SYNTHESIS OF SOME NEW SPIROTHIAZOLIDINONES INCORPORATED WITH QUINAZOLINE MOIETY

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In continuation to our previous work[1,2], together with the importance of the combination of spirothiazolidinones with quinazoline moieties, this work reports the synthesis of some new spirothiazolidinones incorporated with quinazoline moiety.

Our precursors, 2-spiro-1,3-oxathiolan-5-ones *IIIa* – *IIIe* were prepared according to our previously reported method[3], starting with appropriate cyclic ketones.

EXPERIMENTAL

Melting points are uncorrected. ^{1}H NMR spectra were measured on EM-360 90 MHz spectrophotometer and are given in δ ppm relative to TMS. IR spectra were recorded in KBr pellets on a Pye–Unicam SP 200-G spectrophotometer. UV absorbances were measured on a Perkin–Elmer 552 spectrophotometer. Elemental analyses were determined on a Perkin–Elmer 240 C microanalyzer.

Compounds *I* and *II* were prepared according to the reported method[4,5].

Synthesis of 2-Spiro-1,3-oxathiolan-5-ones *IIIa* – *IIIe*. General Procedure

A mixture of the cyclic ketone (0.1 mol), thioglycolic acid (0.1 mol) and *p*-toluenesulfonic acid (0.0001 mol) in dry benzene or toluene was refluxed until the calculated volume of liberated water was removed by a water separator. The reaction mixture was evaporated and the products were collected by filtration and crystallized from the proper solvent. The compounds were confirmed by elemental analyses and spectral data (Table I).

Synthesis of 2-Spirothiazolidin-3-(4′-aminophenyl or 4′-aminobiphenyl)-4-one Derivatives *IVa* – *IVe*, and *Va* – *Ve*. General Procedure

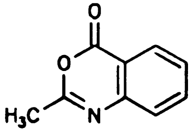
A mixture of 2-spiro-1,3-oxathiolan-5-one (*IIIa* – *IIIe*) (0.01 mol) and *p*-phenylenediamine or benzidine (0.01 mol) in 50 ml absolute ethanol was refluxed for 2 h on water bath. The reaction mixture was evaporated and the products were collected by filtration and crystallized from a proper solvent. The compounds were confirmed by elemental analyses and spectral data (Table II).

Synthesis of 2′-Spirothiazolidin-3′-[3″-(2″-methylquinazolin-4″-onyl)]-4′-one Derivatives *VIa* – *VIe*. General Procedure

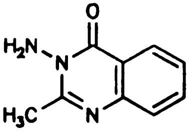
A mixture of 2-spiro-1,3-oxathiolan-5-one (*IIIa* – *IIIe*) (0.001 mol) and 3-amino-2-methylquinazolin-4-one (*II*) (0.001 mol) in 5 ml absolute ethanol was refluxed for 3 h on water bath. The reaction mixture was cooled to room temperature, the product was collected by filtration and crystallized from appropriate solvent. Identity of the compounds was established by elemental analyses and spectral data (Table III).

Synthesis of Spirothiazolidinones *VIIa* – *VIIe*. General Procedure

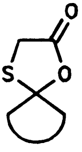
Compound *IVa* – *IVe* (0.01 mol) and *I* (0.01 mol) in 50 ml of absolute ethanol was refluxed for 3 h at 100 °C. Ethanol was removed by distillation under reduced pressure, the product was collected by filtration and crystallized from a proper solvent. The compounds were confirmed by elemental analyses and spectral data (Table IV).



