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4,5-DIALKYL-SUBSTITUTED 3-OXO-(2H)-ISOTHIAZOLE 1,1-DIOXIDES IN REACTIONS WITH DIAZOMETHANE

L. L. Rodina[1]. D. B. Gidon[1], Vs. V. Nikolaev[1], and B. Shulze[2]

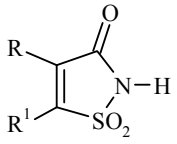
It has been established that the interaction of diazomethane with 4,5-dialkyl-substituted 3-oxo-(2H)-isothiazole 1,1-dioxides proceeds in two stages. Initially alkylation of the sulfonimide nitrogen atom and the carbonyl group oxygen atom occurs (in a ratio of ~ 3:2), then there is a regioselective cycloaddition of diazomethane at the C=C double bond with the formation of the corresponding N-methyloxoisothiazolopyrazolines and 3-methoxyisothiazolopyrazolines.

Keywords: diazomethane, 4,5-dialkyl-3-oxo-(2H)-isothiazole 1,1-dioxides, isothiazolopyrazolines, methylation, 1,3-cycloaddition.

Cycloaddition at the C(4)–C(5) double bond of 3-oxo-(2H)-isothiazole 1,1-dioxide **1** is of practical interest since the resulting heterocyclic adducts may serve as synthons for obtaining substances possessing biological activity and used as medicinal agents [1]. In this series [4+2] cycloaddition to unsubstituted or monosubstituted double bonds is known [2, 3], however cycloaddition to 4,5-disubstituted 3-oxo-(2H)-isothiazole 1,1-dioxides has practically not been studied [4].

In the literature there is reported only one unsuccessful attempt [5] to effect a Diels–Alder reaction at the double bond of such disubstituted heterocycles. This result led the authors to the conclusion that [4π+2π] cycloaddition (to which 1,3-dipolar cycloaddition also belongs) does not go in the case of the disubstituted C(4)–C(5) double bond of 3-oxo-(2H)-isothiazole 1,1-dioxides due to steric hindrance. The study of these reactions is therefore also of definite theoretical interest.

The aim of the present investigation comprises clarification of the possibility of 1,3-cycloaddition of the simplest dipoles at the double dialkyl-substituted C=C bond of the named heterocycles. 4,5-Dimethyl-3-oxo-(2H)-isothiazole 1,1-dioxide (**1a**) and 3-oxo-4,5,6,7-tetrahydro-(2H)-1,2-benzisothiazole 1,1-dioxide (tetrahydrosaccharin) (**1b**) were taken as subjects of the investigation.



1a,b

a R = R[1] = Me, **b** R + R[1] = $(CH_2)_4$

[1]Saint Petersburg State University, Saint Petersburg 198504, Russia; e-mail: lrodina@vn6646.spb.edu. [2]Institute of Organic Chemistry, Leipzig University, Leipzig 04103, Germany; e-mail: bschulze@organik.chemie.uni-leipzig.de. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 595-604, April, 2008. Original article submitted October 30, 2007.

Aliphatic diazo compounds were used as 1,3-dipoles. Oxoisothiazole 1,1-dioxides contain strong electron-withdrawing groups (C=O and SO_2 groups) at the double bond, consequently it must be expected that the maximum contribution to the energy gain on forming a cycloadduct must be introduced by the interaction of the LUMO of the dipolarophile and the HOMO of the dipole. Diazomethane and phenyldiazomethane, having energy-rich, high-lying HOMO were selected as 1,3-dipoles from the broad range of aliphatic diazo compounds [6].

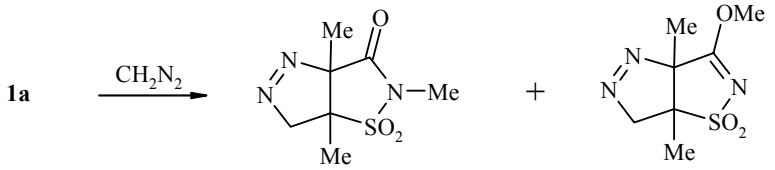
Based on the general chemistry of aliphatic diazo compounds we can imagine three possible directions for their interaction with 3-oxo-(2H)-isothiazole 1,1-dioxides **1a,b**. On the one hand, there is reaction at the nitrogen atom of the amide group, on the other, there is attack at the oxygen atom of the carbonyl group, and also 1,3-dipolar cycloaddition at the C(4)–C(5) double bond.

