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## ISOTHIAZOLO[3,2-*b*]-1,3,4-OXADIAZOLE-5,5-DIOXIDE: SYNTHESIS OF A NEW HETEROPENTALENE SYSTEM

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**Abstract** - Monocyclic, acceptor-substituted *N*-aroylisothiazolium-2-imines (**5a-d**), easily available by cyclocondensation of 2-methyl-3-thiocyanato-2-butenal with aryl hydrazides, are described and the structure of new five-membered azomethine imines (**5**) is determined by X-Ray structure of **5a**. The oxidation of 2-imines (**5**) with hydrogen peroxide in acetic acid gives 3-hydroperoxysultims (*rac-cis* **6**), -sultams (**7**), and 3-oxosultams (**10**). The 3-hydroxysultams (**8a-d**) are obtained by reduction of hydroperoxides (**7**). Surprisingly, after the dehydration of **8a-h** and its 1,5-electrocyclization, a new type of heteropentalenes, the isothiazolo[3,2-*b*]-1,3,4-oxadiazole-5,5-dioxides (**11**) is formed.

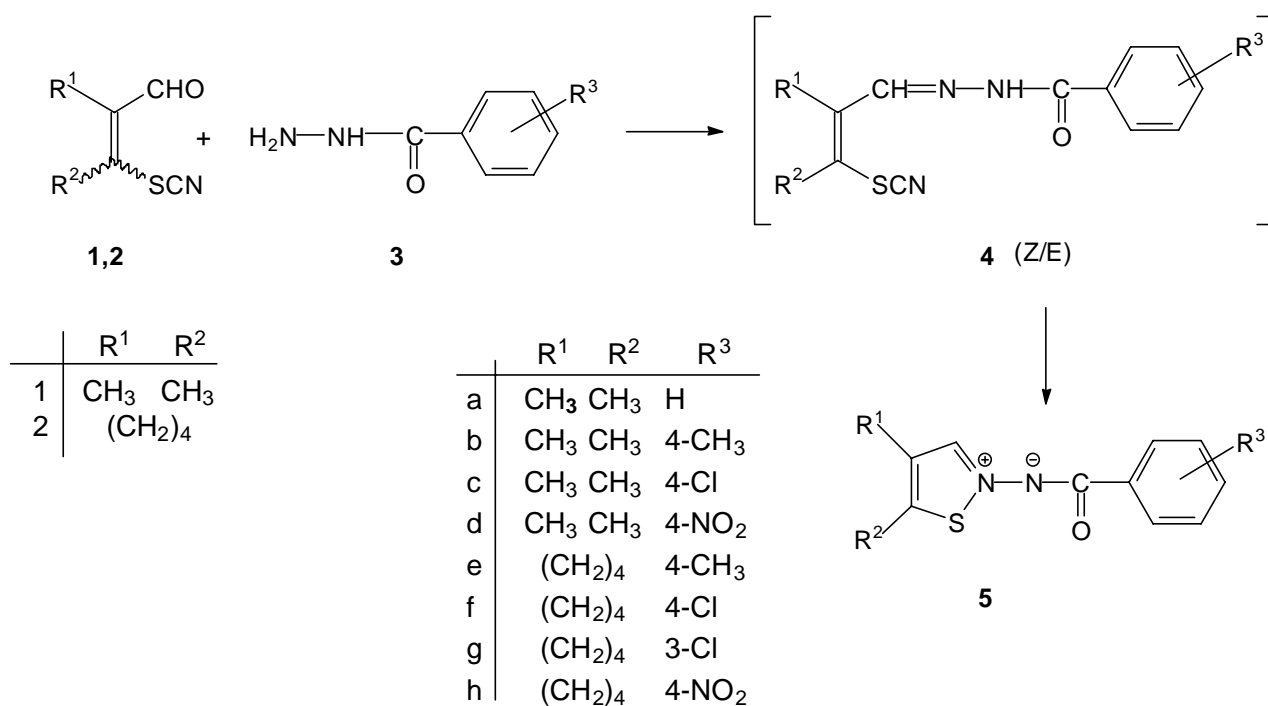
### Introduction

In the course of our research on oxidation of *N*-aroylisothiazolium-2-imines (**5e-h**),<sup>1,2</sup> we investigated the influence of aromatic substituents on the formation of bicyclic 3-hydroperoxysultims (**6f-h**) and 3-hydroperoxysultams (**7e-h**).<sup>3</sup> It was shown that only sultims containing electron-withdrawing groups at the aryl ring are accessible. Using the *N*-benzenesulfonyl analogues<sup>4</sup> of **5**, a ring enlargement to the corresponding 1,2,3-thiadiazines was observed upon oxidation.<sup>5,6</sup> Relatively little is known about the syntheses and use of 1,2,3-thiadiazine heterocycles.<sup>7,8</sup> In this paper we would like to present the synthesis of another class of substances, the hitherto unknown isothiazolo[3,2-*b*]-1,3,4-oxadiazole-5,5-dioxides

(11). These substances containing two condensed five-membered heterocyclic rings are called heteropentalenes.

## RESULTS AND DISCUSSION

The synthesis of the bicyclic precursors (**5–8e–h**) follows a known procedure starting from  $\beta$ -thiocyanatovinyl aldehyde (**2**) and the corresponding benzhydrazides.<sup>1,3</sup> Dimethyl derivatives (**5–8a–d**) were prepared in an analogous way. The reaction of the benzhydrazides (**3**) with the aldehyde (**1**) in ethanol at room temperature gives a mixture of *Z/E*-hydrazones.<sup>4</sup> Cyclisation to **5** occurs on refluxing in ethanol for several hours. The cyclized *N*-aroylisothiazolium-2-imines (**5a–d**) crystallize leaving the unreacted *E*-hydrazone in the mother liquor. Alternative cyclisation of **4** to 1,2,3-thiadiazine is not observed.<sup>9,10</sup>



Scheme 1

The successful ring closure can be determined with IR and <sup>13</sup>C-NMR spectrum, and a disappearing SCN-signal at about 2160 cm<sup>-1</sup> and 110 ppm respectively is observed. In the IR spectra, a shift to significant lower values between 1570 and 1590 cm<sup>-1</sup> takes place. These values are in conformity with other heteroaromatic *N*-aroylimines, and indicate a strong polarization of the carbonyl group. The following NMR spectral signals are characteristic of the imines (**5**) ranging from 8.59 to 8.65 ppm (H-

3), 142.5 to 145.1 ppm (C-3), and 164.1 to 168.8 ppm (CO). The structure of compound (**5a**) can be determined by X-Ray structure analysis (Figure 1).

The bond lengths of the isothiazole ring in the stable azomethine imine (**5a**) and its planar shape indicate electron delocalisation with the participation of the acylamino group. The least square plane of the molecule, calculated without methyl groups and hydrogen atoms, gives a mean deviation of 0.043 Å from this plane. The crystal packing of **5a** is stabilized by a short non-bonded intramolecular S1-O1 1,5-interaction (2.439(1) Å).

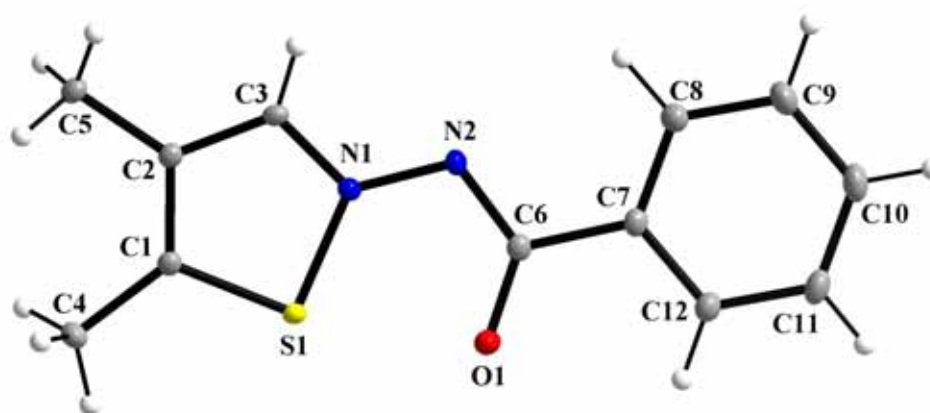


Figure 1. X-Ray crystal structure of **5a**.

