Synthesis of New Derivative of Adipoyl Thiadiazole

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Abstract

This research includes the preparation of new derivatives of adipoyl thiadiazoles, through the reaction of each of hydrazine hydrate , phenyl hydrazine , 2,4-dinitrophenyl hydrazine, semicarbazide and thiosemicarbazid with adipoly chloride in the presence of ethanol (95%). Furthermore, thiadiazoles were made through cyclization of hydrazine , semicarbazide and thiosemicarbazid in alkaline media, such as potassium hydroxide solution in presence of carbon disulfide. The prepared compounds were identified by the physical and spectroscopic methods .

Key words : Thiadiazole, hydrizides, semicarbazide, thiosemicarbazide, adipoly chloride , Carbon disulfide .

Introduction

Research on a new substance possessing anti-bacterial activity has attracted considerable attention owing to the continuous increase in the bacterial resistance.(1) In recent years, attention has been increasingly paid to the synthesis of bis – heterocyclic compounds,which exhibit various biological activities.(2,3,4,5) Keeping these observations in mind and in continuation of our work on the synthesis of heterocyclic compounds containing nitrogen and sulfur.(6,7)Thiadiazoles exhibit a broad spectrum of biological effectiveness ,(8,9,10) such as anti-parkinsonism,(11) hypoglycaemic,(12) anti-histaminic, (13)anti-cancer, (14) anti-inflammatory, (15,16) anti-asthmatic,(17) and anti-hypertensive.(18,19) In the synthesis of heterocyclic sulphur and nitrogen containing compounds, 1,3,4-thiadiazoles are substances of great interest because of their wide use in medicine , agriculture ,(20) and many technological applications.(21) Some of these involve dyes , lubricants , optically active crystals , photo-graphic materials, epoxy resins, etc.(22,23) Thiadiazoles have been found to have hypotensive and anticonculsive activities,(24) Furthermore, infections caused by various microorganisms pose a serious challenge to the medical community and the need for an effective therapy has led to the search for novel antibacterial agents .(25)

Experimental

A- **Instrumental**

Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected . FT-IR spectra were recorded on Shimadzu FT-IR 8400 spectrophotometer as KBr disc. The ^{1}H-NMR was recorded on Bruker model Ultrashild 300 MHZ NMR at Al-Albyt University of Jordon. DMSO-d^6 was used as solvent and TMS as internal reference .

B- **Material**

All chemical compounds were obtained from Fluka and Aldrich .

General procedure for preparation of the hydrazides (1, 3)

Adipoly chloride (5 ml, 0.034 mole) was added to a solution of hydrazine hydrate (3 ml, 0.068 mole) (a product from the reaction of hydrazinium sulphate with 20% of sodium hydroxide) and the precipitate formed was filtered and recrystallized from THF to give a brown crystal of the compound (1), and the same procedure , was used to prepare compound (3) by taking (2.7 ml, 0.027 mole) of phenyl hydrazine to react with adipoly chloride (2 ml, 0.013 mole). The physical properties of the prepared compounds are listed in table (1).

Preparation of N$^{'1}$,N$^{'6}$-bis(2,4-dinitrophenyl)adipohydrazide (5)

To a solution of 2,4-dinitrophenyl hydrazine (2.72 gm,0.013 mole) in ethanol (95%)(20 ml) adipoly chloride (1 ml,0.006 mole) was added slowly with stirring . The reaction mixture was heated at reflux for 3 hours. After cooling, the separated ppt. it was filtered and recrystallized from 50% EtOH: 50% H_2O to give an orange crystal of the compound (5). The same procedure was used to prepare compound 7 and 9 by using 2.05 gm and 2.49 gm from each of the semicarbazide and thiosemicarbazide, respectively, to give the corresponding compounds 7 and 9. The physical properties of the prepared compounds are listed in table (1) .

Preparation of 1,4-di(1,3,4-thiadiazol-2-yl)butane (2)

To a mixture of compound 1 (1.7 gm, 0.01 mole) in a solution of KOH (1.12 gm, 0.02 mole),and (100 ml) of ethanol (95%), carbon disulfide (24 ml, 0.4 mole) was added slowly with stirring. The mixture was refluxed for (5-6) hrs. The mixture was cooled, concentrated under vaccum, and poured slowly with stirring into ice (60 gm) The solution was acidified with dilute hydrochloric acid (10%) to PH (5-6).The product was precipitated and recrystallized from chloroform to give a black brown crystal of the compound (2). The same procedure was used to prepare compounds 4, 6, 8, and 10 by using (3.26 gm, 5.06 gm, 1.41 gm, 1.46 gm) of the compounds: 3, 5, 7, and 9 respectively. The physical properties of the prepared compounds are listed in table(1).