3-Oxo-(2H)-isothiazole 1,1-dioxides **1a,b** were synthesized by the known procedure of [5, 7-9]. The interaction of isothiazole 1,1-dioxides **1** with diazomethane [10] was carried out at 0°C using a tenfold excess of an ether solution of diazomethane.

On adding the first portions of diazomethane to compound **1a** instantaneous heating of the solution and evolution of nitrogen was observed, then the reaction mixture acquired a saturated yellow coloration. The reaction mixture was left at room temperature for 2-3 days (until complete disappearance of the yellow color of the solution). The precipitated solid was separated and dissolved in methylene chloride. According to data of TLC and of ^{1}H NMR of the reaction mixture the initial isothiazolone **1a** had completely reacted and as a result of reaction a mixture was formed of two cycloadducts in a ratio of ~3:2 (according to data of ^{1}H NMR spectroscopy). After processing the reaction mixture one of the adducts was isolated and completely characterized by spectral methods. The second was not successfully isolated from the reaction mixture in a pure state.

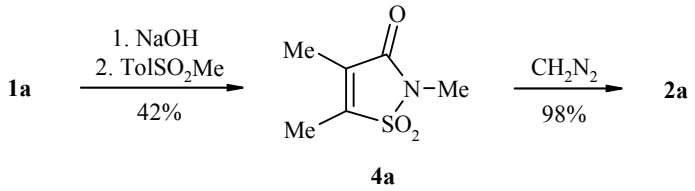
Two groups of signals were observed in the ^{1}H NMR spectrum of the reaction mixture (AB systems with $^2J_{H,H}$ = 19.4 and 19.8 Hz) characteristic of the geminal protons of the CH_2 group of pyrazoline nuclei, and also singlet signals at 3.1 and 4.2 ppm typical of N- and O-methyl groups respectively. On the basis of these data it may be suggested that two adducts, **2a** and **3a**, are present in the reaction mixture of isothiazole dioxide **1a**, being the products of cycloaddition of diazomethane to N- and O-methylated derivatives of isothiazole 1,1-dioxide.

The hydrogen atom of the N–H group of compounds **1a,b** has an acidic character. In particular, saccharins and their nonaromatic analogs are comparable with acetic acid in acidity [11] and must react with diazomethane very readily. In this connection we assume that initially an exothermic interaction occurs of diazomethane with the amide grouping (NH–C=O) of the saccharin, accompanied by the evolution of nitrogen, and leading to the formation of N- and O-methyl derivatives **2a** and **3a**. Then 1,3-dipolar cycloaddition occurs of one further molecule of diazomethane to the double bond of the compounds formed.



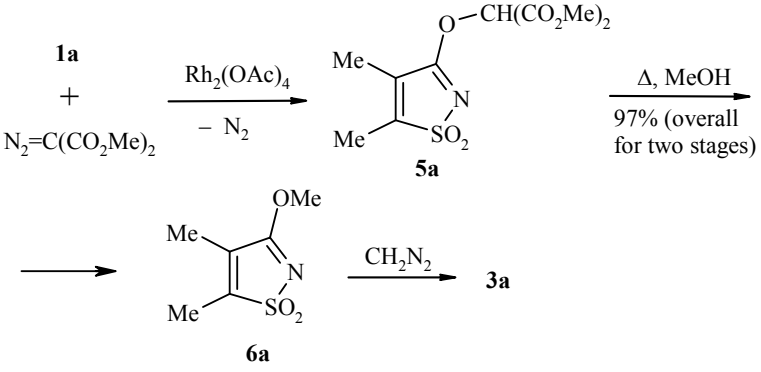
2a **3a**

To confirm this hypothesis we undertook an alternate synthesis of both cycloadducts. Synthesis of compound **2a** was carried out by the scheme shown below. A twofold excess of sodium hydroxide was added to an alcoholic solution of 3-oxo-4,5-isothiazole 1,1-dioxide **1a** and the mixture stirred for 1 h until the formation of the sodium salt of the isothiazolone (check by TLC), then methyl tosylate was added to the reaction mixture.



The isolated N-methylation product of 3-oxo-(2H)-isothiazole 1,1-dioxide – **4a** was reacted with diazomethane, but neither heating of the solution nor evolution of nitrogen were observed. The cycloadduct obtained as a result of this reaction was identical in every parameter with the compound isolated from the reaction mixture of isothiazolone dioxide **1a** with an excess of diazomethane.

