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J. Fahrig[a]; T. H. E. Freysoldt[a]; C. Hartung[a]; J. Sieler[a]; B. Schulze[a]
[a] Institute of Organic Chemistry, University of Leipzig, Leipzig, Germany

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RESEARCH ARTICLE

Oxyfunctionalization of novel diaryl- and triaryl-isothiazolium salts: the first isolable crystalline 3-hydroperoxyisothiazole

J. FAHRIG, T. H. E. FREYSOLDT, C. HARTUNG, J. SIELER and B. SCHULZE*

Institute of Organic Chemistry, University of Leipzig, Johannisallee 29, D-04103 Leipzig, Germany

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Dedicated to Professor Dr. Jürgen Liebscher on the occasion of his 60th birthday.

The synthesis of novel monocyclic di- and triphenyl-substituted hydroperoxysultims *rac-cis* **7** and **8** and sultams **11** and **12**, as well as the 3-oxosultams **15** and **16**, by oxidation of corresponding salts **1** and **2** with H_2O_2 in acetic acid is described. For the first time, it was possible to isolate a 3-hydroperoxide (**3a**) and also to determine the position of the primary oxidizing attack on the C-3 atom of isothiazolium salts **1**, which have generally a much lower oxidation reactivity. Novel 3-hydroxysultams **13** and **14** were obtained by oxidation reaction of salts **1** and **2** with magnesium monoperoxyphthalate (MMPP) in acetonitrile in the ultrasound bath.

Keywords: Isothiazolium salts; Oxidation; Hydroperoxides; Sultams; Sultims; HLE

1. Introduction

Isothiazoles and their oxyfunctionalized derivatives show a wide spectrum of biological and pharmaceutical activities [1–3]. The monocyclic isothiazol-3(2*H*)-ones **A** and **B** are potent industrial microbiocides with antifungal and antibacterial activities [4]. The most famous isothiazole is saccharin **C**, which was first prepared through an oxidative cyclization of *o*-toluenesulfonamide [5]. N-Substituted saccharin derivatives **D–F** show an inhibitory effect on the human leukocyte elastase (HLE) [6]. In recent investigations, we have synthesized 2-phenyl-substituted isothiazol-3(2*H*)-one 1,1-dioxides and demonstrated their activity as potent inhibitors of HLE [7]. Marco and Ingate have synthesized the first monocyclic 2,3-dihydroisothiazole 1,1-dioxide **G**, which has anti-HIV-1-activity [8–12].

Here, we would like to describe the preparation of novel diaryl- and triaryl-substituted isothiazolium salts **1** and **2** and their oxidation cascade to stable monocyclic 3-hydroperoxy-isothiazoles **3** and **4**, and 3-hydroperoxysultims **7** and **8** and -sultams **11** and **12**, as well as

*Corresponding author: Email: bschulze@organik.chemie.uni-leipzig.de

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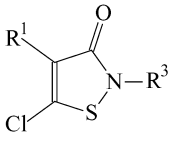
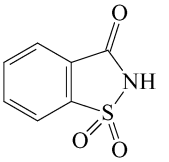
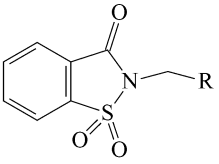
3-hydroxysultams **13** and **14**, respectively. The oxidation reaction is concluded by formation of the 3-oxosultams **15** and **16**.



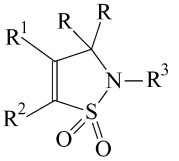
A: $R^3 = CH_3$, $R^1 = H$
B: $R^3 = CH_3(CH_2)_7$, $R^1 = Cl$



C



D: R = OCO-2,6-$Cl_2C_6H_3$
E: R = triazolo, SO_2R^1
F: R = O-heterocyclyl



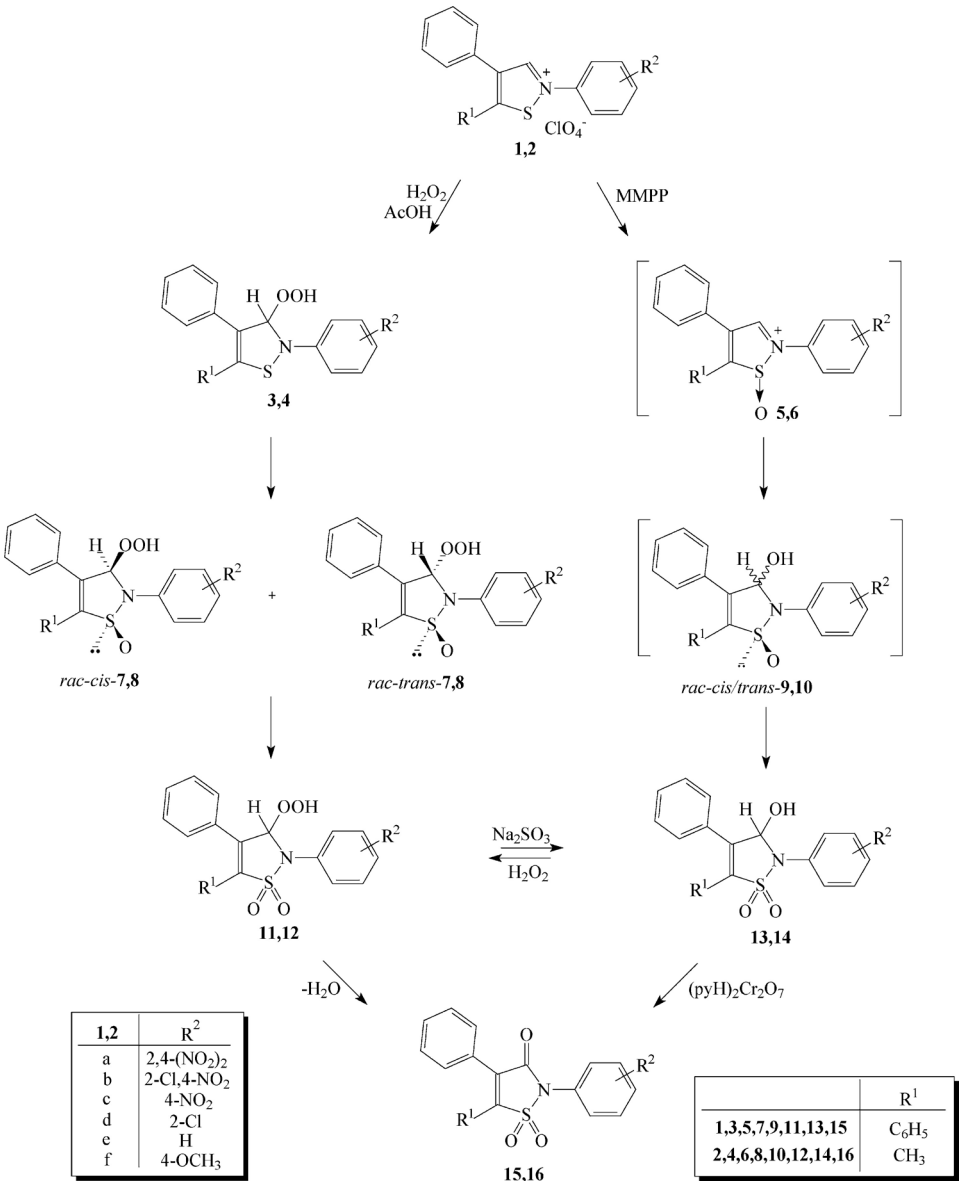
G
R = H, CH_3, $(CH_3)_2CH$
R^1 = OH, NH_2
R^2 = H, CH_3, CN, C_6H_5
R^3 = H, CH_3, $CH_2C_6H_5$

2. Results and discussion

The new isothiazolium salts **1** and **2** were conveniently synthesized by intramolecular cyclocondensation of β-thiocyanatovinyl aldehydes and the variously substituted anilines in the presence of perchloric acid [13].

