

Synthesis and Characterization a New 1,3-Oxazepine Compounds from New Bis-4-Amino-3-mercapto-1,2,4-triazole Derivatives

Atyaf AQ Younus^{1*} and Nasreen R Jber²

¹Department of Chemistry, College of Education for pure Science, University of Al-Anbar, Iraq

²Department of Chemistry, College of Science, Al-Nahrain University, Iraq

***Corresponding author:** Atyaf AQ, College of Education for pure Science, University of Al-Anbar, Iraq, E-mail: yahyaalbayti@yahoo.com

Abstract

The newly derivatives of 4-amino-3-mercapto-1,2,4-triazol containing 1,3-oxazepine derivatives were synthesized by reaction of new synthesis compounds containing imine group (S)₁₋₁₀ with phthalic anhydride, in dry benzene to give compounds (O)₁₋₁₀. All these synthesized compounds have been characterized by elemental analysis and FTIR and some of them were characterized using ¹H-MNR and mass spectroscopy.

Keywords: *Phthalic anhydride; Benzene; Mass spectroscopy; Oxazepine compounds*

Introduction

The development of simple synthesis route to widely used organic compounds ring, using readily available reagents is one of the main objectives of organic synthesis. Heterocyclic compound membered rings have occupied an important place in the field of pharmaceuticals and industries. Amino-1,2,4-triazole system is an important starting material in the synthesis of biologically active and important heterocyclic, which constitute an important class of organic compounds in medicinal, agricultural and industrial field. The synthesis of triazoles fused to another heterocyclic ring has attracted particular attention due to their diverse applications as antibacterial, antidepressant, antiviral, antitumor and anti-inflammatory agents, pesticide herbicides, lubricant and analytical reagents [1,2]. The seven heterocyclic compound membered rings like Oxazepine compounds very important for example Oxazepam is used as an antibiotic, enzyme inhibitor, pharmacological interest [3], and has a biological activity [4].

Citation: Atyaf AQ Younus¹ (2016) Synthesis and Characterization a New 1,3-Oxazepine Compounds from New Bis-4-Amino-3-mercapto-1,2,4-triazole Derivatives, Organic chemistry 12

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Experimental

Preparation of Succinic dihydrazide (II)_a

Dimethyl succinate (5 ml) in 25 ml of ethanol was taken in round bottom flask. To that hydrazine hydrate (6 ml) was added and refluxed for (4 hours). The solution was cooled in ice [5]. The solid crystals was precipitated out and recrystallized with ethanol to give compound (89%), yield, m.p.=170-172°C.

Preparation of terephthalic dihydrazide (II)_b

Dimethyl terephthalate (5 g, mol) solved in (50 ml of ethanol absolute) was taken in round bottom flask. To that hydrazine hydrate (2 ml) was added and refluxed for (4 hours). The solution was cooled in ice [5]. The solid crystals was precipitated out and recrystallized with ethanol to give compound (90%), yield 88%, m.p.=132-135°C.

Preparation of succinic dihydrazide [Bis(potassium dithiocarbazinate)] (III)_a

To a solution of potassium hydroxide (2.24 g, 0.039 mol) in ethanol absolute (150 ml), succinic dihydrazide (2.92 g, 0.02 mol) and carbon disulfide (3 ml) were added as a drops and the mixture was stirred in ice bath (0-6°C) [5]. The yellow solid was precipitated out and the potassium salt obtained in quantitative yield was directly used without purification.

Preparation of terephthalic dihydrazide [Bis(potassium dithiocarbazinate)]

To a solution of potassium hydroxide (1.75 g, 0.031 mol) in ethanol absolute (150 ml), terephthalic dihydrazide (3 g, 0.0076 mol) and carbon disulfide (3 ml) were added as a drops and the mixture was stirred in ice bath (0-6°C) [5]. The yellow solid was precipitated out and recrystallized with ethanol to give compound (88%), yield 84%, m.p.=320°C.

Bis[(3,3'-thio-4,4'-amino-1,2,4-triazole)-5-yl]ethane Preparation

Suspension of potassium salt, was direct used because it was non stable, hydrazine hydrate (2 ml) and water (80 ml) was refluxed for 4 hrs. The color of the reaction mixture changed to green, hydrogen sulfide was evolved and a homogenous solution resulted. A white solid was precipitated by dilution with cold water (100 ml) and acidification with concentrated hydrochloric acid [5]. The product was filtered, washed with cold water (2*30 ml) and recrystallized from ethanol, compound (72%) yield 62%, m.p.=220-222°C.

