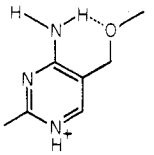
line width was observed for the two NH resonances. The line width at these low pH values was still greater than that of the C6 H resonance, indicating that the N1-protonated species still was undergoing amino hydrogen exchange with solvent hydrogens.

Finally, it is instructive to consider the temperature below which two amino resonances are observable (Table I) as a qualitative measure of the barrier to amino group rotation. First, 1 with a pK similar to that of 4, but with a larger $\Delta\nu$ than 4, has a lower coalescence temperature than 4. The positively charged thiazolium ring of 1 compared to the neutral thiothiazolone of 4 could be the source of the greater barrier to amino rotation in 4. The amino groups of 2 and 3 at low pH's gave rise to two NH resonances (pK_a's for their conjugate acids are 5.7 and 5.9, respectively) even at 25 and 40 °C, respectively. Coalescence of the two resonances was not visible in either one, rather line broadening with increased temperature. Both 2 and 3 likely have higher barriers to amino rotation than 1. Also, 3 exhibits less broadening at the same concentration than 2 at 25 °C; therefore, the barrier in 3 must be larger than in 2. This could be the result of intramolecular stabilization depicted in 8. The barrier to amino



8

rotation estimated for N1′-protonated thiamin at 12 °C in water is about 14.6 kcal/mol, a value consistent with those reported in nonaqueous solvents for some related compounds[23,24] and larger than the nearly 12 kcal/mol measured for neutral thiamin at −40 °C in methanol.[6] The barrier to amino group rotation in compounds 2–4 when N1 protonated is even larger than in thiamin itself but could not be determined, since coalescence was not observed.

These studies demonstrate the need to perform such experiments in water at very low concentrations of compounds to avoid complications due to various exchange phenomena that would mask the subtle changes here described.

(23) See references in ref 6.
(24) Almog, J.; Meyer, A. Y.; Shanan-Atidi, H. *J. Chem. Soc., Perkin Trans. 2* **1972**, 451–458.

Experimental Section

Materials. 4-Amino-5-(methoxymethyl)-2-methylpyrimidine (3) was a gift from Merck Sharpe & Dohme Research Laboratories, Inc., Rahway, NJ. Thiothiamin (4) was a gift from Hoffmann-La Roche Inc., Nutley, NJ. Deuterated solvents were purchased from Stohler Isotope Chemicals and Aldrich Chemical Co. 4-Aminopyrimidine was purchased from Calbiochem.

Methods. Solution pH's were adjusted on small volumes employing a Radiometer GC 2321 or Ingold microelectrode. ^{1}H NMR studies were performed (a) at 360 MHz at the NIH facility at the University of Pennsylvania, School of Medicine, in the proton correlation mode[7] or employing the Redfield technique,[8] and (b) at 500 mHz at the Francis Bitter National Magnet Laboratories of MIT employing the Redfield 2–1–4 pulse technique.[8] The data at 360 and 500 MHz were collected in 80:20 (v/v) H_2O–^2H_2O at variable temperature. The temperature quoted is accurate to ±1 °C. Typically, at each temperature the sample was equilibrated in the probe for at least 10 min prior to recording of the data. The deuterium oxide is required for a stable lock signal. All pH's quoted pertain to apparent readings at a glass electrode and have an uncertainty of less than ±0.1 unit. The solution pH's were always adjusted with HCl or NaOH solutions; hence, Cl^- was the only anion employed.

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Relative Migratory Aptitudes of Alkyl Groups in the Iodination of Ethenyltrialkylborates. A Conformational Analysis

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Relative migratory aptitudes of various alkyl groups have been determined in the iodine-induced rearrangement of bromomagnesium ethenyltrialkylborates. Trialkylboranes of types $R_{3-n}BR'_n$, *B*-R-9-BBN, and $CH(CH_3)_2C(CH_3)_2BRR'$ were complexed with vinylmagnesium bromide and then iodinated. Alkyl rearrangement to the ethenyl terminus, followed by deiodoboration, produced a mixture of 1-alkenes. The overall migratory aptitude order is cyclohexyl > *sec*-butyl > isobutyl > *n*-butyl, bicyclooctyl > thexyl. The magnitude of the migratory aptitude ratios after statistical correction varies with the alkyl substitution pattern in the borate. The migration order is most conveniently explained by consideration of relative conformational stability in the iodinated intermediates before rearrangement.

