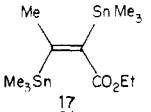
ten-1-ol (31), which was identical with an authentic sample of the same compound obtained by reduction of tiglic aldehyde.



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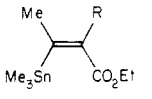
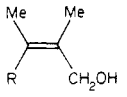


25 R = Me
26 R = $CH_2CH=CH_2$
27 R = $CH_2C_6H_5$
28 R = n-Bu
29 R = 1-hydroxycyclohexyl



30 R = $SnMe_3$
31 R = H

Although direct trapping of intermediates 6 and/or 7 with electrophiles was not successful, it is clear that the methodology described above allows for a two-step conversion of α,β-acetylenic esters into compounds of general structure 11. The latter substances should be readily transformed into highly substituted vinyllithium reagents corresponding to the generalized unsaturated d^3-synthon 13. Work in this area is continuing.

Acknowledgment. Financial support from the Natural Sciences and Engineering Research Council of Canada (NSERCC) and a NSERCC postgraduate scholarship to (J.M.C.) are gratefully acknowledged.

Registry No. 1 (R = Me; R′ = Et), 4341-76-8; 1 (R = Et; R′ = Et), 55314-57-3; 1 (R = *i*-Pr; R′ = Me), 80866-47-3; 1 (R = *n*-C_6H_{13}; R′ = Me), 111-80-8; 1 (R = cyclopropyl; R′ = Me), 80866-48-4; 1 (R = 2-(2-cyclopentyl)ethyl; R′ = Me), 80866-49-5; 1 (R = (3-cyclohexenyl)methyl; R′ = Me), 80866-50-8; 1 (R = *t*-$BuMe_2SiOCH_2$; R′ = Et), 80866-51-9; 1 (R = *t*-$BuMe_2SiOCH_2CH_2$; R′ = Me), 74854-49-2; 14 (R = Me; R′ = Et), 80866-52-0; 14 (R = Et; R′ = Et), 80866-53-1; 14 (R = *i*-Pr; R′ = Me), 80879-50-1; 14 (R = *n*-C_6H_{13}; R′ = Me), 80866-54-2; 14 (R = cyclopropyl; R′ = Me), 80866-55-3; 14 (R = α-(2-cyclopentyl)ethyl; R′ = Me), 80866-56-4; 14 (R = (3-cyclohexenyl)methyl; R′ = Me), 80866-57-5; 14 (R = *t*-$BuMe_2SiOCH_2$; R′ = Et), 80866-58-6; 14 (R = *t*-$BuMe_2SiOCH_2CH_2$; R′ = Me), 80866-59-7; 16 (E = H), 74854-51-6; 25, 80866-60-0; 26, 80866-61-1; 27, 80866-62-2; 28, 80866-63-3; 29, 80866-64-4; 30, 80866-65-5; 31, 497-02-9.

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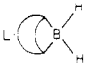
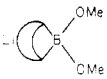
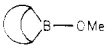
New Powerful Catalysts for the Reduction of Esters by Lithium Borohydride

Summary: The presence of 10 mol % of lithium 9-boratabicyclo[3.3.1]nonane, LiH·9-BBN, or lithium triethylborohydride, $LiEt_3BH$, strongly catalyzes the reduction of esters by lithium borohydride in ether at 25 °C. The corresponding Lewis acid, *B*-methoxy-9-borabicyclo[3.3.1]nonane, B-OMe-9-BBN, also permits the rapid and quantitative reduction of esters by $LiBH_4$ and provides a practical method for the reduction of esters in the presence of reducible groups, such as chloro and nitro.

Sir: We have recently developed an improved conversion of sodium borohydride into lithium borohydride in both diethyl ether (EE) and tetrahydrofuran (THF).[1] A major advantage of lithium borohydride over sodium borohydride is its ready solubility in simple ether solvents.[2] Also, lithium borohydride possesses a much greater selectivity than lithium aluminum hydride so that it is more suitable for selective reductions.[3] One important application appeared to be the reduction of esters, especially in the presence of other reducible groups. Accordingly, we explored this application.