Bis[(3,3'-thio-4,4'-amino-1,2,4-triazole)-5-yl]phenyl Preparation

A suspension of potassium salt of terephthalic dihydrazide (2 g, hydrazine hydrate (2 ml), 0.04 mol) and water (100 ml) was refluxed for (3 hrs), the color of the reaction mixture changed to light green, hydrogen sulfide was evolved and a homogenous solution resulted. A solid was precipitated by dilution with cold water (100 ml) and acidification with concentrated hydrochloric acid [5]. The product was filtered, washed with cold water (2*30 ml) and recrystallized form ethanol.

General procedure for preparation of Schiff bases

Mixture of triazole (0.001 mol) and the corresponding aldehydes (0.002 mol) in ethanol (25 ml) was treated with glacial acetic acid (0.5 ml) and refluxed for (3 hr) [6]. The reaction mixture on cooling was filtered and purified by recrystallization from ethanol.

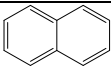
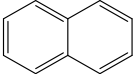
Comp No.	G	Ar	Molecular Formula	Molecular Weight	Solvent	Yield %	Color	m.p. °C
S ₁	-Ph-	P-NO ₂	C ₂₄ H ₁₆ N ₁₀ O ₄ S ₂	572	Ethanol absolute	93%	Yellowish orange	288-290
S ₂	-Ph-	P-Br	C ₂₄ H ₁₆ N ₈ S ₂ Br ₂	639.8	Ethanol absolute	86%	Light yellow	212-215
S ₃	-Ph-	P-CH ₃	C ₂₆ H ₂₂ N ₈ S ₂	510	Ethanol absolute	79%	yellow	150-153
S ₄	-Ph-	P-OCH ₃	C ₂₆ H ₂₂ N ₈ O ₂ S ₂	542	Ethanol absolute	72%	yellow	165-170
S ₅	-Ph-		C ₃₂ H ₂₂ N ₈ S ₂	582	Ethanol absolute	82%	yellow	211-215
S ₆	-CH ₂ -CH ₂ -	P-NO ₂	C ₂₀ H ₁₆ N ₁₀ O ₄ S ₂	524	Ethanol absolute	88%	yellow	156-158
S ₇	-CH ₂ -CH ₂ -	P-Br	C ₂₀ H ₁₆ N ₈ S ₂ Br ₂	591.8	Ethanol absolute	91%	yellow	217-220
S ₈	-CH ₂ -CH ₂ -	P-CH ₃	C ₂₂ H ₂₂ N ₈ S ₂	462	Ethanol absolute	77%	Light yellow	140-143
S ₉	-CH ₂ -CH ₂ -	P-OCH ₃	C ₂₂ H ₂₂ N ₈ O ₂ S ₂	494	Ethanol absolute	72%	yellow	145-147
S ₁₀	-CH ₂ -CH ₂ -		C ₂₈ H ₂₂ N ₈ S ₂	534	Ethanol absolute	88%	Dark yellow	142-144

Table 1: Physical properties of Schiff base compounds (S)₁₋₁₀.

General procedure for preparation of substituted (1,2,4) triazolo (1,3) Oxazepine

Mixture of corresponding Schiff bases (0.001 mol) and (0.002 mol) of phthalic anhydride in dry benzene (30 ml) was refluxed for (4 hr) [7]. The reaction mixture cooled and filtered and recrystallization from ethanol.

