Synthesis And Characterization Of Some 1,3,4 - Thiadiazole Derivatives

Ismaeel Y. Majeed
Iman F. Mustafa
Muhand J. Mahmoud
Dept. of Chemistry/College of Education For pure Science (Ibn Al-Haitham)/ University of Baghdad

Received in :19 February 2013 , Accepted in : 19 May 2013

Abstract

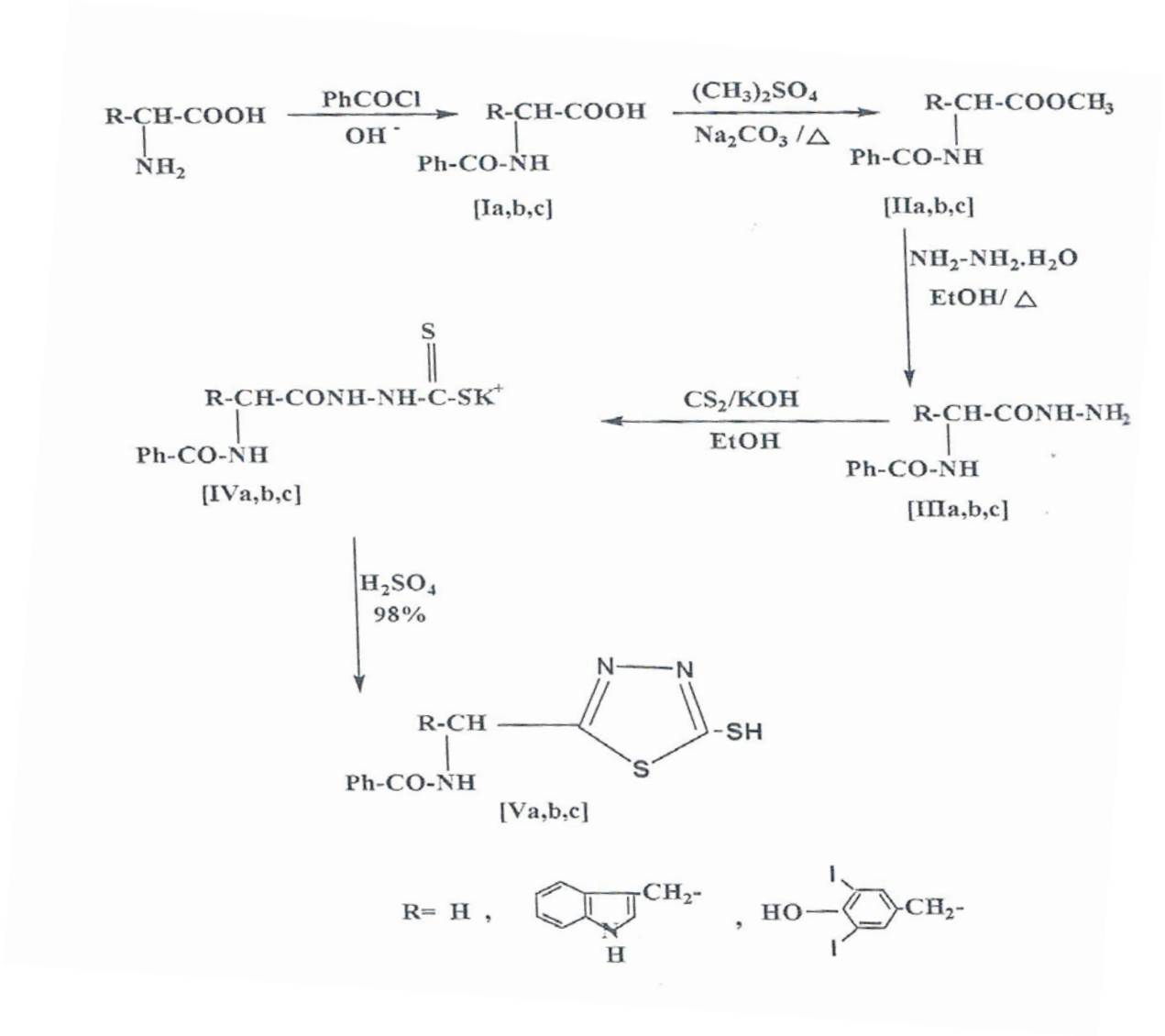
A series of N- benzoyl - 2 – alkyl -1- (2- thio – 1,3,4- thiadiazole -5- yl) , have been synthesized from DL- α– amino acids , The methyl and sulfon thio ethers of these compounds were also prepared , representative samples of the prepared compounds were characterized from their IR- spectrum and elemental analysis .

