Synthesis of New Heterocyclic Derivatives from 4-(3, 5-Dimethyl-1-phenyl-1H-pyrazol-4-ylazo)-benzoic acid

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Date of acceptance 1/3 / 2010

Abstract

In this work pyrazolin derivatives were prepared from the diazonium chloride salt of 4-aminobenzoic acid. Azo compounds were prepared from the reaction of an ethanolic solution of sodium acetate and calculated amount of active methylene compound namely, acetyl acetone to obtain the corresponding hydrazono derivative **(1**). Cyclocondensation reaction of compounds **(1)** with hydrazine hydrate and phenyl hydrazine in boiling ethanol affording the corresponding pyrazoline-5-one derivatives of 4-aminobenzoic acid (**2,3)**. Then compound **(3)** was reacted with thionyl chloride to give the corresponding acid chloride derivative**(4)**, followed by conversion into the corresponding acid hydrazide derivative **(5)** carboxylic acid thiosemicarbazide **(11)**, esters **(14,15)**, thioesters **(16,17)** and amides **(18,19)**, when treated hydrazine hydrate, thiosemicarbazide, alcohols, alkylthiol and secondary amines in dry refluxing benzene; respectively. Schiff's bases **(6-8)** were prepared by refluxing of compound **(5)** with different aldehydes and ketons, then two compounds from the Schiff's bases were cyclized with α-mercapto acetic acid to give **(9** and **10)**. Furthermore, 1,2,4-triazole derivative **(12)** have been also prepared by refluxing thiosemicarbazide derivative with sodium hydroxide solution (4%) followed acidification of the result using (10%)hydrolic acid. Moreover, a thiadiazole derivative **(13)** has been prepared by treatment of thiosemicarbazide derivative with concentrated sulfuric acid as cyclyzing agent. Finally, oxadiazole derivative **(20)** has prepared by condensation of its acid hydrazide derivative with carbon disulfide in basic medium.

Key word: Azo compound, Pyrazol derivatives, active methylene compound

Introduction

Heterocyclic compounds represent an important class of biologically active molecules. Specifically, those containing the pyrazole nucleus have been shown to possess high biological activities as herbicides, fungicides, analgesics, etc [(1)]. Pyrazole derivatives have attracted particular interests during the last twenty five years due to the use of such ring system as the core structure in many drug substances, covering wide range of pharmacological applications [(2, 4)]. Some novel pyrazole derivatives containing sulfonamide moieties as anti microbial agents [(5)]. Various sulfa drugs were coupled with active methylene compounds to give various hydrazones, then novel series of pyrazoles derivatives [(6)]. Moreover; reaction of azo compounds with substituted acetoacetic ester derivatives using acetic acid as solvent [(7)].Azo pyrazolone derivatives were used for this purpose instead of inorganic pigment [(8)], have prepared an azo pyrazolone compound such as barium, strontium, magnesium, manganese, sodium, and especially calcium. The reaction of

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monosubstituted hydrazides with 1,3-dicarbonyl compound is widely used for the synthesis of pyrazoles. [9].

Materials and Methods

Apparatus and Chemicals

Electrothermal 9100 melting point apparatus, Perkin-Elmer 1310 infrared spectrophotometer or a Shimadzu FTIR-800, as KBr discs or thin films, UV-Visible Varian UV-Cary-100 spectrophotometers were used in this work. ^{1}H-NMR spectra was recorded on spectrometer (200MHz) at Silicone Research Center at Wisconsin University, USA. Tetramethylsilane was used as an internal reference and DMSO as solvent. All the chemicals used were supplied by Merck, Fluka and BDH chemicals. The solvents were purified by distillation and dried with calcium chloride.

Synthesis of compounds:

Synthesis of 4-(1-Acetyl-2-oxo-propylazo)-benzoic acid (1) [10]

To an ice-cooled mixture of the active methylene compound (acetyl acetone) (0.01 mole) and sodium acetate (0.05 mole, 4.10 g) in ethanol (50 ml), was added dropwise with stirring to a cooled solution of the diazonium salt over 15 minute. Product was collected and recrystalized from ethanol.

