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Synthesis and Studies on Some Spiro and Fused of Quinone Derivatives

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Authors' contributions

This work was carried out in collaboration between all authors. Author HAS designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Author AKK managed the analyses of the study. Author AMHS managed the literature searches. All authors read and approved the final manuscript.

Research Article

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ABSTRACT

Some new Spiro β-lactam, Spiro thiazolidine derivatives were synthesized by the reaction of new Schiff bases (5a-c, 8a-c) with chloroacetyl chloride and/or mercaptoacetic acid to give new Spiro β-lactam (6a-c, 9a-c) and new Spiro thiazolidinone derivatives (7a-c, 10a-c) . Also, new fused pyrazolo derivatives (12a-c, 13a-c) fused isoxazolo derivatives (14a-c) and pyrimidine derivatives (15a-c, 16a-c) were synthesized by the reaction of new arylidine derivatives (11a-c) with hydrazine hydrate, phenyl hydrazine, hydroxylamine hydrochloride, urea and thiourea, respectively.

Keywords: Spiro β-lactam; spiro thiazolidinone; fused pyrazoles; fused isoxazole; fused pyrimidine's.

1. INTRODUCTION

The importance of heterocyclic compounds in various aspects is beyond estimation and there is always continuous need for the discovery of new heterocyclic compounds to satisfy the requirement of intensive development in industry and various biological aspects [1-3]. A large number of Spiro heterocyclic compounds were prepared [4] and their applications

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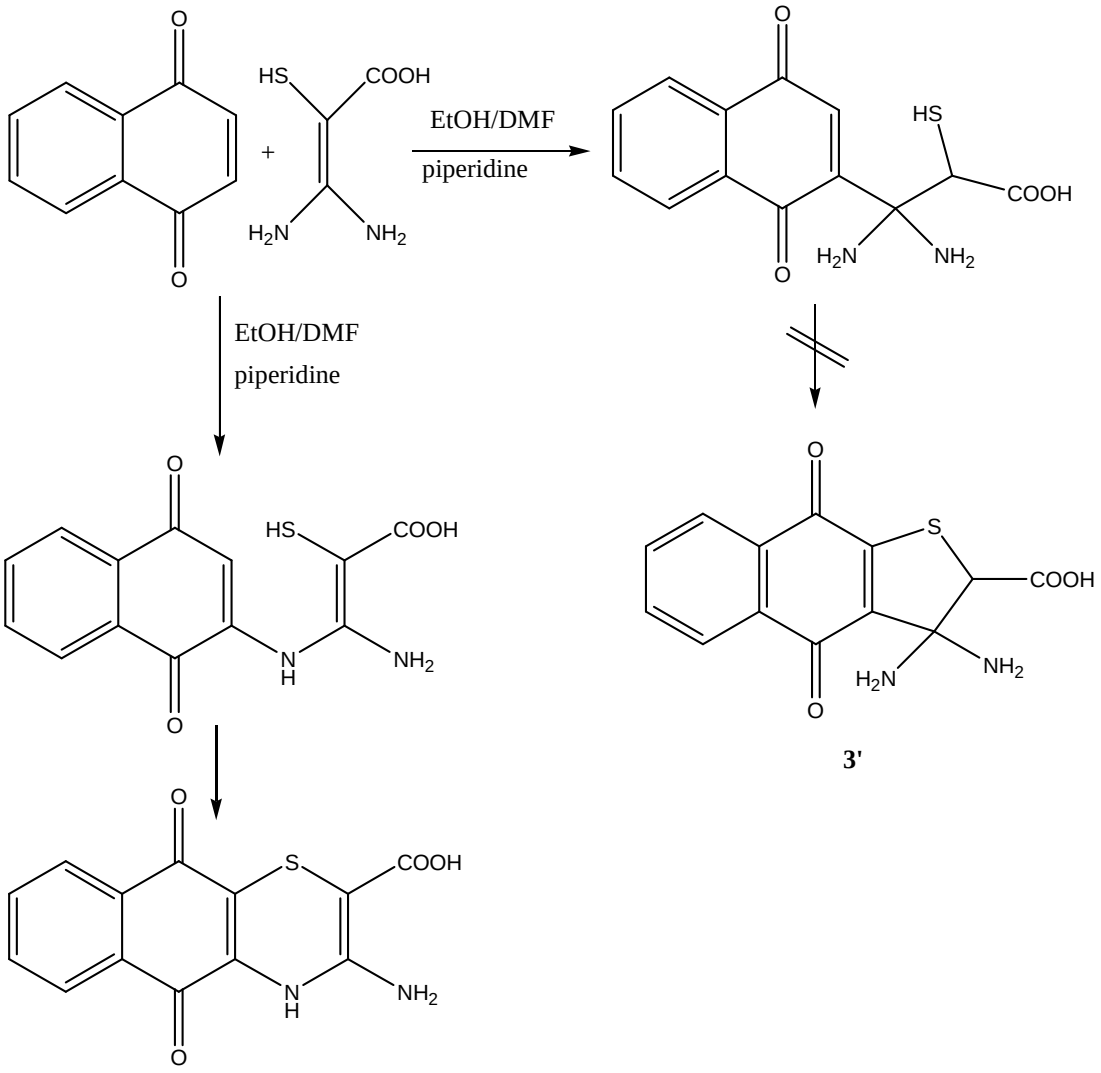
investigated [5]. β-Lactams (azetidin-2-ones) play a neutral role in medicinal chemistry as a key intermediate for the synthesis of penicillin and its analogues. Also, the azolidinone derivatives are used in biological agents such as bactericidal, fungicidal, and insecticidal [6–12] . Also, thiazolidinone compounds have been subject of extensive efforts in the recent past divers biological activities [13-14] such as bacterial, fungicidal, insecticidal, tuberoculostatic, be associated with thiazolidinone derivatives [15-16]. Heterocyclic compounds are very widely distributed in nature and are essential to life in various ways. A series of isolated/fused of pyrazole, isoxazolo, pyrimidine, pyrimidine then, Spiro thiazolodine and Spiro β-lactam derivatives have been synthesized by different methods of chemical reactions [17,18], it has found that undergo various reactions, and as such are excellent and generally starting materials for the development of the organic synthesis. Also, a series of poly fused heterocyclic compounds incorporating 1, 4-naphthoquinone have synthesized by us [19], such as accordion, pyrazine, hydropyrazine, imidazole, phenazine, and bezophenazine derivatives respectively, via a nucleophilic substitution and cyclization reaction. Fused , isolated and Spiro thiazole derivatives were synthesized using 4,5-dihydro-2-ethyl acetate-4-oxothiazole [20] as starting material via different methods of reaction chemistry. The microorganism chosen for the were tested gram positive bacillus bacteria (isolated from air) as well as fungus Aspergillus Niger and Aspergillus Flavus which cause keratomycosis, otomycosis and aspergillosis disease.

