Synthesis and Functionalization of \textit{trans}-2-(2'-Aminocyclohexyloxy)- and \textit{trans}-2-(2'-Azidocyclohexyloxy)acetic Acid

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Summary. Synthesis of the hydrochloride of \textit{trans}-2-(2'-aminocyclohexyloxy)acetic acid (4) from \textit{trans}-2-(2'-azidocyclohexyloxy)acetic acid (1) is described. 4 was acylated at the amino group to give compounds 5-8. 1 was converted into acid chloride (9) and amides 10-13.

Keywords. \textit{trans}-2-(2'-Aminocyclohexyloxy)acetic acid; \textit{trans}-2-(2'-Azidocyclohexyloxy)acetic acid; \textit{trans}-2'-Functionalized 2-cyclohexyloxyacetic acid.

Introduction

In the course of our investigations on the synthesis of potential immunomodulators related to muramyl dipeptide (MDP) [1, 2], \textit{trans}-2-(2'-aminocyclohexyloxy)acetic acid (4) and its synthetic precursor \textit{trans}-2-(2'-azidocyclohexyloxy)acetic acid (1) were needed as key intermediates for the synthesis of some model compounds. Since both carboxylic acids have been unknown so far, we report here our approaches to the synthesis of 1 and 4 and the preparation of some derivatives of the title compounds.

Results and Discussion

We have shown previously [3] that \textit{trans}-2-(2'-azidocyclohexyloxy)acetic acid (1) can be prepared by the alkylation of \textit{trans}-2-azidocyclohexanol [6] with chloroacetic acid and converted \textit{via} its methyl ester 2 into \textit{trans}-octahydro-2\textit{H}-1,4-benzoxazin-3-one (3). However, 1 has not been characterized before, since it could not be
Scheme 1. i: MeOH, H$_2$SO$_4$; ii: NaOH/dioxane; iii: SOCl$_2$; iv: NH$_3$/dioxane; v: L-Ala-OMe-HCl/dioxane; vi: SnCl$_2$-2H$_2$O/MeOH; vii: TsCl, Et$_3$N/dichloromethane; viii: HCl/H$_2$O; ix: Ac$_2$O/NaOH; x: RSO$_2$Cl/NaOH/ether; xi: PhNCO/NaOH; xii: PhNCS/NaOEt; xiii: BOC$_2$O, Et$_3$N/EtOAc