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

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Abstract

The alkylation of 1*H*-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 β-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, 1*H*-1,2,4-triazole, β-aminoalcohol, 2D heteronuclear NMR experiments

Introduction

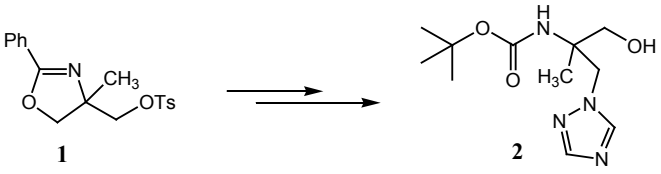
Triazoles constitute an important class of biologically active heterocyclic compounds that have received a great deal of attention since their discovery. Diverse compounds derived from 1,2,4-triazoles have a wide spectrum activities, including antimicrobial [1,2] and antibacterial properties [3,4], human antifungal agents [5], anticancer agents [6], antiviral [7], antitumor activity [8] and in agricultural science as potent fungicides, herbicides and insecticides [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 β-(1,2,4-triazol-1-yl)-L-alanine is known as an important metabolite in plants of the fungicide myclobutanil [11-13] and β-(3-amino-1,2,4-triazol-1-yl)-L-alanine is a metabolite of the weed killer 3-amino-1,2,4-triazole [14].

Materials and Methods

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

Discussion

It is reported that afforded the corresponding 1- and 4-alkylated isomers, with prevalence of the N_1-isomer [15-17]. Reaction of 1*H*-1,2,4-triazole with **1** and K_2CO_3, was carried out in the presence of a catalytic amount of tetrabutylammonium bromide in *N*,*N*'-dimethylformamide at 120°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°C) in the presence of triethylamine [18]. Its structure was established on the basis of NMR spectroscopy (^{1}H, ^{13}C and ^{15}N), 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,

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Table 1: ^{1}H (300 MHz) and ^{13}C (75.47 MHz) NMR spectral data for **2** in DMSO-*d6*, including results obtained by homonuclear 2D shift-correlated **^{1}H COSY** and heteronuclear 2D shift-correlated **HMQC** ($^{1}J_{CH}$)[a]. Chemical shifts (δ, ppm) and coupling constants (*J*, Hz, in parenthesis)[b].

Position	δ_H	δ_C	Correlation ^{1}H-^{1}H	Correlation ^{1}H-^{13}C
(NH) **1**	6.29 (s)	-	1-H	-
2	-	56.66	-	-
3	3.35, 3.45 (AB (2dd), 10.8; 5.6)	64.85	H^1-3, H^2-3, O-H	H^1-3, H^2-3, C-3
(OH) **4**	4.92 (t, 5.6)	-	O-H, H^1-3, H^2-3	-
5	1.18 (s)	20.43	H^1-5, H^2-5, H^3-5	$H^{1,2,3}$-5 ; C-5
6	4.35, 4.51 (AB, 14)	51.74	H^1-6, H^2-6	H^1-6, H^2-6, C-6
9	7.95 (s)	151.61	$H^{3'triazole}$ -9	$H^{3'triazole}$ -9, C-9
11	8.23 (s)	145.24	$H^{5'\text{-triazole}}$ -11	$H^{5'\text{-triazole}}$ -11, C-11
12	-	154.97	-	-
14	-	78.43	-	-
15; 17; 18	1.39 (s)	28.68	$H^{1,2,3}$-15 $H^{1,2,3}$-17 $H^{1,2,3}$-18	$H^{1,2,3}$-15 ; C-15 $H^{1,2,3}$-17; C-17 $H^{1,2,3}$-18 ; C-18

[a]Correlation from C to the indicated hydrogens.

[b]Chemical shifts and coupling constants (*J*) obtained of 1D ^{1}H-NMR spectrum.

