SPIROHETEROCYCLIC SYSTEMS: NEW *N*-SUBSTITUTED SPIROHETEROCYCLIC NAPHTHENES

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Spiro and sulfonamide derivatives have been found to be biologically active[1 – 5]. In view of this importance, we report the synthesis of some new spiroheterocyclic naphthenes *IV – VI*.

EXPERIMENTAL

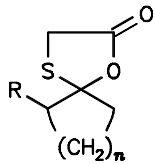
All melting points are uncorrected. IR spectra were recorded in KBr on Pye–Unicam SP-200 G and Perkin–Elmer 599 B spectrophotometers. ^{1}H NMR spectra were recorded on a Varian Em-390 MHz spectrometer in $(CD_3)_2SO$ using TMS as internal standard. Analytical data were obtained using a Perkin–Elmer 240 E microanalyzer.

Synthesis of 1-Oxa-4-thiaspiro[4,4]nonan-2-one (*I*), 1-Oxa-4-thiaspiro[4,5]decan-2-one (*II*) and 1-Oxa-5-methyl-4-thiaspiro[4,5]decan-2-one (*III*)

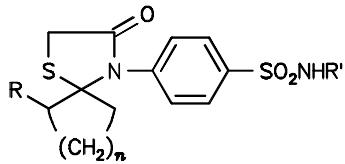
A mixture of cyclopentanone, cyclohexanone or 2-methylcyclohexanone (0.1 mol), mercapto acetic acid (0.1 mol) and *p*-toluene sulfonic acid (150 mg) in dry benzene (300 ml) was refluxed for 5 h on water bath, whereby the liberated water was removed by a water separator, benzene was removed under reduced pressure using a rotary evaporator, the product was collected by filtration and recrystallized from water. Physical properties and microanalytical data are depicted in Table I.

Synthesis of Compounds *IV – VI*

General procedure: A mixture of compound *I*, *II* or *III* and the selected sulfonamide derivative (0.01 mol) in pyridine (10 ml) was heated under reflux for 2 h. A syrupy mass obtained on distilling off the excess of pyridine which was poured into crushed ice containing 5 ml concentrated HCl. The separated solid was filtered, washed with cold water and recrystallized from ethanol. Physical and analytical data are listed in Table I, spectral data for some selected compounds are given in Table II.

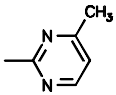
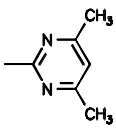


I – III



IV – VI

In formulae *I – VI* : *I*, n = 5, R = H
II, n = 6, R = H
III, n = 6, R = CH_3
IV, n = 5, R = H
V, n = 6, R = H
VI, n = 6, R = CH_3

In formulae *IV – VI* : *a*, R' = H
b, R' = $-COCH_3$
c, R' = $-C(=NH)-NH_2$
d, R' = 
e, R' = 
f, R' = 
g, R' = 
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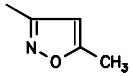
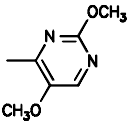
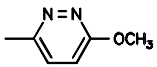
i, R' = 
j, R' = 
k, R' = 

TABLE I
Physical and analytical data of all synthesized compounds

Compound	M.p., °C Yield, %	Formula (M.w.)	Calculated/Found			
			% C	% H	% N	% S
I	134	$C_7H_{10}O_2S$	53.14	6.37	–	20.27
	89	(158.2)	53.05	6.46		20.35
II	146	$C_8H_{12}O_2S$	55.79	7.02	–	18.62
	87	(172.3)	55.68	6.93		18.71
III	155	$C_9H_{14}O_2S$	58.03	7.58	–	17.21
	84	(186.3)	58.12	7.66		17.16
IVa	165	$C_{13}H_{16}N_2O_3S_2$	49.96	5.33	8.97	15.36
	77	(312.5)	50.06	5.41	9.03	15.28
Va	100	$C_{14}H_{18}N_2O_3S_2$	51.51	5.55	8.58	19.64
	78	(326.5)	51.43	5.62	8.66	19.56
VIa	165	$C_{15}H_{20}N_2O_3S_2$	52.92	5.92	8.23	18.84
	73	(340.5)	53.02	6.01	8.32	18.96
IVb	220	$C_{15}H_{18}N_2O_4S_2$	53.21	5.37	14.18	18.96
	87	(354.4)	53.29	5.41	14.23	19.04
Vb	175	$C_{16}H_{20}N_2O_4S_2$	52.16	5.47	7.37	17.40
	89	(368.5)	52.24	5.53	7.26	17.51
VIb	205	$C_{17}H_{22}N_2O_4S_2$	53.38	5.79	7.32	16.77
	83	(382.5)	53.47	5.88	7.25	16.68
IVc	135	$C_{14}H_{18}N_4O_3S_2$	47.44	5.12	15.81	18.09
	82	(354.5)	47.51	5.20	15.90	18.00
Vc	140	$C_{15}H_{20}N_4O_3S_2$	48.89	5.47	13.03	17.40
	87	(368.5)	48.96	5.55	13.10	17.51
VIc	133	$C_{16}H_{22}N_4O_3S_2$	50.24	5.79	14.65	16.76
	78	(382.5)	50.33	5.83	14.72	16.68