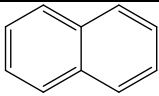
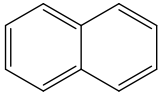
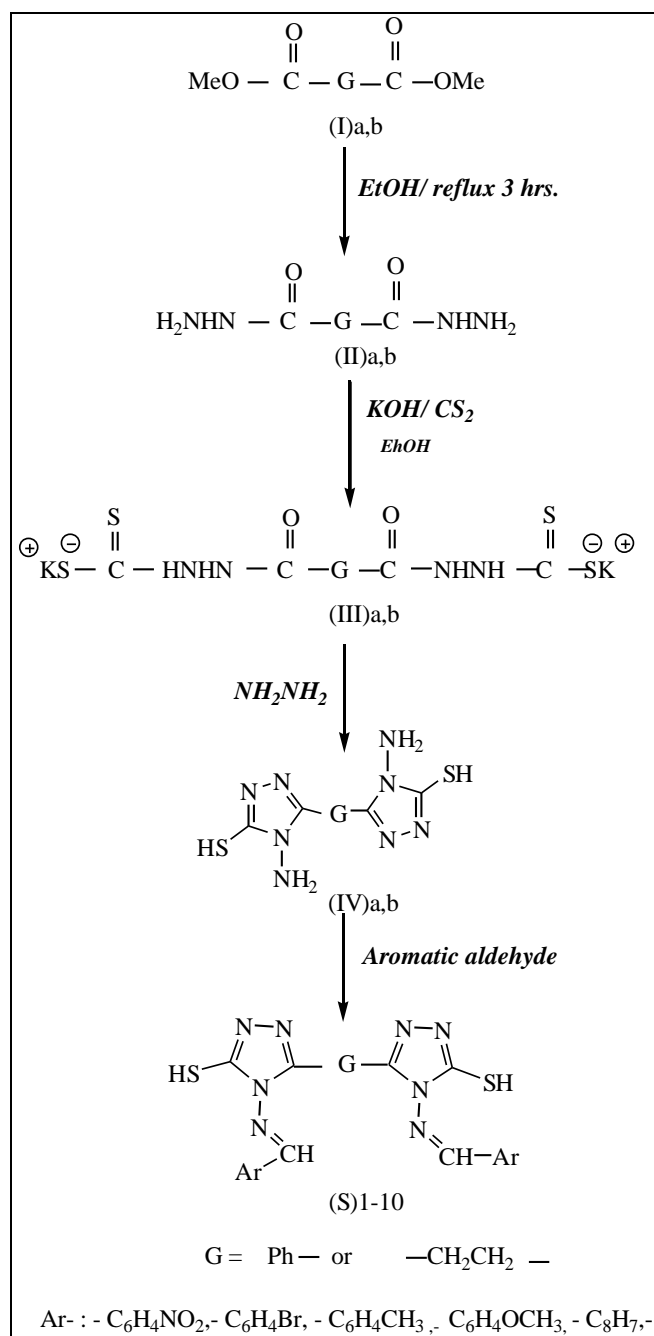
Comp. No.	G	X	Molecular formula	Molecular Weight	Solvent	Yield %	Color	m.p. °C
O ₁	-Ph-	P-NO ₂	C ₄₀ H ₂₄ N ₁₀ O ₁₀ S ₂	868	Benzene	70%	Light yellow	253-255
O ₂	-CH ₂ -CH ₂ -	P-NO ₂	C ₃₆ H ₂₄ N ₁₀ O ₁₀ S ₂	820	Benzene	72%	Yellow	+300
O ₃	-CH ₂ -CH ₂ -	P-CH ₃	C ₃₈ H ₃₀ N ₈ O 6S ₂	758	Benzene	81%	Light yellow	150-153
O ₄	-Ph-	P-CH ₃	C ₄₂ H ₃₀ N ₈ O 6S ₂	806	Benzene	77%	White	218-220
O ₅	-Ph-	P-OCH ₃	C ₄₂ H ₃₀ N ₈ O 8S ₂	838	Benzene	82%	White	187-190
O ₆	-CH ₂ -CH ₂ -	P-OCH ₃	C ₃₈ H ₃₀ N ₈ O 8S ₂	790	Benzene	89%	White	194-197
O ₇	-Ph-		C ₄₈ H ₃₀ N ₈ O 6S ₂	878	Benzene	55%	White	200-203
O ₈	-CH ₂ -CH ₂ -		C ₄₄ H ₃₀ N ₈ O 6S ₂	830	Benzene	65%	White	202-204
O ₉	-Ph-	P-Br	C ₄₀ H ₂₄ N ₈ O 6S ₂ Br ₂	935.8	Benzene	72%	Brown	180-182
O ₁₀	-CH ₂ -CH ₂ -	P-Br	C ₃₆ H ₂₄ N ₈ O 6S ₂ Br ₂	887.8	Benzene	79%	White	195-197

Table 2: Physical properties of Schiff base compounds (O)₁₋₁₀.

Results and Discussion

Synthesis of Bis[(3,3'-thio-4,4'-benzimidineamino-1,2,4-triazole)-5-yl]ethane or phenyl (V)_{a,b}

The title compound was prepared according to the following scheme:



Scheme 1: The synthetic pathway for Schiff base compounds (S)₁₋₁₀.

