Kurzmitteilungen:

Spiroheterocyclic Systems, I:

Spiroheterocycles Related to 1-Oxa-4-thiaspiro[4,4]nonan-2-one and 1-Oxa-4-thiospiro[4,5]decan-2-one

Spiroheterocyclische Systeme, 1. Mitt.: Mit 1-Oxa-4-thiaspiro[4,4]nonan-2-on und 1-Oxa-4-thiaspiro[4,5]decan-2-on verwandte Spiroheterocyclen

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As continuation to our work[1-4], we report herein the synthesis of spirothiazolopyrazoles, spirothiazoloisoxazoles, spirothiazolopyrimidinones, and spirothiazolothiopyrimidinones: Reaction of thioglycolic acid with cyclopentanone or cyclohexanone afforded 1-oxa-4-thiaspiro[4,4]nonan-2-one (**1**) or 1-oxa-4-thiaspiro[4,5]decan-2-one (**2**). Reaction of compounds **1** or **2** with *prim.* alkyl or arylamines in absol. EtOH is very smooth at room temp. or at reflux temp. giving 1-thia-4-(alkyl)arylazaspiro[4,4]nona-3-ones **3a-d** or 1-thia-4-(alkyl)arylazaspiro[4,5]decan-3-ones **4a-d** in 80-95% yields (Scheme 1 and Table 1). Reaction of **3a** or **4a** with aromatic aldehydes yields the corresponding 2-arylidene-1-thia-4-benzylazaspiro[4,4]nonan-3-ones **5a-d** or 2-arylidene-1-thia-4-benzylazaspiro[4,5]decan-3-ones **6a-d** (Table 1, Scheme 1).

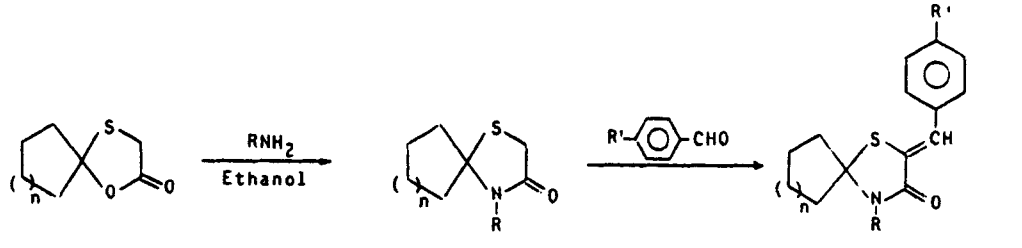
1-Thia-2-(4-nitrobenzylidene)-4-benzylazaspiro[4,4]-nonan-3-one (**5a**) or 1-thia-2-(4-nitrobenzylidene)-4-benzylazaspiro[4,5]-decan-3-one (**6a**) were reacted with hydrazine sulfate, hydroxylamine · HCl, phenyl hydrazine, urea, and thiourea in absol. EtOH and dry pyridine to afford the corresponding spirothiazolopyrazolines **7a,b**, spirothiazoloisoxazolines **8a,b**, spirothiazolophenylpyrazolines **9a,b**, spirothiazolopyrimidinones **10a,b** and spirothiazolothiopyrimidinones **11a,b** (Scheme 2, Table 1).

Experimental Part

Reactions were monitored by TLC.- Melting points: Open glass capillaries; uncorrected.- IR spectra: Pye-Unicam SP 200-G.- ^{1}H-NMR spectra: EM 360 90-MHz spectrophotometer. Elemental analyses: Perkin-Elmer 240 C microanalyser.

1-Oxa-4-thiaspiro[4,4]nonan-2-one (**1**) *and/or 1-oxa-4-thiaspiro[4,5]-decan-2-one* (**2**)

A mixture of cyclopentanone or cyclohexanone (0.1 mole), thioglycolic acid (0.1 mole) and *p*-toluene sulfonic acid (200 mg) in dry benzene (300 ml) was refluxed for 5 h whereby the liberated water was removed by a water separator. The mixture was cooled to room temp., benzene was removed under vac. and the oily residue was left at room temp. for one week to give a solid. The product was treated with Et_2O to form a crystalline compound. Data: Table 1.