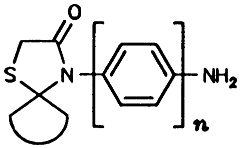
I



II

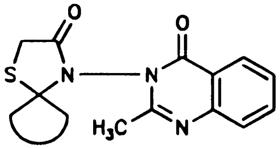


IIIa – *IIIe*

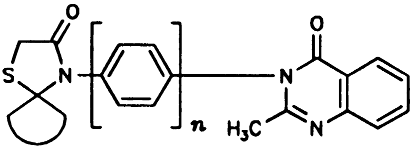


IVa–*IVe*, *n* = 1

Va–*Ve*, *n* = 2



VIa–*VIe*



VIIa–*VIIe*, *n* = 1

VIIIa–*VIIIe*, *n* = 2

In Formulae *III* – *VIII* the spirosystem is based on:

a, cyclopentanone; *b*, cyclohexanone; *c*, 1–tetralone; *d*, fluorenone; *e*, anthrone

TABLE I
Physical and spectral data for compounds *IIIa* – *IIIe*

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found			IR, cm^{-1}	^{1}H NMR
			% C	% H	% S		
IIIa	130 – 132[a] 80	$C_7H_{10}O_2S$ (158.2)	53.15 53.60	6.37 6.29	20.26 20.11	675, 1 265, 1 320, 1 710, 2 920	($(CD_3)_2SO$) 1.5 m, 4 H; 2.1 m, 4 H 3.8 s, 2 H
IIIb	142 – 144[a] 72	$C_8H_{12}O_2S$ (172.2)	55.80 55.71	7.02 6.98	18.62 18.51	700, 1 262, 1 320, 1 695, 2 930	($CDCl_3$) 1.8 m, 6 H; 2.1 m, 4 H; 3.8 s, 2 H
IIIc	124 – 126[a] 65	$C_{12}H_{12}O_2S$ (220.3)	65.51 65.70	5.49 5.30	14.56 14.30	710, 1 320, 1 700, 2 980 – 3 010	($(CD_3)_2SO$) 2.1 – 2.4 m, 2 H; 2.6 m, 2 H; 2.8 t, 2 H; 3.7 s, 2 H; 7 – 7.5 m, 4 H
IIId	192 – 194[a] 80	$C_{15}H_{10}O_2S$ (254.3)	70.93 70.30	3.96 3.60	12.60 12.95	700, 1 320, 1 700, 2 850, 3 030	($(CD_3)_2SO$) 3.7 s, 2 H; 7.1 – 8 m, 8 H
IIIe	220 – 222[b] 75	$C_{16}H_{12}O_2S$ (268.3)	71.63 71.90	4.51 4.35	11.95 11.85	710, 1 700, 2 830, 3 050	($(CD_3)_2SO$) 3.6 s, 2 H; 4.2 s, 2 H; 7.2 – 8.1 m, 8 H

Crystallized from [a] ethanol; [b] ethanol–water (2 : 1).

TABLE II
Physical and spectral data for compounds *IV* and *V*

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found % C	 % H	 % N	 % S	IR, cm^{-1}	^{1}H NMR
IVa	170 – 172[a] 90	$C_{13}H_{16}N_2OS$ (248.3)	62.88 62.65	6.49 6.25	11.28 11.21	12.90 12.75	710, 1 265, 1 325, 1 690, 2 920, 3 400 – 3 350	(CDCl$_3$) 1.3 – 1.6 m, 4 H; 1.7 – 1.9 m, 4 H; 3.7 s, 2 H; 6.7 broad, 2 H; 7 – 7.5 m, 4 H
IVb	200 – 202[b] 90	$C_{14}H_{18}N_2OS$ (262.4)	64.08 64.40	6.91 6.50	10.68 10.43	12.21 12.50	710, 1 690, 2 880, 3 050, 3 400 – 3 350	(CDCl$_3$) 1.3 – 1.5 m, 6 H; 1.6 – 2.0 m, 4 H; 3.7 s, 2 H; 6.5 broad 2 H; 7.0 – 7.5 m, 4 H
IVc	180 – 182[c] 85	$C_{18}H_{18}N_2OS$ (310.4)	69.65 69.50	5.85 5.50	9.03 8.89	10.33 10.10	700, 1 695, 2 885, 3 035, 3 350 – 3 400	((CD$_3$)$_2$SO) 2.1 –2.4 m, 2 H; 2.6 – 2.8 m, 4 H; 3.6 s, 2 H; 6.4 broad, 2 H; 7 – 7.8 m, 8 H
IVd	205 – 207[d] 82	$C_{21}H_{16}N_2OS$ (344.4)	73.24 73.60	4.68 4.35	8.13 8.50	9.30 9.00	700, 1 700, 2 890, 3 035, 3 350 – 3 400	((CD$_3$)$_2$SO) 3.6 s, 2 H; 6.4 broad, 2 H; 7 – 7.8 m, 12 H
IVe	240 – 242[d] 80	$C_{22}H_{18}N_2OS$ (358.5)	73.71 73.40	5.06 5.40	7.82 7.50	8.94 8.50	710, 1 695, 2 920, 3 050, 3 350 – 3 400	((CD$_3$)$_2$SO) 3.7 s, 2 H; 4.1 s, 2 H; 6.9 broad, 2 H; 7.0 – 7.5 m, 8 H; 7.9 – 8.1 m, 4 H

