

Synthesis of Some New 1,2,4-Triazoles Derived from 2-Mercaptobenzimidazole

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Date of acceptance 3/8/2008

Abstract:

New 1,2,4-triazole derivatives of 2-mercaptobenzimidazole (MB) are reported. Ethyl (benzimidazole-2-yl thio) acetate (1) has been prepared by condensing 2-mercaptobenzimidazole with ethylchloroacetate. The ester (1) on reacting with hydrazine hydrate gave the corresponding acetohydrazide(2) which was reacted separately with phenylisocyanate and phenylisothiocyanate, followed by ring closure in an alkaline medium giving 3-[(benzimidazole-2-yl thio) methyl]-4-phenyl-1,2,4-triazole-5-ol and 3-[(benzimidazole-2-yl thio) methyl]-4-phenyl-1,2,4-triazole-5-thiol respectively (6,7). Reaction of acetohydrazide (2) with CS₂ and ethanol/KOH, gave dithiocarbamate salt (8). Cyclization of (8) with hydrazine hydrate gave 3-[(benzimidazole-2-yl thio) methyl]-4-amino-1,2,4-triazole-5-thiol (9).

Furthermore, new Schiff bases (3a-e) were prepared through the reaction of the acetohydrazide (2) with aromatic aldehydes. The prepared compounds were identified by spectral methods FTIR, UV. Measurements of some physical properties and some specific reactions, were carried out.

Introduction

Benzimidazole nucleus play an important role in antimicrobial activity. Number of benzimidazole derivatives were synthesized and evaluated as antifungal, antibacterial[1-4], and as potent anti-HIV agents[5]. In industry, 2-mercaptobenzimidazole is used as antioxidant in the manufacture of industrial rubber[6].

Furthermore, the 1,2,4-triazole compounds are considered as interesting five membered heterocycles since possess important pharmacological activities such as fungicidal, insecticidal, antimicrobial agents and anti-inflammatory[7-8] also as plant growth regulating[9]. Keeping these facts in view, we have synthesized new

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1,2,4-triazole derivatives of 2-mercaptobenzimidazole (6, 7 and 9) and new Schiff bases (3a-e).

Materials and Methods:

Melting points were determined on Gallenkamp melting point apparatus and are uncorrected.

FTIR spectra were recorded on Shimadzu FTIR 8400 spectrophotometer as KBr disc.

U.V spectra were recorded on Shimadzu UV-VIS recorder.

Starting chemical compounds were obtained from Fluka or Aldrich. And the physical properties of the products are listed in table (1).

Preparation of Ethyl(benzimidazole-2-yl thio) acetate [1]

Ethyle chloroacetate (10.6mL, 0.1mol), was added dropwise to a stirred solution of 2-mercaptobenzimidazole (15g, 0.1mol), and anhydrous potassium carbonate (13.8g, 0.1mol) in absolute ethanol (100mL). The reaction mixture was refluxed for 6 hrs. filtered and the solvent was evaporated. The crude product was recrystallized from ethanol to give a white crystals of the ester [1].

Preparation of (Benzimidazole-2-yl thio) acetohydrazide [2]

A mixture of ester [1] (11.8g, 0.05mol) and excess 98% hydrazine hydrate (10mL, 0.2mol) were refluxed for 4 hrs. The reaction mixture was poured in to ice water. The separated precipitate was filtered and recrystallized from ethanol to give a white crystals of the hydrazide [2].

Schiff Base Derivatives of (Benzimidazole-2-yl thio) acetohydrazide [3a-e]

To a hot stirred solution of the hydrazide [2] (0.22g, 0.001 mol) in methanol (5mL), appropriate aromatic aldehyde (0.001mol) was added. The reaction mixture was heated to 70°C for (1-3 hrs.). The separated solid was filtered and recrystallized from ethanol.