Table (1) : Physical properties of the prepared compounds .

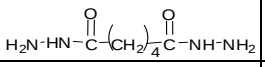
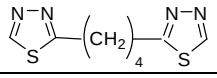
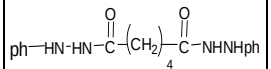
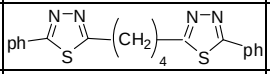
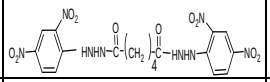
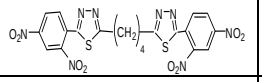
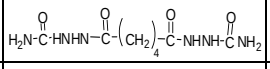
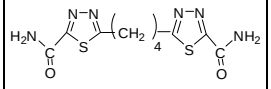
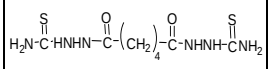
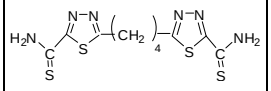
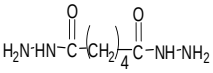
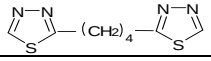
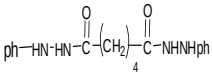
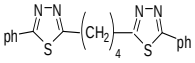
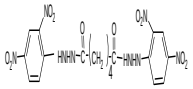
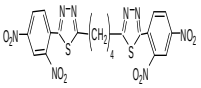
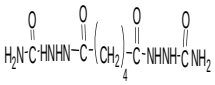
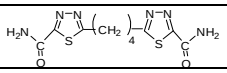
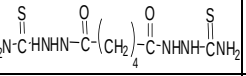
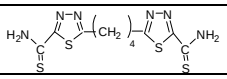
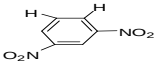
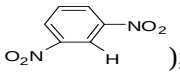
Comp. No.	Comp. Structure	Name of Comp.	m.p °C	Yield %	Colour	Recryst . Solvent
1		Adipohydrazide	146-148	64	Brown	THF
2		1,4-di(1,3,4thiadiazol-2-yl)butane	116-118	71	Black-Brown Crystal	Chloroform
3		$N^{'1}$,$N^{'6}$-diphenyl adipohydrazide	194-198	67	Brown White Crystal	THF
4		1,4-bis(5-phenyl-1,3,4-thiadiazol-2-yl)butane	120-123	71	Black Crystal	Diethyl-Ether
5		$N^{'1}$,$N^{'6}$-bis(2,4-dinitrophenyl)adipohydrazide	158-160	70	Orange Crystal	Ethanol-Water
6		1,4-bis(5-(2,4- dinitrophenyl)-1,3,4-thiadiazol-2-yl) butane	Oily	74	Orange Oily	Chloroform
7		1- Adipoyl semicarbazide	160-162	63	White Crystal	Ethanol-Water
8		5,5'-(butane-1,4-diyl)bis(1,3,4- thiadiazole-2-carboxamide	128-130	23	Brown Crystal	Methanol-Water
9		Adipoyl thio semicarbazide	170-172	61	BrownYellow Crystal	Ethanol-Water
10		5,5'-(butane-1,4-diyl)bis(1,3,4- thiadiazole-2-carbothioamide	144-147	42	Black-Brown Crystal	Ethanol-Water

