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The Preparation and Application of two New Types of Oxazaborolidines

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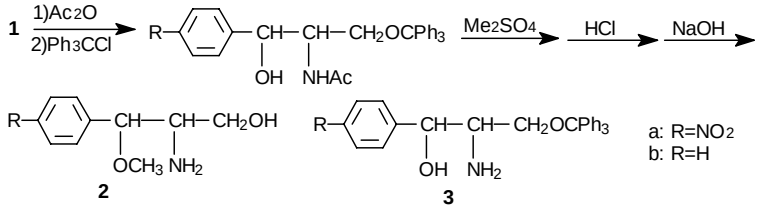
Abstract: Two new type of 1,3,2-oxazaborolidines were prepared from (1s,2s)-2-amino-1-(4-nitrophenyl)-propane-1,3-diol and were used as catalyst in the asymmetric reduction of acetophenone. The influence of the reaction temperature as well as the effect of the structure of catalyst on the enantioselectivity was investigated. The origin of the products' configuration was discussed.

Keywords: 0xazaborolidine, asymmetric catalytic reduction, prochiral ketone.

Stereoselective reduction of the prochiral ketones is one of the most actively studied areas in asymmetric synthesis. In this context,oxazaborolidine catalysed reduction has emerged as one of the most prominent methodology[1].

(1s,2s)-2-amino-1-(4-nitrophenyl)-propane-1,3-diol **1** is a by-product in the chlor-amphenicol manufacture. In this paper, we report the results of the catalytic asy-mmetric reduction of acetophenones with borane in the presence of chiral ligand ari-sing from **1.** The preparation of ligand **2** is scheduled and **3** can be produced from **1**[2].

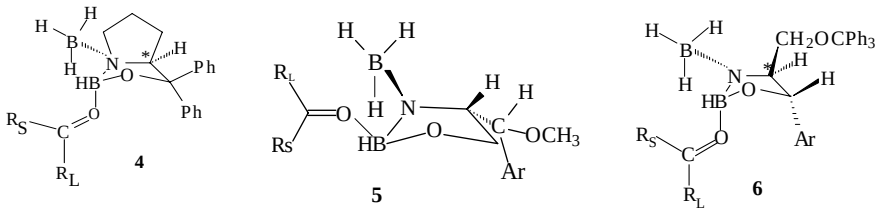


The 10% mol. of **2** or **3** reacted with 1 equiv.of borane at r.t. for two hours, 1 equiv. of prochiral ketone dissolved in THF was added within 1-1.5 hours and then stirred at 40℃ for 5-10 min..After work-up, the obtained product alcohols were subjected to silica gel column chromatography eluting with ethyl acetate: petroleum ether (1:10). The e.e. values and absolute configuration were determined by comparison of their optical rotations with literature[3].

The reactions were proceeded at 0℃,25℃,40-45℃,66℃. But the best result was obtained at 40-45℃. At 0℃,25℃ the reduction did not go to completion even after 24 hours. At 66℃, the non-catalytic pathway is competitive and the e.e. value of product is lowered to about 50%.. The catalytic effect was more dramatic for **2b** then for **2a,** because **2b** has a more basic nitrogen atom. This made it more effective to coordinate

with borane.

According to the reduction mechanism suggested by Corey[1], the main product's configuration is determined by that of the carbon atom which bonds with amino group.



4 **5** **6**

When (*S*)-amino alcohol is used, (*R*)-optically active alcohol is obtained. In the presence of ligand **3** (as **6**), our results confirmed the Corey's mechanism(as **4**). But in the case of **2**, the larger group $ArCH(OCH_3)$ is beneath the heterocycle surface, this made the borane coordinate with nitrogen atom on the β-face like **5** and (*s*)-enantiomer product was obtained.

Table: Enatioselective reduction of acetophenones with 1 equiv. BH_3 and 0.1 equiv. **2** or **3**

entry	Ketones	ligand	e.e.(%)	configuation	yield
1	PhCOMe	**2a**	73.2	S	74.7
2	PhCOMe	**2b**	76.5	S	78.5
3	*p*-CH_3PhCOMe	**2a**	51.5	S	83.2
4	*p*-CH_3PhCOMe	**2b**	74.4	S	81.2
5	*p*-ClPhCOMe	**2a**	65.8	S	80.4
6	*p*-ClPhCOMe	**2b**	71.4	S	79.7
7	*p*-BrPhCOMe	**2a**	61.3	S	82.5
8	*p*-BrPhCOMe	**2b**	66.8	S	82.7
9	*p*-CH_3OPhCOMe	**2a**	23.0	S	54.0
10	*p*-CH_3OPhCOMe	**2b**	64.7	S	82.0
11	PhCOMe	**3a**	43.4	R	80.4
12	PhCOMe	**3b**	78.4	R	78.7
13	*p*-CH_3PhCOMe	**3b**	64.2	R	82.4
14	*p*-BrPhCOMe	**3b**	67.1	R	90.4
15	*p*-CH_3OPhCOMe	**3b**	51.3	R	85.7

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