

Oxidation of Acceptor-substituted Isothiazolium-2-imines to Stable Cyclic Sulfin- and Sulfonamides with 3-Hydroperoxy Function ¹⁾

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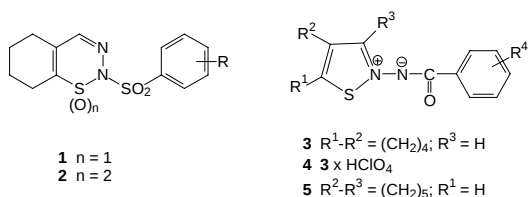
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Abstract. The oxidation of isothiazolium 2-imines **3,5** and their salts **4** to stable 3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1-oxides **7** and 1,1-dioxides **8** and **9** as a

new class of cyclic sultims and sultams is described. The formation of 3-hydroxysultams **10** and isothiazol-3(2H)one 1,1-dioxides **11** is presented.

In the course of our study on the oxidation of *N*-aryl-isothiazolium salts, we have investigated the influence of the donor and acceptor functionality at the aryl ring as well as their stereochemical aspects of the formation of *rac*-*cis*-3-hydroperoxy sultims and sultams [1–4]. Surprisingly, by oxidation of *N*-benzenesulfonylamino isothiazolium salts or the corresponding 2-imines with hydrogen peroxide the ring enlargement products 1,2,3-thiadiazine 1-oxides **1** and 1,1-dioxides **2** can be synthesized easily [5], no hydroperoxides could be isolated. This is a new method for the preparation of 1,2,3-thiadiazines [6, 7].

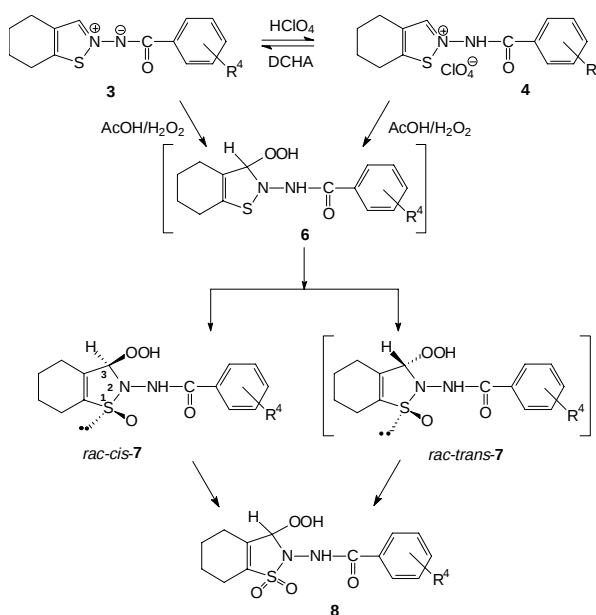
In this paper, we would like to report the synthesis of stable new 3-hydroperoxides of bicyclic *N*-benzoylamino five-membered isothiazole 1-oxides and 1,1-dioxides by oxidation of isothiazolium-2-imines **3, 5** or their salts **4** in good yields for the first time.



Results

The starting materials, bicyclic isothiazolium-2-imines and their salts **3–5** were prepared by cyclocondensation of thiocyanates with benzene hydrazides according to our reported synthesis [8, 9]. The oxidation of **3**, which have electron-withdrawing substituents in the benzoyl ring ($R = Cl, NO_2, CF_3$), with hydrogen peroxide (30%) at 0 °C in acetic acid (Scheme 1) gave the

rac-*cis*-sultims **7c–e, g–i** in moderate yields (13–32%) after one hour as firstly isolatable products. Ring enlargement products like 1,2,3-thiadiazines **1**, which were obtained by the oxidation of *N*-benzenesulfonyl-isothiazolium-2-imines [5], could not be observed.



