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Synthesis of Some Thiazole and Phthalazine Compounds from Schiff bases

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Abstract

It was known that heterocyclic compounds containing S and N have considerable importance which withdraw researchers attention due to their wide medical and biological applications. In the present investigation we have synthesized some ox diazole derivatives (A9-15), phthalazine derivatives (A33-38) and Benzo thiazole-2-yl arylthiazol-4-one (A17-24), thiazoles (A39-41) from schiff base precursors. The thiazole compounds were cyclized using acetic anhydride, thioglycolic acid while phthalazines were cyclized using amyl alcohol in HCl. The synthesized compounds were studied by IR, ¹HNMR spectral methods.

Keywords: Thiazole; Phthalazine; Schiffbases**Introduction**

Schiff base compounds achieved considerable importance due to their biological and medicinal applications [1]. Some thiazoles have prepared from Schiff bases these compounds showed antibacterial activities [2]. It was found that conversion of some biologically active compounds into Schiff bases will increase their effects for example is nicotinic hydrazone was found more active and safer than the corresponding hydrerazieds [3]. Some Schiff bases prepared from aromatic aldehydes and aromatic amines were found to be used as anti-inflammatory agents during the last decade's [4], and many other medical applications 4,5 while 1,3,4-oxadiazoles for example were extensively studied for the last decades especially in pharmaceutical aspects and other applications [5,6]. Oxadiazoles have been synthesized by numerous methods for example the compound 2-(4-(4-bromophenyl (sulfonylphenyl)-5-flurobenzyl) 1,3,4-oxazole was synthesized from the reaction of 1N-(4-bromophenyl sulfonyl benzyl-4N-(4-fluorophenyl) thio simicarbazide with iodine or KI in ethanol [7]. Chepa and co-workers have synthesized 1,3,4-oxadiazole derivatives [8]. Other researchers [9] have prepared oxazoles from the reaction of amino acid ester hydrazides with benzoyl chloride and cyclized the intermediate with POCl₃. 1,3,4-Oxadiazoles have also prepared from succinic anhydride and some hydrazides using POCl₃ for cyclization [10]. In 2012 Sheet and Mohammed [11] have succeeded in synthesizing 1,3,4-oxadiazoles from oxidation of hydrazones using PbO₂. Some thiazole compounds were also found to have medical application [12,13]. There are a lot of methods in the literature for the preparation of thiazole compounds among them, the cyclization of thiosimicarbazides using bromo acetic acid [14]. Tem of researcher have succeeded in synthesizing thiazolidine-4-one from the reaction of hydrazones with thioglycolic acid [14-16]. Phthalazine compounds have also showed many medical application [17,18]. These compounds were prepared by variety of methods among them which is the most common method is the condensation of phthalic ester or anhydride with hydrazine [19]. In 2008 Basheer and Ezzat have synthesized phthalazines by treatment of amino acid hydrazones with saturated solutions of HCl [20].

Experimental

All melting points were measured by Electro thermal melting point apparatus. All the chemical compounds were supplied by BDh, Aldrichand Fulka. The IR measurements were performed using Infrared spectrophotometer, type Tensor27 Bruker, ¹NMR speta were measured (selected compounds in DMSO-d₆ solvent) using Bruker 400MHz/ Gaziosmanpasa University(Turkey), Compound 1 was prepared according to the published procedure [21].



Synthesis of (substituted phenyl, substituted benzoyl hydrazonel (A2-8)

Phenyl hydrazide (0.01 mol.) or 3-Nitrophenyl hydrazide was dissolved in 25 ml of absolute ethanol. Aldehyde or its derivatives was then added. The reaction mixture was refluxed for 2 hours, cooled, stand for 3 hour at r.t. The sp.p.t was filtered off and crystallized from ethanol, Physical and IR spectral data were shown in Tables 1 and 8.