Synthesis of 4-[(3,5-dimethyl-1H-pyrazol-4-yl)diazenyl]benzoic acid (2) [10]

A mixture of azo derivative **(1)** (0.01 mole) and hydrazine hydrate (95 %) (0.012 mole, 0.35 g) in ethanol (30 ml) was heated under reflux for 4 hours. The reaction mixture was concentrated and the reaction product was allowed to cool. The separated product was filtered off, washed with water, and recrystallized from ethanol.

Synthesis of 4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl] benzoic acid (3)[10]

To a solution of compound **(1)** (0.01 mole) in glacial acetic acid (30 ml) , phenyl hydrazine (0.012 mole, 1.3 g) and anhydrous sodium acetate(0.01 mole, 0.82 g) was added. The reaction mixture was heated under reflux for 4 hours. The mixture was poured into ice-cold water and stored in a refrigerator for 12 hours. The crude product, which is separated, was washed with water, dried and recrystallized from ethanol.

Synthesis of 4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl]benzoyl chloride (4))[11]

A mixture of compound **(3)** (0.01 mole, 2.46 g) and thionyl chloride (0.015 mole, 1.78 g) was gently refluxed for 2 hours. After cooling, excess thionyl chloride was removed under reduced pressure. The product was recrystallized from benzene.

Synthesis of 4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl] benzohydrazide (5))[11]

To a stirred solution of compound **(4)** (0.005 mole, 1.32 g) in dry benzene (15 ml), a mixture of hydrazine (95 %) (0.01 mole, 0.35 gm) and benzene (10 ml) was added dropwise. The mixture refluxed for 2 hours, cooling, excess benzene was removed under reduced pressure. Product was recrystallized from ethanol.

Synthesis of Schiff's bases derivatives of 4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl] benzohydrazide (6-8)[11]

To a stirred solution of compound **(5)** (0.01 mole, 2.6 g) in absolute ethanol (30 ml), the appropriate aldehyde or ketone was added (0.01 mole). The mixture was refluxed for 3 hours, cooling, filtered and recrystalized from ethanol.

Synthesis of thiazolidine derivatives of (9 and 10) [12]

A solution of α-mercaptoacetic acid (0.01 mole, 0.92 g) in (15 ml) dry benzene was added slowly with stirring to a solution of compounds **(6 and 7)** (0.01 mole) in (15 ml) of dry benzene. The mixture was refluxed for 10 hours. The solution were concentrated and neuteralized with sodiumbicarbonate solution (10 %). The solid product was filtered and recrystallized from solvent.

Synthesis of 2-{4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl] benzoyl hydrazinecarbothioamide (11)[13]

To a solution of **(4)** (0.005 mole, 1.32 g) in dry benzene (25 ml), thiosemicarbazide (0.005 mole 0.45 g) was added. The mixture was refluxed for 3 hour, cooling, filtered and recrystalized from ethanol.

Synthesis of 5-{4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl) diazenyl]phenyl}-4H-1,2,4- triazole-3-thiol (12)[13]

A mixture of (**11)** (0.001 mole, 0.319 g) and (4%) sodium hydroxide solution (25 ml) was refluxed for 4 hours, cooled, poured into crushed ice and acidified with dilute hydrochloric acid (10 %). The resultant precipitate was filtered, washed with water and recrystallized from ethanol.

Synthesis of 5-{4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl]phenyl}-1,3,4-thiadiazol-2-amine (13)[12]

Compound **(11)** (0.001 mole, 0.32 g) was dissolved in cold concentrated sulfuric acid (10 ml) and stirred at room temperature for 24 hours, poured into crushed ice the product was filtered, recrystalized from ethanol

Esterification of 4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl] benzoyl chloride (14,15)[14]

To a solution of compound **(4)** (0.005 mole, 1.23 g) in dry benzene (25 ml), alkyl, or phenyl alcohol (0.005 mole) was added, the mixture was refluxed for 6 hours, cooling, filtered and recrystalized from appropriate solvent.

Thioesterification of 4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl] benzoyl chloride (16,17)[14]

To a solution of compound **(4)** (0.005 mole, 1.23 g) in dry benzene (25 ml), alkylthiol (0.005 mole) was added, mixture was refluxed for 6 hours The resultant precipitate was filtered, washed with water and recrystallized from appropriate solvent.

