solvolysis of 2-norbornyl derivatives? We believe that steric retardation of ionization of the endo isomer can account for this phenomenon.[6] In fact, Bentley has proposed that "steric hindrance to solvation" of the leaving group in the endo isomer (included in our more general term, steric retardation of ionization) contributes significantly (~50%) to the exo/endo rate ratio with the rest coming from σ-bridging in the exo isomer.[29] Regretably, the present study does not allow for even 50% of the effect being attributed to σ-participation.

We point out that we are not against the existence of σ-bridged cations. As H. C. Brown has pointed elsewhere, "I wish to make it clear that...I did not deny the whole concept. (It would be unscientific to take a dogmatic position that any particular phenomenon is incapable of existence in this fascinating, versatile world of ours.) My position then and now is merely that my students and I have been unable to find any experimental evidence whatsoever for σ-bridging in the solvolysis of norbornyl derivatives."[30]

It is now clear that the 2-norbornyl cation can be prepared and captured in an unsymmetrical state.[31] It clearly does not have the nonclassical stabilization energy that has been postulated for so long. It ill befits serious scientific workers interested in the factor responsible for the high exo/endo rate ratios to ignore these data and results.

(29) Bentley, T. W. *Ann. Rep. B* **1974**, 119.

(30) Brown, H. C. *Chem. Eng. News* **1967**, *45*, 86.

(31) Brown, H. C. "The Nonclassical Ion Problem" (with comments by P. V. R. Schleyer); Plenum Press: New York, 1975; Chapter 12.

# Hydroboration. 73. Relative Rates of Hydroboration of Representative Heterocyclic Olefins with 9-Borabicyclo[3.3.1]nonane

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Relative reactivity studies using the competitive method showed that hydroboration of 2,3-dihydrofuran in THF at 25 °C with 9-borabicyclo[3.3.1]nonane (9-BBN) is 106 times faster than that of cyclopentene, whereas $\Delta^2$-dihydropyran and 2,3,4,5-tetrahydrooxepin react at rates that are 6.4 and 0.034 times those of their corresponding carbocyclic analogues. On the other hand, both 2,3-dihydrothiophene and $\Delta^2$-dihydrothiopyran react slower than cyclopentene and cyclohexene, respectively. In the hydroboration of all of these heterocyclic olefins, boron is exclusively directed to the 3-position. To understand whether the rate differences are due to electronic or steric factors or both, we determined the $^{13}C$ chemical shifts of the olefinic carbons of the heterocycles. The $^{13}C$ chemical shifts show a substantial mesomeric contribution in the ground state in all three oxygen heterocycles and only negligible contribution by sulfur. It is probable that there is a strong mesomeric contribution from oxygen and sulfur to the 3-position in the transition state that controls the direction of hydroboration, giving the 3-substituted boron derivative, and the observed rate, modified by individual conformational effects in each system. The mesomeric effects in the ground state, as indicated by the $^{13}C$ NMR shifts, evidently do not play a significant role either in the reactivity or in the directive effect.

Recently, we undertook a systematic investigation of the hydroboration of heterocyclic olefins with representative hydroborating agents to establish optimum conditions for the hydroboration.[3] It appeared during the course of the investigation that 2,3-dihydrofuran undergoes hydroboration unexpectedly fast. In order to understand the role of the heteroatom on the rate of hydroboration, we undertook a more quantitative study of the relative rates of hydroboration of representative heterocyclic olefins such as 2,3-dihydrofuran, $\Delta^2$-dihydropyran (DHP), 2,3,4,5-tetrahydrooxepin, 2,3-dihydrothiophene, and $\Delta^2$-dihydrothiopyran in comparison with the corresponding carbocyclic analogues. We chose 9-borabicyclo[3.3.1]nonane (9-BBN) as the hydroborating agent, since it is stable, commercially available, and has been more thoroughly studied[4] than other, less stable hydroborating agents. The relative rates were determined at 25 °C in order to permit comparison with the large amount of data available for relative reactivities with 9-BBN at this temperature. It may be noted that a similar relative reactivity study of some of these heterocyclic olefins as compared to their carbocyclic analogs utilizing disiamylborane ($Sia_2BH$) as the hydroborating agent at 0 °C has been described earlier by Zweifel and Plamondon.[5] We present the results of our study in this paper.