The mechanism of the oxidation reaction is shown in scheme 1. The nucleophilic attack of H_2O_2 on C-3 has been recently demonstrated to be the first step of the oxidation process of 2,4-diaryl-substituted salts **2** ($R^1 = CH_3$) to 3-hydroperoxyisothiazole **4** ($R^1 = CH_3$; R^2 = 2-Cl or 2,6-Cl_2) by HPLC-API-MS/MS-coupling [14]. To isolate such 3-hydroperoxyisothiazoles **4**, the oxidation of salts possessing low reactivity must be examined. Baumann *et al.* have already shown that the triaryl-substituted salts **1** ($R^1 = C_6H_5$) are less reactive than the salts **2** and bicyclic isothiazolium salts [14, 15]. Therefore, for this investigation, we carried out the oxidation of the 2,4,5-triphenylisothiazolium perchlorates **1a–c** at different reaction times (10, 15, 20 and 30 min) in H_2O_2 and glacial acetic acid at room temperature; a precipitate was obtained, isolated and characterized. Usually a mixture of **3, 7, 11** and unchanged salt **1** was obtained. In one case, after 15 minutes, only 3-hydroperoxyisothiazole **3a** [$R^1 = C_6H_5$, R^2 = 2,4-$(NO_2)_2$] was found in addition to starting material **1a** (3:1). In the ^{1}H NMR spectrum of 3-hydroperoxyisothiazole **3a** with non-oxidized S-atom, the H-3 proton appears at 6.36 ppm, and in the ^{13}C NMR spectrum the chemical shift of C-3 was found at 96.18 ppm. In the ESI negative-mass spectrum, a molecular mass peak at 436.06 m/z corresponding to structure $C_{21}H_{15}N_3O_6S$ (437.43 g/mol) was observed. Thus, for the first time, we could isolate crystalline 3-hydroperoxyisothiazole **3a** [$R^1 = C_6H_5$, R^2 = 2, 4-$(NO_2)_2$], an intermediate in the oxidation of the salts **1a** and which is a strong acceptor-triphenyl-substituted salt, but possessing reduced oxidation reactivity.

The second attack of oxidant at the S-atom of hydroperoxides **3** and **4** then results in the formation of the stable crystalline 3-hydroperoxysultims *rac-cis* **7a** and *rac-cis* **8d,e** after 1.5–3.5 h at room temperature in H_2O_2/AcOH (21 to 86%, see scheme 1). In the other cases, only a mixture of sultims *rac-cis/trans* **7b,c** and **8a,c** with sultams **11b,c** and **12a,c** was obtained (1.5–23 h). The isolation of sultims **7a–c** and **8a,c–e** was only possible with acceptor- and unsubstituted salts **1** and **2** (see scheme 1). Unexpectedly, for the first time, a pure stable hydroperoxide *rac-cis* **8e** with unsubstituted N-aryl ring could be isolated in 21% yield, despite its parent anilinium ion possessing a relatively high pK_a of 4.63. In former investigations, only stable 3-hydroperoxysultims derived from anilinium ions of pK_a < 3.5 could be obtained [16, 17].



1,2	R^2
a	2,4-$(NO_2)_2$
b	2-Cl,4-NO_2
c	4-NO_2
d	2-Cl
e	H
f	4-OCH_3

	R^1
1,3,5,7,9,11,13,15	C_6H_5
2,4,6,8,10,12,14,16	CH_3

SCHEME 1 Pathway of the oxidation of salts **1** and **2** to 3-oxosultams **15** and **16**.

The stable 3-hydroperoxysultams **11a,c,e** and **f** were obtained after 72–120 h, and **12a,d–f** after 24–96 h at room temperature, while the very stable **11b** and **12c** were obtained after 8 s at 80 °C as pure crystalline products in very good yields (57–95%).

The structure of the 3-hydroperoxysultams **12** was confirmed by X-ray crystal-structure analysis of **12f** ($R^1 = CH_3$, $R^2 = 4\text{-}OCH_3$). The structure of the sultam **12f** presented in figure 1 and the crystallographic data are given in the text.

The isothiazole ring in **12f** is approximately planar. Sultam **12f** shows a helical arrangement of the intermolecular classical O–O–H···O–S–O strong hydrogen bond (3.90 Å) along the 2 screw axis (figure 2) and a weak intermolecular hydrogen bond between the atoms C(1)–H(1)···O(5) (3.24 Å) and C(15)–H(15)···O(4) (3.33 Å).

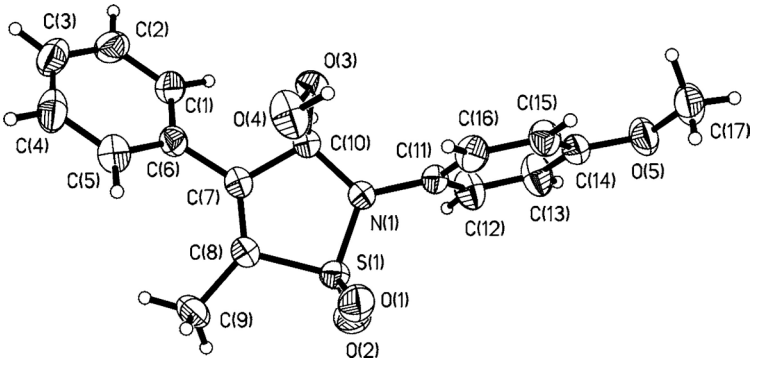


Figure 1. Molecular structure of 3-hydroperoxy-5-methyl-2-(4-methoxyphenyl)-4-phenyl-2,3-dihydroisothiazole 1,1-dioxide **12f** [18]. The selected bond lengths [Å] and angles [°] for **12f** with estimated standard deviations in parentheses are: S(1)–O(1) 1.436(1), S(1)–O(2) 1.431(1), S(1)–N(1) 1.616(2), S(1)–C(8) 1.746(2), O(3)–C(10) 1.407(2), O(3)–O(4) 1.468(2), O(4)–H(10) 1.00(4), N(1)–C(10) 1.444(2), C(10)–C(7) 1.509(2), C(7)–C(8) 1.334(3) and O(1)–S(1)–O(2) 114.86(9), O(1)–S(1)–N(1) 110.79(9), O(2)–S(1)–N(1) 111.77(9), O(1)–S(1)–C(8) 111.21(8), O(2)–S(1)–C(8) 111.84(9), O(3)–O(4)–H(10) 102.0(2), C(8)–C(7)–C(10) 114.1(2), N(1)–C(10)–C(7) 106.7(2), S(1)–N(1)–C(10) 114.2(1), C(10)–O(3)–O(4) 105.9(1).

The structures of the novel 3-hydroperoxy-sultims **7** and **8** and -sultams **11** and **12** were established by IR and NMR spectroscopy and by mass spectrometry. Sultims **7** and **8** have a typical sulfoxide absorption in the IR spectra at 1063–1079 cm^{-1} whereas sultams **11** and **12** exhibit two absorptions at 1126–1159 cm^{-1}/1284–1302 cm^{-1} for the SO_2 group. In their

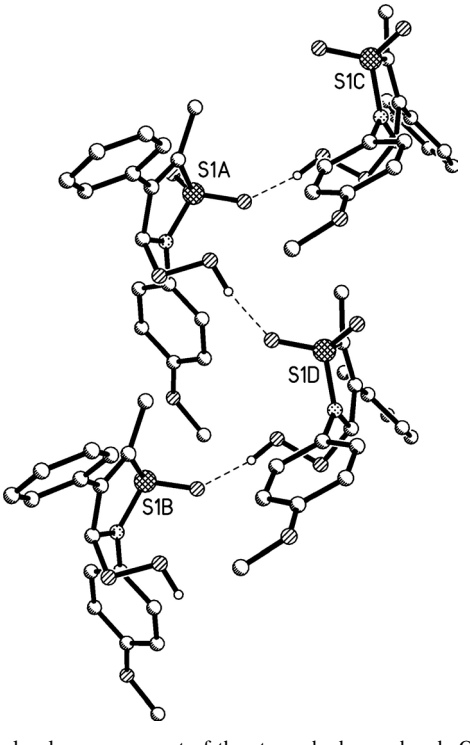


Figure 2. The helical intermolecular arrangement of the strong hydrogen bonds O–O–H···O–S–O of 3-hydroperoxysultam **12f** (Symmetry code for S(1B)-S(1D): $-x, 1/2 + y, 1/2 - z$; Symmetry code for S(1B)-S(1A): $x, 1 + y, z$).