Synthesis of amide derivatives of 4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl] benzoyl chloride (18-19)[14]

To a solution of compound **(4)** (0.005 mole, 1.23 g) in dry benzene (25 ml), secondary amine (0.005 mole) was added, and refluxed for 3 hours The resultant precipitate was filtered, washed with water and recrystallized from appropriate solvent.

Synthesis of 5-{4-[(3,5-dimethyl-1-phenyl-1H-pyrazol-4-yl)diazenyl]phenyl}-1,3,4-oxadiazole-2-thiol (20)[12]

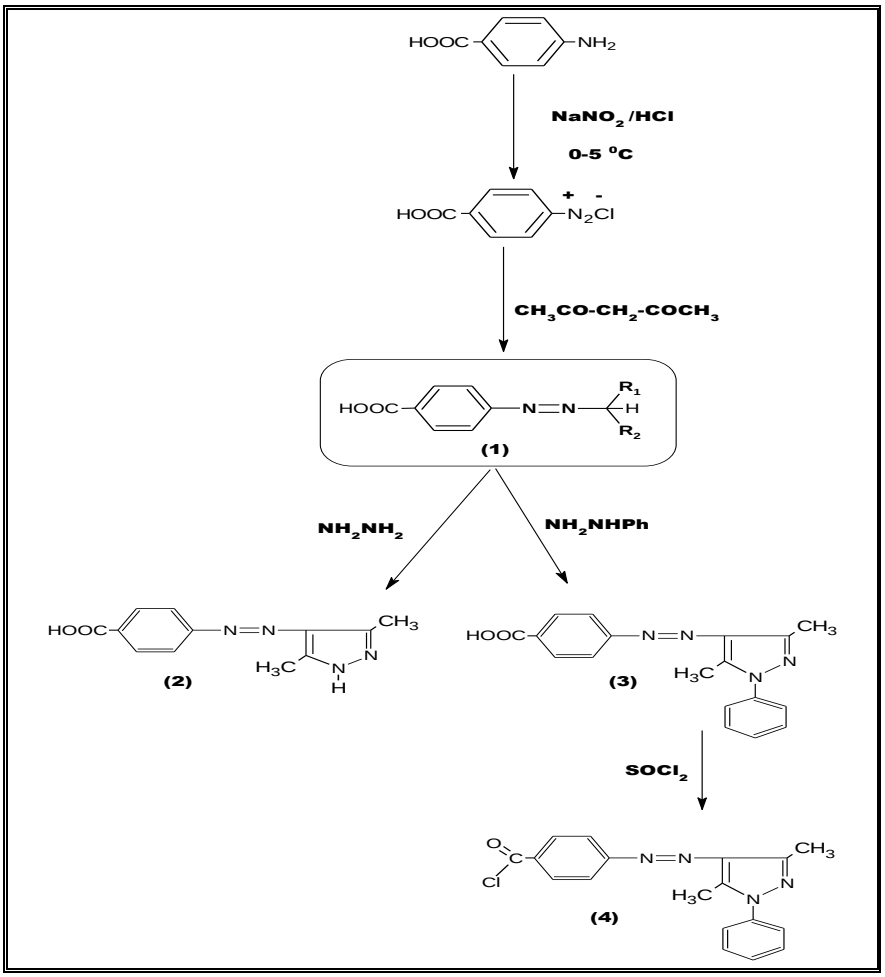
To a mixture of compound **(5)**, (0.01 mole, 2.6 g) and carbon disulfide (0.2 mole, 12 ml) in pyridine (10ml)was added slowly with (10 ml) ethanol (96 %) was added.The mixture was refluxed for (10 hours). The solid product was cooled, concentrated under vacuum and . The recrystallized from chloroform.

Table (1): The physical properties of compounds (1-20)