Key Words :1,3,4 – thiadiazole derivatives , thio – ethers , sulfon compounds .

Introduction

Thiadiazoles and in particular 1,3,4- thiadiazole derivatives were among the various heterocycles that received more attention during the last two decades as antimicrobial agents.[1,2]

Most of the substitutions have been carried out at the 2- and 5- positions of the thiadiazole ring , these inclued , the introduction of a double bond on the thiadiazole ring is reported to have a strong antibacterial activity [3, 4] antifungal[5,6] , antimitotic [7] widely used formedicinal [8] and antihistaminic [9] , substituted thiadiazoles have been reported to display nematocidal [10] and antiinflammatory [11]. Keeping these facts in mind it was thought worth while to synthesize some new [5-(N- benzoyl - alkyl amino) - (1,3,4-thiadiazole -2- thione] derived from N- benzoyl α – amino acids derivatives see (scheme1).



Scheme – 1 –

Experimental

Melting points were determined by using " Electro thermal " melting point apparatus mettler . I.R. spectra were recorded using FTIR – 8300 fourier transforn infared spectrophototmeter schimadzu , for KBr disc . Microanalytical samples were analysed at the Ministry of Oil Laboratories , Baghdad .

- **N- Benzoyl α – amino acid [$I_{a,b,c}$]**

This was carried out following the procedure of vogel [12] .

- **N- Benzoyl methylester of α – amino acid [$II_{a,b,c}$]**

A solution of sodium carbonate (0.01 mole) in water was added gradually with continous stirring to N- benzoyl α – amino acid [$I_{a,b,c}$] (0.01 mole) which was dissolved in dry acetone , to a stirred solution dimethyl sulfate (0.0l mole) was added . The mixture was refluxed for 3hr . Evaporated under reduced pressure and extracted with ethyl acetate .

A syrup was obtaind which showed one spot on T.L.C. (ethyl acetate as a solvent system) .

- **N – Benzoyl α – amino acid hydrazide [$III_{a,b,c}$]**

To a stirred solution of (0.01 mole) of N – benzoyl α – amino methyl ester [$II_{a,b,c}$] in ethanol (10 ml) hydrazine hydrate (0.02 mole) was added . The mixture was refluxed for 3hr . After cooling a white crystalline solid was formed , the crude product was filtered and recrystallized from ethanol .

m.p. of [III_a] = 175 – 177 c^o ,[III_b] = 243-244 c^o ,[III_c]= 230-232 c^o

yield % of [III_a] 73% , [III_b] 82% , [III_c] 86%

- **N- benzoyl α – amino acid xanthate salt : [13] [$IV_{a,b,c}$]**

N- benzoyl α – amino acid hydrazide [$III_{a,b,c}$] (0.0l mole) was mixed with (10 ml) ethanolic KOH solution , a clear solution was thus obtained , carbon disulphide (0.01 mole) (5ml) was now added to it and the resulting solution was stirred for overnight at room temperature , the yellow precipitate is separated and washed with ether .

m.p. of [IV_a]= 140-141 c^o , [IV_b] = 220-222 c^o decom . [IV_c]= 190-192 decom yield %of [IV_a] 74% ,[IV_b] 67% , [IV_c] 62%.

- **[5 – (N- benzoyl - alkyl amino) - 1,3,4 – thiadiazole -2-thione)[13] [$V_{a,b,c}$]**

Xanthate salt (0.01 mole) was dissolved in ice cold conc . Sulphuric acid (10 ml) , the resulting solution was kept at room temperature for 2hr. Stirred at intervals and then poured over crushed ice . It was stirred , diluted with water and flitered , the residue obtained was washed and recrystallized from ethanol – water . Physical properties of compounds [$V_{a,b,c}$] are shown in (Table -1-) .

