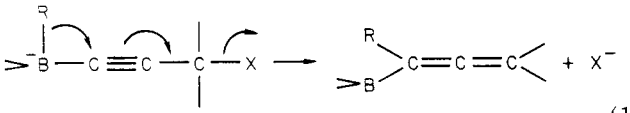
# Communications

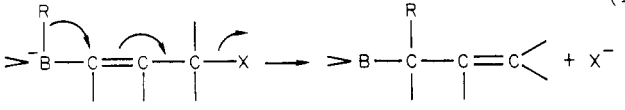
## Stereochemistry at the Migration Terminus of Organoborane Rearrangements. Stereoselective and Enantioselective Formation of Allylic Alcohols

*Summary:* The base-induced migration of an alkyl group from boron to carbon in a γ-acetylvinylborane occurs predominantly in an anti manner with respect to the leaving group to produce a trans allylic alcohol upon oxidation.

*Sir:* One of the most fundamental and synthetically important reactions of organoboranes is the formation of carbon–carbon bonds through the rearrangement of an α-substituted organoborate species.[1] We have recently demonstrated that this reaction occurs with complete inversion at the migration terminus.[2] These rearrangements may be extended to α,β-unsaturated organoborates containing a γ leaving group (eq 1 and 2).[3] The rearrangement of the alkynyl borate (eq 1) occurs with the alkyl



(1)

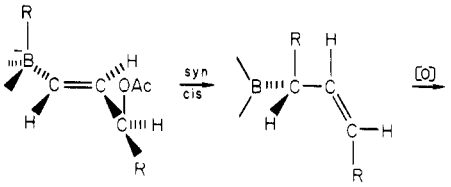


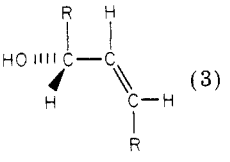
(2)

group migrating predominately (70:30) anti to the leaving group.[4]

The stereochemical situation with the vinylboranes is more complex because the geometry about the double bond of the product must also be considered. Four products are thus possible: syn or anti migration to give a cis olefin and syn or anti migration to give a trans olefin. Closer examination reveals that syn migration to a cis olefin (eq 3) and anti migration to a trans olefin (eq 4) give the same absolute configuration at the migration terminus. Likewise, the syn to trans and anti to cis modes both give the same, but opposite the above, absolute configuration at the migration terminus. The process is further complicated by the fact that an allylic borane may undergo a facile 1,3 boron transposition and a facile protonation to an olefin.[5]

To unravel the stereochemistry of this system we have investigated the rearrangement of chiral dialkyl-γ-acetoxyvinylboranes. The required boranes are readily prepared by hydroboration of (*S*)-3-hydroxy-1-octynyl acetate with either diethyl-[6] or dicyclohexylborane[7] in tetrahydrofuran. The vinylborane is then treated with 3 M aqueous sodium hydroxide at −20 °C to effect the rearrangement. The resulting allyl borinic acid is much less prone to undergo allylic rearrangement or protonation than the corresponding alkylborane.[8] Oxidation (sodium hydroxide/hydrogen peroxide) then produces the allylic alcohol.





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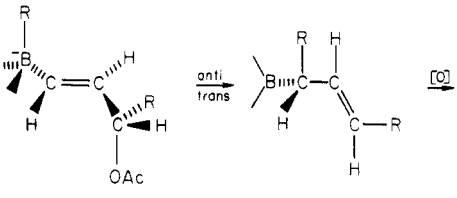

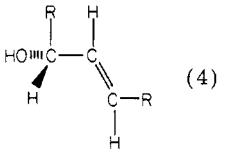

(4)

In both cases only the trans allylic alcohol could be detected. The product from ethyl migration (50% GC yield) was a 75:25 mixture of enantiomers. The cyclohexylborane product (99% GC yield, 86% isolated) was an 87:13 mixture of enantiomers[9] as determined by NMR in the presence of tris[3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorato]europium(III). In each case the major enantiomer was assigned the *R* configuration by comparison with the spectrum of an authentic sample prepared by asymmetric reduction of the appropriate alkynyl ketone.[10] The reaction thus proceeds in a predominately anti mode to give the trans olefin as depicted in eq 4.

In an attempt to maximize the yield based on the migrating alkyl group, thexylcyclohexylborane[11] was investigated. The thexyl group often does not undergo boron

(1) For reviews see: (a) Cragg, G. M. L.; Kock, K. R. *Chem. Soc. Rev.* **1977**, *6*, 393. (b) Negishi, E. *J. Chem. Educ.* **1975**, *52*, 159. (c) Onak, T. "Organoborane Chemistry", Academic Press: New York, 1975. (d) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes", Wiley: New York, 1975. (e) Cragg, G. M. L. "Organoboranes in Organic Synthesis", Marcel Dekker: New York, 1973.