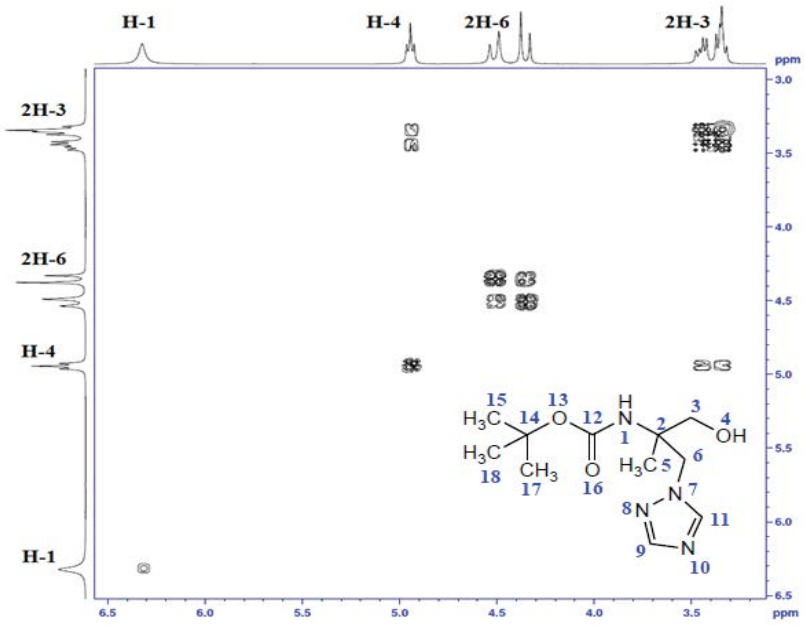

Figure 1: Homonuclear ^{1}H-^{1}H 2D spectrum for compound **2** between 3 and 6.5 ppm.

Table 2: Listing of ^{15}N (400 MHz) NMR spectral data for **2** inDMSO-*d6*, including results obtained by heteronuclear single quantum coherence shift-correlated (**HSQC**) and heteronuclear multiple bond coherence shift-correlated (**HMBC**).

Position	δ_H	δ_N	Correlation ^{1}H-^{15}N
(NH) **1**	7.02 (s)	93.29	H-1,N-1
5	1.24 (s)	93.29	$H^{1,2,3}$-5, N-1
6	4.39, 4.83 (AB, 14)	93.29	$H^{1,2}$-6, N-1
		214.54	$H^{1,2}$-6, N-7
		299.12	$H^{1,2}$-6, N-8
9	7.96 (s)	214.54	$H^{3'triazole}$-9, N-7
		251.97	$H^{3'triazole}$-9, N-10
		299.12	$H^{3'triazole}$-9, N-8
11	8.20 (s)	214.54	$H^{5'\text{-triazole}}$-11, N-7
		251.97	$H^{5'\text{-triazole}}$-11, N-10

Chemical shifts (δ, ppm) and coupling constants (*J*, Hz, in parenthesis) obtained of 1D ^{1}H-NMR spectrum.

^{15}N NMR spectrum of the compound **2** shows four signals corresponding to four nitrogen atoms and assigning each signal to its corresponding nitrogen atom is carried out based mainly on the spectral data ^{1}H-^{15}N HMBC (Figure 3).

Figure 2 and Figure 3).

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_2-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

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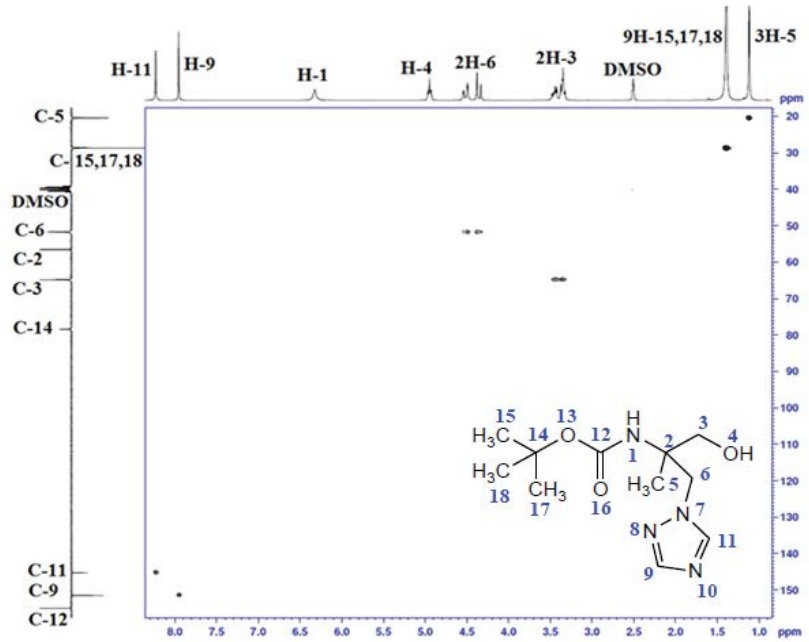

Figure 2: Heteronuclear ^{1}H-^{13}C 2D spectrum for compound **2**.