Table 1: Physical data for compounds (A₂₋₈)

Comp. No.	X	Y	Molecular Formula	m.p. (°C)	Yield (%)	Colour
A3	H	H	C ₁₄ H ₁₂ N ₂ O	204-207*	71	white
A3	4-Cl	H	C ₁₄ H ₁₁ N ₂ OCl	164-167*	80	white
A4	2-OH	H	C ₁₄ H ₁₂ N ₂ O ₂	160-163	65	Yellowish white
A5	H	3-NO ₂	C ₁₄ H ₁₁ N ₃ O ₃	206-208	88	white
A6	4-N(CH ₃) ₂	3-NO ₂	C ₁₆ H ₁₆ N ₄ O ₃	218-220	93	red
A7	2-OH	3-NO ₂	C ₁₄ H ₁₁ N ₃ O ₄	240-244	87	Yellowish white
A8	4-Cl	3-NO ₂	C ₁₄ H ₁₀ N ₃ O ₃ Cl	147-148	91	yellow

Table 8: IR. Spectral Data For Compounds (A2-8)

Comp. No.	X	Y	IR u cm-1 (KBr)			Others
			C=N, (Ar)	C=O amide	N-H	
A2	H	H	1600 15311446	1642	3205	C≡C
A3	4-Cl	H	1604 15791488	1646	3219	690 (C-Cl)
A4	2-OH	H	1622 16091488	1673	3271	3443 (OH)
A5	H	3-NO ₂	1618 15731486	1664	3166	1346 sy (NO ₂) 1536 asy (NO ₂)
A6	4-N(CH ₃) ₂	3-NO ₂	1640 16141481	1656	3238	1364 sy (NO ₂) 1524 asy (NO ₂)
A7	2-OH	3-NO ₂	1612 15751488	1650	3228	1347 sy (NO ₂) 1525 asy (NO ₂)
A8	4-Cl	3-NO ₂	1622 15921474	1672	3298	751 (C-Cl) 1340 sy (NO ₂) 1524 asy (NO ₂)

Synthesis of 2,5-diaryl-3-acetyl-1,3,4-oxadiazoles (A9-15)

Compound (A2-8), (0.003 mol) and 5 ml of acetic anhydride were mixed and refluxed for 2 hours, cooled and 50 gm. Of crushed ice was then added. The mixture was left of r.t for 24 hours. The solid precipitate was filtered and washed with water, dried at r.t. and crystallized from water. The physical properties and IR spectral data shown in Tables (2,9).

Table 2: Physical Data For Compounds (A9-15).

Comp. No.	X	Y	Molecular Formula	m.p. (°C)	Yield (%)	Colour
A9	H	H	C ₁₆ H ₁₄ N ₂ O ₂	61-62	58	white
A10	4-Cl	H	C ₁₆ H ₁₃ N ₂ O ₂ Cl	205-208	73	Yellowish white
A11	2-OH	H	C ₁₆ H ₁₄ N ₂ O ₃	187-190	64	Yellowish white
A12	H	3-NO ₂	C ₁₆ H ₁₃ N ₃ O ₄	100-102	77	Yellowish white
A13	4-N(CH ₃) ₂	3-NO ₂	C ₁₈ H ₁₈ N ₄ O ₄	98-101	86	Yellowish green
A14	2-OH	3-NO ₂	C ₁₆ H ₁₃ N ₃ O ₅	126-129	69	yellow
A15	4-Cl	3-NO ₂	C ₁₆ H ₁₂ N ₃ O ₄ Cl	95-99	72	yellow

Table 9: IR. Spectral Data For Compounds (A9-15)

Comp. No.	X	Y	IR u cm-1 (KBr)				Other	
			N-N	C-O-C		C=N, (Ar)		C=O amide
				Sym.	Asym.			
A9	H	H	1025	1063	1216	1625	1665	
A10	4-Cl	H	1011	1168	1293	1624	1651	813 (C-Cl)
A11	2-OH	H	1018	1063	1259	1624	1664	C≡C 3446 (OH)
A12	H	3-NO ₂	1038	1055	1217	1628	1664	1348 sy (NO ₂) 1533 asy (NO ₂)
A13	4-N(CH ₃) ₂	3-NO ₂	1067	1148	1287	1595	1718	1173 (C-N) 1346 sy (NO ₂) 1534 asy (NO ₂)
A14	2-OH	3-NO ₂	1012	1055	1261	1634	1661	1350 sy (NO ₂) 1532 asy (NO ₂)
A15	4-Cl	3-NO ₂	1018	1110	1221	1649	1734	743 (C-Cl) 1348 sy (NO ₂) 1533 asy (NO ₂)

Synthesis of Arylidenyl 2-benzo-1,3-thiazolyl amine (A16-22)

2-Amino benzo thiazole (0.01 mol) was dissolved in 20 ml of abs. ethanol, substituted aldehydes (0.01 mol) was then added, 2 drops of glacial acetic acid. The reaction mixture was refluxed for 3 hours after completion of the reaction (TLC), the mixture was cooled, water was then added, the solid product was filtered off and crystallized from ethanol, the physical and spectral data were illustrated in (Tables 3,10).