1, n=1
2, n=2

3a-d, n=1
4a-d, n=2

3,4	R
a	Bz
b	Ph
c	Me
d	tBu

5a-d, n=1
6a-d, n=2

5,6	R	R'
a	Bz	NO_2
b	Bz	Cl
c	Bz	OCH_3
d	Bz	H

Scheme 1

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Table 1: Physical data of 1-11a,b

Compd. No.	Molecular Formula (M.W)/Solvent	m.p. °C	Yield %	Micro Analyses % Calcd / Found C	H	N	S	IR(KBr)cm^{-1}	^{1}H NMR(Solvent) δ(TMS)
1	$C_7H_{10}O_2S$ (158.22) (water)	130-2	90	53.16 53.11	6.32 6.29	-	20.25 20.11	675(C-S),1265,1320 (C-O),1710(C=O), 2920(C-H aliph.).	DMSO-d_6 1.3-1.8(4H,m),2.0-2.2 (4H,m),3.8(2H,s).
2	$C_8H_{12}O_2S$ (172.25) (water)	142-4	95	55.81 55.71	6.97 6.88	-	18.60 18.51	700(C-S),1265,1320 (C-O),1695(C=O), 2930(C-H aliph.).	DMSO-d_6 1.7-1.9(6H,m),2.0-2.2 (4H,m),3.9(2H,s).
3a	$C_{14}H_{17}ONS$ (247.36) (ethanol)	160-2	95	68.01 68.00	6.88 6.81	5.66 5.61	12.95 12.81	710(C-S),1685(C=O), 2920(C-H aliph.), 3050(C-H arom.),	DMSO-d_6 1.8(4H,m),2.2(4H,m),3.7 (2H,s),4.0(2H,s),7.0-7.5 (5H,m).
3b	$C_{13}H_{15}ONS$ (233.34) (ethanol)	85-7	85	66.95 66.81	6.43 6.31	6.00 5.89	13.73 13.61	700(C-S),1690(C=O), 2920(C-H aliph.), 3020(C-H arom.).	Acetone d_6 1.3-1.8(4H,m),2.2 (4H,m),3.9(2H,s),7.0-7.5 (5H,m).
3c	$C_8H_{13}ONS$ (171.26) (ethanol)	90-2	85	56.14 56.00	7.60 7.51	8.18 8.11	18.71 18.61	675(C-S),1695(C=O), 2890(C-H aliph.).	DMSO-d_6 1.3-1.8(4H,m),2.0-2.5 (4H,m),3.5(3H,s),3.9(2H,s).
3d	$C_{11}H_{19}ONS$ (213.40) (ethanol)	115-7	80	61.97 61.81	8.92 8.79	6.57 6.42	15.02 15.00	700(C-S),1690(C=O) 2880(C-H aliph.)	Acetone d_6 1.3-1.8(4H,m), 2.2-3.7(13H, m), 3.9(2H,s).
4a	$C_{15}H_{19}ONS$ (261.38) (ethanol)	115-7	80	68.96 68.81	7.27 7.11	5.36 5.22	12.26 12.11	675(C-S),1695(C=O), 2825(C-H aliph.), 3020(CH arom.).	DMSO-d_6 1.6-1.9(6H,m),2.0-2.4 (4H,m),3.7(2H,s),3.9(2H,s), 7.0-7.5.
4b	$C_{14}H_{17}ONS$ (247.36) (methanol)	105-7	85	68.01 68.00	6.88 6.71	5.66 5.51	12.95 12.81	710(C-S),1690(C=O), 2800(C-H aliph.), 3035(C-H arom.).	Acetone d_6 1.4-1.85(6H,m), 2-2.4(4H,m),3.9(2H,s),7.0-7.5 (5H,m).
4c	$C_9H_{15}ONS$ (185.29) (methanol)	120-2	82	58.37 58.12	8.10 8.00	7.56 7.49	17.29 17.11	710(C-S),1680(C=O), 2880(C-H aliph.).	DMSO-d_6 1.7-1.85(6H,m),2.0-2.4 (4H,m),3.4(3H,s),3.9(2H,s).
4d	$C_{12}H_{21}ONS$ (227.37) (ethanol)	127-9	88	63.43 63.32	9.25 9.17	6.16 6.09	14.09 14.00	700(C-S),1695(C=O), 2890(C-H alip.).	(CF_3CO_2H),1.5-2(6H,m),2.0-3.7 (13H,m),3.9(2H,s).
5a	$C_{21}H_{20}O_3N_2S$ (380.46) (water/ethanol) 2:1	110-12 (decomp.)	90	66.31 66.21	5.26 5.16	7.36 7.26	8.42 8.41	700(C-S),1690(C=O), 2880(C-H aliph.), 3080(C-H arom.).	DMSO-d_6 1.3-2.2(4H,m),3.7(2H,s), 6.9(1H,s),7.0-7.8(9H,m).
5b	$C_{21}H_{20}ONSCl$ (369.91) (ethanol/water) 1:1	145-7 (decomp.)	78	68.29 68.00	5.42 5.31	3.79 3.61	8.67 8.57	700(C-S),1695(C=O), 2890(C-H aliph.), 3040(C-H arom.).	Acetone d_6 1.5-1.8(4H,m),2.2 (4H,m),3.7(2H,s),6.9(1H,s), 7.0-7.9-9H,m).
5c	$C_{22}H_{23}O_2NS$ (365.49) (ether)	140-2 (decomp.)	85	72.32 (71.29)	6.30 (6.21)	3.83 (3.71)	8.76 (8.61)	710(C-S),1685(C=O), 2880(C-H aliph.), 3020(C-H arom.).	DMSO-d_6 1.4-1.8(4H,m),2.0-2.4 (4H,m),3.3(3H,s),3.7(2H,s), 6.9(1H,s),7.0-7.9(9H,m).
5d	$C_{21}H_{21}NOS$ (335.47) (ether)	135-7 (decomp.)	80	75.22 75.11	6.26 6.19	4.17 4.11	9.55 9.41	700(C-S),1680(C=O), 2870(C-H aliph.), 3020(C-H arom.).	DMSO-d_6 1.5-2.4(4H,m),3.7(2H,s), 6.9(1H,s),7.0-8.0(10H,m).
6a	$C_{22}H_{22}O_3N_2S$ (394.49) (ether)	165-7 sublm.	90	67.00 66.81	5.58 5.49	7.10 7.00	8.12 8.10	700(C-S),1685(C=O) 2885(C-H aliph.), 3080(C-H arom.).	DMSO-d_6 1.7-1.9(6H,m), 2.0-2.4 (4H,m),3.7(2H,s),6.8(1H,s), 7.0-7.9(9H,m).

