Chemistry of Heterocyclic Compounds, Vol. 48, No. 5, August, 2012 (Russian Original Vol. 48, No. 5, May, 2012)

SYNTHESIS OF BIS-β,β'-SPIRO-PYRROLIDINYL-OXINDOLES, CONTAINING A RHODANINE FRAGMENT

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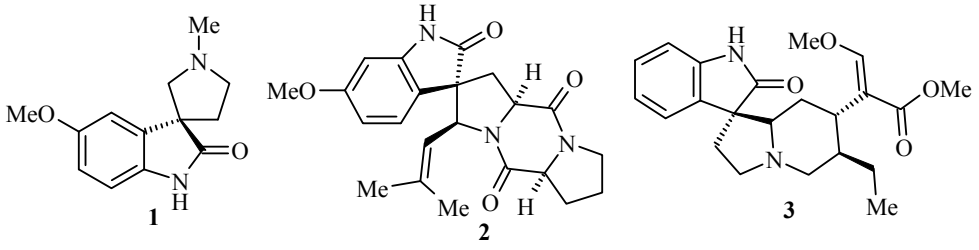
The synthesis of isatilidene derivatives of N-alkylrhodanines has been carried out with dipolarophiles and unstable azomethine ylides, generated in situ from sarcosine and paraformaldehyde. A series of chiral pyrrolidinyl-oxindoles spirofused in the β,β'-positions has been synthesized in the result of cycloaddition in high yield and diastereoselectivity.

Keywords: azomethine ylides, rhodanines, spiro-oxindole, 1,3-dipoles, 1,3-dipolar cycloaddition.

Spirofused pyrrolidinyl-oxindoles have in recent years attracted the attention of specialists in both organic synthesis and medicinal chemistry, as indicated by recently published reviews [1, 2]. This is explained by the fact that many natural, biologically active alkaloids, for example (-)-horsfiline (**1**) [3], spirotryprostatin A (**2**) [4] and rhynchophylline (**3**) [5], contain this structural fragment.



Moreover, the structural rigidity of spiroheterocycle molecules is potentially highly complementary to three-dimensional binding sites in important targets (enzymes, receptors, ion channels), and consequently are of interest in the discovery of new medications.

The many routes towards the synthesis of spiro-pyrrolidinyl-oxindole, which are described in the literature, can be divided into two basic groups: the first is the reaction to form the spiro center; the second is the simultaneous formation of the pyrrolidine ring and the spiro center. The first group involves oxidative rearrangements of tetrahydro-β-carbolines [6-9], intramolecular Mannich reactions [10, 11], intramolecular Heck reactions [12], radical cyclization reactions [13, 14] and the rearrangement of [(*N*-aziridinomethyl-sulfanyl)methylene]-2-oxindoles [15]. The second group involves the many variants of azomethine ylide 1,3-dipolar cycloadditions, described in detail in the papers [16-24] and in the review [25]. The cycloaddition

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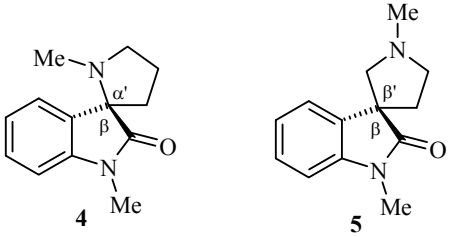
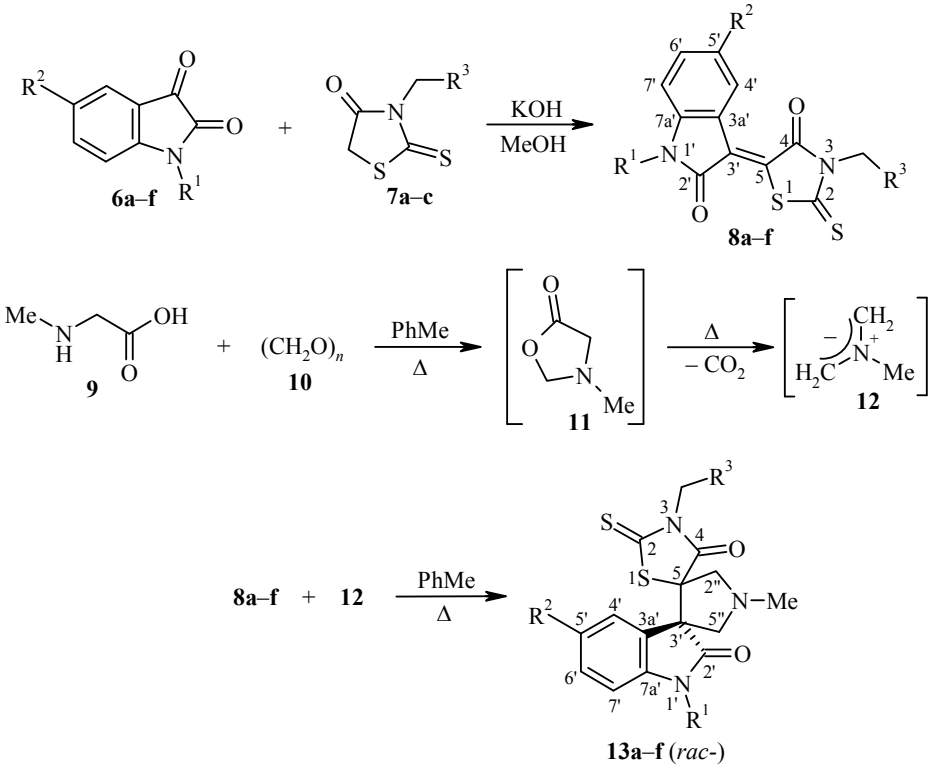
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 5, 859-866, May, 2012. Original article submitted November 30, 2011.