2. RESULTS AND DISCUSSION

In this work, efforts were made to prepare and develop the chemical reactions and applications of a new group of heterocyclic compounds contains two heterocyclic nuclei namely quinolinothiazolidine, piperidinothiazolidine and other isolated systems such as monosubstituted β-lactams. The work covers the preparation of various groups of these heterocyclic molecules with the objects of their use for biological applications especially those carrying a β-lactam ring. The synthesis of newly fused **3-amino-5,10-dioxo-4a,5,10,10a-tetrahydro-4H-naphtho [2,3-b] [1,4] thiazine-2-carboxylic acid(3)**, which, was synthesized by cycloaddition reaction of equimolar ratios of appropriate 3, 3-domino-2-sulfanylprop-2-enoic acid and 1,4-naphthoquinone in ethanol containing piperidine as catalyst. Firstly, the theoretical cycloaddition reaction led to the synthesis of compound **(3)**, but the experimental evidence that depends on the different types of analysis to the reaction product proves that the cycloaddition reaction leads to the formation of compound **(3)** through the electronic socialization according to the suggested mechanism **[Scheme 1]**.



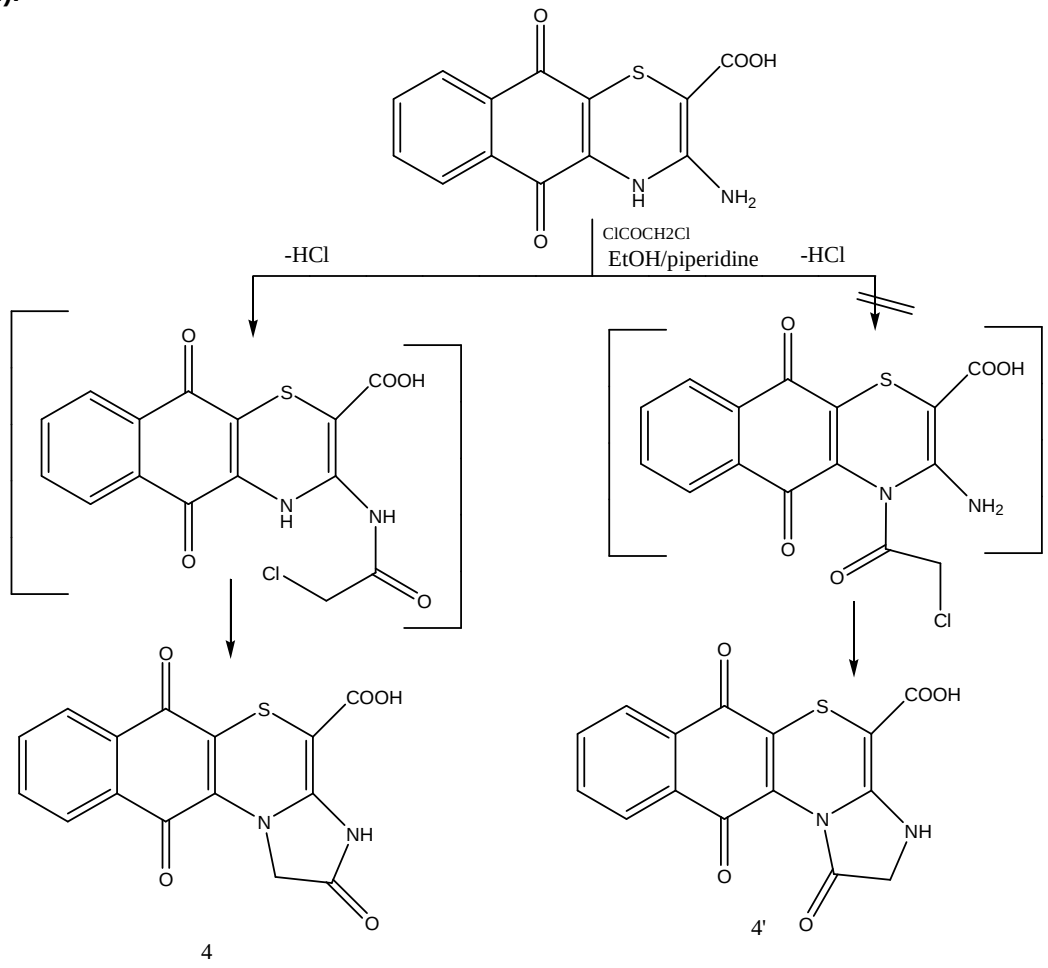
Scheme 1

The structure of the new synthesized **(3)** were confirmed by IR : v 3345-3310(NH, NH_2), 3330(OH), 1710(C=O). ^{1}H NMR (300 MHz, DMSO-d_6) : δ11.0 (s, 1H, COOH), 8-7(m, 4H, Ar-H^+), 2.2(br, 1H, NH), 2.0(br, 2H, NH_2). MS(EI, m/z(%)): 287(M^+). Anal. Calcd. For $C_{13}H_7N_2O_4S$: C, 54.35; H, 2.46; N, 9.75. Found, C, 54.38; H, 2.45; N, 9.80.

The results from ^{1}H-NMR spectra means that the synthesized product **(3)** produced from the reaction of 3,3-diamino-2-mercaptoacrylic acid and 1,4-naphthoquinone is the structural formula of compound **(3)** because of the appearance of the signal peak at δ 3.24-4.30 as a result of fusion of 1,4- naphthoquinone with the unsaturated 3,3-diamino-2-sulfanyl acrylic acid.The presence of amino group attached to C_3 and imino group at C_4, in compound **(3)**, can be cyclized with chloroacetylchloride in ethanol and droplets of pepiridine as catalyst to give fused compound;

2,6,11-trioxo-2,3,5a,6,11,11a-hexahydro-1H-imidazo[1,2-naphtho[2,3-b][1, 4]thiazine-4-carboxylic acid(4). **[Scheme 2]**:

The following suggested reaction illustrates the synthesized fused heterocyclic compound **(4).**



Scheme 2

The structure of the compound **(4)** was confirmed by IR (v_{max}/cm^{-1}): 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 8-7 (m, 4H, Ar-H^{+}), 8.2 (br, 1H, NH), 3.54 (s, 2H, CH_2CO). MS (EI, m/z (%)): 328 (M^{+}). Anal. Calcd. For $C_{15}H_8N_2O_5S$: C, 54.53; H, 2.46; N, 8.53. Found C, 54.50; H, 3.00; N, 8.56.