Table 1: (Continued)

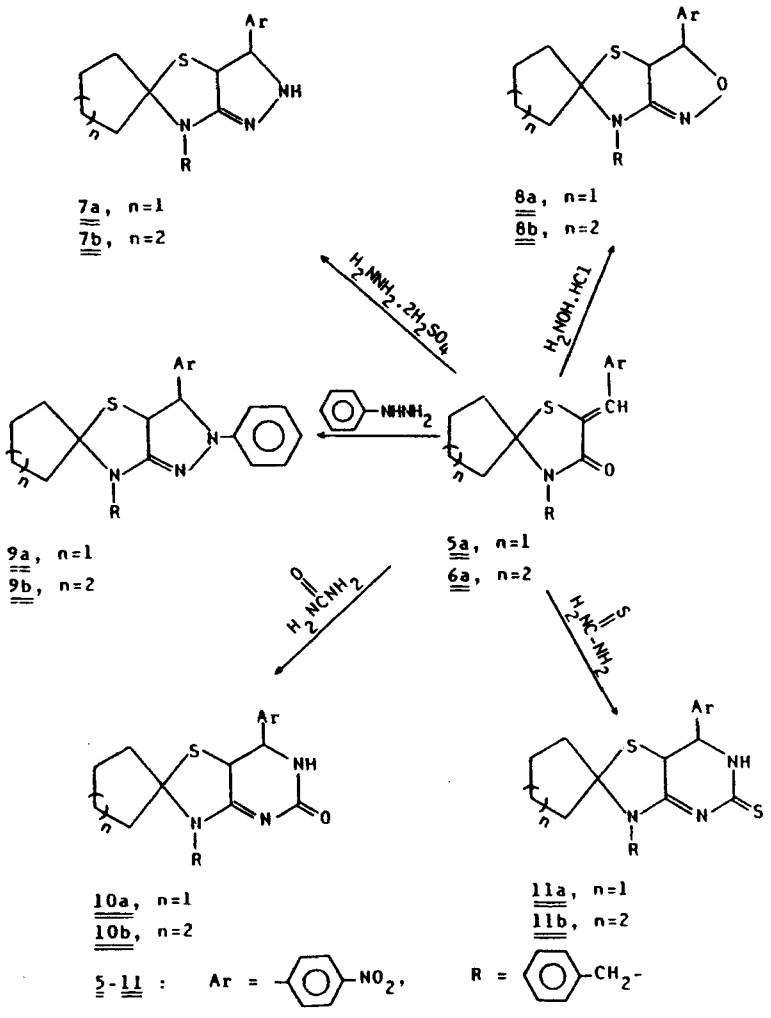
6b	$C_{22}H_{22}ONSCl$ (383.94) (methanol)	159-60 (decomp.)	86	68.92 68.88	5.74 5.69	3.65 3.61	8.35 8.21	710(C-S),1690(C=O), 2890(C-H aliph.), 3100(C-H arom.).	Acetone d_6 1.7-1.9(6H,m), 2.0-2.4 (4H,m),3.7(2H,s),6.8(1H,s), 7.0-8.0(9H,m).
6c	$C_{23}H_{25}O_2NS$ (379.52) (methanol)	165-7	85	72.82 72.71	6.59 6.49	3.69 3.59	8.44 8.41	700(C-S),1690(C=O), 2880(C-H aliph.), 3100(C-H arom.).	DMSO-d_6 1.6-1.9(6H,m), 2.0-2.4 (4H,m),3.3(3H,s),3.7(2H,s),6.7 (1H,s), 7.0-7.8(10H,m).
6d	$C_{22}H_{23}NOS$ (349.50) (ether)	163-5	82	75.64 75.51	6.59 6.49	4.01 4.00	9.16 9.00	700(C-S),1690(C=O), 2880(C-H aliph.), 3100(C-H arom.).	DMSO-d_6 1.6-1.9(6H,m), 2.0-2.4 (4H,m),3.7(2H,s),6.7(1H,S), 7.0-7.8(10H,m).
7a	$C_{21}H_{22}O_2N_4S$ (394.50) (ethanol)	255-7 (decomp.)	80	63.95 63.87	5.58 5.54	14.21 14.11	8.11 8.11	720(C-S),1350,1525 ($-NO_2$),1600(-C=N), 2900(C-H aliph.), 3202(C-H arom.), 3200(NH).	DMSO-d_6 1.3-1.8(4H,m), 2.0-2.2 (4H,m),3.8(2H,s),8.1(1H,s), 4.3(2H,d), 7.0-7.8(9H,m).
7b	$C_{22}H_{24}O_2N_4S$ (408.52) (ethanol)	270-2 (decomp.)	84	64.70 64.61	5.88 5.78	13.72 13.61	7.84 7.71	710(C-S),1356,1525 ($-NO_2$),1600(-C=N), 2890(C-H aliph.), 3202(C-H arom.), 3200(NH).	Acetone d_6 1.6-1.9(6H,m),2.0-2.2 (4H,m),3.7(2H,s),8.1(1H,s),4.3 (2H,d),7.0-7.8(9H,m).
8a	$C_{21}H_{21}O_3N_3S$ (395.48) (methanol)	127-30 (decomp.)	67	63.79 63.61	5.31 5.27	10.63 10.51	8.10 8.00	700(C-S),1356,1525 ($-NO_2$),1600(-C=N), 2890(C-H aliph.), 3020(C-H arom.).	DMSO-d_6 1.5-1.8(4H,m), 2.0-2.2 (4H,m),3.7(2H,s),4(2H,d),7.0-7.8 (9H, m).
8b	$C_{22}H_{23}O_3N_3S$ (409.51) (ethanol)	130-3 (decomp.)	70	64.54 64.39	5.62 5.51	10.26 10.11	7.82 7.69	710(C-S),1356,1525($-NO_2$), 1600(-C=N),2880(C-H aliph.),3020(C-H arom.).	Acetone d_6 1.5-1.9(6H,m), 2.0-2.2(4H,m),3.7(2H,s), 4(2H,d),7.0-7.8(9H,m).
