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SYNTHESIS OF NEW BENZOTRIAZOLE DERIVATIVES

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1H-1,2,3-Benzotriazole convert a vide variety of N-hydroxymethyl amides into their N-Š1-(benzotriazol-1-yl)methyl] amides in very good yield. Synthesized products were confirmed by a combination of elemental analysis, ^{1}H NMR and IR spectral data studies.

Key words: benzotriazole derivatives; amidomethylation; amidomethyl benzotriazoles

INTRODUCTION

Mannich reaction (aminomethylation) of benzimidazole and benzotriazole or substitued benzimidazoles and benzotriazoles with formaldehyde and amines [1–8] is a well known process.

In addition, N-hydroxymethyl derivatives of benzimidazole and benzotriazole give corresponding Mannich bases under the influence of aliphatic or aromatic amines [8, 9–11].

As aminomethylbenzimidazoles or benzotriazoles posses biological [2–7] and corrosion-inhibition activity [1, 8, 9] they can by used as additives in greasing oils [12–15] or in photopolymeryzing paints for improving adhesion [16].

As a part of our programme directed towards the development of new simple procedure for the synthesis of condensed benzimidazole and benzotriazole derivatives, the object of the present work was to examine reactions of 1H-1,2,3-benzotriazole with amino model substances containing CO group such as amides. Thus, the N-hydroxymethylbenzamide was treated with benzotriazole in anhydrous dioxane to give a 90% yield of N-[1-(benzotriazol-1-yl)methyl] benzamide. For the preparation of the other 1-amidomethylbenzotriazoles a number of N-hydroxymethyl amides were used.

EXPERIMENTAL

IR spectra were obtained with a Perkin-Elmer 297 spectrophotometer. The ^{1}H-(250 MHz) NMR spectra were recorded with a Bruker AC 250 E spectrometer with TMS as internal standard.

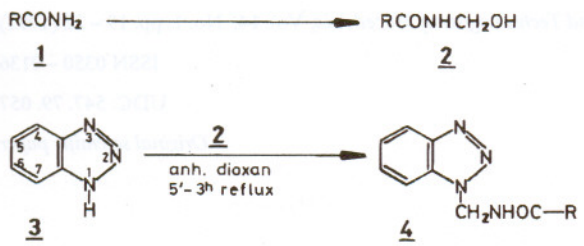
Reactions of 1H-1,2,3-benzotriazole with N-hydroxymethyl amides: General procedure. A mixture of a corresponding methylol (10 mmol) and the benzotriazole (10 mmol) in 10–15 cm^3 anhydrous dioxan (1–2 drops of hydrochloric acid) was refluxed for some time: most of the products (Table I, 4a–f) precipitated during short refluxing period.

In two cases (Table I, 4g–h) the derivatives were isolated when the reaction mixture with stirring is poured directly on ice-water. All the 1-amidomethylbenzotriazoles were purified by repeated recrystalization.

RESULTS AND DISCUSSION

Benzotriazole (3) in reactions with N-methylolamides (2) produces the corresponding N-[1-(benzotriazol-1-yl)methyl] amides (4) (Scheme 1), that were not previously investigated. These compounds are of considerable synthetic interest as substances with potential biological activity.

This method was reported earlier [10, 11] describing the condensation of benzimidazole with N-methylolamides. Thus, refluxing benzotriazole with equimolecular amounts of each of methylols (which were obtained by hydroxymethylation of amides) af-



	R		R
4a	C_6H_5	4e	$p\text{-}NO_2C_6H_4$
4b	$o\text{-}ClC_6H_4$	4f	$CH_2C_6H_5$
4c	$p\text{-}ClC_6H_4$	4g	$o\text{-}FC_6H_4$
4d	$p\text{-}CH_3C_6H_4$	4h	C_5H_4N

Scheme 1

forded 4. Condensation of 2 with 3 in anhydrous dioxan in the presence or catalytical amount of hydrochloric acid gave 4 as the only isolable product.

The N-hydroxymethyl amides (2) used in these reactions were conviently prepared in high yield from the corresponding amides (Table I): benzamide (a), o- (b) and p-chlorobenzamide (c), p-methylbenzamide (d), p-nitrobenzamide (e), phenacetamide (f), o-fluorobenzamide (g), nicotinamide (h) and 35% aqueous formaldehyde solution, usually in the presence of potassium carbonate using standard procedure; the amides (except nicotinamide) were prepared from corresponding chlorides and aqueous amonia [17, 18].

N-[1-(benzotriazol-1-yl)methyl] amides (Table I) have easily been made and readily purified. In many cases they precipitated from reaction mixture (reaction time was dependent upon the structure of the N-methylolamide) in a high state of purity as well as in a good yield. The melting point of each compound was substantially different from that of the initial reagent.

The structure of reaction products were established by elemental analysis, IR and ^1H NMR spectra. The IR spectra of 4 showed ν(NH) at 3365–3270 cm^{-1}, ν(CO) at 1685–1665 cm^{-1} but do not show the band at 1050 cm^{-1} atributable to the C–OH (CH_2OH group); this band is always strong in the spectra of all methylols.