^{1}H NMR spectra, sultims **7** and **8** possess a chemical shift of H-3 proton at 6.32–6.73 ppm, and in their ^{13}C NMR spectra the chemical shift of C-3 appears at 99.07–103.92 ppm. From past investigations, it is known and confirmed with X-ray crystal-structure analysis that the ^{13}C chemical shift of sultims *rac-cis* **7** and **8** is shifted to lower field [16, 17]. Therefore, we also allocated the *rac-cis* **7** and **8** to lower field (99.07–103.92 ppm) and the *rac-trans* **7** and **8** to higher field at 97.60–99.28 ppm. The ^{1}H NMR spectra of 3-hydroperoxysultams **11** and **12** are characterized by the H-3 proton absorption at 6.51–7.29 ppm. The ^{13}C NMR spectra have a chemical shift of C-3 at 90.05–94.85 ppm. In the table 3, the complete data of the sultams **11** and **12** are presented.

As expected [7], the oxidation of the salts **1** and **2** with 30% H_2O_2 in glacial acetic acid at 80 °C for 8–24 h (method A) gave the 3-oxosultams **15e** and **f** and **16d–f** in good yields (42–83%; see tables 1 and 2). By following this procedure, surprisingly, a mixture of **15b** and the respective very stable 3-hydroperoxide **11b** was isolated. After dehydration of **11b** in ethanol and conc. HCl at 80 °C the corresponding pure 3-oxosultam **15b** was obtained (method B).

Another method used to synthesize the 3-oxosultams **15** and **16** is the oxidation of **13** and **14**, which were easily synthesized from isothiazolium salts **1** and **2** with MMPP · $6H_2O$ in CH_3CN, with $(pyH)_2Cr_2O_7$ in CH_2Cl_2 for 8 hs at room temperature (method C).

The symmetrical and antisymmetrical stretching vibration of the SO_2 group in IR spectra at 1139–1159 cm^{-1} and 1249–1332 cm^{-1}, and C=O absorption bands at 1728–1736 cm^{-1}, as well as the chemical shift of C-3 at 159.70–161.83 ppm in ^{13}C NMR spectra, characterize 3-oxosultams **15** and **16**. The inhibitory potential of the new isothiazol-3(2*H*)-one 1,1-dioxides **15** and **16** with stabilizing aryl substituents in the 2-, 4- and/or 5-position will be tested towards various serine proteases.

Furthermore, we investigated the oxidation of isothiazolium salts **1** and **2** with MMPP · $6H_2O$ in an ultrasound bath at 50 °C in CH_3CN. After 3 h, using a one-step-method, the

Table 1. The oxidation of salts **1a–c, e, f** ($R^1 = C_6H_5$).

Salt	R^2	pK_a of anilinium	*rac-cis*-**7** [%]	**11** [%]	**13** [%]	**15** [%][a]
1a	2,4-$(NO_2)_2$	−4.27	86	66		38[7]
1b	2-Cl,4-NO_2	−1.05	97[b]	71	89	58[d]
1c	4-NO_2	1.00	74[c]	67		65[7]
1e	H	4.63		62	83	83
1f	4-OCH_3	5.34		66		68

[a]Method A.
[b]*rac-cis* **7b**/*rac-trans* **7b**/**11b** (4:1:2).
[c]*rac-cis* **7c**/*rac-trans* **7c**/**11c** (4:1:2).
[d]Method B, C (43%).

Table 2. The oxidation of salts **2a, c–f** ($R^1 = CH_3$).

Salt	R^2	pK_a of anilinium	*rac-cis*-**8** [%]	**12** [%]	**14** [%]	**16** [%][a]
2a	2,4-$(NO_2)_2$	−4.27	20[b]	57		48[7]
2c	4-NO_2	1.00	29[c]	95		91[7]
2d	2-Cl	2.65	68	62		61
2e	H	4.63	21	93	48	73
2f	4-OCH_3	5.34	–	78		42

[a]Method A.
[b]*rac-cis* **8a**/*rac-trans* **8a**/**12a** (2:1:1).
[c]*rac-cis* **8c**/*rac-trans* **8c**/**12c** (2:1:2).

Table 3. Analytical data of 3-hydroperoxy-2,4,5-triaryl-2,3-dihydroisothiazole 1,1-dioxides **11** and of 3-hydroperoxy-5-methyl-2,4-diaryl-2,3-dihydroisothiazole 1,1-dioxides **12**.

Cp.	^{1}H-NMR (acetone-d$_6$), δ (ppm), J (Hz)	^{13}C-NMR (acetone-d$_6$), δ (ppm)	Mp (°C)	EI-MS m/z (%)	Molecular formula-molecular weight	IR (cm^{-1})	EA calc./found
11a	6.76 (s, 1H, H-3), 7.46–7.58 (m, 10H, Ar), 8.41 (d, $J = 8.7$ Hz, 1H, Ar), 8.84 (dd, $J = 8.9$ Hz, $J = 2.7$ Hz, 1H, Ar), 9.01 (d, $J = 2.4$ Hz, 1H, Ar), 11.86 (s, 1H, OOH)	94.85 (C-3), 121.04, 122.42, 123.00, 124.80, 129.33, 129.77, 129.94, 130.27, 130.67, 130.75, 130.90, 131.06, 131.18, 131.48, 131.68, 131.74, 131.92, 132.02, 138.25, 138.75	125–130	451.1 ($M^{+\bullet} - H_2O$)	$C_{21}H_{15}N_3O_8S$ 469.4	1157 (SO_2) 1300 (SO_2) 1346 (NO_2) 1539 (NO_2)	C: 53.73/53.56 H: 3.22/3.32 N: 8.95/9.01 O: 27.27/26.99
11b	6.84 (s, 1H, H-3), 7.44–7.61 (m, 10H, Ar), 8.23 (d, $J = 8.7$ Hz, 1H, Ar), 8.44 (dd, $J = 8.6$ Hz, $J = 2.4$ Hz, 1H, Ar), 8.55 (d, $J = 2.4$ Hz, 1H, Ar), 11.67 (s, 1H, OOH)	91.64 (C-3), 123.26, 123.79, 125.95, 126.19, 127.00, 128.80, 128.94, 129.00, 129.11, 129.46, 129.60, 129.80, 130.32, 130.58, 130.71, 130.81, 132.04, 132.91, 133.48, 134.41	153–155	440.2 ($M^{+\bullet} - H_2O$)	$C_{21}H_{15}ClN_2O_6S$ 458.9	1159 (SO_2) 1300 (SO_2) 1348 (NO_2) 1527 (NO_2)	C: 54.97/54.83 H: 3.29/3.40 N: 6.10/5.99 O: 20.92/21.14
11c	7.29 (s, 1H, H-3), 7.44–7.64 (m, 10H, Ar), 7.82, 8.42 (dd, $J_{AB} = 7.2$ Hz, 4H, Ar), 11.72 (s, 1H, OOH)	90.60 (C-3), 117.99, 119.39, 126.54, 126.63, 126.78, 130.02, 130.11, 130.20, 130.67, 130.65, 130.70, 130.77, 130.89, 131.25, 131.61, 132.86, 140.33, 143.58, 147.65, 148.87	145–150	406.0 ($M^{+\bullet} - H_2O$)	$C_{21}H_{16}N_2O_6S$ 424.4	1151 (SO_2) 1294 (SO_2) 1340 (NO_2) 1512 (NO_2)	C: 59.43/59.60 H: 3.80/3.78 N: 6.60/6.52 O: 22.62/22.80
11e	6.93 (s, 1H, H-3), 7.41–7.63 (m, 15H, Ar), 11.41 (s, 1H, OOH)	91.63 (C3), 124.23, 127.15, 130.07, 130.51, 130.79, 130.83, 131.15, 131.20, 131.54	220–225	361.0 ($M^{+\bullet} - H_2O$)	$C_{21}H_{17}NO_4S$ 379.5	1153 (SO_2) 1302 (SO_2)	C: 66.48/66.93 H: 4.52/4.35 N: 3.69/3.40 O: 16.87/16.61
11f	3.84 (s, 3H, OCH_3), 6.67 (s, 1H, H-3), 7.38–7.61 (m, 14H, Ar), 11.28 (s, 1H, OOH)	56.51 (OCH_3), 93.31 (C-3), 130.02, 130.17, 130.33, 130.45, 130.71, 130.78, 130.86, 131.02, 131.08, 131.25, 131.29, 131.42, 131.67, 131.91, 131.97, 132.53, 132.91, 139.01, 140.60, 160.73	135–140	391.2 ($M^{+\bullet} - H_2O$)	$C_{22}H_{19}NO_5S$ 409.5	1151 (SO_2) 1294 (SO_2)	C: 64.53/64.38 H: 4.68/4.82 N: 3.42/3.31 O: 19.54/19.70