TABLE II
(*Continued*)

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found				IR, cm^{-1}	^{1}H NMR
			% C	% H	% N	% S		
Va	170 – 172^d	$C_{19}H_{20}N_2OS$	70.33	6.21	8.64	9.88	700, 1 700, 2 920, 3 050, 3 350 – 3 410	((CD$_3$)$_2$SO) 1.3 – 1.6 m, 4 H; 1.7 – 1.9 m, 4 H; 3.7 s, 2 H; 6.4 broad, 2 H; 7.0 – 7.8 m, 8 H
	90	(324.5)	70.60	6.00	8.40	9.95		
Vb	185 – 187^d	$C_{20}H_{22}N_2OS$	70.97	6.55	8.28	9.47	710, 1 695, 2 890, 3 030, 3 355 – 3 400	((CD$_3$)$_2$SO) 1.3 – 1.5 m, 6 H; 1.6 – 2.0 m, 4 H; 3.7 s, 2 H; 6.5 broad, 2 H; 7.0 – 7.8 m, 8 H
	87	(338.5)	70.80	6.70	8.15	9.28		
Vc	120 – 122^d	$C_{24}H_{22}N_2OS$	74.58	5.74	7.25	8.29	710, 1 700, 2 880, 3 030, 3 350 – 3 400	((CD$_3$)$_2$SO) 2.1 – 2.4 m, 2 H; 2.6 – 2.8 m, 4 H; 3.6 s, 2 H; 6.4 broad 2 H; 7.0 – 7.8 m, 12 H
	80	(386.5)	74.90	5.40	7.50	8.00		
Vd	165 – 167^d	$C_{27}H_{20}N_2OS$	77.12	4.79	6.66	7.63	700, 1 695, 2 925, 3 030, 3 350 – 3 400	((CD$_3$)$_2$SO) 3.6 s, 2 H; 6.4 broad, 2 H; 7.0 – 7.5 m, 8 H; 7.9 – 8.1 m, 8 H
	85	(420.5)	77.60	4.50	6.36	7.80		
Ve	196 – 198^d	$C_{28}H_{22}N_2OS$	77.38	5.10	6.45	7.38	700, 1 695, 2 900, 3 050, 3 350 – 3 400	((CD$_3$)$_2$SO) 3.7 s, 2 H; 4.1 s, 2 H; 6.4 broad, 2 H; 7.0 – 7.8 m, 8 H; 7.9 – 8.2 m, 8 H
	80	(434.6)	77.10	5.20	6.21	7.11		

Crystallized from ^{a} ethanol–water (2 : 1); ^{b} ethanol–water (3 : 1); ^{c} water; ^{d} ethanol.

