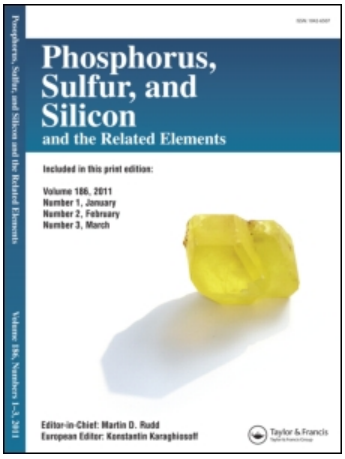

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Synthesis and Studies of Some New Fused/Spiro Heterocyclic Compounds Containing Nitrogen and Sulfur

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Synthesis and Studies of Some New Fused/Spiro Heterocyclic Compounds Containing Nitrogen and Sulfur

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Spiro β-lactam, thiazolidinone derivatives, fused pyrazolo, pyrimidino, pyrimidinthion, and Isoxazolo incorporating new compound 2 has been synthesized by cyclocondensation addition reaction and cycloaddition reaction of monochloroacetyl chloride, mercaptoacetic acid, hydrazinehydrate, phenylhydrazine, urea, thiourea, and hydroxyl amine hydrochloride.

Keywords Mercaptoacetic acid; oxazole; pyrazole; pyrimidine; pyrimidintion; schiff bases; spiro β-lactams; Spiro thiazolidinone

INTRODUCTION

A large number of penicillins are known and used as potent antibiotics,[1] β-lactams and related derivatives have been found to be active compounds having antibacterial activities. Some examples comprise the naturally occurring monobactams and nocardicins.[2] Contrary to penicillins, cephalosporins, or nocardicins, monobactams were not produced by fungi or actinomycetes, but from bacteria, for example Bacillus, pseudomonas.[3] The synthetic oxamazine,[4–6] thiamazins,[7] and monosulfactams[8] showed some antibacterial activity, which raised again a major interest in the area of 2-azetidinone chemistry. Also, thiazole derivatives such as penicillin, which has fused thiazolidine and β-lactam rings were known and used as potent antibiotics.[9] Thiazole derivatives are also associated with a broad spectrum of biological properties, including anticonvulsant,[10,11] antimicrobial,[12–14] antitubercular, and bacteriostatic activities.[15,16] Therefore, compounds containing β-lactam ring, thiazolidinone are expected to possess potential

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biological activities. Our previous work aimed at developing new approaches to the synthesis of polyfunctionally substituted heterocyclic compounds of biological activity.[17–19] Also pyrazoles, oxazole, pyrimidinethione, thioglycolic and β-lactam derivatives play a vital role in many biological processes[20–24] and as synthetic drugs. The chemistry of these heterocyclic compounds has received much attention in recent years. This is principally due to the unique physical and chemical properties of such compounds, which enable their wide application as plant growth regulators,[25] dyes,[26] and corrosion inhibitors.[27]

RESULTS AND DISCUSSION

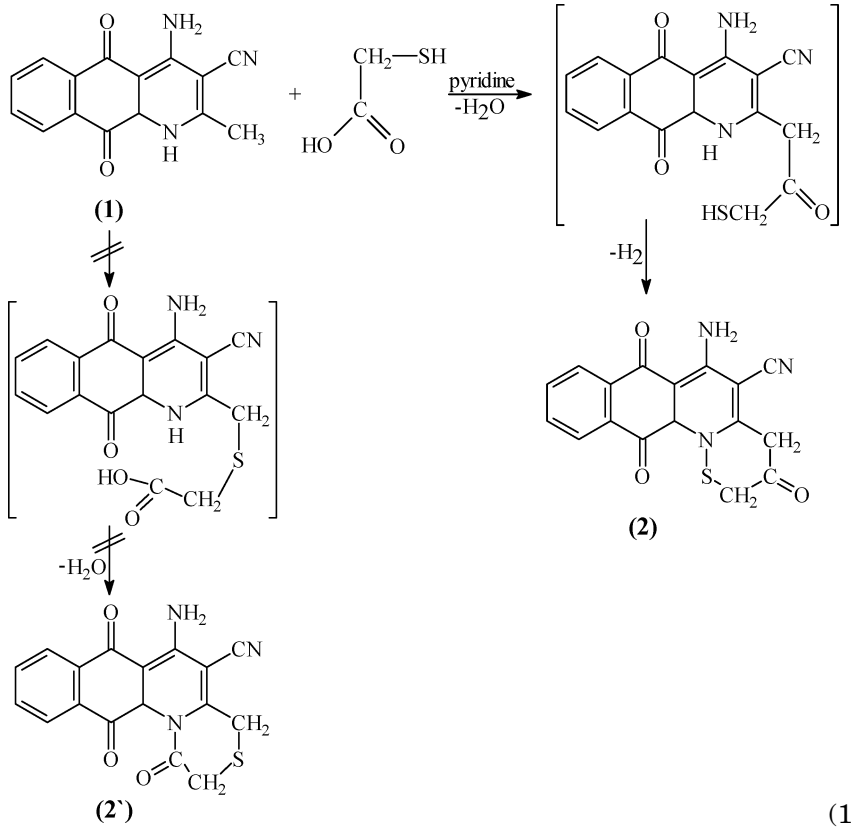
The new compound 2 was synthesized by the reaction of 4-amino-2-methyl-5,10-dioxo-1,5,10,11-tetrahydrobenzo[g]quinoline-3- carbonitrile **1**, which was prepared according to a reported method,[18] with equimolar ratios of mercaptoacetic acid in dry pyridine. The activity of methyl group at C_2 renders it available to react with mercaptoacetic acid through elimination of a molecule of water followed by cyclization to give compound **2**. Thus, compound **2** was prepared according to Equation (1). Structure **2** was preferred over possible **2′** based on elemental analysis, IR, ^{1}H NMR spectrum of the product in DMSO showed singlet at δ 2.81 for 2H and singlet at δ 2.35 for 2H supporting the structure of compound 2 and mass spectral data showed the molecular ion peak at m/z (337). The reaction of compound **1** with mervaptoacetic acid is considered the oxidative cyclization involving the conversion of an amine and a thiol to a sulfenamide.[28,29]

Our approach to the synthesis of the desired spiro compounds started with compounds **3a–c**, which were prepared by the condensation of nitroso compounds such as α-nitroso β-naphthol, p-nitrosophenol, and p-nitroso-N-dimethylaniline with compound **2** in ethanol using a piperidine catalyst, which afforded the new Schiff bases compounds.