Compounds (S)₁₋₁₀ were synthesized by the reaction of Succinic or terephthalic dihydrazide [Bis(potassium dithiocarbazinate)] (III)a,b with hydrazine hydrate to achieve Bis[(3,3'-thio-4,4'-amino-1,2,4-triazole)-5-yl]ethane or phenyl (IV)a,b followed by condensation reaction with different aromatic aldehyde to achieved Bis[(3,3'-thio-4,4'-benzimidineamino-1,2,4-triazole)-5-yl]ethane or phenyl (S)₁₋₁₀.

The structures of all products were identified by using FT-IR and ¹H-NMR for some of them. The all resultant spectral were in correspondence with expected values. The purities of compounds were confirmed by using an elemental analysis. The elemental analysis of compounds (S)₁₋₁₀ are listed in Table 3. The observed values are in well agreement with theoretical values indicating structure of respective compounds.

Comp. No.	Formula	%C		%H		%N		%S	
		Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
S ₁	C ₂₄ H ₁₆ N ₁₀ O ₄ S ₂	50.34	49.88	5.55	4.99	24.47	25.02	11.18	10.96
S ₂	C ₂₄ H ₁₆ N ₈ S ₂ Br ₂	45.01	45.34	2.50	2.61	17.50	18.01	10.00	9.78
S ₃	C ₂₆ H ₂₂ N ₈ S ₂	61.17	61.67	4.31	4.66	21.96	22.21	12.54	12.87
S ₄	C ₂₆ H ₂₂ N ₈ O ₂ S ₂	57.56	56.89	4.05	4.21	20.66	19.88	11.80	11.75
S ₅	C ₃₂ H ₂₂ N ₈ S ₂	65.97	65.11	3.78	4.34	19.24	20.23	10.99	11.09
S ₆	C ₂₀ H ₁₆ N ₁₀ O ₄ S ₂	45.80	46.08	3.05	2.99	26.71	26.05	12.21	12.45
S ₇	C ₂₀ H ₁₆ N ₈ S ₂ Br ₂	40.55	39.43	2.70	2.45	18.92	19.12	10.81	11.12
S ₈	C ₂₂ H ₂₂ N ₈ S ₂	57.14	56.98	4.76	4.35	24.24	24.66	13.85	13.99
S ₉	C ₂₂ H ₂₂ N ₈ O ₂ S ₂	53.44	52.96	4.45	4.51	22.67	23.08	12.95	13.04
S ₁₀	C ₂₈ H ₂₂ N ₈ S ₂	62.92	60.01	4.11	4.58	20.97	21.54	11.98	10.77

Table 3: Elemental analysis (CHNS-O) for compounds (S)₁₋₁₀

The spectroscopic observation of (S)₂ is given: FT-IR (KBr, cm⁻¹) Figure 1 show the appearance of bands at 3110, 2724, 1602 and 841.1 which could be assigned to ν C-H of azomethane group [8], ν S-H, ν C=C and out of plane bending of para-disubstituted benzene ring.