9a	$C_{27}H_{26}O_2N_4S$ (470.60) (ethanol)	115-7 (decomp.)	70	68.93 68.70	5.53 5.41	11.91 11.81	6.80 6.70	700(C-S),1356,1525($-NO_2$), 1600(-C=N),2890(C-H aliph.),3030(C-H arom.).	DMSOd_6 1.3-1.7(4H,m),2.0-2.2 (4H,m),3.7(2H,s),4.3(2H,d), 7.0-8.2(14H,m).
9b	$C_{28}H_{28}O_2N_4S$ (484.62) (ethanol)	120-2 (decomp.)	75	69.42 69.32	5.78 5.62	11.57 11.43	6.61 6.51	710(C-S),1355,1525($-NO_2$), 1600(C=N),2890(C-H aliph.),3020(C-H arom.).	DMSO-d_6 1.5-1.9(6H,m), 2.0-2.2 (4H,m),3.7(2H,s), 4.0(2H,d), 7.0-7.8(14H;m).
10a	$C_{22}H_{22}O_3N_4S$ (422.50) (ethanol)	173-5 (decomp.)	67	62.55 62.45	5.21 5.11	13.27 13.17	7.58 7.48	700(C-S),1350,1520($-NO_2$), 1620(-C=N),1670(C=O),2870 (C-H aliph.),3020(C-H arom.),3100(NH).	Acetone d_6 1.5-1.8(4H,m), 2.0-2.2(4H,m),3.8(2H,s) 8.1(1H,s),4.3(2H,d),7.0-7.9 (10H, m).
10b	$C_{23}H_{24}O_3N_4S$ (436.53) (methanol)	135-7 (decomp.)	65	63.30 63.10	5.5 5.3	12.84 12.61	7.33 7.23	715(C-S),1355,1530(NO_2), 1600(C=N),1680(C=O),2880 (C-H aliph.),3030(C-Harom.)	DMSO-d_6 1.3-1.8(6H,m),2.0-2.2 (4H,m),3.8(2H,s),8.1(1H,s), 4.2(2H,d),7.0-8.0(9H,m).
11a	$C_{22}H_{22}O_2N_4S_2$ (438.57) (methanol)	150-2 (decomp.)	60	60.27 60.10	5.02 5.00	12.78 12.61	14.61 14.40	700(C-S),1110(C=S),1350, 1525(NO_2),2850-2870(C-H aliph.),3020(C-H arom.).	DMSO-d_6 1.4-1.7(4H,m),2.0-2.2 (4H,m),3.7(2H,s),8.1(1H,s), 4.3(2H,d),7.0-7.9(9H,m).
11b	$C_{23}H_{24}O_2N_4S_2$ (452.60) (ethanol)	110-12 (decomp.)	55	61.06 61.00	5.30 5.22	12.38 12.31	7.07 7.00	710(C-S),1100(C=S),1350, 1520(NO_2),2870(C-H aliph), 32020(C-H arom.).	DMSO-d_6 1.3-1.9(6H,m), 2.0-2.2 (4H,m),3.7(2H,s),8.1(1H,s), 4.3(2H,d),7.0-8.0(9H,m).