Table 3: Physical Data for Compounds (A16-22)

Comp. No.	X	Molecular Formula	m.p. (°C)	Yield (%)	Colour
A16	H	C ₁₄ H ₁₀ N ₂ S	92-94	74	Yellowish white
A17	4-N(CH ₃) ₂	C ₁₆ H ₁₅ N ₃ S	56-58	83	Deep yellow
A18	4-NO ₂	C ₁₄ H ₉ N ₃ O ₂ S	86-90	92	Yellowish white
A19	4-OCH ₃	C ₁₅ H ₁₂ N ₂ OS	84-86	61	Yellowish green
A20	4-Cl	C ₁₄ H ₉ N ₂ SCI	87-88	87	orange
A21	2-OH	C ₁₄ H ₁₀ N ₂ OS	99-103	80	Yellowish white
A22	2,6-diCl	C ₁₄ H ₈ N ₂ SCI ₂	127-129	76	Yellow

Table 10: IR. Spectral Data For Compounds (A16-22)

Comp. No.	X	IR u cm-1 (KBr)		Others
		C≡C, C=C, Ar	C=N	
A16	H	1,60,61,445	1642	C≡C
A17	4-N(CH ₃) ₂	1,59,61,487	1650	1165 (C-N)
A18	4-NO ₂	1,59,61,491	1608	1351 sy (NO ₂) 1524 asy (NO ₂)
A19	4-OCH ₃	1,56,91,488	1601	1023 sy (C-O-C) 1253 asy (C-O-C)
A20	4-Cl	1,59,41,446	1603	729 (C-Cl)
A21	2-OH	1,60,01,448	1638	3398 (OH)
A22	2,6-diCl	1,55,31,435	1601	753,776 (C-Cl)

Synthesis of 3-(benzothiazol-2-yl)-2- Arylthiazol -4-one (A17-24)

A compound of Schiff base A16-22 (0.002 mol) was mixed with (0.002) mol of thioglycolic acid in abs-ethanol (25ml), (0.136 mol) of ZnCl₂ anhydrous ZnCl₂ was then added. The reaction mixture was refluxed for 8 hour, cooled, filtered and washed with 3% sodium bicarbonate then with water and crystallized from (Dioxone-water). Physical and spectral data are presented in Tables (4,11).

Table 4: Physical Data For Compounds (A17-24).

Comp. No.	X	Molecular Formula	m.p. (°C)	Yield (%)	Colour
A17	H	C ₁₆ H ₁₂ N ₂ O ₂ S ₂	dec.188	61	white
A19	4-N(CH ₃) ₂	C ₁₈ H ₁₇ N ₃ O ₂ S ₂	dec.232	66	orange
A20	4-NO ₂	C ₁₆ H ₁₁ N ₃ O ₃ S ₂	191-193	70	deepwhite
A21	4-OCH ₃	C ₁₇ H ₁₄ N ₂ O ₂ S ₂	163-165	52	white
A22	4-Cl	C ₁₆ H ₁₁ N ₂ O ₂ S ₂ Cl	178-181	64	Yellowsh white
A23	2-OH	C ₁₆ H ₁₂ N ₂ O ₂ S ₂	265-267	58	white
A24	2,6-diCl	C ₁₆ H ₁₀ N ₂ O ₂ S ₂ Cl ₂	231-233	60	white

Table 11: IR. spectral data for compounds (A18-24)

Comp. No.	X	IR u cm-1 (KBr)				Others
		C-S-C	C-N	C=C, Ar	C=O	
A18	H	757	1219	1,57,21,456	1665	C≡C
A19	4-N(CH ₃) ₂	755	1223	1,61,31,504	1684	697 (C-Cl)
A20	4-NO ₂	762	1266	1,59,51,456	1711	1345 sy (NO ₂) 1519 asy (NO ₂)
A21	4-OCH ₃	826	1278	1,61,21,440	1685	1032 sy (C-O-C) 1254 asy (C-O-C)
A21	4-Cl	758	1287	1,59,31,446	1636	731 (Cl)
A23	2-OH	754	1277	1,60,11,445	1708	3400(OH)
A24	2,6-Cl	809	1274		1704	753,777 (C-Cl)