- **[5- (N – benzoyl – methyl amino) - 1,3,4 – thiadiazole –2 –thio ether] [14] [$VI_{a,b,c}$] .**

The compounds [$V_{a,b,c}$] (0.01 mole) , were dissolved in dioxane (10 ml) , which contained (0.01 mole) potassium hydroxide , alkyl iodide (0.01 mole) was added drop wise with stirring , the reactans were refluxed 1hr . and monitored by (T.L.C) . After evaporating the solvent under reduced pressure , water was added , and the crude product was extracted with ethyl acetate and dried over anhydrous sodium sulphate . Evaporation of the organic solvent gave a solid that was crystallized from (benzene – petroleum ether 40 – 60) physical properties are shown in (Table – 1 -) .

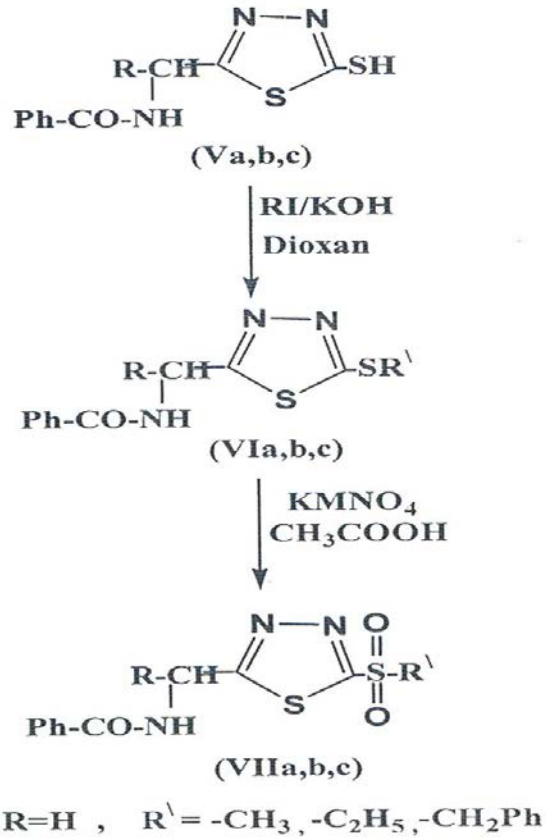
- **[5- (N – benzoyl –alkyl amino) – 2- methyl sulphonyl – 1,3,4 – thiadiazole)] [15] [$VII_{a,b,c}$] .**

The alkyl thioether [$VI_{a,b,c}$] (0.01 mole) was dissolved in 80% aqueous acetic acid (3 ml) , to this solution of potassium permanganate (0.03 mole) in water (5 ml) , was added during a period of 0.5hr . 30% hydrogen peroxide was added in a quantity sufficient to

discharge the colour . Work – up neutralization with sodium hydrogen carbonate soluation , extracting with ethyl acetate and evaporation of the organic solvent .

Results and Discussion

In the present work a series of 1,3,4 – thiadiazole derivatives were synthesized from glycine , DL – 3-5- diiodo tyrosine and DL- trptophan as outlined in (scheme 1) . The key intermediates. N- benzoyl (α- amino acid hydrazide) [III $_{a,b,c}$] were prepared by the reaction of methyl ester of (N- benzoyl - α- amino acid) [I $_{a,b,c}$] with hydrazine . The IR spectra showed the normal secondary amide stretching of the acid hydrazide which appeared at (1640 – 1600 cm^{-1}) as compared to stretching of the carbonyl group in the corresponding esters , which appeared at (1740 – 1660 cm^{-1}) .