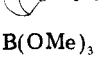
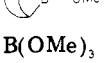
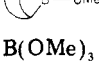
The reduction of esters proceeds smoothly but relatively slowly. The reaction is considerably faster in EE than in THF. However, even in refluxing EE, typical esters such as ethyl caproate required 5 h and ethyl benzoate ~24 h to go to completion. On the other hand, lithium triethylborohydride[4] and lithium 9-boratabicyclo[3.3.1]no-

Table I. Rate of Reduction of Ethyl Caproate by $LiBH_4$ in the Presence of Various Catalysts in Ether at 25 °C[a]

	% reaction					
catalyst	0.5 h	1 h	2 h	4 h	8 h	24 h
no catalyst	17	28	41	65	100	100
$LiEt_3BH$	80	100	100			
	100	100				
$LiEt_3BOMe$	83	98	100			
	100	100				
$BF_3\cdot OEt_2$	21	35	50	73	100	100
$BH_3\cdot THF$	10	14	18	26	53	62
n-Bu_3B	22	98	100			
	100	103				
n-OctB$(OMe)_2$	92	100				
$(MeO)_3B$	52	100				
$(PhO)_3B$	14	30	45	68	98	
$(n$-$DodO)_3B$[b]		26	46		100	

[a] [Ester] = 1.0 M; [$LiBH_4$] = 1.0 M; [catalyst] = 0.1 M. [b] *n*-Dod = *n*-dodecyl.

Table II. Reduction of Esters by $LiBH_4$ in Refluxing Ether[a]

		% reaction					
ester	catalyst	0.5 h	1 h	2 h	4 h	8 h	24 h
ethyl caproate	none	26	41	61	90	99[b]	
		100[c]	101				
	$B(OMe)_3$	100[d]	100				
ethyl benzoate	none	12	20	30	44	67[e]	
		60	100[e]	102			
	$B(OMe)_3$	29	46	65	86[e]	100	
ethyl pivalate	none	9	15	20	29	45	
		39	74	93	104	104	
	$B(OMe)_3$	68	102	104			

[a] [Ester] = 1.0 M; [$LiBH_4$] = 1.0 M; [catalyst] = 0.1 M. [b] 5 h. [c] 0.25 h. [d] 0.75 h. [e] Solution turns cloudy.

(1) Brown, H. C.; Choi, Y. M.; Narasimhan, S. *Inorg. Chem.* **1981**, *20*, 4454.

(2) Brown, H. C.; Kramer, G. W.; Levy, A. B.; Midland, M. M. "Organic Syntheses via Boranes"; Wiley-Interscience: New York, 1975; P 258.

(3) (a) Schlesinger, H. I.; Brown, H. C. *J. Am. Chem. Soc.* **1940**, *62*, 342. (b) Nystrom, R. F.; Chaikin, S. W.; Brown, W. G. *Ibid.* **1949**, *71*, 3245.

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Table III. Reduction of Esters by Lithium Borohydride in Refluxing Ether in the Presence of *B*-Methoxy-9-BBN or Methyl Borate[a]

ester	catalyst	product	rctn time, h	% yield[b]	mp (°C) or bp (°C/torr) found	mp (°C) or bp (°C/torr) reported (ref)
ethyl caproate	$(MeO)_3B$	1-hexanol	1.0	82	76-78/15	158/760 (11)
methyl stearate	B-MeO-9-BBN	1-octadecanol[c]	0.5	97	58-60	58-60 (12)
ethyl cyclohexanecarboxylate	$(MeO)_3B$	(hydroxymethyl)-cyclohexane	1.0	80	84-86/15	83/14 (13)
ethyl pivalate	$(MeO)_3B$	2,2-dimethyl-propanol	1.0	81	52-53	52-53 (14)
ethyl 1-adamantanecarboxylate	$(MeO)_3B$	1-adamantane-carbinol[c]	1.0	90	115-117	115-118 (15)
ethyl benzoate	B-MeO-9-BBN	benzyl alcohol	2.0	81	96-98/15	93/10 (16)
ethyl 4-chlorobenzoate	B-MeO-9-BBN	4-chlorobenzyl[c] alcohol	1.0	90	70-71	70-72 (12)
ethyl 3-chloropropionate	$(MeO)_3B$	1-hydroxy-3-chloropropane	0.5	84	60-62/15	160-162/760 (17)
ethyl 4-nitrobenzoate	B-MeO-9-BBN	4-nitrobenzyl[c] alcohol	0.5	78 (91)[d]	91-93	92-94 (12)

[a] Ester = 20 mmol (2.0 M); $LiBH_4$ = 11 mmol (1.1 M); catalyst = 2 mmol (0.2 M). [b] All of the products were fully characterized by ^1H NMR. Unless otherwise stated, yields represent pure isolated products. [c] Isolated by removing the solvent after the reaction, hydrolyzing the residue, filtering, washing with 3 M NaOH, and drying. [d] Crude yield.

nane[5,6] reduce esters very rapidly, the reaction being complete within 5 min.