1-[Benzimidazole-2-yl thio) methyl carbonyl]-4-phenyl semicarbazide or thiosemicarbazide [4,5]

Ethanolic solution of the hydrazide [2] (2.2g, 0.01mol) and phenyl isocyanate (1.08mL, 0.01 mol) or phenyl isothiocyanate (1.2mL, 0.01mol) was stirred at room temperature overnight. The precipitate

was filtered, washed with ethanol, to get compounds [4,5] respectively.

3-[(Benzimidazole-2-yl thio) methyl]-4-phenyl-1,2,4-triazole-5-ol or -5-thiol [6,7]

The semicarbazide [4] (3.4g, 0.01mol) or thiosemicarbazide [5] (3.57g, 0.01mol) was refluxed in 10% sodium hydroxide solution (25 mL) for 6 hrs., cooled, poured onto ice water, stirred and filtered, to gave [6,7] compounds.

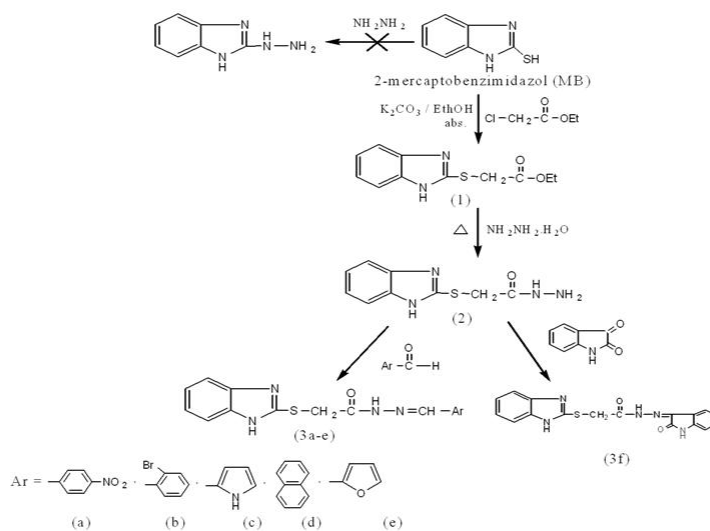
Potassium-3-[(benzimidazole-2-yl thio) methyl] dithiocarbazate [8]

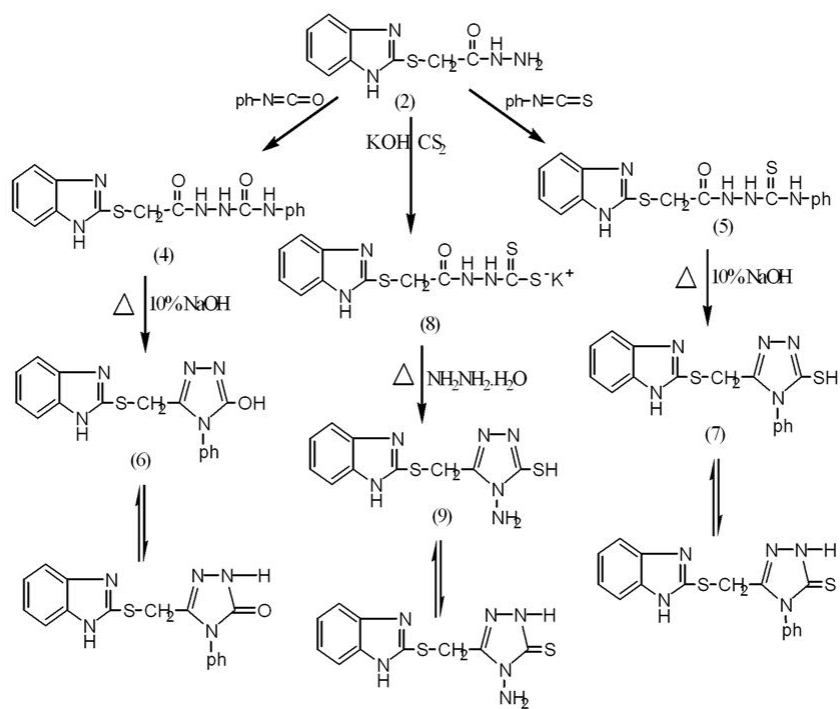
To a stirred ethanolic solution of KOH (1.68g, 0.03mol) in (20 mL), hydrazide [2] (2.2g, 0.01mol) then CS₂ (1.8mL, 0.03mol) were added slowly. The reaction mixture was stirred

overnight. Dry ether (20mL) was added and the yellow ppt. was filtered, washed with ether and vacuum dried. The salt [8] was obtained in almost quantitative yield and was employed in the next step without further purification.