The key stages of obtaining compound **3a** are the O-alkylation of the imide carbonyl group with diazo compounds and the subsequent transesterification of the O-alkylimidate under the action of methanol [12, 13].

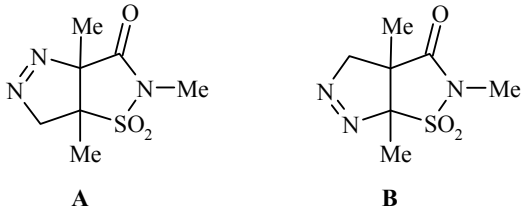


In the first stage of the synthesis, as a result of the catalytic decomposition of diazomalonic acid dimethyl ester with dirhodium tetraacetate [14] in the presence of isothiazolone 1,1-dioxide, the O-alkylimidate **5a** was obtained [15], which on boiling in methanol led to the isolation of 3-methoxyisothiazole 1,1-dioxide **6a** in high yield. Treatment of the synthesized O-methylation product of isothiazole 1,1-dioxide with an excess of diazomethane **6a** led to the formation of a compound the spectral data of which were completely in accord with the spectral characteristics of cycloadduct **3a.**

The second stage of the process **5a→6a** is evidently the nucleophilic substitution at the sp^2-hybridized carbon atom C(3) of the heterocycle. Proceeding from literature data on analogous conversions on acyclic imidates [13], we propose that the most probable reaction mechanism comprises the addition of methanol at the C=N double bond of imidate **5a** with subsequent fission of dimethyl tartronate [12].

Analogous results were obtained from the reaction of diazomethane with tetrahydrosaccharin **1b**, and also on carrying out the set of conversions **1b→4b→2b** and **1b→5b→3b** (see EXPERIMENTAL).

A choice between structures **A** and **B** for cycloadduct **2a** and clarification of the direction of addition of diazomethane to the C=C double bond of isothiazole 1,1-dioxides **4a,b** and **6a,b** was made with the aid of HETCOR and HMBC methods of two-dimensional NMR spectroscopy.



It is evident that in the case of structure **A** cross peaks must be observed in the HMBC spectrum of pyrazole **2a** for the carbon atoms of the CH_2 and C=O groups with the protons of different bridge methyl groups, while for structure **B** the signals of the carbon atoms of the methylene and carbonyl groups must give cross peaks in the HMBC spectra with the very same methyl group. The investigations carried out showed that the carbon atom of the CH_2 group of pyrazole **2a** at 86.9 ppm gives a cross peak with the protons of the methyl group at 1.5, but the carbon of the carbonyl group at 162.6 gives a cross peak with the protons of the other CH_3 group (at 1.7 ppm), which indicates conclusively in favor of structure Δ^1-pyrazole **A**.

The structure of pyrazoline **2a**, one of the cycloadducts of diazomethane obtained with 4,5-dialkyl-substituted isothiazole 1,1-dioxides 1, was established unequivocally with the aid of X-ray structural analysis (Fig. 1 and Tables 1, 2). According to the data obtained the isothiazole (N(1)–S(1)–C(3)–C(2)–C(1)) and pyrazole (C(3)–C(4)–N(3)–N(2)–C(2)) rings are not completely planar and the mean deviation from the plane of the first was 0.864, and of the second 0.0852 Å, i.e. an order of magnitude less. The dihedral angle between the planes of these rings was 111.1°.

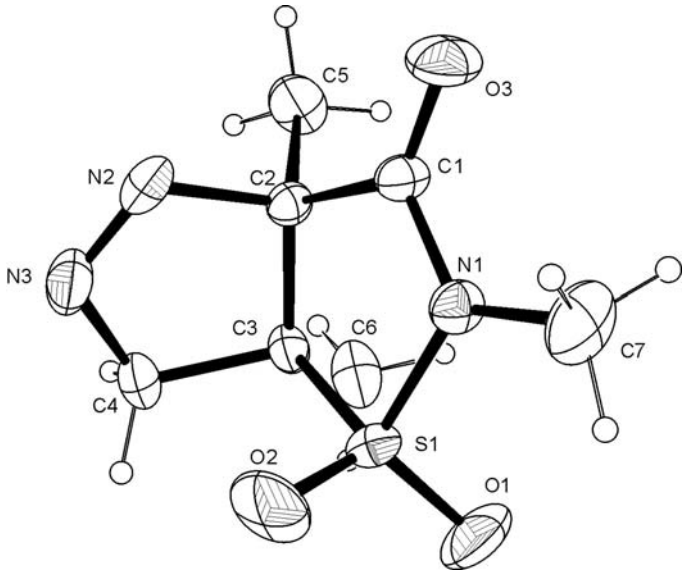


Fig. 1. Molecular structure of compound **2a** according to data of X-ray structural analysis.