Table I

Physical and spectroscopic data of N-[1-(benzotriazol-1-yl)methyl]amides [4]

4	R	Formula (M_r)	Yield (%)	M.p. (°C)	Found (Requiered) / % C	H	N	IR ν (NH), ν(CO)	^1H NMR δ/ppm
a	C_6H_5	$C_{14}H_{12}N_4O$ (252.132)	90	165–166	66.72 (66.64)	4.70 (4.79)	22.39 (22.21)	3325, 1673	6.33 (N $\underline{CH_2}$), 7.32–7.90 (5H, aromatics), 7.37 (H-5), 7.52 (H-6), 7.99 (H-4), 8.05 (H-7).
b	$o\text{-}ClC_6H_4$	$C14H_{11}ClN_4O$ (286.718)	70	143–144	58.50 (58.62)	4.02 (3.83)	19.45 (19.54)	3312, 1684	6.19 (N$\underline{CH_2}$), 7.38–7.47 (o-ClC_6H_4), 7.44 and 7.61 (H-5 and H-6), 8.03 and 8.06 (H-7 and H-4).
c	$p\text{-}ClC_6H_4$	$C14H_{11}ClN_4O$ (286.718)	88	222–223	58.72 (58.62)	3.94 (3.83)	19.62 (19.54)	3318, 1672	6.23 (N$\underline{CH_2}$), 7.40–7.92 (4H, p-ClC_6H_4), 7.38 and 7.52 (H-5 and H-6), 7.96 and 8.05 (H-4 and H-7), 9.89 (NH).
d	$p\text{-}CH_3C_6H_4$	$C_{15}H_{14}N_4O$ (266.149)	92	172–173	67.58 (67.64)	5.25 (5.30)	21.10 (21.04)	3338, 1667	2.38 (tolyl CH_3), 6.33 (N $\underline{CH_2}$), 7.38 and 7.53 (H-5 and H-6), 8.03 (2H, H-7 and H-4).
e	$p\text{-}NO_2C_6H_4$	$C14H_{11}N_5O_3$ (297.126)	98	< 250	56.50 (56.55)	3.70 (3.73)	23.40 (23.56)	3270, 1680	6.24 (N $\underline{CH_2}$), 7.42 and 7.60 (H-5 and H-6), 8.04 (2H, H-7 and H-4), 8.09-8.31 (4H, p-$NO_2C_6H_4$), 10.24 (N$\underline{H}$)
f	$CH_2C_6H_5$	$C_{15}H_{14}N_4O$ (266.149)	85	142–143	67.50 (67.64)	5.10 (5.30)	20.90 (21.04)	3290, 1678	3.62 (benzyl CH_2), 6.04 (N $\underline{CH_2}$), 6.81 (N$\underline{H}$), 7.17-7.29 (5H, C_6H_5), 7.40 and 7.52 (H-5 and H-6), 7.93 and 8.02 (H-7 and H-4).
g	$o\text{-}FC_6H_4$	$C14H_{11}FN_4O$ (270.124)	65	135–136	62.39 (62.19)	4.20 (4.10)	20.65 (20.74)	3364, 1663	6.35 (N $\underline{CH_2}$), 7.03–7.56 (3H, o-FC_6H_4), 7.36 (H-5), 7.50 (H-6), 7.99 (N$\underline{H}$), 8.00 (H-4), 8.01 (H-7), 8.10 (1H, aromatic).
h	C_5H_4N	$C_{13}H_{11}N_5O$ (253.194)	70	183–184	61.58 (61.63)	4.25 (4.38)	27.78 (27.66)	3320, 1673	6.36 (N $\underline{CH_2}$), 7.39 (H-5), 7.54 (H-6), 8.01 (H-4), 8.05 (H-7), 7.40, 8.29, 8.72, 9.19 four nicotinics H. 8.13 (N$\underline{H}$).

As known, the reactions of alkylation, acylation and aminomethylation of benzotriazole predominantly give products at the N-1 position although there are a few reports of the N-2 alkylation [19, 20].

Thus, starting from benzotriazole one could expect that the products should be the corresponding N-1 benzotriazole derivative (Scheme 1) and in our discussion this has been assumed. However, it has been known from literature [3] that aminomethylbenzotriazoles, prepared by a Mannich reaction (from dialkylamines), exist in solution in an equilibrium between N-1 and N-2 substituted forms although the major component is N-1 isomer (Scheme 2).

Scheme 2

However, N-1 and N-2 substituted benzotriazoles can be distiguished by a ^{1}H NMR spectroscopy [21, 22].

The aromatic region of the spectra of all amidomethylbenzotriazoles (4) consists of two major multiplets with spliting pattern expected for the N-1 substituted benzotriazoles; one centred at ca. 7.5 p.p.m. (two triplets H-5 and H-6) and second at about 8 p.p.m. (two dublets H-7 and H-4). This argument suggested that the our new compounds existed mainly in the form I (Table II).

Table II

H-1 NMR data of compound 4a–h (benzotriazole patern only)

Compound /solvent	Aromatic proton resonances (δ)			
4a/$CDCl_3$	7.37	7.52	7.99	8.05
4b/DMSO	7.44	7.61	8.03	8.06
4c/$CDCl_3$	7.38	7.52	7.96	8.05
4d/$CDCl_3$	7.38	7.53	8.03	8.03
4e/DMSO	7.42	7.60	8.04	8.04
4f/$CDCl_3$	7.40	7.52	7.93	8.02
4g/$CDCl_3$	7.36	7.50	8.00	8.01
4h/$CDCl_3$	7.39	7.54	8.01	8.05

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Резиме

СИНТЕЗА НА НОВИ БЕНЗОТРИАЗОЛНИ ДЕРИВАТИ

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Клучни зборови: бензотриазолни деривати; амидометилирање; амидометилбензотриазоли.

Со реакција на поголем број N-хидроксиметиламиди со бензотриазол настануваат N-[1-(бензотриазол-1-ил)метил]амиди во многу добри приноси. Структурата на новосинтетизираните соединенија е дискутирана врз основа на IR и ^{1}H NMR спектралните податоци.