SPIROHETEROCYCLIC SYSTEMS. V. SYNTHESIS OF 3-SUBSTITUTED-10-SPIRO(1′-CYCLOALKANE)-THIAZOLO[4,3-*a*]QUINAZOLIN-4-ONES

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Spiro derivatives show photochromic properties, biological activity and optical properties[1 - 6]. Quinazoline derivatives have well known biological activities[7]. Thiazolidinones derivatives have considerable importance as drugs[8 - 11] and herbicides[12].

EXPERIMENTAL

The time required for completion of the reactions was monitored by thin layer chromatography. Melting points were determined in open glass capillaries and are uncorrected. IR spectra (wavenumbers in cm^{-1}) were recorded in KBr pellets on a Pye–Unicam SP G spectrophotometer. ^1H NMR spectra were measured in $CDCl_3$ using TMS as internal standard on EM 360 90 MHz NMR spectrophotometer. Chemical shifts are given in ppm (δ-scale).

1-Thia-4-(2′-carboxyphenyl)azaspiro[4,4]nonan-3-one (*IV*)

1-Oxa-4-thiaspiro[4,4]nonan-2-one (*II*, ref.[13]) (1.58 g, 0.01 mol) was dissolved in 20 ml of absolute ethanol. To this solution (1.37 g, 0.01 mol) of anthranilic acid (*I*) was added portionwise and the mixture was refluxed for 1 h. The solvent was concentrated under reduced pressure and the reaction mixture was cooled to room temperature whereby *IV* was precipitated as pale yellow crystals; yield 2.43 g (95%), m.p. 125 – 127 °C.

1-Thia-4-(2′-carboxyphenyl)azaspiro[4,5]decan-3-one (*V*)

This compound was prepared in similar way as the compound *IV* from 1-oxa-4-thiaspiro[4,5]decan-2-one (*III*); yield 92%, pale yellow crystals, m.p. 110 – 112 °C.

10-Spiro(1′-cyclopentane)thiazolo[4,3-*a*]benzoxazin-4-one (*VI*)

A solution of 2.77 g (0.01 mol) of 1-thia-4-(2′-carboxyphenyl)azaspiro[4,4]nonan-3-one (*IV*) in 25 ml acetic anhydride was heated at 90 °C on a water bath for 6 h. The reaction mixture was cooled to room temperature whereby 2.33 g (90%) of *VI* was precipitated as pale yellow crystals; m.p. 200 – 202 °C.

10-Spiro(1′-cyclohexane)thiazolo[4,3-*a*]benzoxazin-4-one (*VII*)

This compound was prepared in similar way as *VI* from 1-thia-4-(2′-carboxyphenyl)azaspiro[4,5]decan-3-one (*V*); yield 85%, pale yellow crystals, m.p. 140 – 142 °C.

10-Spiro(1′-cyclopentane)thiazolo[4,3-*a*]quinazolin-4-one (*VIIIa*)

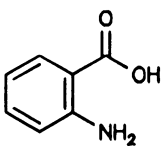
An amount of 0.25 g (0.001 mol) of compound *VI* was fused with 1 g of ammonium acetate at 150 – 180 °C for 2 h. The reaction mixture was cooled to room temperature, diluted with 10 ml cold water whereby *VIIIa* was precipitated as white powder; yield 0.23 g (89%), m.p. 170 – 172 °C.

10-Spiro(1′-cyclohexane)thiazolo[4,3-*a*]quinazolin-4-one (*IXa*)

This compound was prepared in similar way as *VIIIa* from *VII*; yield 90%, m.p. 192 – 194 °C.

3-Hydroxy-10-spiro(1′-cyclopentane)thiazolo[4,3-*a*]quinazolin-4-one (*VIIIb*)

An amount of 0.259 g (0.001 mol) of *VI* was dissolved in 10 ml pyridine, to this solution was added 0.069 g, (0.001 mole) of hydroxylamine hydrochloride. The reaction mixture was heated at 70 °C on a water bath



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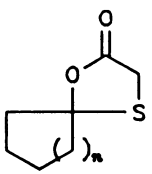
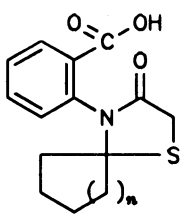
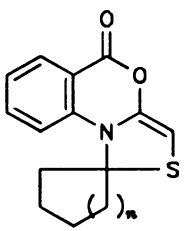


