).



**12a**: R = Et    **13a**: 73%
b: R = n-$C_4H_9$    b: 75%



**14a**: R = Et    **15a**: 78%
b: R = n-$C_4H_9$    b: 82%

A typical experimental procedure involves addition of 1 equivalent of reagent **2**[10] to a tetrahydrofuran solution of an enol borane (generated from the corresponding organoborane and α-diazoketone, 20 mmol scale)[9] at *ca*. -10°C, allowing the mixture to warm to room temperature overnight, then removing solvent (atmospheric pressure) and distilling the product.[11]

The regio- and stereocontrol, the mild neutral conditions, and the operational simplicity of this one-flask procedure render it an attractive route to enol silyl ethers. Combined with recent observations[12] that the reverse exchange, $-\mathrm{OBR}_2 \longrightarrow \mathrm{OSiMe}_3$, is also readily achieved, an expanded accessibility to either class of important intermediates is now available.[13]

## References and Notes

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5. Imidazole is also highly effective in removing boron-containing by-products from reaction mixtures containing sensitive functionality,[2] Ph.D. Thesis of J.O., University of Alberta, 1979. The polymeric nature of dialkylboraimidazole adducts have been described earlier, K.D. Müller, L. Komorowski, and K. Niedenzu, *Synth. React. Inorg. Met. Org. Chem.*, **8**, 149 (1978).

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7. W. Fenzl, R. Köster, and H.-J. Zimmerman, *Liebigs Ann. Chem.*, 2201 (1975), have demonstrated the 1,4-addition of triethylborane to several enones to occur with varying stereoselectivity.

8. In contrast to the conjugate addition process, the enol borane-forming reaction of $R_3B$ reagents and α-diazoketones is characterized by preferential migration of primary alkyl groups.[9]

9. The enol boranes were prepared by standard procedures; J. Hooz and S. Linke, *J. Amer. Chem. Soc.*, **90**, 5936 (1968); H. Kono and J. Hooz, *Org. Synth.*, **53**, 77 (1973).

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11. If inadvertent partial hydrolysis occurs, the pure enol silyl ethers may be isolated by chromatography on silica gel (2% ether in hexane elution) at -20°C for the more sensitive acyclic cases, and at room temperature for the more stable cyclohexanone derivatives.

12. I. Kuwajima, M. Kato, and A. Mori, *Tetrahedron Lett.*, 4291 (1980); M. Wada, *Chem. Lett.*, 153 (1981).

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