The structure of these newly synthesized Schiff bases compounds **3a–c** were confirmed by elemental analysis and infrared spectra, which showed absorption bands at 1620–1580 cm^{-1} attributed to C=N and a characteristic band attributed to C=O at 1700–1696 cm^{-1} and 3310 attributed to NH_2.[30]

The formation of Schiff bases **3a–c** is expected to owing suggested mechanism, (c.f. Equation [2]).

The first step in the previous mechanism involves the formation of carboanion (a) using piperidine as a catalyst, which abstracted a proton from the active hydrogen center; accordingly, it was added itself on the polarized aromatic nitroso compounds forming the intermediate compound (b) to uptake a proton from the piperidinium ion forming

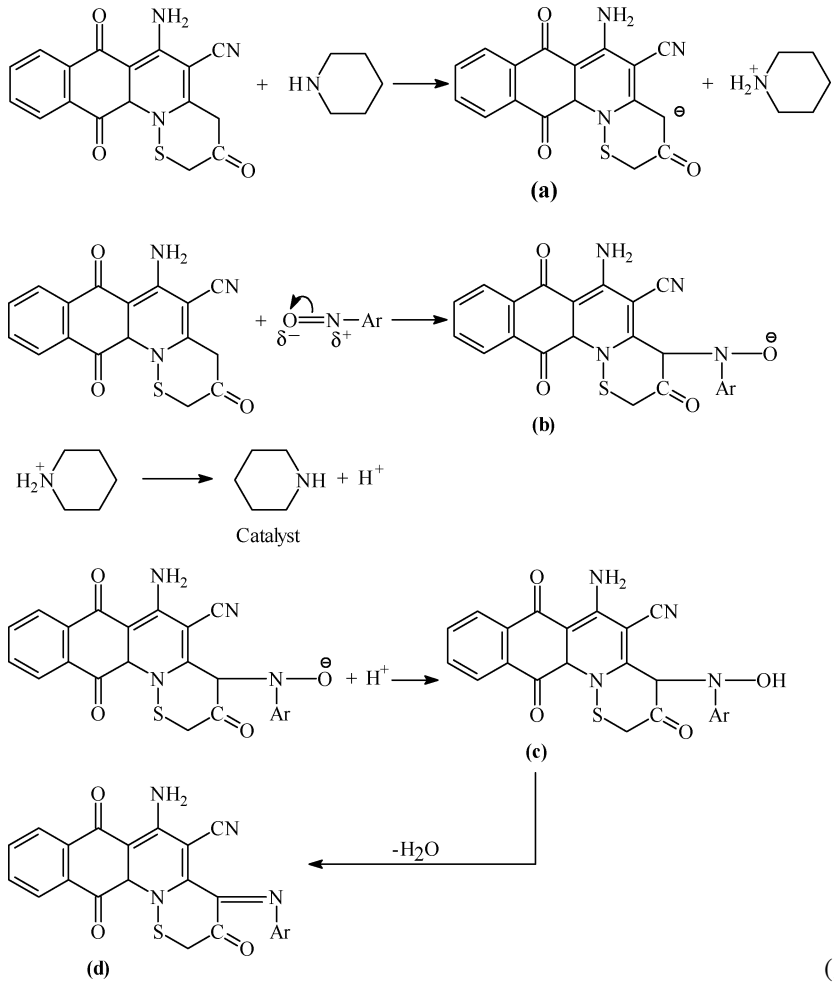


(1)

compound (c). The latter compound (c) lost a mole of water to produce the Schiff base compound **3a–c**.

Compound **3a–c** underwent cycloaddition with chloroacetyl chloride to give spiro lactam **4a–c**. The cycloaddition proceeded smoothly in dry xylene in the presence of a triethylamine catalyst[19,31] to afford **4a–c**. The reaction of compound **3a–c** with chloroacetyl chloride proceeded through a [2 + 2] cycloaddition; the cycloaddition reaction was assumed to go through the following suggested mechanism (c.f. Equation [3]).

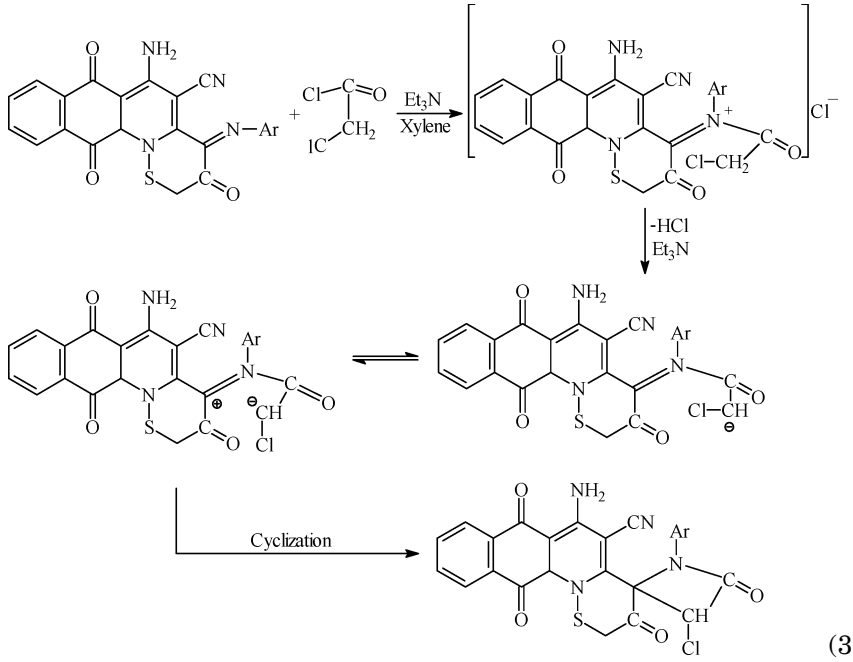
The structure of spiro lactams **4a–c** confirmed by analytical data and infrared spectra, which showed the disappearance of the absorption band of C=N at 1580 cm^{-1}, also showed a C-N absorption band at 1225 cm^{-1} and C=O of a β-lactam ring at 1765 cm^{-1} and ^1H NMR spectrum, which showed signals at δ 6.65 (s, NH_2), multiplet signals at δ 8–7 for aromatic protons, at δ 4.22 singlet for β-lactam carbon proton, at δ 2.56 (s, S-CH_2).