3-[(Benzimidazole-2-yl thio) methyl]-4-amino-1,2,4-triazole-5-thiol [9]

A suspension of potassium salt [8] (0.01mol) in excess hydrazine hydrate (5mL) was refluxed until the evolution of H₂S was ceased; during reflux the colour of the reaction mixture changed to green and a homogenous solution resulted. After cooling, the reaction mixture was acidified with 10%HCl to yield a white precipitate. Physical properties are listed in Table(1).



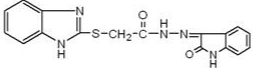
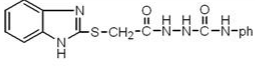
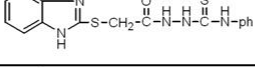
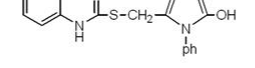
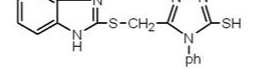
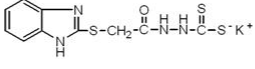
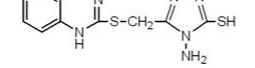




Scheme (2)

Table (1): Physical properties of the prepared compounds

Comp. no.	Molecular Formula	Comp. Structure	m.p. °C	Yield %	Colour	Recryst. solvents
1	C ₁₁ H ₁₂ N ₂ O ₂ S		100	88	White	Ethanol
2	C ₉ H ₁₀ N ₄ OS		230	68	White	Ethanol/water
3	C ₁₀ H ₉ N ₄ OSAr					
3a	C ₁₆ H ₁₃ N ₅ O ₃ S	Ar =	288-290	85	Red	Methanol
3b	C ₁₆ H ₁₃ N ₄ OSBr	Ar =	245-250	46	Pale yellow	Methanol
3c	C ₁₄ H ₁₃ N ₅ OS	Ar =	145-148	79	Deep violete	Methanol

3d	C ₂₀ H ₁₆ N ₄ OS	Ar = 	256d.	52	Deep yellow	Methanol
3e	C ₁₄ H ₁₂ N ₄ O ₂ S	Ar = 	224-226	83	Brown	Methanol
3f	C ₁₈ H ₁₅ N ₃ O ₂ S		326-328	65	Orange	Methanol
4	C ₁₆ H ₁₅ N ₃ O ₂ S		154d.	80	White	Ethanol
5	C ₁₆ H ₁₅ N ₃ O ₂ S ₂		145d.	82	White	Ethanol
6	C ₁₆ H ₁₃ N ₃ OS		172d.	69	White	Chloroform
7	C ₁₆ H ₁₃ N ₃ S ₂		180d.	77	Pink	Ethanol/water
8	C ₁₆ H ₉ N ₄ OS ₂ K		>350	90	White	-
9	C ₁₆ H ₁₆ N ₆ S ₂		310	64	White	Ethanol/water

Results and Discussion

In the present work the synthesis of some new 1,2,4-triazoles and Schiff base derivatives were achieved from 2-mercaptobenzimidazole, the synthetic route used is shown in schemes (1 and 2).

Ethyl(benzimidazole - 2 - yl thio) acetate [1] was prepared by condensing 2 - mercaptobenzimidazole with ethylchloro acetate. The FTIR spectrum indicated the presence of a $\nu_{C=O}$ ester (1743 cm^{-1}) and ν_{S-CH_2} (1683 cm^{-1})[10], also hydroxamic acid test improved the presence of ester group. The UV spectrum show a band at λ_{max} (287 nm), improving that the

reaction was carried on the S not on N in the 2-mercaptobenzimidazole ring[11].

