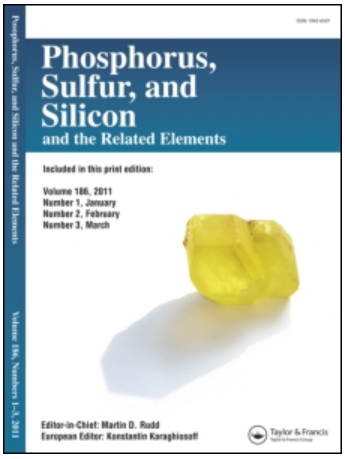

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SYNTHESIS AND CYCLIZATION OF 3-[3'(2'-SPIROTHIAZOLIDIN-4'-ONYL)] QUINAZOLIN-4-ONE DERIVATIVES

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SYNTHESIS AND CYCLIZATION OF 3-[3′(2′-SPIROTHIAZOLIDIN-4′-ONYL)] QUINAZOLIN-4-ONE DERIVATIVES

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The reaction of 3-(3H)-aminoquinazolin-4-one derivatives 4a-c with 2-spiro-1,3-oxathiolan-5-one derivatives 7a-f in ethanol yielded 3-[3′(2′-spirothiazolidin-4′-one)]quinazolin-4-one derivatives 8a-r in excellent yield. Cyclization of compounds 8a-r with sodium hydroxide in ethanol or with fusion with anhydrous sodium acetate gave the spirothiazolopyrazoloquinazolinone derivatives 9a-r. All the synthesized spiro heterocyclic derivatives were identified by conventional methods (IR, ^{1}H NMR) and elemental analyses.

Keywords: Spiroheterocycles; Spirothiazoloquinazolinones; Spiropyrazoloquinazolinones; cyclizations; NMR

INTRODUCTION

Spiro derivatives have anticovulant[1], antibacterial, antitubercular, anticancer activity[2]. They are also used as a potential dopamine D_2 receptor radioligand for SPECT[3], as potential anxiolytic[4], antiamnesia[5] as well as used in ophthalmic photochromic lenses[6]. Also spiroheterocycles were used as PDE1 and PDE5, GMP phosphodiesteras inhibitors[7], as nitric oxide syntase inhibitors[8]. Photoisomerization[9,10] and the utilization of spiroheterocycles as herbicides and pesticides were studied[11] and their application as potential topical agents for vaginal infections are also reported[12]. The syn-

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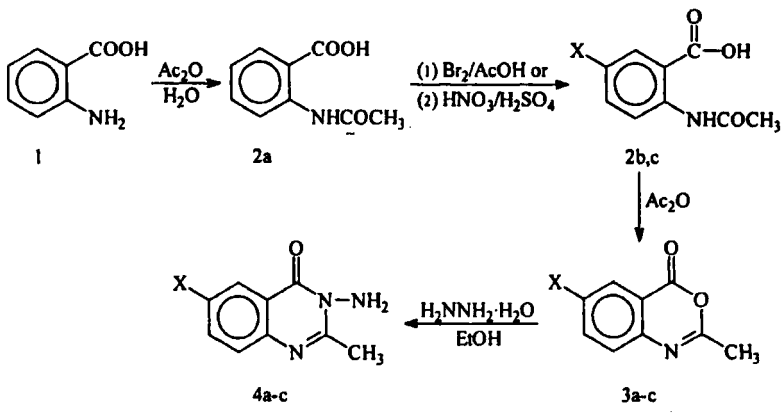
thesis of spiro derivatives as antitumor derivatives of illudin S[13], analogs of dehydroilludin M[14], as potential muscarinic agonists[15] and as antifungal agent[16] has been carried out.

It is of interest to note that pyrazole derivatives are used as pharmaceuticals[17–14]. Also quinazolin-4-one derivatives showed diverse biological activity[25], for example azolylquinazolines and related compounds were used as protein tyrosine kinase inhibitors[26]. Fused aryl pyridoquinazolinones were prepared to be used as anticancer agents[27–33]. Substituted quinazolinediones and quinazolinones were used as potent fibrinogen receptor antagonists[34]. As a consequence of all the forgoing observation and as a continuation of our previous work[35–40], we report herein the synthesis of some spirothiazolopyrazolquinazolinone derivatives.