reaction of unstabilized azomethine ylides generated *in situ* from active carbonyl compounds and an *N*-alkyl-α-amino acid is a good preparative method, that is important for creating large compound libraries for bioscreening [25]. However, in the described reactions of such type, where isatin is used as the carbonyl component to generate the azomethine ylide, the structures formed have the oxindole fragment spirofused with pyrrolidine ring at the α'-position (substructure of type **4**), and not at the β'-position as in natural compounds.



In the present work, to synthesize spirocycles with β,β'-spirofused oxindole and pyrrolidine rings of type **5,** we have used the previously unknown isatilidenerhodanines **8a-f**, formed from the corresponding isatins **6** and *N*-alkylrhodanines **7** (Tables 1, 2). The azomethine ylide **12** was generated *in situ* as a result of decarboxylation of the 5-oxazolidinone **11**, formed by the interaction of sarcosine **9** and paraformaldehyde **10** [26].



6, 8, 13 a,**b**,**e** R^1 = H, **c**,**d**,**f** R^1 = Me; **a** R^2 = H, **b** R^2 = Br, **c** R^2 = Cl, **d** R^2 = F, **e** R^2 = OMe, **f** R^2 = Me; **7a**, **8**, **13 a**,**b** R^3 = vinyl, **7b**, **8**, **13 c**,**f** R^3 = furan-2-yl, **7c**, **8**, **13 d**,**e** R^3 = Ph

The three-component reaction of 1,3-dipolar cycloaddition of the azomethine ylide **12** to the dipolarophiles **8a-f** occurs in high yield and gives the bis-spiroheterocycles **13a-f** (Tables 1-3). In the course of the reaction, the solution loses the deep red-brown color of the rhodanine isatilidene derivative **8a-f**, and a pale-yellow color appears. TLC data indicated a complete disappearance of the dipolarophiles in 7-8 hours from the start of the reaction.

Table 1. Physicochemical Characteristics of Compounds **8a-f** and **13a-f**

Compound	Empirical formula	Found, % / Calculated, %			Mp, °C	Yield, %
		C	H	N		
8a	$C_{14}H_{10}N_2O_2S_2$	55.23 / 55.61	3.47 / 3.33	9.32 / 9.26	308-310	91
8b	$C_{14}H_9BrN_2O_2S_2$	44.09 / 44.10	2.33 / 2.38	7.43 / 7.35	266-272	83
8c	$C_{17}H_{11}ClN_2O_3S_2$	52.55 / 52.24	2.67 / 2.84	7.39 / 7.17	236-240	88
8d	$C_{19}H_{13}FN_2O_2S_2$	59.45 / 59.36	3.58 / 3.41	7.21 / 7.29	282-284	62
8e	$C_{19}H_{14}N_2O_3S_2$	59.65 / 59.67	3.77 / 3.69	7.33 / 7.32	292-302	76
8f	$C_{18}H_{14}N_2O_3S_2$	58.33 / 58.36	3.85 / 3.81	7.50 / 7.56	296-306	70
13a	$C_{17}H_{17}N_3O_2S_2$	57.05 / 56.80	5.03 / 4.77	11.94 / 11.69	224-226	73
13b	$C_{17}H_{16}BrN_3O_2S_2$	46.43 / 46.58	3.87 / 3.68	9.38 / 9.59	265-267	90
13c	$C_{20}H_{18}ClN_3O_3S_2$	53.70 / 53.63	4.17 / 4.05	9.51 / 9.38	182-186	82
13d	$C_{22}H_{20}FN_3O_2S_2$	59.77 / 59.84	4.65 / 4.57	9.63 / 9.52	170-172	88
13e	$C_{22}H_{21}N_3O_3S_2$	60.46 / 60.12	5.21 / 4.82	9.15 / 9.56	132-138	75
13f	$C_{21}H_{21}N_3O_3S_2$	59.13 / 59.00	4.89 / 4.95	9.95 / 9.83	152-154	84