(2)

Spirothiazolidinone **5a–c** was prepared by the cycloaddition of mercaptoacetic acid (1:1 molar ratios) in dioxane in the presence of triethylamine as catalyst was heated under reflux on a steam bath for 15 h. and afforded the corresponding compound **5a–c**. The cycloaddition reaction was assumed to go through the following suggested mechanism (c.f., Equation [4]).

The structure of thiazolidinone derivatives **5a–c** was identified from the correct elemental analysis and infrared spectra, which showed an absorption band at 1680–1640 cm^{-1} attributed to C=O group and ^{1}H-NMR spectrum, which showed a singlet signal at 2.45 for CH_2 of the thiazolidinone ring.

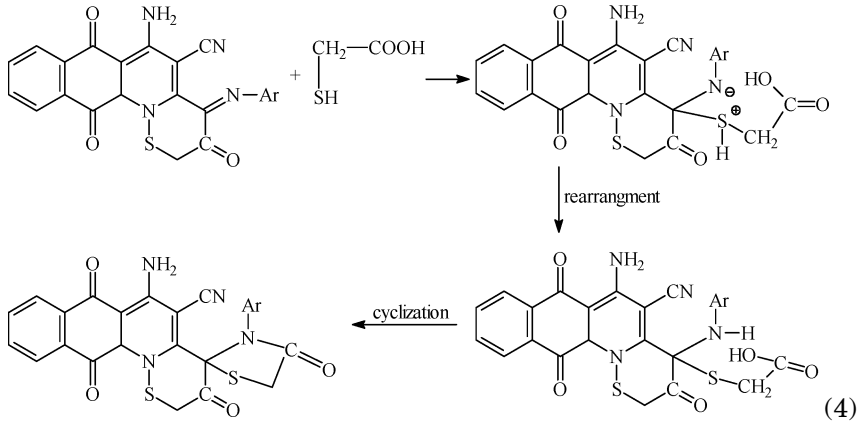


(3)

The activity of carbonyl group in compound **2** lead compound **2** was easily condensed with different aromatic amine in dry DMF and few drops of piperidine as a catalyst to give new Schiff bases derivatives **6a–c**. The structure of compound **6a–c** were confirmed by elemental analysis and infrared spectra, which showed absorption bands at 1625–1580 cm^{-1} attributed to C=N and a characteristic band attributed to C=O at 1710–1699 cm^{-1} and 3310 attributed to NH_2.[28]

The formation of Schiff bases **6a–c** is expected to using the same suggested mechanism of compound **3a–c**.

Compound **6a–c** underwent cycloaddition with chloroketene to give spiro lactam **7a–c**. The cycloaddition proceeded smoothly in toluene in the presence of a triethyl amine catalyst[19,29] to afford **7a–c**. The formation of newly spiro thiazolidinone **7a–c** is expected to owing the same suggested mechanism of compound **4a–c**. The structure of spiro lactams **7a–c** confirmed by analytical data and infrared spectra, which showed the disappearance of the absorption band of C=N at 1580 cm^{-1}, also showed a C-N absorption band at 1527 cm^{-1} and C=O of a β-lactam ring at 1760 cm^{-1} and ^{1}H-NMR spectrum, which showed signals at δ 6.69 (s, NH_2), multiplet signals at δ 8–7 for aromatic protons, at δ 4.25 singlet for β-lactam carbon proton, at δ 2.52 (s, S-CH_2).



(4)

Spiro thiazolidinone **8a–c** was prepared by the cycloaddition of mercaptoacetic acid in dioxane in the presence of triethyl amine as a catalyst was heated under reflux for 15 h. and afforded the corresponding compound **8a–c**, the cycloaddition reaction was assumed to go through the same suggested mechanism of formation of compound **5a–c**.

The structure of thiazolidinone derivatives **8a–c** was identified from the correct elemental analysis and infrared spectra, which showed an absorption band at 1685–1645 cm^{-1} attributed to C=O group and ^{1}H-NMR spectrum, which showed a singlet signal at 2.39 for CH_2 of the thiazolidinone ring.

The activity of the methylene group in compound **2** lead compound **2** was easily condensed with different aromatic aldehydes in ethanol as a solvent using piperidine catalyst to give **9a–c**. The structure of compound **9a–c** was confirmed by elemental analysis and IR, which revealed the presence of peak NH_2 at 2300–3100 cm^{-1}, C=O 1725–1670 cm^{-1}, and C=C 1610–1585 cm^{-1}; also, its structures were confirmed by ^{1}H-NMR and mass spectral data (c.f. Tables I and II).

The activity of the exocyclic group C=C in compound **9a–c** in conjugation with the carbonyl group was demonstrated by a reaction with hydrazines, hydroxylamine hydrochloride, urea, and thiourea. The nature of the structure of the products for the previously mentioned reaction, according to the different methods of analysis, elemental analysis, IR, and mass spectra, gave us the agreements that the reaction is carried out by condensation addition reaction through the α, β-unsaturated ketonic system. Thus, the chemical work covers the implementation of the following fused heterocyclic compounds and the details are as follows (c.f. Equation [4]).

