PREPARATION OF POTASSIUM 9-ALKYL-9-BORATABICYCLO[3.3.1]NONANES AND THEIR STEREOSELECTIVITY IN THE REDUCTION OF CYCLIC KETONES

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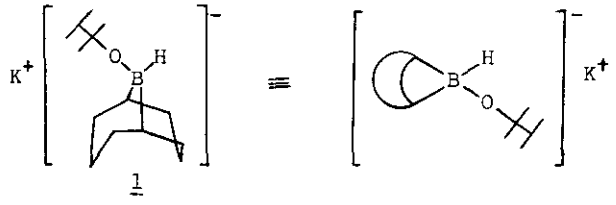
Abstract — Potassium 9-alkyl-9-boratabicyclo[3.3.1]nonanes (K 9-R-9-BBNHs) possessing a wide range of steric requirements were prepared from the reaction of the corresponding 9-alkyl-9-borabicyclo[3.3.1]nonanes (9-R-9-BBNs) and excess potassium hydride, and the stereoselectivities of these reagents in the reduction of representative cyclic ketones were examined. All reagents showed high stereoselectivities, with the stereoselectivities generally increasing with increasing steric requirements of the alkyl substituent. Especially, the tert-butyl derivative, K 9-TB-9-BBNH, achieved the most favorable stereoselectivity, comparable to that by lithium trisiamylborohydride at 0°C.

Potassium hydride, the most favorable hydride-donor among the common alkali metal hydrides (LiH, NaH, KH), reacts readily with organoboranes, such as trialkylboranes[1], trialkoxyboranes[2], 9-alkoxy-9-BBN[3], and cyclic boronic esters[4], producing the corresponding stable potassium trisubstituted borohydrides. These borohydrides thus formed possess unique reducing characteristics,[2-bcd,3] especially showing a high degree of stereoselectivity toward typical cyclic ketones.[2-c,3]

Among the trisubstituted borohydrides, potassium 9-alkoxy-9-boratabicyclo[3.3.1]nonanes (K 9-OR-9-BBNHs) showed an interesting feature in the stereoselectivity toward cyclic ketones. Thus, the stereoselectivity generally increases with increasing steric requirements of the alkoxy substituent on boron of 9-BBN.[3-b] Finally, the stereoselectivity achieved by the thexyloxy (2,3-dimethyl-2-butoxy) derivative[3-a] (1) approached to that by lithium tri-sec-butylborohydride[5].



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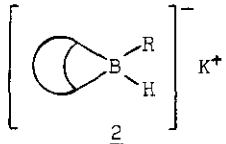
This outcome encouraged us to explore a general procedure of the syntheses of the potassium 9-alkyl-9-boratabicyclo[3.3.1]nonanes (K 9-R-9-BBNHs) (2) for possible examination of their stereoselective reducing characteristics.



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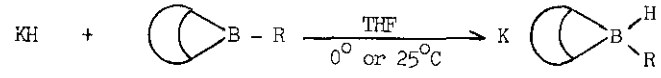
A representative series of 9-alkyl-9-BBN with various steric requirements of the R group were prepared by hydroborating the corresponding olefins with 9-BBN (R = sec-amyl, neohexyl, thexyl, n-octyl, cyclohexyl),[6] by treating 9-methoxy-9-BBN with the corresponding alkyllithium (R = n-butyl, tert-butyl, phenyl)[7], and by hydroborating propargyl bromide with 2 equiv 9-BBN followed by ring closure (R = cyclopropyl)[8]. The ^{11}B nmr spectra and physical properties of these 9-alkyl-9-BBN are summarized in Table I.

Table I. ^{11}B nmr Spectra and Physical Properties of 9-Alkyl-9-borabicyclo[3.3.1]nonanes

9-Alkyl-9-BBN[a]	^{11}B nmr chemical shift, δ[b]	bp(°C) / torr	n_D^{20}
9-n-butyl-9-BBN	+87.7	94-96 / 11	1.4722
9-t-butyl-9-BBN	+85.5	63 / 6	1.4728
9-sec-amyl-9-BBN	+87.7	118 / 12	1.4809
9-neohexyl[c]-9-BBN	+88.2	127-130 / 16	1.4835
9-thexyl[d]-9-BBN	+87.5	115-117 / 9	1.4840
9-n-octyl-9-BBN	+80.6	127 / 7	1.4810
9-cyclopropyl-9-BBN	+84.2	96 / 11	1.5192
9-cyclohexyl-9-BBN	+88.4	120-124 / 15	1.5082
9-phenyl-9-BBN	+80.9	134-138 / 10	1.5535

a) Viscous liquids, very reactive toward air. b) All chemical shifts are reported to $BF_3.OEt_2$ with chemical shifts downfield from $BF_3.OEt_2$ assigned as positive in THF. c) neohexyl = 3,3-dimethyl-1-butyl. d) thexyl = 2,3-dimethyl-2-butyl.