1-Thia-4-alkyl(aryl)azaspiro[4,4]nonan-3-one **3a-d** *or 1-thia-4-alkyl(aryl)azaspiro[4,5]decan-3-one* **4a-d**

A mixture of **1** or **2** (0.01 mole) and the prim. aliphatic (aromatic) amine (0.01 mole) in absol. EtOH (100 ml) was stirred at room temp. for 2 h, then concentrated under vac., and the product was collected by filtration and crystallized from a proper solvent (Table 1).

2-Arylidene-1-thia-4-benzylazaspiro[4,4]nonan-3-ones **5a-d** *or 2-arylidene-1-thia-4-benzylazaspiro[4,5]decan-3-ones* **6a-d**

A mixture of **3a** or **4a** (0.01 mole) and the aromatic aldehyde (0.012 mole) was fused for 5 min at 150°C to give an oily product which was left over night to afford the crude solid product which was triturated with Et_2O and collected by filtration (Table 1).



Scheme 2

Spiroheterocycles **7-11**

A mixture of **5a** or **6a** (0.001 mole) and the proper reagent (hydrazine sulfate, hydroxylamine · HCl, phenylhydrazine, urea, or thiourea) (0.001 mole) in EtOH/pyridine (50 ml 1:1) was refluxed gently for 2 h. The mixture was cooled and diluted with cold 5 % aqueous HCl whereby the desired products precipitated. They were crystallized from suitable solvents (Table 1).

References

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