The ester [1] through reaction with hydrazine hydrate, gave (benzimidazole-2-yl thio) acetohydrazide [2]. FTIR spectrum showed a shift in the $\nu_{C=O}$ band from (1743 cm^{-1}) to (1666 cm^{-1}) amide I. Absorption at (3317 , 3278 and 3155 cm^{-1}) could be attributed to $-NH_2$ group asym. and sym., and $-NH$ group stretching band respectively.

The Schiff bases (3a-f) were obtained in good yield through the reaction of hydrazide [2] with different aromatic aldehydes (scheme 1). The

structured of all the synthesized compounds were confirmed by FTIR and UV spectral. UV spectrums of the Schiff bases (3a-f) show a shift of band to higher λ_{\max} (red shift) because of the chromophore groups on aromatic ring. The characteristic absorption bands are listed in (Table 2) and the FTIR spectra of (3f) is shown in Figure (1).

The hydrazide [2] was converted to semicarbazide [4] and thiosemicarbazide [5] by the reaction with phenylisocyanate or phenylisothiocyanate at room temperature (scheme 2). FTIR spectral data showed absorption at (1695 cm^{-1}) $\nu\text{C}=\text{O}$ in semicarbazide [4] and (1234 cm^{-1}) $\nu\text{C}=\text{S}$ in thiosemicarbazide [5], also showed the out-of-plane C-H bending at ~ 750 and 690 cm^{-1} .

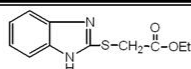
Treatment of compounds [4] and [5] with 10% sodium hydroxide solution afford intramolecular cyclization to give the 3-[(benzimidazole-2-yl thio)]-4-phenyl-1,2,4-triazole-5-ol [6] and 3-[(benzimidazole-2-yl thio)methyl]-4-phenyl-1,2,4-triazole-5-thiol [7] respectively. The structures of hydroxyl-triazole [6] and thio-triazole [7] were identified from FTIR and UV. The FTIR spectrum of [6] showed $\nu\text{O}-$

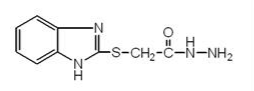
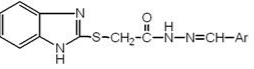
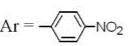
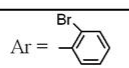
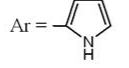
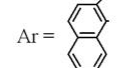
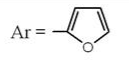
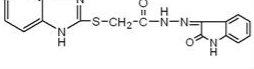
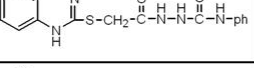
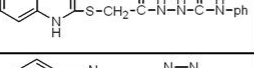
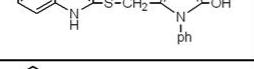
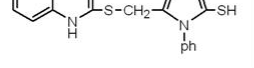
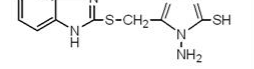
H vibration at (3448 cm^{-1}) broad and $\nu\text{C}=\text{N}$ at (1596 cm^{-1}). FTIR spectrum of [7] (Figure 2) showed $\nu\text{N}-\text{H}$ vibration at (3232 cm^{-1}), $\nu\text{C}=\text{N}$ band at (1627 cm^{-1}), $\nu\text{C}=\text{S}$ at (1180 cm^{-1}) and out-of-plane C-H bending at (748 and 649 cm^{-1}).

On the other hand, Hoggarth's method[12] has been used for the preparation of 3-[(benzimidazole-2-yl thio)methyl]-4-amino-1,2,4-triazole-5-thiol [9] by reaction of hydrazide [2] with CS_2 in ethanolic KOH gave the dithiocarbazate salt [8] in excellent yield, which, was then cyclized by refluxing with 98% hydrazine hydrate to give a moderate yield of triazole derivative[9] [13]. FTIR spectrum (Figure 3) showed absorptions at ($3286-3163\text{ cm}^{-1}$) asym. and sym. for $-\text{NH}_2$ group which overlap with absorption N-H group, and (1203 cm^{-1}) for C=S due to thio-thion structure formation[14].