	R^4		R^4
a	H	f	2- NO_2
b	4- CH_3	g	3- NO_2
c	2-Cl	h	4- NO_2
d	3-Cl	i	3- CF_3
e	4-Cl		

Scheme 1 Oxidation of bicyclic isothiazolium-2-imines **3** or their salts **4** to stable 3-hydroperoxy-sultims *rac*-*cis*-**7** and sultams **8**

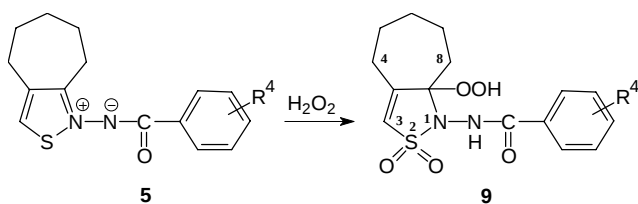
¹⁾ Presented in part at the Fourth Conference on Iminium Salts, Stimpfach-Rechenberg (Germany), September 14–16, 1999

The characteristic spectral data of the stable *rac-cis*-**7** are the IR absorption of the SO bond at 1050–1070 cm⁻¹ and the chemical shift of C(3) in ¹³C NMR (acetone-d₆), which appears at 101.7–101.9 ppm. These spectroscopic data are in good agreement with the *cis*-configuration of the *cis*-2-aryl-3-hydroperoxysultims [3].

When same oxidation of the imines **3** is carried out at room temperature the corresponding 1,1-dioxides **8a–i** were isolated (32–58%) after 8h. The hydroperoxides **8** melt with elimination of water followed by crystallization of the formed 3-oxosultams **11** in a few cases. The melt of **11** can be observed at 10–20 degrees above the melting point of **8**. The characteristic ¹³C chemical shifts of the C-3 atoms in **8** are 94.2–94.5 ppm, and typical SO₂ absorption bands in the IR spectra are at 1160–1190 and 1290–1330 cm⁻¹.

The mechanism of the oxidation is assumed to begin with nucleophilic attack of hydrogen peroxide at C-3 of the imines **3**. The first intermediate **6** could not be isolated. The next step is the oxidation of the sulfur atom with formation of the *rac-cis*- and *rac-trans*-3-hydroperoxy sultims **7**. We could only isolate *rac-cis*-**7** when there is an acceptor substituents at the benzoyl ring. These acceptor substituents reduce the electron density in the benzoyl ring of **7c–i**. The *cis*-attack in **6** is preferred because of the hydrogen bond between the oxidants and the 3-hydroperoxy group on the *syn*-side. There is an additional stabilization of *rac-cis*-**7** by electrostatic interaction between the electron-poor aromatic ring and the sulfur of the isothiazole ring. The *rac-trans*-**7** are more reactive than *rac-cis*-**7** and so they are more rapidly oxidized to give the sultams **8**.

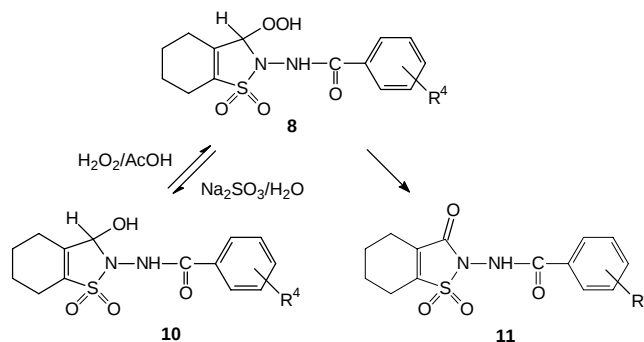
The oxidation with 30% H₂O₂ in acetic acid at room temperature of the isothiazolium-1-imines **5a,g,h** containing substituents in the 3- and 4-position of the isothiazole ring, gave sultams **9a,g,h**, respectively. The corresponding sultims could not be isolated (Scheme 2). The hydroperoxide structure of **9a** was confirmed by X-ray crystal-structure analysis [10]. This is the first X-ray analysis of a hydroperoxide in the 2-benzoylamino serie. The isothiazole ring of **9a** is a planar one with a flat endocyclic N-atom attached to the SO₂ group. The crystals of **9a** show two intermolecular H-bonds between one O-atom of the SO₂ group and the H-atom of the NH-group of a second molecule of **9a**, and a intramo-



Scheme 2 Oxidation of isothiazolium-1-imines **5** to stable hydroperoxides **9**

lecular H-bond between the O-atom of the exocyclic carbonyl group and the H-atom of the HOO-group [10].