Synthesis of ethyl- N – benzoyl glycinate [22] (A25)

Dry HCl gas was prepared and passed through (80 ml) of absolute ethanol till saturation. To this solution was added (0.067 mol.) N-benzoyl glycine. The mixture was refluxed at 90°C for 2 hours under dry conditions. After completion of reaction (TLC monitoring). The hot solution was added to 150 ml of water, neutralized with 3% sodium carbonate. The solid product was filtered, dried at r.t and crystallized of 75%, published MP. Is 60.5°C.

Synthesis of substituted benzaldehyde N- benzoyl glycolyl hydrazones (A27-32)

Equimolar amounts of compound [26] and substituted aldehyde (0.005 mol.) were dissolved in 20 ml. Of ethanol (abs). The mixture was refluxed for 2 hours, cooled. The solid product was crystallized from ethanol, physical and spectral data are presented in (Tables 5,12).

Table 5: Physical Data for Compounds (A27-32).

Comp. No.	X	Molecular formula	m.p. (°C)	Yield (%)	Colour
A27	H	C ₁₆ H ₁₅ N ₃ O ₂	181-184	87	white
A28	4-N(CH ₃) ₂	C ₁₈ H ₂₀ N ₄ O ₂	214-216	74	white to yellow
A29	4-NO ₂	C ₁₆ H ₁₄ N ₄ O ₄	226-227	70	Yellowsh white
A30	4-Cl	C ₁₆ H ₁₄ N ₃ O ₂ Cl	212-214	65	white
A31	2-Cl	C ₁₆ H ₁₄ N ₃ O ₂ Cl	146-150	79	white
A32	3-NO ₂	C ₁₆ H ₁₄ N ₄ O ₄	228-230	83	white

Table 12: IR. Spectral Data For Compounds (A27-32)

Comp. No.	X	IR u cm-1 (KBr)				Others
		C=C, Ar	C=N	C=O	N-H	
A27	H	1,61,21,489	1635	1685	3308	C≡C
A28	4-N(CH ₃) ₂	1,55,81,495	1616	1676	3197	1180 (C-N)
A29	4-NO ₂	1,57,01,487	1602	1699	3362	1348 sy (NO ₂) 1539 asy (NO ₂)
A30	4-Cl	1,60,11,489	1635	1685	3315	713 (C-Cl)
A31	2-Cl	1,56,61,467	1608	1685	3360	704 (C-Cl)
A32	3-NO ₂	1,57,71,487	1603	1691	3342	1348 sy (NO ₂) 1523 asy (NO ₂)

Synthesis of 1-benzamideo methyl substituted phthalazines (A33-38)

A compound of (A27-32), 0.001 mol. was dissolved in 10 ml of amyl alcohol saturated with dry HCl gas. The mixture was heated on steam bath for 1.5 hour and then refluxed for one hour. After completion of the reaction (TLC monitored), cooled and washed with 20% NaOH then with water and filtered. The solid product was crystallized from dioxane, physical and IR spectral data are presented in (Tables 6,13).

Table 6: Physical Data For Compounds(A33-38).

Comp. No.	X	Molecular formula	m.p. (°C)	Yield (%)	Colour
A33	H	C ₁₆ H ₁₃ N ₃ O	> 350	48	brown
A34	4-N(CH ₃) ₂	C ₁₈ H ₁₈ N ₄ O	dec.337	80	Yellowsh green
A35	4-NO ₂	C ₁₆ H ₁₂ N ₄ O ₃	307-308	66	yellow
A36	4-Cl	C ₁₆ H ₁₂ N ₃ OCl	> 350	60	white
A37	2-Cl	C ₁₆ H ₁₂ N ₃ OCl	> 350	52	white
A38	3-NO ₂	C ₁₆ H ₁₂ N ₄ O ₃	193-195	71	Deep yellow

Table 13: IR. Spectral data for compounds (A33-38)