The electrophilic iodine-induced rearrangement of α,β-unsaturated organoborates is a valuable method for producing substituted alkenes[1–3] and alkynes.[4] However, there remain the synthetic and theoretical problems of

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Table I. Percent Alkyl Group Migration in the Iodination of Ethenyltrialkylborates

compd	trialkylborane[a] R	trialkylborane[a] R'	% of alkene products[b] $RCH=CH_2$	% of alkene products[b] $R'CH=CH_2$	% migration[c]
		For RR'_2B			
1	*n*-butyl	cyclohexyl	7	93	69
2	*sec*-butyl	cyclohexyl	24	76	45
3	isobutyl	cyclohexyl	10	90	72
4	cyclohexyl	*n*-butyl	52	48	52
5	cyclohexyl	*sec*-butyl	41	59	33
6	cyclohexyl	isobutyl	44	56	52
7	cyclohexyl	9-BBN	81	19[d]	63
8	*n*-butyl	9-BBN	31	69[d]	73
9	*sec*-butyl	9-BBN	61	39[d]	36
10	isobutyl	9-BBN	45	55[d]	95
		For $CH(CH_3)_2C(CH_3)_2BRR'$			
11	*n*-butyl	*n*-butyl	100		45
12	isobutyl	*n*-butyl	69	31	28

[a] R_3B in the corresponding bromomagnesium ethenyltrialkyborate. [b] Determined by GC analysis utilizing an internal standard. Percentages are reported as the average of at least two experiments and deviate by ±3%. [c] Based on the millimoles of R_3B. [d] Alkene product determined from 1-vinyl-5-cyclooctanol (see text).

prediction and interpretation of relative migratory aptitudes of alkyl groups in unsymmetrically substituted organoborates. The previous report[5] of alkyl group mobility in the iodination of ethynyltrialkylborates was the first systematic attempt to compare migratory aptitudes in an internal competitive migration. The complementary study of migration in ethenyltrialkylborates is reported here.

Analysis and Results

The iodine-induced rearrangement of bromomagnesium ethenyltrialkylborates, followed by spontaneous deiodoboration, produces the corresponding alkyl-substituted olefins[3] (eq 1 and 2). Since only one alkyl group is

$$R_3B + MgBrCH{=}CH_2 \xrightarrow{THF} [R_3BCH{=}CH_2]MgBr \quad (1)$$

$$[R_3BCH{=}CH_2]MgBr \xrightarrow[THF]{I_2,\ -78\ °C} RCH{=}CH_2 + R_2BI + MgBrI \quad (2)$$

transferred during the irreversible reaction, iodination of unsymmetrical trialkylborates produces a mixture of alkenes in amounts which depend on the relative rates of alkyl group migration in the intramolecular competition. Mixed trialkylboranes of types $R'R_2B$, R'_2RB, and $CH(CH_3)_2C(CH_3)_2BRR'$ were chosen in order to interpret migratory aptitudes in terms of both inherent reactivity of individual alkyl–boron bonds and substitution pattern dependence. The experimental results are reported in Tables I and II.

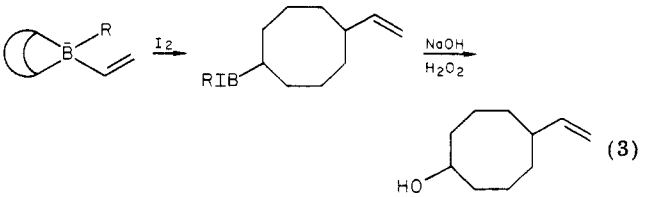
Although the reaction also occurs in the presence of hydroxide, that procedure[3b] produced significant amounts of alkyl iodide[6] from symmetrical primary trialkylborates. Without base, less than 10% primary alkyl iodides, which are formed slower than the alkenes, were present. The extent of migration was comparable both in the absence of base (−78 °C, 15 min) and in the presence of base (0 °C, 15 min).