Several attempts have been carried out to prepare 2-hydrazinobenzimidazole by the reaction of 2-mercaptobenzimidazole with 98% hydrazine hydrate, but all attempts have been failed and no achievements were obtained by this way[15].

Table (2): UV and FTIR absorption spectra data of the prepared compounds

Comp. no.	Comp. structure	UV, (EtOH) λ_{\max} (nm)	FTIR (cm^{-1})						
			$\nu\text{N}-\text{H}$	$\nu\text{C}-\text{H}$ aromatic	$\nu\text{C}-\text{H}$ aliphatic	$\nu\text{C}=\text{O}$	$\nu\text{C}=\text{C}$ & $\nu\text{C}=\text{N}$	O-O-P $\delta\text{C}-\text{H}$	Other bands
1		257	3139	3016	2970, 2877	1743	1620, 1581	748	S-CH ₂ 2638

2		283	3317, 3278, 3155		2993	1666	1550	740	
3									
3a	Ar = 	257 411	3200			1643	1566	848 740	NO ₂ (asym.) 1512 NO ₂ (sym) 1334
3b	Ar = 	357,332 239	3200			1650	1580	740	C-Br 509
3c	Ar = 	327,300 243	3147	3070	2970, 2839	1635	1581	740	
3d	Ar = 	386,328 290,240	3240	3062	2954, 2877	1650			
3e	Ar = 	327 239	3263	3055	2970, 2869	1643	1589	732	C-O-C 1218
3f		452,242	3178	3062	2900, 2800	1681	1620 1566	725	N-H Lactam 3400
4		257,245	3236		2862	1695		750, 692	
5		297	3190	3060	2920, 2858	1631		746, 692	C=S 1234
6		301,238	3119	3016	2939 2846	1620	1580	748, 686	O-H 3448
7		301,257 245	3232	3020		1627	1596	748, 694	
9		300	3286 3163	3062	2893			748	C=S 1203

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تحضير بعض مركبات 1, 2, 4- ترايزول الجديدة المشتقة من 2- مركبتوبنزاميدازول

زينب عبد الزهرة خضير المصري*

* قسم الكيمياء , كلية العلوم , جامعة بغداد

الخلاصة:

تم في هذا البحث تحضير عدد من مشتقات 1, 2, 4- ترايزول من خلال تفاعل 2- مركبتوبنزاميدازول مع اثيل كلورواستيت ليعطي اثيل (بنزاميدازول-2- ثايو) استيت [1] , ثم تحويل الاستر الناتج الى مشتق الهيدرازيد [2] الذي يتفاعل مع كل من الفينيل ايزوسيانات او الفينيل ايزوثايوسيانات ليعقبها غلق حلقي في وسط قاعدي ليعطي المركبين 3- [(بنزاميدازول - 2 - ثايو) مثيل] - 4 - فنيل - 1 , 2 , 4 - ترايزول - 5 - اول و 3- [(بنزاميدازول - 2 - ثايو) مثيل] - 4 - فنيل - 1 , 2 , 4 - ترايزول - 5 - ثايول على التوالي .
كما ان تفاعل مشتق الهيدرازيد [2] مع ثاني كبريتيد الكربون وهيدروكسيد البوتاسيوم ليعطي ملح ثنائي ثايوكاربازييت والذي يغلق حلقياً مع الهيدرازين المائي ليعطي مركب 3- [(بنزاميدازول - ثايو) مثيل] - 4 - امينو - 1 , 2 , 4 - ترايزول - 5 ثايول .
كذلك حضرت قواعد شيف جديدة من تفاعل مشتق الهيدرازيد [2] مع الديهايدات اروماتية مختلفة .
شخصت المركبات المحضرة بالطرائق الطيفية [FTIR , U.V] وتعيين بعض خواصها الفيزيائية.