Comp. No.	X	IR u cm-1 (KBr)			Others
		C=N	C=O	N-H	
A33	H	1614	1650	3417	C≡C
A34	4-N(CH ₃) ₂	1604	1621	3406	1178 (C-N)
A35	4-NO ₂	1599	1599	3441	1346 sy (NO ₂) 1519 asy (NO ₂)
A36	4-Cl	1600	1626	3385	815 (C-Cl)
A37	2-Cl	1614	1635	3383	873 (C-Cl)
A38	3-NO ₂	1630	1630	3437	1356 sy (NO ₂) 1529 asy (NO ₂)

Synthesis of 2-Aryl-3- (N- benzoyl glycolyl amido)-3-methyl thiazolidine -4-one (A39-41)

Equimolar amounts of compound (A33-38) and 2-mercapto propionic acid, 0.001 each were refluxed in 20 ml of absolute ethanol and 0.136 mol of ZnCl₂ (anhydrous) for 8 hours, cooled and washed with NaHCO₃ 3% then with water, filtered and the solid product was crystallized from ethanol, physical and IR spectral data were shown in (Tables 7,14).

Table 7: Physical Data For Compounds (A39-41)

Comp. No.	X	Molecular formula	m.p. (°C)	Yield (%)	Colour
A39	H	C ₁₉ H ₁₉ N ₃ O ₃ S	dec.327	72	yellow
A40	4-NO ₂	C ₁₉ H ₁₈ N ₄ O ₅ S	232-234	63	Yellowish white
A41	2-Cl	C ₁₉ H ₁₈ N ₃ O ₃ SCl	dec.352	56	white

Table 14: IR. Spectral Data for Compounds (A39-41)

Comp. No.	X	C-S-C	IR ν cm ⁻¹ (KBr)			Others
			C=O amide	C=O lactam	N-H	
A39	H	854	1683	1695	3309	
A40	4-NO ₂	690	1708	1734	3373	1346 sy (NO ₂) 1510 asy (NO ₂)
A41	2-Cl	752	1683	1712	3358	700 (C-Cl)

Results and Discussion

According to the previous studies heterocyclic compounds were found to have a wide range of medical and biological application [24-26] and are important for human life. For this reasons we are here to discuss the preparation of new series of heterocyclic compounds derived from Schiff bases.

Synthesis of (substituted phenyl, substituted benzoyl hydra zones (A2-8)

The above compounds were synthesized from the condensation of phenyl hydrazine with some substituted benzaldehydes as mentioned in the experimental part. The IR spectra for the synthesized compounds were as follows: 1642-1673 cm⁻¹ for C=O amide, 1600-1640 cm⁻¹ for C=N stretching which sometimes appeared within the aromatic C=C region as shown in (Tables 8) while N-H stretching band appeared within, 3166-3299 cm⁻¹.

Synthesis of 2,5-dianyl-3-Acetyl-1,3,4-oxadiazole (A9-15)

Similar compounds have shown to have significant biological and pharmaceutical effects. These compounds were prepared by numerous methods as it was mentioned in the experimental part among them is the condensation of Schiff base with acetic anhydride so we prepared these compound using this method. The obtained compounds were characterized by the following IR absorption bands: 1651-1734 cm⁻¹ for C=O and at 1595-1645 cm⁻¹ for C=N while C-O-C was appeared at 1055-1168, 1216-1293 cm⁻¹ for symmetry and asymmetry. Stretching vibration. The other bands were indicated in (Table 9). The 1H NMR of compound (A9) showed the following signals; 1.918ppm singlet for 3H of O=C-CH₃, 2.509ppm. As singlet band related to 1H of O-C-H proton while the aromatic protons 10H appeared at 7.198- 8.479ppm.

Synthesis of arylidine-2-benzo-1,3-thiadiazolene amine (A16-22)

The above compounds were prepared by condensation of 2-Amino benzothiazole with some substituted benzaldehydes as it was mentioned in the experimental part. These compounds were characterized by the absorption bands as indicated in (Table 10):1601-1650 cm⁻¹ for C=C aromatic in which sometimes appeared within the C=N absorption region.