RESULTS AND DISCUSSION

Because of the importance of the spiroheterocyclic derivatives and quinazolinone derivatives, it is very interesting to synthesize some new fused spiroheterocyclic derivatives incorporated with quinazolinones. To reach our goal, 3-(3H)-aminoquinazolin-4-ones *4a-c* were prepared by simple standard well known procedures, then allowed to react with 2-spiro-1,3-oxathiolan-5-one derivatives. For the synthesis of 3-(3H)-aminoquinazolin-4-ones 4a-c, anthranilic acid 1 was acetylated with acetic anhydride followed by addition of cold water to afford acetylanthranilic acid 2a. It was brominated with bromine in acetic acid or nitrated with concentrated nitric and sulfuric acid mixture to yield *2b,c*. Compounds *2a-c* were cyclized with acetic anhydride to yield the benzoxazinone derivatives *3a-c* which reacted with hydrazine hydrate to afford 3-(3H)-aminoquinazolin-4-one derivatives *4a-c* (Scheme 1).

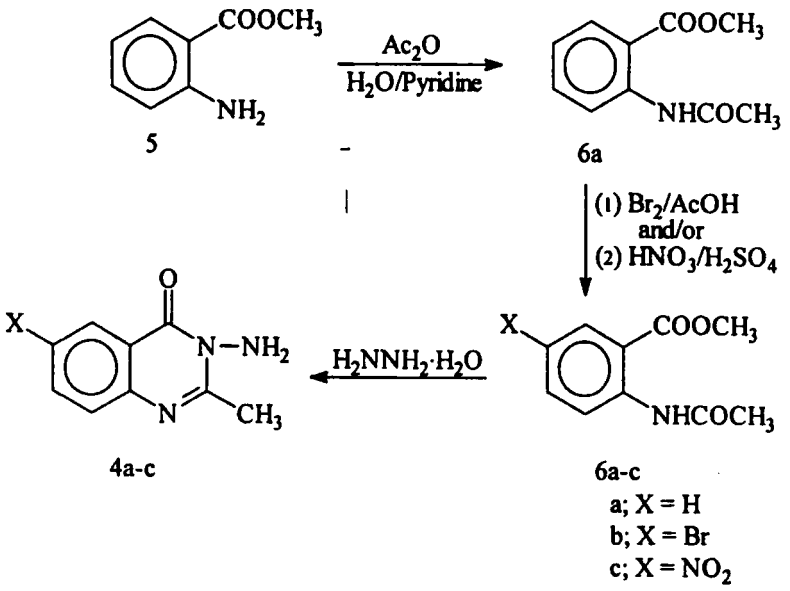
The preparation of 3-(3H)-aminoquinazolin-4-one derivatives *4a-c* was achieved by another procedure starting from methyl anthranilate 5 which was acetylated with acetic anhydride to yield acetyl methyl anthranilate 6a. Bromination of 6awith bromine in acetic acid and nitration of 6a with a H_2SO_4/HNO_3 mixture yielded the bromo derivative 6b and the nitro derivative 6c respectively. The reaction of compounds 6a-c with hydrazine hydrate afforded the aminoquinazolin-4-one derivatives *4a-c* (Scheme 2).



1 2a 2b,c 3a-c 4a-c

a; X = H
b; X = Br
c; $X = NO_2$

SCHEME 1

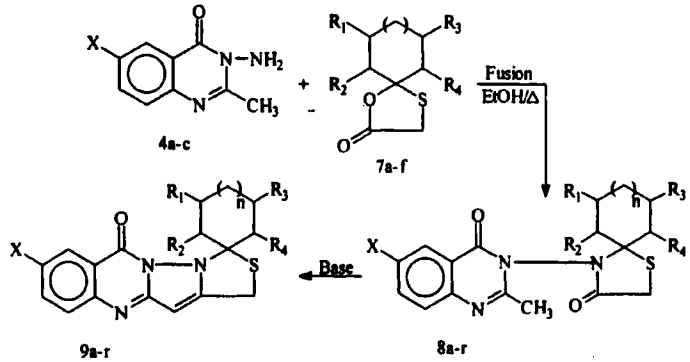


5 6a 6a-c 4a-c

a; X = H
b; X = Br
c; $X = NO_2$

SCHEME 2

The reaction of 3-(3H)-aminoquinazolin-4-one derivatives *4a-c* with 2-spiro-1,3-oxathiolan-5-one derivatives 7a-f in ethanol yielded -[3′(2′-spirothiazolidin-4′-one)]-quinazolin-4-one derivatives *8a-r* in excellent yield (Scheme 3).



4a-c 7a-f 9a-r 8a-r

In compounds 8a-r and 9a-r.