TABLE III
Physical and spectral data of compounds *VI*

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found % C	 % H	 % N	 % S	IR, cm^{-1}	^{1}H NMR
VIa	162 – 164[a] 82	$C_{16}H_{17}N_3O_2S$ (316.8)	60.66 60.63	5.41 5.15	13.27 13.70	10.12 10.00	710, 1 265, 1 320, 1 700, 2 925, 3 030	($CDCl_3$) 1.3 – 1.6 m, 4 H; 1.7 – 1.9 m, 4 H; 2.8 s, 3 H; 3.6 s, 2 H; 7.9 – 8.2 m, 4 H
VIb	173 – 175[a] 80	$C_{17}H_{19}N_3O_2S$ (329.4)	62.00 61.70	5.81 5.45	12.76 12.38	9.73 9.90	700, 1 265, 1 320, 1 710, 2 950, 3 050	($(CD_3)_2SO$) 1.3 – 1.5 m, 6 H; 1.6 – 2.0 m, 4 H; 2.8 s, 3 H; 3.6 s, 2 H; 7.9 – 8.2 m, 4 H
VIc	250 – 252[a] 82	$C_{21}H_{19}N_3O_2S$ (377.5)	66.82 66.90	5.07 5.30	11.14 11.00	8.48 8.60	710, 1 265, 1 320, 1 710, 2 900, 3 030	($(CD_3)_2SO$) 2.1 – 2.9 m, 2 H; 2.6 – 2.8 m, 4 H; 2.8 s, 3 H; 3.6 s, 2 H; 7.0 – 7.5 m, 4 H; 7.9 – 8.2 m, 4 H
VId	150 – 152[b] 75	$C_{24}H_{17}N_3O_2S$ (411.5)	70.05 70.50	4.16 4.00	10.21 10.40	7.79 7.50	1 260, 1 325, 1 700, 2 925, 3 050	(CF_3COOH) 2.8 s, 3 H; 3.6 s, 2 H; 7 – 7.5 m, 8 H; 7.9 – 8.2 m, 4 H
VIe	275 – 277[a] 70	$C_{25}H_{19}N_3O_2S$ (425.7)	70.57 70.70	4.50 4.20	9.88 9.50	7.54 7.20	1 260, 1 325, 1 700, 2 895, 3 030	(CF_3COOH) 2.8 s, 3 H; 3.6 s, 2 H; 4.1 s, 2 H; 7 – 7.5 m, 8 H; 7.9 – 8.2 m, 4 H

Crystallized from [a] ethanol; [b] ethanol–water (5 : 1).

TABLE IV
Physical and spectral data of compounds *VIIa* – *VIIe* and *VIIIa* – *VIIIe*

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found				IR, cm^{-1}	^{1}H NMR
			% C	% H	% N	% S		
VIIa	360^a 70	$C_{22}H_{21}N_3O_2S$ (391.5)	67.50 67.30	5.41 5.10	10.74 10.50	8.19 8.00	710, 1 700, 2 950, 3 050	(CF_3COOH) 1.3 – 1.6 m, 4 H; 1.7 – 1.9 m, 4 H; 2.8 s, 3 H; 3.6 s, 2 H; 7 – 7.4 m, 4 H; 7.9 – 8.2 m, 4 H
VIIb	310 – 312^a 70	$C_{23}H_{23}N_3O_2S$ (405.5)	68.13 68.50	5.72 5.70	10.37 10.60	7.90 7.60	710, 1 700, 2 925, 3 030	(CF_3COOH) 1.3 – 1.5 m, 6 H; 1.6 – 2.0 m, 4 H; 2.8 s, 3 H; 3.4 s, 2 H; 7.0 – 7.5 m, 4 H; 7.9 – 8.2 m, 4 H
VIIc	210 – 212^a 68	$C_{27}H_{23}N_3O_2S$ (453.6)	71.50 71.30	5.11 5.30	9.27 9.70	7.07 7.00	710, 1 700, 2 925, 3 030	(CF_3COOH) 2.1 – 2.4 m, 2 H; 2.6 – 2.8 m, 4 H; 2.9 s, 3 H; 3.7 s, 2 H; 7. – 7.5 m, 8 H; 7.9 – 8.2 m, 4 H
VIId	270 – 272^a 65	$C_{30}H_{21}N_3O_2S$ (487.6)	73.90 73.60	4.34 4.10	8.62 8.35	6.58 6.25	700, 1 700, 2 890, 3 050	($(CD_3)_2SO$) 2.8 s, 3 H; 3.6 s, 2 H; 6.9 – 7.5 m, 12 H; 7.9 – 8.2 m, 4 H
VIIe	275 – 277^a 70	$C_{31}H_{23}N_3O_2S$ (501.6)	74.23 74.60	4.62 4.20	8.38 8.60	6.39 6.15	700, 1 700, 2 890, 3 040	($(CD_3)_2SO$) 2.8 s, 3 H; 3.7 s, 2 H; 4.10 s, 2 H; 7.0 – 7.8 m, 12 H 7.9 – 8.2 m, 4 H

