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A Convenient Method for the Synthesis of Chiral N-Protected 1, 2-Amino Alcohols *via* the Reduction of the Aminoketones

Zheng Hong ZHOU*, Yi Long TANG, Kang Ying LI, Bing LIU, Chu Chi TANG

State Key Laboratory of Elemento-Organic Chemistry
Institute of Elemento-Oganic Chemistry, Nankai University, Tianjin 300071

Abstract: A series of optically active N-protected 1,2-amino alcohols were synthesized *via* the reduction of the corresponding α-aminoketones starting from the readily available L-amino acids.

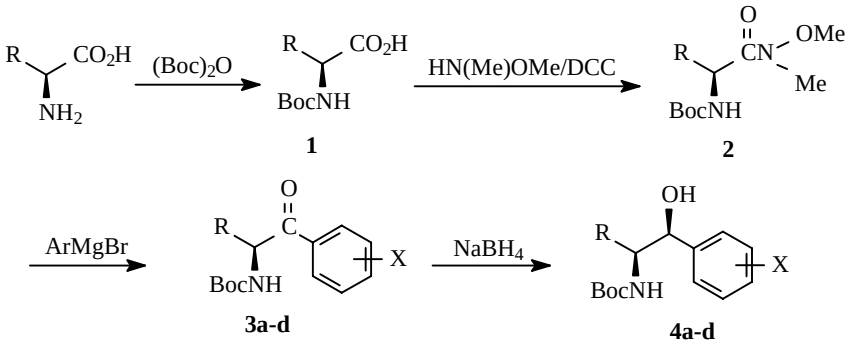
Keywords: Optically active, 1,2-amino alcohol, α-aminoketone, reduction.

The preparation of chiral 1,2-amino alcohols by synthetic method and the isolation of their enantiomeric and/or diastereomeric forms, as well as the knowledge of their configuration were of great importance in pharmacological research on anaesthetics, analgesics *etc*. It was well known that the receptorial centers were very stereoselective towards the above drugs in many cases. Moreover, 1,2-amino alcohols are the important building blocks in the synthesis of various natural products[1] and bicyclic amidines and guanidines[2]. In addition, the enantiomers of chiral amino alcohols could be employed in the asymmetric synthesis of optically active compounds[3], mainly in the formation of complex hydrides[4,5], or in the asymmetric reaction of unsaturated molecules in the presence of metal catalysts[6]. Therefore, the synthesis of optically active 1,2-amino alcohols has attracted much attention of the organic chemists. An efficient method for the synthesis of chiral N-protected α-aminoketones and related 1,2-amino alcohols starting from the L-amino acids (**Scheme 1**) is described in this letter.

The readily available L-amino acids were converted to the corresponding N-*tert*-butoxycarbony protected amino acids 1. The condensation of 1 with N,O-dimethylhydroxylamine[7] afforded the corresponding N-protected Weinreb amides **2**. Grignard reaction of the amides **2** with arylmagnesium bromide provided the pivotal -aminoketone derivatives **3**. Reduction of the ketones **3** with sodium borohydride resulted in the exclusive formation of the corresponding 1,2-*syn*-amino alcohols **4** in high yield (the assigned stereochemistry of compounds **4** was determined according to the literature[8]). The experimental data of the ketones **3** and the 1,2-amino alcohols **4** were summarized in the **Table 1**.

* E-mail: z.h.zhou@eyou.com

Scheme 1



a: R = CH_3, X = H; b: R = CH_3, X = 4-CH_3; c: R = $PhCH_2$, X = H; d: R = $PhCH_2$, X = 4-CH_3. Boc = *tert*-butoxycarbonyl; DCC = N,N-dicyclohexylcarbodiimide.

Table 1 Experimental data of the compounds **3**, **4**

Compd.	R	X	mp/°C	Yield/ %	$[\alpha]_{20}^{D}$
3a	CH_3	H	Thick liquid	47.5	0 (c 0.9, $CHCl_3$)
3b	CH_3	4-CH_3	99~100	59.6	–66.0 (c 0.94, $CHCl_3$)
3c	$PhCH_2$	H	94~96	58.1	+52.3 (c 1, $CHCl_3$)
3d	$PhCH_2$	4-CH_3	89~91	47.3	+51.2 (c 0.5, $CHCl_3$)
4a	CH_3	H	86~87	82.3	+9.8 (c 1, $CHCl_3$)
4b	CH_3	4-CH_3	128~129	97.6	–70.4 (c 1.02, $CHCl_3$)
4c	$PhCH_2$	H	136~137	77.1	–24.8 (c 0.71, $CHCl_3$)
4d	$PhCH_2$	4-CH_3	131~134	92.3	–25.3 (c 0.3, $CHCl_3$)

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