(2) Midland, M. M.; Zolopa, A. R.; Halterman, R. L. *J. Am. Chem. Soc.* **1979**, *101*, 248.

(3) Zweifel, G.; Horng, A.; Snow, J. T. *J. Am. Chem. Soc.* **1970**, *92*, 1427. Zweifel, G.; Horng, A. *Synthesis*, **1973**, 672. Leung, A. T.; Zweifel, G. *J. Am. Chem. Soc.* **1974**, *96*, 5620. Zweifel, G.; Backlund, S. J.; Leung, T. *Ibid.* **1978**, *100*, 5561. Midland, M. M. *J. Org. Chem.* **1977**, *42*, 2650.

(4) Midland, M. M.; McDowell, D. C. *J. Organomet. Chem.* **1978**, *156*, C5.

(5) Mikhailov, B. M. *Organomet. Chem. Rev., Sect. A* **1972**, *8*, 1.

(6) Koster, R.; Binger, P. *Inorg. Synth.* **1974**, *15*, 141.

(7) Brown, H. C.; Mandal, A. K.; Kulkarni, S. U. *J. Org. Chem.* **1977**, *42*, 1392.

(8) Mikhailov, B. M.; Pozdnev, V. F. *Izv. Akad. Nauk SSSR, Ser. Khim.*, **1967**, 1477.

(9) The enantiomeric purity of the cyclohexyl product could be increased to 86% by using hexane as a solvent and lithium triethylcarboxide as a base at −78 °C. However, the product of 1,3 boron transposition, 1-cyclohexyl-1-heptene-3-ol, was also a major product.

(10) Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *J. Am. Chem. Soc.*, in press. The alkynyl alcohol was reduced to the trans allylic alcohol with lithium aluminum hydride and to the cis allylic alcohol with disiamylborane.

(11) Reference 1d, p 74.

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to carbon migrations.[12] The reaction gives an 80:20 mixture of cyclohexyl and thexyl group migration products in an overall 100% GC yield. Interestingly, the thexyl product was 80% enantiomerically pure while the cyclohexyl product was 44% enantiomerically pure. This increase in enantioselectivity with increasing degree of substitution at the $\alpha$-carbon of the migrating alkyl group as well as the exclusive formation of the trans double bond seems to indicate that conformational effects about the $sp^2$–$sp^3$ bonds may be playing an important role in the stereochemical outcome of the reaction.

The overall transformation described here accomplishes an alkylation and a 1,3 alcohol transposition with a high degree of stereoselectivity both at the new alcohol center and about the double bond. Optically active propargyl alcohols are now readily available,[10,13] and dialkylboranes are becoming readily available. This reaction should therefore provide an effective method for preparing a variety of enantiomeric materials such as those found in many natural products. We are continuing to explore these possibilities.

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**Registry No.** (*S*)-*trans*-1-diethylbora-3-acetoxy-1-octene, 72390-37-5; (*S*)-*trans*-1-dicyclohexylbora-3-acetoxy-1-octene, 72390-38-6; (*R*)-*trans*-4-decen-3-ol, 72441-82-8; (*S*)-*trans*-4-decen-3-ol, 72441-83-9; (*R*)-*trans*-1-cyclohexyl-2-octen-1-ol, 72390-39-7; (*S*)-*trans*-1-cyclohexyl-2-octen-1-ol, 72390-40-0; (*R*)-*trans*-2,3,3-trimethyl-5-undecen-4-ol, 72390-41-1; (*S*)-*trans*-2,3,3-trimethyl-5-undecen-4-ol, 72390-42-2; (*S*)-3-hydroxy-1-octynyl acetate, 54315-38-7; diethylborane, 5518-25-2; dicyclohexylborane, 1568-65-6; thexylcyclohexylborane, 72390-43-3.

(12) Negishi, E.; Brown, H. C. *Synthesis* **1974**, 77.
(13) Pirkle, W. H.; Hauske, J. R. *J. Org. Chem.* **1977**, *42*, 1839.
(14) Alfred P. Sloan Foundation Fellow, 1978–1980.

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## Anomalous Behavior of Tosylates in Elimination Reactions

*Summary:* Deprotonation of the tosyl methyl group affects the behavior of tosylates in elimination reactions.