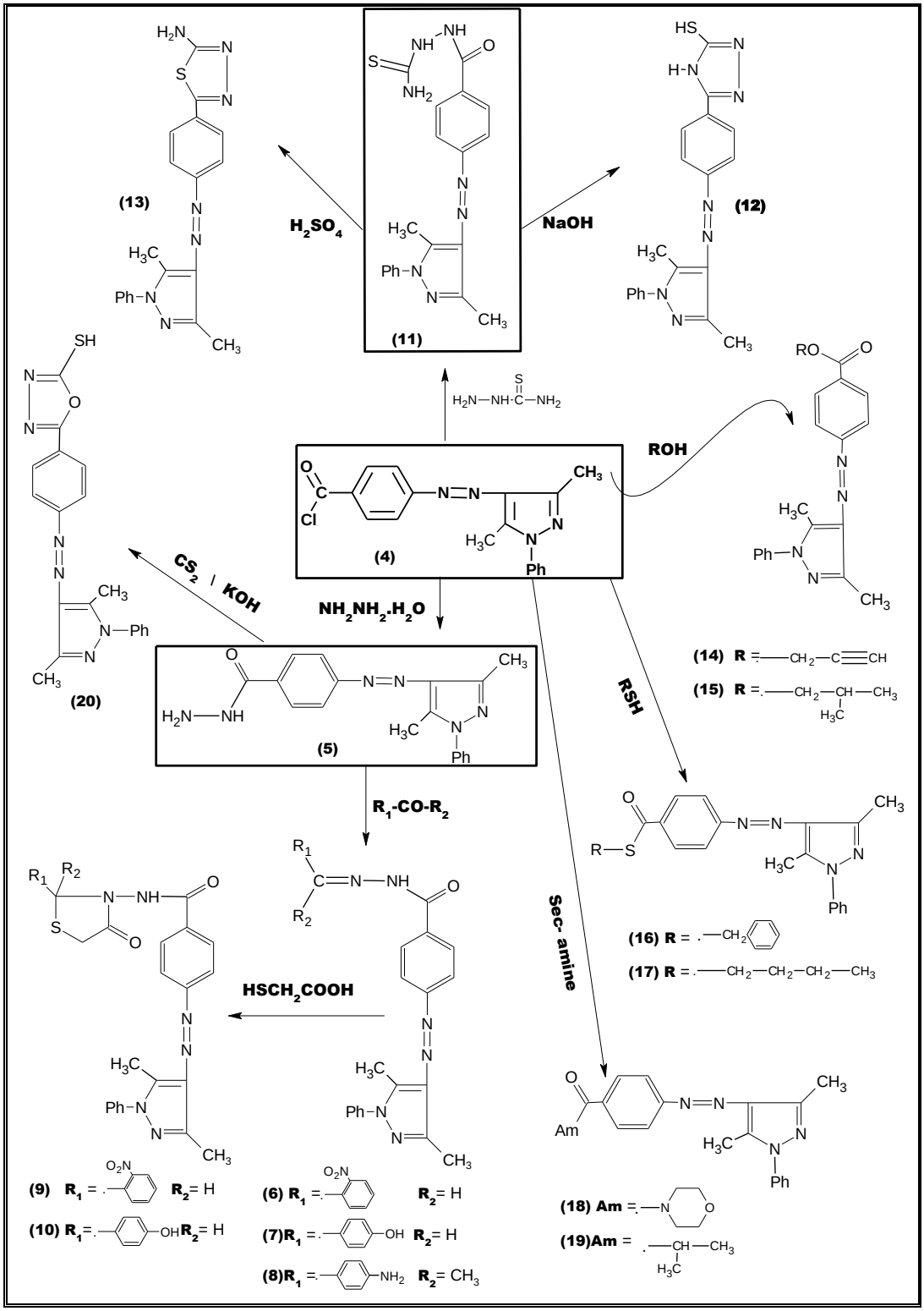
Compound Number	Molecular Formula	M.P/ ˚C	Color	Purification solvent	Yield (%)
1	$C_{12}H_{12}N_2O_4$	210-212	Greenish-Yellow	Ethanol	80
2	$C_{12}H_{12}N_4O_2$	215-217	Pale-Yellow	Ethanol	56
3	$C_{18}H_{16}N_4O_2$	230-233	Pale -Green	Ethanol	70
4	$C_{18}H_{15}ClN_4O$	208 dec	Deep-Orange	Benzene	66
5	$C_{18}H_{18}N_6O$	240-241	Pale Brown	Ethanol	70
6	$C_{25}H_{23}N_7O_3$	249-250	Brown	Ethanol	68
7	$C_{25}H_{24}N_6O_2$	256-259	Pale-green	Ethanol/water	82
8	$C_{26}H_{27}N_7O$	271 dec.	Yellow	Ethanol	78
9	$C_{27}H_{24}N_7O_4S$	270dec	Deep-Green	Chloroform	40
10	$C_{27}H_{25}N_6O_3S$	287 dec.	Brown	Chloroform	57
11	$C_{19}H_{21}N_7OS$	275 dec.	Brown	Ethanol	66
12	$C_{19}H_{19}N_7S$	224-226	Brownish-red	Ethanol	33
13	$C_{19}H_{19}N_7S$	290 dec.	Pale-Green	Ethanol	54
14	$C_{21}H_{20}N_4O_2$	189-191	Yellow	Benzene	88
15	$C_{22}H_{26}N_4O_2$	160-163	Pale Brown	Chloroform	83
16	$C_{25}H_{24}N_4OS$	190 dec	Brown	Benzene	30
17	$C_{22}H_{26}N_4OS$	159-162	Brown	Chloroform	56
18	$C_{22}H_{25}N_5O_2$	203-207	Pale Brown	Chloroform	60
19	$C_{20}H_{23}N_5O$	200 dec	Yellow	Chloroform	76
20	$C_{18}H_{18}N_6OS$	230-234	Brown	Chloroform	43