We then examined the possibility that small quantities of these compounds could catalyze the reduction of esters by lithium borohydride. Indeed, we observed a remarkable enhancement of the rate in the presence of 10 mol % of $LiEt_3BH$ or LiH·9-BBN (Figure 1). It appeared that the reduction of esters by $LiEt_3BH$ or LiH·9-BBN must produce species capable of enhancing the reaction being regenerated under the reaction conditions.

We also observed strong catalytic effects by $LiEt_3BOMe$ and $LiB(OMe)_2$-9-BBN (Table I).

We deduced that the recycling intermediates must be Et_3B[7] and B-OMe-9-BBN. We used both tri-*n*-butylborane[8] and B-OMe-9-BBN and confirmed this prediction (Table I). Indeed, we discovered that B-OMe-9-BBN is a far more powerful catalyst than *n*-Bu_3B or any of the other species examined (Table I). Thus, the esters ethyl caproate and ethyl benzoate are reduced in 0.25 h and 1.0 h, respectively, in refluxing ethyl ether (Table II). A further advantage of this reagent is its easy removal from the products. Thus, after the reduction is complete, simple treatment of the reaction mixture with 3 M sodium hydroxide extracts the catalyst from the organic layer into the aqueous phase.[9]

Finally, we established that methyl borate is also a good catalyst, although less effective than B-OMe-9-BBN (Table I). However, it proved to be especially effective for the reduction of the sterically hindered ester, ethyl pivalate (Table II). It also possesses the major advantage of ready removal from the reaction mixture by simple washing with water.

Thus, merely by adding 10 mol % of these catalysts, the reduction of aliphatic, aromatic, and sterically hindered esters by lithium borohydride can be readily completed in 1–2 h (Table III). The selective reduction of the ester group in the presence of such readily reducible groups as chloro and nitro is also readily effected by these catalysts (Table III).

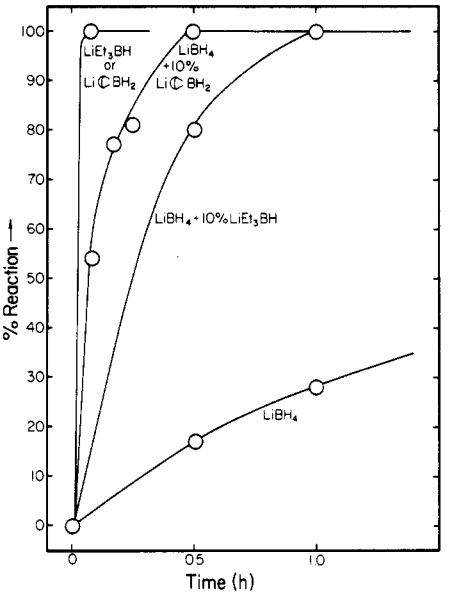
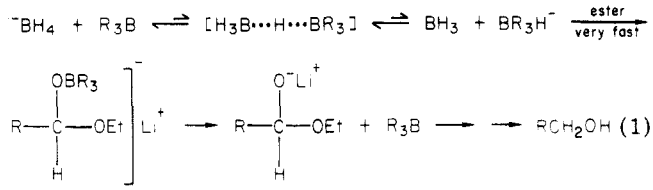


Figure 1. Reduction of ethyl caproate by $LiBH_4$ in ether at 25 °C in the presence of $LiEt_3BH$ or Li-9-BBNH: [ester] = 1.0 M, [$LiBH_4$] = 1.0 M, [catalyst] = 0.1 M.

