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

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In our previous work, we found that chiral dialkylmonoaalkoxyborohydrides 1 afforded higher optical induction than the corresponding trialkylborohydrides 2 for the reduction of prochiral ketones. Accordingly, well-defined, new chiral borohydride reagents of 1 were synthesized and their asymmetric reducing properties were investigated. 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. On the other hand, DCHGF 4 is a monosaccharide derivative, 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

![Chemical structure](attachment:image.png)

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+460). 5 was converted in-

![Chemical structure](attachment:image.png)
to the corresponding hydride reagent, 9-O-
(1,2:5,6-di-O-cyclohexylidene-D-
glucofuranosyl)-9-borastacyclo [3.3.1] nonane 6
by treatment with excess potassium hydride (25°C,
6 h) in essentially quantitative yield: 11B NMR
δ -1.3 (br.s); IR ν νK-H 2012 cm⁻¹. This reagent
was analyzed for stoichiometric ratio of

Asymmetric reductions for 9 selected represen-
tative classes of ketones 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 in 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-di-
methylocyclopetanone, 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
α-keto ester, methyl benzoformate to give α-
hydroxy ester, methyl mandelate of 92% ee as well
as K glucoride. 3a,5,8 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-butan-2-one, and 62% ee
for 4-phenyl-3-butan-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

<table>
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<tr>
<th>ketone</th>
<th>time (h)</th>
<th>yield (%)</th>
<th>ee*</th>
<th>config.</th>
<th>ee* config.</th>
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<td>98</td>
<td>58</td>
<td>R</td>
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<td>90</td>
<td>80</td>
<td>R</td>
<td>84</td>
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<td>16</td>
<td>95</td>
<td>62</td>
<td>R</td>
<td>61</td>
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</table>

*([H]:[cpd] = 1:1:0.5, [ketone] = 0.3 M). By GC analysis.
GC yield of styrene oxide. Mainly 1,4 reduction. Determined by capillary GC analysis of MTPA ester. Determined by capillary GC analysis of (R)-menthyl carbon-
ate. 4 [α]D = -37.28 (c 1.05, benzene) as styrene oxide.
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°C via a double ended
needle. After 16 h, the unreacted hydride was
destroyed by addition of methanol at -78°C. The
solvent was pumped off under reduced pressure,
followed by hydrogen peroxide oxidation. (pH 7
buffer solution in ethyl ether, 0°C, 3 h). The
aqueous layer was extracted with ethyl ether. The
etheral 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

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MTPA ester* of the product: 92% ee enriched S configuration.

ACKNOWLEDGEMENT

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REFERENCES AND NOTES

4. (a) R. C. Hockett, R. L. Miller and A. Scataglione, J. Am. Chem. Soc., 71, 3072 (1949); [α]D = −2.20 (c 2.27, EtOH); (b) Present work: [α]D = 2.84 (c 2.43, EtOH).
8. The asymmetric reductions for the other aliphatic ketones are under investigation.