The hydroperoxides **8** are converted into the novel 3-hydroxysultams **10a,b,d,e,g–i** by reduction with Na₂SO₃ in water in high yields (71–90%). Typical in the ¹H NMR spectra of **10** is the 3-H proton absorption at 5.54–5.70 ppm. The ¹³C signal of the C-3 atoms appears between 83.6–85.4 ppm in acetone-d₆.



Scheme 3 Synthesis of 3-hydroxy-sultams **10** and 2-benzoylamino-tetrahydro-saccharines **11**

The oxo-products **11** were separated as by-products from the oxidation to 1-oxides **7** and 1,1-dioxides **8**. The conversion of the hydroperoxides **8** into 3-oxosultams **11a,b,d,h** by thermolysis in ethanol via elimination of water is a better way. The IR spectra of the 1,1-dioxides **11** show two carbonyl absorption bands at 1760 cm⁻¹ for (3-C=O) and 1650–1680 cm⁻¹ (for NHCO) and absorptions for the SO₂ group at 1160–1180 cm⁻¹ and 1270–1290 cm⁻¹. The signal of the C-3 atoms in the ¹³C spectra are found at 165.0 ppm. Furthermore, we found that 3-hydroxysultams **10** can be reoxidized to the hydroperoxides **8** with H₂O₂ (Scheme 3). We will give a report later about the elimination of water of the sultams **10** to give firstly oxidizing isothiazolium 2-imines as educts for new bicyclic systems. First attempts to use the novel 3-hydroperoxy-sultams **8** as oxidizing agents were also carried out.

Conclusion

In summary, it has been shown in contrast to our earlier report [5], that the oxidation of acceptor-substituted isothiazolium-2-imines **3** and **5** with H₂O₂ in acetic acid leads also to stable 3-hydroperoxy-2-benzoylamino-hexahydro-1,2-benzisothiazole 1-oxides *rac-cis*-**7** and 1,1,-dioxides **8**. No ring enlargement products to 1,2,3-thiadiazines are observed.

Furthermore, a new efficient route to 3-hydroxy-sultams **10**, which are versatile educts for new bicyclic compounds, has been found.

Experimental

IR: ATI Mattson Genesis Series FTIR Unicam Analytical Systems. – UV/Vis: Beckman DU 650 Spectrophotometer. – NMR: Varian Unity 400 Spectrometer, TMS internal standard. – Elemental analysis: Heareus- CHN–O–S-RAPID-Analyser. – MS: Quadrupol VG-12-250 of Analytical Instruments Manchester. – Melting points were determined on a Boëtius micro melting point apparatus and have been corrected.

N-Benzoyl-4,5,6,7-tetrahydro-1,2-benzisothiazolium-2-imines **3a–k** (General Procedure)

The imines **3a,b,e,f,h** and salts **4a,b,e,f,h** were described in [8]. The new imines **3c,d,g,i** and perchlorates **4c,g** were prepared according [8].

N-(2-Chlorobenzoyl)-4,5,6,7-tetrahydro-1,2-benzisothiazolium-2-imine (**3c**)

Yield 55%; *m.p.* 179–181 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1590 m (CO), 1540 s, 1450 m, 1350 s, 910 s. – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 257.5 (3.81); 335.5 (4.09). – $\text{C}_{14}\text{H}_{13}\text{ClN}_2\text{OS}$ (292.77) Perchlorate **4c**: *m.p.* 143–146 °C.