In the ^{1}H NMR spectra of compounds **13a-f**, the signals of the diastereotopic methylene groups 2"-CH_2 and 5"-CH_2 appear as AB quartets in the range from 3 to 4 ppm. In comparison with the downfield part of the ^{1}H NMR spectrum of the dipolarophiles **8a-f**, an upfield shift of the signal of the proton at the atom 4'-C is observed in the spectra of compounds **13a-f**, because of the disappearance of the influence of the rhodanine fragment carbonyl group (Table 2).

The structure of compound **13a** was shown unambiguously by X-ray structural analysis (Figure, Tables 4 and 5). The central five-membered ring C(5),C(3'),C(5"),N(1"),C(2") has an "envelope" conformation with one atom C(2") out of the plane of the remaining four pyrrolidine ring atoms. The 2-oxindole and rhodanine fragments at atoms C(5) and C(3') form a torsion angle C(2')–C(3')–C(5)–S(1), equal to 34.7°.

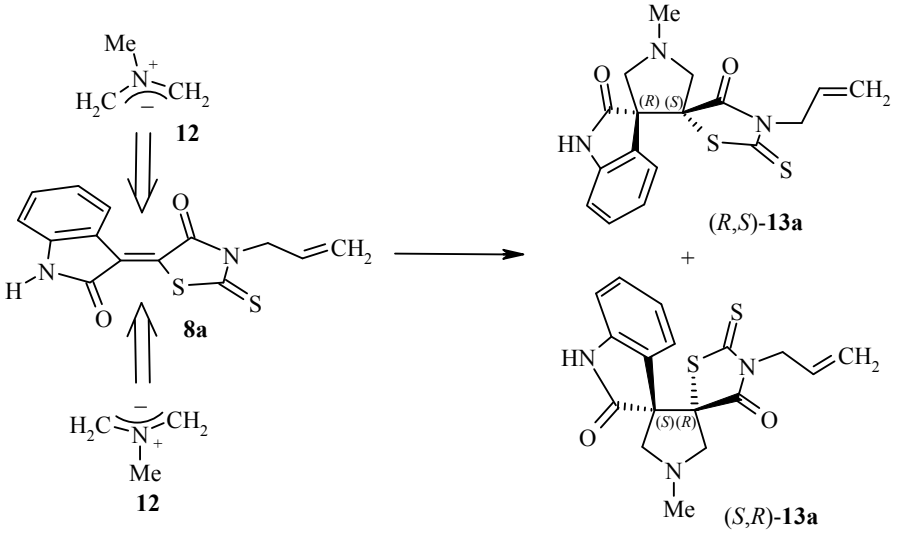


Table 2. ^{1}H NMR Spectra of Compounds **8a-f** and **13a-f**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)
8a	4.67 (2H, d, *J* = 5.3, NCH_2); 5.10-5.25 (2H, m, CH=C$\underline{H}_2$); 5.75-5.95 (1H, m, C$\underline{H}$=CH_2); 6.95 (1H, d, *J* = 7.8, H-7'); 7.08 (1H, dd, *J* = 7.8, *J* = 7.8, H-6'); 7.42 (1H, dd, *J* = 7.8, *J* = 7.8, H-5'); 8.79 (1H, d, *J* = 7.8, H-4'); 11.27 (1H, s, NH)
8b	4.67 (2H, d, *J* = 5.1, NCH_2); 5.21 (2H, dd, *J* = 5.4, *J* = 1.1, CH=C$\underline{H}_2$); 5.75-5.94 (1H, m, C$\underline{H}$=CH_2); 6.96 (1H, d, *J* = 8.4, H-7'); 7.46 (1H, dd, *J* = 8.4, *J* = 2.1, H-6'); 8.50 (1H, d, *J* = 2.1, H-4'); 11.41 (1H, s, NH)
8c	3.24 (3H, s, NCH_3); 5.27 (2H, s, NCH_2Fur); 6.35-6.45 (1H, m, H-4 Fur); 6.48 (1H, d, *J* = 3.3, H-3 Fur); 7.20 (1H, d, *J* = 8.2, H-7'); 7.55-7.67 (2H, m, H-6', H-5 Fur); 8.85 (1H, d, *J* = 1.7, H-4')
8d	2.33 (3H, s, NCH_3); 5.30 (2H, s, NCH_2Ph); 7.03 (1H, d, *J* = 7.5, H-7'); 7.20-7.40 (6H, m, H Ph, H-6'); 8.66 (1H, s, H-4')
8e	3.75 (3H, s, OCH_3); 5.27 (2H, s, NCH_2); 6.86 (1H, d, *J* = 8.6, H-7'); 7.04 (1H, dd, *J* = 8.6, *J* = 2.5, H-6'); 7.21-7.43 (5H, m, H Ph); 8.46 (1H, d, *J* = 2.5, H-4'); 11.08 (1H, s, NH)
8f	2.40 (3H, s, 5'-CH_3); 3.26 (3H, s, NCH_3); 5.36 (2H, s, NCH_2Fur); 6.31 (1H, dd, *J* = 3.2, *J* = 1.9, H-4 Fur); 6.44 (1H, d, *J* = 3.2, H-3 Fur); 6.74 (1H, d, *J* = 7.9, H-7'); 7.20-7.30 (1H, m, H-6'); 7.32-7.37 (1H, m, H-5 Fur); 8.81 (1H, s, H-4')
