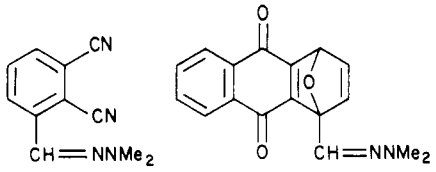

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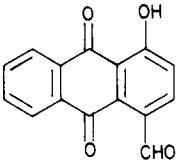

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$J_{2,3}$ = 3.8 Hz) and is of particular interest for further elaboration into analogues of mitoxanthone of current interest in cancer chemotherapy.[10]

5-Methylfurfural dimethylhydrazone (1, R = CH_3) and maleic anhydride in chloroform over 16 h at room temperature gave 3 (R = CH_3, X = O) as bright orange prisms, mp 135–136 °C, but in reduced yield (74%). Similarly 1 (R = CH_3) and *N*-ethylmaleimide gave 3 (R = CH_3, X = NEt) after purification by chromatography (silica, $CHCl_3$) as bright yellow needles, mp 145–146 °C, also in reduced yield (65%). However, the corresponding dimethylhydrazones from 5-nitrofural and 2-acetylfuran did not undergo reactions with these dienophiles.

Furfural and DMAD yield a thermally labile 1:1 cycloadduct in very modest yield; however, the dienic nature of the furan ring is enhanced in its acetal and diacetate, the yields of cycloadducts being increased significantly.[11] Aldehyde dialkylhydrazones have been shown[12] to have enamine characteristics, and we find that introduction of the dimethylhydrazonyl group into the furan system results in an increase in its HOMO energy[13] relative to that of furan and 2-vinylfuran. The conformational preference of the aldehyde group[14] does not favor the cisoid azadiene form of the hydrazone, and these factors apparently enhance addition across the furan moiety. The hydrazone also assists in the spontaneous ether fission in the initial cycloadducts derived from maleic anhydride and *N*-ethylmaleimide, facilitating the dehydration to the benzenoid system. However, in the naphthoquinone cycloadduct, ready air oxidation of the quinone–hydroquinone tautomer in the initial cycloadduct prevents dehydrative aromatization. Protonation is needed to assist in the ether fission, and under these acid conditions the aldehyde is obtained.

Extension of these cycloadditions to unsymmetrical dienophiles and to other hydrazones is currently under study in this laboratory.

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Registry No. 1 (R = H), 14064-21-2; 1 (R = Me), 92011-68-2; 3 (R = H, X = O), 92054-27-8; 3 (R = H, X = NEt), 92011-69-3; 3 (R = CH_3, X = O), 92011-70-6; 3 (R = CH_3, X = NEt), 92011-71-7; 4, 14671-41-1; 5, 92011-72-8; 6, 92011-73-9; 7, 92011-74-0; maleic anhydride, 108-31-6; fumaronitrile, 764-42-1; thiophene-2-carbaldehyde dimethylhydrazone, 69819-67-6; 1,4-naphthoquinone, 130-15-4; *N*-ethylmaleimide, 128-53-0.

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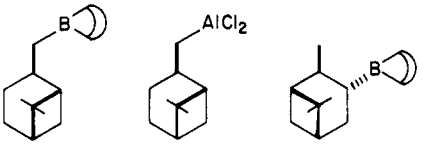
Asymmetric Reduction of Ketones with *B*-(*cis*-10-Pinanyl)-9-borabicyclo[3.3.1]nonane. Observation of a Change in Enantioselection between Similar Organoborane and Organoaluminum Reagents

Summary: The title reagent reduces prochiral ketones of moderate steric bulk in modest to good enantiomeric excesses of the *S* alcohols. This absolute configuration is the opposite of that obtained with a similar organoaluminum reagent.

Sir: During our initial investigation of enantioselective trialkylborane reducing agents, we found that the adduct of (−)-β-pinene and 9-BBN (*cis*-myrtanylborane, 1) reduced



1 2 3

benzaldehyde-*d*[1] and acetophenone to the corresponding *S* alcohol in moderate enantiomeric excess (ee). Recently, Giacomelli has demonstrated that the dichloroaluminum reagent **2**, derived from (−)-β-pinene, reduces a variety of alkyl and aromatic ketones to the *R* alcohols.[2] This discrepancy in the absolute configuration of the products derived from similar reducing agents has prompted us to reexamine asymmetric reductions with the *cis*-myrtanylborane. We find that in general **1** and **2** provide products of the opposite configuration. These results may have important mechanistic implications for reductions with these reagents.

A variety of ketones were examined (Table I) in order to evaluate the scope and potential of reductions with *cis*-myrtanylborane. In all cases the procedures developed for Alpine-borane,[3,4] **3**, were followed. Thus, 5.0 mmol of ketone was added to 7.5 mmol of *cis*-myrtanylborane[5] at

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(3) *B*-3-Pinanyl-9-borabicyclo[3.3.1]nonane is commercially available from Aldrich Chemical Co. under the trademark Alpine-Borane.