Selected distances (Å), angles and torsion angles (°):

C1-C2 1.377(2), C3-N1 1.332(1), N1-N2 1.376(1), N2-C6 1.334(2), C6-C7 1.493(2), S1-O1 2.439(2), C1-S1-N1 90.82(5), C3-N1-S1 112.2(1), C3-N1-N2 120.9(1), N1-N2-C6 112.9(1), N2-C6-C7 114.6(1), C3-N1-S1-C1 0.48, C1-S1-N2-N1 0.59, C2-C3-N1-N2 179.78, S1-N1-N2-C6 5.68, N1-N2-C6-O1 1.85, N2-C6-C7-C8 1.82.

The imines (**5**) are oxidized to the hydroperoxy sultams (**7a-d**) with 30% H<sub>2</sub>O<sub>2</sub> / glacial acetic acid at room temperature. In the case of acceptor-substituted compounds (**5c,d**), two stable *rac-cis* hydroperoxysultams (**6c,d**) can be isolated using a reaction temperature of 0°C. These sultams can be easily determined by their <sup>13</sup>C-NMR spectral signal at C-3 (102.2 and 100.8 ppm). The prolongation of the reaction time at room temperature gives the corresponding hydroperoxy sultams (**7c,d**) with <sup>13</sup>C-NMR spectral signals of C-3 at higher field ranging from 93.8 to 94.7. If the oxidation is carried out for 8 hrs at 80 °C 3-oxosultams (**10c,d**) are formed with compounds having an acceptor substituent at the aromatic ring. The <sup>13</sup>C-NMR spectra show characteristic values of 160 ppm for C-3. The X-Ray structure of **10d** (Figure 2) shows two intermolecular hydrogen bonds.

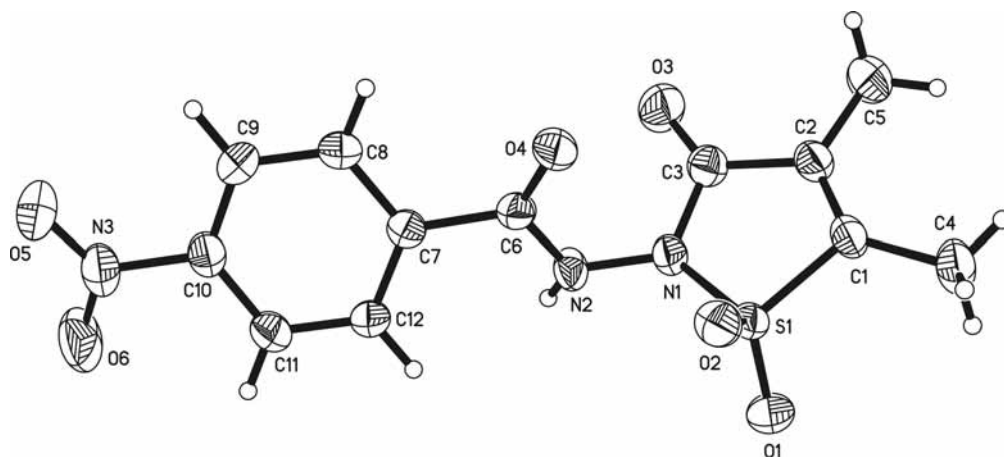


Figure 2. X-Ray crystal structure of **10d**.

Selected distances (Å), angles and torsion angles (°):

C1-C2 1.336(2), C2-C3 1.491(2), C3-N1 1.403(2), N1-N2 1.3823(17), S1-O4 3.501,  
 N1-S1-C1 92.59(7), C3-N1-S1 112.77(11), C3-N1-N2 121.52(12), C6-N2-N1  
 118.93(13), N2-C6-C7 113.84(13), C3-N1-S1-C1 9.41, C1-S1-N2-N1 161.34, C2-C3-  
 N1-N2 162.0, S1-N1-N2-C6 90.01, N1-N2-C6-O4 5.14, N2-C6-C7-C8 25.97.

The oxygen of the hydrazido-carbonyl group and one oxygen of the SO<sub>2</sub>-group act as acceptor atoms. The 1-dimensional chains are formed along the crystallographic b-axis by translation of the lattice constant value ( $b = 4.759(1)$  Å). Thus the phenyl ring are stacked with the same value (Figure 3).

Usually the reduction of the hydroperoxide to the corresponding hydroxy compound (**8**) is achieved by stirring with aqueous Na<sub>2</sub>SO<sub>3</sub> for several hours (method A).<sup>3</sup> Now, by stirring the hydroperoxide (**7**) in DMSO and gentle warming for a few minutes (method B), we found another way of reduction. After that, a small amount of water was added, the mixture was lyophilised, and the 3-hydroxysultams (**8a-d**) were obtained in excellent yields.

The short reaction time and significantly higher yields are the advantages of the new method. The characteristic <sup>13</sup>C-NMR spectral signals at C-3 for hydroxy compounds (**8a-d**) show values between 83.8 and 85.5 ppm.

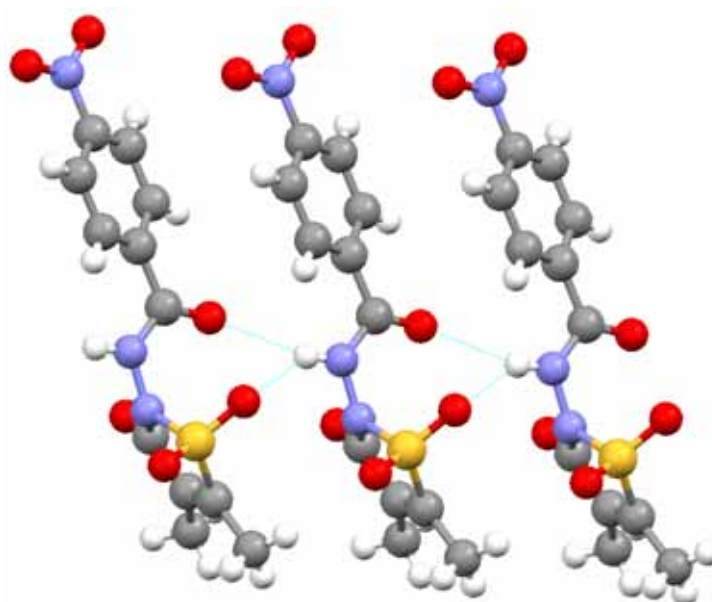
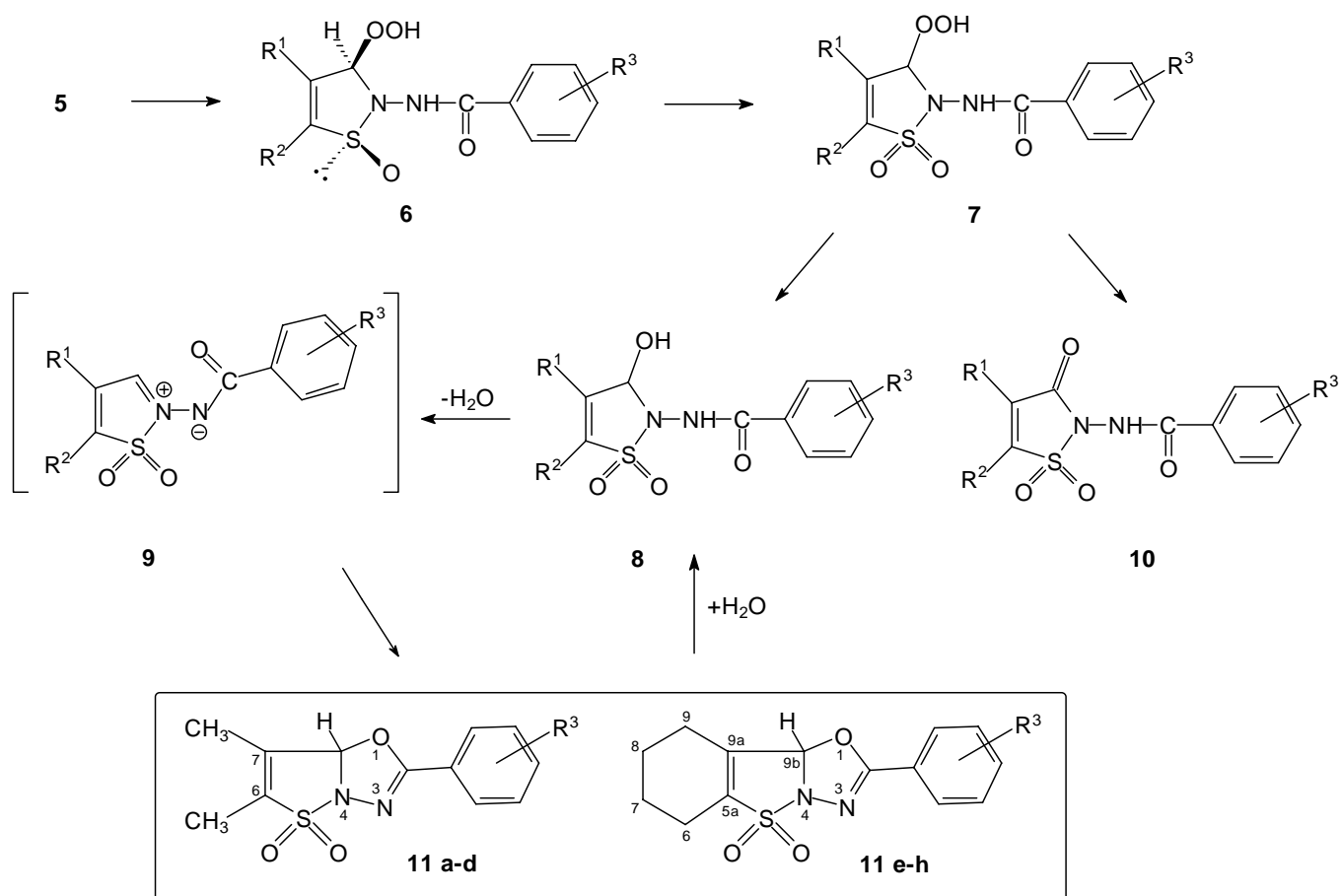