Compd. No. 8&9	X	n	R_1	R_2	R_3	R_4
a	H	0	H	H	H	H
b	Br	0	H	H	H	H
c	NO_2	0	H	H	H	H
d	H	1	H	H	H	H
e	Br	1	H	H	H	H
f	NO_2	1	H	H	H	H
g	H	0	H	H		
h	Br	0	H	H		
j	H	1	H	H		
k	Br	1	H	H		
l	NO_2	1	H	H		
m	H	0				
n	Br	0				
o	NO_2	0				
p	H	1				
q	Br	1				
r	NO_2	1				

SCHEME 3

The structures of the prepared compounds *8a-r* were assigned on the basis of elemental analyses, IR, ^{1}H-NMR, ^{13}C-NMR and mass spectroscopy (Table I). The IR spectrum of 8g showed characteristic strong absorption bands at 3050 cm^{-1} corresponding to the stretching vibrations of the aromatic carbon-hydrogen bond, and the band 2917 cm^{-1} is due to the aliphatic carbon-hydrogen bond. The band at 1677 cm^{-1} corresponds to the stretching vibrations of the carbonyl group of the quinazoline and thiazolidine rings. The bands at 1630 cm^{-1} is indicative for the C=N stretching and 700 cm^{-1} for C-S bond of thiazolidine ring. The ^{1}H-NMR spectrum of 8g (DMSO-d_6) showed the following signals: δ 2.43 (2H, t) for the methylene protons of the indan moiety, δ 2.59 (2H, t) for the benzylic methylene protons of the indan residue, δ 2.40 (3H, s) for the methyl group protons at $C_2$of the quinqzoline ring, δ 3.60 (2H, s) for the methylene protons of the thiazolidine ring and δ 7.40–8.20 ppm (8H, m) for the aromatic protons of both the quinazoline and the indan rings. The ^{13}C-NMR spectrum of 8g (DMSO-d_6) showed the following signals: 22.79, 27.84, 28.81, 119.67, 120.49, 125.83, 126.42, 126.56, 128.29, 132.06, 133,82, 142.25, 144.60, 146.66, 152.85, 155.46, 155,79, 159.99, 174.67, 197.45 ppm.

For the synthesis of the target compounds spirothiazolopyrazoloquinazolinones *9a-r*, attempted cyclization reactions of *8a-r* were carried out, by reaction of *8a-r* with sodium hydroxide (20%) in ethanol or with anhydrous sodium acetate to give the desired spirothiazolopyrazoloquinazolinones *9a-r* in good yields (Scheme 3, Table II). The chemical structures of *9a-r* are based on their elemental analyses and their spectral data (Table II). The IR spectrum of 9a showed characteristic strong absorption bands at 3030 cm^{-1} corresponding to the aromatic carbon-hydrogen stretching vibrations, 2917 cm^{-1} for the aliphatic carbon-hydrogen stretching vibrations, 1677 cm^{-1} corresponding to the stretching vibrations of the carbonyl group of the quinazoline ring, 1630 $cm^{-1}$for the C=N stretching and 710 cm^{-1} for C-S stretching vibrations. The ^{1}H-NMR spectrum of 9a (DMSO-d_6) showed the following signals: δ 1.30–1.60 (4H, m), 1.70–1.90 (4H, m) for the methylene protons of the cyclopentane moiety, 3.20 (2H, s) for the methylene protons of the thiazole ring, 5.10 (1H, s) for the H atom of pyrazole ring and 7.20–8.10 ppm (4H, m) for the aromatic protons of the quinazoline ring.

TABLE I Physical data of 3-[3-[3'-(2'-spirothiazolidin 4'-one]quinazolin-4-one derivatives 8a-r.