TABLE 1. Main Bond Lengths (*d*) in the Compound **2a** Molecule

Bond	*d*, Å	Bond	*d*, Å
C(1)–O(3)	1.199(3)	C(3)–S(1)	1.812(2)
C(1)–N(1)	1.371(3)	C(4)–N(3)	1.459(4)
C(1)–C(2)	1.512(3)	C(7)–N(1)	1.468(3)
C(2)–C(5)	1.525(3)	N(1)–S(1)	1.645(2)
C(2)–N(2)	1.519(3)	N(2)–N(3)	1.236(3)
C(2)–C(3)	1.528(3)	O(1)–S(1)	1.415(2)
C(3)–C(6)	1.522(3)	O(2)–S(1)	1.425(2)
C(3)–C(4)	1.531(3)		

TABLE 2. Main Valence (ω) and Torsional (τ) Angles in the Compound **2a** Molecule

Angle	ω, deg.	Angle	τ, deg.
O(3)–C(1)–N(1)	123.5(2)	N(1)–C(1)–C(2)–C(5)	-142.8(2)
O(3)–C(1)–C(2)	125.7(2)	N(1)–C(1)–C(2)–N(2)	100.0(2)
N(1)–C(1)–C(2)	110.75(17)	N(1)–C(1)–C(2)–C(3)	-12.3(3)
C(1)–C(2)–C(5)	111.56(19)	C(1)–C(2)–C(3)–C(6)	-99.5(2)
C(1)–C(2)–N(2)	107.17(18)	C(5)–C(2)–C(3)–C(6)	28.9(3)
C(5)–C(2)–N(2)	107.30(18)	N(2)–C(2)–C(3)–C(6)	145.9(2)
C(1)–C(2)–C(3)	110.92(16)	C(1)–C(2)–C(3)–C(4)	133.95(19)
C(5)–C(2)–C(3)	115.7(2)	C(5)–C(2)–C(3)–C(4)	-97.7(2)
N(2)–C(2)–C(3)	103.46(17)	N(2)–C(2)–C(3)–C(4)	19.3(2)
C(6)–C(3)–C(2)	117.9(2)	C(1)–C(2)–C(3)–S(1)	20.9(2)
C(6)–C(3)–C(4)	114.95(19)	C(5)–C(2)–C(3)–S(1)	149.21(16)
C(2)–C(3)–C(4)	101.62(17)	N(2)–C(2)–C(3)–S(1)	-93.75(15)
C(6)–C(3)–S(1)	109.53(17)	C(6)–C(3)–C(4)–N(3)	-147.7(2)
C(2)–C(3)–S(1)	102.51(13)	C(2)–C(3)–C(4)–N(3)	-19.2(2)
C(4)–C(3)–S(1)	109.36(16)	S(1)–C(3)–C(4)–N(3)	88.7(2)
N(3)–C(4)–C(3)	105.9(2)	C(2)–C(1)–N(1)–C(7)	-177.4(2)
C(1)–N(1)–C(7)	123.3(2)	C(2)–C(1)–N(1)–S(1)	-4.2(2)
C(1)–N(1)–S(1)	115.25(14)	C(1)–C(2)–N(2)–N(3)	-131.4(2)
C(7)–N(1)–S(1)	121.12(18)	C(5)–C(2)–N(2)–N(3)	108.7(2)
N(3)–N(2)–C(2)	112.1(2)	C(3)–C(2)–N(2)–N(3)	-14.1(2)
N(2)–N(3)–C(4)	112.63(19)	C(2)–N(2)–N(3)–C(4)	1.4(3)
O(1)–S(1)–O(2)	116.86(18)	C(3)–C(4)–N(3)–N(2)	11.9(3)
O(1)–S(1)–N(1)	108.27(13)	C(1)–N(1)–S(1)–C(3)	15.41(18)
O(2)–S(1)–N(1)	109.41(15)	C(7)–N(1)–S(1)–C(3)	-171.2(2)
O(1)–S(1)–C(3)	114.10(14)	C(6)–C(3)–S(1)–N(1)	105.60(17)
O(2)–S(1)–C(3)	110.41(12)	C(2)–C(3)–S(1)–N(1)	-20.34(14)
N(1)–S(1)–C(3)	95.60(9)	C(4)–C(3)–S(1)–N(1)	-127.60(16)