Results and Discussion

For the synthesis of the target 4-aminobenzoic acid derivatives in this work, the reaction sequences are outlined in schemes **(1 and 2)**.



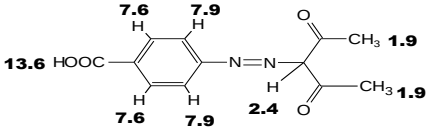
Scheme (1)



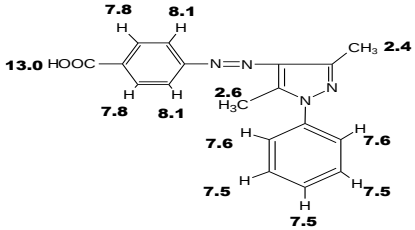
Scheme (2)

The prepared diazonium chloride of 4-aminobenzoic acid was added to an ethanolic solution of sodium acetate and calculated amount of active methylene compound, namely, acetylacetone to afford the corresponding hydrazono derivatives**(1,2)** as shown in Scheme (1). The IR spectrum of compound **(1)** shows a characteristic bands at (1720 cm^{-1}), (1690 cm^{-1}) corresponding to the (C=O) stretching vibration of acetyl and carboxylic acid groups, respectively, bands at (1545 cm^{-1}) due

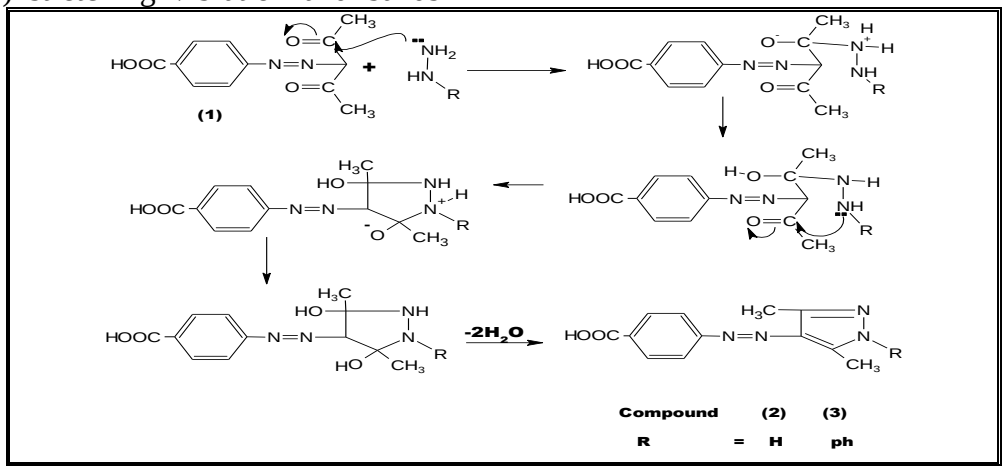
to stretching vibration of azo group [15] ,and at (2600-3100 cm^{-1}) refers to the stretching vibration of hydroxyl group in carboxylic acid. The U.V. spectrum of this compound has λ_{max} (MeOH) at (366.0nm and 257.0 nm) due to (π-π^*) transition. The ^{1}H-NMR spectrum of compound **(1)** showed a singlet at δ (1.9 ppm) integrated for six protons attributed to the two methyl groups. The spectrum also shows signal at δ (2.45) ppm integrated for one proton assigned for the proton of the active methylene group. Aromatic protons appeared as AB quartet at (7.9 and 7.6 ppm) for p-substituted ring integrated for four protons. A signal at δ (13.6) ppm, integrated for one proton, which may be attributed to the proton of the carboxylic acid group.