Our approach to the synthesis of the desired Spiro systems started with compounds 5 (a-c) and 8 (a-c), which:

Preparation of compound 2, 6, 11-Trioxo-1-phenylimino-2,3,6,11-tetrahydro-1H-5-thia-3,11b-diaza-cyclopenta[a]anthracene-4-carboxylic acid (5a-c) : by condensation of compound (4) with aromatic nitroso derivatives such as, {α-nitroso-β-naphthol, β-nitroso-α–naphthol, p-

nitroso-phenol}, in absolute ethanol and in the presence of piperidine as catalyst. The following reaction illustrates the formation of 5 (a-c) [Scheme 3].

Preparation of compound 6,11-Dioxo-2-phenylimino-2,3,6,11-tetrahydro-1H-5-thia-3,11b-diaza-cyclopenta[a]anthracene-4-carboxylic acid (8a-c) : by condensation of compound (4) with aromatic aniline derivatives such as, {aniline, 4-hydroxyaniline, 4-Nitro-aniline}, in absolute ethanol and droplets of piperidine as catalyst.

Synthesis of 3-chloro-1-aryl-2,5,9,14-tetraoxo-8-thia-1,6,15-triaza-spiro[3,4]octan-2-one[a]anthracene-7-carboxylic acid (6a-c) and 3-chloro-1-phenyl-8-thia-1,5,6-triaza-spiro[3,4]octan-2-one[a]anthracene-7-carboxylic acid (9a-c): were achieved through the interaction of **5 (a-c)** and **8 (a-c)** with equimolar ratio of chloroacetyl chloride in a mixture of absolute ethanol and dimethylformamide with droplets of piperidine as catalyst **[Scheme 3]**. The structure of Spiro-β-Lactam **6 (a-c)** and **9 (a-c)** was confirmed by IR and ^{1}H-NMR spectra **[cf. Experimental section]** and their elemental analysis **[**cf. **Tables 1,2]**.

Synthesis of 1-phenyl-2,10,15-trioxo-4,9-dithia-1,7,16-triaza-spiro[5, 5]nonan-2-one[a]anthracene-8-carboxylic acid (7a-c) :and 4-phenyl-1, 10-dithia-4, 7, 8-triaza-spiro[5, 5]nonan-3-one[a]anthracene-9-carboxylic acid (10a-c):

These compounds were prepared by the cycloaddition of mercaptoacetic acid with the previously prepared Schiff bases **5 (a-c)** and **8 (a-c)** in a mixture of absolute ethanol/ dimethylformamide with the presence of piperidine as catalyst to give the corresponding Spiro-thiazolidinone **7 (a-c)** and **10 (a-c)**. The structure of these compounds were confirmed by IR and ^{1}H-NMR spectra **[cf. Experimental section]** and their elemental analysis **[**cf. **Tables 1,2]**.

Synthesis of 1-[(E)-1-arylmethylidene]-2,6,11-trioxo-2,3,5a,6,11,11a-hexa-hydro-1H-imidazo[1,2-d]naphtho[2,3-b][1,4]thiazine-4-carbox-ylic acid (11a-c):

The activity of methylene group in C_1 of compound **(4)** promoted us to explore the possibility of utilizing some new Schiff bases prepared by the condensation of compound **(4)** with equimolar ratio of aromatic aldehyde derivatives in a mixture of absolute ethanol and DMF containing piperidine as catalyst to give the corresponding new Spiro-schiff base arylidine derivatives **11 (a-c) [Scheme 4]**. The structure of new Spiro Schiff base **11 (a-c)** was confirmed by IR and ^{1}H-NMR spectra **[cf. Experimental section]** and their elemental analysis **[**cf. **Table 2]**.

Synthesis of 2-acetyl-3-phenyl-2,3,3a,8-tetrahydro-6-thia-1,2,3b,8tetraaza-cyclopenta[a]indene[a']anthracene-7-carboxylic acid (12a-c):

The presence of active methylene group adjacent to the active carbonyl group in compound **11 (a-c)**, leads to, the formation of new Spiro-heterocyclic derivatives. This can be achieved, by cycloaddition, between equimolar ratios of compound **11 (a-c)** with hydrazine hydrate, in a mixture of EtOH/DMF in the presence of droplets of glacial AcOH as catalyst to proceed compound **12 (a-c)[Scheme 4]**. The structures of these compounds were confirmed by IR and ^{1}H-NMR spectra **[cf. Experimental section]** and their elemental analysis **[Table 3]**.

Table 1. Physical and analytical data for the synthesized compounds (5a-c, 6a-c, 7a-c)

Comp. NO.	Yield %	M.P (ºC)	Solvent	Mol. Form. (Mol. Wt)	Elemental analysis [Calc. / Found (%)]				MS (M^+)
					C	H	N	S	
5a	61	265	Ethanol /DMF	$C_{25}H_{15}O_6N_3S$ (485.468)	61.85 61.82	3.11 3.11	8.66 8.63	6.60 6.56	485
5b	62	272	Ethanol /DMF	$C_{25}H_{15}O_6N_3S$ (485.468)	61.85 61.89	3.11 3.08	8.66 8.69	6.60 6.55	485
5c	61	278	Ethanol /DMF	$C_{21}H_{13}O_6N_3S$ (435.408)	57.93 57.96	3.01 2.99	9.65 9.67	7.36 7.30	435
6a	67	275	Ethanol /DMF	$C_{27}H_{16}O_7N_3SCl$ (561.949)	57.71 57.67	2.87 2.90	7.48 7.40	5.71 5.65	561
6b	65	276	Ethanol /DMF	$C_{27}H_{16}O_7N_3SCl$ (561.949)	57.71 57.75	2.87 2.85	7.48 7.54	5.71 5.76	561
6c	65	270	Ethanol /DMF	$C_{23}H_{16}O_7N_3SCl$ (513.907)	53.75 53.70	3.14 3.10	8.18 8.00	6.24 6.30	513
7a	58	222	Ethanol /DMF	$C_{27}H_{19}O_7N_3S_2$ (561.586)	57.75 57.80	3.41 3.40	7.48 7.50	11.42 11.45	561
7b	58	277	Ethanol /DMF	$C_{27}H_{19}O_7N_3S_2$ (561.586)	57.75 57.70	3.41 3.45	7.48 7.42	11.42 11.50	561
7c	58	243	Ethanol /DMF	$C_{23}H_{16}O_7N_3S_2$ (511.527)	54.01 53.99	3.35 3.35	8.21 8.25	21.54 21.60	511