Scheme – 2 –

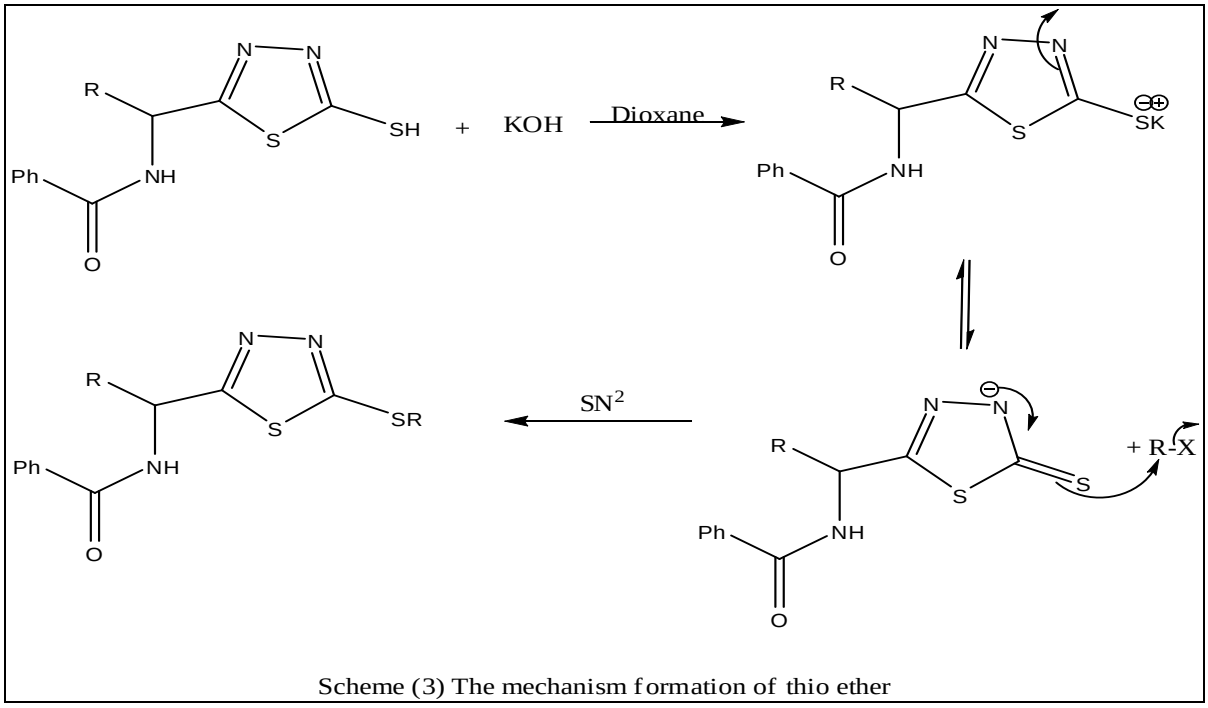
Treating the acid hydrazides [III $_{a,b,c}$] with carbon disulphide in alkalin medium gave yellow solids ,which are characterized as N- benzoyl-α-amino acid Xanthate salt [IV$_{a,b,c}$],The IR spectra showed to stretching bands at (3300 – 3330 cm^{-1}) which could be attributed to – NH group , and the disappearance of – NH_2 bands at (3290 – 3275 cm^{-1}) which could be due to obtain the reaction . Another characteristic bands were observed at (1074 – 1050 cm^{-1}) which could be due to C = S , then the bands at (1630 – 1635 cm^{-1}) were obtained which could be attributed to a secondary amide (*V* C=O amide I) and abroad band was obtained at (1670 – 1640 cm^{-1}) which could be attributed to the (amide II) .

Then treated the xanthate salt [IV $_{a,b,c}$] with Conc. sulphuric acid , to obtain 1,3,4 – thiadiazole [V $_{a,b,c}$] .

IR spectra showed stretching bands at (1065 – 1060 cm-1) , (2233-2490cm^{-1}) which could be attributed (C = S) [16] , -SH stretching and the disappearance of the C=O

hydrazide (amid I) indicated the reaction is obtained , and a strong stretching band appeared at (1485 – 1488 cm^{-1}) which could be due to (N – C=S)[17] stretching band in thiadiazole ring . See (figure -1-)

Alkylation of compounds [$V_{a,b,c}$] with alkyl iodide in basic medium see (scheme -2-) afforded [5- (N- benzoyl alkyl amino - 1,3,4 – thiadiazole -2- thio ether] [$VI_{a,b,c}$] in 80% yield .

