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## 신

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새로운 키랄수소화븡소 환원제. Potassium 9-0-(1,2:5,6-Di-0-Cyclohexylidene -*a*-D-glucofuranosyl)-9-Boratabicyclo [3.3.1] nonane 의 합성 및 비대칭 환원성에 관한 연구

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# A New Chiral Borohydride Reagent. Preparation and Asymmetric Raducing Properties of Potassium 9-0-(1,2:5,6-Di-O-Cyclohexylidenea -D-glucofuranosyl)-9-Boratabicyclo [3.3.1] nonane

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In our previous work, we found that chiral dialkylmonoalkoxyborohydrides 1 afforded higher optical induction than the corresponding trialkylborohydrides 2 for the reduction of prochiral ketones.1 Accordingly, well-defined, new chiral borohydride reagents of 1 were synthesized



and their asymmetric reducing properties were investigated.<sup>2</sup> Among them, DIPGF 3 have proven to be a highly effective chiral auxiliary for the asymmetric reduction of several types of prochiral ketones with K glucoride.3 On the other hand, DCHGF 4 is a monosaccharide derivative,4 in which substituents at C-1, C-2 and C-5, C-6 are different from those of 3. If the new chiral borohydride using 4 as a chairall auxiliary could be prepared, we expected 4 would provide different steric effects from those of 3 in transition state of asymmetric incubation, giving unique asymmetric reducing properties. Therefore we tested the possibility. Thus, 4 was treated with 9-BBN in





at 25°C to give the borinic ester, 9-O-DCHGF-9-BBN 5 (viscous oil, 96% yield, 11B NMR 56. 03(s): MS, M<sup>+</sup> 460). 5 was converted in-



to the corresponding hydride reagent, 9-O-(1,2:5,6-di-O-cyclohexylidene--Dglucofuranosyl)-9-boratabicyclo [3.3.1] nonane **6** by treatment with excess potassium hydride (25°C, 6 h) in essentially quantitative yield: <sup>11</sup>B NMR  $\delta$ -1.3 (br.s); IR  $\nu_{B-H}$  2012 cm<sup>-1</sup>. This reagent was analyzed for stoichiometric ratio of K:B:H=1:1:1.

Asymmetric reductions for 9 selected representative classes of ketones<sup>5</sup> with 6 were carried out in THF at -78°C. The results are compared with them by K glucoride and summarized in Table 1. Generally, the rates of reduction for the selected ketones examined with this reagent were somewhat slower than those by K glucoride under the same reaction condition. Thus the reduction of unhindered aliphatic ketone, 3-methyl-2- butanone, proceeded to completion within 12 h to give 58% ee. The optical induction is noteworthy as compared with 36% ee by K glucoride.3a,5.8 For relatively hindered aliphatic ketone, 2,2-dimethylcyclopentanone, high optical yield (80% ee) was obtained, although the reduction was very sluggish, requiring 4 days for 90% reduction. This reagent provided the best result in the reduction of a-keto ester, methyl benzolformate to give ahydroxy ester, methyl mandelate of 92% ee as well as K glucoride.<sup>3a,c,5</sup> The asymmetric reduction for other ketones examined appeared essentially same optical inductions as those given by K glucoride, giving 77% ee for acetophenone, 55% ee for 3-acetylpyridine, 78% ee for 2-chloroacetophenone, 60% ee for trans-4-phenyl-3-buten-2-one, and 62% ee for 4-phenyl-3-butyn-2-one. Absolute configurations for the product alcohols are exactly same as those given by K glucoride.3a The reduction of 2-cyclohexenone, unfortunately, gave 1,4-addition product mainly. The results indicated that steric difference at C-1, C-2 and C-5, C-6 in 3 and 4 provided almost no effects in asymmetric induction for such ketones

Table 1. Asymmetric reduction of representative ketones with 6 in THF at -78 °C<sup>o</sup>

katana		4			K glucoride <sup>/</sup>	
Retone	time	yield(%) <sup>ø</sup>	%ee⁴	config.	%ee	config
٦.	1 <b>2 h</b>	98	58	R	36	R
$\dot{\mathbf{Q}}$	4 d	90	80⁄	R	84	R
O <sup>L</sup>	30 h	97	77	R	78	R
Q <sup>i</sup>	30 h	96	55	R	70	R
O <sup>L</sup> "	24 h	80¢	78¢	΄S	77	s
QU.	16 h	85	92	S	<del>9</del> 2	\$
Oni	24 h	93	60	R	60	R
δ.	16 h	d	-	-	-	-
()*×	16 h	95	62	R	61	R

<sup>a</sup>[H<sup>-</sup>]:[cpd] = 1.1:1.0, [ketone] = 0.3M. <sup>b</sup>By GC analysis. <sup>c</sup>GC yield of styrene oxide. <sup>d</sup>Mainly 1,4 reduction. <sup>c</sup>Determined by capillary GC analysis of MTPA ester.<sup>6</sup> / Determined by capillary GC analysis of (-)menthyl carbonate.<sup>7</sup>  $s[\alpha]_{B}^{p_{2}}-37.28$  (c 1.05, benzene) as styrene oxide. Based on calculated[ $\alpha$ ]]<sup>b</sup> + 46.84 (c 1.08, benzene); G. Berti, F. Bottari, P. L. Ferrorini, and B. J. Maccia. J. Org. Chem. 30, 4091 (1965). <sup>k</sup>Data taken from ref. 3a and 5.

examined except 3-methyl-2-butanone. The following procedure is representative. The flask was charged with 5.5 mmol of 6 in THF (0.5 M, 11 ml) and cooled to  $-78^{\circ}$ C via a double ended needle. After 16 h, the unreacted hydride was destroyed by addition of methanol at  $-78^{\circ}$ C. The solvent was pumped off under reduced pressure, followed by hydrogen peroxide oxidation. (pH 7 buffer solution in ethyl ether,  $0^{\circ}$ C, 3 h). The aqueous layer was extacted with ethyl ether. The ethereal extracts were concentrated in vacuo and the product, methyl mandelate, was obtained by bulb-to bulb distillation. (GC yield: 85%). Optical purity was measured by capillary GC analysis of MTPA ester<sup>6</sup> of the product: 92% ee enriched S configuration.

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- 8. The asymmetric reductions for the other aliphatic ketones are under investigation.

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