TABLE I Elemental Analysis of New Compound

Comp. no.	Solvent of crystallization	M.p. °C	Yield %	Color	Formula (mol. wt)	Analytical data found/required (%) C	H	N	S	Cl	MS (m/z)
2	Ethanol	296	60	Brown	$C_{17}H_{11}O_3N_3S$	6.53	3.29	12.46	9.51	—	337
					(337)	6.50	3.28	12.43	9.49	—	
3a	Ethanol	>300	45	Green	$C_{27}H_{16}O_4N_4S$	65.85	3.27	11.38	6.51	—	493
					(492)	65.82	3.26	11.36	6.48	—	
3b	Ethanol	>300	55	Deep Brown	$C_{23}H_{14}O_4N_4S$	62.44	3.19	12.66	7.25	—	442
					(442)	62.42	3.16	12.65	7.23	—	
3c	Ethanol	>300	50	Red	$C_{25}H_{19}O_3N_5S$	63.95	4.09	14.92	6.83	—	469
					(469)	63.92	4.07	14.90	6.81	—	
4a	Methanol	>300	70	Orange	$C_{29}H_{17}O_5N_4SCl$	61.22	3.01	9.85	5.64	6.23	568
					(568)	61.19	2.99	9.84	5.61	6.21	
4b	Ethanol	>300	60	Red	$C_{25}H_{15}O_5N_4SCl$	57.86	2.91	10.80	6.18	6.83	518
					(518)	57.83	2.89	10.79	6.15	6.81	
4c	Methanol	>300	55	Brown	$C_{27}H_{20}O_4N_5SCl$	59.39	3.69	12.83	5.87	6.49	546
					(546)	59.38	3.66	12.80	5.84	6.47	546
5a	Methanol	>300	45	Violet	$C_{29}H_{18}O_5N_4S_2$	61.69	2.86	9.92	11.36	—	546
					(564)	61.66	2.84	8.89	11.34		
5b	Methanol	>300	40	Move	$C_{25}H_{16}O_5N_4S_2$	58.13	3.12	10.85	12.42	—	516
					(516)	58.13	3.12	10.84	12.42		
5c	Ethanol	>300	49	Greenish Blue	$C_{27}H_{21}O_4N_5S_2$	59.65	3.89	12.88	11.80	—	543
					(543)	59.63	3.87	12.88	11.80		
6a	Methanol	>300	50	Pale Green	$C_{23}H_{16}O_2N_4S$	66.98	3.91	13.58	7.77	—	412
					(412)	66.97	3.90	13.58	7.77		
6b	Methanol	>300	54	Green	$C_{23}H_{16}O_3N_4S$	64.47	3.76	13.08	7.48	—	428
					(428)	64.47	3.76	13.07	7.46	—	
6c	Methanol	>300	59	Green	$C_{23}H_{15}O_4N_5S$	60.39	3.30	15.31	7.01	—	457
					(457)	60.39	3.30	15.30	7.01		

7a	Ethanol	>300	60	Brown	$C_{25}H_{17}O_3N_4SCl$	61.41	3.50	11.46	6.56	7.25	488
					(488)	61.39	3.50	11.45	6.54	7.24	
7b	Methanol	>300	65	Red Brown	$C_{25}H_{17}O_4N_4SCl$	59.47	3.93	11.10	6.35	7.02	504
					(504)	59.45	3.93	11.08	6.33	7.01	
7c	Methanol	>300	63	Broan	$C_{25}H_{16}O_5N_5SCl$	56.24	3.02	13.12	6.01	6.64	533
					(533)	56.22	3.01	13.09	6.01	6.64	
8a	Methanol	>300	49	Red	$C_{25}H_{18}O_3N_4S$	61.71	3.73	11.51	13.18	—	486
					(486)	61.70	3.71	11.49	13.16		
8b	Ethanol	>300	43	Reddish Brown	$C_{25}H_{17}O_4N_4S$	59.87	3.42	11.17	12.79	—	501
					(501)	59.87	3.42	11.15	12.79		
8c	Ethanol	>300	47	Violet	$C_{25}H_{17}O_5N_2S$	56.49	3.22	13.18	12.06	—	531
					(531)	56.47	3.21	13.18	12.05	—	
9a	Methanol	>300	45	Brown	$C_{24}H_{15}O_3N_3S$	67.84	3.55	9.88	7.54	—	425
					(533)	67.84	3.55	9.87	7.52	—	
9b	Methanol	>300	48	Brown	$C_{24}H_{15}O_4N_3S$	65.30	3.42	9.52	7.26	—	441
					(441)	65.29	3.40	9.52	7.23	—	
9c	Ethanol	>300	55	Reddish Brown	$C_{24}H_{14}O_5N_4S$	61.27	3.00	11.91	6.82	—	470
					(470)	61.27	2.99	11.90	6.82		
10a	Methanol	>300	58	Green	$C_{26}H_{19}O_3N_5S$	64.85	3.98	14.54	6.66	—	481
					(481)	64.85	3.98	14.53	6.66	—	
10b	Ethanol	>300	53	Green	$C_{26}H_{19}O_4N_5S$	62.77	3.85	14.08	6.44	—	497
					(497)	62.76	3.85	14.08	6.43	—	
10c	Ethanol	>300	55	Greenish Blue	$C_{26}H_{18}O_5N_6S$	59.31	3.45	15.96	6.09	—	526
					(526)	59.31	3.45	15.95	6.08	—	
11a	Methanol	>300	53	Green Yellow	$C_{30}H_{21}O_2N_5S$	69.89	4.11	13.58	6.22	—	515
					(515)	69.88	4.10	13.58	6.20	—	

(Continued on next page)

TABLE I Elemental Analysis of New Compound (*Continued*)