12a	2.27 (s, 3H, 5-CH_3), 6.56 (s, 1H, H-3), 7.55–7.69 (m, 6H, Ar), 8.30 (d, $J = 8.6$ Hz, 1H, Ar), 8.77 (dd, $J = 8.7$ Hz, $J = 2.7$ Hz, 1H, Ar), 11.64 (s, 1H, OOH)	8.91 (5-CH_3), 94.64 (C-3), 122.20, 129.10, 129.60, 129.80, 130.81, 131.35, 133.42, 135.83, 137.86, 138.47, 149.22	120–122	389.0 ($M^{+\bullet} - H_2O$)	$C_{16}H_{13}N_3O_8S$ 407.4	1132 (SO_2) 1302 (SO_2)	C: 47.18/47.40 H: 3.22/3.09 N: 10.32/10.50 O: 31.42/31.00
12c	2.27 (s, 3H, 5-CH_3), 7.07 (s, 1H, H-3), 7.56–7.75 (m, 5H, Ar), 8.01, 8.45 (d, $J_{AB} = 9.2$ Hz, 4H, Ar), 11.53 (s, 1H, OOH)	8.44 (5-CH_3), 90.05 (C-3), 118.58, 125.81, 129.69, 129.80, 130.77, 131.19, 134.40, 138.93, 142.68, 144.12	193–196	344.0 ($M^{+\bullet} - H_2O$)	$C_{16}H_{14}N_2O_6S$ 362.4	1126 (SO_2) 1294 (SO_2) 1342 (NO_2) 1510 (NO_2)	C: 53.03/53.40 H: 3.89/3.89 N: 7.73/7.90 O: 26.49/26.22
12d	2.31 (s, 3H, 5-CH_3), 6.52 (s, 1H, H-3), 7.46–7.67 (m, 9H, Ar), 11.28 (s, 1H, OOH)	8.90 (5-CH_3), 92.85 (C-3), 128.82, 129.47, 129.63, 129.69, 129.84, 130.53, 130.98, 131.51, 131.56, 131.76, 134.86	123–126	($M^{+\bullet} - H_2O$)	$C_{16}H_{14}ClNO_4S$ 351.8	1132 (SO_2) 1296 (SO_2)	C: 54.62/54.70 H: 4.01/3.92 N: 3.98/3.94 O: 18.19/18.30
12e	2.27 (s, 3H, 5-CH_3), 6.83 (s, 1H, H-3), 7.30–7.75 (m, 10H, Ar), 11.30 (s, 1H, OOH)	7.92 (5-CH_3), 90.78 (C-3), 122.52, 125.60, 128.64, 128.79, 128.96, 129.17, 129.47, 129.81, 129.94, 130.02, 130.37, 130.44	108–110	300.1 ($M^{+\bullet} - H_2O$)	$C_{16}H_{15}NO_4S$ 317.4	1128 (SO_2) 1290 (SO_2)	C: 60.55/60.70 H: 4.76/4.78 N: 4.41/4.41 O: 20.17/20.01
12f	2.20 (s, 3H, 5-CH_3), 3.82 (s, 3H, *p*-OCH_3), 6.51 (s, 1H, H-3), 6.98, 7.02 (d, $J_{AB} = 7.0$ Hz, 4H, Ar), 7.48–7.66 (m, 5H, Ar)	8.12 (5-CH_3), 55.19 (*p*-OCH_3), 92.46 (C-3), 114.65, 127.31, 128.46, 128.83, 129.05, 129.61, 131.19, 134.35, 138.20, 144.82, 158.46	152–153	329.0 ($M^{+\bullet} - H_2O$)	$C_{17}H_{17}NO_5S$ 347.4	1130 (SO_2) 1284 (SO_2)	C: 58.78/58.90 H: 4.93/4.69 N: 4.03/3.99 O: 23.03/22.95

acceptor-**13b**, and donor-substituted 3-hydroxysultams **13e** and **14e** were obtained as colourless crystals in very high yields (48–89%). The reaction mechanism is shown in scheme 1. The primary attack in this oxidation sequence with MMPP is in contrast to that of the H_2O_2/AcOH system [14, 15]. The first step of this oxidation occurred by attack of MMPP at the sulfur atom of salts **1** and **2** to form the reactive, not-isolable S-oxide intermediates **5** and **6**, which reacted with the nucleophilic oxygen of water to give **13** and **14**. The *rac-cis/trans* sultims **9 and 10** could not be isolated.

This new synthesis with MMPP·$6H_2O$ for 3-hydroxysultams **13** and **14** is better than the oxidation–reduction pathway of the salt **1b** *via* the 3-hydroperoxide **11b**, and the reduction with Na_2SO_3. Using the MMPP method, the hydroxide **13b** was isolated in 89% yield, and when the oxidation–reduction process was applied only a 58% total yield was obtained.

The 3-hydroxysultams **13** and **14** displayed the characteristic IR band of the sulfonyl group at 1130–1157 cm^{-1} and 1290–1298 cm^{-1}. In the ^1H NMR spectra of **13** and **14**, the H-3 proton absorptions appear at 6.16–6.43 ppm, and the OH-function at 6.57–6.65 ppm. The typical ^{13}C NMR data are 81.40–83.58 ppm for C-3.

In further investigations, we want to analyse the reaction of isothiazolium salts **1** and **2** with other O- or N-nucleophiles, *e.g.* MMPP · $6H_2O$ in alcohol, to form 3-alkoxy-sultims and -sultams.

Conclusions

In summary, the oxidation of diaryl- and triaryl-substituted isothiazolium salts **1** and **2** is a convenient method to synthesize 3-hydroperoxysultims **7** and **8**, the corresponding sultams **11** and **12**, and also 3-hydroxysultams **13** and **14**. Moreover, we could isolate for the first time the 3-hydroperoxyisothiazole **3a** after 15 min in H_2O_2/AcOH at room temperature, and, unexpectedly, the pure 3-hydroperoxysultim *rac-cis* **8e** with unsubstituted N-aryl ring as a crystalline product. The solid-state structure of the sultam **12f** was measured with X-ray crystallography. Furthermore, three routes to synthesize 3-oxosultams **15** and **16** have been found and established by oxidation of the precursors. The new synthesized di- and triaryl-substituted isothiazol-3(2*H*)-one 1,1-dioxides **15** and **16** are potent inhibitors of the human leukocyte elastase [7, 21].