N-(3-Chlorobenzoyl)-4,5,6,7-tetrahydro-1,2-benzisothiazolium-2-imine (**3d**)

Yield 84%; *m.p.* 186–187 °C (ethanol). – IR (KBr): ν/cm^{-1} = 2950 m, 1590 m (CO), 1530 s, 1450 m, 1350 s, 1260 m, 920 m. – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 255.0 (3.95); 348.5 (4.11). – ^1H NMR (DMSO- d_6): δ/ppm = 9.04 (s, 1H, 3-H); 7.96 (s, 1H, *o*-H); 7.93 (d, 1H, J = 7.5 Hz, *p*-H); 7.49 (m, 2H, *o/m*-H); 2.86 (t, 2H, CH_2), 2.64 (t, 2H, CH_2); 1.81 (m, 4H, 2 CH_2). – ^{13}C NMR (DMSO- d_6): δ/ppm = 164.7 (CO); 152.1 (C-7a); 142.8 (C-3); 138.2 (*m*-C); 132.9 (*i*-C); 130.1; 129.9; 126.8, 125.7 (4CH, arom.); 125.6 (C-3a); 22.6, 21.8, 21.7, 21.4 (4 CH_2). – MS (m/z , %) = 292 (M^+ 25); 231 (13); 201 (8); 139 (100); 111 (81); 91 (15); 75 (20). $\text{C}_{14}\text{H}_{13}\text{ClN}_2\text{OS}$ Calcd.: C 57.43 H 4.48 N 9.57 O 5.47 (292.77) Found: C 57.44 H 4.47 N 9.76 O 5.69.

N-(3-Nitrobenzoyl)-4,5,6,7-tetrahydro-1,2-benzisothiazolium-2-imine (**3g**)

Yield 65%; *m.p.* 218–220 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1590 s (CO), 1530 s (NO_2), 1370 s, 1350 s (NO_2), 710 s. – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 258.0 (4.11); 348 (4.16). $\text{C}_{14}\text{H}_{13}\text{N}_3\text{O}_3\text{S}$ (303.54). Perchlorate **4g**: *m.p.* 166–170 °C.

N-(3-Trifluoromethylbenzoyl)-4,5,6,7-tetrahydro-1,2-benzisothiazolium-2-imine (**3i**)

Yield 78%; *m.p.* 167–169 °C (2-propanol). – IR (KBr): ν/cm^{-1} = 2950 m, 1605 m (CO), 1540 s, 1460 s, 1370 s, 1320 s, 1280 s, 1150 s, 1120 s, 1070 s, 1050 s. – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 258.5 (3.57); 347.5 (3.93). $\text{C}_{15}\text{H}_{13}\text{F}_3\text{N}_2\text{OS}$ (326.34).

N-Benzoyl-5,6,7,8-tetrahydro-4H-cyclohepta[c]-isothiazolium-1-imines **5a,g,h** (General Procedure)

The imine **5a** is described in [8]. The new imines **5g,h** were prepared according [8] from 2-thiocyanatomethylene-cycloheptanone and substituted benzhydrazide.

N-(3-Nitrobenzoyl)-5,6,7,8-tetrahydro-4H-cyclohepta[c]-isothiazolium-1-imine (**5g**)

Yield 29%; *m.p.* 196–197 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1591 m (CO), 1526 s (NO_2), 1347 s (NO_2), 716 m. – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 207.0 (4.29); 223.5 (4.09). – MS (m/z , %) = 317 (M^+ 30); 150 (70); 104 (40); 97 (100); 76 (36). $\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_3\text{S}$ (317.37).

N-(4-Nitrobenzoyl)-5,6,7,8-tetrahydro-4H-cyclohepta[c]-isothiazolium-1-imine (**5h**)

Yield 41%; *m.p.* 248–249 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1595 s (CO), 1517 s (NO_2), 1341 s (NO_2), 715 m. – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 209.5 (4.39); 266.0 (4.36); 351.5 (4.31). – ^1H NMR (DMSO- d_6): δ/ppm = 8.41 (s, 1H, 3-H); 8.27 (m, 4H arom.H); 3.51 (m, 2H, CH_2); 2.84 (m, 2H, CH_2), 1.86 (m, 4H, CH_2); 1.64 (m, 2H, CH_2). – ^{13}C NMR (DMSO- d_6): δ/ppm = 163.7 (CO); 159.0 (C-8a); 148.4 (*p*-C); 142.7 (*i*-C); 136.3 (C-3); 133.4 (C-3a); 128.4 (*o*-C); 123.3 (*m*-C); 31.0, 29.8, 28.7, 27.1, 25.2 (5 CH_2). – MS (m/z , %) = 317 (M^+ 65); 150 (100); 105 (43); 98 (77); 76 (26).