One possible explanation of such catalytic effects might be the coordination of the Lewis acid with the oxygen atom of the carbonyl group.[7] Such coordination could increase the electron deficiency of the carbonyl carbon, facilitating attack by borohydride. However, we observed that the presence of BF_3·OEt_2 and BH_3·THF did not catalyze the reaction. Consequently, we sought an alternative explanation. We propose that a rapid mobile equilibrium involving transfer of hydride from borohydride to the Lewis acid produces a small quantity of the substituted borohydrides which have been previously demonstrated to be powerful reagents for the reduction of esters (eq 1). In terms of this mechanism, BF_3·OEt_2 might form BF_3H^-, which would either be a poor hydrogen donor or would disproportionate into $LiBH_4$ and $LiBF_4$. Hence, no catalytic effect would be observed (Table I). Hydride transfer to BH_3 would give the same reagent. If $B_2H_7^-$ is formed, it is known to be less reactive than borohydride,[10] so the

(4) Brown, H. C.; Kim, S. C.; Krishnamurthy, S. *J. Org. Chem.* **1980**, *45*, 1.
(5) Brown, H. C.; Singaram, B.; Mathew, C. P. *J. Org. Chem.* **1981**, *13*, 2712.
(6) The reducing properties of lithium 9-boratabicyclo[3.3.1]nonane have been explored by C. P. Mathew (unpublished research).
(7) Professor Nung Min Yoon of Sogang University, Seoul, Korea, has informed us that he and his students have observed a catalytic effect of triethylborane on the reduction of epoxides and esters by lithium borohydride in THF. His observations are being published concurrently.
(8) Because of its lower flamability, tri-*n*-butylborane was used in our tests.
(9) *B*-Methoxy-9-BBN forms the hydroxy derivative which is soluble in sodium hydroxide as the "ate" complex.



rate would be retarded, as observed (Table I).

This procedure offers a simple mild conversion of esters to alcohols. The selective reduction of the ester group in the presence of reducible groups appears to be readily achieved. Consequently, this development markedly enhances the utility of the reagent, $LiBH_4$, for the convenient reduction of esters and their selective reduction in the presence of many reducible functional groups. The full scope of such selective reductions is currently under investigation.

Acknowledgment. We thank the U.S. Army Research Office (ARO DAAG-29-79-C-0027) for financial support of this study.

Registry No. $LiBH_4$, 16949-15-8; LiH-9-BBH, 76448-08-3; $LiEt_3BH$, 22560-16-3; $LiB(OMe)_2$-9-BBN, 81095-46-7; $LiEt_3BOMe$, 81130-65-6; B-OMe-9-BBN, 38050-71-4; BF_3·OEt_2, 109-63-7; BH_3·THF, 14044-65-6; Bu_3B, 122-56-5; $OctB(OMe)_2$, 81044-43-1; $(MeO)_3B$, 121-43-7; $(PhO)_3B$, 1095-03-0; $(DodO)_3B$, 2467-15-4; ethyl caproate, 123-66-0; ethyl benzoate, 93-89-0; ethyl pivalate, 3938-95-2; methyl stearate, 112-61-8; ethyl cyclohexanecarboxylate, 3289-28-9; ethyl 1-adamantanecarboxylate, 2094-73-7; ethyl 4-chlorobenzoate, 7335-27-5; ethyl 3-chloropropionate, 3938-95-2; ethyl 4-nitrobenzoate, 99-77-4.

(10) Krishnamurthy, S.; Brown, H. C. *J. Org. Chem.* **1980**, *45*, 849.
(11) Hovorka, F.; Lenkelma, H. P.; Stanford, S. C. *J. Am. Chem. Soc.* **1938**, *60*, 823.
(12) Brown, H. C.; Subba Rao, B. C. *J. Am. Chem. Soc.* **1956**, *78*, 2582.
(13) Heirs, G. S.; Adams, R. *J. Am. Chem. Soc.* **1926**, *48*, 2388.
(14) *Beilstein 1*, 431.
(15) Stetter, M.; Schwarz, M.; Hirschhorn, A. *Chem. Ber.* **1959**, *92*, 1629.
(16) Chaikin, S. W.; Brown, W. G. *J. Am. Chem. Soc.* **1949**, *71*, 122.
(17) Henry, L. *Chem. Zentralbl.* **1907**, *1*, 1314.