3. Experimental

3.1 *General*

Mp: Boetius micro-melting-point apparatus; corrected. IR spectra: Genisis FTIR Unicam Analytical System (ATI Mattson); KBr pellets; values in cm^{-1}. ^1H NMR: Varian Gemini-200 and 300; δ in ppm rel. to TMS as internal standard. ^{13}C NMR spectra: 50 or 100 MHz, recorded on the named spectrometers. MS: Quadrupole-MS VG 12-250; 70 eV. Elemental analysis: Heraeus CHNO Rapid Analyzer.

3.2 *Synthesis of 2,4,5-triarylisothiazolium perchlorates (1) and 5-methyl-2,4-diarylisothiazolium perchlorates (2)*

The new salts **1b,e,f** and **2d** were prepared according to literature procedure [13]. Compounds **1a,c** and **2a,c** were described in [7], **2e** in [22], and **2f** in [23].

3.2.1 2-(2-Chloro-4-nitrophenyl)-4,5-diphenylisothiazolium perchlorate (1b). Yield 57%; mp 273–277 °C; ^{1}H NMR (DMSO-d_6) δ (ppm) 7.41–7.65 (m, 10H, Ar), 8.35 (d, 1H, Ar), 8.56 (dd, $J = 8.6$ Hz, $J = 2.3$ Hz, 1H, Ar), 8.75 (d, $J = 2.4$ Hz, 1H, Ar), 9.97 (s, 1H, H-3); ^{13}C NMR (DMSO-d_6) δ (ppm) 123.90, 125.67, 125.89, 125.90, 128.43, 129.23, 129.38, 129.62, 129.74, 129.83, 131.06, 131.15, 132.40, 134.95, 138.68, 149.53, 161.16 (C-3), 169.27; IR (KBr) ν (cm^{-1}) 1093 (ClO_4^-), 1350 (NO_2), 1531 (NO_2); ESI-MS (m/z) 393.0 (M-ClO_4)$^+$; elemental analysis for $C_{21}H_{14}Cl_2N_2O_6S$ (493.3): Calculated (%) C, 51.13; H, 2.86; N, 5.68; S, 6.50. Found (%) C, 51.10; H, 2.74; N, 5.58; S, 6.66.

3.2.2 2,4,5-Triphenylisothiazolium perchlorate (1e). Yield 81%; mp 210–212 °C; ^{1}H NMR (DMSO-d_6) δ (ppm) 7.51–7.65 (m, 10H, Ar), 7.77–7.80 (m, 3H, Ar), 8.03–8.08 (m, 2H, Ar), 10.03 (s, 1H, H-3); ^{13}C NMR (DMSO-d_6) δ (ppm) 123.35, 125.92, 128.90, 129.13, 129.38, 129.58, 129.65, 130.60, 131.61, 132.15, 135.35, 136.66, 157.48 (C-3), 165.42; IR (KBr) ν (cm^{-1}) 1092 (ClO_4^-); ESI-MS (m/z) 313.0 (M - ClO_4)$^+$; elemental analysis for $C_{21}H_{16}ClNO_4S$ (413.9): Calculated (%) C, 60.94; H, 3.90; N, 3.38. Found (%) C, 60.43; H, 4.04; N, 3.26.

3.2.3 2-(4-Methoxyphenyl)-4,5-diphenylisothiazolium perchlorate (1f). Yield 42%; mp 146–149 °C; ^{1}H NMR (DMSO-d_6) δ (ppm): 3.92 (s, 3H, OCH_3), 7.30–7.59 (m, 10H, Ar), 7.97, 8.01 (d, $J_{AB} = 8.8$ Hz, 4H, Ar), 9.94 (s, 1H, H-3); ^{13}C NMR (DMSO-d_6) δ (ppm) 55.96 (OCH_3), 115.43, 125.01, 125.90, 128.90, 129.04, 129.30, 129.47, 129.55, 129.62, 131.96, 135.06, 157.23 (C-3), 161.36, 164.48; IR (KBr) ν (cm^{-1}) 1113 (ClO_4^-); ESI-MS (m/z) 344.1 (M - ClO_4)$^+$; elemental analysis for $C_{22}H_{18}ClNO_5S$ (443.9): Calculated (%) C, 59.53; H, 4.09; N, 3.16; S, 7.22. Found (%): C, 59.70; H, 3.89; N, 3.33; S, 7.07.

3.2.4 2-(2-Chlorophenyl)-5-methyl-4-phenylisothiazolium perchlorate (2d). Yield 83%; mp 148–149 °C; ^{1}H NMR (DMSO-d_6) δ (ppm) 2.96 (s, 3H, 5-CH_3), 7.61–7.73 (m, 9H, Ar), 9.81 (s, 1H, H-3); ^{13}C NMR (DMSO-d_6) δ (ppm) 15.00 (5-CH_3), 129.48, 129.73, 129.97, 130.23, 130.29, 131.64, 134.24, 134.48, 137.08, 160.15 (C-3), 170.07; IR (KBr) ν (cm^{-1}): 1086 (ClO_4^-); ESI-MS (m/z) 286.1 (M - ClO_4)$^+$; elemental analysis for $C_{16}H_{13}Cl_2NO_4S$ (386.3): Calculated (%) C, 49.75; H, 3.39; N, 3.63. Found (%) C, 49.60; H, 3.19; N, 3.61.

3.3 *Synthesis of 3-hydroperoxy-2-(2,4-dinitrophenyl)-4,5-diphenyl-2,3-dihydroisothiazole (3a)*

H_2O_2 (0.7 mL, 30%) was added to a stirred suspension of **1a** (0.26 mmol) in AcOH (0.7 mL) at room temperature. After dissolution of salt **1a**, a colourless precipitate of **3a** and unchanged salt **1a** (3:1) was obtained after 15 min, and the title product isolated.

3.3.1 3-Hydroperoxy-2-(2,4-dinitrophenyl)-4,5-diphenyl-2,3-dihydroisothiazole (3a). Yield 96% (mixture with **1a**); mp 180–183$^{\cdots}$ 270–275 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 6.36 (s, 1H, H-3), 7.42–7.75 (m, 10H, Ar), 8.75 (d, $J = 8.60$ Hz, 1H, Ar), 9.05 (dd, $J = 8.6$ Hz, $J = 2.4$ Hz, 1H, Ar), 9.29 (d, $J = 2.4$ Hz, 1H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm) 96.18 (C-3), 116.81, 121.35, 127.62, 128.57, 128.91, 129.02, 129.31, 129.55, 129.77, 129.91, 130.18, 130.49, 131.77, 132.98, 133.62, 134.81, 139.35; IR (KBr) ν (cm^{-1}) 1344 (NO_2), 1534 (NO_2); ESI-MS (m/z) 436.1 (M - H)$^-$; $C_{21}H_{15}N_3O_6S$ (437.4).