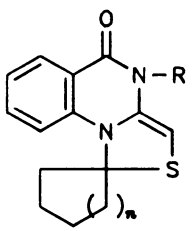
II, $n = 1$
III, $n = 2$



IV, $n = 1$
V, $n = 2$



VI, $n = 1$
VII, $n = 2$



VIII, $n = 1$
IX, $n = 2$

In formulae *VIII*, *IX* : *a*, R = H; *b*, R = OH; *c*, R = CH_3; *d*, R = $CH_2CH(CH_3)_2$; *e*, R = C_6H_5; *f*, R = $CH_2C_6H_5$; *g*, R = 4-$NO_2C_6H_4$; *h*, R = 4-$CH_3COC_6H_4$; *i*, R = 1-naphthyl

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TABLE I
Physical and analytical data of spiro compounds *IV* – *IX*[a]

Compound	M. p., °C Yield, %	Formula (M. w.)	IR	^{1}H NMR
IV	125 – 127 95	$C_{14}H_{15}NO_3S$ (277.3)	3 050 (CH arom.); 2 830 (CH aliph.); 1 700 (C=O); 700 (C–S)	1.30 – 1.70 m, 4 H (2 × CH_2, cyclopentane); 1.80 – 2.30 m, 4 H (2 × CH_2, cyclopentane); 3.40 s, 2 H (CH_2CO); 7.00 – 7.60 m, 4 H (arom.); 9.10 s, 1 H (COOH)
V	110 – 112 92	$C_{15}H_{17}NO_3S$ (291.4)	3 070 (CH arom.); 2 830 (CH aliph.); 1 715 (C=O); 710 (C–S)	1.23 – 1.40 m, 6 H (3 × CH_2, cyclohexane); 1.60 – 1.90 m, 4 H (2 × CH_2, cyclohexane); 3.36 s, 2 H (CH_2CO); 7.00 – 7.60 m, 4 H (arom.); 9.00 s, 1 H (COOH)
VI	200 – 202 90	$C_{14}H_{13}NO_2S$ (259.3)	3 050 (CH arom.); 2 920 (CH aliph.); 1 710 (C=O); 1 320 (C–O), 1 265	1.30 – 1.60 m, 4 H (2 × CH_2, cyclopentane); 1.70 – 1.90 m, 4 H (2 × CH_2, cyclopentane); 7.60 m, 4 H (arom.); 8.2 s, 1 H (H-2)
VII	140 – 142 85	$C_{15}H_{15}NO_2S$ (273.4)	3 070 (CH arom.); 2 890 (CH aliph.); 1 710 (C=O); 1 330 (C–O), 1 270	1.24 – 1.40 m, 6 H (3 × CH_2, cyclohexane); 1.60 – 2.00 m, 4 H (2 × CH_2, cyclohexane); 7.00 – 7.50 m, 4 H (arom.); 3.38 s, 1 H (H-2)
VIIIa	170 – 172 89	$C_{14}H_{14}N_2OS$ (258.3)	3 340 (NH); 3 060 (CH arom.); 2 860 (CH aliph.); 1 710 (C=O)	1.37 – 1.70 m, 4 H (2 × CH_2, cyclopentane); 1.85 – 2.10 m, 4 H (2 × CH_2, cyclopentane); 3.80 s, 1 H (NH); 7.00 – 7.70 m, 4 H (arom.); 8.35 s, 1 H (H-2)
VIIIb	170 – 172 87.6	$C_{14}H_{14}N_2O_2S$ (274.5)	3 400 (OH); 3 070 (CH arom.); 2 850 (CH aliph.); 1 715 (C=O)	1.40 – 1.70 m, 4 H (2 × CH_2, cyclopentane); 1.80 – 2.10 m, 4 H (2 × CH_2, cyclopentane); 5.10 s, 1 H (NOH); 7.00 – 7.70 m, 4 H (arom.); 8.30 s, 1 H (H-2)
VIIIc	155 – 157 75	$C_{15}H_{16}N_2OS$ (272.4)	3 070 – 3 040 (CH arom.); 2 870, 2 850 (CH aliph.); 1 710 (C=O)	1.40 – 1.70 m, 4 H (2 × CH_2, cyclopentane); 1.80 – 1.95 m, 4 H (2 × CH_2, cyclopentane); 3.20 s, 3 H (CH_3N); 7.00 – 7.70 m, 4 H (arom.); 8.20 s, 1 H (H-2)