13a	2.64 (3H, s, NCH_3); 3.30 (1H, d, *J* = 10.4) and 3.69 (1H, d, *J* = 10.4, 2"-CH_2); 3.47 (1H, d, *J* = 10.9) and 3.91 (1H, d, *J* = 10.9, 5"-CH_2); 4.29-5.71 (2H, m, C$\underline{H}_2$CH=CH_2); 5.10 (2H, dd, *J* = 17.5, *J* = 10.3, CH=C$\underline{H}_2$); 5.48-5.72 (1H, m, C$\underline{H}$=CH_2); 6.87 (1H, d, *J* = 7.4, H-7'); 6.93 (1H, dd, *J* = 7.4, *J* = 7.4, H-6'); 7.15-7.30 (2H, m, H-4',5'); 8.68 (1H, s, NH)
13b	2.63 (3H, s, NCH_3); 3.28 (1H, d, *J* = 10.4) and 3.66 (1H, d, *J* = 10.4, 2"-CH_2); 3.46 (1H, d, *J* = 10.8) and 3.89 (1H, d, *J* = 10.8, 5"-CH_2); 4.45 (1H, dd, *J* = 14.5, *J* = 6.3) and 4.61 (1H, dd, *J* = 14.5, *J* = 5.3, C$\underline{H}_2$CH=CH_2); 5.15 (1H, d, *J* = 17.1) and 5.26 (1H, d, *J* = 10.1, CH=C$\underline{H}_2$); 5.54-5.73 (1H, m, C$\underline{H}$=CH_2); 6.75 (1H, d, *J* = 8.2, H-7'); 7.32 (1H, d, *J* = 1.9, H-4'); 7.38 (1H, dd, *J* = 8.2, *J* = 1.9, H-6'); 7.89 (1H, s, NH)
13c	2.62 (3H, s, 1"-CH_3); 3.18 (1H, d, *J* = 10.4) and 3.70 (1H, d, *J* = 10.4, 2"-CH_2); 3.18 (3H, s, 1'-CH_3); 3.48 (1H, d, *J* = 10.7) and 3.90 (1H, d, *J* = 10.7, 5"-CH_2); 5.05 (1H, d, *J* = 15.0) and 5.12 (1H, d, *J* = 15.0, NCH_2Fur); 6.20-6.28 (2H, m, H-3,4 Fur); 6.72 (1H, d, *J* = 8.2, H-7'); 7.20-7.35 (3H, m, H-5 Fur, H-4',6')
13d	2.61 (3H, s, 1"-CH_3); 3.17 (1H, d, *J* = 10.6) and 3.67 (1H, d, *J* = 10.6, 2"-CH_2); 3.19 (3H, s, 1'-CH_3); 3.47 (1H, d, *J* = 10.6) and 3.89 (1H, d, *J* = 10.6, 5"-CH_2); 5.00 (1H, d, *J* = 14.0) and 5.17 (1H, d, *J* = 14.0, NCH_2Ph); 6.71 (1H, dd, *J* = 8.4, *J* = 4.2, H-7'); 6.87 (1H, dd, *J* = 8.1, *J* = 2.5, H-4'); 6.95 (1H, dd. d, *J* = 8.4, *J* = 6.3, *J* = 2.5, H-6'); 7.12-7.32 (5H, m, H Ph)
13e	2.63 (3H, s, NCH_3); 3.29 (1H, d, *J* = 10.3) and 3.66 (1H, d, *J* = 10.3, 2"-CH_2); 3.46 (1H, d, *J* = 10.7) and 3.88 (1H, d, *J* = 10.7, 5"-CH_2); 3.49 (3H, s, OCH_3); 5.05 (1H, d, *J* = 14.4) and 5.12 (1H, d, *J* = 14.4, NCH_2Ph); 6.65-6.80 (3H, m, H-4',6',7'); 7.07-7.22 (5H, m, H Ph); 7.87 (1H, s, NH)
13f	2.21 (3H, s, 5'-CH_3); 2.63 (3H, s, 1"-CH_3); 3.17 (1H, d, *J* = 10.4) and 3.71 (1H, d, *J* = 10.4, 2"-CH_2); 3.18 (3H, s, 1'-CH_3); 3.47 (1H, d, *J* = 10.7) and 3.92 (1H, d, *J* = 10.7, 5"-CH_2); 5.06 (2H, s, NCH_2Fur); 6.15 (1H, d, *J* = 3.2, H-3 Fur); 6.24 (1H, dd, *J* = 3.2, *J* = 1.9, H-4 Fur); 6.68 (1H, d, *J* = 7.7, H-7'); 7.00-7.12 (2H, m, H-4',6'); 7.25-7.28 (1H, m, H-5 Fur)