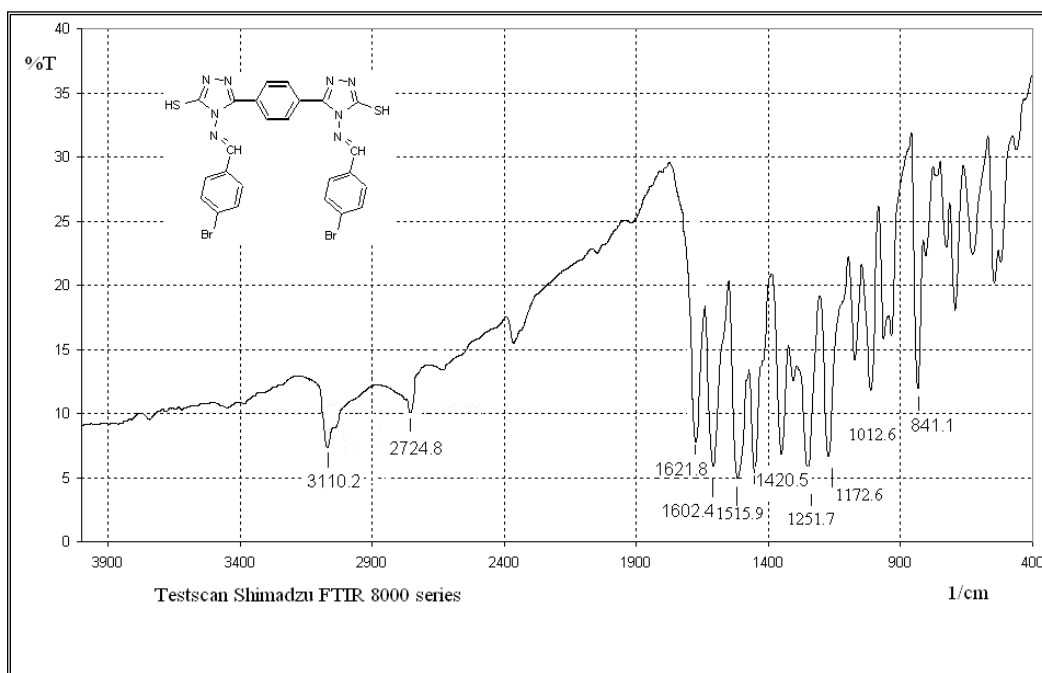


Figure 1: FTIR spectrum of Bis[(3,3'-thio-4,4'-(4''-benzylideneamino)-1,2,4-triazole)-5-yl] phenyl (S)₂.

¹HNMR (DMSO-d₆), δ in ppm) Figure 2: 7.61-7.50 (d-d, 12H, arom. H), 8.2 (s, 2H, CH = N), 12.6(s, 2 H, SH). Table 4 shows the FT-IR absorption bands for synthesizes compounds.

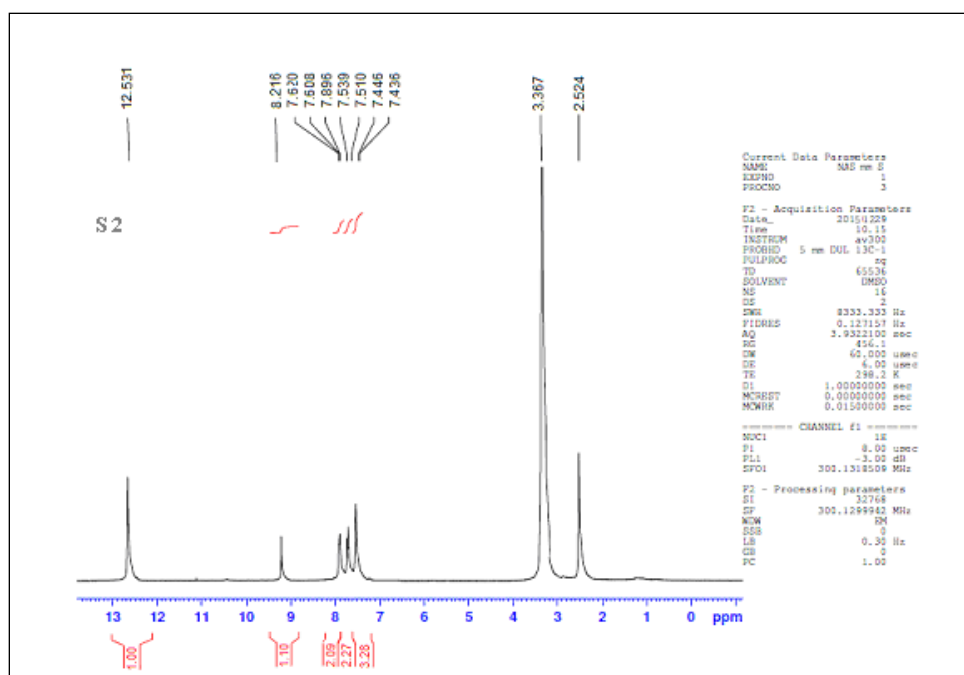


Figure 2: ¹HNMR spectrum of Bis[(3,3'-thio-4,4'-(4''-benzimidineamino)-1,2,4-triazole-5-yl] phenyl (S₂).