Comp. no.	Solvent of crystallization	M.p. °C	Yield %	Color	Formula (mol. wt)	Analytical data found/required (%) C	H	N	S	Cl	MS (m/z)
11b	Ethanol	>300	60	Green	$C_{30}H_{21}O_3N_5S$	67.78	3.98	13.17	6.03	—	531
					(531)	67.77	3.98	13.16	6.02	—	
11c	Methanol	>300	62	Green	$C_{30}H_{20}O_4N_6S$	64.28	3.60	14.99	5.72	—	560
					(560)	64.28	3.59	14.97	5.71	—	
12a	Methanol	>300	46	Brown	$C_{24}H_{16}O_3N_4S$	65.44	3.66	12.72	7.28	—	440
					(440)	65.42	3.66	12.71	7.28	—	
12b	Methanol	>300	40	Red	$C_{24}H_{16}O_4N_4S$	63.15	3.53	12.27	7.02	—	456
					(456)	63.15	3.53	12.26	7.02	—	
12c	Ethanol	>300	43	Reddish Brown	$C_{24}H_{15}O_5N_5S$	59.38	3.11	14.43	6.61	—	485
					(485)	59.37	3.11	14.41	6.60	—	
13a	Methanol	>300	45	Orange	$C_{25}H_{17}O_4N_6S$	64.23	3.67	14.98	6.86	—	—
					(467)	64.23	3.66	14.96	6.85		
13b	Ethanol	>300	50	Brown Red	$C_{25}H_{17}O_4N_6S$	60.36	3.44	16.89	6.45	—	497
					(497)	60.36	3.44	16.89	6.43		
13c	Methanol	>300	45	Violet	$C_{25}H_{16}O_5N_6S$	58.59	3.15	16.40	6.26	—	512
					(512)	58.58	3.15	16.39	6.26		
14a	Methanol	>300	60	Blue	$C_{25}H_{17}O_2N_5S_2$	62.09	3.54	14.48	13.26	—	—
					(483)	62.09	3.54	14.46	13.25		
14b	Ethanol	>300	63	Green Blue	$C_{25}H_{17}O_3N_6S_2$	58.47	3.34	16.36	12.49	—	513
					(513)	58.46	3.33	16.36	12.49		
14c	Methanol	>300	67	Violet Blue	$C_{25}H_{16}O_4N_6S_2$	56.81	3.05	15.90	12.13	—	528
					(528)	56.80	3.05	15.90	12.11		

TABLE II Selected IR, ^{1}H-NMR Spectra Data for the New Compounds Listed in Table I

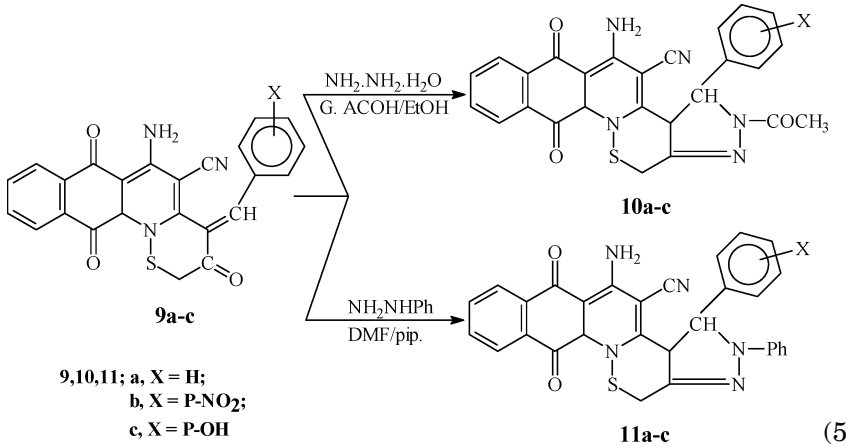
Comp. No.	IR (cm^{-1})	^{1}H-NMR δ (ppm)
2	1680 (2C═O), 2216 (C≡N), 3300 (NH_2), 1720 (C═O).	2.35 (s, 2H), 2.88 (s, 2H), 6.77 (s, NH_2), 8–7 (m, 5H, aromatic protons).
3a	1620–1580 (C═N), 1700–1696 (C═O), 1726 (C═O), 2220 (C≡N), 3100–34oo (OH, NH_2).	2.53 (s, 2H), 6.75 (s, NH_2), 8.0–7.1 (m, 12H, aromatic protons, OH protons).
3b	1625–1585 (C═N), 1700–1690 (C═O), 1730 (C═O), 2215 (C≡N), 3100–3450 (OH, NH_2).	2.56 (s, 2H), 6.73 (s, NH_2), 8.1–7.2 (m, 9H, aromatic protons, OH protons).
3c	1628–1580 (C═N), 1705–1695 (C═O), 1733 (C═O), 2211 (C≡N), 3330 (NH_2).	1.13 (d.s., 6H), 2.54 (s, 2H), 6.70 (s, NH_2), 8.1–7.1 (m, 11H, aromatic protons).
4a	1690–1685 (C═O), 1722 (C═O), 2218 (C≡N), 3150–3400 (OH, NH_2).	2.56 (s, 2H), 4.22 (s, 1H), 6.65 (s, NH_2), 8–7 (m, 12H, aromatic protons, OH protons).
4b	1695–1670 (C═O), 1725 (C═O), 2213 (C≡N), 3150–3400 (OH, NH_2).	2.57 (s, 2H), 4.19 (s, 1H), 6.69 (s, NH_2), 8–7 (m, 10H, aromatic protons, OH protons).
4c	1699–1675 (C═O), 1728 (C═O), 2215 (C≡N), 3320 (NH_2).	1.15 (d.s., 6H), 2.52 (s, 2H), 6.69 (s, NH_2), 8–7 (m, 10H, aromatic protons).
5a	1690–1665 (C═O), 1712 (C═O), 2212 (C≡N), 3100–3400 (OH, NH_2).	2.45 (s, 2H), 2.56 (s, 2H), 6.66 (s, NH_2), 8–7 (m, 12H, aromatic protons, OH protons).
5b	1695–1660 (C═O), 1715 (C═O), 2210 (C≡N), 3150–3400 (OH, NH_2).	2.46 (s, 2H), 2.58 (s, 2H), 6.69 (s, NH_2), 8–7 (m, 10H, aromatic protons, OH protons).
5c	1699–1660 (C═O), 1716 (C═O), 2215 (C≡N), 3334 (NH_2).	1.12 (s, 6H), 2.43 (s, 2H), 2.55 (s, 2H), 6.65 (s, NH2), 8–7 (m, 9H, aromatic protons).
6a	1623–1580 (C═N), 1710–1699 (C═O), 1710 (C═O), 2218 (C≡N), 3325 (NH_2).	2.33 (s, 2H), 2.12 (s, 2H), 6.59 (s, NH_2), 8–7 (m, 10H, aromatic protons).
6b	1625–1575 (C═N), 1700–1590 (C═O), 1713 (C═O), 2220 (C≡N), 2100–3400 (OH, NH_2).	2.34 (s, 2H), 2.09 (s, 2H), 6.57 (s, NH_2), 8–7 (m, 10H, aromatic protons, OH protons).
6c	1625–1580 (C═N), 1700–1595 (C═O), 1715 (C═O), 2225 (C≡N), 3328 (NH_2).	2.36 (s, 2H), 2.15 (s, 2H), 6.62 (s, NH_2), 8–7 (m, 9H, aromatic protons).
7a	1790–1585 (C═O), 2223 (C≡N), 3335 (NH_2).	2.32 (s, 2H), 2.52 (s, 2H), 4.25 (s, 1H), 6.69 (s, NH_2), 8–7 (m, 10H, aromatic protons).