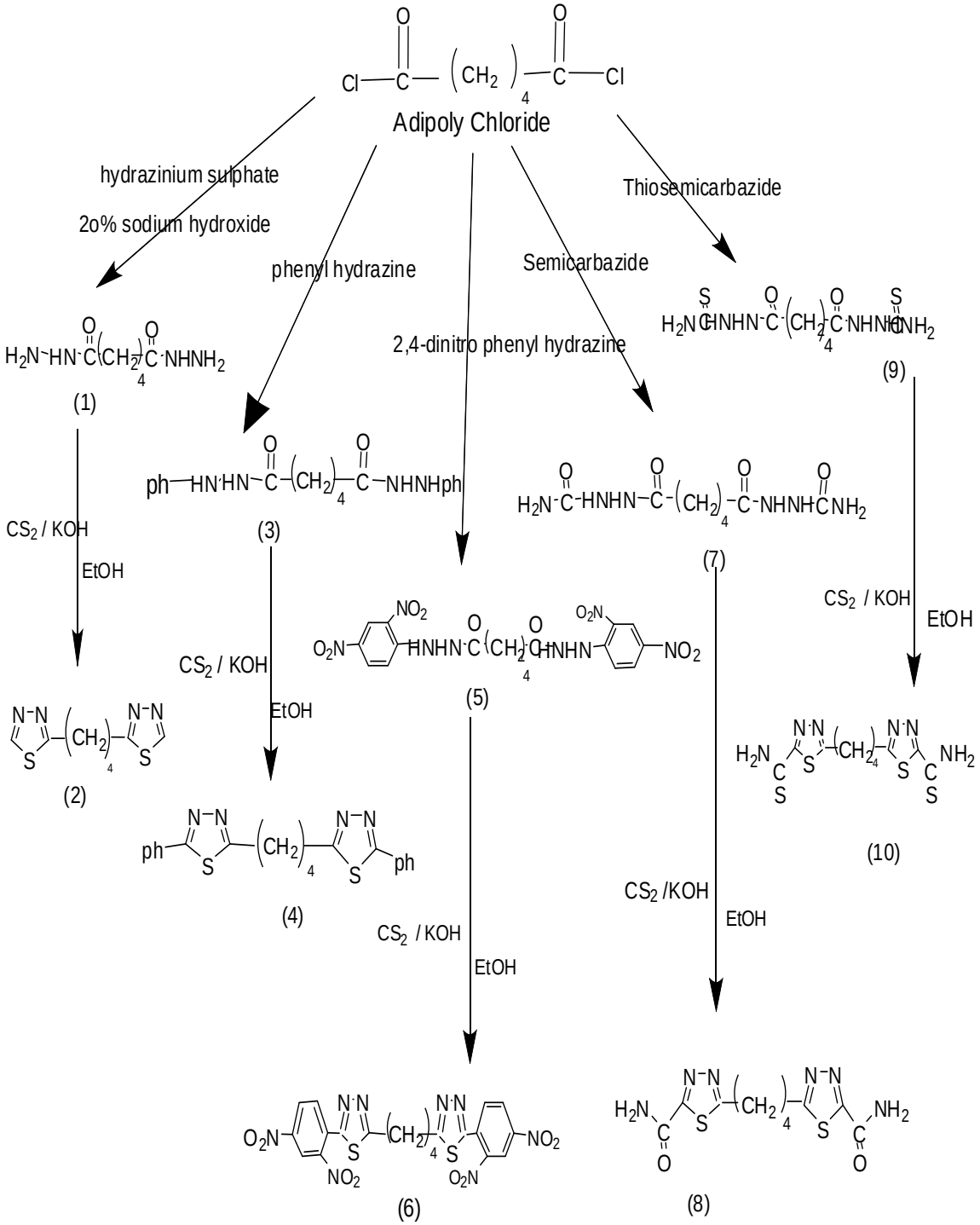
Table (2) : The solubility of the prepared compounds in different solvents

Comp.No.	Comp.Structure	C_2H_5OH	CH_3OH	DMF	H_2O	Benzene	$CHCl_3$	CH_2Cl_2
1		+	+	+	-	-	-	-
2		+	+	+	-	-	-	+
3		-	+	+	-	-	-	+
4		÷	÷	-	-	÷	+	÷
5		÷	+	÷	÷	÷	÷	÷
6		+	+	-	+	÷	÷	÷
7		÷	+	+	+	-	-	-
8		÷	÷	-	-	-	-	+
9		÷	+	÷	÷	-	-	+
10		÷	÷	-	-	-	-	-

(+) Soluble (-) Insoluble (÷) Partially soluble

Results and Discussion

The synthesis of new derivatives of hydrazine and thiadiazole were achieved from the reaction of adipoly chloride with different compounds ,such as hydrazine hydrate ,phenyl hydrazine ,2,4-dinitrophenyl hydrazine, semicarbazide and thiosemicarbarzide to afford compounds 1 , 3 , 5 , 7 and 9 . These compounds were treated with carbon disulfide to afford 2,4,6,8 and 10 compounds, as shown in Scheme I . The structures of (1, 2, 3, 4, 5, 6, 7, 8, 9 and 10) compounds were confirmed by physical properties which are listed in table (1) by spectral methods,such as FT-IR and some by ^{1}H-NMR and the determination of their solubility in different solvents .FT-IR spectra of the compounds (1, 3, 5, 7 and 9) showed the absorption at ν(1693-1620)cm^{-1} for(C=O) amid group and the disappearance the absorption at ν (1800-1700)cm^{-1}for carbonyl of acid chloride, while ^{1}H-NMR spectral data of compound (1) showed δ ppm 10(s, H, NH); 7.4-7.6 (d, 2H, -NH_2); 1.2-3.8 (m, 4H, $(CH_2)_4$); and for compound (5) δ ppm 6.5 (s, H, NH); 7-7.6 (d, 2H, ) ; 7.9 (s, H, ); 1.1-3.9 (m, 4H , $(CH_2)_4$) . The data are listed in table (4) .The derivatives of adipoyl thiadiazole (2,4,6,8 and 10) showed the absorption of (C=N) at ν (1627-1594) cm^{-1}, (1462-1415) cm^{-1} of (N-N) bending , (1404-1338) cm^{-1} of (C-N), and (702 -605) cm^{-1}of (C-S) .The compounds (2,3, 4, 5 and 6) showed the absorption bands at ν (3136-3082) cm^{-1}of(C-H)aromatic at (1670-1505) cm^{-1}of (C=C) and of (C-H) aliphatic at (2974-2937) cm^{-1},while the ^{1}H-NMR spectral data of compound (2) showed δppm (2.3-3.4) (m, 4H, $(CH_2)_4$) .The data was listed in table(4)