$\text{C}_{15}\text{H}_{15}\text{N}_3\text{O}_3\text{S}$ Calcd.: C 56.76 H 4.76 N 13.24 S 10.10 (317.37) Found: C 56.50 H 4.63 N 13.10 S 10.24.

2-Benzoylamino-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1-oxides **7c–i** (General Procedure)

H_2O_2 (5 ml, 30%) was added to a stirred suspension of **3** or **4** (1.68 mmol) in AcOH (8 ml) at 0 °C. After 1 h the formed 1-oxide **7** was filtrated and recrystallized from EtOH.

2-(2-Chlorobenzoylamino)-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1-oxide (**7c**)

Yield 19%; *m.p.* 145–147 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1655 s (CO), 1305 m, 1060 s (SO). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 209 (4.65); 280 (4.27).

$\text{C}_{14}\text{H}_{15}\text{ClN}_2\text{O}_4\text{S}$ (342.79)

Calcd.: C 49.05 H 4.41 N 8.17 O 18.67 S 9.35

Found: C 49.15 H 4.36 N 8.14 O 18.60 S 9.39.

2-(3-Chlorobenzoylamino)-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1-oxide (**7d**)

Yield 32%; *m.p.* 152–153 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3432 s, 2933 m, 1644 s (CO), 1565 m, 1087 s (SO). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 232.0 (4.00); 289 (4.28).

$\text{C}_{14}\text{H}_{15}\text{ClN}_2\text{O}_4\text{S}$ (342.80)

Calcd.: C 49.05 H 4.41 N 8.17 O 18.67 S 9.35

Found: C 49.16 H 4.59 N 7.98 O 18.60 S 9.33.

2-(4-Chlorobenzoylamino)-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1-oxide (**7e**)

Yield 17%; *m.p.* 128–131 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3330 m, 3180 m, 1660 s (CO), 1540 s, 1330 m, 1070 s (SO). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 240.0 (4.23). – ^1H NMR (acetone- d_6): δ/ppm = 11.06 (s, 1H, OOH); 10.43 (s, 1H, NH); 7.99 (d, 2H, J_{AB} = 6.54 Hz, *o*-H); 7.57 (d, 2H, J_{AB} = 6.54 Hz, *m*-H); 5.66 (s, 1H, 3-H); 2.37 (m, 4H, 2 CH_2), 1.74 (m, 4H, 2 CH_2). – ^{13}C NMR (acetone- d_6): δ/ppm = 168.0 (CO); 144.2 (C-7a); 142.3 (C-3a); 139.6 (*p*-C); 132.2 (*i*-C); 130.9, 130.4 (*o/m*-C); 101.9 (C-3); 25.0, 23.3, 22.5, 22.4 (4 CH_2). – MS (m/z , %) = 324 ($\text{M}^+ - \text{H}_2\text{O}$, 71); 308 (14); 261 (9); 139 (100); 111 (30); 75 (6).

$C_{14}H_{15}ClN_2O_4S$ (342.80)

Calcd.: C 49.05 H 4.41 N 8.17 O 18.67 S 9.35

Found: C 48.99 H 4.53 N 8.22 O 18.50 S 9.66.