Table 2. Physical and analytical data for the synthesized compounds (8_{a-c}, 9_{a-c}, 10_{a-c})

Comp. NO.	Yield %	M.P (ºC)	Solvent	Mol. Form. (Mol. Wt.)	Elemental analysis [Calc. / Found (%)]				MS (M^+)
					C	H	N	S	
8a	45	285	Ethanol /DMF	$C_{21}H_{15}O_4N_3S$ (405.426)	62.21 62.15	3.73 3.70	10.36 10.30	7.91 7.85	405
8b	55	289	Ethanol /DMF	$C_{21}H_{15}O_5N_3S$ (421.425)	59.85 59.80	3.59 3.57	9.97 9.90	7.61 7.55	421
8c	75	293	Ethanol /DMF	$C_{21}H_{14}O_6N_4S$ (450.424)	56.00 55.98	3.13 3.11	12.44 12.46	7.12 7.20	450
9a	60	291	Ethanol /DMF	$C_{23}H_{16}O_5N_3SCl$ (481.908)	57.32 57.35	3.35 3.34	8.72 8.75	6.65 6.60	481
9b	61	296	Ethanol /DMF	$C_{23}H_{16}O_6N_3SCl$ (497.907)	55.48 55.42	3.24 3.22	8.44 8.40	6.44 6.50	497
9c	65	299	Ethanol /DMF	$C_{23}H_{15}O_7N_4SCl$ (526.906)	52.43 52.40	2.87 2.90	10.63 10.50	9.06 9.10	526
10a	62	320	Ethanol /DMF	$C_{23}H_{17}O_5N_3S_2$ (479.528)	57.61 57.55	3.57 3.55	8.76 8.80	13.37 13.45	479
10b	50	315	Ethanol /DMF	$C_{23}H_{17}O_6N_3S_2$ (495.527)	55.75 55.70	3.46 3.45	8.48 8.40	12.94 12.84	479
10c	60	325	Ethanol /DMF	$C_{23}H_{16}O_7N_4S_2$ (524.527)	52.67 52.73	3.07 3.10	10.68 10.76	12.23 12.30	524
11a	35	250	Ethanol /DMF	$C_{22}H_{24}N_2O_5S$ 428.50	5.65 5.62	61.67 61.70	6.54 6.62	7.48 7.55	428
11b	45	285	Ethanol /DMF	$C_{22}H_{24}N_2O_6S$ ~~444.14~~	59.44 59.40	5.45 5.42	6.31 6.24	7.20 7.28	445
11c	50	265	Ethanol /DMF	$C_{22}H_{23}N_3O_7S$ 473.13	55.80 55.75	4.90 4.94	8.88 8.80	6.76 6.70	475

Table 3. Physical and analytical data for the synthesized compounds (12_{a-c}, 13_{a-c}, 14_{a-c})

Comp. NO.	Yield %	M.P (ºC)	Solvent	Mol. Form. (Mol. Wt.)	Elemental analysis [Calc. / Found (%)]				MS (M^+)
					C	H	N	S	
12a	58	340	Ethanol /DMF	$C_{24}H_{18}O_5N_4S$ (474.488)	60.75 60.70	3.82 3.79	11.81 11.90	6.76 6.70	474
12b	58	343	Ethanol /DMF	$C_{24}H_{18}O_6N_4S$ (490.488)	58.77 58.83	3.70 3.69	11.42 11.48	6.54 6.48	490
12c	60	348	Ethanol /DMF	$C_{24}H_{17}O_7N_5S$ (519.486)	55.49 55.54	3.30 3.25	13.48 13.40	6.17 6.10	519
13a	61	Over 350	Ethanol /DMF	$C_{28}H_{20}O_4N_4S$ (508.548)	66.13 66.10	3.96 3.94	11.02 11.00	6.31 6.29	508
13b	60	Over 350	Ethanol /DMF	$C_{28}H_{20}O_5N_4S$ (524.547)	64.11 64.01	3.84 3.80	10.68 10.60	6.11 6.19	524
13c	63	Over 350	Ethanol /DMF	$C_{28}H_{19}O_6N_5S$ (553.545)	60.75 60.70	3.46 3.44	12.65 12.60	5.79 5.70	553
14a	40	Over 350	Ethanol /DMF	$C_{22}H_{15}O_5N_3S$ (433.436)	60.96 60.92	3.49 3.45	9.96 9.94	7.40 7.32	433
14b	55	Over 350	Ethanol /DMF	$C_{22}H_{15}O_6N_3S$ (449.435)	58.79 58.82	3.36 3.38	9.35 9.40	7.13 7.20	449
14c	65	Over 350	Ethanol /DMF	$C_{22}H_{14}O_7N_4S$ (478.435)	55.23 55.25	2.95 2.95	11.71 11.65	6.70 6.65	478

Synthesis of 2-phenyl-3-phenyl-2,3,3a,8-tetrahydro-6-thia-1,2,3b,8tetraaza-cyclopenta[a]indene[a']anthracene-7-carboxylic acid (13a-c):

By cyclocondensation reaction of Schiff base derivatives **11 (a-c)** with phenyl hydrazine in a mixture of EtOH/DMF in the presence of piperidine as catalyst to synthesized Spiro-heterocyclic derivatives **13 (a-c)[Scheme 4]**. The structures of these compounds were confirmed by IR and ^{1}H-NMR spectra **[cf. Experimental section]** and their elemental analysis **[Table 3]**.

Synthesis of 3-phenyl-3,3a-dihydro-8H-2-oxa-6-thia-1,3b,8-triaza-cyclopenta[a]indene[a']anthracene-7-carboxylic acid (14a-c):

By cyclocondensation reaction of Schiff base derivatives **11 (a-c)** with hydroxylamine hydrochloride in a mixture of EtOH/DMF in the presence of NaOH (2-3 droplets) as catalyst to synthesize Spiro-aryl-ISO-oxazolo heterocyclic derivatives **14 (a-c)[Scheme 4]**.The structures of these compounds were confirmed by IR and ^{1}H-NMR spectra **[cf. Experimental section]** and their elemental analysis **[Table 3]**.