Table II. Relative Alkyl Group Migratory Aptitudes (M) in the Iodination of Ethenyltrialkylborates

compd	trialkylborane[a] R	trialkylborane[a] R'	M(R/R')[b]
	For $R_{3-n}BR'_n$		
1	dicyclohexyl	*n*-butyl	6.6
2	dicyclohexyl	*sec*-butyl	1.6
3	dicyclohexyl	isobutyl	4.5
4	cyclohexyl	di-*n*-butyl	2.2
5	cyclohexyl	di-*sec*-butyl	1.4
6	cyclohexyl	diisobutyl	1.6
	For *B*-R'-9-BBN		
7	9-BBN	cyclohexyl	0.12
8	9-BBN	*n*-butyl	1.1
9	9-BBN	*sec*-butyl	0.32
10	9-BBN	isobutyl	0.61
	For $CH(CH_3)_2C(CH_3)_2BRR'$		
12	isobutyl	*n*-butyl	2.2

[a] R_3B in the corresponding bromomagnesium ethenyltrialkylborate. [b] The ratios were calculated from the percentages of alkene products from each trialkylborate rearrangement. The statistical correction for trialkylborates ($R_{3-n}BR'_n$) and 9-BBN-B-R' is $M(R/R') = (n/3 - n)(\%R/\%R')$.

The product of bicyclic bond migration from each *B*-ethenyl-*B*-alkyl-substituted 9-BBN was analyzed after the intermediate was oxidized to 1-vinyl-5-cyclooctanol (eq 3).



(3)

Among the several thexylborates examined [$CH(CH_3)_2C(CH_3)_2BRR'$], significant alkyl migration occurred only in the relatively unhindered thexyl-di-*n*-butylborate and thexylisobutyl-*n*-butylborate (**11**, **12**). For the others

(1) (a) Zweifel, G.; Arzoumanian, H.; Whitney, C. C. *J. Am. Chem. Soc.* **1967**, *89*, 3652. (b) Zweifel, G.; Polston, N. L.; Whitney, C. C. *Ibid.* **1968**, *90*, 6243. (c) Brown, H. C.; Basavaiah, D.; Kulkarni, S. U. *J. Org. Chem.* **1982**, *47*, 171.

(2) Evans, D. A.; Crawford, T. C.; Thomas, R. C.; Walker, J. A. *J. Org. Chem.* **1976**, *41*, 3947.

(3) (a) Utimoto, K.; Uchida, K.; Yamaya, M.; Nozaki, H. *Tetrahedron* **1977**, *33*, 1945. (b) Miyaura, N.; Tagami, H.; Itoh, M.; Suzuki, A. *Chem. Lett.* **1974**, 1411. (c) Akimoto, I.; Sano, M.; Suzuki, A. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1587.

(4) (a) Suzuki, A.; Miyaura, N.; Aiko, S.; Itoh, M.; Brown, H. C.; Sinclair, J. A.; Midland, M. M. *J. Am. Chem. Soc.* **1973**, *95*, 3080. (b) Midland, M. M.; Sinclair, J. A.; Brown, H. C. *J. Org. Chem.* **1974**, *39*, 731.

(5) Slayden, S. W. *J. Org. Chem.* **1981**, *46*, 2311.

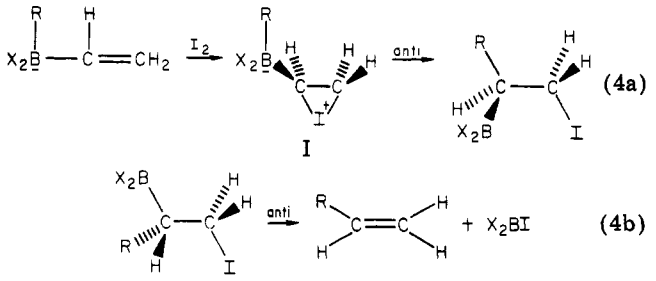
(6) Brown, H. C.; Rathke, M. W.; Rogic, M. M. *J. Am. Chem. Soc.* **1968**, *90*, 5038.