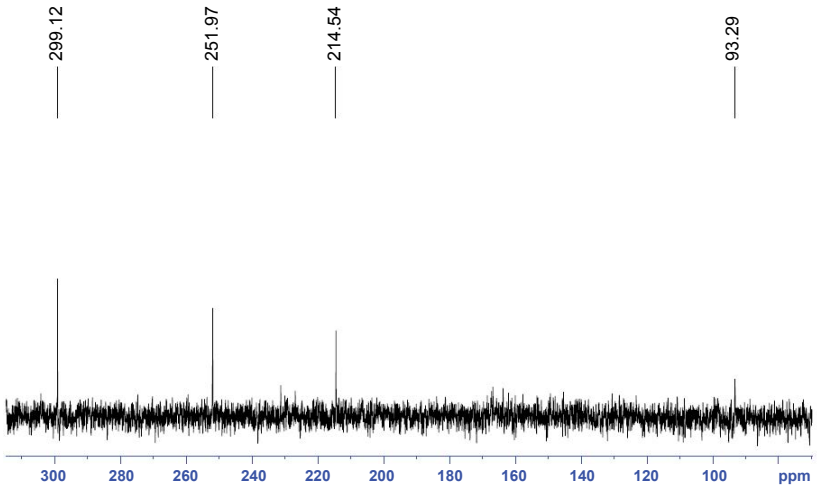

Figure 3: ^{15}N NMR spectrum of the compound **2**.

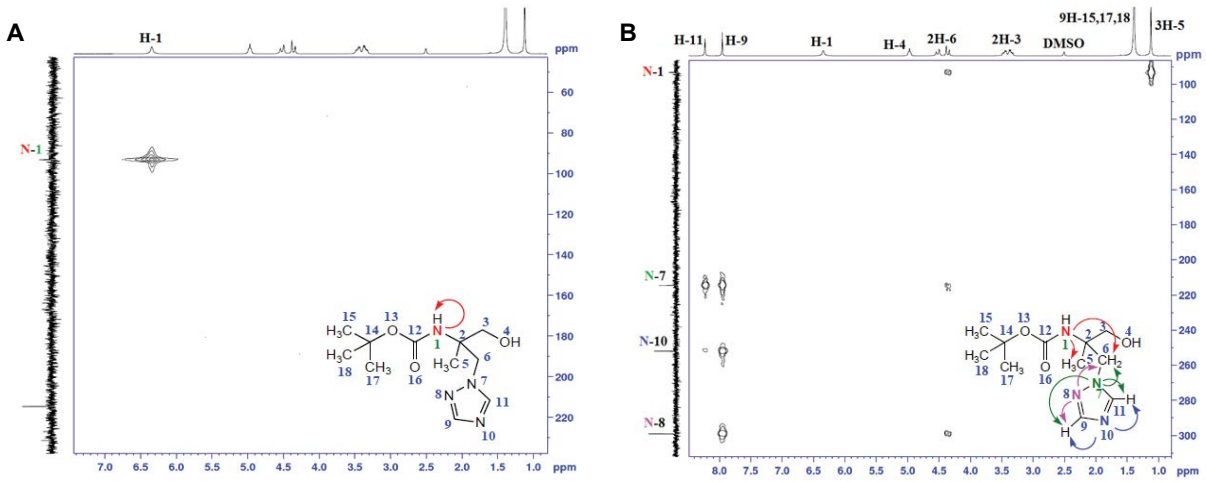

Figure 4A: ^{1}H – ^{15}N HSQC spectrum for compound **2**; (**B**): ^{1}H-^{15}N HMBC spectrum for compound **2**.