TABLE IV
(*Continued*)

Compound	M. p., °C Yield, %	Formula (M. w.)	Calculated/Found % C	 % H	 % N	 % S	IR, cm^{-1}	^{1}H NMR
VIIIa	200 – 202^{b} 75	$C_{28}H_{25}N_3O_2S$ (467.6)	71.92 71.60	5.39 5.00	8.99 8.70	6.85 6.50	700, 1 700, 2 925, 3 030	($(CD_3)_2SO$) 1.3 – 1.6 m, 4 H; 1.7 – 1.9 m, 4 H; 2.8 s, 3 H; 3.7 s, 2 H; 6.9 – 7.6 m, 8 H; 7.9 – 8.2 m, 4 H
VIIIb	280 – 282^{b} 70	$C_{29}H_{27}N_3O_2S$ (481.3)	72.37 72.70	5.66 5.30	8.73 8.90	6.66 6.30	700, 1 700, 2 920, 3 035	($(CD_3)_2SO$) 1.3 – 1.5 m, 6 H; 1.6 – 2.0 m, 4 H; 2.8 s, 3 H; 3.4 s, 2 H; 6.8 – 7.6 m, 8 H; 7.9 – 8.2 m, 4 H
VIIIc	250 – 252^{c} 75	$C_{33}H_{27}N_3O_2S$ (529.7)	74.83 74.50	5.14 5.20	7.93 7.70	6.05 6.20	710, 1 700, 2 920, 3 050	(CF_3COOH) 2.1 – 2.4 m, 2 H; 2.6 – 2.8 m, 4 H; 2.8 s, 3 H; 3.3 s, 2 H; 6.8 – 8.2 m, 4 H
VIIId	182 – 184^{b} 72	$C_{36}H_{25}N_3O_2S$ (563.7)	76.71 76.50	4.47 4.25	7.46 7.30	5.68 5.50	710, 1 710, 2 920, 3 035	(CF_3COOH) 2.8 s, 3 H; 3.7 s, 2 H; 6.9 – 8.2 m, 16 H; 8.1 – 8.3 m, 4 H
VIIIe	163 – 165^{b}	$C_{37}H_{27}N_3O_2S$ (577.7)	76.93 76.80	4.71 4.30	7.27 7.50	5.55 5.30	700, 1 700, 2 900, 3 050	(CF_3COOH) 2.8 s, 3 H; 3.6 s, 2 H; 4.1 s, 2 H; 6.8 – 8.0 m, 16 H; 8.1 – 8.3 m, 4 H

Crystallized from ^{a} ethanol–water; ^{b} ethanol; ^{c} dioxane–water (1 : 1).

Synthesis of Spirothiazolidinones *VIIIa* – *VIIIe*. General Procedure

Compound *Va* – *Ve* (0.01 mol) and *I* (0.01 mol) in 50 ml of absolute ethanol was refluxed for 2 h on water bath. The reaction mixture was concentrated under reduced pressure, the product was collected by filtration and crystallized from proper solvent. The identity of the compounds was confirmed by elemental analyses and spectral data (Table IV).

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