Synthesis of 4,9,13-trioxo-11-aryl-3a,4,9,9a,10a,11,12,13-octahydro-1H-naphth-o[2',3':5,6][1,4]thiazino[3,4-f]purine-2-carboxylic acid (15a-c):

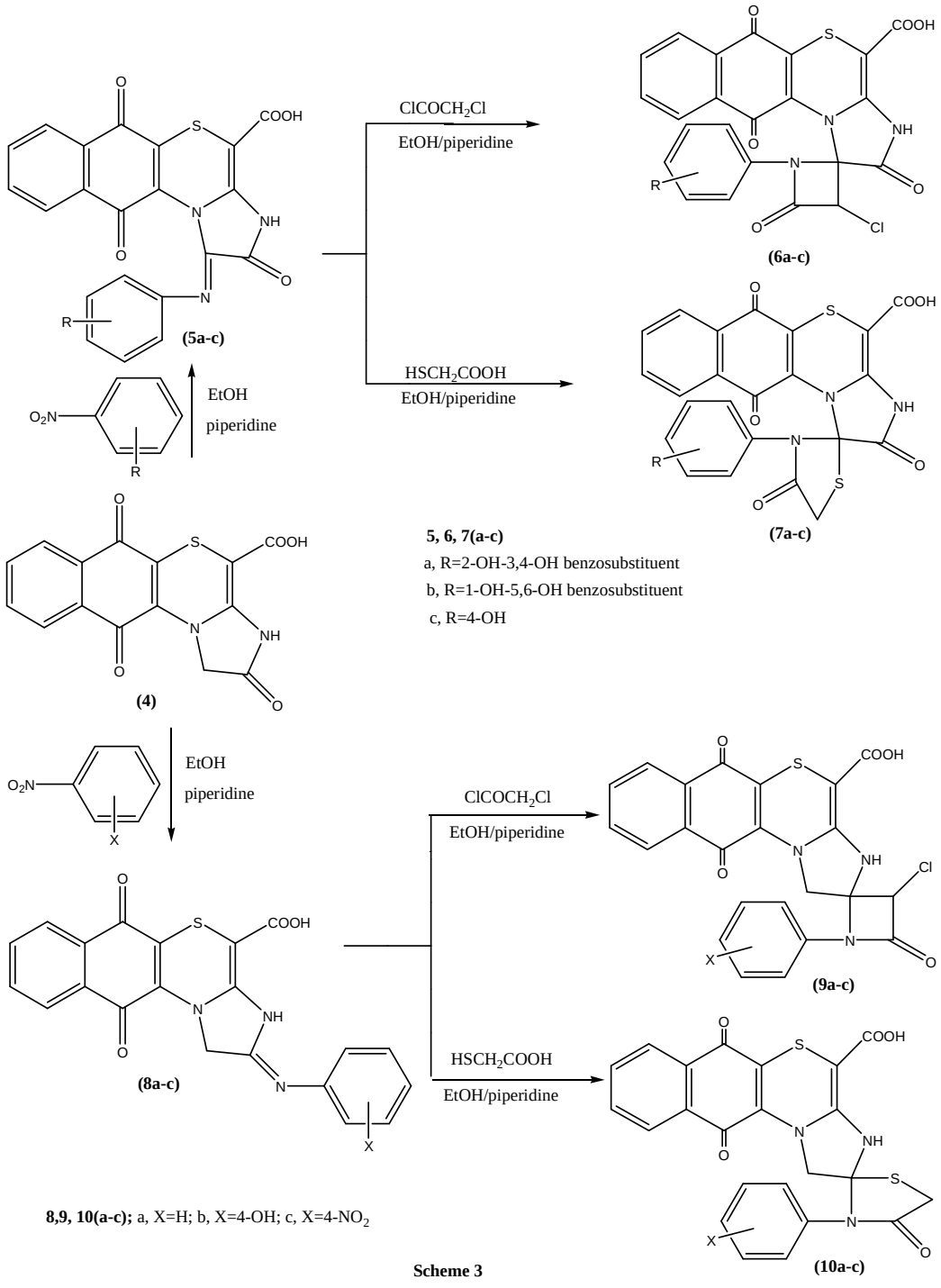
By cyclocondensation reaction of Schiff base derivatives **11 (a-c)** with urea in EtOH with HCl (2-3 droplets) as catalyst to synthesize Spiro-aryl pyrimidinone heterocyclic derivatives **15 (a-c)[c.f. Scheme 3]**. The structures of these compounds were confirmed by their elemental analysis, IR and ^{1}H-NMR spectra **[cf. Experimental section]**.

Synthesis of 5,13-dioxo-12-aryl-10-thioxo-5,10,11,12,12a,13-hexahydro-8H-6thia-8,9,11,12b-tetraaza-indeno [1,2-a] anthracene-7-carboxylic acid (16a-c):

By cyclocondensation reaction of Schiff base derivatives **11 (a-c)** with thiourea in EtOH containing NaOH (2-3 droplets) as catalyst to synthesize Spiro-aryl thiopyrimidino heterocyclic derivatives **16 (a-c)[Scheme 4]**. The structures of these compounds were confirmed by IR and ^{1}H-NMR spectra **[cf. Experimental section]** and their elemental analysis**[Table4]**.

Table 4. Physical and analytical data for the synthesized compounds (15_{a-c}, 16_{a-c})