Figure 3. Polymer arrangement of **10d** by hydrogen bonds  
 $\text{SO}_2 \cdots \text{NH}'$  (2.238 Å) and  $\text{O}_4 \cdots \text{NH}'$  (2.521 Å).

We expected the formation of the dehydrated azomethin imine (**9**) upon refluxing the hydroxysultams (**8a-h**) in toluene, but we surprisingly isolated the cyclisation product, isothiazolo[3,2-*b*]-1,3,4-oxadiazole-5,5-dioxide (**11b-h**). The mechanism of this reaction can be explained with an elimination-cyclisation cascade-reaction. The elimination of water from **8** produces an unstable *N*-aroylisothiazole-2-imine 1,1-dioxide (**9**), which reacts *via* a 1,5-electrocyclization to the novel heteropentalene (**11**).

The structure of **8d** was investigated with NMR spectrum in DMSO- $d_6$  ( $^1\text{H}$ ,  $^{13}\text{C}$ , HMQC, HMBC, (1,1)-ADEQUATE). The NH at 10.90 ppm gives in the HMBC (8 Hz) spectrum a correlation cross peak to the carbonyl group at 165.13 ppm (caused by coupling *via* two bonds). A cross peak to this carbonyl group was also found from the H-2',6' protons of the aryl ring (coupling *via* three bonds). The OH appears in the proton spectrum as broadened singlet at 7.18 and H-3 at 5.51 ppm (corresponding to C-3 at 84.04 (HMQC)). In HMBC, only the  $\text{CH}_3$  singlet at 1.92 ppm shows a cross peak to 84.04, indicating that this methyl group is bonded to C-4. Additionally, a correct assignment was possible with the use of an (1,1)-ADEQUATE spectrum. Therefore, cross peaks from 5.51 ppm (H-3) to 225.1 (the sum of carbon chemical shifts of C-3 and C-4), from 1.92 ppm to 153.9 (sum of  $\text{CH}_3$  and C-4), and from 2.01 ppm to 136.9 (the sum of the other  $\text{CH}_3$  and C-5) furnish the carbon connection in the heterocyclic part of the molecule.



Scheme 2

The structure of diazepamantene (**11d**) was also established using NMR spectroscopic methods ( $^1\text{H}$ ,  $^{13}\text{C}$ , HMQC, HMBC). The ring formation could be identified especially from the HMBC spectrum. The singlet of H-6a proton at 6.80 ppm (corresponding to C-6a at 95.68 ppm (HMQC)) gives (besides expected cross peaks to 139.06 (C-6) and 131.68 (C-5)) a cross peak to C-2 at 157.52 ppm (C,H coupling via three bonds). Also a cross peak to 157.52 was found from the H-2',6' signal at 8.09 ppm.

When, after 3 days, **11d** was measured in water containing DMSO- $d_6$ , two sets of signals could be observed in the  $^{13}\text{C}$  NMR spectrum. One corresponds to **11d**, but the other to **8d**. This means that **11d** can be easily hydrolysed back to **8d**. Therefore, a quantitative ring opening of **11d** could be also achieved by refluxing the compound with water containing toluene.

## EXPERIMENTAL

Melting points were measured on a Boetius micro-melting-point apparatus and are corrected. Spectral data were recorded on the following spectrometers: IR spectra, ATI Mattson Genesis FTIR Unicam Analytical System;  $^1\text{H}$ -NMR /  $^{13}\text{C}$ -NMR, Varian Gemini 200, Varian Gemini 300, Bruker DRX 600, Bruker DRX 700,  $\sigma$  in ppm rel. to TMS as internal standard,  $J$  in Hz; EI-MS, VG 12-250 and Thermo

Electron MAT95XP, 70 eV, ESI-MS Bruker APEX II (7 Tesla); Elemental analysis, Heraeus CHNO Rapid Analyzer.

***N*-Aroylisothiazolium-2-imines (5):**

(*Z/E*)-2-Methyl-3-thiocyanato-2-butenal (**1**) (1.4g, 10 mmol) was dissolved in ethanol (30 mL) and a suspension of the hydrazide (**3**) (10 mmol) in water (30 mL) was added. After stirring at rt for 1 h, a mixture of *Z/E*-hydrazones precipitates was filtered off and refluxed in ethanol (60 mL) for 3-4 h. After cooling, the crystals were filtered off and re-crystallized from ethanol to yield compound (**5**).

***N*-Benzoyl-4,5-dimethyl-isothiazolium-2-imine (5a):**

Yield: (60%, colorless needles); mp 153-155 °C; IR (KBr)  $\nu$ : 3060, 1589 (CO), 1532, 1363, 1046  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.65 (s, 1H, H-3), 8.17 (m, 2H, H-Ar), 7.45 (m, 3H, H-Ar), 2.45 (s, 3H,  $\text{CH}_3$ ), 2.23 (s, 3H,  $\text{CH}_3$ );  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 168.2 (CO), 149.5 (C-5), 142.7 (C-3), 135.7 (C-1'), 130.7 (C-4'), 128.3 (Ar-CH), 127.8 (Ar-CH), 123.8 (C-4), 11.4 ( $\text{CH}_3$ ), 11.2 ( $\text{CH}_3$ ). EI-MS  $m/z$  232 ( $\text{M}^+$ , 12), 105 (100), 77 (57), 67 (4), 59 (11). *Anal.* Calcd for  $\text{C}_{12}\text{H}_{12}\text{N}_2\text{OS}$ : C 62.04; H 5.21; N 12.06; S 13.80. Found: C 61.96; H 4.99; N 12.38; S 13.66.

**Crystal Data for 5a:**  $\text{C}_{12}\text{H}_{12}\text{N}_2\text{OS}$ , MW 232.22, triclinic, space group P-1,  $a = 6.602(2)$ ,  $b = 7.178(4)$ ,  $c = 12.291(3)$  Å,  $\alpha = 78.6(3)$ ,  $\beta = 89.5(11)$ ,  $\gamma = 71.00(1)$ ,  $V = 539.0$  Å<sup>3</sup>,  $F(000) = 244$ ,  $Z = 2$ ,  $T = 20$  °C,  $\mu(\text{MoK}\alpha) = 0.278$   $\text{mm}^{-1}$ ,  $D = 1.431$   $\text{g}\cdot\text{cm}^{-3}$ , GOF = 0.95,  $wR(F^2) = 0.1033$  (all 3678 data),  $R = 0.0385$  (3309 data with  $I > 2\sigma I$ ).

Crystallographic measurements were made using a AXS BRUKER 1K CCD-detector (graphite monochromated  $\text{MoK}\alpha$  radiation ( $\lambda=0.71073$  Å); empirical absorption correction using SADABS<sup>11</sup>. The structures were solved using direct methods, and refined in the anisotropic approximation for the non-hydrogen atoms using SHELXS-86 and SHELXL-97.<sup>12,13</sup> All hydrogen atoms were located by difference Fourier map and refined isotropically.