3.4 *Synthesis of 3-hydroperoxy-2,4,5-triaryl-2,3-dihydroisothiazole 1-oxides (rac-cis 7) and 3-hydroperoxy-5-methyl-2,4-diaryl-2,3-dihydroisothiazole 1-oxides (rac-cis 8)*

3.4.1 General procedure. H_2O_2 (0.7 mL, 30%) was added to a stirred suspension of a salt **1a–c** or **2a,c–e** (0.26 mmol) in AcOH (0.7 mL) at room temperature. After dissolution of **1** or **2**, a colourless precipitate of **7a–c** or **8a,c–e** was obtained after 1.5–23 h and was isolated. The crude product was washed with water. The oxidation of salts **1b** and **c** and **2a** and **c** gave a mixture of *rac-cis* **7** with *rac-trans* **7** and sultams **11** as well as *rac-cis* **8** with *rac-trans* **8** and sultams **12** (see also tables 1 and 2)

3.4.2 3-Hydroperoxy-2-(2,4-ditrophenyl)-4,5-diphenyl-2,3-dihydroisothiazole 1-oxide (*rac-cis* 7a). Yield 86%; mp 123–126 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 6.59 (s, 1H, H-3), 7.39–7.53 (m, 10H, Ar), 8.32 (d, $J = 8.9$ Hz, 1H, Ar), 8.67 (dd, $J = 8.9$ Hz, $J = 2.6$ Hz, 1H, Ar), 8.86 (d, $J = 2.6$ Hz, 1H, Ar), 11.37 (s, 1H, OOH); ^{13}C NMR (acetone-d_6) δ (ppm) 102.59 (C-3) 121.51, 121.62, 123.25, 128.21, 128.62, 128.83, 128.90, 129.08, 129.15, 129.26, 129.41, 129.64, 129.80, 129.91, 130.07, 130.35, 130.43, 131.33, 131.42, 135.06; IR (KBr) ν (cm^{-1}) 1072 (SO), 1344 (NO_2), 1535 (NO_2); EI-MS (m/z) 435.1 ($M^{+\bullet} - H_2O$); elemental analysis for $C_{21}H_{15}N_3O_7S$ (453.4): Calculated (%) C, 55.63; H, 3.33; N, 9.27. Found (%) C, 55.74; H, 3.22; N, 9.09.

3.4.3 2-(2-Chloro-4-nitrophenyl)-3-hydroperoxy-4,5-diphenyl-2,3-dihydroisothiazole 1-oxide (*rac-cis* 7b). Yield 97%; mp 119–123 °C; ^{1}H NMR (acetone-d_6) δ (ppm)[a] 6.49 (s, 1H, H-3), 7.38–7.59 (m, 10H, Ar), 8.05 (d, $J = 8.7$ Hz, 1H, Ar), 8.16 (d, $J = 8.7$ Hz, 1H, Ar), 8.37–8.41 (m, 1H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm)[b] 101.50 (C-3), 113.49, 123.17, 123.28, 124.36, 125.61, 125.72, 128.78, 128.83, 128.93, 129.22, 129.28, 129.36, 129.40, 129.55, 129.66, 129.79, 130.42, 133.59, 133.93; IR (KBr) ν (cm^{-1}) 1063 (SO), 1348 (NO_2), 1522 (NO_2); EI-MS (m/z) 424.3 ($M^{+\bullet} - H_2O$); elemental analysis for $C_{21}H_{15}ClN_2O_5S$ (442.9): Calculated (%) C, 56.95; H, 3.41; N, 6.33. Found (%) C, 56.83; H, 3.28; N, 6.29. NMR data for *rac-trans* **7b**: [a]6.73 (s, 1H, H-3); [b]97.60 (C-3);

3.4.4 3-Hydroperoxy-2-(4-nitrophenyl)-4,5-diphenyl-2,3-dihydroisothiazole 1-oxide (*rac-cis* 7c). Yield 74%; mp 130–133 °C; ^{1}H NMR (acetone-d_6) δ (ppm)[a] 7.02 (s, 1H, H-3), 7.37–7.64 (m, 10H, Ar), 8.26–8.33 (m, 4H, Ar), 11.22 (s, 1H, OOH); ^{13}C NMR (acetone-d_6) δ (ppm)[b] 100.64 (C-3), 117.99, 126.79, 130.02, 130.20, 130.47, 130.65, 130.70, 130.77, 130.89, 131.00, 131.17, 131.59, 131.90, 132.86, 140.33, 147.65; IR (KBr) ν (cm^{-1}) 1072 (SO), 1344 (NO_2), 1535 (NO_2); EI-MS (m/z) 406.0 ($M^{+\bullet} - H_2O$); elemental analysis for $C_{21}H_{16}N_2O_6S$ (424.4): Calculated (%) C, 59.43; H, 3.80; N, 6.60. Found (%) C, 59.22; H, 3.71; N, 6.69.

NMR data for *rac-trans* **7c**: [a]7.09 (s, 1H, H-3); [b]98.66 (C-3).

3.4.5 3-Hydroperoxy-2-(2,4-dinitrophenyl)-5-methyl-4-phenyl-2,3-dihydroisothiazole 1-oxide (*rac-cis* 8a). Yield 20%; mp 98–101 °C; ^{1}H NMR (acetone-d_6) δ (ppm)[a] 2.29 (s, 3H, CH_3), 6.56 (s, 1H, H-3), 7.47–7.66 (m, 5H, Ar), 7.81 (d, $J = 9.5$ Hz, 1H, Ar), 8.28 (dd, $J = 9.5$ Hz, $J = 2.7$ Hz, 1H, Ar), 8.93–8.96 (m, 1H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm)[b] 10.60 (CH_3), 99.07 (C-3), 117.28, 122.21, 123.83, 129.11, 129.60, 129.73, 129.96, 130.02, 130.56, 130.82, 131.08, 137.88, 139.16, 146.10; IR (KBr) ν (cm^{-1}) 1070 (SO), 1348 (NO_2), 1535 (NO_2); EI-MS (m/z) 392.1 ($M^{+\bullet}$+ H); elemental analysis for $C_{16}H_{13}N_3O_7S$ (391.4): Calculated (%) C, 49.10; H, 3.35; N, 10.74. Found (%) C, 49.19; H, 3.28; N, 10.69.

NMR data for *rac-trans* **8a**: [a]6.55 (s, 1H, H-3); [b]99.28 (C-3).

3.4.6 3-Hydroperoxy-2-(4-nitrophenyl)-5-methyl-4-phenyl-2,3-dihydroisothiazole 1-oxide (*rac-cis* 8c). Yield 68%; mp 134–136 °C; ^{1}H NMR (acetone-d_6) δ (ppm)[a] 2.37 (s, 3H, CH_3), 6.48 (s, 1H, H-3), 7.01–7.51 (m, 5H, Ar), 7.82–8.01 (m, 4H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm)[b] 12.28 (CH_3), 103.92 (C-3), 108.92, 110.85, 113.98, 114.22, 125.70, 126.52, 126.87, 129.36, 129.50, 129.70, 129.81, 130.34, 130.54, 130.68; IR (KBr) ν (cm^{-1}) 1070 (SO), 1342 (NO_2), 1504 (NO_2); EI-MS (m/z) 328.1 ($M^{+\bullet} - H_2O$); elemental analysis for $C_{16}H_{14}N_2O_5S$ (346.4): Calculated (%) C, 55.48; H, 4.07; N, 8.09. Found (%) C, 55.36; H, 3.98; N, 8.08.

NMR data for *rac-trans* **8c**: [a]6.68 (s, 1H, H-3); [b]98.41 (C-3).

3.4.7 2-(2-Chlorophenyl)-3-hydroperoxy-5-methyl-4-phenyl-2,3-dihydroisothiazole 1-oxide (*rac-cis* 8d). Yield 68%; mp 115–117 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 2.27 (s, 3H, 5-CH_3), 6.32 (s, 1H, H-3), 7.46–7.86 (m, 9H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm) 11.26 (5-CH_3), 101.82 (C-3), 128.24, 128.85, 129.02, 129.11, 129.23, 129.90, 130.35, 130.54, 130.94, 132.63, 134.47, 135.39, 139.13, 143.14; IR (KBr) ν (cm^{-1}) 1066 (SO); EI-MS (m/z) 335.0 ($M^{+\bullet}$); elemental analysis for $C_{16}H_{14}ClNO_3S$ (335.8): Calculated (%) C, 57.23; H, 4.20; N, 4.17. Found (%) C, 57.32; H, 4.07; N, 4.23.