(Continued on next page)

TABLE II Selected IR, ^{1}H-NMR Spectra Data for the New Compounds Listed in Table I (*Continued*)

Comp. No.	IR (cm^{-1})	^{1}H-NMR δ (ppm)
7b	1765–1589 (C═O), 2221 (C≡N), 3330 (NH_2).	2.36 (s, 2H), 2.50 (s, 2H), 4.23 (s, 1H), 6.67 (s, NH_2), 8–7 (m, 10H, aromatic protons, OH protons).
7c	1760–1585 (C═O), 2227 (C≡N), 3335 (NH_2).	2.37 (s, 2H), 2.54 (s, 2H), 4.26 (s, 1H), 6.73 (s, NH_2), 8–7 (m, 9H, aromatic protons).
8a	1690–1590 (C═O), 17.28 (C═O), 2219 (C≡N), 3333 (NH_2).	2.31 (s, 2H), 2.55 (s, 2H), 2.39 (s, 2H), 6.75 (s, NH_2), 8–7 (m, 10H, aromatic protons).
8b	1695–1585 (C═O), 1731 (C═O), 2216 (C≡N), 3150-3400 (OH, NH_2).	2.32 (s, 2H), 2.53 (s, 2H), 2.37 (s, 2H), 6.77 (s, NH_2), 8–7 (m, 9H, aromatic protons, OH protons).
8c	1600–1585 (C═O), 1735 (C═O), 2229 (C≡N), 3340 (NH_2).	2.34 (s, 2H), 2.56 (s, 2H), 2.42 (s, 2H), 6.79 (s, NH_2), 8–7 (m, 9H, aromatic protons).
9a	1610–1585 (C═O), 1725–1670 (C═O), 2220 (C≡N), 3100-3400 (NH_2).	2.45 (s, 2H), 6.82 (s, NH_2), 8.1–7.01 (m, 11H, aromatic protons).
9b	1600–1585 (C═C), 1720–1675 (C═O), 2225 (C≡N), 3150-3400 (NH_2).	2.43 (s, 2H), 6.83 (s, NH_2), 8.1–7.01 (m, 11H, aromatic protons, OH protons).
9c	1610–1580 (C═C), 1725–1670 (C═O), 2227 (C≡N), 3150-3400 (OH, NH_2).	2.48 (s, 2H), 6.85 (s, NH_2), 8.1–7.01 (n, 1oH, aromatic protons).
10a	1715–1670 (C═O), 2215 (C≡N), 3100–3400 (NH_2).	1.21 (s, 3H), 2.46 (s, 2H), 6.87 (s, NH_2), 8.1–7.01 (m, 12H, aromatic protons).
10b	1710–1675 (C═O), 2227 (C≡N), 3100–3400 (NH_2).	1.23 (s, 3H), 2.45 (s, 2H), 6.84 (s, NH_2), 8.1–7.01 (m, 12H, aromatic protons, OH protons).
10c	1705–1670 (C═O), 2220 (C≡N), 3150–3400 (OH, NH_2).	1.25 (s, 3H), 2.46 (s, 2H), 6.87 (s, NH_2), 8.1–7.01 (m, 11H, aromatic protons).
11a	1700–1660 (C═O), 1710 (C═O), 2210 (C≡N), 3100-3400 (NH_2).	2.51 (s, 2H), 6.85 (s, NH_2), 8.1–7.01 (m, 17H, aromatic protons).
11b	1690–1670 (C═O), 1714 (C═O), 2216 (C≡N), 3100-3400 (NH_2).	2.49 (s, 2H), 6.86 (s, NH_2), 8.1–7.01 (m, 17H, aromatic protons, OH protons).

11c	1695–1665 (C═O), 1716 (C═O), 2208 (C≡N), 3100–3400 (OH, NH_2).	2.53 (s, 2H), 6.89 (s, NH_2), 8.1–7.01 (m, 16H, aromatic protons).
12a	1699–1660 (C═O), 1719 (C═O), 2213 (C≡N), 3150–3400 (NH_2).	2.48 (s, 2H), 6.88 (s, NH_2), 8.1–7.01 (m, 12H, aromatic protons).
12b	1695–1660 (C═O), 1722 (C═O), 2222 (C≡N), 3100–3400 (NH_2).	2.5 (s, 2H), 6.70 (s, NH_2), 8.1–7.01 (m, 12H, aromatic protons, OH protons).
12c	1690–1670 (C═O), 1715 (C═O), 2217 (C≡N), 3100–3400 (OH, NH_2).	2.54 (s, 2H), 6.75 (s, NH_2), 8.1–7.01 (m, 11H, aromatic protons).
13a	1695–1645 (C═O), 1718 (C═O), 2219 (C≡N), 3100–3400 (NH_2, NH).	2.55 (s, 2H), 6.77 (s, NH_2), 8.1–7.01 (m, 12H, aromatic protons, 10.23 (brs, NH).
13b	1690–1645 (C═O), 1720 (C═O), 2215 (C≡N), 3100–3400 (NH_2, NH).	2.51 (s, 2H), 6.74 (s, NH_2), 8.1–7.01 (m, 12H, aromatic protons, OH protons), 10.26 (brs, NH).
13c	1695–1640 (C═O), 1723 (C═O), 2210 (C≡N), 3150–3400 (OH, NH_2, NH).	2.56 (s, 2H), 6.79 (s, NH_2), 8.1–7.01 (m, 11H, aromatic protons), 10.35 (brs, NH).
14a	1690–1640 (C═O), 1716 (C═O), 2216 (C≡N), 3100–3400 (NH_2, NH).	2.53 (s, 2H), 6.78 (s, NH_2), 8.1–7.01 (m, 12H, aromatic protons), 10.39 (brs, NH).
14b	1699–1645 (C═O), 1719 (C═O), 2223 (C≡N), 3100–3400 (NH_2, NH).	2.54 (s, 2H), 6.79 (s, NH_2), 8.1–7.01 (m, 12H, aromatic protons, OH protons), 10.43 (brs, NH).
14c	1700–1640 (C═O), 1722 (C═O), 2214 (C≡N), 3100–3400 (NH_2, NH).	2.58 (s, 2H), 6.82 (s, NH_2), 8.1–7.01 (m, 11H, aromatic protons), 10.45 (brs, NH).



