Journal of Kerbala University , Vol. 6 No.4 Scientific. 2008

Synthesis of Some New Azo Schiff Bases and Tetrazole Derivatives from 2-Amino -1,3,4-thiadiazole-5-thiol

Zaid H.Abood, Rahman T. Haiwal ,Ibrahem L.Kadum, Khulood O.Gzar ,Sajid M.Radhi , Rabab K.Hameem and Sawsan K.Abbas
Chemistry Department ,College of Science ,University of Kerbala
Kerbala-Iraq

Abstract:

In this paper new azo schiff bases and tetrazole derivatives of 2-Amino-1,3,4-thiadiazole-5-thiol have been prepared.2-Amino-1,3,4-thiadiazole-5-thiol [1] was prepared by the reaction of thiosemicarbazide with carbon disulfide in alcoholic sodium carbonate solution .Compound [1] was converted to the diazonium salt which was directly converted to the azo derrivative [2] via a coupling reaction with salicyldehyde.The new azo Schiff bases derivatives [3-6] were prepared by condensation of aldehyde group of the new azo aldehyde derivative [2] with some primary amines (3-Amino phenol, 3-Bromo aniline ,2-phenyl ethyl amine) and with 2,4- Dinitro phenyl hydrazine respectively in absolute ethanol. The resulting imines [3-6] were converted to the corresponding tetrazole derivatives[7-10] through 1,3-dipolar cycloaddition reaction with sodium azide in tetrahydrofuran. All new synthesized derivatives were identified by their melting points,elemental analysis and FT-IR spectra. They have long been known to posses hypnotics activities and it is hoped that our compounds would do so.

الخلاصة :

تم في هذا البحث تحضير مشتقات قواعد شف وتترازول جديدة تحتوي في تركيبها على مجموعة ازو من المركب ٢-امينو -١،٣،٤- ثايادايازول-5- ثايول. حضر المركب البادى ٢-امينو -١،٣،٤- ثايادايازول-٥- ثايول [1] من تفاعل الثايو سيميكاربزايد مع ثنائي كبريتيد الكاربون في محلول كاربونات الصوديوم الكحولي . ثم تحويل المركب [1] الى ملح الدايازونيوم والذي تم تحويلة مباشرة الى مشتق الازو المقابل [2] عن طريق تفاعل الازدواج مع السالسالديهايد . تم تحضير مشتقات قواعد شف الجديدة الحاوية على مجموعة الازو [3-6] عن طريق تكاثف مجموعة الديهايد مشتق الازوالديهايد الجديد [2] مع بعض الامينات الاولية (٣- امينو فينول ، ٣-برومو انيلين ،٢- فنيل اثيل امين) ومع ٢،٤- ثنائي نتروفنيل هيدرازين وعلى التوالي في الايثانول المطلق . تم تحويل الايمينات الناتجة [3-6] الى مشتقات التترازول المقابلة [7-10] عن طريق تفاعل الاضافة الحلقية ٣,١ - ثنائية القطب مع ازيد الصوديوم في رباعي هيدروفيوران . ثبت نقاط انصهار المركبات الجديدة المحضرة ، وشخصت بوساطة التحليل الدقيق للعناصر واطياف الاشعة تحت الحمراء . ومن المؤمل ان تمتلك هذة المشتقات الجديدة فعالية بايولوجية واهمية طبية على غرارمشتقات ١،٣،٤- ثايادايازول الاخرى .

Introduction

Azo schiff bases are prepared by the acid-catalysed condensation of primary amines , hydrazines and hydrazides with azoaldehydes[1] .These derivatives are well known to have a wide range of biological activities such as antiviral[2] ,antibacterial[3-8],antifungal[3-4,9],anticonvulsant[10] and anticancer[11-14]. Several methods for the synthesis of tetrazole ring have been reported[15-19],but the most direct one is via [2+3] cycloaddition of azides and nitriles[20] .Tetrazole derivatives showed fungicidal and antiviral activity[21]. Tetrazoles also serve as precursors for synthesis of further interesting heterocycles[22].

We reported here the synthesis of some tetrazole derivatives via [2+3] cycloaddition of some new azo schiff bases derivatives and sodium azide .All prepared derivatives are containing azo group which may increase the biological activities[14,23-25].