(R, R′ = diisobutyl; di-*sec*-butyl; cyclohexyl, *sec*-butyl; isobutyl, cyclohexyl, *n*-butyl; *sec*-butyl, *n*-butyl) less than 10% alkyl migration was observed. No product of thexyl migration was detected by GC analysis on several packed columns or by GC/MS on capillary columns. Furthermore, oxidation of the iodinated reaction mixture with alkaline hydrogen peroxide produced thexyl alcohol in nearly quantitative yield. Thus, the thexyl ligand does not compete with primary or secondary alkyl group migration. Thexyl does migrate during the iodination, under alkaline conditions, of several trivalent thexylalkenylboranes.[1b,2] That it is not observed in this system may be due to inhibition of iodine attack on the less sterically accessible tetraorganoborates. The addition of vinylmagnesium bromide to the trialkylboranes at room temperature was slightly exothermic in all cases except with the thexyldialkylboranes. The formation of vinyl iodide during iodination of the hindered thexylborates also indicated a slow complexation. After the ethenylthexylborates were stirred for 24 h at room temperature, iodination produced much less vinyl iodide but no improvement in alkyl migration yield.

Discussion

The relative migratory aptitudes determined from each set of isomeric ethenyltrialkylborates are consistent (Table II). Overall, the order is cyclohexyl > *sec*-butyl > isobutyl > *n*-butyl, bicyclooctyl > thexyl, or, generally, secondary > primary > tertiary. Also, the magnitude of the relative migratory aptitudes (*M*) for each pair of cyclohexylbutylborates is dependent on the substitution pattern, except for the cyclohexyl-*sec*-butylborates (**2**, **5**), the only instance where the statistically corrected ratios correspond.

The reaction pathway (eq 4) involving a cyclic iodonium

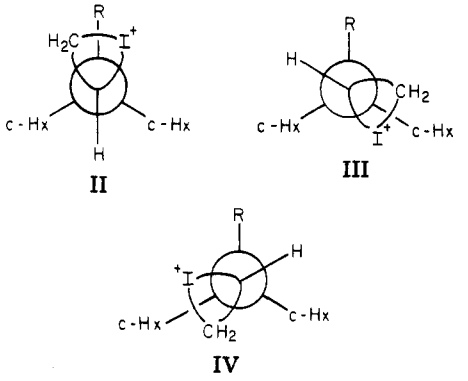


intermediate is proposed by analogy with the iodination of trivalent alkenylboranes.[1] Because of the high geometrical isomeric purity (>92%) of the disubstituted olefin products in those reactions, it was suggested[1b] that each step proceeds stereoselectively[7,8] as shown. The relative rates of the iodination and migration steps are not known, although calculations[9] on ethynylborates suggest that a rate-limiting electrophilic attack precedes a fast, highly exothermic rearrangement.[10]

The simplest general explanation of the data presented here is that the alkene product composition is largely determined by the relative stabilities of the transitions states leading to the various conformations of I which permit the anti migration from boron to carbon.[11] The rationalization thus depends on the following assumptions: (1) the rate of carbon–boron bond rotation in the reacting ethenylborate is faster than the rate of iodination; (2) iodine attack is the rate-limiting step; (3) anti migration occurs in a cyclic iodonium ion intermediate; (4) the rate of migration is faster than carbon–boron bond rotation in I; (5) deiodoboration occurs completely from all rearranged intermediates.