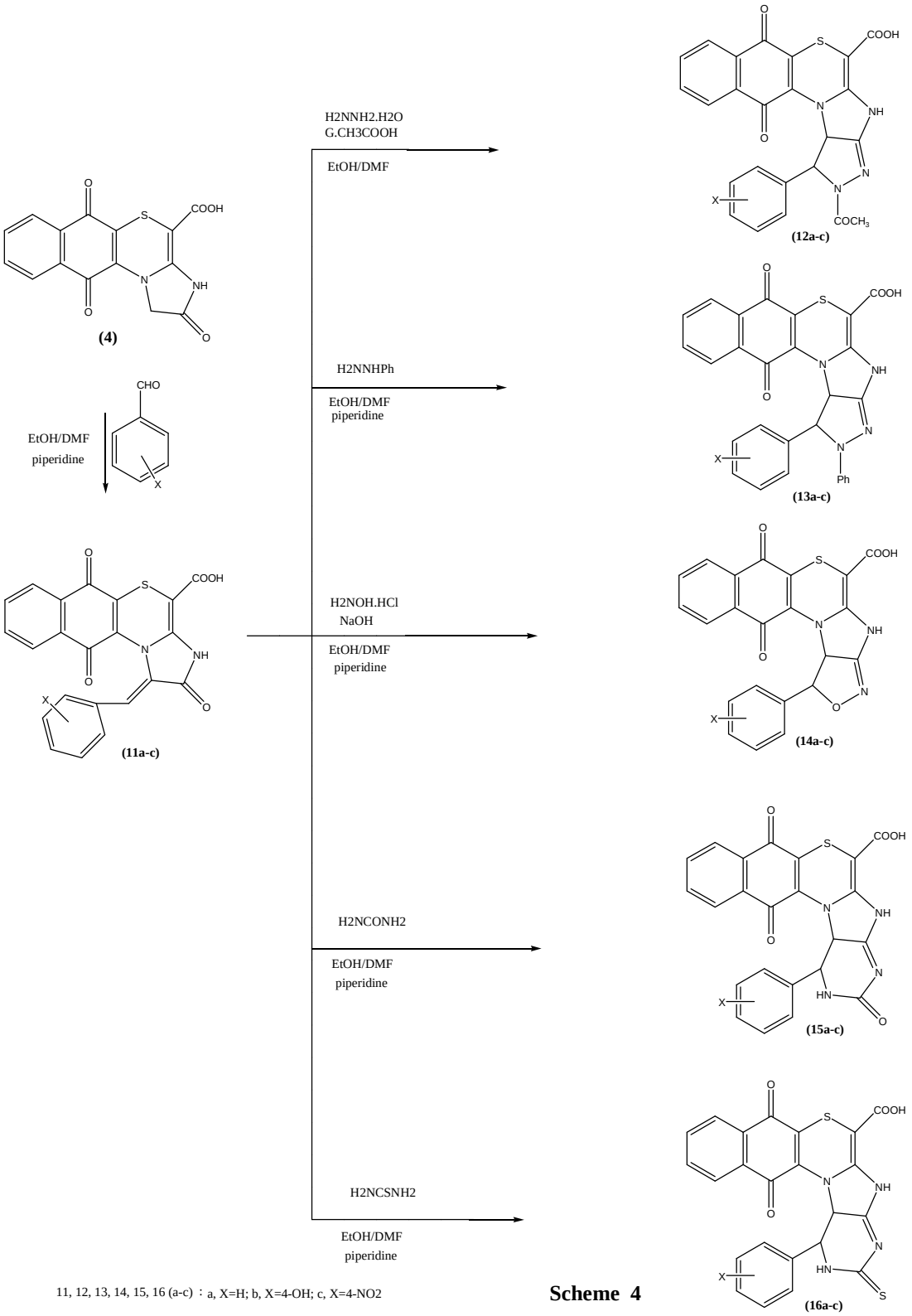
Comp. NO.	Yield %	M.P (ºC)	Solvent	Mol. Form. (Mol. Wt)	Elemental analysis [Calc. / Found (%)]				MS (M^+)
					C	H	N	S	
15a	68	Over 350	Ethanol /DMF	$C_{23}H_{16}O_5N_4S$ (460.461)	59.99 59.95	3.50 3.46	12.17 12.08	6.96 6.90	460
15b	66	Over 350	Ethanol /DMF	$C_{23}H_{16}O_6N_4S$ (476.460)	57.98 58.06	3.38 3.44	11.76 11.80	6.73 6.80	476
15c	70	Over 350	Ethanol /DMF	$C_{23}H_{15}O_7N_5S$ (505.459)	54.65 54.60	2.99 2.95	13.86 13.80	6.34 6.26	505
16a	67	Over 350	Ethanol /DMF	$C_{23}H_{16}O_4N_4S_2$ (476.522)	57.97 58.00	3.38 3.40	11.67 11.70	13.46 13.53	476
16b	45	Over 350	Ethanol /DMF	$C_{23}H_{16}O_5N_4S_2$ (492.521)	56.09 56.05	3.27 3.24	11.38 11.32	13.02 13.10	492
16c	65	Over 350	Ethanol /DMF	$C_{23}H_{15}O_6N_5S_2$ (521.525)	52.97 52.93	2.90 2.88	13.43 13.47	12.30 12.35	521



5, 6, 7(a-c)
a, R=2-OH-3,4-OH benzosubstituent
b, R=1-OH-5,6-OH benzosubstituent
c, R=4-OH

8,9, 10(a-c); a, X=H; b, X=4-OH; c, X=4-NO_2

Scheme 3



11, 12, 13, 14, 15, 16 (a-c)：a, X=H; b, X=4-OH; c, X=4-NO2

Scheme 4

EXPERIMENTAL

All melting points for the synthesized compounds are (uncorrected) measured on a Gallen-Kamp melting point apparatus with a digital thermometer type MFB-595-010M. The elemental analysis were done on a Perkin-Elmer 240ºC elemental analyzer system Gmbh VAR IDEL $V_{2.3}$ 2007 CHNS mode. (Cairo University). IR spectra were measured as KBr discs on a Pye Unicom Sp 1100 infrared spectrophotometer Shimadzu (υ. Cm^{-1}). ^{1}H-NMR spectra were recorded for $CDCl_3$ and DMSO solution on a Varian T-60 NMR spectrometer using TMS as an internal reference (chemical shifts in δ ppm) at 450 MHz (Cairo University). Mass spectra were recorded on a Hp.Ms 5988 spectrometer. Elemental analysis was carried out at the micro analytical of Cairo University.

Synthesis of 3-amino-5,10-dioxo-4a,5,10,10a-tetrahydro-4H-naphtho[2,3-b] [1,4] thiazine-2-carboxylic acid (3):

A solution of the equimolar ratio of appropriate urea was reacted with mercaptoacetic acid in ethanol (20 ml) containing few drops of piperidine, where, the mixture was treated with 1,4-naphthoquinone (0.01 ml) and heated under reflux for 10-13 hr. (monitored by TLC control). The solvent was then evaporated under reduced pressure. Pour onto acidified ice/water by drops of HCl conc., the formed solid product was collected by filtration and crystallized from ethanol to give (53 % yields) of deep brown powder of **(3)**. M.p.: 320ºC. The structure of the new synthesized **(3)** were confirmed by IR : ν 3345-3310(NH, NH_2), 3330(OH), 1710(C=O). ^{1}H NMR (300 MHz, DMSO-d_6) : δ11.0 (s, 1H, COOH), 8-7(m, 4H, Ar-H^+), 2.2(br, 1H, NH), 2.0(br, 2H, NH_2). MS(EI, m/z(%)): 314.32(M^+). Anal. Calcd. For $C_{15}H_{10}N_2O_4S$: C, 57.3; H, 3.21; N, 8.91. Found, C, 57.35; H, 3.20; N, 9.00.

Synthesis of 2,6,11-trioxo-2,3,5a,6,11,11a-hexahydro-1H-imidazo[1,2-d] naphtho[2 , 3-b][1,4]thiazine-4-carboxylic acid (4);

By reaction of equimolar ratios of appropriate compound **(3)** (2.80 g , 0.01 mole) and chloroacetylchloride (0.11 g, 0.01 mole) was condensed until fused for about ½h, then, added ethanol (30 ml) in presence of (0.5 ml) piperidine as catalyst. The experimental evidence that depends on the different types of analysis to the reaction product proves that the reaction leads to the formation of compound **(4)** according to the suggested reaction. M.p.: 230ºC. The structure of the compound **(4)** was confirmed by IR (ν_{max}/cm^{-1}): 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 8-7 (m, 4H, Ar-H^+), 8.2 (br, 1H, NH), 3.54 (s, 2H, CH_2CO). MS (EI, m/z (%)): 330.31 (M^+). Anal. Calcd. For $C_{15}H_{10}N_2O_5S$: C, 54.54; H, 3.05; N, 8.49. Found C, 54.50; H, 3.00; N, 8.56.