Experimental

Chemicals

The following chemicals have been used in this work according to their manufactures .

Table(1) : Chemicals and their manufactures

Chemicals	Supplied from
Thiosemicarbazide	Fluka
Sodium carbonate(anhydrous)	BDH
Carbon disulfide	Fluka
Conc.Hydrochloric acid	Merck
Sodium nitrite	BDH
Chemicals	**Supplied from**
Sodium hydroxide	BDH
Ethanol(absolute)	BDH
Glacial acetic acid	BDH
Salicyldehyde	Fluka
3-Aminophenol	BDH
3-Bromoaniline	BDH
2-Pheyl ethyl amine	Fluka
2,4- Dinitrophenyl hydrazine	Merck
Tatrahydrofuran	BDH
Sodium azide	Merck

General Notes

All solvents used were redistilled. Thin layer chromatography were performed on asilica-gel SG - 40 (Merck). Spots were visualized with iodine vapour. The melting points were determined with Stuart Melting Point Apparatus. The FT-IR spectra were recorded on FT - IR - 8400S, Schimadzu-Spectrophotometer and using KBr discs.Elemental analysis measured on EA-1108 Carlo-Erba elemental analyzer.

Preparation Methods:

1) Synthesis of 2-Amino-1,3,4-thiadiazole-5-thiol [1]

A mixture of(5g,0.0549mole)of thiosemicarbazide and(2.912g,0.0274 4mole) of anhydrous sodium carbonate was dissolved in(25m**L**) absolute ethanol , to this solution (5g,0.0657mole) of carbon disulfide was added . The reaction mixture was refluxed on a water bath at 60 ºC for 24hrs.The reaction mixture was then allowed to cool down to room temperature , then (25m**L**) of distilled water was added with stirring to the mixture , the solution was carefully acidified with conc.hydrochloric acid to give pale yellow precipitate . The product was filltered under reduced pressure , washed well with cold distilled water and recrystallized from distilled water , yield 85% , m.p=(231-233ºC) ,reported (232-233ºC) [(26)] .

2) Synthesis of 2-Hydroxy-5-(5-mercapto-[1,3,4] -thiadiazol-2-ylazo)-benzaldehyde [2]

To a mixture of 2-Amino-1,3,4-thiadiazole-5-thiol [1] (2g ,0.015mole) and distilled water (10m**L**) contained in a small beaker , conc. hydrochloric acid (4m**L**) was added. The mixture was cold at (0ºC) in an ice bath . a solution of sodium nitrite (1.3g ,0.0188 mole) in (10m**L**) of distilled water was added dropwise with stirring to the mixture, the temperature of the ice bath was controlled between (0-5ºC) . a solution of (1.834g ,0.015 mole) of salicyldehyde

in (15m**L**) of (10%) sodium hydroxide solution in (150m**L)** beaker was prepared and cold to (5ºC) by immersion in an ice bath. The salicyldehyde solution was stirred vigorously ,the cold diazonium salt solution was added very slowly to the salicyldehde solution , a red colour developed and red crystals soon separated .when all the diazonium salt solution was added , the mixture was allowed to stand in an ice bath for 30 min.with occasional stirring. The solution was filtered , washed well with distilled water then with alittle alcohol , recrystallized from ethanol and dried upon filter paper,yield 70%,m.p=(179-181ºC).

3)Synthesis of azo schiff bases derivatives[3-6]

Azo benzaldehyde derivative [2] (0.4g,0.0015mole) was dissolved in (15 m**L**) of absolute ethanol containing a drop of glacial acetic acid, then equimolar amounts(0.0015mole) of some primary amines (3-Amino phenol ,3-Bromoaniline , 2-phenyl ethyl amine) and 2,4-Dinitrophenyl hydrazine were added dropwise and respectively. The reaction mixture was refluxed with stirring on awater bath at (60ºC) for 2hrs.Then the mixture was allowed to cool to room temperature , the coloured precipitate was filtered and recrystallized from ethanol , yields % and melting points are given in Table (2).