Two chiral centers are formed as a result of the cycloaddition, so that formally four stereoisomers of compound **13** may be formed – ((*R*,*R*), (*R*,*S*), (*S*,*R*), and (*S*,*S*)). However, since [3+2] cycloaddition is a concerted process (not ionic), the chiral centers are formed simultaneously, which leads to the formation of only two stereoisomers – the enantiomers (*R*,*S*) and (*S*,*R*). The absence in the ^{1}H NMR spectra of signals for even traces of the other two possible isomers ((*R*,*R*) and (*S*,*S*)) serves as an experimental confirmation of this.

As a result of the equal probability of addition of the azomethine ylide **12** to the enantiotopic faces of the dipolarophile **8a** (from above or below), a racemic mixture of the isomers (*R*,*S*)-**13a** and (*S*,*R*)-**13a** is formed, as is also confirmed by the packing of the bis-spirocycle molecules in the unit cell, according to X-ray crystallographic data.

Table 3. ^{13}C NMR Spectra of Bis-spirooxindoles **13a-f**

Com-pound	Chemical shifts, δ, ppm (*J*, Hz)
13a	41.8 (1''-CH_3); 46.1 (NCH_2); 60.2 (C-5); 61.6 (C-5''); 62.7 (C-2''); 66.1 (C-3'); 111.9 (C-7'); 113.7 (C-5'); 118.1 (CH=$\underline{C}H_2$); 126.2 (C-6'); 128.0 (C-4'); 129.5 ($\underline{C}$H=CH_2); 132.6 (C-3a'); 142.4 (C-7a'); 174.7 (C-2'); 177.5 (C-4); 198.6 (C-2)
13b	41.8 (1''-CH_3); 46.1 (NCH_2); 60.2 (C-5); 61.6 (C-5''); 62.7 (C-2''); 66.1 (C-3'); 111.9 (C-7'); 113.7 (C-5'); 118.1 (CH=$\underline{C}H_2$); 126.2 (C-6'); 128.0 (C-4'); 129.5 ($\underline{C}$H=CH_2); 132.6 (C-3a'); 142.4 (C-7a'); 174.7 (C-2'); 177.5 (C-4); 198.6 (C-2)
13c	26.4 (1'-CH_3); 40.7 (1''-CH_3); 41.8 (NCH_2); 59.7 (C-5''); 62.2 (C-5); 63.7 (C-3'); 66.2 (C-2''); 109.4 (C-3 Fur); 110.6 (C-7'); 110.7 (C-4 Fur); 125.2 (C-3a'); 125.2 (C-4'); 126.9 (C-5'); 129.7 (C-6'); 142.9 (C-5 Fur); 143.4 (C-7a'); 147.2 (C-2 Fur); 174.4 (C-2'); 175.7 (C-4); 198.2 (C-2)