Comp. No.	G	X	νAr H	ν CH=N	ν C=C	γ para-Sub.	Other
S ₁	-Ph-		3081	3100	1600	838	1554 1345 (NO ₂)
S ₂	-Ph-		3067	3110	1602	841	-
S ₃	-Ph-		3068	3114	1598	844	2987 and 2877 (C-H Aliphatic)
S ₄	-Ph-		3080	3100	1597	839	1100 (C-O)
S ₅	-Ph-		3077	3110	1600	-	-
S ₆	-CH ₂ -CH ₂ -		3063	3102	1603	832	15564 1353 (NO ₂)

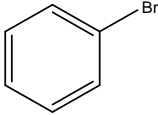
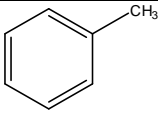
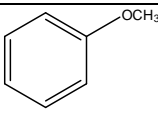
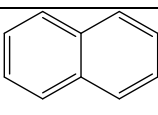
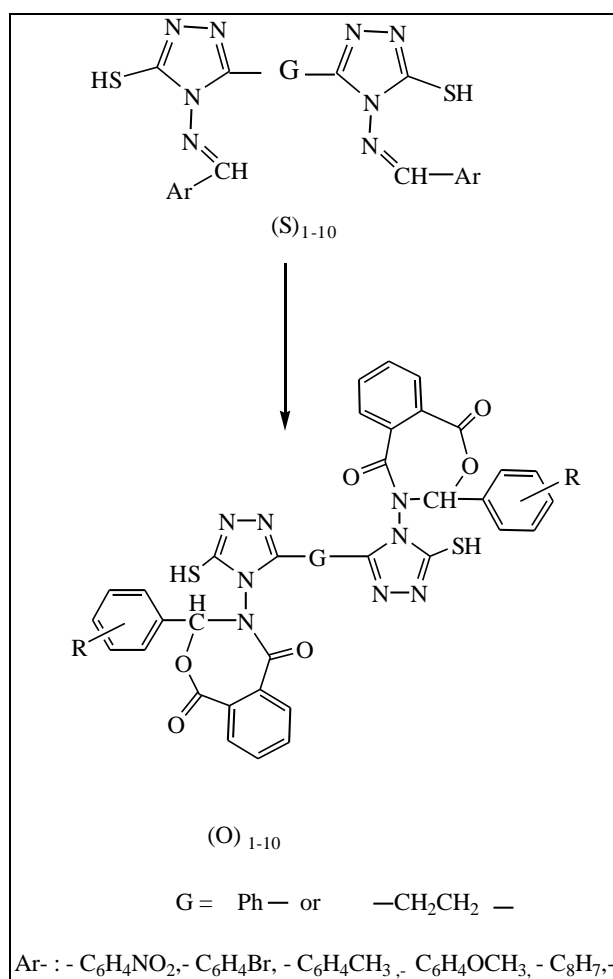
S ₇	-CH ₂ -CH ₂ -		3058	3098	1602	840	2997 and 2854 (C-H Aliphatic)
S ₈	-CH ₂ -CH ₂ -		3044	3097	1600	836	2965 and 2878 (C-H Aliphatic)
S ₉	-CH ₂ -CH ₂ -		3056	3112	1594	827	2987 and 2877 (C-H Aliphatic)
S ₁₀	-CH ₂ -CH ₂ -		3071	3110	1597	-	2981 and 2876 (C-H Aliphatic)

Table 4: Characteristic FTIR absorption bands of synthesized compounds (S)₁₋₁₀.

Synthesis of substituted (1,2,4) triazolo (1,3) Oxazepine (O)₁₋₁₀

The title compound was prepared according to the following scheme



Scheme 2: The synthetic pathway for substituted (1,2,4) triazolo (1,3) Oxazepine (O)₁₋₁₀.

Compounds (O)₁₋₁₀ were synthesized by the reaction of Schiff base compounds (S)₁₋₁₀ with phthalic anhydride in benzene to give 1,3-Oxazepine-4,7-dione derivatives compounds. Cycloaddition is achieved by ring formation that results from the addition of π electrons either $\delta \pi$ bonds with formation of new δ bonds [9].

The structures of all products were identified by using FT-IR and ¹H-NMR for some of them. The purities of compounds were confirmed by using an elemental analysis. The elemental analysis of compounds (O)₁₋₁₀ are listed in Table 5.