Synthesis of 2, 6, 11-Trioxo-1-phenylimino-2,3,6,11-tetrahydro-1H-5-thia-3,11b-diaza-cyclopenta[a]anthracene-4-carboxylic acid (5a-c) :

A solution of equimolar ratio of compound **(4)** (0.33 g, 0.01 mole) was treated with different aromatic nitroso compounds (α-naphthol, β-naphthol, 4-nitrosophenol, respectively, 0.01 mole) in an equimolar ratio, were dissolved in ethanol (40 ml) and (0.5 ml) of piperidine as catalyst was added. The reaction mixture was heated under reflux for 8-10h. The mixture was allowed to cool at room temperature, filtered, washed several times with water, dried, collected, and crystallized from the proper solvent to give **5(a-c)**. The structure of the compound **5a** as example was confirmed by IR (ν_{max}/cm^{-1}): 3360, 3554(OH), 3350-

3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 10H, Ar-H^{+}), 2.5 (br, 1H, NH).

Synthesis of3-chloro-1-aryl-2,5,9,14-tetraoxo-8-thia-1,6,15-triaza-spiro[3,4]octan-2-one[a]anthracene-7-carboxylic acid (6a-c) :

A solution of equimolar ratio of **5(a-c)** (4.86 g, 4.86 g, 4.36 g, respectively, 0.01 mole) and chloroacetyl chloride (1.13 g, 0.01 mole) in a mixture of ethanol (40 ml) in the presence of (0.5 ml) of piperdine was refluxed for 8-10h. The filtrate was evaporated under reduced pressure, poured into ice water where the product was separated, filtered, washed several times with water and crystallized from the proper solvent to give **6(a-c)**. The structure of the compound **6**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 10H, Ar-H^{+}), 7.6(s, 1H, β-Lactam-H^{+}), 2.5 (br, 1H, NH).

Synthesis of1-phenyl-2,10,15-trioxo-4,9-dithia-1,7,16-triaza-spiro[5, 5]nonan-2-one[a]anthracene-8-carboxylic acid (7a-c) :

A solution of equimolar ratio of **5(a-c)** (4.86 g, 4.86 g, 4.36 g, respectively, 0.01 mole) and mercaptoacetic acid (0.092 g, 0.01 mole) in a mixture of ethanol (40 ml) in the presence of (0.5) ml of piperdine was refluxed for 8-10h. The filtrate was evaporated under reduced pressure, poured into ice water where the product was separated, filtered, washed several times with water and crystallized from the proper solvent to give **7(a-c)**. The structure of the compound **7**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 10H, Ar-H^{+}),3.54 (s, 2H, CH_2CO), 2.5 (br, 1H, NH).

Synthesis of 6,11-Dioxo-2-phenylimino-2,3,6,11-tetrahydro-1H-5-thia-3,11b-diaza-cyclopenta[a]anthracene-4-carboxylic acid (8a-c) :

A solution of an equimolar ratio of compound **(4)** (3.32 g, 0.01 mole) in ethanol (30 ml) and dimethylformamide was reacted with different aromatic amines {aniline, 4-hydroxyaniline, 4-nitroaniline (0.93 g, 1.09 g, 1.38 g, respectively, 0.01 mole)} in the presence of catalytic amount of piperidine (0.5 ml). The reaction mixture was heated under reflux for 8-10h. The solvent was then evaporated under reduced pressure or at the room temperature and the residue was treated with ice water acidified by HCl. The solid product was collected by filtration and crystallized from the proper solvent to give **8(a-c)**. The structure of the compound **7**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 10H, Ar-H^{+}),3.54 (s, 2H, CH_2CO), 2.5 (br, 1H, NH).

Synthesis of3-chloro-1-phenyl-8-thia-1,5,6-triaza-spiro[3,4]octan-2-one[a]anthracene-7-carboxylic acid (9a-c) :

A solution of an equimolar ratio of compound **8(a-c)** (0.41 g, 0.42 g, 0.45 g, respectively, 0.01 mole) in ethanol (30 ml) and dimethyl-formamide was treated with $ClCOCH_2Cl$ (0.112 g, 0.01 mole) in the presence of catalytic amount of piperidine (0.5 ml). The reaction mixture was heated under reflux for 8-10h. The solvent was then evaporated under reduced

pressure or at the room temperature and the residue was treated with ice water acidified by HCl. The solid product was collected by filtration and crystallized from the proper solvent to give **9(a-c)***.* The structure of the compound **9**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 10H, Ar-H^{+}), 7.8(s, 1H, β-Lactam-H^{+}), 3.54 (s, 2H, CH_2CO), 2.5 (br, 1H, NH).

Synthesis of4-phenyl-1, 10-dithia-4, 7, 8-triaza-spiro[5, 5]nonan-3-one[a]anthracene-9-carboxylic acid (10a-c) :

A solution of equimolar ratio of compound **8(a-c)** (0.41 g, 0.42 g, 0.45 g, respectively, 0.01 mole) in ethanol (30 ml) and dimethylformamide was treated with $HSCH_2COOH$ (0.092 g, 0.01 mole) in the presence of catalytic amount of piperidine (0.5 ml). The reaction mixture was heated under reflux for 6-8h. The solvent was then evaporated under reduced pressure and the residue was treated with ice water acidified by HCl. The solid product was collected by filtration and crystallized from the proper solvent to give **10(a-c)**. The structure of the compound **10**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 10H, Ar-H^{+}), 3.54 (s, 2H, CH_2CO), 2.5 (br, 1H, NH).

Synthesis of 1-[(E)-1-arylmethylidene]-2,6,11-trioxo-2,3,5a,6,11,11a-hexa-hydro-1H-imidazo[1,2-d]naphtho[2,3-b][1,4]thiazine-4-carbox-ylic acid (11a-c) :

A solution of an equimolar ratio of compound **4**(0.32 g, 0.01 mol) in ethanol (30 ml) and dimethylformamide was treated with different aromatic aldehyde derivatives {benzaldehyde, 4-hydroxybenzaldehyde, 4-nitrobenzaldehyde, respectively, (0.106 g, 0.122 g, 0.151 g, 0.01 mol)} in the presence of catalytic amount of piperidine (0.5 ml). The reaction mixture was heated under reflux for 8-10h. The solution was then evaporated under reduced pressure and the residue was treated with ice water acidified by HCl. The solid product was collected by filtration and crystallized from the proper solvent to give **11(a-c)**. The structure of the compound **11**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 10H, Ar-H^{+}), 5.6(s, 1H, CH olifinic), 2.5 (br, 1H, NH).