13d	26.4 (1'-CH_3); 41.8 (1''-CH_3); 47.3 (NCH_2); 60.0 (C-5''); 61.9 (C-5); 63.6 (C-3'); 66.4 (C-2''); 110.1 (d, J_{C-F} = 8.3, C-7'); 113.0 (d, J_{C-F} = 26.0, C-6'); 116.0 (d, *J* = 27.2, C-4'); 124.8 (d, J_{C-F} = 8.5, C-3a'); 126.9 (C-2,6 Ph); 127.6 (C-4 Ph); 128.4 (C-3,5 Ph); 134.2 (*i*-C Ph); 140.7 (d, J_{C-F} = 1.9, C-7a'); 158.0 (d, J_{C-F} = 239.3, C-5'); 174.8 (C-2'); 175.9 (C-4); 198.9 (C-2)
13e	41.8 (1''-CH_3); 47.2 (NCH_2); 55.0 (5'-OCH_3); 60.4 (C-5''); 62.2 (C-5); 63.6 (C-3'); 66.8 (C-2''); 110.5 (C-4'); 112.2 (C-7'); 114.4 (C-6'); 125.3 (C-4 Ph); 126.7 (C-2,6 Ph); 127.3 (C-3a'); 128.4 (C-3,5 Ph); 134.2 (*i*-C Ph); 136.0 (C-7a'); 154.8 (C-5'); 174.9 (C-2'); 178.0 (C-4); 199.3 (C-2)
13f	20.9 (5'-CH_3); 26.2 (1'-CH_3); 40.7 (1''-CH_3); 42.0 (NCH_2); 59.8 (C-5''); 61.9 (C-5); 63.2 (C-3'); 66.0 (C-2''); 108.9 (C-7'); 109.1 (C-4 Fur); 110.6 (C-3 Fur); 122.9 (C-3a'); 125.4 (C-4'); 129.9 (C-6'); 131.9 (C-5'); 142.0 (C-7a'); 142.9 (C-5 Fur); 147.5 (C-2 Fur); 174.7 (C-2'); 175.9 (C-4); 198.6 (C-2)

Thus, the preparative methods have been developed for the synthesis of rhodanine isatilidene derivatives based on both *N*-alkyl derivatives and NH-containing isatins, and also related bis-spiroheterocycles, opening another route to compounds including the structural fragment of natural alkaloids.

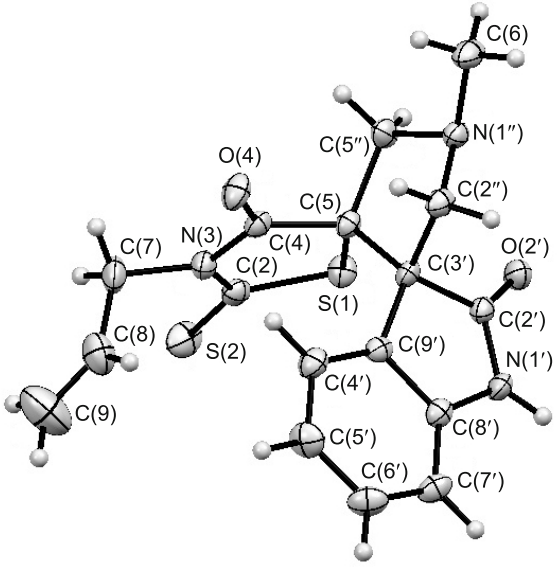


Fig. 1. Molecular structure of compound **13a** with the atoms pepresented by 50% probability thermal vibration ellipsoids.

The high diastereoselectivity of the cycloaddition reactions and the presence of three points of diversification in the bis-spiroheterocycles allows the synthesis of a wide range of potentially biologically active compounds.