Attempts to carry out the cycloaddition of an aryl-substituted homolog of diazomethane, *viz*. phenyldiazomethane, to 4,5-dialkyl-substituted 3-oxo-(2H)-isothiazole 1,1-dioxides **1a,b** were unsuccessful. After maintaining an ether solution of isothiazoles **1** with a fivefold excess of phenyldiazomethane for 15 days at room temperature, the formation of the presumed cycloadduct was not observed according to data of TLC and ^{1}H NMR spectra of the reaction mixture. Probably the bulky aryl group in the 1,3-dipole hinders the interaction of dialkylisothiazolone dioxides with phenyldiazomethane.

We have therefore established for the first time, that on interacting an excess of diazomethane with 4,5-dialkyl-substituted 3-oxo-(2H)-isothiazolone 1,1-dioxides, initially parallel alkylation of the N and O atoms of the ambident NH-C=O system of the isothiazolone occurs with the formation of a mixture of N- and O-methyl derivatives in a ratio of ~3:2. Subsequent cycloaddition of diazomethane to the C=C bond of the N- and O-methylisothiazole 1,1-dioxides proceeds regioselectively and leads to the formation of bicyclic Δ^1-pyrazoles. Under analogous conditions phenyldiazomethane does not react with disubstituted 3-oxo-(2H)-isothiazole 1,1-dioxides.

EXPERIMENTAL

The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker DRX 400 (400 and 100 MHz respectively) instrument and on a Bruker DRX 600 (600 and 150 MHz respectively) in $CDCl_3$ solution, internal standard was TMS. The IR spectra were recorded on an ATI Mattson Genesis Series FTIR instrument, with Fourier

transformation, in KBr disks. The UV spectra were obtained on a Beckman DU 650 instrument, the mass spectra by electron impact with direct insertion of sample into the ionization chamber, energy of ionizing electrons was 70 eV. Separation of reaction mixtures was carried out by flash chromatography on Chemapol L 40/100 silica gel or silica gel Merck 0.063-0.2 mm. The course of reactions was followed by TLC on Silufol UV-vis (254 nm) plates, visualization was in UV light and/or iodine vapor.

Methylene chloride was redistilled over P_2O_5 immediately before use, petroleum ether of bp 35-65°C was used.

Diazomethane was obtained by the method given in [10]. A 40% KOH solution (30 ml) was added to ether (10 ml), the mixture was cooled to 5°C and N-nitrosomethylurea (10 g) was added with stirring to the mixture. The dark-yellow ether layer of diazomethane was separated by decantation and dried for 3 h with granulated potassium hydroxide.

Phenyldiazomethane was obtained analogously from N-nitrosobenzylurea [10].

Diazomalonic Acid Dimethyl Ester. *p*-Nitrobenzenesulfonyl azide (12.1 g: 50 mmol) was added to a solution of dimethyl malonate (8 g, 50 mmol) in methylene chloride (10 ml). A solution of triethylamine (5.05 g, 50 mmol) in methylene chloride (5 ml) was then added dropwise with stirring and cooling, and the reaction mixture was left for 24 h at ~ 20°C. *p*-Nitrotoluenesulfonylamide was filtered off, the reaction mixture was washed with a 3% solution of NaOH (2 g, 50 mmol) in water (65 ml), dried over $MgSO_4$, the solvent was distilled, the oily substance obtained was chromatographed on a column (silica gel Merck 0.063-0.3 mm) in the system petroleum ether–Et_2O, 1:1. The isolated diazo compound was distilled in vacuum. Yield of diazomalonic ester was 9 g (90%); bp 44-45°C (0.1 mm Hg). The data corresponded to those given in the literature [12].

4,5-Dimethyl-3-oxo-(2H)-isothiazole 1,1-Dioxide (1a) was obtained by the method of [5, 11], mp 164°C.