Comp. No.	Yield (%)	M.P. (°C)	Molecular formula (Solvent of Crystallization)	Microanalyses-Calculated / Found				(%) Br	IR (KBr) cm^{-1}	^{1}H-NMR (DMSO-d_6), δ (TMS)	^{13}C-NMR (DMSO-d_6), δ (TMS)
				C	H	N	S				
8a	86	162–164	$C_{18}H_{17}N_3O_2S$ (ethanol)	60.95 60.63	5.39 5.15	13.33 13.20	10.5 10.00	– –	3030 (CH arom), 2917 (CH aliph), 1677 (C=O), 1630 (C=N), 700 (C-S).	1.30–1.60(4H, m, $2CH_2$), 1.70–1.90 (4H, m, $2CH_2$), 2.40(3H, s, CH_3),3.60 (2H, s, CH_2), 7.10–8.20 (4H, m, aromatic protons).	-
8b	82	172–174	$C_{18}H_{16}N_3O_2SBr$ (ethanol)	48.85 48.60	4.07 4.00	10.68 10.68	8.14 8.00	20.10 20.00	3050 (CH arom), 2917 (CH aliph),1677 (C=O), 1630 (C=N), 700 (C-S).	1.30–1.60 (4H, m, $2CH_2$), 1.70–1.90 (4H, m, $2CH_2$), 2.30(3H, s, CH_3),3.60 (2H, s, CH_2), 7.80–8.20 (3H, m, aromatic protons).	-
8c	86	180–182	$C_{18}H_{16}N_4O_4S$ (ethanol)	53.33 53.20	4.44 4.30	15.55 15.30	8.88 8.70	– –	3050 (CH arom), 2917 (CH aliph),1677 (C=O), 1630 (C=N), 710 (C-S).	1.30–1.60 (4H, m, $2CH_2$), 1.70–1.90 (4H, m, $2CH_2$), 2.30(3H, s, CH_3),3.40 (2H, s, CH_2), 7.50–8.20 (3H, m, aromatic protons).	-
8d	87	173–175	$C_{17}H_{19}N_3O_2S$ (ethanol)	62.00 61.90	5.77 5.60	12.76 12.60	9.72 9.65	– –	3030 (CH arom), 2917 (CH aliph),1677 (C=O), 1620 (C=N), 700 (C-S).	1.30–1.50 (6H, m, $2CH_2$), 1.60–2.00 (4H, m, $2CH_2$), 2.30(3H, s, CH_3),3.60 (2H, s, CH_2), 7.40–8.20 (4H, m, aromatic protons).	-
8e	85	165–167	$C_{17}H_{18}N_3O_2SBr$ (ethanol)	50.12 50.00	4.42 4.40	10.31 10.10	7.86 7.60	19.41 19.20	3030 (CH arom), 2917 (CH aliph),1677 (C=O), 1620 (C=N), 700 (C-S).	1.30–1.50 (6H, m, $2CH_2$), 1.60–2.00 (4H, m, $2CH_2$), 2.30(3H, s, CH_3),3.60 (2H, s, CH_2), 7.50–8.20 (3H, m, aromatic protons).	-
8f	85	182–184	$C_{17}H_{18}N_4O_4S$ (ethanol)	54.54 54.30	4.81 4.60	14.97 14.70	8.55 8.30	– –	3040 (CH arom), 2917 (CH aliph),1677 (C=O),1630 (C=N).	1.30–1.50 (6H, m, $2CH_2$), 1.60–2.00 (4H, m, $2CH_2$), 2.30(3H, s, CH_3),3.46 (2H, s, CH_2), 7.40–8.10 (3H, m, aromatic protons).	-