Crystallographic data for the structure reported in this paper was deposited with the Cambridge Crystallographic Data Centre as no. CCDC-270926 for **5a**. Copies of the data can be obtained free of charge on application to ccdc, 12 Union Road, Cambridge CB21EZ, UK (fax (+44) 1223-336-033; email: deposit@ccdc.cam.ac.uk).

**4,5-Dimethyl-*N*-(4-methylbenzoyl)isothiazolium-2-imine (5b):**

Yield: (18%, pink needles); mp 211-213 °C; IR (KBr)  $\nu$ : 1580 (CO), 1530, 1360, 1170, 920  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.59 (s, 1H, H-3), 8.03 (d, 2H,  $J = 8.3$  Hz, H-Ar), 7.21 (d, 2H,  $J = 8.3$  Hz, H-Ar), 2.44 (s, 3H,  $\text{CH}_3$ ), 2.39 (s, 3H, Ph- $\text{CH}_3$ ), 2.17 (s, 3H,  $\text{CH}_3$ );  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 168.8 (CO), 149.3 (C-5), 142.5 (C-3), 141.1 (C-4'), 133.5 (C-1'), 129.4 (Ar-CH), 128.1 (Ar-CH), 123.9 (C-4), 11.9 (Ph- $\text{CH}_3$ ), 11.6 ( $\text{CH}_3$ ), 11.4 ( $\text{CH}_3$ ). EI-MS  $m/z$  246 ( $\text{M}^{+\bullet}$ , 35), 218 (8), 175 (6), 119 (100), 91 (25). *Anal.* Calcd for  $\text{C}_{13}\text{H}_{14}\text{N}_2\text{OS}$ : C 63.39; H 5.73; N 11.37; S 13.02. Found: C 63.42; H 5.54; N 11.20; S 13.31.

***N*-(4-Chlorobenzoyl)-4,5-dimethylisothiazolium-2-imine (5c):**

Yield: (32%, yellow prisms); mp 214-216 °C; IR (KBr)  $\nu$ : 3080, 1590 (CO), 1520, 1370, 750  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 9.02 (s, 1H, H-3), 7.98 (d, 2H,  $J = 8.4$ , H-Ar), 7.48 (d, 2H,  $J = 8.4$ , H-Ar), 2.46 (s, 3H,  $\text{CH}_3$ ), 2.19 (s, 3H,  $\text{CH}_3$ );  $^{13}\text{C-NMR}$  ( $\text{DMSO-d}_6$ )  $\delta$ : 165.1 (CO), 149.9 (C-5), 144.0 (C-3), 134.7 (C-4'), 133.8 (C-1'), 128.8 (Ar-CH), 128.0 (Ar-CH), 124.1 (C-4), 10.8 ( $\text{CH}_3$ ), 10.3 ( $\text{CH}_3$ ). MS  $m/z$  266 ( $\text{M}^{+\bullet}$ , 18), 139 (100), 111 (20), 75 (11). *Anal.* Calcd for  $\text{C}_{12}\text{H}_{11}\text{N}_2\text{OClS}$ : C 54.03; H 4.16; N 10.50; S 12.02. Found: C 54.07; H 4.34; N 10.83; S 12.40.

**4,5-Dimethyl-*N*-(4-nitrobenzoyl)isothiazolium-2-imine (5d):**

Yield: (42%, yellow prisms); mp 278-279 °C; IR (KBr)  $\nu$ : 1570 (CO), 1540 ( $\text{NO}_2$ ), 1340 ( $\text{NO}_2$ ), 710  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 8.60 (s, 1H, H-3), 8.26 (m, 4H, H-Ar), 2.47 (s, 3H,  $\text{CH}_3$ ), 2.45 (s, 3H,  $\text{CH}_3$ );  $^{13}\text{C-NMR}$  ( $\text{CDCl}_3$ )  $\delta$ : 164.1 (CO), 151.2 (C-5), 148.4 (C-4'), 145.1 (C-3), 142.1 (C-1'), 128.3 (Ar-CH), 124.6 (C-4), 123.5 (Ar-CH), 11.1 ( $\text{CH}_3$ ), 10.5 ( $\text{CH}_3$ ). EI-MS  $m/z$  277 ( $\text{M}^{+\bullet}$ , 56), 150 (100), 104 (28), 76 (32). *Anal.* Calcd for  $\text{C}_{12}\text{H}_{11}\text{N}_3\text{O}_3\text{S}$ : C 51.98; H 4.00; N 15.15; S 11.56. Found: C 52.11; H 3.71; N 15.41; S 11.60.

**2-Aroylamino-4,5-dimethyl-3-hydroperoxy-2,3-dihydroisothiazole 1-oxide (6):**

Isothiazolium-2-imine (**5**) (1.7 mmol) was dissolved in glacial acetic acid (8 mL), cooled to 0 °C, and then hydrogen peroxide (30%, 1 mL, 8.8 mmol) was added. After 5 min, another 4 mL (35 mmol) of hydrogen peroxide was given to the solution and stirring was continued at 0 °C for 60 min. The precipitate was filtered off, washed with ether, and recrystallized from ethanol.

**2-(4-Chlorobenzoylamino)-4,5-dimethyl-3-hydroperoxy-2,3-dihydroisothiazole 1-oxide (6c):**

Yield: (16%, colorless crystals); mp 131 - 132 °C; IR (KBr)  $\nu$ : 3190, 2320, 1650 (CO), 1530, 1320, 1060 (SO)  $\text{cm}^{-1}$ ;  $^1\text{H-NMR}$  ( $\text{Acetone-d}_6$ )  $\delta$ : 11.11 (s, 1H, OOH), 10.46 (s, 1H, NH), 7.98 (d, 2H,  $J = 8.9$  Hz, H-Ar), 7.57 (d, 2H,  $J = 8.9$  Hz, H-Ar), 5.62 (s, 1H, H-3), 2.02 (s, 3H,  $\text{CH}_3$ -C5), 1.95 (s, 3H,  $\text{CH}_3$ -C4);  $^{13}\text{C-NMR}$



NMR (Acetone- $d_6$ )  $\delta$ : 168.1 (CO), 141.0 (C-4), 139.6 (Ar-C), 132.1 (C-5), 130.9 (Ar-CH), 130.4 (Ar-CH), 130.1 (Ar-C), 102.2 (C-3), 13.3 (CH<sub>3</sub>), 11.0 (CH<sub>3</sub>). EI-MS  $m/z$  316 ( $M^{+\bullet}$ , 4), 299 (15), 266 (12), 234 (73), 206 (48), 180 (41), 156 (87), 139 (100), 111 (33), 75 (14). *Anal.* Calcd for C<sub>12</sub>H<sub>13</sub>N<sub>2</sub>O<sub>4</sub>ClS: C 45.50; H 4.14; N 8.84; S 10.12. Found: C 45.16; H 4.20; N 8.90; S 10.29.

**3-Hydroperoxy-4,5-dimethyl-2-(4-nitrobenzoylamino)-2,3-dihydroisothiazole 1-oxide (6d):**

Yield: (45%, colorless prisms); mp 144-146 °C; IR (KBr)  $\nu$ : 1650 (CO), 1600, 1530 (NO<sub>2</sub>), 1340 (NO<sub>2</sub>), 1060 (SO) cm<sup>-1</sup>; <sup>1</sup>H-NMR (CDCl<sub>3</sub>)  $\delta$ : 10.95 (s, 1H, NH), 8.32 (d, 2H,  $J$  = 10.12 Hz, H-Ar), 8.21 (d, 2H,  $J$  = 10.12 Hz, H-Ar), 5.56 (s, 1H, H-3), 2.13 (s, 3H, CH<sub>3</sub>-C4), 2.02 (s, 3H, CH<sub>3</sub>-C5); <sup>13</sup>C-NMR (CDCl<sub>3</sub>)  $\delta$ : 166.3 (CO), 150.9 (C-4'), 140.1 (C-4), 136.9 (C-1'), 133.5 (C-5), 129.7 (C-2',6'), 124.5 (C-3',5'), 100.8 (C-3), 13.5 (CH<sub>3</sub>), 11.6 (CH<sub>3</sub>). EI-MS  $m/z$  309 ( $M^{+\bullet}$ -H<sub>2</sub>O, 9), 277 (11), 244 (59), 217 (36), 150 (100), 104 (27), 76 (14). *Anal.* Calcd for C<sub>12</sub>H<sub>13</sub>N<sub>3</sub>O<sub>6</sub>S: C 44.03; H 4.00; N 12.84; S 9.78. Found: C 44.01; H 4.14; N 12.66; S 9.95.