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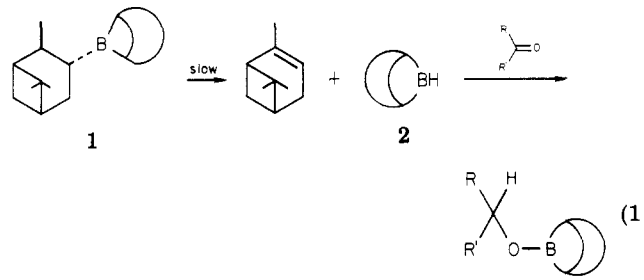
Improved Procedure for the Asymmetric Reduction of Prochiral Ketones by *B*-(3-Pinanyl)-9-borabicyclo[3.3.1]nonane

Summary: An improved experimental procedure gives good optical induction in the reduction of nonacetylenic prochiral ketones, using the chiral trialkylborane *B*-(3-pinanyl)-9-borabicyclo[3.3.1]nonane (Midland's reagent).

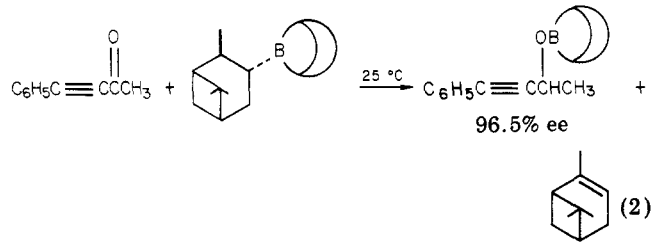
Sir: Recently, *B*-(3-pinanyl)-9-borabicyclo[3.3.1]nonane (1) was shown to be a very useful chiral reducing agent for the reduction of aldehydes and acetylenic ketones.[1] In addition to giving excellent chemical yields and optical induction, the reagent has several advantages in being readily available in both *d* and *l* forms, requiring mild reaction conditions and simple workup procedures, while exhibiting high chemoselectivity (many other readily reducible functionalities are tolerated).

However, the reagent is not useful for the reduction of simple, nonacetylenic ketones, possibly of even greater interest. The difficulty in this case apparently arises from the very slow reaction at room temperature under such conditions. The usual reduction by a cyclic mechanism is replaced by an alternate mechanism involving a prior dissociation of the reagent (eq 1). Reduction of the ketone



by the dissociation product, 9-borabicyclo[3.3.1]nonane (9-BBN, 2), produces inactive product. Increasing the temperature as a means of enhancing the rate of reaction is self-defeating, since it leads to enhanced dissociation of the reagent.[2]

It occurred to us that it should be possible to increase the rate of reaction as well as to minimize the undesirable dissociation by carrying out the reaction in more concentrated solutions. Accordingly, we carried out the reduction of 4-phenyl-3-butyn-2-one (3, eq 2) in a 2 M THF solution



(the original workers had used a 0.5 M solution of 9-BBN in THF to prepare the reagent and slightly more dilute solutions for the actual reductions). The reaction went to completion in ~20 h (as against 48 h in the original procedure) and the alcohol obtained had a specific rotation of +69.6°, substantially higher than the value of +51.8° achieved by Midland and co-workers in their original procedure.[1] This specific rotation of the alcohol represents an optical purity of 96.5% on the basis of Midland's value of 51.8° for 72% ee. Since we had started with α-pinene of 92% ee, this value appears to be a little high. This discrepancy may be due to the fact that Midland and co-workers used NMR shift reagents to determine optical purity and the rotation reported by them may be a little low. Encouraged, we then tried the neat reagent. In this case, the reaction went to completion in ~8–12 h, using only 40% excess reagent, and the alcohol obtained had the same optical purity as the one from the 2 M THF reaction.

Encouraged by this result, we applied this procedure (neat conditions) to the reduction of acetophenone and other representative aliphatic ketones (eq 3–5). In most cases, using 100% excess reagent, the reaction went to completion in 7–10 days at room temperature. Moderate to good optical induction was realized (all results reported are for reagent from 92% ee α-pinene). Thus, acetophenone was reduced to α-methylbenzyl alcohol in an enantiomeric excess of 78%. In the aliphatic series, 2-

(1) Midland, M. M.; Tramontano, A.; Zderic, S. A. *J. Am. Chem. Soc.* **1977**, *99*, 5211. Midland, M. M.; Greer, S.; Tramontano, A.; Zderic, S. A. *Ibid.* **1979**, *101*, 2352. Midland, M. M.; McDowell, D. C.; Hatch, R. L.; Tramontano, A. *Ibid.* **1980**, *102*, 867.

(2) Midland, M. M.; Petre, J. E. *J. Am. Chem. Soc.*, in press.

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