TABLE I
(*Continued*)

Compound	M.p., °C Yield, %	Formula (M.w.)	Calculated/Found			
			% C	% H	% N	% S
IVd	178	$C_{18}H_{19}N_3O_3S_2$	55.51	4.92	10.79	16.46
	75	(389.5)	55.63	5.01	10.88	16.38
Vd	220	$C_{19}H_{21}N_3O_3S_2$	55.45	5.14	10.21	15.58
	79	(411.6)	55.56	5.23	10.30	15.62
VId	195	$C_{20}H_{23}N_3O_3S_2$	56.32	5.43	9.85	15.03
	72	(426.5)	56.44	5.52	9.93	15.12
IVe	227	$C_{17}H_{18}N_4O_3S_2$	52.29	4.65	14.35	16.42
	86	(390.5)	52.33	4.72	14.46	16.51
Ve	238	$C_{18}H_{20}N_4O_3S_2$	53.45	4.98	13.85	15.85
	84	(404.5)	53.54	5.03	13.96	15.93
VIe	248	$C_{19}H_{22}N_4O_3S_2$	54.53	5.29	13.39	15.32
	80	(418.5)	54.62	5.33	13.44	15.41
IVf	235	$C_{18}H_{20}N_4O_3S_2$	50.34	4.98	13.85	15.85
	78	(404.5)	50.41	5.06	13.76	15.93
Vf	220	$C_{19}H_{22}N_4O_3S_2$	54.53	5.29	13.39	15.32
	82	(418.5)	54.66	5.34	13.44	15.41
VIf	215	$C_{20}H_{24}N_4O_3S_2$	55.52	5.59	12.97	14.82
	72	(432.6)	55.61	6.06	13.06	14.91
IVg	190	$C_{19}H_{22}N_4O_3S_2$	54.53	5.29	13.39	15.32
	81	(418.5)	54.61	5.33	13.44	15.42
Vg	225	$C_{20}H_{24}N_4O_3S_2$	55.54	5.59	12.95	14.83
	84	(432.6)	55.62	6.08	13.04	14.91
VIg	202	$C_{21}H_{26}N_4O_3S_2$	56.47	5.86	12.57	14.36
	78	(446.7)	56.58	5.93	12.65	14.44

TABLE I
(*Continued*)

Compound	M.p., °C Yield, %	Formula (M.w.)	Calculated/Found			
			% C	% H	% N	% S
IVh	185	$C_{16}H_{17}N_3O_3S_3$	48.59	4.33	10.62	24.32
	89	(395.5)	48.71	4.40	10.69	24.42
Vh	208	$C_{17}H_{19}N_3O_3S_3$	49.86	4.68	10.26	23.48
	92	(409.5)	49.99	4.76	10.35	23.56
VIh	190	$C_{18}H_{21}N_3O_3S_3$	51.03	4.99	10.08	16.33
	87	(423.7)	51.15	5.09	10.18	16.41
IVi	155	$C_{17}H_{19}N_3O_4S_2$	51.89	4.87	10.68	16.29
	81	(393.5)	51.97	4.96	10.77	16.35
Vi	160	$C_{18}H_{21}N_3O_4S_2$	53.05	5.19	10.31	15.74
	83	(407.5)	53.19	5.24	10.41	15.81
VIi	150	$C_{19}H_{23}N_3O_4S_2$	54.13	5.49	9.97	15.23
	77	(421.6)	54.26	5.57	10.10	15.32
IVj	145	$C_{19}H_{22}N_4O_5S_2$	50.65	4.92	12.44	14.23
	79	(450.5)	50.77	5.03	12.54	14.32
Vj	170	$C_{20}H_{24}N_4O_5S_2$	51.71	5.20	12.27	12.06
	81	(464.6)	51.89	5.29	12.33	12.16
VIj	200	$C_{21}H_{26}N_4O_5S_2$	52.71	5.87	11.71	13.40
	74	(478.6)	52.84	5.78	11.82	13.51
IVk	168	$C_{18}H_{20}N_4O_4S_2$	51.40	4.80	13.32	15.26
	81	(420.6)	51.52	4.89	13.41	15.33
Vk	186	$C_{19}H_{22}N_4O_4S_2$	54.50	5.30	13.41	15.33
	86	(418.7)	54.63	5.40	13.48	15.28
VIk	175	$C_{20}H_{24}N_4O_4S_2$	55.51	5.59	12.97	14.83
	78	(432.7)	55.61	5.63	13.05	14.91