TABLE I
(*Continued*)

Compound	M. p., °C Yield, %	Formula (M. w.)	IR	^{1}H NMR
VIIId	152 – 154 78	$C_{18}H_{22}N_2OS$ (314.5)	3 060 – 3 040 (CH arom.); 2 870 (CH aliph.); 1 715 (C=O)	1.10 d, 6 H ($(CH_3)_2$); 1.20 d, 2 H (NCH_2); 1.30 – 1.6 m, 5 H (2 × CH_2, cyclopentane and CH); 1.70 – 1.85 m, 4 H (2 × CH_2, cyclopentane); 7.00 – 7.75 m, 4 H (arom.); 8.15 s, 1 H (H-2)
VIIIe	92 – 94 82	$C_{19}H_{18}N_2OS$ (322.4)	3 050 (CH arom.); 2 850 (CH aliph.); 1715 (C=O)	1.50 – 1.70 m, 4 H (2 × CH_2, cyclopentane); 1.70 – 1.85 m, 4 H (2 × CH_2, cyclopentane); 7.10 – 7.80 m, 9 H (arom.); 8.2 s, 1 H (H-2)
VIIIf	98 – 100 80	$C_{20}H_{20}N_2OS$ (336.5)	3 045 (CH arom.); 2 855 (CH aliph.); 1 710 (C=O)	1.40 – 1.60 m, 4 H (2 × CH_2, cyclopentane); 1.75 – 1.90 m, 4 H (2 × CH_2, cyclopentane); 3.2 s, 2 H (CH_2Ph); 7.00 – 7.50 m, 9 H (arom.); 8.17 s, 1 H (H-2)
VIIIg	127 – 129 85	$C_{20}H_{17}N_3O_3S$ (379.4)	3 050 (CH arom.); 2 850 (CH aliph.); 1 710 (C=O)	1.37 – 1.55 m, 4 H (2 × CH_2, cyclopentane); 1.65 – 1.85 m, 4 H (2 × CH_2, cyclopentane); 6.85 – 7.55 m, 8 H (arom.); 8.20 s, 1 H (H-2)
VIIIh	195 – 197 86	$C_{21}H_{20}N_2O_2S$ (364.5)	3 045 (CH arom.); 2 840 (CH aliph.); 1 715 (C=O)	1.40 – 1.60 m, 4 H (2 × CH_2, cyclopentane); 1.70 – 1.95 m, 4 H (2 × CH_2, cyclopentane); 2.3 s, 3 H (CH_3); 6.90 – 7.40 m, 8 H (arom.); 8.20 s, 1 H (H-2)
VIIIi	180 – 182 87	$C_{24}H_{20}N_2OS$ (384.5)	3 055 (CH arom.); 2 860 (CH aliph.); 1 710 (C=O)	1.35 – 1.65 m, 4 H (2 × CH_2, cyclopentane); 1.70 – 1.95 m, 4 H (2 × CH_2, cyclopentane); 6.80 – 7.70 m, 11 H (arom.); 8.20 s, 1 H (H-2)
IXa	192 – 194 90	$C_{15}H_{16}N_2OS$ (272.4)	3 340 (NH); 3 050 (CH arom.); 2 820 (CH aliph.); 1 715 (C=O)	1.18 – 1.40 m, 6 H (3 × CH_2, cyclohexane); 1.60 – 2.00 m, 4 H (2 × CH_2, cyclohexane); 3.85 s, 1 H (NH); 7.10 – 7.70 m, 4 H (arom.); 8.19 s, 1 H (H-2)
IXb	180 – 182 78	$C_{15}H_{16}N_2O_2S$ (288.4)	3 400 (OH); 3 050 (CH arom.); 2 870 (CH aliph.); 1 715 (C=O)	1.20 – 1.45 m, 6 H (3 × CH_2, cyclohexane); 1.60 – 2.00 m, 4 H (2 × CH_2, cyclohexane); 5.10 s, 1 H (NOH); 7.00 – 7.67 m, 4 H (arom.); 8.75 s, 1 H (H-2)

TABLE I
(*Continued*)