Comp. No.	Yield (%)	M.P. (°C)	Molecular formula (Solvent of Crystallization)	Microanalyses-Calculated/ Found				(%) Br	IR (KBr) cm^{-1}	^{1}H-NMR (DMSO-d_6), δ (TMS)	^{13}C-NMR (DMSO-d_6), δ (TMS)
				C	H	N	S				
8g	83	116–118	$C_{20}H_{17}N_3O_2SBr$ (ethanol)	66.11 66.00	4.68 4.40	11.57 11.30	8.81 8.60	- -	3030 (CH arom), 2920 (CH aliph),1677 (C=O),1620 (C=N).	2.43 (2H, m, CH_2), 2.59 (2H, t, CH_2), 2.40(3H, s, CH_3), 3.60 (2H, s, CH_2),7.40–8.20 (8H, m, aromatic protons).	22.79, 27.84, 28.18, 119.67, 120.49, 125.83,132.06, 133.82, 142 25, 144.60, 146.66, 152.85,155.46, 155.79, 159.99, 174.67, 197.45.
8h	76	210–212	$C_{20}H_{16}N_3O_2SBr$ (ethanol)	54.42 54.20	3.62 3.40	9.52 9.30	7.25 7.10	17.91 17.80	3040 (CH arom), 2920 (CH aliph),1677 (C=O),1620 (C=N).	2.40 (2H, m, CH_2), 2.60 (2H, t, CH_2), 2.40 (3H, s, CH_3), 3.60 (2H, s, CH_2),7.40–8.30 (7H, m, aromatic protons).	-
8i	75	180–182	$C_{20}H_{16}N_4O_4SBr$ (ethanol)	58.82 58.60	3.92 3.70	13.72 13.50	7.84 7.60	- -	3030 (CH arom), 2917 (CH aliph), 1677 (C=O),1620 (C=N), 710 (C-S).	2.40 (2H, m, CH_2), 2.60 (2H, t, CH_2), 2.40 (3H, s, CH_3), 3.60 (2H, s, CH_2),7.10–8.30 (7H, m, aromatic protons).	-
8j	61	90–92	$C_{21}H_{19}N_3O_2S$ (ethanol)	66.84 66.80	5.03 5.00	11.14 11.10	8.48 8.30	- -	3040 (CH arom), 2917 (CH aliph), 1677 (C=O), 1630 (C=N), 700 (C-S).	2.30 (2H, m, CH_2), 2.40 (2H, t, CH_2), 2.60 (2H, s, CH_2), 2.40 (3H, s, CH_3),3.60 (2H, s, CH_2), 7.10–8.10 (7H, m, aromatic protons).	21.82, 22.79, 27.84, 28.18, 119.67, 120.49,125.88, 126.16, 126.42, 126.56, 126.92, 133.35,133.82, 142.25, 146.66, 152.85, 155.46, 155.79,159.99, 174.67, 197.45.
8k	62	228–230	$C_{21}H_{18}N_3O_2S$ (ethanol)	55.58 55.20	3.95 3.70	9.23 9.10	7.03 7.00	17.36 17.10	3030 (CH arom), 2917 (CH aliph),1677 (C=O),1620 (C=N), 700 (C-S).	2.30 (2H, m, CH_2), 2.40 (2H, t, CH_2), 2.60 (2H, s, CH_2), 2.40 (3H, s, CH_3),3.60 2H, s, CH_2), 7.10–8.10 (7H, m, aromatic protons).	-
8L	65	185–187	$C_{21}H_{18}N_4O_2S$ (ethanol)	59.71 59.60	4.26 4.10	13.27 13.10	7.58 7.40	- -	3050 (CH arom), 2917 (CH aliph),1677 (C=O),1620 (C=N), 710 (C-S).	2.30 (2H, m, CH_2), 2.40 (2H, t, CH_2), 2.60 (2H, s, CH_2), 2.40 (3H, s, CH_3),3.60 (2H, s, CH_2), 7.10–8.20 (7H, m, aromatic protons).	-

Comp. No.	Yield (%)	M.P. (°C)	Molecular formula (Solvent of Crystallization)	Microanalyses-Calculated/ Found				(%) Br	IR (KBr) cm^{-1}	^{1}H-NMR (DMSO-d_6), δ (TMS)	^{13}C-NMR (DMSO-d_6), δ (TMS)
				C	H	N	S				
8m	61	110–112	$C_{24}H_{17}N_3O_2S$ (ethanol)	70.07 70.00	4.13 4.00	10.21 10.10	7.78 7.70	- -	3050 (CH arom), 2917 (CH aliph), 1677 (C=O), 1620 (C=N), 710 (C-S).	2.40 (3H, m, CH_3), 2.90 (2H, s, CH_2), 7.10–8.30 (12H, m, aromatic protons).	27.70, 28.85, 119.67, 120.49, 125.83, 126.16, 126.42, 126.56, 126.92, 127.40, 133.35, 133.82, 142.25, 142.50, 144.60, 146.66, 146.54, 152.85, 155.46, 155.79, 155.99, 174.67, 197.45.
8n	60	160–162	$C_{24}H_{16}N_3O_2SBr$ (ethanol)	58.89 58.70	3.27 3.20	8.58 8.40	6.54 6.40	16.15 16.10	3030 (CH arom), 2917 (CH aliph), 1677 (C=O), 1620 (C=N), 710 (C-S).	2.40 (3H, m, CH_3), 2.90 (2H, s, CH_2), 7.10–8.20 (11H, m, aromatic protons).	-
8o	59	176–178	$C_{25}H_{19}N_3O_4S$ (ethanol)	63.15 63.00	3.50 3.40	12.28 12.10	7.01 7.00	- -	3030 (CH arom), 2917 (CH aliph), 1630 (C=O), 1630 (C=N), 710 (C-S).	2.40 (3H, m, CH_3), 2.90 (2H, S, CH_2), 7.10–8.20 (11H, m, aromatic protons).	-
8p	58	190–192	$C_{25}H_{19}N_3O_2S$ (ethanol)	70.58 70.50	4.47 4.40	9.88 9.80	7.52 7.49	- -	3040 (CH arom), 2917 (CH aliph), 1677 (C=O), 1630 (C=N), 710 (C-S).	2.85 (2H, m, CH_2), 2.90 (2H, S, CH_2), 2.40 (3H, S, CH_3), 7.10–8.20 (12H, m, aromatic protons).	26.70, 27.80, 28.85, 119.67, 120.67, 121.40, 125.83, 126.16, 126.42, 126.50, 126.92, 127.40, 133.35, 133.82, 142.25, 142.50, 144.60, 146.66, 146.84, 152.85, 155.46, 155.79, 159.99, 174.67, 197.45.
8q	58	254–256	$C_{25}H_{18}N_4O_4S$ (ethanol)	59.64 59.50	3.57 3.40	8.34 8.20	6.36 6.20	15.70 15.50	3040 (CH arom), 2917 (CH aliph), 1677 (C=O), 1620 (C=N), 710 (C-S).	2.40 (3H, m, CH_3), 2.80 (2H, s, CH_2), 7.40–8.10 (11H, m, aromatic protons).	
8r	55	176–178	$C_{25}H_{18}N_4O_4S$ (ethanol)	63.82 63.60	3.82 3.60	11.91 11.70	6.80 6.70	- -	3040 (CH arom), 2917 (CH aliph), 1677 (C=O), 1620 (C=N), 710 (C-S).	2.40 (3H, m, CH_3), 2.80 (2H, s, CH_2), 2.90 (2H, s, CH_2), 7.20–8.10 (11H, m, aromatic protons).	