To the extent that the relative conformational stabilities of I reflect the free-energy differences between their corresponding transition states, the competitive intramolecular migratory aptitudes partly depend on the populations of conformations produced, if the conformers go directly to their respective rearrangement products. Because of the contracted bond angles in the cyclic iodonium ion, the most important factor affecting conformational stability is assumed to be the magnitude of the steric interactions of the methylene group and iodine atom on the terminus with the alkyl group on boron which is gauche to both of them.[12]

Consider the iodonium ion (shown for one enantiomer) generated from a dicyclohexylbutylborate. When R = *sec*-butyl, the effective sizes of the three secondary groups, and thus the relative stabilities and populations of conformations II–IV, are approximately the same, and migration from each rotamer should be nearly equal. This is reflected in the alkene product distribution which is approximately the 2:1 statistical mixture for cyclohexyl/*sec*-butyl migration. However, when R = *n*-butyl or isobutyl, the relative energy of II is expected to decrease with the decreased steric interaction of the effectively smaller butyl groups with the iodine and methylene. The anti migration of cyclohexyl in the most stable iodonium conformation (II) accounts for the preponderance of cyclohexyl migration product. Only a small amount of butyl migration from higher energy III is observed. When (*trans*-1-hexenyl)dicyclohexyl-*n*-butylborate was iodinated, a 91:9 ratio of 1-cyclohexyl-1-hexene/5-decene was produced. Evidently steric bulk on the β-carbon of the terminus does not greatly affect the migration ratio.



On the bicyclic ring of the 9-BBN's, the β-hydrogens offer significant steric interference with the methylene hydrogens on the terminus, as in conformation VII. This

(7) (a) Ayers, R. L.; Michejda, C. J.; Rack, E. P. *J. Am. Chem. Soc.* **1971**, *93*, 1389. (b) Zanger, M.; Rabinwitz, J. L. *J. Org. Chem.* **1975**, *40*, 248.

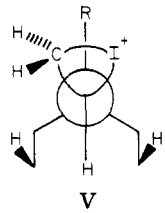
(8) Woods, W. G.; Bengelsdorf, I. S. *J. Org. Chem.* **1966**, *31*, 2769.

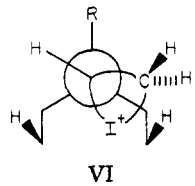
(9) (a) Bentley, T. W. *J. Org. Chem.* **1982**, *47*, 60. (b) Pelter, A.; Bentley, T. W.; Harrison, C. R.; Subrahmanyam, C.; Laub, R. J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2419.

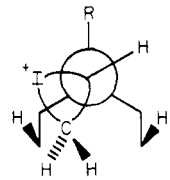
(10) Iodine reacts faster with the triple bond than with the double bond in mixed alkenylalkynylborates. Negishi, E.; Lew, G.; Yoshida, T. *J. Chem. Soc., Chem. Commun. 1973*, 874.

(11) (a) Eliel, E. L. "Stereochemistry of Carbon Compounds"; McGraw-Hill: New York, 1962; Chapters 6, 8. (b) Hammett, L. P. "Physical Organic Chemistry", 2nd ed.; McGraw-Hill: New York, 1970; Chapter 5. (c) Benjamin, B. M.; Schaeffer, H. J.; Collins, C. J. *J. Am. Chem. Soc.* **1957**, *79*, 6160.

(12) Alternate interpretations can be formulated which depend upon different assumptions concerning the relative rates of the various processes. In each case, provided that the important interactions affecting the stability of the ground states, transition states, or products are steric, the observed migratory aptitude order can be explained. However, more experimental evidence must be adduced before any mechanistic claims can be substantiated.


V

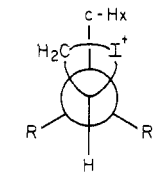

VI

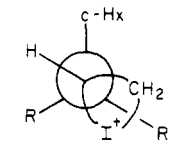

VII

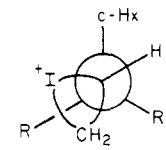
energy-raising steric factor reduces the relative abundance of that conformation and thus the amount of bicyclic migration product from it. Inspection of molecular models also suggests that the gauche interactions of the terminus are more severe with the cyclohexyl group (V, R = cyclohexyl) than with the bicyclic group (VI). This analysis accounts for the larger observed migratory aptitude of cyclohexyl from conformation VI. Furthermore, as the effective bulk of R decreases from cyclohexyl to *n*-butyl, the relative stability of V compared to VI should increase. The consequent increase of bicyclic migration in the observed migration products reinforces this conclusion. The greater primary group migration (73%) from *B*-isopropenyl-*B*-alkyl-substituted 9-BBN[3b] derives from the relative instability of V when the α-hydrogen on the terminus is replaced by a methyl group.