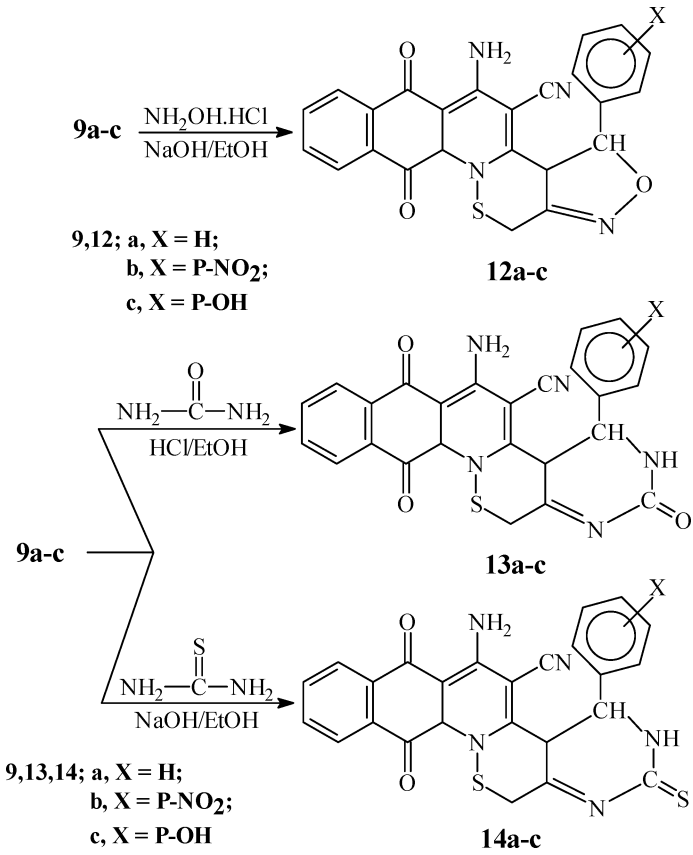
(5)

N-acetyl (phenyl) derivatives of compounds **10a–c** and **11a–c** were synthesized by the interaction of **9a–c** with equimolecular ratios of hydrazine hydrate or phenylhydrazine in the presence of glacial acetic acid and piperidine as a catalyst, respectively.

The structures of **10a–c** and **11a–c** were confirmed by elemental analysis, IR, ^{1}H NMR, and mass spectra (c.f. Tables I and II). The structure of compound **10a** was confirmed by elemental analysis, IR, and an ^{1}H NMR spectrum, which revealed the presence of singlet signal at δ 6.65 for NH_2 and a multiplet signal at δ 8–7 for aromatic protons, at δ 2.56 (s, CH_3), δ 2.45 (s, CH_2-S), δ 2.23 (d, CH), δ 1.65 (d, CH), and mass spectral data showed the molecular ion peak at m/z (481). Also, the structure of compound **11a** was confirmed by elemental analysis, IR, and an ^{1}H NMR spectrum, which revealed the presence of singlet signal at δ 6.67 for NH_2 and a multiplet signal at δ 8–6 for aromatic protons, at δ 2.49 (s, CH_2S), δ 1.61 (d, CH), and δ 1.12 (d, CH), and mass spectral data showed the molecular ion peak at m/z (515).

Isoxazolino derivatives of compounds **12a–c** were synthesized by the reaction of **9a–c** with equimolecular ratios of hydroxylamine hydrochloride in the presence of sodium hydroxide [c.f. Equation (5)]. The structures of **12a–c** were confirmed by elemental analysis, IR, ^{1}H-NMR, and mass spectra (c.f. Tables I and II).

Pyrimidine and pyrimidinethion derivatives of compounds **13a–c** and **14a–c** were synthesized by the reaction of **9a–c** with equimolecular ratios of urea and/or thiourea in ethanol containing 20 ml of hydrochloric acid and/or in the presence of sodium hydroxide, respectively [c.f. Equation (6)]. The structures of compounds **13a–c** and **14a–c** were confirmed by analytical and spectral analysis (c.f. Tables I and II).



(6)

EXPERIMENTAL

Melting points were uncorrected and determined using Kofler m.p. apparatus. IR spectra were recorded on a Pye Unicam SP3-100 spectrophotometer using the KBr water technique. ^{1}H NMR spectra were recorded on a Varian EM-39090 MHz spectrometer using TMS as an internal standard. MS spectra were measured on SSQ-7000 apparatus at 70 eV. Elemental analyses were carried out at the Microanalytical center of Cairo University (Cairo, Egypt) and at the Microanalytical Unit at Assiut University (Assiut, Egypt). The characterization data of all newly synthesized compounds are given in Tables I and II.

4-Amino-2-methyl-5,10-dioxo-1,5,10,11-tetrahydrobenzo[g]quinoline-3-carbonitrile 1

This compound was prepared according to a reported method.[18]

The Synthesis of New Compound 2

A mixture of 1 (2.65 g, 0.01 mmol) and mercaptoacetic acid (0.92 g, 0.01 mmol) in dry pyridine (20 ml) was heated under reflux on a steam bath for 13 h. The solid product that separated after cooling was collected and recrystallized from the proper solvent to give **2** as green crystals.