4) Synthesis of tetrazole derivatives [7-10]

A mixture of (0.0009mole) of prepared azo schiff bases [3-6] in (15 m**L**) of tetrahydrofuran and sodium azide (0.058g,0.0009mole) was heated under reflux on a water bath at (50-55ºC) for 4hrs,the temperature of the water bath was controlled at this range during the reaction proceeding, the reaction mixture was then allowed to cool to room temperature , filtered and recrystallized from ethanol, yields % and mellting points are shown in Table (2).

Comp. No.	M.P.^{O}C	Yield %	M.F	M.Wt g/mole	C.H.N analysis					
					Calculated%			Found%		
[1]	231-233	85	$C_2H_3N_3S_2$	133	C	H	N	C	H	N
					-	-	-	-	-	-
[21	179-181	70	$C_9H_6N_4O_2S_2$	266	40.60	2.25	21.05	40.39	2.38	21.16
[3]	153-155	75	$C_{15}H_{11}N_5O_2S_2$	357	50.42	3.08	19.60	50.31	3.19	19.43
[4]	129-130	70	$C_{15}H_{10}N_5OS_2Br$	420	42.85	2.38	16.66	42.74	2.22	16.53
[5]	130-132	81	$C_{17}H_{15}N_5OS_2$	369	55.28	4.06	18.97	55.02	4.17	18.88
[6]	158-160	72	$C_{15}H_{10}N_8O_5S_2$	446	40.35	2.24	25.11	40.22	2.15	25.21
[7]	140-141	64	$C_{15}H_{10}N_8O_2S_2$	398	45.22	2.51	28.14	45.12	2.73	28.01
[8]	119-120	58	$C_{15}H_9N_8OS_2Br$	461	39.04	1.95	24.29	39.18	1.89	24.18

[9]	123-124	68	$C_{17}H_{14}N_8OS_2$	410	49.75	3.41	27.31	49.63	3.55	27.26
[10]	148-149	55	$C_{15}H_9N_{11}O_5S_2$	٤٨٧	36.96	1.84	31.62	36.82	1.79	31.73

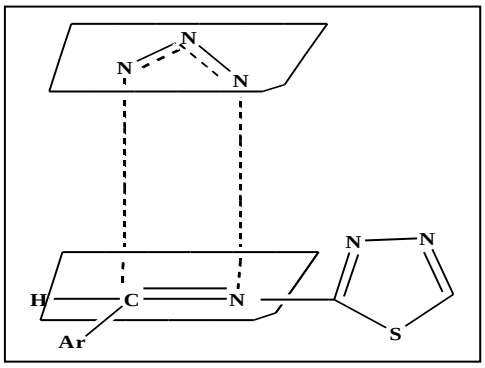
Table (2): Melting points , percent yields and C.H.N analysis of the prepared compounds (1-10)

Results and Discusion

Azo Schiff bases can be prepared via a condensation reaction between primary amines with azoaldehydes[1] , therefore we prepared 2-Amino-1,3,4-thiadiazole-5-thiol, by the reaction of thiosemicarbazide with carbon disulfide in alcoholic sodium carbonate solution ,as a primary amine which was then converted to the corresponding diazonium salt , by the reaction with hydrochloric acid and sodium nitrite , which was directly converted to the azo aldehyde derivative [2] as a product of coupling reaction with salicyldehyde .Aldehyde group of this new substituted benzaldehyde was condensed with various primary aromatic amines are 3-Amino phenol ,3-Bromo aniline ,2-phenyl ethyl amine and 2,4-Dinitro phenyl hydrazine respectively to give four new azo Schiff bases derivatives [3-6] which were then introduced in a 1,3-dipolar cyclo addition reaction with sodium azide to give four new tetrazole derivatives [7-10] containing azo group as well as 1,3,4-thiadiazole hetrocyclic ring as a trial to develop the biological activity of thiadiazole ring .

Reaction mechanism of azide addition to the imine group systematically investigated as [3+2] cycloaddition which christened as a 1,3-dipolar cycloaddition .it is involved the addition of unsaturated systems, dipolarphiles,to 1,3-dipoles ,a molecule possessing resonance contributors in which a positive and negative charge are located in 1,3-position relative to each other . The addition results in a five-member ring .Azide are a prominent class of 1,3-dipols and azide 1,3-dipolar cycloadditions are of great synthetic value and have been studied mechanistically in great detail.