The relative migratory aptitudes of the secondary bicyclooctyl carbon in the *B*-Bu-9-BBN's are lower than the relative migratory aptitudes of the secondary cyclohexyl carbon in the butyldicyclohexylborates. If the important destabilizing gauche interactions are more severe for cyclohexyl than for bicyclooctyl, then the population ratio of II/III would be greater than the population ratio of V/VI (when IV and VII are ignored). Therefore, the cyclohexyl/butyl product ratios should be larger than the corresponding bicyclooctyl/butyl product ratios. That the observed product distributions and relative migratory aptitudes are consistent with those predicted supports this assessment.

The conformational stabilities of the dibutylcyclohexylborates VIII–X are nearly equal when R = *sec*-butyl,

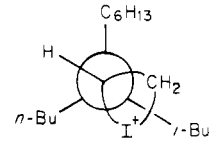

VIII

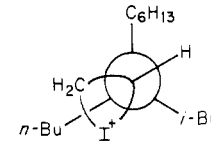

IX

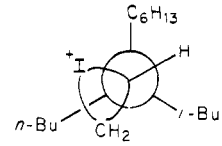

X

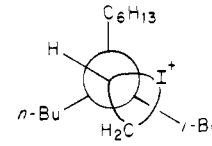
and the product distribution approaches the expected 2:1 statistical mixture. The close correspondence of the statistically corrected migratory aptitudes for the two secondary-substituted *sec*-butylcyclohexylborates (**2**, **5**) shows the similarity of their contributions to migratory aptitude regardless of the substitution pattern. As the effective size of the butyl group decreases, the relative stability of VIII should also decrease. For R = *n*-butyl, VIII may be unimportant, and thus the ~50:50 mixture of cyclohexyl/*n*-butyl migration products from IX and X is reasonable. The analysis of diisobutylcyclohexylborate may be considered as an intermediate case. Because of β-branching in the isobutyl group and the resulting destabilizing gauche interactions with the terminus in IX and X, the possibility of some isobutyl migration from VIII cannot be discounted. Also, if the methylene group is effectively larger than iodine, then X may be deemed slightly more stable than IX. Taken together, these factors would lead to the prediction of somewhat more isobutyl than cyclohexyl migration. This is observed to be the case.

The steric congestion around the ethenyl group in some of the thexylborates may preclude the requisite iodonium ion formation. In those cases where butyl migration does occur (**11**, **12**), the conformations in which the thexyl is


XI


XII


XIII


XIV

gauche to both the iodine and the methylene are clearly unstable and are not considered further. For the other four conformations (XI–XIV) of thexylisobutyl-*n*-butylborate, XI and XII may be less stable due to the gauche interactions between the methylene hydrogens and the large tertiary group, if it is assumed that methylene is effectively larger than iodine. In XIII and XIV, the iodine is gauche to the thexyl and thus either *n*-butyl or isobutyl migrates. The greater migration of isobutyl results from the more favorable gauche interaction of the terminus with the *n*-butyl group in XIII.

Conclusion

The application of conformational concepts to this problem of competitive migratory aptitudes has explanatory and predictive value. The rationale proceeds as follows. Iodination of ethenyltrialkylborates in the slow step produces a cyclic iodonium ion intermediate from which a fast anti alkyl group migration occurs. The migratory product distribution may depend, therefore, on the relative conformational stabilities of the intermediate, in so far as their populations reflect the stabilities of the transition states leading to them. This interpretation generally explains the results presented here, and predictions based on this hypothesis may aid in devising future synthetic strategies.