TABLE II Physical data of spirothiazolopyrazoloquinazolinones *9a-r*

Comp. No.	*Yield (%)*	*M.P. (°C*	*Molecular formula (Solvent of Crystallization)*	*Microanalyses-Calculated/ Found (%)*					*IR (KBr) cm^{-1} δ (TMS)*	*^{1}H-NMR (DMSO-d_6). δ (TMS)*
				C	*H*	*N*	*S*	*Br*		
9a	66	90–92	$C_{16}H_{15}N_3O_2S$ (ethanol)	64.64 64.40	5.05 5.00	14.14 14.10	10.77 10.77	– –	3030 (CH arom), 2917 (CH aliph), 1677 (C=O), 1630 (C=N), 710 (C-S).	1.30–1.60 (4H, m, $2CH_2$), 1.70–1.90 (4H, m, $2CH_2$), 3.20 (2H, s, CH_2), 5.10 (1H, s, CH),7.20–8.10 (4H, m, aromatic protons).
9b	61	228–230	$C_{16}H_{14}N_3OSBr$ (ethanol)	51.20 51.10	3.73 3.50	11.20 11.10	8.53 8.40	21.06 21.00	3040 (CH arom), 2917 (CH aliph), 1677 (C=O), 1620 (C=N), 710 (C-S).	1.30–1.60 (4H, m, $2CH_2$), 1.70–1.90 (4H, m, $2CH_2$), 3.20 (2H, s, CH_2), 5.10 (1H, s, CH),7.20–8.10 (3H, m, aromatic protons).
9c	60	170–172	$C_{16}H_{14}N_3O_3S$ (ethanol)	56.14 56.10	4.09 4.00	16.37 16.20	9.35 9.15	– –	3050 (CH arom), 2917 (CH aliph), 1677 (C=O), 1630 (C=N), 700 (C-S).	1.30–1.60 (4H, m, $2CH_2$), 1.70–1.90 (4H, m, $2CH_2$), 3.20 (2H, s, CH_2), 5.10 (1H, s, CH),7.20–8.10 (3H, m, aromatic protons).
9d	63	95–97	$C_{17}H_{17}N_3OS$ (ethanol)	65.59 65.40	5.46 5.30	13.50 13.20	10.38 10.10	– –	3040 (CH arom), 2917 (CH aliph), 1677 (C=O), 1630 (C=N), 700 (C-S).	1.30–1.60 (6H, m, $3CH_2$), 1.60–2.00 (4H, m, $2CH_2$), 3.20 (2H, s, CH_2), 5.00 (1H, s, CH),7.30–8.20 (4H, m, aromatic protons).
9e	60	150–152	$C_{17}H_{16}N_3OS$ (ethanol)	52.44 52.30	4.11 4.10	10.79 10.60	8.22 8.10	20.30 20.20	3050 (CH arom), 2917 (CH aliph), 1677 (C=O), 1630 (C=N), 710 (C-S).	1.30–1.60 (6H, m, $3CH_2$), 1.60–2.00 (4H, m, $2CH_2$), 3.10 (2H, s, CH_2), 5.00 (1H, s, CH),7.20–8.10 (3H, m, aromatic protons).
9f	58	188–190	$C_{17}H_{16}N_4O_3S$ (ethanol)	57.30 57.10	4.49 4.30	15.73 15.60	8.98 8.70	– –	3050 (CH arom), 2917 (CH aliph), 1677 (C=O), 1620 (C=N).	1.30–1.60 (6H, m, $3CH_2$), 1.60–2.00 (4H, m, $2CH_2$), 3.20 (2H, s, CH_2), 5.10 (1H, s, CH),7.30–8.10 (3H, m, aromatic protons).