Comp. No.	Formula	%C		%H		%N		%S	
		Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
O ₁	C ₄₀ H ₂₂ N ₁₀ O ₁₀ S ₂	55.29	55.78	2.53	3.01	16.12	16.73	7.37	8.01
O ₂	C ₃₆ H ₂₂ N ₁₀ O ₁₀ S ₂	52.68	52.98	3.41	4.06	17.07	12.43	7.80	8.02
O ₃	C ₃₈ H ₂₈ N ₈ O ₆ S ₂	60.15	59.76	3.69	2.88	14.77	15.11	8.44	9.07
O ₄	C ₄₂ H ₂₈ N ₈ O ₆ S ₂	62.53	62.81	3.47	3.67	13.89	14.05	8.06	8.65
O ₅	C ₄₂ H ₂₈ N ₈ O ₈ S ₂	60.14	60.45	3.34	3.02	13.36	13.82	7.63	8.11
O ₆	C ₃₈ H ₂₈ N ₈ O ₈ S ₂	57.72	57.32	3.54	4.12	14.17	14.09	8.01	7.88
O ₇	C ₄₈ H ₂₈ N ₈ O ₆ S ₂	65.60	66.65	3.18	3.81	12.75	13.17	7.28	7.85
O ₈	C ₄₄ H ₂₈ N ₈ O ₆ S ₂	63.61	62.91	3.37	3.76	13.49	13.77	7.71	8.10
O ₉	C ₄₀ H ₂₂ N ₈ O ₆ S ₂ Br ₂	51.33	52.03	2.35	3.09	11.96	12.09	6.83	7.08
O ₁₀	C ₃₆ H ₂₂ N ₈ O ₆ S ₂ Br ₂	48.65	48.42	2.47	3.05	12.61	13.11	7.20	6.96

Table 5: Elemental analysis (CHNS-O) for compounds (O)₁₋₁₀.

Spectroscopic observation of (O₆) for example is given: FT-IR (KBr, cm⁻¹) Figure 3: 1737 (C=O of lactone stretching), 1700 (C=O of lactam stretching)⁽⁹⁾, 3078 (Ar-H), 2977-2884 (ν C-H, aliphatic stretching), 1597 (ν C=C), 1257 (ν C-O), 842 (out of plane bending for para-substituted benzene ring).

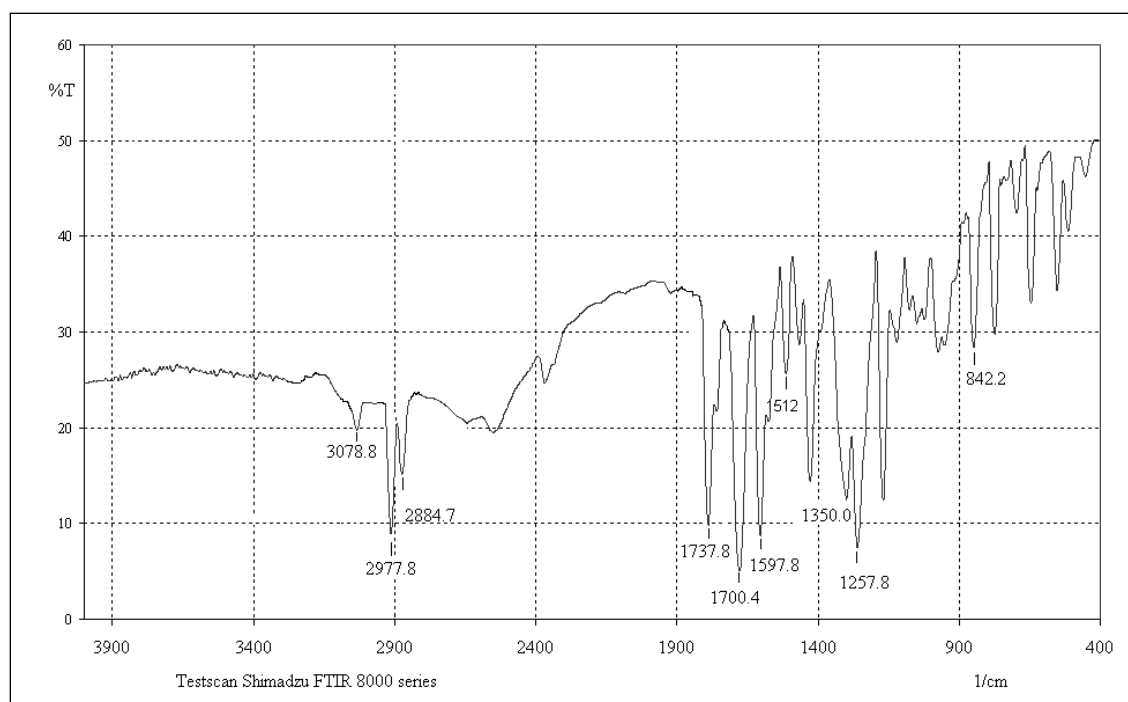


Figure 3: FTIR spectrum of compound (O)₆.