Interaction of 4,5-Dimethyl-3-oxo-(2H)-isothiazole 1,1-Dioxide (1a) with Diazomethane. A tenfold excess of an ether solution of diazomethane was added slowly with stirring and cooling at 0°C to an ether solution of 4,5-dimethyl-3-oxo-(2H)-isothiazole 1,1-dioxide (500 mg, 2.85 mmol). On adding the first portions of diazomethane instant decolorization and warming of the solution was observed, and also evolution of gas. When decolorization of the solution and evolution of gas had finished, the remaining solution of diazomethane was added rapidly and the reaction mixture acquired a saturated yellow coloration.The reaction mixture was left at room temperature protected from light for 2-3 days (until complete disappearance of the yellow color from the solution). The precipitated solid was then dissolved in methylene chloride, and filtered from undissolved polymethylene. According to data of TLC and ^{1}H NMR spectra a mixture was formed in the reaction mixture of two cycloadducts **2a** and **3a** in a ratio of 3:2, compound **2a** was isolated by crystallization from methylene chloride.

The reaction of tetrahydrosaccharin with diazomethane was carried out analogously. According to data of ^{1}H NMR spectroscopy a mixture of cycloadducts **2b** and **3b** was obtained, also in a 3:2 ratio.

2,4,5-Trimethyl-3-oxo-(2H)-isothiazole 1,1-Dioxide (4a). Sodium hydroxide (0.32 g) was added to a solution of compound **1a** (0.55 g, 3.35 mmol) in alcohol (10 ml), the mixture was stirred at room temperature for 1 h (check for the disappearance of the starting material by TLC). Methyl tosylate (1.4 g, 7.5 mmol) was added to the obtained suspension, and the mixture boiled for 30 min. The reaction mixture was dissolved in water (100 ml), extracted with methylene chloride (5×10 ml), and the extract evaporated in vacuum. The oil obtained crystallized on adding a small amount of alcohol. The solid was filtered off and recrystallized from chloroform. Yield was 0.25 g (42%); mp 69-70°C. IR spectrum, ν, cm^{-1}: 2959 (CH_3), 1733 (CO), 1322 (SO_2), 1161 (SO_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.8 (3H, s, CH_3); 2.0 (3H, s, CH_3); 3.1 (3H, s, N–CH_3). ^{13}C NMR spectrum, δ, ppm: 11.2 (CH_3); 11.6 (CH_3); 20.7 (N–CH_3); 160.3 (C=O); 130.1 (C-4, α-C=O); 151.0 (C-5, α-SO_2). Mass spectrum, *m/z* (I_{rel}, %): 175 $[M]^+$ (55). Found, %: C 41.26; H 5.10; N 7.93. $C_6H_9NO_3S$. Calculated, %: C 41.13; H 5.18; N 7.99.

2-Methyl-3-oxo-4,5,6,7-tetrahydro-(2H)-1,2-benzisothiazole 1,1-Dioxide (4b) (2-methyltetrahydro-saccharin) was obtained from tetrahydrosaccharin (0.7 g). Yield was 0.38 g (51%); mp 85°C. IR spectrum, ν, cm^{-1}:

2955 (CH_3, CH_2), 1730 (C=O), 1332 (SO_2), 1162 (SO_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.8 (2H, m, CH_2); 1.9 (2H, m, CH_2); 2.4 (2H, m, CH_2); 2.5 (2H, m, CH_2); 3.1 (3H, s, N–CH_3). ^{13}C NMR spectrum, δ, ppm: 18.9 (CH_2); 20.6 (CH_2); 21.0 (CH_2); 23.5 (CH_2); 21.4 (N–CH_3); 160.5 (C=O); 136.7 (C-9, α-C=O); 146.2 (C-8, α-SO_2). Mass spectrum, *m/z* (I_{rel}, %): 201 $[M]^+$ (35). Found, %: C 47.72; H 5.65; N 6.79. $C_8H_{11}NO_3S$. Calculated, %: C 47.70; H 5.52; N 6.96.

2,7,8-Trimethyl-3-oxoisothiazolo[4,5-*c*]pyrazoline 1,1-Dioxide (2a). A tenfold excess of an ether solution of diazomethane was added to compound **4a** (100 mg, 5.7 mmol). The reaction mixture was left at room temperature in the dark until complete disappearance of the yellow color from the solution. The ether was distilled off in vacuum, the residue was crystallized from methylene chloride having first filtered off polymethylene from the solution. Yield was 122 mg (98.5%); mp 127°C (decomp.). IR spectrum, ν, cm^{-1}: 2926 (CH_3, CH_2), 1735 (CO), 1328 (SO_2), 1161 (SO_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.5 (3H, s, CH_3); 1.7 (3H, s, CH_3); 3.0 (3H, s, N–CH_3); 4.7 (1H, d, ^2J = 19.4, CH_2); 5.5 (1H, d, ^2J = 19.4, CH_2). ^{13}C NMR spectrum, δ, ppm: 15.6 (CH_3); 15.9 (CH_3); 24.9 (N–CH_3); 86.9 (CH_2); 162.6 (CO); 104.9 (C-8, α-C=O); 63.4 (C-7, α-SO_2). Mass spectrum, *m/z* (I_{rel}, %): 217 $[M]^+$ (5). Found, %: C 39.20; H 5.21; N 19.71. $C_7H_{11}NO_3S$. Calculated, %: C 38.70; H 5.06; N 19.35.