Comp. No.	*Yield (%)*	*M.P. (°C*	*Molecular formula (Solvent of Crystallization)*	*Microanalyses-Calculated/ Found (%)*					*IR (KBr) cm^{-1} δ (TMS)*	*^{1}H-NMR (DMSO-d_6), δ (TMS)*
				C	*H*	*N*	*S*	*Br*		
9g	55	85–87	$C_{20}H_{15}N_3OS$ (ethanol)	69.56 69.40	4.34 4.20	12.17 12.10	9.27 9.20	– –	3040 (CH arom), 2920 (CH aliph), 1680 (C=O), 1620 (C=N), 710 (C-S).	2.43 (2H, t, CH_2), 2.60 (2H, t, CH_2), 3.20 (2H, s, CH_2), 5.10 (1H, s, CH), 7.40–8.20 (8H, m,aromatic protons).
9h	53	180–182	$C_{20}H_{14}N_3OSBr$ (ethanol)	56.73 56.60	3.30 3.20	9.92 9.70	7.56 7.40	18.67 18.50	3040 (CH arom), 2930 (CH aliph), 1680 (C=O), 1620 (C=N), 710 (C-S).	2.40 (2H, s, CH_2), 2.60 (2H, t, CH_2), 3.10 (2H, s, CH_2), 5.00 (1H, s, CH), 7.40–8.10 (7H, m,aromatic protons).
9I	52	150–152	$C_{20}H_{14}N_4O_3S$ (ethanol)	61.53 61.40	3.58 3.40	14.35 14.20	8.20 8.10	– –	3050 (CH arom), 2940 (CH aliph), 1680 (C=O), 1630 (C=N), 710 (C-S).	2.40 (2H, s, CH_2), 2.60 (2H, t, CH_2), 3.10 (2H, S, CH_2), 5.00 (1H, S, CH), 7.40–8.10 (7H, m,aromatic protons).
9j	52	95–97	$C_{21}H_{17}N_3O_5$ (ethanol)	70.19 70.10	4.73 4.60	11.69 11.40	8.91 8.70	– –	3050 (CH arom), 2940 (CH aliph), 1680 (C=O), 1630 (C=N), 710 (C-S).	2.30 (2H, t, CH2), 2.40 (2H, t, CH2), 2.60 (2H, t, CH_2), 3.20 (2H, s, CH), 5.10(1H, s, CH), 7.40-8.10 (7H, m, aromatic protons).
9k	50	120–122	$C_{21}H_{16}N_3OSBr$ (ethanol)	57.66 57.60	3.66 3.60	9.61 9.40	7.32 7.20	18.07 18.00	3040 (CH arom), 2940 (CH aliph), 1680 (C=O), 1630 (C=N), 700 (C-S).	2.30 (2H, t, CH_2), 2.40 (2H, t, CH_2), 2.60 (2H, t, CH_2), 3.20 (2H, t, CH_2), 5.10 (1H, s, CH), 7.20-8.10 (7H, m, aromatic protons).
9L	50	170–172	$C_{21}H_{16}N_4O_3S$ (ethanol)	62.37 62.20	3.96 3.70	13.86 13.60	7.92 7.70	– –	3040 (CH arom), 2920 (CH aliph), 1680 (C=O), 1630 (C=N), 700 (C-S).	2.30 (2H, t, CH_2), 2.40 (2H, t, CH_2), 2.60 (2H, t, CH_2), 3.20 (2H, s, CH), 5.00 (1H, s, CH), 7.40-8.10 (7H, m, aromatic protons).
9m	55	200–202	$C_{24}H_{15}N_3OS$ (ethanol)	73.28 73.10	3.81 3.60	10.68 10.60	8.14 8.00	– –	3050 (CH arom), 2940 (CH aliph), 1680 (C=O), 1630 (C=N), 710 (C-S).	2.40 (2H, s, CH_2), 2.60 (2H, t, CH_2), 3.20 (2H, s, CH_2), 5.00 (1H, s, CH), 7.10–8.00 (7H, m,aromatic protons).