**2-Aroylamino-3-hydroperoxy-2,3-dihydroisothiazole 1,1-dioxide (7):**

*N*-Aroylisothiazolium-2-imine (**5**) (1.6 mmol) was suspended in glacial acetic acid (8 mL). Hydrogen-peroxide 30 % (5 mL, 44 mmol) was added over a period of 4 h at rt and the mixture stirred overnight. The product crystallized upon standing at 4 °C and was recrystallized from ethanol.

**2-Benzoylamino-4,5-dimethyl-3-hydroperoxy-2,3-dihydroisothiazole 1,1-dioxide (7a):**

Yield: (18%, colorless crystals); mp 155-158 °C; IR (KBr)  $\nu$ : 3310, 1660 (CO), 1520, 1300 (SO<sub>2</sub>), 1170 (SO<sub>2</sub>) cm<sup>-1</sup>; <sup>1</sup>H-NMR (Acetone- $d_6$ )  $\delta$ : 11.35 (s, 1H, OOH), 9.88 (s, 1H, NH), 7.97 (m, 2H, H-Ar), 7.66 (m, 1H, H-Ar), 7.60 (m, 2H, H-Ar), 5.68 (s, 1H, H-3), 2.28 (s, 3H, CH<sub>3</sub>-C5), 1.93 (s, 3H, CH<sub>3</sub>-C4); <sup>13</sup>C-NMR (Acetone- $d_6$ )  $\delta$ : 160.5 (CO), 139.2 (C-4), 138.6 (Ar-C), 133.8 (C-5), 133.3 (Ar-C), 129.7 (Ar-CH), 128.7 (Ar-CH), 93.8 (C-3), 11.7 (CH<sub>3</sub>-C4), 7.6 (CH<sub>3</sub>-C5). EI-MS  $m/z$  280 ( $M^{+\bullet}$ -H<sub>2</sub>O, 43), 264 (33), 199 (25), 161 (7), 146 (43), 105 (100). *Anal.* Calcd for C<sub>12</sub>H<sub>14</sub>N<sub>2</sub>O<sub>5</sub>S: C 48.31; H 4.73; N 9.39; S 10.73. Found: C 48.52; H 5.01; N 9.29; S 10.60.

**4,5-Dimethyl-3-hydroperoxy-2-(4-methylbenzoylamino)-2,3-dihydroisothiazole 1,1-dioxide (7b):**

Yield: (35%, colorless prisms); mp 211-214 °C; IR (KBr)  $\nu$ : 3210, 2920, 2490, 2360, 1650 (CO), 1420, 1300 (SO<sub>2</sub>), 1170 (SO<sub>2</sub>) cm<sup>-1</sup>; <sup>1</sup>H-NMR (Acetone- $d_6$ )  $\delta$ : 11.52 (s, 1H, OOH), 9.95 (s, 1H, NH), 7.91 (d, 2H,  $J$  = 8.2 Hz, H-Ar), 7.34 (d, 2H,  $J$  = 8.2 Hz, H-Ar), 5.04 (s, 1H, H-3), 2.40 (s, 3H, Ph-CH<sub>3</sub>), 2.21 (s, 3H, CH<sub>3</sub>-C5), 2.00 (s, 3H, CH<sub>3</sub>-C4); <sup>13</sup>C-NMR (Acetone- $d_6$ )  $\delta$ : 160.9 (CO), 145.2 (Ar-C), 139.3 (C-4),

133.9 (C-5), 130.9 (Ar-CH), 130.7 (Ar-C), 129.4 (Ar-CH), 94.5 (C-3), 22.2 (Ph-CH<sub>3</sub>), 12.4 (CH<sub>3</sub>-C5), 8.3 (CH<sub>3</sub>-C5). EI-MS *m/z* 294 (M<sup>+</sup>-H<sub>2</sub>O, 11), 278 (30), 160 (60), 135 (15), 119 (100), 91 (26). *Anal.* Calcd for C<sub>13</sub>H<sub>16</sub>N<sub>2</sub>O<sub>5</sub>S: C 49.99; H 5.16; N 8.97; S 10.27. Found: C 50.01; H 5.34; N 9.07; S 10.57.

**2-(4-Chlorobenzoylamino)-3-hydroperoxy-4,5-dimethyl-2,3-dihydroisothiazole 1,1-dioxide (7c):**

Yield: (37%, colorless crystals); mp 156 - 159 °C; IR (KBr) *v*: 3300, 1670 (CO), 1600, 1480, 1280 (SO<sub>2</sub>), 1160 (SO<sub>2</sub>), 1100 cm<sup>-1</sup>; <sup>1</sup>H-NMR (Acetone-d<sub>6</sub>) *δ*: 11.41 (s, 1H, OOH), 10.12 (s, 1H, NH), 8.02 (d, 2H, *J* = 8.6 Hz, H-Ar), 7.60 (d, 2H, *J* = 8.6 Hz, H-Ar), 5.67 (s, 1H, H-3), 2.03 (s, 3H, CH<sub>3</sub>-C5), 1.97 (s, 3H, CH<sub>3</sub>-C4); <sup>13</sup>C-NMR (Acetone-d<sub>6</sub>) *δ*: 169.4 (CO), 140.0 (C-4), 139.2 (Ar-C), 133.9 (C-5), 131.2 (Ar-CH), 131.0 (Ar-CH), 130.5 (Ar-C), 94.6 (C-3), 12.4 (CH<sub>3</sub>-C4), 8.3 (CH<sub>3</sub>-C5). EI-MS *m/z* 314 (M<sup>+</sup>-H<sub>2</sub>O, 66), 298 (25), 180 (58), 155 (24), 139 (100), 111 (22), 75 (12). *Anal.* Calcd for C<sub>12</sub>H<sub>13</sub>N<sub>2</sub>O<sub>5</sub>ClS: C 43.31; H 3.94; N 8.41; S 9.62. Found: C 42.66; H 4.01; N 8.52; S 9.75.

**4,5-Dimethyl-3-hydroperoxy-2-(4-nitrobenzoylamino)-2,3-dihydroisothiazole 1,1-dioxide (7d):**

Yield: (53%, colorless crystals); mp 234-237 °C; IR (KBr) *v*: 3310, 1690 (CO), 1530 (NO<sub>2</sub>), 1350 (NO<sub>2</sub>), 1290 (SO<sub>2</sub>), 1170 (SO<sub>2</sub>) cm<sup>-1</sup>; <sup>1</sup>H-NMR (Acetone-d<sub>6</sub>) *δ*: 11.36 (s, 1H, OOH), 10.36 (s, 1H, NH), 8.44 (d, 2H, *J* = 9.0 Hz, H-Ar), 8.30 (d, 2H, *J* = 9.0 Hz, H-Ar), 5.79 (s, 1H, H-3), 2.11 (s, 3H, CH<sub>3</sub>-C5), 2.08 (s, 3H, CH<sub>3</sub>-C4); <sup>13</sup>C-NMR (Acetone-d<sub>6</sub>) *δ*: 166.7 (CO), 152.2 (C-4'), 137.9 (C-4), 134.1 (C-1'), 132.4 (Ar-CH), 130.5 (C-4), 125.3 (Ar-CH), 94.7 (C-3), 12.5 (CH<sub>3</sub>-C4), 8.4 (CH<sub>3</sub>-C5). EI-MS *m/z* 325 (M<sup>+</sup>-H<sub>2</sub>O, 65), 308 (51), 192 (45), 167 (84), 150 (100), 137 (11), 121 (31), 104 (16), 65 (28). *Anal.* Calcd for C<sub>12</sub>H<sub>13</sub>N<sub>3</sub>O<sub>7</sub>S: C 41.98; H 3.82; N 12.24; S 9.34. Found: C 42.04; H 4.00; N 12.43; S 9.61.