Compound	M. p., °C Yield, %	Formula (M. w.)	IR	^{1}H NMR
IXc	160 – 162 82	$C_{16}H_{18}N_2OS$ (286.4)	3 050 (CH arom.); 2 850 (CH aliph.); 1 715 (C=O)	1.20 – 1.45 m, 6 H (3 × CH_2, cyclohexane); 1.70 – 1.95 m, 4 H (2 × CH_2, cyclohexane); 3.15 s, 3 H (NCH_3); 6.80 – 7.60 m, 4 H (arom.); 8.15 s, 1 H (H-2)
IXd	135 – 136 80	$C_{19}H_{24}N_2OS$ (328.5)	3 060 (CH arom.); 2 870 (CH aliph.); 1 710 (C=O)	1.10 d, 6 H ($(CH_3)_2C$); 1.30 d, 2 H (NCH_2); 1.3 – 1.5 m, 7 H (3 × CH_2, cyclohexane and CH); 1.65 – 1.95 m, 4 H (2 × CH_2, cyclohexane); 7.1 – 7.7 m, 4 H (arom.); 8.20 s, 1 H (H-2)
IXe	100 – 102 75	$C_{20}H_{20}N_2OS$ (336.5)	3 050 (CH arom.); 2 850 (CH aliph.); 1 715 (C=O)	1.4 – 1.65 m, 6 H (3 × CH_2, cyclohexane); 1.70 – 1.95 m, 4 H (2 × CH_2, cyclohexane); 7.10 – 7.60 m, 9 H (arom.); 8.20 s, 1 H (H-2)
IXf	107 – 109 80	$C_{21}H_{22}N_2OS$ (350.5)	3 060 (CH arom.); 2 870 (CH aliph.); 1 710 (C=O)	1.35 – 1.55 m, 6 H (3 × CH_2, cyclohexane); 1.65 – 1.80 m, 4 H (2 × CH_2, cyclohexane); 3.3 s, 2 H (CH_2Ph); 7.0 – 7.5 m, 9 H (arom.); 8.15 s, 1 H (H-2)
IXg	187 – 189 85	$C_{21}H_{19}N_3O_3S$ (393.5)	3 050 (CH arom.); 2 850 (CH aliph.); 1 715 (C=O)	1.30 – 1.50 m, 6 H (3 × CH_2, cyclohexane); 1.60 – 1.80 m, (2 × CH_2, cyclohexane); 7.0 – 7.5 m, 8 H (arom.); 8.25 s, 1 H (H-2)
IXh	200 – 202 85	$C_{22}H_{22}N_2O_2S$ (378.5)	3 060 (CH arom.); 2 860 (CH aliph.); 1 710 (C=O)	1.35 – 1.50 m, 6 H (3 × CH_2, cyclohexane); 1.60 – 1.85 m, 4 H (2 × CH_2, cyclohexane); 2.3 s, 3 H (CH_3CO); 6.90 – 7.40 m, 8 H (arom.); 8.20 s, 1 H (H-2)
IXi	192 – 194 87	$C_{25}H_{22}N_2OS$ (398.5)	3 050 (CH arom.); 2 850 (CH aliph.); 1 715 (C=O)	1.20 – 1.45 m, 6 H (3 × CH_2, cyclohexane); 1.65 – 1.8 m, 4 H (2 × CH_2, cyclohexane); 6.80 – 7.40 br m, 11 H (arom.); 8.2 s, 1 H (H-2)

[a] Satisfactory microanalysis obtained C ± 0.23, H ± 0.31, N ± 0.31, S ± 0.30.

for 1 h. Pyridine was removed under reduced pressure and the residue was poured into 10 ml of cold 10% hydrochloric acid whereby *VIIIb* was precipitated as pale yellow powder; yield 0.24 g (87.6%), m.p. 170 – 172 °C.

3-Hydroxy-10-spiro(1′-cyclohexane)thiazolo[4,3-*a*]quinazolin-4-one (*IXb*)

This compound was prepared in similar way as *VIIIb* from compound *VII*; yield 78%, m.p. 180 – 182 °C.

3-Alkyl(aryl)-10-spiro(1′-cycloalkane)thiazolo[4,3-*a*]quinazolin-4-ones (*VIIIc – VIIIi*, *IXc – IXi*)

An amount of 0.001 mol of *VI* or *VII*, respectively, was dissolved in absolute ethanol and to this solution a 0.001 mol of primary aliphatic and/or aromatic amine was added, then the mixture was heated on water bath for 2 h. The reaction mixture was cooled to room temperature whereby *VIIIc – VIIIi* and *IXc – IXi* were precipitated (Table I).

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