Comp. No.	Yield (%)	M.P. (°C	Molecular formula (Solvent of Crystallization)	Microanalyses-Calculated/ Found (%)					IR (KBr) cm^{-1} δ (TMS)	^{1}H-NMR (DMSO-d_6), δ (TMS)
				C	H	N	S	Br		
9n	53	180–182	$C_{24}H_{14}N_3OSBr$ (ethanol)	61.14 61.00	2.97 2.80	8.91 8.70	6.79 6.60	17.77 16.50	3040 (CH arom), 2940 (CH aliph), 1680 (C=O), 1630 (C=N), 710 (C-S).	2.30 (2H, s, CH_2), 5.00 (1H, s, CH), 7.20–8.10 (12H, m, aromatic protons).
9o	50	165–167	$C_{24}H_{14}NO_3S$ (ethanol)	65.75 65.50	3.19 3.10	12.78 12.50	7.30 7.20	– –	3050 (CH arom), 2940 (CH aliph), 1680 (C=O), 1630 (C=N), 700 (C-S).	2.30 (2H, s, CH_2), 5.00 (1H, s, CH), 7.40–8.10 (11H, m, aromatic protons).
9p	50	160–162	$C_{25}H_{17}N_3OS$ (ethanol)	73.71 73.50	4.17 4.10	10.31 10.10	7.86 7.50	– –	3040 (CH arom), 2950 (CH aliph), 1680 (C=O), 1630 (C=N), 700 (C-S).	2.70 (2H, s, CH_2), 5.00 (1H, s, CH), 7.40–8.18 (11H, m, aromatic protons).
9q	53	170–172	$C_{25}H_{16}N_3OSBr$ (ethanol)	61.85 61.70	3.29 3.20	8.65 8.50	6.59 6.40	16.28 16.10	3050 (CH arom), 2940 (CH aliph), 1680 (C=O), 1630 (C=N), 710 (C-S).	2.40 (2H, s, CH_2), 3.20 (2H, s, CH_2), 5.00 (1H, s, CH), 7.20–8.10 (12H, m, aromatic protons).
9r	50	220–222	$C_{25}H_{16}N_4O_3S$ (ethanol)	66.37 66.10	3.53 3.40	12.38 12.10	7.07 7.00	– –	3050 (CH arom), 2940 (CH aliph), 1685 (C=O), 710 (C-S).	2.70 (2H, s, CH_2), 3.20 (2H, s, CH_2), 5.00 (1H, s, CH), 7.40–8.20 (11H, m, aromatic protons).

EXPERIMENTAL

The time required for completion of each reaction was monitored by TLC. Melting points are uncorrected. The ^{1}H-NMR (δ ppm) spectra were measured on an EM-360 90-MHz spectrophotometer using TMS as internal standard. A Varian FT-80 spectrophotometer was used to obtain all ^{13}C-NMR (δ, ppm) spectra. IR (υ cm^{-1}) spectra were recorded on a Pye-Unicam SP 200-G spectrophotometer and the E I mass spectra were recorded on a Varian-MAT 311 A spectrometer. Elemental analyses were determined on a Perkin-Elmer 240 C microanalyser.

Preparation of 3-amino-2-methyl-3H-quinazolin-4-ones 4a-c

These compounds were prepared according to the reported method[35].

Preparation of 2-spiro-1,3-oxathiolan-5-ones 7a-f

These compounds also were prepared according to the reported method[36,37].

Synthesis of 3-[3'-(2'-spirothiazolidin-4'-one]quinazolin-4-one derivatives 8a-r, General Procedure

Each compound *4a-c* (0.01 mole) was fused with compound *7a-f* (0.01 mole) for ¼ hr, then 25 ml of absolute ethanol was added to the reaction mixture. The reaction mixture was refluxed for 6 hrs, cooled to room temperature whereby compounds *8a-r* precipitated and filtered off. They were dried and recrystallized from ethanol. Results are reported in Table I.

Synthesis of spirothiazolopyrazoloquinazolinones 9a-r

Method 1; General Procedure

Each compound *8a-r* (0.01 mole) was fused with anhydrous sodium acetate (0.01 mole) f½ hr, then cooled to room temperature, poured into cold water whereby compounds *9a-r* were precipitated. They were filtered off, dried and recrystallized from ethanol. The obtained results are listed in Table II.

Method 2; General Procedure

Each compound *8a-r* (0.01 mole) was dissolved in 25 ml of absolute ethanol, to this solution a few drops (½ ml) of 20% alcoholic sodium hydroxide solution was added. The reaction mixture was refluxed for 6 hrs. At the end of the refluxing time, the reaction mixture was cooled to room temperature, poured into 25 ml of 10% hydrochloric acid solution whereby compounds *9a-r* were precipitated, filtered off, dried and recrystallized from ethanol. results are shown in Table II.

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