Hydrazons are easily undergoing cyclocondensation reaction with hydrazine hydrate or phenyl hydrazine in boiling ethanol affords to the corresponding pyrazoline derivatives of 4-aminobenzoic acid. The IR spectrum of compound **(2) ,**shows the appearance of a band at (1618 cm^{-1}) refer to (C=N) bond stretching vibration and the appearance of strong bands in the (3345 cm^{-1}), attributed to (N-H) stretching vibration and bands of (C=O) carboxylic acid appeared at (1680 cm^{-1}), and $(OH)_{st}$ appear at (2700-3230cm^{-1}) ,band at (1575 cm^{-1}) due to stretching vibration of azo group [15]. The IR spectrum of compound **(3)** shows the disappearance the characteristic band of acetyl carbonyl group at (1720 cm^{-1}), and appearance a band at (1618 cm^{-1}) refer to(C=N) bond stretching vibration, band at (1550 cm^{-1}) due to stretching vibration of azo group and appearance of a band at (1310 cm^{-1}) due to (N-Ph) stretching vibration which give a good indication for the cyclization . The ^{1}H-NMR spectrum of compound **(3)** showed two signals, assigned for the two methyl groups of pyrazol ring at δ (2.48) [16] and (2.65) ppm each integrated for three protons. Aromatic protons appeared at the region δ (7.8 and 8.1) ppm as AB quartet for p-substituted ring, (7.4-7.6) ppm integrated for 5 protons of the other ring [16]. The proton of the carboxylic acid group appeared at δ (13.0) ppm, integrated for one proton.



The mechanism of this cyclocondensation reaction may be:



Scheme (3)

The IR spectrum of compound **(4),** shows the disappearance of the hydroxyl group of the starting material and appearance of the new (C=O) band at (1790 cm^{-1}), for the acetyl chloride. The spectrum also shows an absorption band at (750 cm^{-1}) refering to (C-Cl) band. The IR spectrum of compound **(5),** shows an absorption band at (1710 cm^{-1}) for (C=O) stretching vibration and at (3290 cm^{-1}) for (N-H) and (3450-3500 cm^{-1}) for (NH_2) stretching vibration. The success of the reaction has been confirmed by comparing the (C=O) absorption in the acid chloride and hydrazide derivatives [17]. The Schiff's bases **(6-8)** have been synthesized by the condensation of **(5)** with appropriate aromatic aldehydes or ketones in the presence of absolute ethanol as a solvent. The IR spectrum of compound **(6),** shows the characteristic band at (3333 and 3165 cm^{-1}) due to (NH) stretching vibrations, at (1657 cm^{-1}) for (C=O) of amide group and at (1635 cm^{-1}) due to (C=N) stretching vibration. The spectrum also shows absorption band at (1360, 1515 cm^{-1}) for the asymmetrical and symmetrical vibration for aromatic (NO_2), respectively. The U.V. spectrum of this compound, has λ_{max} (MeOH) at (400.0nm and 331.0 nm) due to (π-π^*) transition. Other bands of the synthesized Schiff's bases **(6-8)** are listed in table (2). The IR spectrum of compound **(10)** revealed a strong band around (1717 cm^{-1}) for amide carbonyl group of thiadiazole-4-one and (1680 cm^{-1}) for the amide carbonyl group. The spectrum also shows absorption band at (759 cm^{-1}) due to (C-S-C) group and near (3400) and (3300 cm^{-1}) due to the two (NH) stretching vibrations which interfere with the (OH) stretching vibration, Band at (1547 cm^{-1}) due to stretching vibration of azo group .The IR spectrum of compound **(11),** shows the main characteristic bands at (1220 cm^{-1}) refers to (C=S) stretching vibration, (3300-3450 cm^{-1}) due to (NH_2) asymmetric and symmetrical bands respectively, interfered with (NH), band at (3350 cm^{-1}) of the ring system. In addition, the success of reaction has been confirmed by the disappearance of (C=O) at (1790 cm^{-1}) in acid chloride, and appearance of (C=O) band at (1682 cm^{-1}) in the acid thiosemicarbazide. The IR spectrum of compound **(12),** shows characteristic (S-H) stretching vibration as weak band at (2700 cm^{-1}) and (C=S) stretching vibration as weak band at (1233 cm^{-1}) which confirmed the tautomersim between thion and thiol form and an absorption band at (1644 cm^{-1}) due to (C=N) stretching vibration of triazole. The U.V. spectrum of this compound, has λ_{max} (MeOH) at (377.0 nm and 256.5 nm) due to (π - π^*) transition. The IR spectrum of compound **(13)** shows absorption band at (1260 cm^{-1}) due to (N-N) stretching vibration and at (3300-3450 cm^{-1}) due to (NH_2) stretching vibration, band at (1540 cm^{-1}) due to stretching vibration of azo group ,an absorption band at (1630 cm^{-1}) due to (C=N) stretching vibration. The U.V. spectrum of this compound, has λ_{max} (MeOH) at (426.0nm and 356.0 nm) responsible for (π - π^*). The IR spectrum of compound **(14),** shows the disappearance of (C-Cl) stretching band and appearance of absorption band at (1728 cm^{-1}) due to (C=O) stretching vibration, appearance of sharp band (C≡C-H) stretching band at (3255 cm^{-1}) and band at (2145 cm^{-1}) for (C≡C) assymetrical stretching vibration [18] . The success of the reaction has been confirmed by the appearance of the triple bond of the acetylenic group. The IR spectrum of compound **(16),** shows band at (1690 cm^{-1}) due to (C=O) stretching vibration which had appeared at (1790 cm^{-1}) in acid chloride compound **,** band at (690 cm^{-1}) due to (C-S) stretching vibration. The U.V. spectrum of compound **(16),** has λ_{max}