¹HNMR spectrum of compound (O)₅ (DMSO-d₆, δ in ppm) Figure 4: 7.22 -7.90 (d-d, 20H, arom. H), 7.21(s, 2H), 12.13 (s, 2H, SH) [10], 3.35 (s, 6H, OCH₃). Table 6 shows the FT-IR absorption bands for synthesizes compounds.

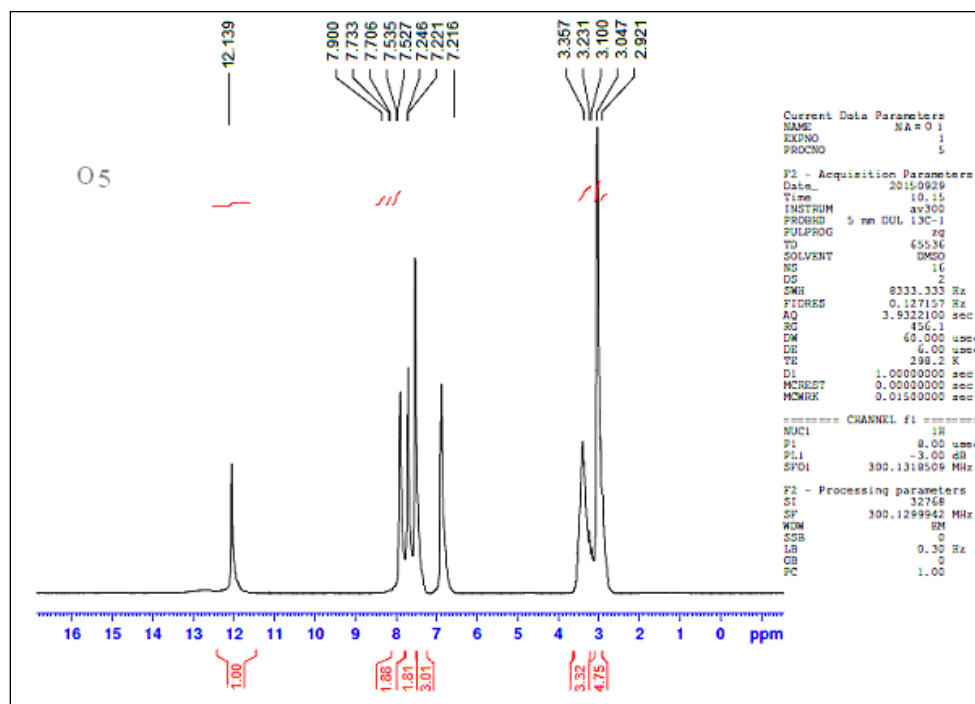


Figure 4: ¹HNMR spectrum of compound (O)₅.

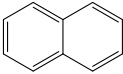
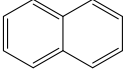
Comp. No.	G	X	ν Ar H	ν C=O lactone	ν C=O lactome	γ para-Sub.	Other
O ₁	-Ph-	P-NO ₂	3080	1741	1688	838	1554 1345 (NO ₂)
O ₂	-CH ₂ . CH ₂ .	P-NO ₂	3065	1738	1702	841	1564 1353 (NO ₂)
O ₃	-CH ₂ -CH ₂ -	P-CH ₃	3076	1735	1698	844	2987 and 2877 (C-H Aliphatic)
O ₄	-Ph-	P-CH ₃	3065	1729	1697	839	1100 (C-O)
O ₅	-Ph-	P-OCH ₃	3074	1724	1700	-	-
O ₆	-CH ₂ -CH ₂ -	P-OCH ₃	3078	1737	1700	842	1257 (C-O) 2977 and 2885 (C-H Aliphatic)
O ₇	-Ph-	Ar= 	3064	1731	1702	840	
O ₈	-CH ₂ -CH ₂ -		3056	1738	1700	836	2965 and 2878 (C-H Aliphatic)
O ₉	-Ph-	P-Br	3049	1734	1694	827	
O ₁₀	-CH ₂ -CH ₂ -	P-Br	3068	1732	1697	-	2981 and 2876 (C-H Aliphatic)

Table 6: Characteristic FTIR absorption bands of synthesizes compounds (S)₁₋₁₀.

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