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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

1. Xu W, Song B, Bhadury P, Song Y, Hu D (2010) Synthesis and crystal structure of novel sulfone derivatives containing 1,2,4-triazole moieties. Molecules 15: 766-779.
2. Karabasanagouda T, Adhikari AV, Shetty NS (2007) Synthesis and antimicrobial activities of some novel 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles and 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazines carrying thioalkyl and sulphonyl phenoxy moieties. Eur J Med Chem 42: 521-529.
3. Tehranchian S, Akbarzadeh T, Fazeli MR, Jamalifar H, Shafiee A (2005) Synthesis and antibacterial activity of 1-[1,2,4-triazol-3-yl] and 1-[1,3,4-thiadiazol-2-yl]-3-methylthio-6,7-dihydrobenzo[c]thiophen-4(5H) ones. Bioorg Med Chem Lett 15: 1023-1025.
4. Foroumadi A, Soltani F, Moshafi MH, Ashraf-Askari R (2003) Synthesis and in vitro antibacterial activity of some N-(5-aryl-1,3,4-thiadiazole-2-yl)piperazinyl quinolone derivatives. Farmaco 58: 1023-1028.
5. Chen Q, Zhu XL, Jiang LL, Liu ZM, Yang GF (2008) Synthesis, antifungal activity and CoMFA analysis of novel 1,2,4-triazolo[1,5-a]pyrimidine derivatives. Eur J Med Chem 43: 595-603.
6. Holla BS, Poojary KN, Rao BS, Shivananda MK (2002) New bis-aminomercaptotriazoles and bis-triazolothiadiazoles as possible anticancer agents. Eur J Med Chem 37: 511-517.
7. Al-Soud YA, Al-Dweri MN, Al-Masoudi NA (2004) Synthesis, antitumor and antiviral properties of some 1,2,4-triazole derivatives. Farmaco 59: 775-783.
8. DemirbaÅŸ N, Ugurluoglu R, DemirbaÅŸ A (2002) Synthesis of 3-alkyl(aryl)-4-alkylidenamino-4,5-dihydro-1H-1,2,4-triazol-5-ones and 3-alkyl-4-alkylamino-4,5-dihydro-1H-1,2,4-triazol-5-ones as antitumor agents. Bioorg Med Chem 10: 3717-3723.
9. Crispino GA, Goudar JS (2001) Process for the preparation of a triazolinone herbicide. US Pat 6268506 B1.
10. Song BA, Hu DY, Zheng S, Huang RM, Yang S, et al. (2001) Synthesis and bioactivity of phosphorodithioate compounds containing 1,2,4-triazole. Chin J Org Chem 21: 524-529.
11. Arnold M, Evrard D, Leander J, Lodge D, Schoep D, et al. (1993) Tetrazole amino acids as competitive NMDA antagonists. Bioorg Med Chem Lett 3: 43-48.
12. Ebert B, Lenz S, Brehm L, Bregnedal P, Hansen JJ, et al. (1994) Resolution, absolute stereochemistry, and pharmacology of the S-(+)- and R-(-)-isomers of the apparent partial AMPA receptor agonist (R,S)-2-amino-3-(3-hydroxy-5-phenylisoxazol-4-yl)propionic acid [(R,S)-APPA]. J Med Chem 37: 878-884.
13. Ikegami F, Murakoshi I (1994) Enzymic synthesis of non-protein b-substituted alanines and some higher homologues in plants. Phytochemistry 35: 1089-1104.
14. Dunnill P, Fowden L (1965) The amino acids of seeds of the Cucurbitaceae. Phytochemistry 4: 933-944.
15. Bulger PG, Cotterell IF, Cowden CJ, Davies AJ, Dolling UH (2000) An investigation into the alkylation of 1,2,4-triazole. Tetrahedron Lett 41: 1297-1301.
16. Boukallaba K, Elachqar A, El Hallaoui A, Alami A, El Hajji S, et al. (2006) Synthesis of new alpha-heterocyclic alpha-aminophosphonates. Phosphor Sulfur Silicon 108: 819-823.
17. Bentama A, El Hadrami EM, El Hallaoui A, Elachqar A, Lavergne JP, et al. (2003) Synthesis of new alpha-heterocyclic alpha-aminoesters. Amino Acids 24: 423-426.
18. Aouine Y, Faraj H, Alami A, El-Hallaoui A, Elachqar A, et al. (2011) Simple and efficient synthesis of racemic 2-(tert-butoxycarbon-ylamino)-2-methyl-3-(1H-1,2,4-triazol-1-yl)propanoic acid, a new derivative of Î²-(1,2,4-triazol-1-yl) alanine. Molecules 16: 3380-3390.

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