The common features of this type of reactions is best accommodated by a T.S. geometry in which the dipolarphile and its ligands lies in one plane , and the azide lies in a parallel plane above or below , so that the orbitals perpendicular to the planes interact to form bonds , Scheme (1).



Scheme(1): Approximate transition state geometry for azide addition

The structures of synthesized compounds were shown in scheme (2).
Synthesized compounds [1-10] were characterized by melting points, C.H.N. microanalysis, as it was shown in Table (2), and FT-IR spectra as it was shown in Table (3).

Compound [1] showed identical melting point with that published [27]. Compound [1] was also characterized with FT-IR spectrum which showed the following characteristic bands: the two bands at 3400cm^{-1} and 3280cm^{-1} were due to asymmetric and symmetric stretching vibrations of (-NH_2) group respectively an absorption band at 3090cm^{-1} was due to the (-NH) stretching vibration (tautomeric form). The absorption bands at 2920cm^{-1} and 2770cm^{-1} were attributable to the intramolecularly hydrogen bonded of (-NH) group [27]. The (-SH) stretching band found as very weak shoulder at 2600cm^{-1}. A band at 1600cm^{-1} was due to the (C=N) stretching vibration of the thiadiazole ring moiety. The sharp bands at 1530cm^{-1} and1495cm^{-1} are due to the (-NH) bending and (C-N) stretching vibrations respectively. Also, the absorption bands at (1360, 1320,1280)cm^{-1} are due to the presence of (=N-N-C-) cyclic grouping [28]. Moreover, the absorption band at 1070cm^{-1} for the (C=S) group stretching vibration gives evidence that compound [1] can exist in two tautomeric forms, thiol form [**1$_a$**] and thion form [**1$_b$**] [29]. Beside this, the band at 750cm^{-1}due to (C-S) bond stretching is good evidence for the structure given to the product.

| **1$_a$** | | **1$_b$** |

FT-IR spectrum of compound [2], azo aldehyde derivative, showed disappearance of absorption bands at 3400cm^{-1} and 3280 cm^{-1} attributed to the (-NH_2) stretching frequency and appearance of a broad band at the range (3440-3360)cm^{-1} assignable to υ(-OH).The absorption band at 3150cm^{-1} due to the υ(C-H) aromatic. The band at 2870cm^{-1} due to the υ(C-H) aliphatic of aldehyde group (-CHO). Furthermore, the absorbtion band at 1625cm^{-1} due to the υ (C=O) of aldehyde group, we notice that the value was shifted to the lower frequency due to the intramolecular hydrogen bonding with ***Ortho*** hydroxy group. FT-IR spectrum also showed appearance of a weak absorption band at 1575 cm^{-1} for υ(N=N).The absorption band at 1540 cm^{-1} due to the υ (C=N) of the thiadiazole ring. The three absorption bands at (1560cm^{-1}, 1500cm^{-1}, 1460cm^{-1}) due to the υ(C=C) of the aromatic ring. The absorption band at 840cm^{-1} was due to the δ(C-H) aromatic out of plane . FT-IR spectrum also showed a strong band at 1050cm^{-1} was attributed to the υ(C=S) of thion tautomeric form.

FT-IR spectrum of Schiff bases derivatives, compounds [3-6] , showed disappearance of the absorption band at 1625cm^{-1} attributed to the υ(C=O) of aldehyde group in compound [2]. On the other hand, the FT-IR spectrum of compounds [3-6] showed appearance of absorption bands due to the exocyclic imine group stretching vibration υ(C=N)at(1620cm^{-1},1620cm^{-1},1620cm^{-1},1615cm^{-1})respectively. Moreover, FT-IR spectrum also showed appearance of another important characteristic absorption bands found in Table (3). FT-IR spectrum of tetazole derivatives, compounds [7-10], showed disappearance of absorption bands attributed to the exocyclic imine group stretching vibration υ(C=N) at (1620cm^{-1}, 1620cm^{-1}, 1620cm^{-1},1615cm^{-1}) respectively which is good evidence for the success of a 1,3-dipolar cycloaddition reactions. Beside this, the FT-IR spectrum of these compounds were devoid of a strong band at (2160-2120)cm^{-1} attributed to the stretching frequency of azide

group. FT-IR spectrum of these compounds also showed appearance of another important characteristic absorption bands shown in Table (3).