(MeOH) at (292.0 nm) responsible for (π - π^*) transition. The IR spectrum of compound **(18),** shows the main characteristic bands at (1635 cm^{-1}) due to (C=O) of amide and at (1160 cm^{-1}) due to (C-O-C) stretching vibration. The U.V. spectrum of compound **(18)**, has λ_{max} (MeOH) at (310.0 nm) due to (π- π^*) transition. The IR spectrum of compound **(20),** shows absorption band at (3350 cm^{-1}) which corresponds to (NH) stretching vibration, the spectrum also shows a band at (1640 cm^{-1}) due to (C=N) stretching vibration. Another band for (C-O-C) stretching vibration appears at (1170 cm^{-1}), band at (1566 cm^{-1}) due to stretching vibration of azo group ,an absorption band at (1640 cm^{-1}) due to (C=N) stretching vibration. The U.V. spectrum of this compound, has λ_{max} (MeOH) at (410.0 nm and 300.0 nm) due to (π - π^*) transition.

Table (2): Spectral data for compounds (1-20)

Compound Number	UV λ_{max} (nm)	ν(C=O)	ν(C=N)	ν(N=N)	ν(C-H)al ν(C-H)ar	Others
1	366 257	1720(acetyl) 1690 (acid)	------	1545	2980 3050	2600-3100 $(OH)_{st}$
2	398 268	1680(acid)	1618	1575	2900 3030	2700-3230$(O-H)_{st}$ 3345 $(N-H)_{st}$
3	300 270	1690(acid)	1620	1550	2970 3070	2600-3250(O-H) 1310(N-Ph)
4	344 240	1790	1610 interfere with C=C	1585	2950 3050	750 $(C-Cl)_{st}$ 3350 $(N-H)_{st}$
5	328	1710	1610 interfere with C=C	1563	2970 3080	3450-3500 $(NH)_{st}$ 3290 $(NH)_{st}$
6	400 331	1657	1635	1540	2995 3040	3165-3333$(N-H)_{st}$ 1360-1515$(NO_2)_{st}$
7	333	1655	1620 Interfere with C=C	1545	2950 3075	3230 $(N-H)_{st}$
8	290	1665	1620	1550	2940 3030	3300-3425 $(NH_2)_{st}$ Interfere with 3275 $(N-H)_{st}$
9	381 277	1708 1675	1638	1525	2960 3020	3400$(NH)_{st}$ 1340,1520$(NO_2)_{st}$ 748$(C-S-C)_{st}$
10	409 290	1717(thia) 1680(amid)	1663	1547	2920 3050	3300-3400$(NH)_{st}$ Interfere with 3100-3400$(OH)_{st}$ 759$(C-S-C)_{st}$ 790 p-sub
11	405 266	1682	1630 interfere with C=C	1540	2960 3050	1220 $(C=S)_{st}$ 3350 $(NH)_{st}$ Interfere with 3300-3450 $(NH_2)_{st}$
12	377 256.5	---------	1644	1555	2970 3080	1233 $(C=S)_{st}$ 2700$(SH)_{st}$ 3300 $(NH)_{st}$
13	426 356	----------	1630 interfere with C=C	1540	2900 3050	1260 (N-N) 3250 $(NH)_{st}$ Interfere with 3300-3450 $(NH_2)_{st}$