Table 4. Basic Bond Lengths (*l*) in the Molecule of the Bis-spiroheterocycle **13a**

Bond	*l*, Å	Bond	*l*, Å	Bond	*l*, Å
S(1)–C(2)	1.737(2)	N(3)–C(4)	1.380(3)	C(6)–H(6A)	0.9600
S(1)–C(5)	1.826(2)	N(3)–C(7)	1.481(3)	C(6)–H(6B)	0.9600
N(1')–C(2')	1.353(3)	C(3')–C(9')	1.517(3)	C(6)–H(6C)	0.9600
N(1')–C(8')	1.401(3)	C(3')–C(5)	1.570(3)	C(7')–C(8')	1.379(3)
N(1')–H(1'A)	0.8600	O(4)–C(4)	1.208(3)	C(7')–H(7'A)	0.9300
N(1")–C(2")	1.457(3)	C(4')–C(9')	1.384(3)	C(7)–C(8)	1.505(4)
N(1")–C(6)	1.465(3)	C(4')–C(5')	1.395(3)	C(7)–H(7A)	0.9700
N(1")–C(5")	1.470(3)	C(4')–H(4'A)	0.9300	C(7)–H(7B)	0.9700
S(2)–C(2)	1.638(2)	C(4)–C(5)	1.531(3)	C(8')–C(9')	1.405(3)
O(2')–C(2')	1.219(3)	C(5)–C(5")	1.558(3)	C(8)–C(9)	1.282(4)
C(2')–C(3')	1.546(3)	C(5")–H(5"A)	0.9700	C(8)–H(8A)	0.9300
C(2)–N(3)	1.373(3)	C(5")–H(5"B)	0.9700	C(9)–H(9A)	0.9300
C(2")–C(3')	1.539(3)	C(5')–C(6')	1.393(3)	C(9)–H(9C)	0.9300
C(2")–H(2"A)	0.9700	C(5')–H(5'A)	0.9300	C(6)–H(6A)	0.9600
C(2")–H(2"B)	0.9700	C(6')–C(7')	1.380(3)		

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra of $CDCl_3$ solutions with TMS as internal standard were recorded on a Bruker DPX-250 spectrometer (250 MHz and 60 MHz, respectively). Elemental analyses were carried out using the combustion method of Pregl and Dumas. Melting points were determined in glass capillaries with APTI apparatus, TLC of the reaction mixtures were carried out on Silufol 245 plates with EtOAc as eluent. *N*-Benzylrhodanine was synthesized by method [27] and *N*-furfurylrhodanine by method [28].

3-(4-Oxo-2-thioxo-1,3-thiazolidin-5-ylidene)-1,3-dihydro-2*H*-indol-2-ones 8a-f (General Method). The 40% aqueous KOH solution (0.01 ml) was added to a solution of equimolar quantities (0.01 mol) of isatin **6** and rhodanine **7** in methanol (30 ml). After 20 min, the precipitate was filtered off and washed with MeOH.

Bis-β,β'-spirooxindoles 13a-f (General Method). A dipolarophile **8a-f** (0.1 mmol), sarcosine **9** (0.036 g, 0.4 mmol), and paraformaldehyde **10** (0.012 g, 0.4 mmol) were suspended in toluene (40 ml). The reaction mixture was refluxed for 8 h. After 1 h the reaction mixture became homogenous and began to lose color. The reaction course was monitored by change in the reaction mixture color. The reaction mixture was cooled, toluene was evaporated in vacuum, and the residue was recrystallized from MeOH.

X-ray Crystallographic Study of Compound 13a. Crystals of compound **13a** ($C_{17}H_{17}N_3O_2S_2$, M = 359.46) obtained by recrystallization from methanol, monoclinic, space group $C_{2/c}$, at 163 K: a 26.975(7), b 8.056(17), c 16.156(4) Å; α 90, β 109.13(2), γ 90°; V 3315.8 (14) Å^3; Z 8; d_{calc} 1.44 g/cm^3; F(000) 1504. Intensities of 4255 reflections were determined on a Bruker SMART CCD diffractometer (λ(MoKα) 0.71073 Å, ω-scanning, $2\theta_{max}$ 28°), and 3933 independent reflections (R_{int} 0.0116) were used in further calculations. The structure was solved by direct methods and refined by full-matrix least-squares method in F^2 in the anisotropic-isotropic approximation. The positions of H atoms were calculated geometrically and refined in the isotropic approximation using the "rider" model. The final values of the probability factors for compound **13a** were: *wR*2 0.0828 and *GOOF* 1.008 for all independent reflections (*R*1 0.0503 was calculated for *F* for 2543 fixed reflections with $I > 2\sigma(I)$). All calculations were carried out with the SHELXTL PLUS 5.10 suite of programs [29]. The X-ray data for the bis-spiroheterocycle **13a** have been deposited in the Cambridge Crystallographic Data Center (deposit CCDC 714445).