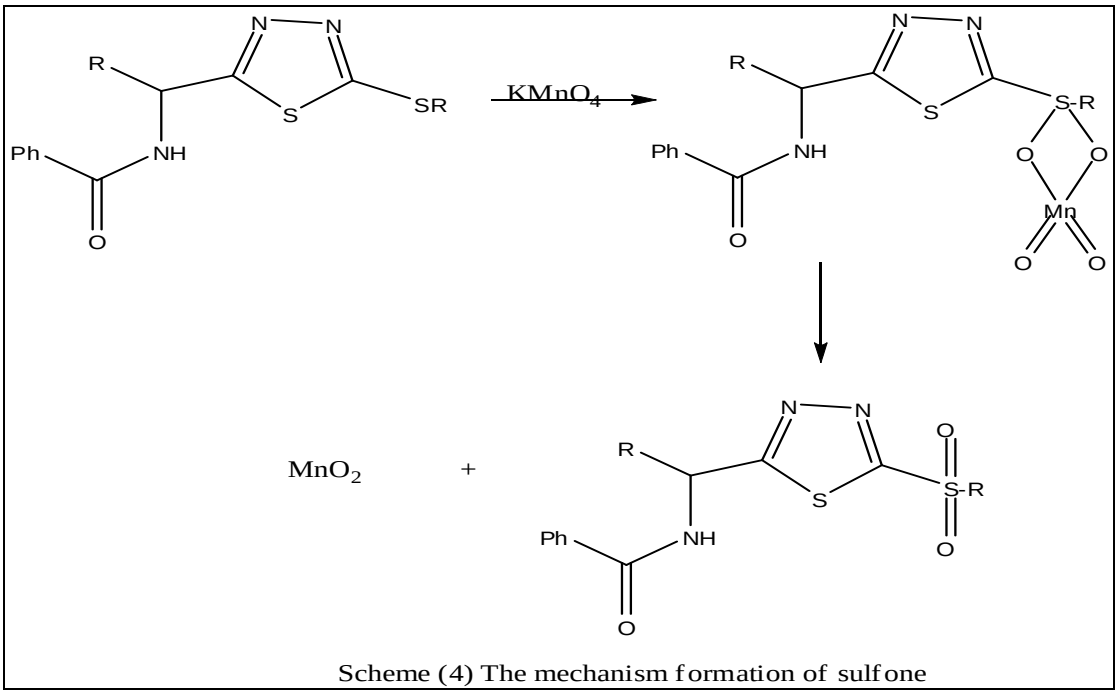


Scheme (3) The mechanism formation of thio ether

The IR spectra of these compounds showed the disappearance of the C=S and the SH stretching's at (1065-1060cm^{-1}) (2233-2490cm^{-1}) respectively . New bands at (1423 cm^{-1}) and at (1303 cm^{-1}) appeared which could be attributed to the new -S-CH_3 stretching band in compound [VI_a] , then another characteristic band was observed at (1410 cm^{-1}) which could be due to (-SCH_2)[18] in compound [VI_b] . See (figure -2-) .

The sulphones [$VII_{a,b,c}$] were prepared by oxidation of [$VI_{a,b,c}$] with potassium permanganate and hydrogen peroxide see (scheme -2-) .

The IR spectra are characterized by the sulphone 0=S=0 absorption[18] bands at (1319 – 1325 cm^{-1}) and (1155 – 1159cm^{-1}) see (figure -3-) .



Scheme (4) The mechanism formation of sulfone

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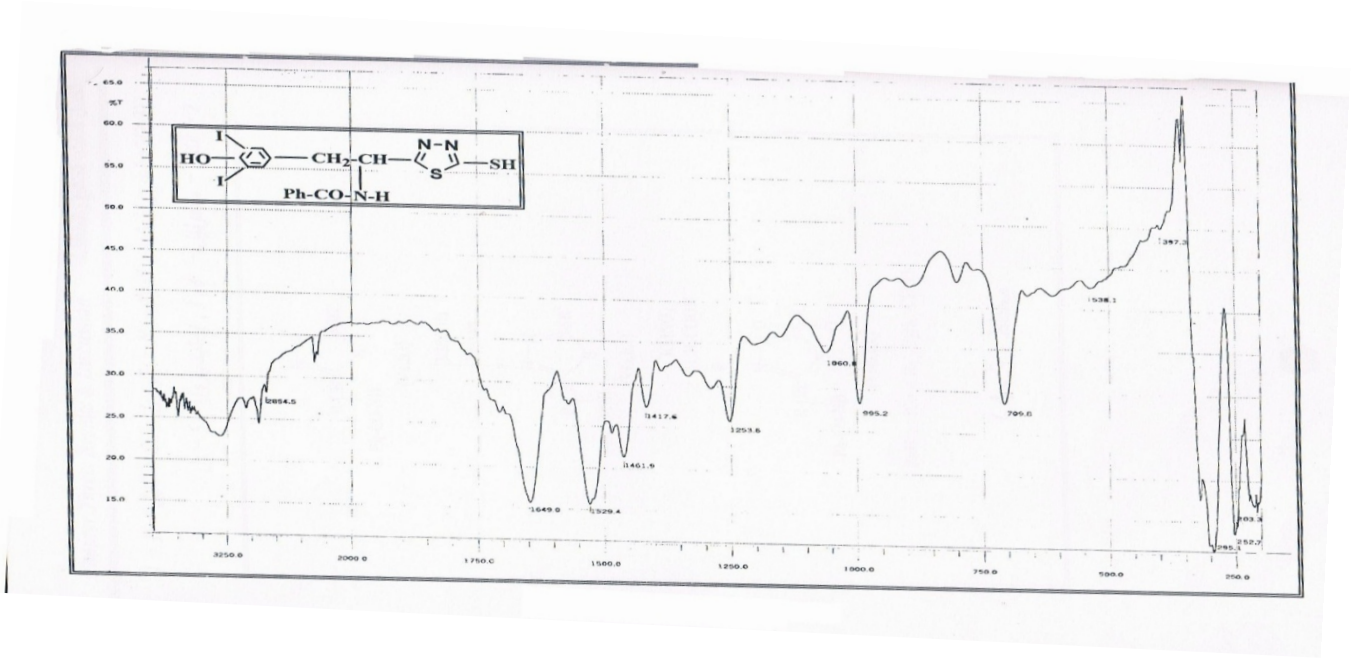