The potassium 9-alkyl-9-BBNH derivatives were prepared by adding the neat 9-alkyl-9-BBN to a vigorously stirred suspension of ca. 50 mole % excess potassium hydride (free of oil) in THF either at 0°C or 25°C (eq 1).



(1)

The products prepared in this study appear to be very stable toward disproportionation. The reaction conditions are summarized in Table II.

Table II. Reaction of Potassium Hydride with Representative 9-Alkyl-9-BBN in Tetrahydrofuran[a]

9-Alkyl-9-BBN	Temp (°C)	Time
9-n-butyl-9-BBN	0	instantly
9-t-butyl-9-BBN	25	24 h
9-sec-amyl-9-BBN	25	6 h
9-neohexyl[b]-9-BBN	25	6 h
9-thexyl[c]-9-BBN	25	24 h
9-n-octyl-9-BBN	25	3 h
9-cyclopropyl-9-BBN	25	24 h
9-cyclohexyl-9-BBN	25	24 h
9-phenyl-9-BBN	0	instantly

a) The solutions were 1.0 M in 9-alkyl-9-BBNs and approximately 50% excess of potassium hydride utilized. b) neohexyl = 3,3-dimethyl-1-butyl. c) thexyl = 2,3-dimetheyl-2-butyl.

Solutions of the K 9-R-9-BBNH derivatives in THF display typical strong absorptions around 2000 cm^{-1} in the ir, attributed to the B-H stretching vibration. The ^{11}B nmr spectra exhibit clean doublets in the region some -10 ppm upfield from the standard, $BF_3.OEt_2$. The results are summarized in Table III.

Table III. Infrared and ^{11}B nmr Spectra of Potassium 9-Alkyl-9-boratabicyclo[3.3.1]nonanes in Tetrahydrofuran

K 9-alkyl-9-BBNH	IR ν(B-H), cm^{-1}	^{11}B NMR chemical shift[a], δ (multiplicity)	$J_{(B-H)}$ Hz
potassium 9-n-butyl-9-BBNH	1990	-13.4 (d)	70
potassium 9-t-butyl-9-BBNH	1980	- 8.9 (d)	75
potassium 9-sec-amyl-9-BBNH	2000	-12.8 (d)	67
potassium 9-neohexyl[b]-9-BBNH	2000	-12.6 (d)	63
potassium 9-thexyl[c]-9-BBNH	2000	-10.3 (d)	74
potassium 9-n-octyl-9-BBNH	1995	-14.0 (d)	65
potassium 9-cyclopropyl-9-BBNH	1990	-13.8 (d)	70
potassium 9-cyclohexyl-9-BBNH	1980	-11.9 (d)	62.5
potassium 9-phenyl-9-BBNH	2000	-13.5 (d)	53

a) All chemical shifts are relative to $BF_3.OEt_2$ with chemical shifts upfield from $BF_3.OEt_2$ assigned as negative. b, c) See corresponding footnotes in Table II.

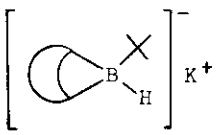
The stereoselectivity of these new reagents toward representative group of cyclic ketones was examined at 0° and -25°C. The results are summarized in Table IV.

Table IV. Stereoselective Reduction of Cyclic Ketones with Potassium 9-Alkyl-9-boratabicyclo[3.3.1]-nonanes (K 9-R-9-BBNHs) in Tetrahydrofuran at 0° and -25°C [a,b,c]

Ketones	Temp °C	R in K 9-R-9-BBNH							
		n-Bu	t-Bu	sec-amyl	neohexyl[d]	n-octyl	cyclopropyl	cyclohexyl	phenyl
cyclohexanone									
2-methyl-	0	97.5	99.5	99.5	98	98	92	99.5	90.5
	-25	-	99.5	99.5	-	-	-	99.5	-
3-methyl-	0	66.5	98	96	67	67.5	60.5	83.5	46.5
	-25	-	99	96.5	-	-	-	84	-
4-methyl-	0	61	94	90	61.5	62	58.5	93.5	53.5
	-25	-	94.5	90.5	-	-	-	93.5	-
4-tert-butyl-	0	52.5	98.5	96.5	53	53	54	83.5	44.5
	-25	-	98.5	96.5	-	-	-	86.5	-
3,3,5-trimethyl-	0	98	99	99	98.5	98.5	96.5	99	98
	-25	-	99.5	99.5	-	-	-	99.5	-
norcamphor	0	92.5	95.5	95.5	93.5	e	93	94.5	94.5
	-25	-	96.5	96	-	-	-	96	-
camphor	0	99.5	99.9	99.9	99.5	99.5	96.5	99.5	98.5
	-25	-	99.9	99.9	-	-	-	99.9	-

a) A 2:1 ratio for reagent : ketone was used. b) The yields of alcohols were quantitative and the figures are percentage of the less stable isomers. c) Heterogeneous reaction at -25°C. d) neohexyl = 3,3-dimethyl-1-butyl. e) GC analysis was impossible due to complete overlap of n-octanol and exo-norborneol peaks.