3.4.8 3-Hydroperoxy-5-methyl-2,4-diphenyl-2,3-dihydroisothiazole 1-oxide (*rac-cis* 8e). Yield 21%; mp 134–136 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 2.23 (s, 3H, 5-CH_3), 6.72 (s, 1H, H-3), 7.39–7.70 (m, 10H, Ar), 11.03 (s, 1H, OOH); ^{13}C NMR (DMSO-d_6) δ (ppm) 12.20 (5-CH_3), 99.13 (C-3), 119.36, 124.54, 130.06, 130.37, 130.47, 130.63, 130.82; IR (KBr) ν (cm^{-1}) 1079 (SO); EI-MS (m/z) 301.0 ($M^{+\bullet}$); elemental analysis for $C_{16}H_{15}NO_3S$ (301.4): Calculated (%) C, 63.77; H, 5.02; N, 4.65. Found (%) C, 63.67; H, 5.12; N, 4.49.

3.5 *Synthesis of 3-hydroperoxy-2,4,5-triaryl-2,3-dihydroisothiazole 1,1-dioxides (11) and 3-hydroperoxy-5-methyl-2,4-diaryl-2,3-dihydroisothiazole 1,1-dioxides (12)*

3.5.1 General procedure. H_2O_2 (0.7 mL, 30%) was added to a suspension of **1a–c,e,f** or **2a,c–f** (0.26 mmol) in AcOH (0.7 mL). The solution was stirred for 24–120 h at room temperature. The crude product **11** or **12** was washed with water, see table 3.

3.6 *Synthesis of 3-hydroxy-2,4,5-triaryl-2,3-dihydroisothiazole 1,1-dioxides (13b,e) and 3-hydroxy-5-methyl-2,4-diaryl-2,3-dihydroisothiazole 1,1-dioxides (14e)*

3.6.1 General procedure. *Method A*: MMPP · $6H_2O$ (1.56 mmol) was added to a suspension of a salt **1b,e** or **2e** (0.26 mmol) in acetonitrile (4 mL). The mixture was left in an ultrasound bath for 3 h at 50 °C. The excess of MMPP was decomposed by addition of sodium thiosulfate, the generated acid was neutralized with saturated aqueous $NaHCO_3$, and the mixture was extracted with Et_2O (3 × 3 mL). The combined organic layers were dried over $MgSO_4$. The solvent was evaporated off and a 3-hydroxysultam **13b,e** or **14e** was obtained. *Method B*: 3-Hydroperoxide **11b** (0.26 mmol) was added to a solution of $Na_2SO_3 \cdot 5H_2O$ (0.52 mmol) in distilled water (4 mL). The suspension was stirred for 24 h at room temperature. After stirring, the mixture was extracted with Et_2O (3 × 3 mL). The combined organic layers were dried over $MgSO_4$. The solvent was evaporated off and compound **13b** was obtained.

3.6.2 2-(2-Chloro-4-nitrophenyl)-3-hydroxy-4,5-diphenyl-2,3-dihydroisothiazole 1,1-dioxide (13b). Yield 89% (Method A)/63% (Method B); mp 225–230 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 6.43 (d, $J = 8.8$ Hz, 1H, H-3), 6.57 (d, $J = 8.8$ Hz, 1H, OH), 7.38–7.58 (m, 10H, Ar), 8.09 (d, $J = 8.8$ Hz, 1H, ar), 8.39 (dd, $J = 8.7$ Hz, $J = 2.6$ Hz, 1H, Ar), 8.50 (d, $J = 2.6$ Hz, 1H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm) 83.58 (C-3), 123.67, 126.38, 127.87, 129.52, 129.95, 130.09, 130.38, 130.51, 130.69, 130.97, 131.29, 131.43, 131.96, 132.69, 134.06, 135.20, 136.51, 137.27, 138.49, 143.05; IR (KBr) ν (cm^{-1}) 1157 (SO_2), 1298 (SO_2), 1350 (NO_2), 1525 (NO_2); EI-MS (m/z) 442.0 ($M^{+\bullet}$); elemental analysis for $C_{21}H_{15}ClN_2O_5S$ (442.9): Calculated (%) C, 56.95; H, 3.41; N, 6.33. Found (%) C, 57.12; H, 3.67; N, 6.09.

3.6.3 3-Hydroxy-2,4,5-triphenyl-2,3-dihydroisothiazole 1,1-dioxide (13e). Yield 83%; mp 195–200 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 6.16 (d, $J = 9.9$ Hz, 1H, H-3), 6.65 (d, $J = 9.9$ Hz, 1H, OH), 7.38–7.66 (m, 15H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm) 81.40 (C-3), 121.90, 128.38, 128.67, 128.94, 129.21, 129.33, 129.44, 129.53, 129.69, 129.80, 129.93, 130.11, 130.44, 130.55, 130.69, 130.89, 131.26, 131.86, 132.77, 133.42; IR (KBr) ν (cm^{-1}) 1147 (SO_2), 1292 (SO_2); EI-MS (m/z) 361.0 ($M^{+\bullet} - H_2$); elemental analysis for $C_{21}H_{17}NO_3S$ (363.4): Calculated (%) C, 69.40; H, 4.71; N, 3.85. Found (%) C, 69.50; H, 4.72; N, 3.96.

3.6.4 3-Hydroxy-5-methyl-2,4-diphenyl-2,3-dihydroisothiazole 1,1-dioxide (14e). Yield 48%; mp 125–132 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 2.18 (s, 3H, CH_3), 5.96 (d, $J = 8.8$ Hz, 1H, H-3), 6.50 (d, $J = 10.0$ Hz, 1H, OH), 7.18–7.64 (m, 10H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm) 7.81 (CH_3), 81.88 (C-3), 121.80, 125.01, 128.61, 128.74, 128.91, 129.16, 129.42, 129.67, 129.89, 129.98, 130.33, 130.39; IR (KBr) ν (cm^{-1}) 1130 (SO_2), 1290 (SO_2); EI-MS (m/z) 299.0 ($M^{+\bullet} - H_2$); elemental analysis for $C_{16}H_{15}NO_3S$ (301.4): Calculated (%) C, 63.77; H, 5.02; N, 4.65. Found (%) C, 63.30; H, 4.93; N, 4.46.

3.7 *Synthesis of 2,4,5-triarylisothiazol-3(2H)-one 1,1-dioxides(15) and 5-methyl-2,4-diarylisothiazol-3(2H)-one 1,1-dioxides (16)*

3.7.1 General procedure. *Method A*: H_2O_2 (0.7 mL, 30%) was added to a suspension of **1b,e,f** or **2d–f** (0.26 mmol) in AcOH (0.7 mL). The solution was stirred for 8–24 h at 80 °C. After cooling, the 3-oxosultams **15** and **16** were isolated.

Method B: By following procedure A, a mixture containing **15b** and respective hydroperoxide **11b** was isolated in this case. The mixture was dissolved in ethanol (4 mL), and conc. HCl (0.3 mL) was added. The mixture was refluxed for 6–8 h. After cooling, the corresponding 3-oxosultam **15b** was isolated by filtration.

Method C: $(pyH)_2Cr_2O_7$ (0.65 mmol) was added to a solution of **13b** (0.26 mmol) in CH_2Cl_2 (1 mL). The suspension was stirred for 8 h at room temperature. Purification was by column chromatography (Al_2O_3, EtOAc). The combined organic layers were washed successively with aq. Na_2CO_3 (10%) and saturated aq. NaCl, and dried over Na_2SO_4. The solvent was evaporated off and the 3-oxosultam **15b** was obtained. Compounds **15a** and **c** and **16a** and **b** were described in [7].