TABLE II
IR and ^{1}H NMR spectra of some representative compounds

Compound	IR, cm^{-1}	^{1}H NMR, δ ppm
IVb	720 (C–S), 2 900 (C–H aliph.), 3 202 (C–H arom.), 3 210 (NH), 1 710 (C=O), 1 345 (SO_2 asym), 1 155 (SO_2 sym)	1.3 – 1.9 m (4 H), 4.0 s (2 H), 2.6 s (3 H), 7.0 – 7.8 m (4 H, arom.), 9.3 s (1 H, NH)
IVd	715 (C–S), 2 900 (C–H aliph.), 3 205 (C–H arom.), 3 210 (NH), 1 700 (C=O), 1 340 (SO_2 asym), 1 160 (SO_2 sym)	1.4 – 1.8 m (4 H), 4.1 s (2 H), 6.8 – 7.7 m (8 H, arom.), 9.5 s (1 H, NH)
Ve	725 (C–S), 2 900 (C–H aliph.), 3 205 (C–H arom.), 3 200 (NH), 1 710 (C=O), 1 350 (SO_2 asym), 1 160 (SO_2 sym)	1.3 – 1.7 m (4 H), 4.1 s (2 H), 7.0 – 7.8 m (7 H, arom.), 9.4 s (1 H, NH)
Vf	720 (C–S), 2 900 (C–H aliph.), 3 205 (C–H arom.), 3 220 (NH), 1 710 (C=O), 1 355 (SO_2 asym), 1 160 (SO_2 sym)	1.4 – 1.9 m (5 H), 4.1 s (2 H), 2.7 s (4 H), 7.0 – 7.9 m (6 H, arom.), 9.3 s (1 H, NH)
Vg	720 (C–S), 2 900 (C–H aliph.), 3 205 (C–H arom.), 3 230 (NH), 1 710 (C=O), 1 355 (SO_2 asym), 1 160 (SO_2 sym)	1.3 – 1.8 m (5 H), 4.0 s (2 H), 2.5 s (6 H), 7.1 – 7.8 m (5 H, arom.), 9.2 s (1 H, NH)
Vh	715 (C–S), 2 900 (C–H aliph.), 3 205 (C–H arom.), 3 220 (NH), 1 700 (C=O), 1 355 (SO_2 asym), 1 160 (SO_2 sym)	1.4 – 1.7 m (5 H), 4.0 s (2 H), 7.0 – 7.7 m (6 H, arom.), 9.2 s (1 H, NH)
Vj	715 (C–S), 2 900 (C–H aliph.), 3 205 (C–H arom.), 3 210 (NH), 1 700 (C=O), 1 360 (SO_2 asym), 1 155 (SO_2 sym)	1.4 – 1.8 m (5 H), 4.1 s (2 H), 7.1 – 7.9 m (5 H arom.), 9.1 s (1 H, NH), 3.85 s (6 H, OCH_3)
Vk	725 (C–S), 2 900 (C–H aliph.), 3 205 (C–H arom.), 3 230 (NH), 1 700 (C=O), 1 360 (SO_2 asym), 1 160 (SO_2 sym)	1.4 – 1.8 m (5 H), 4.1 s (2 H), 7.0 – 7.8 m (6 H arom.), 9.1 s (1 H, NH), 3.76 s (3 H, CH_3)
Vi	725 (C–S), 2 900 (C–H aliph.), 3 202 (C–H arom.), 3 230 (NH), 1 710 (C=O), 1 360 (SO_2 asym), 1 160 (SO_2 sym)	1.3 – 1.8 m (5 H), 4.1 s (2 H), 7.1 – 7.7 m (6 H, arom.), 9.2 s (1 H, NH), 3.8 s (3 H, CH_3)
VId	730 (C–S), 2 900 (C–H aliph.), 3 202 (C–H arom.), 3 220 (NH), 1 700 (C=O), 1 355 (SO_2 asym), 1 155 (SO_2 sym)	1.4 – 1.9 m (4 H), 4.1 s (2 H), 2.7 s (3 H, CH_3), 7.3 – 7.9 m (8 H, arom.), 9.5 s (1 H, NH)
VIe	730 (C–S), 2 900 (C–H aliph.), 3 202 (C–H arom.), 3 220 (NH), 1 710 (C=O), 1 360 (SO_2 asym), 1 155 (SO_2 sym)	1.4 – 1.9 m (4 H), 4.1 s (2 H), 2.8 s (3 H, CH_3), 7.2 – 7.8 m (7 H arom.), 9.3 s (1 H, NH)

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