## Results and Discussion

The competitive method reported earlier[6] to determine the relative reactivity of two olefins toward hydroboration was adopted for this study. The two olefins to be compared were mixed in equimolar amounts (0.5 M in THF) and reacted with 1 equiv of 9-BBN (0.5 M in THF) at 25 °C. An inert hydrocarbon was added as internal standard. After the hydroboration was complete, the mixture was analyzed by GC for residual olefins. A stripper column ($^1/_8$ in. × 12 in.—20% THEED on Chromosorb W, 80–100

(1) Postdoctoral research associate on Grant DAAG 850062 from the United States Army Research Office.

(2) Postdoctoral research associate on Grant GM 10937-22 from the National Institutes of Health.

(3) Brown, H. C.; Vara Prasad, J. V. N.; Zee, S.-H. *J. Org. Chem.* **1985**, *50*, 1582.

(4) Brown, H. C.; Knights, E. F.; Scouten, C. G. *J. Am. Chem. Soc.* **1974**, *96*, 7765.

(5) Zweifel, G.; Plamondon, J. *J. Org. Chem.* **1970**, *35*, 898.

(6) Brown, H. C.; Liotta, R.; Scouten, C. G. *J. Am. Chem. Soc.* **1976**, *98*, 5297.

0022-3263/85/1950-5583$01.50/0 

**Table I. Relative Reactivities of Olefins toward 9-BBN in THF at 25 °C (1-Hexene = 100)**

| hetero and related olefins | relative rates |
|---|---|
| 2-methyl-4,5-dihydrofuran | 1003 |
| 2,3-dihydrofuran | 678 |
| 2-methyl-1-heptene | 307 |
| 1-hexene | 100 |
| 4-methoxy-1-butene | 69 |
| 3,3-dimethyl-1-butene | 18.5 |
| cycloheptene | 6.9 |
| cyclopentene | 6.4 |
| 1-methyl-1-cyclopentene | 1.59 |
| 2,5-dihydrofuran | 1.54 |
| $\Delta^2$-dihydropyran | $3.07 \times 10^{-1}$ |
| 2,3,4,5-tetrahydrooxepin | $2.31 \times 10^{-1}$ |
| 2,3-dihydrothiophene | $1.38 \times 10^{-1}$ |
| cyclohexene | $4.8 \times 10^{-2}$ |
| $\Delta^2$-dihydrothiopyran | $4.5 \times 10^{-3}$ |

mesh) was used to retain the intermediate organoborane and not allow it to pass into the second column ($^1/_8$ in. × 12 ft—10% SP-2100 on Chromosorb W, 80–100 mesh). With these values in hand, along with the initial concentration of each olefin, the relative rate was obtained by using the Ingold–Shaw expression:[7] relative rate = $k_X/k_Y = (\ln [X]_i - \ln [X]_f)/(\ln [Y]_i - \ln [Y]_f)$, where $[X]_i$ and $[Y]_i$ are the initial concentrations and $[X]_f$ and $[Y]_f$ are the residual concentrations of X and Y, the two olefins being compared.

The relative rates are summarized in Table I.

We observed that 2,3-dihydrofuran reacts 106 times faster than does cyclopentene, the corresponding carbocycle, toward hydroboration with 9-BBN. The earlier study with $Sia_2BH$[5] showed a relative reactivity of 21.8.

| rel react | | |
|---|---|---|
| 9-BBN, 25 °C | 1.00 | 106 |
| $Sia_2BH$, 0 °C | 1.00 | 21.8 |

This major difference in reactivity appeared to be worth looking into in detail in order to account for the much higher reactivity of the oxygen heterocycle. The rapidity of the reaction may be due either to electronic effects of the oxygen atom or to its effect on the conformation of the molecule. Analysis of the hydroboration product showed a 100% regioselectivity at the position $\beta$ to the heteroatom. This prompted us to turn our attention toward the probable mesomeric effect of the oxygen atom.

Moving the double bond one carbon atom away from the oxygen lone pair reduces the reactivity drastically. Thus, 2,5-dihydrofuran reacts 4.2 times slower than does cyclopentene and 440 times slower than does 2,3-dihydrofuran. In the case of $Sia_2BH$, a slightly higher reactivity for 2,5-dihydrofuran is reported.[5]

| rel react | | | |
|---|---|---|---|
| 9-BBN, 25 °C | 0.24 | 1.00 | 106 |
| $Sia_2BH$, 0 °C | 1.26 | 1.00 | 21.8 |

Evidently, with the mesomeric interaction being absent in the 2,5-isomer, the inductive effect of the oxygen atom deactivates the double bond toward hydroboration. A similar deactivation is noted in the open chain system: 4-methoxy-1-butene reacts at 0.69 the rate of 1-hexene.