In general, the degree of stereoselectivity exhibits a close correlation with the bulkiness of alkyl substituent in the reagent (2). However, it should be pointed out that the stereoselectivity achieved at 0°C with the tert-butyl derivative, potassium 9-tert-butyl-9-BBNH (K 9-TB-9-BBNH) (3), is exceptionally high, comparable to the results with lithium trisiamylborohydride at that temperature. This



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reagent has α-methyl substituted tertiary alkyl group on boron, which is more effective than those have β- or γ-methyl substituted bulkier alkyl groups on boron.

In conclusion, a new class of reducing agents, potassium 9-alkyl-9-BBNHs containing a wide variety

of alkyl groups are readily prepared by treating 9-alkyl-9-BBN with potassium hydride in tetrahydrofuran at 0° or 25°C. The reagents possessing a bulky alkyl substituent reveal an excellent stereoselectivity in the reduction of cyclic ketones at 0° and -25°C. Of these, the selectivity exhibited at 0°C by potassium 9-tert-butyl-9-BBNH (K 9-TB-9-BBNH) approaches that achieved with lithium trisiamylborohydride at that temperature.

In addition, in the course of systematic study of the reducing characteristics, we found these reagent possess excellent selectivities on the reduction of organic functional groups. We are investigating these in detail.

EXPERIMENTAL

Infrared spectra were recorded on a Perkin-Elmer 1330 spectrophotometer by using sealed liquid cells. ^{11}B nmr spectra were recorded with a Bruker WP 80 SY spectrometer. The chemical shifts reported are in δ(ppm) relative to $BF_3.OEt_2$. GC analyses were performed with a Hewlett-Packard 5790 A FID chromatograph equipped with a Hewlett Packard 3390 A integrator / plotter. The alcohol products were analyzed using a 12 ft x 0.125 in. column packed with 15% THEED on 100 / 120 mesh Supelcoport or 10% Carbowax 20 M on 100 / 120 mesh Supelcoport with the use of a suitable internal standard and authentic sample.

Preparation of 9-R-9-BBNHs — The 9-R-9-BBNs containing sec-amyl, neohexyl, tert-butyl, n-octyl, or cyclohexyl groups were prepared by hydroboration of the corresponding olefins with 9-BBN in THF according to the published procedure.[6] The 9-n-butyl-, 9-tert-butyl-, and 9-phenyl-9-BBNs were prepared by treating 9-methoxy-9-BBN with the corresponding alkyllithium in pentane[7]. 9-Cyclopropyl-9-BBN was synthesized by dihydroboration of propargyl bromide with 2 equiv 9-BBN followed by ring closure with sodium hydroxide.[8] The physical and spectral properties of freshly distilled products are summarized in Table I.

Preparation of K 9-R-9-BBNHs — The preparation of potassium 9-tert-butyl-9-BBNH (K 9-TB-9-BBNH) is representative. Into an oven-dried 100-ml flask, equipped with a side arm, a condenser, and an adaptor connected to a mercury bubbler, was placed 3.6 g of potassium hydride (90 mmol) as an oil suspension and the oil medium was removed by washing with THF (3 x 10 ml). To this oil-free potassium hydride were added 25 ml of THF and 10.62 g of 9-TB-9-BBN (60 mmol). The reaction mixture was stirred vigorously at 25°C for 24 h to give K 9-TB-9-BBNH in a pure form : ^{11}B nmr δ-8.9 (d, J_{B-H} = 75 Hz) ; ir ν(B-H) 1980 cm^{-1}.

Stereoselective Reactions — The reaction of 2-methylcyclohexanone with K 9-TB-9-BBNH is representative to explore the stereoselectivity. In a 50-ml flask was placed 1.7 ml of a 1.2 M solution of the reagent in THF (2.0 mmol). The flask was maintained at 0°C and 1.0 ml of a precooled 1.0 M solution

of 2-methylcyclohexanone solution in THF (1.0 mmol) was added. The reaction mixture was stirred at 0°C for 2 h (12 h at -25°C) and then quenched by addition of 0.5 ml of H_2O. The organoborane was oxidized with alkaline hydrogen peroxide. The aqueous layer was saturated with anhydrous potassium carbonate, and the organic layer was separated and dried. GC analysis revealed the presence of 100% 2-methylcyclohexanol containing 99.5% of the cis isomer. The results are summarized in Table IV.

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