2-Methyl-3-oxo-4,5,6,7-tetrahydro-(2H)-1,2-benzisothiazolo[4,5-*c*]pyrazoline 1,1-Dioxide (2b) was obtained analogously from N-methyltetrahydrosaccharin **4b** (100 mg, 5.35 mmol). Yield was 120 mg (96%); mp 132°C (decomp.). IR spectrum, ν, cm^{-1}: 2948 (CH_3, CH_2), 1729 (CO), 1332 (SO_2), 1158 (SO_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.2 (1H, m, CH_2); 1.3 (1H, m, CH_2); 1.4 (1H, m, CH_2); 1.6 (1H, m, CH_2); 1.7 (1H, m, CH_2); 1.9 (1H, m, CH_2); 2.2 (1H, s, CH_3); 2.8 (1H, s, CH_3); 3.0 (3H, s, N–CH_3); 4.7 (1H, d, ^2J = 19.2, CH_2); 5.5 (1H, d, ^2J = 19.2, CH_2). ^{13}C NMR spectrum, δ, ppm: 18.5 (CH_2); 19.5 (CH_2); 25.2 (CH_2); 27.4 (CH_2); 25.3 (N–CH_3); 83.1 (CH_2); 162.7 (C=O); 100.1 (C-3a, α-C=O); 63.7 (C-7a, α-SO_2). Mass spectrum, *m/z* (I_{rel}, %): 243 $[M]^+$ (6). Found, %: C 44.81; H 5.77; N 16.80. $C_9H_{13}NO_3S$. Calculated, %: C 44.39; H 5.39; N 17.27.

3-Methoxy-4,5-dimethylisothiazole 1,1-Dioxide (6a). Dimethyl diazomalonate (0.43 g, 2.71 mmol) was added to a solution of compound **1a** (0.39 g, 2.42 mmol). Then dirhodium tetraacetate (11 mg, 0.024 mmol) was added with stirring and the mixture was left stirring for 5 h. At the end of the decomposition of the diazo compound (check by TLC), the reaction mixture was chromatographed on a small column of silica gel, eluting with a pentane–ether, 1:1 mixture. After distilling off the solvent, yellow-green oily **5a** was obtained which without further purification was dissolved in methyl alcohol (10 ml) and boiled for 3 h. The solvent was distilled in vacuum, and the residue washed with a small volume of ether. Yield was 0.41 g (97%); mp 75-76°C. IR spectrum, ν, cm^{-1}: 2956 (CH_3), 1577 (C=N), 1321 (SO_2), 1173 (SO_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.8 (3H, s, CH_3); 2.1 (3H, s, CH_3); 4.0 (3H, s, O–CH_3). ^{13}C NMR spectrum, δ, ppm: 8.6 (CH_3); 8.9 (CH_3); 58.3 (O–CH_3); 172.9 (C=O); 128.0 (C-3, α-C=O); 150.7 (C-5, α-SO_2). Mass spectrum, *m/z* (I_{rel}, %): 175 $[M]^+$ (45). Found, %: C 41.33; H 5.23; N 8.00. $C_6H_9NO_3S$. Calculated, %: C 41.13; H 5.18; N 7.99.