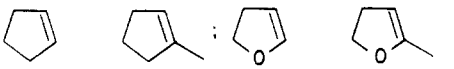
| rel react | | |
|---|---|---|
| 9-BBN, 25 °C | 1.00 | 0.69 |

(7) Ingold, C. K.; Shaw, F. R. *J. Chem. Soc.* **1927**, 2818.

A system where the mesomeric and inductive effects contribute in the same direction so as to enrich electronically the hydroboration center should show a larger reactivity than 2,3-dihydrofuran. 2-Methyl-4,5-dihydrofuran was considered an appropriate example to test this prediction. Indeed, as anticipated, a significant acceleration in the rate of hydroboration was observed. A similar effect is noted in hydroboration with $Sia_2BH$.[5]

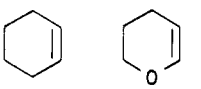
| rel react | | |
|---|---|---|
| 9-BBN, 25 °C | 1.00 | 631 |
| $Sia_2BH$, 0 °C | 1.00 | 454 |

It is interesting to note here that even though 1-methylcyclopentene is less reactive than cyclopentene, attributed to probable steric factors,[6] the trend is reversed in the case of the heterocyclic system.



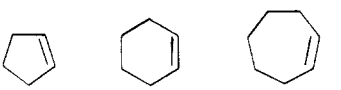
| rel react | | | | |
|---|---|---|---|---|
| 9-BBN, 25 °C | 1.00 | 0.25 | 1.00 | 1.5 |
| $Sia_2BH$, 0 °C | | | 1.00 | 2.08 |

To verify the effectiveness of the ostensible mesomeric contribution of the oxygen lone pair in increasing the rate of hydroboration in heterocycles, dihydropyran (DHP) was compared with cyclohexene toward hydroboration with 9-BBN. To our surprise, we found that the effect was only marginal. The same is true for the reaction with $Sia_2BH$ as well.[5]



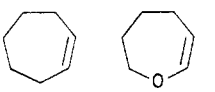
| rel react | | |
|---|---|---|
| 9-BBN, 25 °C | 1.00 | 6.4 |
| $Sia_2BH$, 25 °C | 1.00 | 1.19 |

In an attempt to explain the anomaly in the rate enhancement between the electronically similar five- and six-membered oxygen heterocyclic olefins, 2,3-dihydrofuran and DHP, respectively, as compared to the corresponding carbocyclic analogues, the hydroboration of the seven-membered homologue, 2,3,4,5-tetrahydrooxepin was studied. Cyclopentene reacts much faster than does cyclohexene and cycloheptene is as reactive as cyclopentene in hydroboration with 9-BBN.



| rel react | | | |
|---|---|---|---|
| 9-BBN, 25 °C | 133 | 1.00 | 143 |

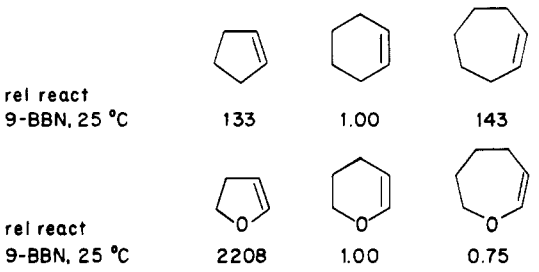
Presumably, just as cyclopentene and cycloheptene have the same rate, 2,3,4,5-tetrahydrooxepin was expected to have the enhanced rate exhibited by 2,3-dihydrofuran. Much to our surprise, we found that 2,3,4,5-tetrahydrooxepin reacts 30 times slower than cycloheptene.



| rel react | | |
|---|---|---|
| 9-BBN, 25 °C | 1.00 | 0.034 |

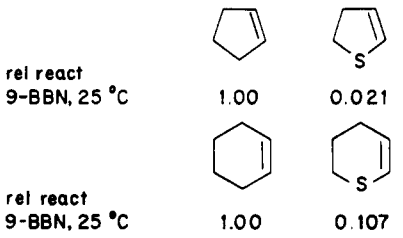
Of great significance in this context is the fact that the similarity in the reaction rates for five- and seven-membered carbocyclic olefins is not observed in the heterocycles, with the seven-membered homologue being even less reactive than the six-membered heterocycle. While the five- and seven-membered carbocyclic olefins exhibit the same rate, the six- and seven-membered heterocyclic ole-

fins exhibit approximately the same rate.