3.7.2 2-(2-Chloro-4-nitrophenyl)-4,5-diphenylisothiazol-3(2H)-one 1,1-dioxide (15b). Yield 58% (Method B)/43% (Method C); mp 180–185 °C; ^{1}H NMR (acetone-d_6) δ (ppm): 7.50–7.70 (m, 10H, Ar), 8.10 (d, $J = 8.7$ Hz, 1H, Ar), 8.52 (dd, $J = 8.6$ Hz, $J = 2.4$ Hz, 1H, Ar), 8.65 (d, $J = 2.4$ Hz, 1H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm) 125.01, 126.31, 127.45, 128.57, 130.19, 131.04, 131.96, 132.09, 133.35, 134.17, 134.72, 134.81, 137.61,

146.60, 151.15, 159.81 (C-3); IR (KBr) ν (cm^{-1}) 1151 (SO_2), 1302 (SO_2), 1344 (NO_2), 1531 (NO_2), 1736 (CO); EI-MS (m/z) 440.1 ($M^{+\bullet}$); elemental analysis for $C_{21}H_{13}ClN_2O_5S$ (440.9): Calculated (%) C, 57.21; H, 2.97; N, 6.35. Found (%) C, 57.30; H, 3.18; N, 6.42.

3.7.3 2,4,5-Triphenylisothiazol-3(2*H*)-one 1,1-dioxide (15e). Yield 83% (Method A); mp 231–233 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 7.47–7.68 (m, 15H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm) 123.59, 126.01, 128.43, 129.31, 129.82, 130.12, 130.14, 130.33, 130.39, 130.51, 130.62, 131.01, 131.33, 132.24, 134.41, 144.63, 160.11 (C-3); IR (KBr) ν (cm^{-1}) 1142 (SO_2), 1295 (SO_2), 1733 (CO); EI-MS (m/z) 361.0 ($M^{+\bullet}$); elemental analysis for $C_{21}H_{15}NO_3S$ (361.4): Calculated (%) C, 69.79; H, 4.18; N, 3.88. Found (%) C, 69.98; H, 4.22; N, 3.76.

3.7.4 2-(4-Methoxyphenyl)-4,5-diphenylisothiazol-3(2*H*)-one 1,1-dioxide (15f). Yield 68% (Method A); mp 178–179 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 3.89 (s, 3H, OCH_3), 7.13, 7.18 (d, $J_{AB} = 9.0$ Hz, 4H, Ar), 7.46–7.59 (m, 10H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm) 56.02 (OCH_3), 115.95, 122.32, 126.22, 128.54, 129.37, 130.21, 130.39, 131.08, 131.26, 131.34, 132.27, 161.83 (C-3); IR (KBr) ν (cm^{-1}) 1144 (SO_2), 1294 (SO_2), 1728 (CO); EI-MS (m/z) 391.0 ($M^{+\bullet}$); elemental analysis for $C_{22}H_{17}NO_4S$ (391.4): Calculated (%) C, 67.50; H, 4.38; N, 3.58. Found (%) C, 67.70; H, 4.29; N, 3.51.

3.7.5 2-(2-Chlorophenyl)-5-methyl-4-phenylisothiazol-3(2*H*)-one 1,1-dioxide (16d). Yield 61% (Method A); mp 193–195 °C; ^{1}H NMR (acetone-d_6) δ (ppm): 2.50 (s, 3H, 5-CH_3), 7.55–7.68 (m, 9H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm): 9.88 (5-CH_3), 128.39, 128.58, 129.95, 130.13, 130.26, 130.33, 131.55, 131.81, 132.41, 133.71, 135.39, 136.24, 145.94, 159.70 (C-3); IR (KBr) ν (cm^{-1}) 1159 (SO_2), 1332 (SO_2), 1735 (CO); EI-MS (m/z) 334.0 ($M^{+\bullet}$); elemental analysis for $C_{16}H_{12}ClNO_3S$ (333.8): Calculated (%) C, 57.57; H, 3.62; N, 4.20. Found (%):C, 57.70; H, 3.72; N, 4.07.

3.7.6 5-Methyl-2,4-diphenylisothiazol-3(2*H*)-one 1,1-dioxide (16e). Yield 73% (Method A); mp 103–104 °C; ^{1}H NMR (acetone-d_6) δ (ppm) 2.40 (s, 3H, 5-CH_3), 7.28–7.67 (m, 10H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm) 9.39 (5-CH_3), 121.06, 127.35, 129.18, 129.53, 129.60, 129.98, 130.63, 130.66, 130.89, 134.49, 143.29, 159.77 (C-3), 166.61; IR (KBr) ν (cm^{-1}) 1139 (SO_2), 1249 (SO_2), 1731 (CO); EI-MS (m/z) 299.0 ($M^{+\bullet}$); elemental analysis for $C_{16}H_{13}NO_3S$ (299.4): Calculated (%) C, 64.20; H, 4.38; N, 4.68. Found (%) C, 64.10; H, 4.21; N, 4.66.

3.7.7 5-Methyl-2-(4-methoxyphenyl)-4-phenylisothiazol-3(2*H*)-one 1,1-dioxide (16f). Yield 42% (Method A); mp 119–120 °C; ^{1}H NMR (acetone-d_6) δ (ppm: 2.50 (s, 3H, 5-CH_3), 3.92 (s, 3H, *p*-OCH_3), 7.16–7.19 (m, 4H, Ar), 7.47–7.71 (m, 5H, Ar); ^{13}C NMR (acetone-d_6) δ (ppm): 8.40 (5-CH_3), 55.35 (*p*-OCH_3), 115.25, 121.74, 127.64, 128.77, 130.34, 130.38, 130.54, 134.43, 143.55, 161.12 (C-3); IR (KBr) ν (cm^{-1}) 1145 (SO_2), 1249 (SO_2), 1731 (CO); EI-MS (m/z) 329.0 ($M^{+\bullet}$); elemental analysis for $C_{17}H_{15}NO_4S$ (329.4): Calculated (%) C, 61.99; H, 4.59; N, 4.25. Found (%) C, 61.70; H, 4.52; N, 4.29.

3.8 *X-ray structural analysis of 3-hydroperoxy-5-methyl-2-(4-methoxyphenyl)-4-phenyl-2,3-dihydroisothiazole 1,1-dioxide 12f*

3.8.1 Crystal data. $C_{17}H_{17}NO_5S$, FW 347.4, $T = 223(2)$ K. Crystal system Monoclinic. Space group $P2(1)/c$, $a = 11.0779(8)$ Å, $b = 8.1501(6)$ Å, $c = 18.9432(13)$ Å, β 106.3570(10)°, $V = 1641.1(2)$ Å^3, $Z = 4$, $\rho = 1.406$ mg/m^3, Absorption coeff. 0.224 mm^{-1}.

Crystal size $0.30 \times 0.20 \times 0.10\,\text{mm}^3$. Range for data collection 2.24–28.29°, index ranges $-14 \leq h \leq 12$, $-10 \leq k \leq 10$, $-17 \leq l \leq 24$. Reflections collected 10128, independent reflections 3990 [$R_{(\text{int})} = 0.0377$]. Absorption correction SADABS, Max./Min. transmission 0.9779/0.9358, data/parameters 3990/285. Final R indices [$I > 2\sigma(I)$] $R^1 = 0.0426$, $wR^2 = 0.0854$, R indices (all data) $R^1 = 0.0868$, $wR^2 = 0.0952$, Lgst. Diff peak/hole $0.276/-0.308\,\text{e}\,\text{Å}^{-3}$.

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[18] Crystals were obtained from acetone. The intensities were measured on a Siemens SMART CCD diffractometer. Data collection and cell refinement are listed in the text. The structure was solved by direct methods with SHELX-97 [19]. The refinement was done with SHELXL-97 [20]. Crystallographic data for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre, CCDC No. 268977 for **12f**. Copies of the data can be obtained, free of charge, from CCDC, 12 Union Road, Cambridge, CB2 1EZ. UK [fax: +44(1233)336033; e-mail: deposit@ccdc.cam.ac.uk; internet: http://www.ccdc.cam.ac.uk].
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