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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. π-Facial selectivities of up to 99:1 are observed. © 1998 Elsevier Science Ltd. All rights reserved.

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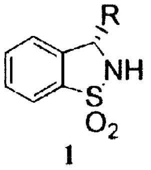
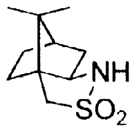
Chiral auxiliary-based reactions constitute an important class of asymmetric syntheses[1]. Recently, Oppolzer and co-workers reported new sultam auxiliaries **1**, which contained useful features compared to the well-known camphorsultam **2**. Sultams **1a** and **1b** were demonstrated to be useful 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**-**1c**) as the chiral auxiliary, which are prepared similarly through an asymmetric Ru-catalyzed transfer hydrogenation of sulfonylimines **3**.[1]



1

	R		R
a	Me	**d**	*i*-Bu
b	*t*-Bu	**e**	*i*-Pr
c	Bn		



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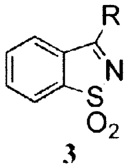

3

The azidation was carried out using 2,4,6-triisopropylbezenesulfonyl azide (trisyl-N_3) 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

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[1] Enantiopurity (%ee) of the products (crude/purified), yields and physical data {$[\alpha]_D$ (c, $CHCl_3$), 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.

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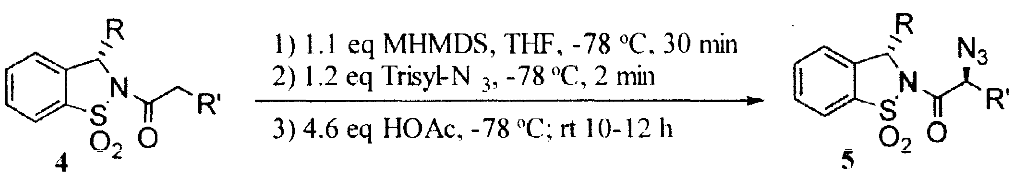
NaHMDS was used as the base, compared to the case of KHMDS. The opposite trend was observed in the case of Evans' oxazolindinone auxiliary. In all cases, diastereoselectivities of 95:5 or more were observed when NaHMDS was used. Excellent π-facial selectivities (>98:2) and high yields were observed when sultam **1b** was employed as the chiral auxiliary (entry 4 and 9). Hydrolysis of the azidation product **5b** (R = *t*-Bu; R' = CH_2Ph) under basic conditions ($LiOH$-H_2O_2 in THF-H_2O, 0 °C) followed by an acidic work-up afforded the corresponding α-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,[a] %	d.s.[b]
1	Me	$CH_2CH=CH_2$	Na	72	95:5
2	*i*-Pr	$CH_2CH=CH_2$	Na	73	95:5
3	*i*-Bu	$CH_2CH=CH_2$	Na	77	96:4
4	*t*-Bu	$CH_2CH=CH_2$	Na	96	>98:2
5	CH_2Ph	$CH_2CH=CH_2$	Na	72	96:4
6	*i*-Bu	$CH_2CH=CH_2$	K	45	93:7
7	*t*-Bu	$CH_2CH=CH_2$	K	63	93:7
8	*i*-Bu	CH_2Ph	Na	55	>98:2
9	*t*-Bu	CH_2Ph	Na	85	99:1
10	*i*-Bu	CH_2Ph	K	54	98:2
11	*t*-Bu	CH_2Ph	K	79	>98:2

[a] Isolated by column chromatography on silica gel. [b] Determined by ^1H NMR analysis.

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