3-Methoxy-4,5,6,7-tetrahydro-1,2-benzisothiazole 1,1-Dioxide (6b) was obtained by an analogous method from tetrahydrosaccharin **1b** (0.47 g, 2.5 mmol). Yield was 0.49 g (98%), oily substance. IR spectrum, ν, cm^{-1}: 2960 (CH_3, CH_2), 1575 (C=N), 1321 (SO_2), 1167 (SO_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm : 1.7 (2H, m, CH_2); 1.9 (2H, m, CH_2); 2.2 (2H, m, CH_2); 2.4 (2H, m, CH_2); 4.0 (3H, s, O–CH_3). ^{13}C NMR spectrum, δ, ppm: 18.3 (CH_2); 19.3 (CH_2); 20.0 (CH_2); 22.6 (CH_2); 59.1 (O–CH_3); 172.9 (C=O); 135.9 (C-3, α-C=O); 146.1 (C-5, α-SO_2). Mass spectrum, *m/z* (I_{rel}, %): 201 $[M]^+$ (23). Found, %: C 47.92; H 5.69; N 6.90. $C_8H_{11}NO_3S$. Calculated, %: C 47.70; H 5.52; N 6.96.

3-Methoxyisothiazolo[4,5-*c*)pyrazoline 1,1-Dioxide (3a). A tenfold excess of an ether solution of diazomethane was added to compound **6a** (100 mg, 5.7 mmol). The reaction mixture was left at room temperature without access to light until complete disappearance of the yellow color of the solution. The ether was distilled in vacuum, the solid was recrystallized from methylene chloride, after first filtering polymethylene from the solution. Yield 118 mg (95%); mp 138°C (decomp.). IR spectrum, ν, cm^{-1}: 2945 (CH_3, CH_2), 1568 (C=N), 1323 (SO_2), 1155 (SO_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.5 (3H, s, CH_3); 1.7 (3H, s, CH_3); 4.2 (3H, s, N–CH_3); 4.8 (1H, d, ^2J = 19.8, CH_2); 5.7 (2H, d, ^2J = 19.8, CH_2). ^{13}C NMR spectrum, δ, ppm: 15.7 (CH_3); 16.2 (CH_3); 59.0 (O–CH_3);

88.1 (CH_2); 173.5 (C=O); 104.9 (C-3a, α-C=O); 64.8 (C-7a, α-SO_2). Mass spectrum, *m/z* (I_{rel}, %): 217 $[M]^+$ (3). Found, %: C 39.51; H 5.25; N 19.79. $C_7H_{11}NO_3S$. Calculated, %: C 38.70; H 5.06; N 19.35.

3-Methoxy-4,5,6,7-tetrahydro-1,2-benzisothiazolo[4,5-*c*]pyrazoline 1,1-Dioxide (3b) was obtained by an analogous method from 3-methoxytetrahydrosaccharin **6b** (100 mg, 5.35 mmol). Yield 116 mg (89%), oily substance. IR spectrum, ν, cm^{-1}: 2931 (CH_3, CH_2), 1570 (C=N), 1325 (SO_2), 1163 (SO_2). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm (*J*, Hz): 1.2 (1H, m, CH_2); 1.3 (1H, m, CH_2); 1.4 (1H, m, CH_2); 1.5 (1H, m, CH_2); 1.7 (1H, m, CH_2); 1.9 (1H, m, CH_2); 2.2 (1H, s, CH_3); 2.4 (1H, s, CH_3); 4.1 (3H, s, N–CH_3); 4.7 (1H, d, ^2J = 19.2, CH_2); 5.5 (1H, d, ^2J = 19.2, CH_2). ^{13}C NMR spectrum, δ, ppm: 18.7 (CH_2); 19.9 (CH_2); 25.5 (CH_2); 27.5 (CH_2); 60.2 (O–CH_3); 84.3 (CH_2); 173.7 (C=O); 101.7 (C-3a, α-C=O); 65.3 (C-7a, α-SO_2). Mass spectrum, *m/z* (I_{rel}, %): 243 $[M]^+$ (4). Found, %: C 44.81; H 5.77; N 16.80. $C_9H_{13}NO_3S$. Calculated, %: C 44.53; H 5.42; N 16.60.

X-Ray Structural Investigation. Colorless monocrystals of size 0.40×0.40×0.30 mm were obtained on crystallizing adduct **2a** from methylene chloride. The crystals of cycloadduct **2a** were rhombic: a = 10.8266(15), b = 12.8833(17), c = 14.2472(19) Å, V = 1987.2(5) $Å^3$, ρ_{calc} = 1.452 mg/m^3, space group *Pbca*. Recording was carried out at 293(2) K on a Siemens SMART CCD diffractometer using radiation of wavelength 0.71073 Å. Calculation of absorption was carried out using SADABS program [16], and the SHELXS97 program was used to process the structural data [17].

The final divergence factor R [$I > 2\sigma(I)$], R^1 = 0.0441, ωR^2 = 0.1337.

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