**2-Aroylamino-3-hydroxy-2,3-dihydroisothiazole 1,1-dioxide (8):**

Method A: Na<sub>2</sub>SO<sub>3</sub>·7H<sub>2</sub>O (587 mg, 2.33 mmol) was dissolved in H<sub>2</sub>O (7.5 mL) at rt. 3-Hydroperoxyisothiazole 1,1-dioxide (7) (1 mmol) was added and stirred for 8 h. The crude product (8) was filtered off, washed with water, and recrystallized from ethanol.

Method B: The hydroperoxysultam (7) (1 mmol) was dissolved in DMSO (5 mL), gently heated to 50 °C for 5 min, and stirred at rt for another 20 min. Water (3 mL) was added and lyophilised to yield the hydroxysultam (8). **8e-h** was prepared according to lit.<sup>1,3</sup>

**2-Benzoylamino-4,5-dimethyl-3-hydroxy-2,3-dihydroisothiazole 1,1-dioxide (8a):**

Yield: (95 %, colorless syrup, method B); IR (KBr) *v*: 3411, 1677 (CO), 1304 (SO<sub>2</sub>), 1176, 1145 (SO<sub>2</sub>), 1072, 1024 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>) *δ*: 10.57 (s, 1H, NH), 8.18 (s, 1H, OH), 7.89 (d, 2H, *J* = 7.4 Hz,

H-Ar), 7.64 (m, 1H, H-Ar), 7.50 (d, 2H,  $J = 7.4$  Hz, H-Ar), 5.50 (s, 1H, H-3), 1.98 (s, 3H,  $CH_3$ -C5), 1.89 (s, 3H,  $CH_3$ -C4);  $^{13}C$ -NMR (DMSO- $d_6$ )  $\delta$ : 166.1 (CO), 141.4 (C-4), 132.6 (Ar-C), 132.1 (Ar-C), 129.3 (C-5), 128.4 (Ar-CH), 127.6 (Ar-CH), 83.8 (C-3), 11.9 ( $CH_3$ -C4), 7.3 ( $CH_3$ -C4). EI-MS  $m/z$  282 ( $M^{+\bullet}$ , 10), 137 (20), 119 (65), 105 (100), 91 (15). *Anal.* Calcd for  $C_{12}H_{14}N_2O_4S$ : C 51.05; H 5.00; N 9.92; S 11.34. Found: C 51.41; H 4.98; N 9.64; S 11.05.

**4,5-Dimethyl-3-hydroxy-2-(4-methylbezoylamino)-2,3-dihydroisothiazole 1,1-dioxide (8b):**

Yield: (71 %, colorless prisms, method A); mp 165-168 °C (ethanol, decomp); IR (KBr)  $\nu$ : 2925, 1670 (CO), 1305 ( $SO_2$ ), 1160 ( $SO_2$ ), 1150  $cm^{-1}$ ;  $^1H$ -NMR (Acetone- $d_6$ )  $\delta$ : 10.68 (s, 1H, NH), 7.94 (d, 2H,  $J = 8.4$  Hz, H-Ar), 7.63 (d, 2H,  $J = 8.4$  Hz, H-Ar), 5.63 (s, 1H, H-3), 2.90 (s, 3H, Ph- $CH_3$ ), 2.39 (s, 3H,  $CH_3$ ), 1.98 (s, 3H,  $CH_3$ );  $^{13}C$ -NMR (Acetone- $d_6$ )  $\delta$ : 167.8 (CO), 144.1 (C-4'), 142.1 (C-4), 131.8 (C-5), 131.3 (C-1'), 130.6 (Ar-CH), 129.2 (Ar-CH), 85.6 (C-3), 22.1 (Ph- $CH_3$ ), 12.9 ( $CH_3$ -C4), 8.3 ( $CH_3$ -C5). EI-MS  $m/z$  296 ( $M^{+\bullet}$ , 25), 214 (20), 174 (20), 135 (15), 119 (100), 105 (15), 91 (35), 65 (25). *Anal.* Calcd for  $C_{13}H_{16}N_2O_4S$ : C 52.69; H 5.44; N 9.45; S 10.82. Found: C 52.63; H 5.73; N 9.40; S 10.95.

**2-(4-Chlorobezoylamino)- 4,5-dimethyl-3-hydroxy-2,3-dihydroisothiazole 1,1-dioxide (8c):**

Yield: (69 %, colorless crystals, method A); mp 188-190 °C (ethanol); IR (KBr)  $\nu$ : 3253, 1664 (CO), 1596, 1320 ( $SO_2$ ), 1178 ( $SO_2$ ), 1060  $cm^{-1}$ ;  $^1H$ -NMR (Acetone- $d_6$ )  $\delta$ : 9.42 (s, 1H, NH), 7.86 (d, 2H,  $J = 8.2$  Hz, H-Ar), 7.31 (d, 2H,  $J = 8.2$  Hz, H-Ar), 5.52 (d, 1H,  $J = 7.8$  Hz, H-3), 2.03 (s, 3H,  $CH_3$ -C5), 1.93 (s, 3H,  $CH_3$ -C4);  $^{13}C$ -NMR (Acetone- $d_6$ )  $\delta$ : 165.3 (CO), 141.6 (C-4), 141.6 (C-4'), 137.1 (C-5), 130.9 (C-1'), 129.6 (Ar-CH), 128.7 (Ar-CH), 83.9 (C-3), 12.0 ( $CH_3$ -C4), 7.4 ( $CH_3$ -C4). *Anal.* Calcd for  $C_{12}H_{13}N_2O_4ClS$ : C 45.50; H 4.14; N 8.84. Found: C 45.30; H 4.45; N 8.53. ESI-MS  $m/z$  339 [ $M+Na$ ] $^+$ .

**4,5-Dimethyl-3-hydroxy-2-(4-nitrobenzoylamino)-2,3-dihydroisothiazole 1,1-dioxide (8d):**

Yield: (95 %, colorless prisms, method B); mp 166-168 °C (ethanol); IR (KBr)  $\nu$ : 3281, 1746, 1682 (CO), 1602, 1520 ( $NO_2$ ), 1350 ( $NO_2$ ), 1317 ( $SO_2$ ), 1176 ( $SO_2$ ), 1147, 1059  $cm^{-1}$ ;  $^1H$ -NMR (DMSO- $d_6$ , 700 MHz)  $\delta$ : 10.90 (s, 1H, NH), 8.36 (2H,  $J = 7.0$  Hz, H-3',5'), 8.12 (2H,  $J = 7.0$  Hz, H-2',6'), 7.18 (br s, 1H, OH), 5.51 (br s, 1H, H-3), 2.01 (s, 3H,  $CH_3$ -C5), 1.92 (s, 3H,  $CH_3$ -C4);  $^{13}C$ -NMR (DMSO- $d_6$ , 176 MHz, HMQC, HMBC, (1,1)-ADEQUATE)  $\delta$ : 165.13 (CO), 149.71 (C-4'), 141.77 (C-4), 137.95 (C-1'), 129.50 (C-5), 129.45 (C-2',6'), 123.87 (C-3',5'), 84.04 (C-3), 12.10 ( $CH_3$ -C4), 7.45 ( $CH_3$ -C5). ESI-MS  $m/z$  350 [ $M+Na$ ] $^+$ . *Anal.* Calcd for  $C_{12}H_{13}N_3O_6S$ : C 44.03; H 4.00; N 12.84; 9.78. Found: C 44.16; H 3.91; N 12.71; S 9.94.

**2-Aroylamino-4,5-dimethylisothiazol-3(2H)-one 1,1-dioxide (10):**

Isothiazolium-2-imine (**5**) (1.7 mmol) was suspended in glacial acetic acid (10 mL) and hydrogen peroxide (30%, 5 mL, 44 mmol) was added. The mixture was stirred at 80°C for 8 h. The precipitate which was formed after 3-4 days was filtered off, washed with ether, and recrystallized from ethanol.

**2-(4-Chlorobenzoylamino)-4,5-dimethylisothiazol-3(2H)-one 1,1-dioxide (10c):**

Yield: (15 %, yellow needles); mp 175-178 °C; IR (KBr)  $\nu$ : 3324, 1755 (CO), 1673 (CO), 1341 (SO<sub>2</sub>), 1189 (SO<sub>2</sub>), 1093, 735 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 10.43 (s, 1H, NH), 8.03 (m, 2H, H-Ar), 7.60 (m, 2H, H-Ar), 2.33 (s, 3H, CH<sub>3</sub>), 2.07 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C-NMR (Acetone-d<sub>6</sub>)  $\delta$ : 166.2 (CO), 160.1 (C-3), 148.1 (C-5), 140.0 (C-4'), 134.4 (C-4), 132.8 (Ar-CH), 131.1 (Ar-CH), 130.2 (C-1'), 9.92 (CH<sub>3</sub>), 9.04 (CH<sub>3</sub>). ESI-MS  $m/z$  337 [M+Na]<sup>+</sup>, 315 [M+H]<sup>+</sup>. *Anal.* Calcd for C<sub>12</sub>H<sub>11</sub>N<sub>2</sub>O<sub>4</sub>ClS: C 45.79; H 3.52; N 8.90; S 10.11. Found: C 45.85; H 3.42; N 8.65; S 9.92.