Synthesis of 3-(benzothiazole-2-yl)-2-aryl thiazoline-4-one (A17-24)

These compounds were appeared by the condensation of the Schiff base (A9-15) with thioglycolic acid using anhydrous ZnCl₂. The synthesized compounds were identified by IR and 1H NMR, IR spectral data revealed the presence of the following absorption bands:1636-1171 cm⁻¹ assigned

for C=O stretch of the thiazolidone, 754-826 cm⁻¹ related for C-N stretch while C=C of the aromatic absorbed with the range of 1437-1613 cm⁻¹ as shown in (Table 11). The 1NMR spectrum for compound (A20) showed the following resonating signals 27ppm for S-CH singlet, 4.01ppm belongs to 2H of CH₂ and doublet signed at 6.87, 6.899 for 2H aromatic while the second signed of the aromatic proton appeared at 7.36, 7.346. Benzothiazole protons were found at 7.4-8.0ppm.

Compound (23) showed resonating signal at 2.5ppm corresponds for 2H of CH₂ (cyclic) and the spectrum showed a multiple signal at 7.31-7.43 belongs to 3H of ArH and finally a multiple signal of 5.07-8.02ppm assigned for 4H of benzothiazole.

Synthesis of Ethyl-n-benzoyl glycinate (A25)

This compound was prepared by esterification of N-benzoyl glycine, IR spectrum of this compound showed the following absorption bands: 1759 cm⁻¹ for C=O ester, 1641 cm⁻¹ for C=O Amide while C=C Aromatic appeared at 1493-1600 cm⁻¹ together with N-H at 3338 cm⁻¹.

Synthesis of N-benzoyl glyciyl hydrazides (A26)

The IR spectrum of the above compound revealed the formation of the hydrazide compound through the absorption of this group C=O at lower value and the presence of N-H band at 3194-3488 cm⁻¹ while the C=C appeared at 1491-1577 cm⁻¹.

Synthesis of N-benzoyl glyciyl hydrazones (A27-32)

The above compounds were identified by IR studies which showed the following absorption bands; 1602-1635 cm⁻¹ for C=N, 1467-1621 cm⁻¹ for Aromatic C=C, 3197-3362 cm⁻¹ belongs to N-H while the C=O of the corresponding hydrazide appeared at 1676-1699 cm⁻¹ as indicated in (Table 12).

Synthesis of 1-Benzamido methyl substituted phthalazines (A33-38)

The series of compounds were appeared from the corresponding hydrazones with amyl alcohol in presence of HCL. IR spectrum of these compounds showed the following absorption bands: 1599-1630 cm⁻¹ for C=N, 1599-1650 cm⁻¹ belongs to the amide C=O while the NH appeared at 3383-3441 cm⁻¹ as shown in (Table 13). The 1H NMR spectrum of compound (33) exhalted the following signals 8.44 ppm for the diazine protons, 8.32 ppm for 5,8 protons of benzene ring, 8.23 ppm d of d for 6,7 protons of the benzene ring, 7.80-7.84ppm for the phenyl ring protons adjacent to the carbonyl, NH at 5.84ppm and 3.23 ppm singlet for the CH₂ protons.

Synthesis of -2-Aryl-3-N-benzoylgiyl amindo-5-methyl thiazolidine-4-one (A39-41)

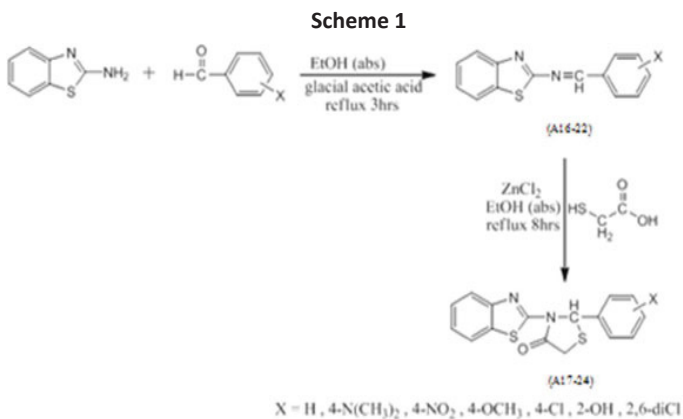
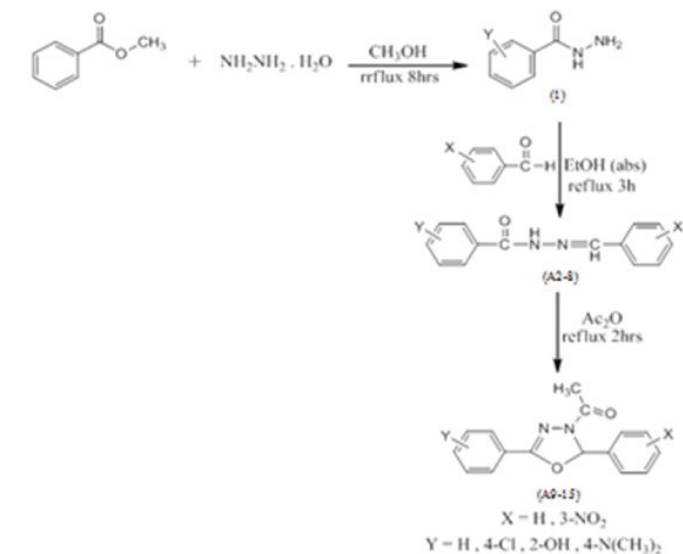
This series of compounds were prepared by the cyclization of the corresponding hydra zones using ZnCl₂ in absolute ethanol the role of ZnCl₂ is to catch the OH group of the thio glycolic acid and make the carbonyl of this acid available (more positive) for the nitrogen attack and cyclization. These compounds were identified by IR which showed the following absorption bands; 1695-1734cm⁻¹ belongs to C=O of thiazole ring, C=O Amide at 1683-1708 cm⁻¹ while the N-H stretching appeared at 3309-3373 cm⁻¹ as indicated in Table (14).