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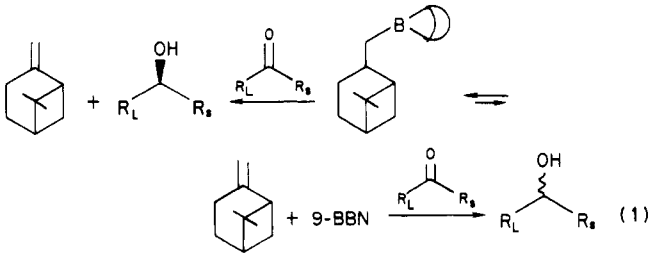
Table I. Reduction of Ketones with Reagents 1 and 2

	1			2[a]
ketone	reactn time, days	% yield[b] (isolated)	% ee[c]	% ee
acetophenone	3	50	33 *S*	32 *R*
α-tetralone	3	80	66 *S*	86 *R*
2-octanone	3	82	11 *S*	
2,2-dimethyl-3-butanone	10 (2)[d]		23 *S* (64 *S*)[d]	11 *R*
4-methylpentyn-3-one	0.5	60	66 *R*[e]	
2-methyl-4-nonyn-3-one				78 *R*[e]

[a] From ref 2. [b] In all cases reduction was 100% complete. [c] Determined by ^{1}H NMR using chiral shift reagent. [d] Values in parentheses are at 5000 atm. [e] The configuration changes because of the change in priorities.

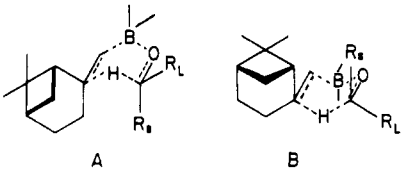
0 °C. The mixture was stirred at room temperature. Upon completion (>97% reduction) the product was worked up in the usual manner.[4] The enantioselectivities are largely determined by the size of the groups flanking the carbonyl. Interestingly, the absolute configuration of the products is the same as that obtained from Alpine-Borane,[4] **3** (derived from (+)-α-pinene), even though the pinene ring systems are of the opposite absolute configuration. However, for alkyl and aromatic ketones, the opposite absolute configuration is obtained with reagent **2**. In the case of acetylenic ketones, the rule of steric size is followed with the borane reagents **1** and **3** (acetylene is smaller than alkyl) but a reversal is noted with the aluminum reagent **2**.

In addition to the bimolecular process leading to enantioselective reduction, competition studies indicate that an unusually facile dehydroboration process occurs.[6] When reagent **1** is allowed to exchange with 1-octene at 77 °C, the dehydroboration–exchange proceeds with a half-life of less than 3 h. In cases in which reduction of a ketone is slow, dissociation of the trialkylborane followed by reduction of the ketone with 9-BBN can become an important side reaction (eq 1). We have previously shown



that pressures above 2000 atm can completely suppress the dehydroboration side reaction.[4a] Indeed, when 2,2-dimethyl-3-butanone was reduced at 5000 atm, reduction was complete in only 2 days and provided alcohol of 64% ee while the same reaction at 1 atm required 10 days and produced alcohol of only 23% ee. Other ketones showed similar improvements in both rate and enantiomeric excess, indicating that the rate of dehydroboration is approximately 4% per day under the usual reaction conditions.

It has been assumed that these organometallic reductions occur through a six-centered transition state. We have further postulated that Alpine-borane and other organoborane reductions occur via a "boat-like" transition state wherein the boron and β-hydrogen may assume a planar orientation which is favorable for the developing alkene double bond.[7] Our examination of models suggests that two such transition states, leading to opposite enantiomeric products, may be competing. In both models only



the orientation with the large group occupying the preferred equitorial position is shown. In all cases examined model A, may be used to predict the major product from reductions with **1**.

On the basis of the change in configuration obtained from **1** and **2**, caution must be used in extrapolating these models to actual transition states. It is believed that organoboranes are monomeric in solution so that these models may approach the transition state. However, aluminum compounds are oligomeric. Thus the aggregated nature of the reagent, as well as the possibility of intervention by optically active aluminum alkoxide species in the oligomer, should be considered.

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Registry No. **1**, 79919-20-3; **2**, 87682-10-8; 1-octene, 111-66-0; *trans*-myrtanylborane, 79919-21-4; acetophenone, 98-86-2; α-tetralone, 529-34-0; 2-octanone, 111-13-7; 2,2-dimethyl-3-butanone, 75-97-8; 4-methypentyn-3-one, 13531-82-3; 2-methyl-4-nonyn-3-one, 63098-60-2; (*S*)-α-methylbenzenemethanol, 1445-91-6; (*S*)-1,2,3,4-tetrahydronaphthalen-1-ol, 53732-47-1; (*S*)-2-octanol, 6169-06-8; (*S*)-2,2-dimethyl-3-butanol, 1517-67-5; (*R*)-4-methyl-1-pentyn-3-ol, 73522-97-1; (*R*)-α-methylbenzenemethanol, 1517-69-7; (*R*)-1,2,3,4-tetrahydronaphthalen-1-ol, 23357-45-1; (*R*)-2,2-dimethyl-3-butanol, 1572-96-9; (*R*)-2-methyl-4-nonyn-3-one, 87682-13-1.

(5) The reagent may be formed overnight at room temperature under "neat" conditions. Thus, 10.0 mmol of a THF solution of 9-BBN and 11.0 mmol of (−)-β-pinene are mixed at room temperature and the solvent removed under reduced pressure. The *cis*-myrtanylborane formed is a translucent clear semisolid. Reflux for more than 2 h in THF causes significant isomerization, forming *trans*-myrtanylborane. Our preliminary results indicate that the *cis*- and *trans*-myrtanylboranes reduce prochiral ketones to opposite enantiomeric products.

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