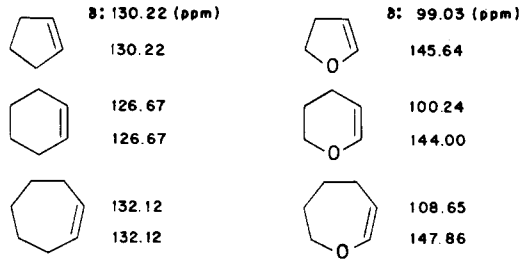

Zweifel and Plamondon gave a plausible explanation[5] for the differences in reactivities of 2,3-dihydrofuran and DHP as compared to their carbocyclic analogues. Besides the increased steric hindrance factors, the reduced mesomeric interaction of the nonbonded pair of electrons on the oxygen with the double bond in the less planar DHP was considered responsible for the lower reactivity of DHP. The same explanation could be extended to account for the behavior of 2,3,4,5-tetrahydrooxepin.

Further in the investigative process, we studied the behavior of the corresponding sulfur analogues toward hydroboration with 9-BBN. The results show a vast



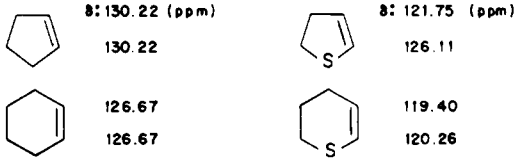

difference in the behavior of the rates as compared to the oxygen heterocycles, though the regioselectivity is the same for both the oxygen and sulfur heterocycles. In the hydroboration of both these heterocycles, boron is exclusively directed toward the 3-position.

We felt that a look into the electronic environments of these heterocyclic olefins was desirable. $^{13}C$ NMR chemical shifts are known to give an approximate picture of the electron density around the carbon atoms.[8] We recorded the $^{13}C$ NMR spectra of all the compounds in question and the $^{13}C$ NMR shifts are given in Table II. The data show a very high shielding at the $\beta$-carbons with a corresponding deshielding for the $\alpha$-carbons for all three oxygen heterocycles, which, predominantly, is due to the mesomeric contribution of the oxygen lone pair. This is in conformity




with the regioselectivity of hydroboration of these heterocyclic olefins. However, the differences in the rates of hydroboration seem difficult to reconcile with the observed shifts at the $\beta$-position of the double bond.

In the case of the sulfur heterocycles, an insignificant shielding at the $\beta$-carbon is observed which can be explained by a poor mesomeric contribution from sulfur.




But the direction of hydroboration is similar to that of the oxygen heterocycle, giving the 3-substituted boron derivative. Thus, though the $^{13}C$ NMR chemical shifts of the oxygen heterocycles are in conformity with the regioselectivity, they do not explain the rates of hydroboration observed. In the case of sulfur heterocycles, the observed regioselectivity is not in conformity with the $^{13}C$ NMR shifts.

It must be noted that the $^{13}C$ NMR chemical shifts can at best give a picture of the electron density in the ground state. Probably, there is a strong mesomeric contribution from the oxygen and sulfur to the 3-position in the transition state that controls the direction of hydroboration. On the other hand, the rates must be influenced by both mesomeric contribution and by conformational effects in the transition state. The conformations of these heterocycles may be quite different from those of the corresponding carbocycles. Moreover, the conformations of the sulfur systems may be significantly different from those of the oxygen derivatives. The C–S–C and C–O–C bond angles as well as the C–S and C–O bond lengths vary considerably.[9] If conformational factors are responsible for the differences in the rates of hydroboration of sulfur and oxygen heterocycles, they may as well be responsible for the differences in the behavior of the five-, six-, and seven-membered oxygen heterocycles. The mesomeric effects in the ground state as indicated by the $^{13}C$ NMR shifts evidently do not play a significant role either in the reactivity or in the directive effect.

Though the exact reasons as to why 2,3-dihydrofuran reacts faster than cyclopentene are not known, this reaction provides a selective hydroboration of dihydrofuran systems in the presence of carbocyclic olefins and hence may be of considerable value in synthetic organic chemistry.