Synthesis of2-acetyl-3-phenyl-2,3,3a,8-tetrahydro-6-thia-1,2,3b,8tetraaza-cyclopenta[a]indene[a']anthracene-7-carboxylic acid (12a-c) :

A solution of Spiro-arylidino derivatives **11(a-c)** (4.74 g, 4.90 g, 4.19 g, respectively, 0.01 mole) in a mixture of ethanol (20 ml) and dimethylformamide (15 ml) as solvent, hydrazine hydrate (0.50 g, 0.01 mole) was added followed by glacial acetic acid (5 ml). The reaction mixture was concentrated and filtered. These produced substances were washed with water and the precipitates were separated, filtered, washed several times with water, dried, collected and crystallized from the proper solvent to give **12(a-c)**. The structure of the compound **12**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 10H, Ar-H^{+}), 5.2(d, 1H, CH pyrazoline-H^{+}), 3.6 (d, 1H, pyrazolidine-H^{+}), 2.3(s, 3H, CH_3CO), 2.1(br, 1H, NH).

Synthesis of2-phenyl-3-phenyl-2,3,3a,8-tetrahydro-6-thia-1,2,3b,8tetraaza-cyclopenta[a]indene[a']anthracene-7-carboxylic acid (13a-c) :

A solution of Spiro-Arylidino derivatives **11(a-c)** (4.74 g, 4.90 g, 4.19 g, respectively, 0.01 mole) in a mixture of ethanol (20 ml) and dimethylformamide (15 ml) as solvent, added phenyl hydrazine (1.08 g, 0.01 mole) in the presence of (0.5 ml) of piperidine as catalyst. The reaction mixture was refluxed for 10-12h (monitored by TLC). The reaction mixture was concentrated, cooled, poured into ice water acidified by concentrated HCl acid. The solid substances were collected by filtration, washed with water for several times an crystallized from the proper solvent to give **13(a-c)**. The structure of the compound **13**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 15H, Ar-H^{+}), 5.2(d, 1H, CH pyrazoline-H^{+}), 3.6 (d, 1H, pyrazolidine-H^{+}), 2.1(br, 1H, NH).

Synthesis of 3-phenyl-3,3a-dihydro-8H-2-oxa-6-thia-1,3b,8-triaza-cyclopenta[a]indene[a']anthracene-7-carboxylic acid (14a-c):

A solution of Spiro-arylidino derivatives **11(a-c)** (4.74 g, 4.90 g, 4.19 g, respectively, 0.01 mole) was refluxed with hydroxylamine hydrochloride (0.69 g, 0.01 mole) in the presence of (0.5 ml) of NaOH as a catalyst and a mixture of ethanol (30 ml) and dimethylformamide (15 ml) as a solvent for 8-11h (monitored by TLC). The reaction mixture was filtered hot, the filtrate was concentrated and poured into ice-water, where, the products were separated, filtered, washed several times with water an crystallized from the proper solvent to give **14(a-c)**. The structure of the compound **14**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8-7 (m, 10H, Ar-H^{+}), 5.2(d, 1H, CH pyrazoline-H^{+}), 3.6 (d, 1H, pyrazolidine-H^{+}), 2.1(br, 1H, NH).

Synthesis of 4,9,13-trioxo-11-aryl-3a,4,9,9a,10a,11,12,13-octahydro-1H-naphth-o[2',3':5,6][1,4]thiazino[3,4-f]purine-2-carboxylic acid (15a-c):

A solution of Spiro-arylidino derivatives **11(a-c)** (4.18 g, 4.34 g, 4.62, respectively 0.01 mole) was refluxed with urea (0.6 g, 0.01 mole) in the presence of HCl (0.5 ml) as a catalyst and a mixture of ethanol and dimethylformamide as a solvent, for 8-10h. The reaction mixture was filtered hot from unreacted materials, and the filtrate was concentrated and poured into ice water and the products were separated, filtered, washed several times with water and crystallized from the proper solvent to give **15(a-c)**. The structure of the compound **15**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8.3(br, 1H, m, pyrimidine-H^{+}), 8-7(m, 10H, Ar-H^{+}), 5.2(d, 1H, CH pyrazoline-H^{+}), 3.6 (d, 1H, pyrazolidine-H^{+}), 2.1(br, 1H, NH).

Synthesis of 5,13-dioxo-12-aryl-10-thioxo-5,10,11,12,12a,13-hexahydro-8H-6thia-8,9,11,12b-tetraaza-indeno[1,2-a]anthracene-7-carboxylic acid (16a-c):

A solution of Spiro-arylidino derivatives **11(a-c)** (4.18 g, 4.34 g, 4.62, respectively 0.01 mole) was refluxed with thiourea (0.67 g, 0.01 mole) in the presence of NaOH (0.5 ml) as a catalyst and a mixture of ethanol and dimethylformamide as a solvent, for 8-10h. The reaction mixture was filtered hot from unreacted materials, and the filtrate was concentrated and poured into ice water and the products were separated, filtered, washed several times with

water and crystallized from the proper solvent to give **16(a-c**). The structure of the compound **16**a as example was confirmed by IR (v_{max}/cm^{-1}): 3360, 3554(OH), 3350-3320(NH), 1720, 1640(C=O). The ^{1}H-NMR spectrum of the product in [DMSO-d6] gave a singlet at δ 11 (s, 1H, COOH), 10.5(s, 1H, OH), 8.3(br, 1H, m, pyrimidine-H^{+}), 8-7(m, 10H, Ar-H^{+}), 5.2(d, 1H, CH pyrazoline-H^{+}), 3.6 (d, 1H, pyrazolidine-H^{+}), 2.1(br, 1H, NH).

4. CONCLUSION

The Spiro β-lactam derivatives (6a-c, 9a-c) and the Spiro thiazolidinone derivatives (7a-c, 10a-c), also, the fused pyrazolo derivatives(12a-c, 13a-c), the fused isoxazolo derivatives (14a-c) and the pyrimidine derivatives (15a-c, 16a-c), such heterocyclic compounds were known to be of special value in medicinal chemistry and some of them are suitable intermediates in the synthesis of penicillin, cephalosporin's, and their analogous.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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