The Synthesis of New Schiff Bases Derivatives 3a–c

A mixture of 2 (3.37 g, 0.01 mmol), aromatic nitroso compounds (0.01 mmol), and a few drops of piperidine (0.5 ml) in ethanol (15 ml) was heated under reflux for 8 h, concentrated, and allowed to cool. The precipitate that formed was collected and recrystallized from the proper solvent to give **3a–c**.

The Synthesis of Spiro Lactam Derivatives 4a–c

A mixture of **3a–c** (0.01 mmol) and chloroacetyl chloride (1.13 g, 0.01 mmol) in dry xylene (30 ml) and triethylamine (0.01 ml) as catalyst was heated under reflux for 14 h. The solid that separated up on cooling was filtered off and crystallized from the proper solvent to give **4a–c**.

The Synthesis of Spiro Thiazolidinone Derivatives 5a–c

A mixture of **3a–c** (0.01 mmol), mercaptoacetic acid (0.92 g, 0.01 mmol) and triethylamine (0.01 ml) in dioxane (20 ml) was heated under reflux on a steam bath for 15 h. The solid product that separated after cooling was collected and recrystallized from the proper solvent to give **5a–c**.

The Synthesis of Schiff Bases Derivatives 6a–c

A mixture of 2 (3.37 g, 0.01 mmol) aromatic amine (0.01 mmol), and few drops of piperidine (0.5 ml) in dry DMF (30 ml) was heated under reflux for 7 h. the solvent was then evaporated under reduced pressure, and the residue was treated with ice water. The solid product was collected and crystallized from the proper solvent to give **6a–c**.

The Synthesis of New Spiro Lactam Derivatives 7a-c

A mixture of **6a–c** (0.01 mmol), chloroacetyl chloride (1.13 g, 0.01 mmol) in toluene (20 ml) and triethylamine (0.01 ml) was heated to reflux under magnetic stirring for 12 h. Concentration in vacuo gave a residue, which was taken up in acetone and chromatographed on silica gel plates (cyclohexane 7/ethyl acetate 7.5) to afford a crude material, which was crystallized from the proper solvent to give **7a–c**.

Synthesis of New Spiro Thiazolidinone Derivatives 8a–c

A mixture of **6a–c** (0.01 mmol), mercaptoacetic acid (0.92 g, 0.01 mmol) in dioxane (30 ml) and triethyl amine catalyst (0.01 mmol) was stirred under reflux for 15 h. Concentration in vacuo afforded a crude material, which was dissolved in ethylacetate and chromatographed on silica gel (hexane 4/ethyl acetate 1) to give a solid substance, which was crystallized from the proper solvent to give **8a–c**.

Synthesis of Arylidene Compound Derivatives 9a–c

To a mixture of 2 (3.37 g, 0.01 mmol) and different aromatic aldehyde (0.01 mmol) in absolute ethanol (20 ml) was added piperidine (5 drops). The mixture was heated under reflux for 6 h. the crystalline product thus obtained after cooling was collected and recrystallized from the proper solvent to give **9a–c**.

The Reaction of Compound 9a–c with Hydrazine Hydrate to Give N-Acetyl-pyrazolo Derivatives 10a–c

A magnetically stirred mixture of compound **9a–c** (0.01 mmol) and hydrazine hydrate (0.50 g, 0.01 mmol) in ethanol (30 ml) in the presence of glacial acetic acid and piperidine as a catalyst was heated to reflux for 10 h. On cooling to room temperature, the precipitate was collected and boiled with petroleum ether (60–80°C). The residue was treated with ice water, and the solid obtained was collected and crystallized from the proper solvent to give **10a–c**.

The Reaction of Compound 9a–c with Phenylhydrazine to Give N-phenylhydrazine to Give N-phenyl-pyrazolo Derivatives11a–c

A mixture of **9a–c** (0.01 mmol) and phenylhydrazine (1.08 g, 0.01 mmol) in dry DMF (30 ml) in the presence of a catalytic amount of piperidine

(0.1 ml) was heated under reflux on a steam bath for 14 h. The solvent was then evaporated under reduced pressure, and the residue was treated with cold water. The solid product was collected and crystallized from the proper solvent to give **11a–c**.

The Reaction of Compound 9a–c with Hydroxylamine Hydrochloride to Give Isoxazolo Derivatives 12a–c

A mixture of **9a–c** (0.01 mmol) in absolute ethanol (20 ml) was treated with hydroxylamine hydrochloride (0.69 g, 0.01 mmol) in the presence of sodium hydroxide as a catalyst. The reaction mixture was heated under reflux for 13 h. The reaction mixture was filtered hot. The solvent was then evaporated under reduced pressure, and the remaining resin was boiled with petroleum ether (60–80°C). The solid product was collected and crystallized from the proper solvent to give **12a–c**.

The Reaction of Compound 9a–c with Urea to Give Pyrimidino Derivatives 13a–c

A mixture of **9a–c** (0.01 mmol) and urea (0.60 g, 0.01 mmol) in ethanol (30 ml) was added Conc. HCl (20 ml). The mixture was heated under reflux for 15 h. It was then filtered hot and allowed to cool; the solvent evaporated under reduced pressure, and the residue was treated with crushed ice and neutralized with 5N NaOH. The solid product was collected and crystallized from the proper solvent to give **13a–c**.

The Reaction of Compound 9a–c with Thiourea to Give Thio-pyrimidino Derivatives 14a–c

A mixture of **9a–c** (0.01 mmol) and thiourea (0.76 g, 0.01 mmol) in dry DMF (20 ml) was added sodium hydroxide as catalyst. The reaction mixture was heated under reflux for 13 h. It was then filtered hot; the solvent evaporated under reduced pressure to dryness, and the residue treated with petroleum ether (60–80°C). The excess of petroleum ether was removed, and the residue was treated with cold water. The solid product was collected and crystallized from the proper solvent to give **14a–c**.

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