**4,5-Dimethyl-2-(4-nitrobenzoylamino)isothiazol-3(2H)-one 1,1-dioxide (10d):**

Yield: (36 %, yellow needles); mp 243-244 °C; IR (KBr)  $\nu$ : 3338, 1762 (CO), 1688 (CO), 1518 (NO<sub>2</sub>), 1345 (NO<sub>2</sub>), 1319 (SO<sub>2</sub>), 1186 (SO<sub>2</sub>), 1110, 1086, 716 cm<sup>-1</sup>; <sup>1</sup>H-NMR (Acetone-d<sub>6</sub>)  $\delta$ : 10.74 (s, 1H, NH), 8.43 (m, 2H, H-Ar), 8.32 (m, 2H, H-Ar), 2.39 (s, 3H, CH<sub>3</sub>), 2.17 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C-NMR (Acetone-d<sub>6</sub>)  $\delta$ : 165.1 (CO), 160.3 (C-3), 150.0 (C-5), 145.1 (C-4'), 137.5 (C-4), 132.4 (C-1'), 130.9 (Ar-CH), 125.1 (Ar-CH), 9.9 (CH<sub>3</sub>), 9.1 (CH<sub>3</sub>). EI-MS  $m/z$  325 (M<sup>+</sup>, 5), 150 (100), 134 (7), 120 (25), 104 (30), 92 (15), 76 (17). *Anal.* Calcd for C<sub>12</sub>H<sub>11</sub>N<sub>3</sub>O<sub>6</sub>S: C 44.31; H 3.41; N 12.92; S 9.84. Found: C 44.80; H 3.30; N 12.50; S 9.66.

**Crystal Data for 10d:** C<sub>12</sub>H<sub>11</sub>N<sub>3</sub>O<sub>6</sub>S, MW 325.30, monoclinic, space group P2(1),  $a = 4.759(1)$ ,  $b = 11.754(1)$ ,  $c = 25.362(2)$  Å,  $\alpha = 90$ ,  $\beta = 91.69(1)$ ,  $\gamma = 90$ ,  $V = 1418.1$  Å<sup>3</sup>,  $F(000) = 672$ ,  $Z = 4$ ,  $T = -60$  °C,  $\mu(\text{MoK}\alpha) = 0.263$  mm<sup>-1</sup>,  $D = 1.524$  g.cm<sup>-3</sup>,  $\text{GOF} = 0.984$ ,  $wR(F^2) = 0.0857$  (all 3321 data),  $R = 0.0330$  ( $I > 2\sigma I$ ).

Crystallographic measurements were made using a STOE IPDS1-Diffractometer (graphite monochromated MoK $\alpha$  radiation ( $\lambda = 0.71073$  Å); empirical absorption correction using SADABS.<sup>11</sup> The structures were solved using direct methods, and refined in the anisotropic approximation for the non-hydrogen atoms using SHELXS-86 and SHELXL-97.<sup>12,13</sup> All hydrogen atoms were located by difference Fourier map and refined isotropically.

Crystallographic data for the structure reported in this paper was deposited with the Cambridge

Crystallographic Data Centre as no. CCDC-279070 for **10d**. Copies of the data can be obtained free of charge on application to ccdc, 12 Union Road, Cambridge CB21EZ, UK (fax (+44) 1223-336-033; email: deposit@ccdc.cam.ac.uk).

**2-Aryl-isothiazolo[3,2-*b*]- and 2-Aryl-6,7,8,9-tetrahydro-1,2-benzisothiazolo[3,2-*b*]-1,3,4-oxadiazole 5,5-dioxide (11):**

The 3-hydroxyisothiazole (**8a-h**) (0.13 mmol) was dissolved in 10 mL of dry toluene and refluxed for 6 h. The solvent was evaporated to give **11a-h** as colorless solids.

**6,7-Dimethyl-2-isothiazolo[3,2-*b*]-1,3,4-oxadiazole 5,5-dioxide (11a):**

Yield: (50 %, colorless solid); mp 211-214 °C; IR (KBr)  $\nu$ : 1624 (C=N), 1334 (SO<sub>2</sub>), 1178 (SO<sub>2</sub>), 1071, 776, 689 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$ : 7.87 (d, 2H, *J* = 7.2 Hz, H-Ar), 7.66 (m, 1H, H-Ar), 7.57 (t, 2H, *J* = 7.4 Hz, H-Ar), 6.74 (s, 1H, H-7a), 2.07 (s, 6H, CH<sub>3</sub>); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>)  $\delta$ : 158.8 (C-2), 139.1 (C-7), 130.2 (C-6), 129.6 (Ar-CH), 128.2 (Ar-CH), 126.5 (Ar-CH), 123.0 (C-1'), 95.1 (C-7a), 11.0 (CH<sub>3</sub>-C7), 7.7 (CH<sub>3</sub>-C6). CI-MS *m/z* 265 ([M+H]<sup>+</sup>, 100), 247 (31), 146 (53), 113 (20), 105 (43). *Anal.* Calcd for C<sub>12</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>S: C 54.53; H 4.58; N 10.60; S 12.11. Found: C 54.82; H 4.64; N 10.49; S 12.27.

**6,7-Dimethyl-2-(4-methylphenyl)isothiazolo[3,2-*b*]-1,3,4-oxadiazole 5,5-dioxide (11b):**

Yield: (60 %, colorless solid); mp 218-221 °C; IR (KBr)  $\nu$ : 1621 (C=N), 1322 (SO<sub>2</sub>), 1189 (SO<sub>2</sub>), 1079, 824, 748 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$ : 7.73 (d, 2H, *J* = 8.1 Hz, H-Ar), 7.35 (d, 2H, *J* = 8.1 Hz, H-Ar), 6.66 (s, 1H, H-7a), 2.38 (s, 3H, Ph-CH<sub>3</sub>), 2.03 (s, 6H, CH<sub>3</sub>); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>)  $\delta$ : 158.9 (C-2), 143.0 (C-4'), 139.0 (C-7), 131.5 (C-6), 129.7 (Ar-CH), 127.3 (Ar-CH), 120.2 (C-1'), 94.9 (C-7a), 21.2 (Ph-CH<sub>3</sub>), 11.8 (CH<sub>3</sub>-C7), 7.0 (CH<sub>3</sub>-C6). EI-MS *m/z* 278 (M<sup>+</sup>, 8), 214 (M<sup>+</sup>-SO<sub>2</sub>, 4), 160 (33), 119 (100), 91 (42), 65 (18). *Anal.* Calcd for C<sub>13</sub>H<sub>14</sub>N<sub>2</sub>O<sub>3</sub>S: C 56.10 H 5.07; N 10.06; S 11.50. Found: C 56.26; H 5.37; N 9.89; S 11.62.

**2-(4-Chlorophenyl)-6,7-dimethyl-isothiazolo[3,2-*b*]-1,3,4-oxadiazole 5,5-dioxide (11c):**

Yield: (71 %, colorless solid); mp 194-196 °C; IR (KBr)  $\nu$ : 1746, 1620 (C=N), 1596, 1336 (SO<sub>2</sub>), 1181 (SO<sub>2</sub>), 1094, 1012, 834 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-*d*<sub>6</sub>)  $\delta$ : 7.87 (d, 2H, *J* = 8.4 Hz, H-Ar), 7.63 (d, 2H, *J* = 8.4 Hz, H-Ar), 6.74 (s, 1H, H-7a), 2.52 (s, 3H, CH<sub>3</sub>), 2.32 (s, 3H, CH<sub>3</sub>); <sup>13</sup>C-NMR (DMSO-*d*<sub>6</sub>)  $\delta$ : 158.1 (C-2), 139.0 (C-7), 137.5 (C-4'), 131.5 (C-6), 129.3 (Ar-CH), 129.1 (Ar-CH), 121.8 (C-1'), 95.3 (C-7a), 11.6 (CH<sub>3</sub>-C7), 6.9 (CH<sub>3</sub>-C6). EI-MS *m/z* 298 (M<sup>+</sup>, 37), 233 (10), 180 (74), 139 (100), 111 (66), 75 (32). *Anal.* Calcd for C<sub>12</sub>H<sub>11</sub>N<sub>2</sub>O<sub>3</sub>ClS: C 48.24; H 3.71; N 9.38 S 10.73. Found: C 47.90; H 3.84; N 9.59.