Fig.(1): (compound V c)

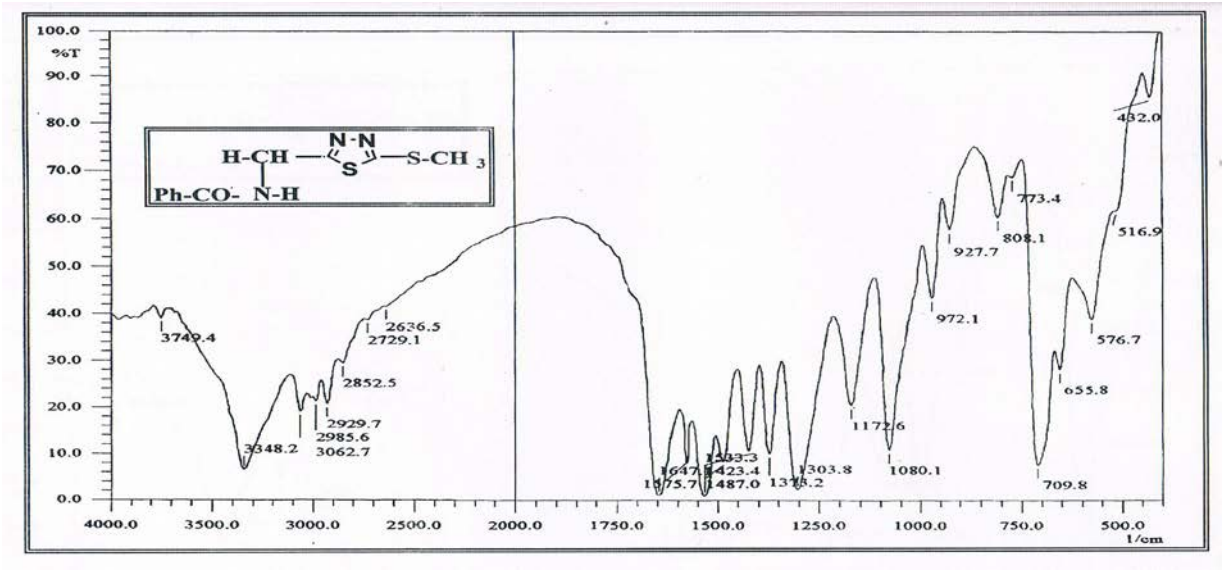


Fig. (2) :(compound VI a)