## Experimental Section

The organoboranes were always handled with extreme care under an atmosphere of prepurified nitrogen.[10] All glassware, syringes, and needles were oven-dried at 130 °C before use, assembled hot, and cooled under nitrogen. $^{11}B$ and $^{13}C$ NMR were recorded in a Varian FT-80A spectrometer. All GC analyses were carried out with a Varian Aerograph Series 1200 gas chromatograph using a $^1/_8$ in. × 12 ft column packed with 10% SP-2100 on Chromosorb W (80–100 mesh). A stripper column of 20% THEED on Chromosorb W (80–100 mesh) was used to trap the borane components of the reaction mixture.

**Materials.** 9-BBN was purchased from Aldrich Chemical Company, and a standard solution in THF was made and estimated by using standard procedure.[10] THF was distilled over benzophenone ketyl and stored under nitrogen atmosphere in an ampule. 2,3,4,5-Tetrahydrooxepin,[11] 2,3-dihydrothiophene,[12] $\Delta^2$-dihydrothiopyran,[13] and 4-methoxy-1-butene[14] were prepared

(8) Stothers, J. B. "Carbon-13 NMR Spectroscopy"; Academic Press: New York, 1972. Nelson, G. L.; Williams, E. A. "Progress in Physical Organic Chemistry"; Wiley: New York, 1976; Vol. 12, pp 229–342.

(9) The C–O–C bond angle is 111.72° whereas the C–S–C bond angle is 99.1°. The $^{sp^3}$C–O bond length is 1.41 Å, whereas the $^{sp^3}$C–S bond length is 1.81 Å. March, J. "Advanced Organic Chemistry", 3rd ed.; Wiley: New York, 1985; p 19 and 21.

(10) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975; Chapter 9.

(11) Inoue, Y.; Matsumoto, N.; Hakushi, T.; Srinivasan, R. *J. Org. Chem.* **1981**, *46*, 2267.

(12) Sosnovsky, G. *Tetrahedron* **1962**, *18*, 903.

(13) Parham, W. E.; Christensen, W.; Groen, S. H.; Dodson, R. M. *J. Org. Chem.* **1964**, *29*, 2211.

Table II. $^{13}C$ NMR Chemical Shifts for the Heterocyclic Olefins $\overline{X—C^1=C^2—C(C)_n}$ and Their Parent Compounds

| X | n | $^{13}C$ shifts (±0.05 ppm)[a] $C_1$ | $C_2$ |
|---|---|---|---|
| O | 1 | 145.64 | 99.03 |
| O | 2 | 144.00 | 100.24 |
| O | 3 | 147.86 | 108.65 |
| C | 1 | 130.22 | 130.22 |
| C | 2 | 126.67 | 126.67 |
| C | 3 | 132.12 | 132.12 |
| S | 1 | 126.11 | 121.75 |
| S | 2 | 120.26 | 119.40 |
|  | | 125.90 | 125.90 |

[a] $Me_4Si$ at 0.00 is used as internal standard.

as in literature. All other olefins were obtained from commercial sources and distilled under nitrogen over LAH. The internal standards were kept over 5-Å molecular sieves under nitrogen atmosphere and used as such.

**Procedure.** To an oven-dried, nitrogen-cooled reaction flask fitted with a connecting tube was added 5.0 mmol each of alkenes X and Y and a suitable internal standard (*n*-heptane, 0.5 mL). Several minute aliquots (1 μL) were removed and analyzed by GC to determine the response factors of the two alkenes using a $^1/_8$ in. × 12 ft column of SP-2100 on Chromosorb W protected by a $^1/_8$ in × 12 ft column of THEED on Chromosorb W. 9-BBN in THF (10 mL of 0.5 M) was then added. The reaction mixture was kept at 25 °C. After the reaction was over, samples were removed and analyzed by GC to determine the amounts of residual alkenes. From the initial and final quantities of alkenes, the relative reactivities were calculated by using the Ingold–Shaw expression: relative rate = $k_X/k_Y$ = (ln $[X]_i$ − ln $[X]_f$)/(ln $[Y]_i$ − ln $[Y]_f$) where $[X]_i$ and $[Y]_i$ are the initial concentrations and $[X]_f$ and $[Y]_f$ are the final concentrations of X and Y, respectively.