**6,7-Dimethyl-2-(4-nitrophenyl)-isothiazolo[3,2-*b*]-1,3,4-oxadiazole 5,5-dioxide (11d):**

Yield: (95 %, colorless solid); mp 189-192 °C; IR (KBr)  $\nu$ : 1682, 1635 (C=N), 1596, 1341 (SO<sub>2</sub>), 1180 (SO<sub>2</sub>), 1080, 1006, 851 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>, 600 MHz)  $\delta$ : 8.35(2H, *J* = 8.8 Hz, H-3',5'), 8.09 (2H, *J* = 8.4 Hz, H-2',6'), 6.80 (s, 1H, H-7a), 2.05 (s, 6H, 2 x CH<sub>3</sub>); <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>, 150 MHz, HMQC, HMBC)  $\delta$ : 157.52 (C-2), 149.70 (C-4'), 139.06 (C-7), 131.68 (C-6), 128.83 (C-2',6'), 128.77 (C-1'), 124.24 (C-3',5'), 95.68 (C-7a), 11.63 (CH<sub>3</sub>-C7), 7.00 (CH<sub>3</sub>-C6). ESI-MS *m/z* 310 [M+H]<sup>+</sup>. *Anal.* Calcd for C<sub>12</sub>H<sub>11</sub>N<sub>3</sub>O<sub>5</sub>S: C 46.60; H 3.58; N 13.59; S 10.35. Found: C 46.85; H 3.72; N 13.65; S 10.54.

**2-(4-Methylphenyl)-6,7,8,9-tetrahydro-1,2-benzisothiazolo[3,2-*b*]-1,3,4-oxadiazole 5,5-dioxide (11e):**

Yield: (82 %, colorless solid); mp 182-184 °C; IR (KBr)  $\nu$ : 1623 (C=N), 1338 (SO<sub>2</sub>), 1172 (SO<sub>2</sub>), 1126, 1076, 569 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 7.83 (d, 2H, *J* = 8.2 Hz, H-Ar), 7.36 (d, 2H, *J* = 8.2 Hz, H-Ar), 6.67 (s, 1H, H-9b), 2.39 (s, 3H, Ph-CH<sub>3</sub>), 2.50 (m, 4H, 2 CH<sub>2</sub>), 1.78 (m, 4H, 2 CH<sub>2</sub>); <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 159.3 (C-2), 143.2 (C-4'), 142.6 (C-9a), 134.7 (C-5a), 129.8 (Ar-CH), 127.4 (Ar-CH), 120.3 (C-1'), 94.6 (C-9b), 22.7 (Ph-CH<sub>3</sub>), 21.3 (CH<sub>2</sub>), 20.8 (CH<sub>2</sub>), 20.2 (CH<sub>2</sub>), 18.3 (CH<sub>2</sub>). EI-MS *m/z* 304 (M<sup>+</sup>, 6), 240 (10), 119 (100), 91 (47), 65 (6). *Anal.* Calcd for C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O<sub>3</sub>S: C 59.19; H 5.30; N 9.20. Found: C 59.02; H 5.36; N 9.44.

**2-(4-Chlorophenyl)-6,7,8,9-tetrahydro-1,2-benzisothiazolo[3,2-*b*]-1,3,4-oxadiazole 5,5-dioxide (11f):**

Yield: (38 %, colorless solid); mp 236-240 °C; IR (KBr)  $\nu$ : 1626 (C=N), 1597, 1341 (SO<sub>2</sub>), 1173 (SO<sub>2</sub>), 1124, 1088, 615, 570 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 7.87 (d, 2H, *J* = 8.6 Hz, H-Ar), 7.63 (d, 2H, *J* = 8.6 Hz, H-Ar), 6.75 (s, 1H, H-9b), 2.40 (m, 4H, 2 CH<sub>2</sub>), 1.71 (m, 4H, 2 CH<sub>2</sub>); <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 158.3 (C-2), 142.4 (C-9a), 137.5 (C-4'), 134.6 (C-5a), 129.3 (Ar-CH), 128.7 (Ar-CH), 121.9 (C-1'), 94.8 (C-9b), 22.5 (CH<sub>2</sub>), 20.7 (CH<sub>2</sub>), 20.1 (CH<sub>2</sub>), 18.2 (CH<sub>2</sub>). EI-MS *m/z* 324 (M<sup>+</sup>, 7), 260 (7), 139 (100), 111 (29), 91 (8). *Anal.* Calcd for C<sub>14</sub>H<sub>13</sub>N<sub>2</sub>O<sub>3</sub>ClS: C 51.77; H 4.03; N 8.63; S 9.86. Found: C 51.69; H 4.06; N 8.59; S 10.11.

**2-(3-Chlorophenyl)-8,9,10,11-tetrahydro-1,2-benzisothiazolo[3,2-*b*]-1,3,4-oxadiazole 5,5-dioxide (11g):**

Yield: (51 %, colorless crystals); mp 172-174 °C; IR (KBr)  $\nu$ : 1638 (C=N), 1568, 1337 (SO<sub>2</sub>), 1167 (SO<sub>2</sub>), 1127, 1081 cm<sup>-1</sup>; <sup>1</sup>H-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 7.76 (s, 1H, H-3Ar), 7.63 (m, 3H, H-4,5,6Ar), 6.68 (s, 1H, H-9b), 2.33 (m, 4H, 2 CH<sub>2</sub>), 1.63 (m, 4H, 2 CH<sub>2</sub>); <sup>13</sup>C-NMR (DMSO-d<sub>6</sub>)  $\delta$ : 158.6 (C-2), 143.2 (C-9a), 135.2 (Ar-C), 133.2 (C-5a), 126.7 (4C, Ar-CH), 125.4 (Ar-C), 95.6 (C-9b), 23.1 (CH<sub>2</sub>), 21.3 (CH<sub>2</sub>), 20.7

(CH<sub>2</sub>), 18.9 (CH<sub>2</sub>). EI-MS m/z 324 (M<sup>+</sup>, 8), 260 (7), 139 (100), 111 (44), 91 (10), 75 (22). *Anal.* Calcd for C<sub>14</sub>H<sub>13</sub>N<sub>2</sub>O<sub>3</sub>ClS: C 51.77; H 4.03; N 8.63. Found: C 51.65; H 3.99; N 8.70.

**2-(4-Nitrophenyl)-6,7,8,9-tetrahydro-1,2-benzisothiazolo[3,2-b]-1,3,4-oxadiazole 5,5-dioxide (11h):**

Yield: (47 %, colorless solid); mp 248-250 °C; <sup>1</sup>H-NMR (CDCl<sub>3</sub>) δ: 8.29 (d, 2H, *J* = 8.8 Hz, H-Ar), 8.08 (d, 2H, *J* = 8.8 Hz, H-Ar), 6.35 (d, 1H, *J* = 1.9 Hz, H-9b), 2.45 (m, 4H, 2 CH<sub>2</sub>), 1.83 (m, 4H, 2 CH<sub>2</sub>); <sup>13</sup>C-NMR (CDCl<sub>3</sub>) δ: 158.3 (C-2), 150.6 (C-4'), 141.5 (C-9a), 137.6 (C-5a), 130.1 (C-1'), 129.5 (C-2',6'), 124.6 (C-3',5'), 96.3 (C-9b), 23.7 (CH<sub>2</sub>), 21.8 (CH<sub>2</sub>), 21.3 (CH<sub>2</sub>), 19.7 (CH<sub>2</sub>). EI-MS m/z 335 (M<sup>+</sup>, 10), 271 (8), 150 (100), 91(65). *Anal.* Calcd for C<sub>14</sub>H<sub>13</sub>N<sub>3</sub>O<sub>5</sub>S: C 50.14; H 3.91; N 12.53; S 9.56. Found: C 50.33; H 3.97; N 12.41.

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