Experimental Section

General Methods. All manipulations were performed in an atmosphere of prepurified nitrogen. Glassware, syringes, and needles were oven dried and then cooled while being flushed with nitrogen. GC analyses were performed on a Bendix 2300 gas chromatograph. Peak integration was carried out by using a Hewlett-Packard 3380S integrator. The alkene products were identified by coinjection with authentic samples, and thermal response factors were calculated relative to decane as an internal standard.

Materials. Tetrahydrofuran (Mallinckrodt) and cyclohexene (Eastman) were dried with lithium aluminum hydride and distilled under nitrogen. 2,3-Dimethyl-2-butene (Aldrich), vinylmagnesium bromide (Aldrich), isobutylene (Matheson), 1-butene (Matheson), and *cis*-2-butene (Linde) were used as received. Borane–tetrahydrofuran (Aldrich) and 9-BBN–THF (Aldrich) were titrated according to a standard procedure[13] to determine hydride molarity.

Synthesis of Trialkylboranes. The standard procedures for synthesis of the trialkylboranes were carried out as previously reported.[5]

Reaction of Trialkylboranes with Vinylmagnesium Bromide and Iodine. Vinylmagnesium bromide (6.25 mmol)

(13) Brown, H. C. "Organic Synthesis via Boranes"; Wiley: New York; 1975.

was added to the flask containing the trialkylborane (5 mmol), and the solution was then stirred for 1 h at room temperature. After the trialkylborate solution was cooled to −78 °C, iodine in THF (5.0 mL, 1 M) was added slowly to the vigorously stirred solution. Aliquots were withdrawn and quenched with sodium thiosulfate solution. The organic phase was analyzed by GC (10% DC 710, Chromosorb W, 6 ft × 0.25 in.) for the 1-alkene products.

Oxidation of Trialkylboranes. A 2-mL aliquot of the trialkylborane solution (~0.5 M) was delivered via syringe to a glassware assembly identical with that described above. The solution was cooled to 0 °C, 1 mL of 3 N NaOH was then added, followed by 1 mL of 30% H_2O_2. The mixture was stirred either at 50 °C for 1 h or at room temperature overnight. After the addition of K_2CO_3, the organic phase was separated and dried over anhydrous $MgSO_4$.

Oxidation of Dialkyliodoboranes. The iodinated reaction mixture was quenched with 3 mL of saturated sodium thiosulfate solution and warmed to 0 °C. The upper organic layer was transferred via a double-tipped needle to an identical glassware assembly. Oxidation was achieved by addition of 5 mL of 3 N NaOH and 5 mL of 30% hydrogen peroxide at 0 °C, and the resulting mixture was heated at 50 °C for 1 h. After addition of sodium thiosulfate and saturation of the mixture with K_2CO_3, the organic phase was separated and dried over K_2CO_3.

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Registry No. RR^1_2B (R = butyl; R^1 = cyclohexyl), 6917-84-6; RR^1_2B (R = *sec*-butyl; R^1 = cyclohexyl), 77123-47-8; RR^1_2B (R = isobutyl; R^1 = cyclohexyl), 6917-83-5; RR^1_2B (R = cyclohexyl; R^1 = butyl), 38103-70-7; RR^1_2B (R = cyclohexyl; R^1 = *sec*-butyl), 77123-48-9; RR^1_2B (R = cyclohexyl; R^1 = isobutyl), 77123-49-0; RR^1_2B (R = cyclohexyl; R^1 = 9-BBN), 53535-83-4; RR^1_2B (R = butyl; R^1 = 9-BBN), 23532-74-3; RR^1_2B (R = *sec*-butyl; R^1 = 9-BBN), 53317-06-9; RR^1_2B (R = isobutyl; R^1 = 9-BBN), 63942-77-8; $CH(CH_3)_2C(CH_3)_2BRR^1$ (R = butyl; R^1 = butyl), 42928-38-1; $CH(CH_3)_2C(CH_3)_2BRR^1$ (R = isobutyl; R^1 = butyl), 77136-28-8; $RCH{=}CH_2$ (R = butyl), 592-41-6; $RCH{=}CH_2$ (R = *sec*-butyl), 760-20-3; $RCH{=}CH_2$ (R = isobutyl), 691-37-2; $RCH{=}CH_2$ (R = cyclohexyl), 695-12-5; 1-vinyl-5-cyclooctanol, 81626-24-6; vinyl bromide, 593-60-2.