14	395	1728	1615	1555	2950 3080	3255 (C≡C)st 2145 (C≡C)st 3350 $(NH)_{st}$
15	400 260	1725	1617	1583	2900 3050	3350 (NH)st
16	455 311	1690	1620	1550	2975 3100	3300$(NH)_{st}$ 690$(C-S)_{st}$
17	398 285	1700	1612	1558	2980 3050	3270 $(NH)_{st}$ 675$(C-S)_{st}$
18	310	1635	1625 interfere with (C=O)	1550	2950 3080	1160(C-O-C) 3350 (NH)st
19	337 288	1648	1625)	1550	2950 3050	3300 (NH)
20	410 300	---------	1640	1566	2970 3080	1170 $(C-O-C)_{st}$ 2750$(SH)_{st}$ 1200 $(C=S)_{st}$ 3350 (NH)

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تحضير مشتقات حلقات غير متجانسة جديدة من 4-(5،3-داي مثيل -1-فنيل ،1-Hبايرازول ، بلزو، حامض البنزوك

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الخلاصة

تناول هذا البحث تحضير بعض مركبات البايرازولين المشتقة من ملح كلوريد الدايزونيوم للمركب 4-امينو حامض البنزويك. تم تحضير مركبات الازو عن طريق مفاعلة ملح كلوريد الدايزونيوم مع مركب حاوي على مجموعة المثلين الفعالة مثل (acetyl acetone) باستخدام الايثانول كمذيب بوجود خلات الصوديوم حيث تم الحصول على المشتق (**1**) . تمت مفاعلة المركب (**1**) مع الهيدرازين والفنيل هيدرازين في الايثانول للحصول على مشتق البايرازولين (**2**) و(**3**). بعدها اجري تفاعل المركب (**3**) مع كلوريد الثايونيل للحصول على مشتق حامض الكلوريد (**4**), و تم تحويل هذا المشتق الى مشتق الهايدرازيد (**5**) ,ثايوسميكاربازايد حامض الكاربوكسيل (**11**), استرات (**15,14**), استرات الثايول (**17,16**) والامايد (**19,18**) بالمفاعلة مع الهايدرازين, الثايوسمي كاربازايد, الكحولات, ثايولات الالكيل, و الامينات الثانوية في درجة غليان البنزين الجاف , على التوالي. تضمن البحث ايضا تحضير عدد من قواعد شف(**6-8**), بمعاملة المركب (**5**) مع عدد من الالديهايدات و الكيتونات الاروماتية المختلفة, و من ثم غلق حلقي لاثنين من هذه القواعد بمفاعلتها مع (α-mercapto acetic acid) للحصول على(**9 , 10**). حضر مشتق 1و2و4-الترايازول(**12**) عن طريق مفاعلة مشتق الثايوسيميكاربازايد(**11**) مع محلول هيدروكسيد الصوديوم (4%) ثم تحميض الناتج باستخدام حامض الهيدروكلوريك (10%) . ايضا تم تحضير مشتق الثاياديازول (**13**) من معاملة مشتق الثايوسيميكاربازايد مع حامض الكبريتيك المركز, واخيرا و ضمن نفس الاطار تم تحضير مشتق الاوكساديازول (**20**) من تصعيد مشتق هيدرازيد الحامض مع CS_2 و KOH في الايثانول المطلق.