Conclusions

According to the above results it was clear that the intermediate compounds were cyclized into the corresponding thiazoles, thiadiazoles and diazines (Figure 1).

In general, the temporal pattern of gender gap in suicide mortality fluctuations was similar for three countries: sharp decrease in the mid of 1980s, dramatic increase in the 1990s followed by a decline. While the trends in the gender gap have been similar in three countries during the Soviet period, there was significant discrepancy after the collapse of the

Soviet Union in 1991. In particular, in Belarus, the gender gap in suicide rates increased steadily up to 2000, reaching an all-time high, and then started to decrease. The graphical evidence suggests that in all countries, the temporal pattern of alcoholic psychoses incidence rate fits closely with the changes in the gender gap in suicide mortality (Figures 2-4).

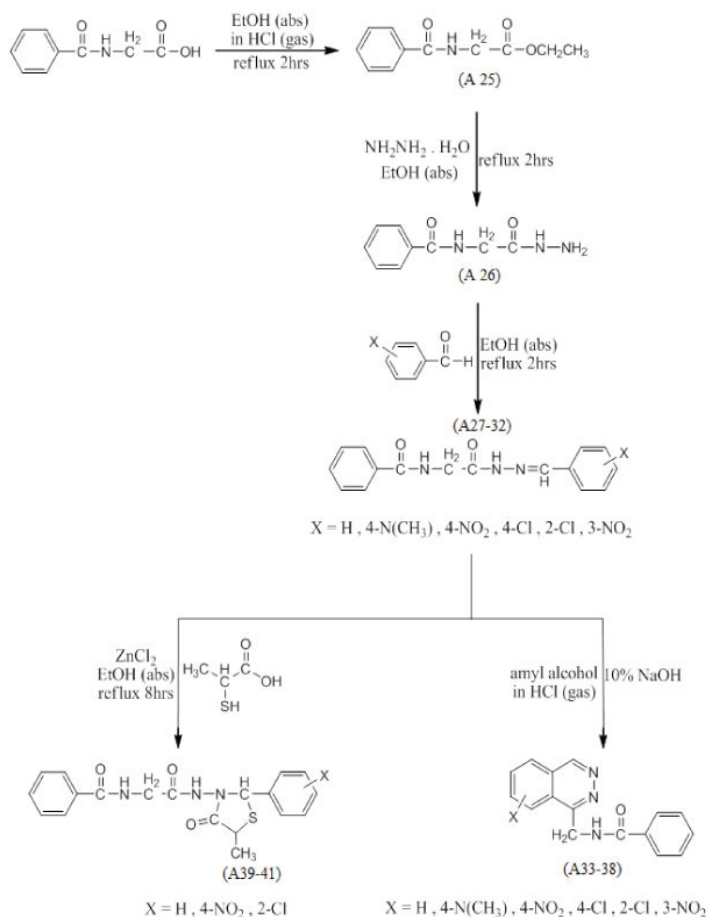


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