Ring Transformation of 1,3,4-Oxadiazole to *s*-Triazole-Fused Heterocycles. New Synthetic Route for Thiazolo[2,3-*c*]-*s*-triazole and 7*H*-*s*-Triazolo[3,4-*b*][1,3,4]thiadiazine

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s-Triazole-fused heterocycles have been synthesized by an intramolecular transformation of some 1,3,4-oxadiazole ketones with ammonia or hydrazine. The α-[(1,3,4-oxadiazol-2-yl)thio] ketone **2m** gave thiazolo[2,3-*c*]-*s*-triazole (**4m**), accompanied by a small amount of the hydrazide **9m** on treatment with ammonium acetate in acetic acid. Similar treatment of ketones **2a** and **2b** afforded only the hydrazides **9a** and **9b**, respectively. Ketones **2a–n** reacted with hydrazine hydrate in acetic acid to give 7*H*-*s*-triazolo[3,4-*b*][1,3,4]thiadiazines **5a–n**. However, ketones **2o–q**, with substituents α to the carbonyl group, could not be converted to the corresponding fused-ring systems. Mechanisms for these transformations are proposed.

s-Triazolo-fused heterocycles can be prepared by ring closure of hydrazino-substituted heterocycles with a carboxylic acid, cyanogen bromide, or carbon disulfide.[1] An alternative route involves reaction of a substituted *s*-triazole such as 4-amino-3-mercapto-1,2,4-triazole with a bifunctional compound.[2] Although *s*-triazoles can be prepared from 1,3,4-oxadiazoles and amines at elevated temperatures,[3] just as pyrroles are formed from furans and amines,[4] these ring transformations have been limited to the preparation of monocyclic systems. We have undertaken an investigation of the synthesis of *s*-triazolo-fused heterocycles by intramolecular ring closure of substituted 1,3,4-oxadiazoles (**2**) with ammonia or hydrazine. We here report new synthetic routes to a thiazolo[2,3-*c*]-*s*-triazole (**4m**) and the 7*H*-*s*-triazolo[3,4-*b*][1,3,4]thiadiazines (**5a–n**).

Table I. Yields and Melting Points of α-(1,3,4-Oxadiazol-2-yl)thio Ketones (2a–q)[a]

compd	R^1	R^2	R^3	yield, %	mp, °C[b]
2a	Ph	H	CH_3	95	97–98
2b	Ph	H	Ph	84	162–164
2c	4-ClC_6H_4	H	CH_3	76	145–146
2d	4-ClC_6H_4	H	Ph	95	170–172
2e	4-BrC_6H_4	H	CH_3	94	140–141
2f	4-BrC_6H_4	H	Ph	81	168–170
2g	2-pyridyl	H	CH_3	74	106–107
2h	2-pyridyl	H	Ph	89	145
2i	3-pyridyl	H	CH_3	63	115–117
2j	3-pyridyl	H	Ph	89	144–146
2k	4-pyridyl	H	CH_3	100	112–114
2l	4-pyridyl	H	Ph	79	155–157
2m	C_2H_5	H	CH_3	88	oil
2n	C_2H_5	H	Ph	84	69–71
2o	Ph	CH_3	Ph	62	135–137
2p	Ph	$(CH_2)_4$		84	108–110
2q	Ph	Ph	Ph	100	153–155

[a] All microanalyses were within 0.4% of the theoretical values. [b] All ketones except **2m** were recrystallized from EtOH. **2m** was purified on a silica gel column with $CHCl_3$ as the eluent.

Results and Discussion

Reactions of Ketones 2a,b,m with Ammonia. Mercapto ketones **2a–q** were prepared in high yields (Table

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