Characterization of the Structure of \textit{tert}-butyl[1-hydroxy-2-methyl-3-(1H-1,2,4-triazol-1-yl)]propan-2-ylcarbamate Using 2D Heteronuclear NMR Experiments

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Abstract

The alkylation of 1H-1,2,4-triazole with an O-tosyloxazoline derivative, followed by an oxazoline ring-opening reaction and protection of amine function, leads normally to obtain two regioisomers of \(\beta\)-aminoalcohols. After purification by column chromatography of the crude reaction product, only a single product is obtained. Hence, there is need of its identification by spectroscopic study.

Keywords

Oxazoline, 1H-1,2,4-triazole, \(\beta\)-aminoalcohol, 2D heteronuclear NMR experiments

Introduction

Triazoles constitute an important class of biologically active heterocyclic compounds that have received a great deal of attention since their discovery. Diverse compounds derived from 1,2,4-triazoles have a wide spectrum activities, including antimicrobial \cite{[1,2]} and antibacterial properties \cite{[3,4]}, human antifungal agents \cite{[5]}, anticancer agents \cite{[6]}, antiviral \cite{[7]}, antitumor activity \cite{[8]} and in agricultural science as potent fungicides, herbicides and insecticides \cite{[9,10]}. Amino acids containing the 1,2,4-triazole moiety and their derivatives represent a well-known group of organic compounds also presenting biological activity. Thus \(\beta-(1,2,4\text{-triazol-1-yl})\text{-L-alanine}\) is known as an important metabolite in plants of the fungicide myclobutanil \cite{[11-13]} and \(\beta-(3\text{-amino-1,2,4\text{-triazol-1-yl})\text{-L-alanine}\) is a metabolite of the weed killer 3-amino-1,2,4-triazole \cite{[14]}.

Materials and Methods

NMR spectra (\(1H, 13C\) and \(15N\)) were recorded on a Bruker AM 300 (operating at 300.13 MHz for \(1H\), at 75.47 MHz for \(13C\) and at 30.41 MHz for \(15N\)) spectrometer (Centre Universitaire Régional d’Interface, Fez-Morocco). NMR data are listed in ppm and are reported relative to tetra-methylsilane (\(1H, 13C\)).

Discussion

It is reported that afforded the corresponding 1- and 4-alkylated isomers, with prevalence of the N\(_1\)-isomer \cite{[15-17]}. Reaction of 1H-1,2,4-triazole with 1 and K\(_2\)CO\(_3\), was carried out in the presence of a catalytic amount of tetrabutylammonium bromide in \(N,N\)dimethylformamide at 120\(^\circ\)C for 12 hours. The previous reaction stage is followed by an oxazoline ring-opening reaction carried out in acidic medium. The aminoalcohol derivative 2, which is the aim of this paper, is obtained after addition of tert-butoxycarbonyl anhydride Boc to the intermediate product in a mixture of water/dioxane (1/2) at (0 < T < 5\(^\circ\)C) in the presence of triethylamine \cite{[18]}. Its structure was established on the basis of NMR spectroscopy (\(1H, 13C\) and \(15N\)), in addition to MS data and elemental analysis.

The definite assignment the chemical shifts of protons, carbons and nitrogens of compound 2 are shown in table 1 and table 2 (Figure 1, 2).

![Figure 1](image-url)

![Figure 2](image-url)
This interaction $^1$H-$^15$N has allowed us to make the following observations:

- A signal at 93.29 ppm attributed to the carbamate nitrogen N-1: correlation between CH$_3$, CH$_2$-triazole and the amidic nitrogen.
- A signal at 214.54 ppm attributed to the N-7 of the 1,2,4-triazole ring: correlation between the two triazole protons, CH$_2$-triazole and N-7 nitrogen at position 1 of the 1,2,4-triazole ring.
- A signal at 251.97 ppm attributed to the N-10 of the 1,2,4-triazole ring: interaction between the two triazole protons and the N-10 located in the position 4 of the 1,2,4-triazole ring.
- A signal at 299.12 ppm attributed to N-8 of the 1,2,4-triazole ring: interaction between CH$_3$-triazole, triazole proton H-9 and N-8 at position 2 of the 1,2,4-triazole ring.

Further, the analysis of $^1$H-$^15$N HMBC spectrum of compound 2 confirms that the nucleophilic substitution reaction of 1,2,4-triazole...
Figure 2: Heteronuclear $^1$H-$^{13}$C 2D spectrum for compound 2.

Figure 3: $^{15}$N NMR spectrum of the compound 2.

Figure 4A: $^1$H – $^{15}$N HSQC spectrum for compound 2; (B): $^1$H-$^{15}$N HMBC spectrum for compound 2.

and O-tosyloxazoline derivative 1 is carried out on the nitrogen in position 1 of the 1,2,4-triazole ring and its structure has been clearly identified (Figure 4).

References


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