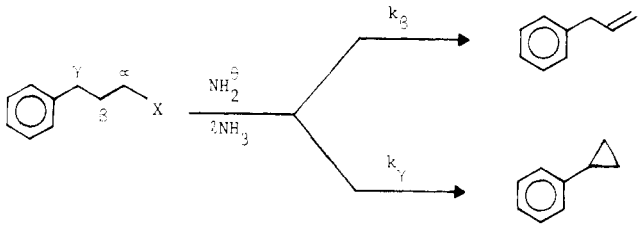
*Sir:* Alkyl halides or sulfonate esters serve as the substrates for the great majority of displacement and elimination reactions. Tosylate is often the leaving group of choice as its preparation from the corresponding alcohol takes place under mild conditions which avoid the stereochemical uncertainties and skeletal rearrangements associated with the conversion of an alcohol to a halide.[1] There are several instances, however, where tosylates resist displacement,[2,3] and a recent paper[4] has noted the failure of a tosylate to undergo $\gamma$-elimination. Accordingly, we are prompted to present our observations concerning the anomalous behavior of the tosylate leaving group in elimination reactions.

Table I. Elimination from 3-Phenylpropyl Derivatives[5]

| X | type[a] | X | type[a] |
|---|---|---|---|
| I[b] | $\beta$ | F | $\gamma$ |
| Br | $\beta$ | OTs | $\gamma$ |
| Cl | $\beta$, $\gamma$ | | |

[a] Type of elimination. $\beta$ elimination is accompanied by alkylation of the salt of propenylbenzene to give diphenylhexenes. [b] Unpublished observations from this laboratory.

Scheme I




Our interest in tosylate as a "problem" leaving group stems from an investigation of the base-induced elimination reactions of a series of 3-phenylpropyl derivatives (Table I, Scheme I). In moving through the halogen series, we observe a gradual shift from $\beta$ to $\gamma$ elimination. As the halogen becomes less polarizable and more tightly bound to the $\alpha$-carbon, leaving group ability decreases. Since tosylate is generally ranked between bromide and chloride in reactivity,[6] one might expect this ester to undergo predominantly $\beta$ elimination. It is therefore surprising that tosylate joins the poorer leaving group fluoride in giving $\gamma$-elimination (Table I). As a possible rationale for the poor leaving ability of tosylate under these conditions, we speculated that the tosyl methyl protons might be preferentially abstracted by the strong base.[7]

Evidence that this is the case was obtained by quenching a mixture of 3-phenylpropyl tosylate (1) and potassium amide with methyl iodide. The recovered ester showed substantial alkylation (70%), providing the ethyl derivative **2**[8] (eq 1); the $\gamma$-elimination product, phenylcyclopropane, was isolated in 20% yield (Scheme I). That deprotonation of the tosyl ester alters the reaction pathway can be seen by removal of the suspect methyl group. When the analogous benzenesulfonate (**3**) was subjected to excess potassium amide in liquid ammonia (eq 2), 3-phenyl-1-

(1) House, H. O. "Modern Synthetic Reactions", 2nd ed.; Benjamin, W. A.: Menlo Park, CA, 1972; p 531.
(2) (a) Meyers, A. I.; Nabeya, A.; Adicker, H. W.; Politzer, I. R. *J. Am. Chem. Soc.* **1969**, *91*, 763. (b) Still, W. C.; MacDonald, T. I. *Ibid.* **1974**, *96*, 5561.
(3) Seebach, D.; Wilka, E.-M. *Synthesis* **1976**, 476 and references therein.
(4) Chang, Y. H.; Pinnick, H. W. *J. Org. Chem.* **1978**, *43*, 373. The corresponding mesylate also failed to cyclize.
(5) Bumgardner, C. L. *Chem. Commun.* **1965**, 374.
(6) (a) Lowry, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry"; Harper and Row: New York, 1976; pp 192, 374–5. (b) Leaving group ability is generally correlated with the strength of the conjugate acid of the leaving group: March, J. In "Advanced Organic Chemistry: Reactions, Mechanism, and Structure", 2nd ed; McGraw-Hill: New York, 1977; p 325. (c) See also: Stirling, C. J. M. *Acc. Chem. Res.* **1979**, *12*, 198.
(7) (a) Rash, F. H.; Hauser, C. R. *J. Org. Chem.* **1967**, *32*, 3379. (b) During the course of this study, benzylic metalation, aryl metalation, and one-electron transfer have been suggested as possible side reactions of tosylates with certain organolithiums.[3] (c) Although benzylic metalation of tosylhydrazones had been suggested as a complicating factor in the Shapiro olefin synthesis, a recent study has shown that metalation is directed ortho to the tosyl sulfonyl: Chamberlain, A. R.; Stemke, J. E.; Bond, F. T. *J. Org. Chem.* **1978**, *43*, 147.
(8) Determined by NMR analysis of the ratio of the tosyl methyl to the $A_2X_3$ system of the *p*-ethyl derivative. The mass spectrum showed a new molecular ion indicative of the alkylated material.

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