Adipoly Chloride
hydrazinium sulphate
2o% sodium hydroxide
phenyl hydrazine
2,4-dinitro phenyl hydrazine
Semicarbazide
Thiosemicarbazide
(1)
(2)
(3)
(4)
(5)
(6)
(7)
(8)
(9)
(10)
CS2 / KOH
EtOH

Scheme (I)

Table (3) : FT-IR absorption spectra data (cm^{-1}) of the prepared compounds .

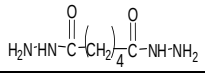
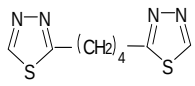
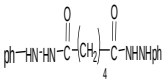
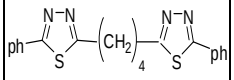
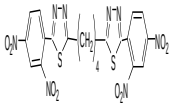
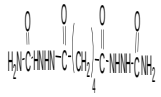
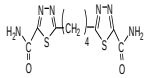
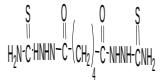
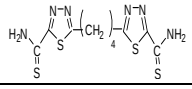
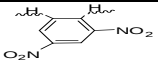
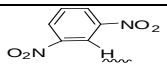
Comp.No.	Comp.Structure	ν NH_2 νNH	νC=Oamide	νC-H aromatic	νC=C	νC=N	N-NBending ν C-N	Other bands
1		3479 3314	1693			1620	1427 1357	C-H alph . 2926
2				3136		1616	1462 1377	ν C-H alph. 2951 ν(C-S)613
3		3356 3206	1662	3082	1505 1551		1456 1332	ν C-H alph 2951
4				3082	1670 1521	1594	1456 1379	ν C-H alph 2937 ν(C-S)690
5		3321 3248	1648	3101	1620 1593		1496 1338	ν C-H alph 2958 ν(C-NO_2) 1323
6				3101	1616 1569	1616	1415 1338	ν C-H alph. 2974 $\nu(C-S)666$ ν(C-NO_2) 1320
7		3283 3182	1685	3066			1481 1384	ν C-H alph. 2978
8		3313	1689			1616	1462 1392	ν C-H alph. 2924 ν(C-S) 605
9		3255 3128	1620				1369	ν C-H alph. 2924 ν(C-S) 705
10		3317				1627	1454 1404	ν C-H alph. 2968 ν(C-S) 702

Table (4) : ^{1}H-NMR Spectral data for selected compounds

Comp. No.	^{1}H-NMR parameters (ppm) δ-H
1	10 (s, H, NH); 7.4-7.6 (d, 2H, -NH_2); 1.2-3.8 (m, 4H, (CH_2))
2	2.3-3.4 (m, 4H, $(CH_2)_4$),)
5	6.5 (s, H, NH); 7-7.6 (d, 2H, ); 7.9 (s, H, ); 1.1-3.9 (m, 4H, $(CH_2)_4$)

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تخليق مشتقات جديدة للأدايبويل ثايادايازول

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الملخص

تضمن هذا البحث مفاعلة ادايبولي كلورايد مع الهيدرازين ومشتقاته التي هي فنيل هيدرازين ، ٢،٤-داينتروفنيل هيدرازين،سيمي كاربازايد و ثايوسيمي كاربازايد بعد ذلك عوملت نواتج هذا التفاعل بثاني كبريتيد الكاربون مع هيدروكسيد البوتاسيوم وبوجود الايثانول تكونت حلقات غير متجانسة وهي عبارة عن الثايادايازول ومشتقاته . تم اثبات . التراكيب عن طريق FT-IR و ^{1}H-NMR و تعيين نقاط انصهارها وذوبانيتها في مذيبات مختلفة .