**Relative Reactivities.** It is important in relative reactivity studies to choose substrate pairs such that their relative rates do not differ by a factor of more than 10. The olefin pairs studied were 2-methyl-4,5-dihydrofuran/2,3-dihydrofuran, 2,3-dihydrofuran/2-methyl-1-heptene, 2-methyl-1-heptene/1-hexene, 1-hexene/4-methoxy-1-butene, 1-hexene/3,3-dimethyl-1-butene, 3,3-dimethyl-1-butene/cycloheptene, cycloheptene/cyclopentene, cyclopentene/1-methylcyclopentene, cyclopentene/2,5-dihydrofuran, 1-methylcyclopentene/$\Delta^2$-dihydropyran, $\Delta^2$-dihydropyran/2,3,4,5-tetrahydrooxepin, $\Delta^2$-dihydropyran/4-methyl-1-cyclohexene, 4-methyl-1-cyclohexene/cyclohexene, cyclohexene/2,3-dihydrothiophene, and cyclohexene/$\Delta^2$-dihydrothiopyran. The results are summarized in Table I.

**Acknowledgment.** We thank Dr. J. Chandrasekharan of our Department for helpful suggestions. We gratefully acknowledge support from the United States Army Research Office (Grant DAAG 850062) and the National Institutes of Health (Grant GM 10937-22) in this research.

(14) Brown, H. C.; Lynch, G. J. *J. Org. Chem.* **1981**, *46*, 531.

# Chiral Synthesis via Organoboranes. 4. Synthetic Utility of Boronic Esters of Essentially 100% Optical Purity. Synthesis of Homologated Boronic Acids and Esters of Very High Enantiomeric Purities

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2-Alkyl-1,3,2-dioxaborinanes, $R^*BO_2(CH_2)_3$, of essentially 100% optical purity, prepared by the asymmetric hydroboration of readily available prochiral olefins with subsequent removal of the chiral auxiliary, can be homologated to α-chloroalkyl derivatives, $R^*CHClBO_2(CH_2)_3$, of essentially 100% ee by reaction with $LiCHCl_2$. The intermediates $R^*CHClBO_2(CH_2)_3$ are smoothly reduced with KIPBH to give the corresponding one-carbon-homologated boronic esters $R^*CH_2BO_2(CH_2)_3$ in very high optical purity. The operation can be repeated to produce $R^*CH_2CH_2BO_2(CH_2)_3$ etc. Consequently, it is now possible to synthesize a wide variety of optically active boronic esters, not available by direct asymmetric hydroboration, either (+) or (−), in essentially 100% ee, and to convert these into synthetically valuable compounds.

The transfer of alkyl groups from boron to carbon is one of the most valuable synthetic reactions of organoboranes. It can be achieved under remarkably mild conditions in a number of ways. In particular, the complete replacement of boron in a trialkylborane by a functionalized carbon can be achieved by carbonylation,[2] cyanidation,[3] or reaction with the anion derived from dichloromethyl methyl ether (DCME),[4] i.e., under neutral, acidic, or basic conditions, respectively (eq 1–3).

$$R_3B \xrightarrow[2.\ [O]]{1.\ CO} R_3COH \quad (1)$$

$$R_3B \xrightarrow[2.\ (CF_3CO)_2O]{1.\ CN^-} R_3COH \quad (2)$$

$$R_3B \xrightarrow[2.\ base\ \ 3.\ [O]]{1.\ Cl_2CHOMe} R_3COH \quad (3)$$

(1) (a) Postdoctoral research associate on Grant CHE 79-18881 of the National Science Foundation. (b) Postdoctoral research associate on Grant GM 10937-22 of the National Institutes of Health. (c) Visiting Professor on a grant from the Ministry of Education of the Republic of Korea.

(2) Brown, H. C. *Acc. Chem. Res.* **1969**, *2*, 65.

(3) (a) Pelter, A.; Hutchings, M. G.; Rowe, K.; Smith, K. *J. Chem. Soc., Perkin Trans. 1* **1975**, 138. (b) *Ibid.* **1975**, 129.

(4) (a) Brown, H. C.; Carlson, B. A. *J. Org. Chem.* **1973**, *38*, 2422. (b) Carlson, B. A.; Brown, H. C. *J. Am. Chem. Soc.* **1973**, *95*, 6876.

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