Table 5. Valence Angles (ω) in the Molecule of the Bis-spiroheterocycle **13a**

Angle	ω, deg.	Angle	ω, deg.
C(2)–S(1)–C(5)	93.85(11)	N(1")–C(5")–C(5)	106.30(17)
C(2')–N(1')–C(8')	111.41(18)	N(1")–C(5")–H(5"A)	110.5
C(2')–N(1')–H(1'A)	124.3	C(5)–C(5")–H(5"A)	110.5
C(8')–N(1')–H(1'A)	124.3	N(1")–C(5")–H(5"B)	110.5
C(2")–N(1")–C(6)	112.7(2)	C(5)–C(5")–H(5"B)	110.5
C(2")–N(1")–C(5")	106.29(17)	H(5"A)–C(5")–H(5"B)	108.7
C(6)–N(1")–C(5")	112.82(18)	C(6')–C(5')–C(4')	120.3(2)
O(2')–C(2')–N(1')	126.7(2)	C(6')–C(5')–H(5'A)	119.8
O(2')–C(2')–C(3')	125.31(19)	C(4')–C(5')–H(5'A)	119.8
N(1')–C(2')–C(3')	108.01(18)	C(7')–C(6')–C(5')	121.3(2)
N(3)–C(2)–S(2)	126.49(18)	C(7')–C(6')–H(6'A)	119.4
N(3)–C(2)–S(1)	111.37(16)	C(5')–C(6')–H(6'A)	119.4
S(2)–C(2)–S(1)	122.14(14)	N(1")–C(6)–H(6A)	109.5
N(1")–C(2")–C(3')	103.31(17)	N(1")–C(6)–H(6B)	109.5
N(1")–C(2")–H(2"A)	111.1	H(6A)–C(6)–H(6B)	109.5
C(3')–C(2")–H(2"A)	111.1	N(1")–C(6)–H(6C)	109.5
N(1")–C(2")–H(2"B)	111.1	H(6A)–C(6)–H(6C)	109.5
C(3')–C(2")–H(2"B)	111.1	H(6B)–C(6)–H(6C)	109.5
H(2"A)–C(2")–H(2"B)	109.1	C(8')–C(7')–C(6')	117.9(2)
C(2)–N(3)–C(4)	117.21(18)	C(8')–C(7')–H(7'A)	121.1
C(2)–N(3)–C(7)	122.3(2)	C(6')–C(7')–H(7'A)	121.1
C(4)–N(3)–C(7)	120.41(19)	N(3)–C(7)–C(8)	111.9(2)
C(9')–C(3')–C(2")	112.55(18)	N(3)–C(7)–H(7A)	109.2
C(9')–C(3')–C(2')	101.86(17)	C(8)–C(7)–H(7A)	109.2
C(2")–C(3')–C(2')	108.97(18)	N(3)–C(7)–H(7B)	109.2
C(9')–C(3')–C(5)	122.63(18)	C(8)–C(7)–H(7B)	109.2
C(2")–C(3')–C(5)	101.25(17)	H(7A)–C(7)–H(7B)	107.9
C(2')–C(3')–C(5)	109.27(17)	C(7')–C(8')–N(1')	127.7(2)
C(9')–C(4')–C(5')	119.1(2)	C(7')–C(8')–C(9')	122.2(2)
C(9')–C(4')–H(4'A)	120.4	N(1')–C(8')–C(9')	110.08(19)
C(5')–C(4')–H(4'A)	120.4	C(9)–C(8)–C(7)	124.3(3)
O(4)–C(4)–N(3)	123.5(2)	C(9)–C(8)–H(8A)	117.9
O(4)–C(4)–C(5)	124.1(2)	C(7)–C(8)–H(8A)	117.9
N(3)–C(4)–C(5)	112.43(18)	C(4')–C(9')–C(8')	119.2(2)
C(4)–C(5)–C(5")	110.18(18)	C(4')–C(9')–C(3')	133.1(2)
C(4)–C(5)–C(3')	111.21(17)	C(8')–C(9')–C(3')	107.47(19)
C(5")–C(5)–C(3')	103.89(17)	C(8)–C(9)–H(9A)	120.0
C(4)–C(5)–S(1)	104.86(15)	C(8)–C(9)–H(9C)	120.0
C(5")–C(5)–S(1)	114.06(15)	H(9A)–C(9)–H(9C)	120.0
C(3')–C(5)–S(1)	112.80(15)	N(1")–C(5")–C(5)	106.30(17)

This work was carried with the financial support of the Russian Foundation for Basic Research (project No 09-03-00726-a) and the Foundation for the Assistance of Small Innovation Enterprises (project No. 9653/10 (2009-2010)).

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