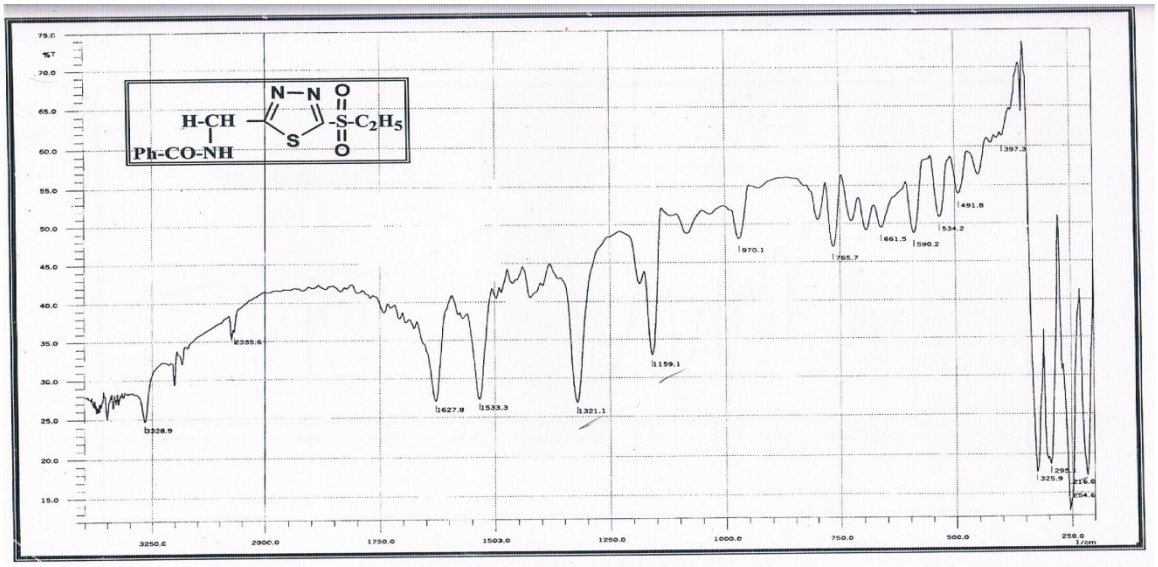
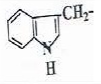
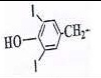


Fig.(3): (compound VII $_b$)

Table (1) :Physical properties of compounds [V – VII] a,b,c

Com. No .	Molecular formula	Molecular weight	R	R '	Yield %	m.p. c°	Analysis %					
							Cal cd. %			found%		
							C	H	N	C	H	N
V a	$C_{10}H_9N_3S_2O$	251	H	-	85	98-99	47.80	3.58	16.73	47.78	3.57	16.72
V b	$C_{18}H_{16}N_4S_2O$	368		-	73	124-126	58.69	4.37	15.21	58.60	4.21	15.01
Vc	$C_{17}H_{13}N_3S_2O_2I_2$	611		-	78	105-106	33.38	2.12	6.87	33.36	2.10	6.85
VI a	$C_{11}H_{11}N_3S_2O$	265	H	CH_3	89	78-79	49.81	4.15	15.84	49.79	4.14	15.83
VI b	$C_{12}H_{13}N_3S_2O$	279	H	C_2H_5	81	81-83	51.61	4.65	15.05	51.60	4.63	15.03
VI c	$C_{17}H_{15}N_3S_2O$	341	H	CH_2Ph	83	93-94	59.82	4.39	12.31	59.71	4.25	12.11
VII a	$C_{11}H_{11}N_3S_2O_3$	297	H	CH_3	88	125-127	44.44	3.70	14.14	44.21	3.52	14.12
VII b	$C_{12}H_{13}N_3S_2O_3$	311	H	C_2H_5	91	172-173	46.30	4.18	13.50	46.29	4.16	13.49
VII c	$C_{17}H_{15}N_3S_2O_3$	373	H	CH_2Ph	93	120-122	54.64	4.02	11.26	54.55	3.85	11.12

تحضير وتشخيص بعض مشتقات (4,3,1) ثايودايزول وتشخيصها

إسماعيل ياسين مجيد
إيمان فيصل مصطفى
مهند جميل محمود
قسم الكيمياء / كلية التربية للعلوم الصرفة (ابن الهيثم) / جامعة بغداد

استلم البحث في : 19 شباط 2013 ، قبل البحث : 19 آيار 2013

الخلاصة

تم في هذا البحث تحضير سلسلة من المركبات N- بنزويل -2- الكيل -1- (2- ثايو – 4,3,1 – ثايودايزول -5- يل) من (الفا حمض اميني) وقد اجريت لهذه المركبات عملية الالكلة بهاليدات الالكيل وتحويلها الى مركبات الثايو اثير ، وكذلك اجريت عملية الاكسدة لمركب الثايو اثير وتحويله الى مركب السلفون .
وقد شخصت هذه المركبات باستخدام مطيافيه الأشعة تحت الحمراء ، وتحليل العناصر .

الكلمات المفتاحية : مشتقات 1 و3و4-ثاياديازول ، ثايو ايثرات ،مركبات السلفون.