

# The Evaluation of Chiral Benzosultams As Auxiliaries in Asymmetric Azidation Reaction

Kyo Han Ahn,\* Seung-Ki Kim, and Chul Ham

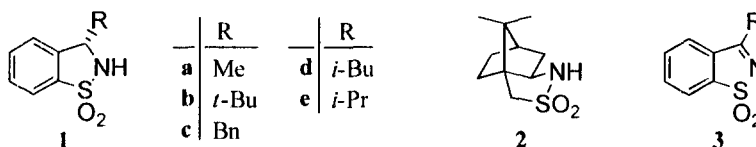
Department of Chemistry and Center for Biofunctional Molecules, POSTECH, San 31 Hyoja-dong, Pohang 790-784, Republic of Korea

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**Abstract.** Several chiral 3-substituted benzosultams, synthesized through an enantioselective Ru(II)-catalyzed transfer hydrogenation of corresponding sulfonylimines, are evaluated as chiral auxiliaries in the asymmetric azidation reaction of their *N*-acyl derivatives.  $\pi$ -Facial selectivities of up to 99:1 are observed. © 1998 Elsevier Science Ltd. All rights reserved.

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Chiral auxiliary-based reactions constitute an important class of asymmetric syntheses[1]. Recently, Oppolzer and co-workers reported new sultam auxiliaries **1**, which contained useful features compared to the well-known camphorsultam **2**. Sultams **1a** and **1b** were demonstrated to be useful chiral auxiliaries in several asymmetric reactions such as alkylation, aldol[2], and cycloaddition reactions[3,4]. Recently, we achieved an efficient two-step synthesis of chiral sultams **1b** and **1c**, which involved no chromatographic separation[5]. Herein, we wish to report the asymmetric azidation reaction employing several sultams (**1a–1e**) as the chiral auxiliary, which are prepared similarly through an asymmetric Ru-catalyzed transfer hydrogenation of sulfonylimines **3**.<sup>1</sup>



The azidation was carried out using 2,4,6-triisopropylbenzenesulfonyl azide (trisyl-N<sub>3</sub>) as an azide-transferring agent, according to the procedure of Evans and co-workers[6,7]. The results are summarized in Table 1. Interestingly, better enantioselectivities were obtained when

<sup>1</sup> Enantiopurity (%ee) of the products (crude/purified), yields and physical data { $[\alpha]_D$  (c, CHCl<sub>3</sub>), mp (°C)} of purified ones: **1a**:

86.8/100, 61%, -30.8 (1.0), 90.3–91.1; **1d**: 89.8/100, 54%, -75.0 (1.0), 76.6–77.3; **1e**: 67.4/100, 58%, -75.8 (1.4), 117.1–118.0.

NaHMDS was used as the base, compared to the case of KHMDS. The opposite trend was observed in the case of Evans' oxazolidinone auxiliary. In all cases, diastereoselectivities of 95:5 or more were observed when NaHMDS was used. Excellent  $\pi$ -facial selectivities (>98:2) and high yields were observed when sultam **1b** was employed as the chiral auxiliary (entry 4 and 9). Hydrolysis of the azidation product **5b** ( $R = t\text{-Bu}$ ;  $R' = \text{CH}_2\text{Ph}$ ) under basic conditions ( $\text{LiOH}\cdot\text{H}_2\text{O}_2$  in  $\text{THF}\text{-H}_2\text{O}$ ,  $0^\circ\text{C}$ ) followed by an acidic work-up afforded the corresponding  $\alpha$ -azidocarboxylic acid (**6**) and chiral auxiliary **1b** in 94% and 90% yields, respectively. Comparison of the optical rotation of **6** with the literature value of its antipode[7] established the absolute stereochemistry generated. The observed facial selectivity can be explained by assuming that a metal ( $Z$ )-enolate chelated to the sulfonyl oxygen(s) reacts with trisyl azide.

Table 1. Diastereoselective Azidation of *N*-Acyl-sultams **4**

Entry	R	R'	M	Yield, <sup>a</sup> %	d.s. <sup>b</sup>
1	Me	$\text{CH}_2\text{CH}=\text{CH}_2$	Na	72	95:5
2	<i>i</i> -Pr	$\text{CH}_2\text{CH}=\text{CH}_2$	Na	73	95:5
3	<i>i</i> -Bu	$\text{CH}_2\text{CH}=\text{CH}_2$	Na	77	96:4
4	<i>t</i> -Bu	$\text{CH}_2\text{CH}=\text{CH}_2$	Na	96	>98:2
5	$\text{CH}_2\text{Ph}$	$\text{CH}_2\text{CH}=\text{CH}_2$	Na	72	96:4
6	<i>i</i> -Bu	$\text{CH}_2\text{CH}=\text{CH}_2$	K	45	93:7
7	<i>t</i> -Bu	$\text{CH}_2\text{CH}=\text{CH}_2$	K	63	93:7
8	<i>i</i> -Bu	$\text{CH}_2\text{Ph}$	Na	55	>98:2
9	<i>t</i> -Bu	$\text{CH}_2\text{Ph}$	Na	85	99:1
10	<i>i</i> -Bu	$\text{CH}_2\text{Ph}$	K	54	98:2
11	<i>t</i> -Bu	$\text{CH}_2\text{Ph}$	K	79	>98:2

<sup>a</sup> Isolated by column chromatography on silica gel.

<sup>b</sup> Determined by  $^1\text{H}$  NMR analysis.

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