3-Hydroperoxy-2-(3-nitrobenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1-oxide (7g)

Yield 20%; *m.p.* 143–146 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3250 m, 2970 m, 1650 s (CO), 1560 m, 1540 s (NO₂), 1340 s (NO₂), 1060 s (SO). – UV (ethanol): λ_{max}/nm (lg ϵ) = 257.5 (3.82). – ¹H NMR (acetone-*d*₆): δ/ppm = 11.12 (s, 1H, OOH); 10.76 (s, 1H, NH); 8.79 (s, 1H, *o*-H); 8.49 (m, 1H, *p*-H); 8.39 (m, 1H, *o*-H); 7.87 (m, 1H, *m*-H); 5.72 (s, 1H, 3-H); 2.40 (m, 4H, 2CH₂), 1.77 (m, 4H, 2CH₂). – ¹³C NMR (acetone-*d*₆): δ/ppm = 167.1 (CO); 149.9 (*m*-C); 144.5 (*i*-C); 144.1 (C-7a); 142.4 (C-3a); 135.2, 131.9, 128.3, 124.0 (4CH arom.); 101.9 (C-3); 25.0, 23.2, 22.5, 22.4 (4CH₂). – MS (*m/z*, %) = 353 (M⁺ 5); 335 (36); 271 (47); 270 (63); 150 (100); 141 (26); 104 (29); 76 (20).

$C_{14}H_{15}N_3O_6S$ (353.35)

Calcd.: C 47.59 H 4.28 N 11.89 O 27.17 S 9.06

Found: C 47.58 H 4.41 N 11.62 O 27.40 S 9.08.

3-Hydroperoxy-2-(4-nitrobenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1-oxide (7h)

Yield 13%; *m.p.* 144–146 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3360 m, 3170 s, 1660 s (CO), 1530 s (NO₂), 1350 s (NO₂), 1070 s (SO). – UV (ethanol): λ_{max}/nm (lg ϵ) = 261.0 (4.14).

$C_{14}H_{15}N_3O_6S$ (353.35)

Calcd.: C 47.59 H 4.28 N 11.89 O 27.17 S 9.06

Found: C 47.58 H 4.40 N 11.68 O 27.10 S 9.30.

3-Hydroperoxy-2-(3-trifluoromethylbenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1-oxide (7i)

Yield 27%; *m.p.* 155–157 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3401 s, 2939 s, 1665 s (CO), 1333 s, 1169 s, 1127 s, 1075 s (SO). – UV (ethanol): λ_{max}/nm (lg ϵ) = 228.0 (4.01); 291.0 (4.44).

$C_{15}H_{15}F_3N_2O_4S$ (376.35)

Calcd.: C 47.87 H 4.02 N 7.44 O 17.01 S 8.02

Found: C 47.93 H 4.22 N 7.59 O 16.97 S 8.32.

2-Benzoylamino-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxides 8a–k (General Procedure)

H₂O₂ (5 ml, 30%) was added to a stirred suspension of **3** or **4** (1.68 mmol) in AcOH (8ml) at room temperature. After 8 h the formed 1,1-dioxide **8** was filtrated off, washed with ether and recrystallized from EtOH.

2-Benzoylamino-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (8a)

Yield 33%; *m.p.* 182–185 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3350 s, 1660 s (CO), 1300 s (SO₂), 1170 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ϵ) = 231.0 (4.07). – ¹H NMR (CDCl₃): δ/ppm = 11.65 (s, 1H, OOH); 10.07 (s, 1H, NH); 8.00 (m, 2H, *o*-H); 7.67 (m, 1H, *p*-H); 7.56 (m, 2H, *m*-H); 5.71 (s, 1H, 3-H); 2.41 (m, 4H, 2CH₂), 1.8 (m, 4H, 2CH₂). – ¹³C NMR (acetone-*d*₆): δ/ppm = 166.7 (CO); 142.4 (C-7a); 136.9 (*i*-C); 134.4 (*p*-C); 133.0 (C-3a); 130.3 (*m*-C); 129.4 (*o*-C); 94.4 (C-3); 23.9, 22.3, 22.2, 19.9 (4CH₂). – MS (*m/z*, %) = 306 (M⁺ – H₂O, 5); 291 (5); 226 (1); 122 (3); 105 (100); 77 (27). $C_{14}H_{16}N_2O_5S$ (324.35)

Calcd.: C 51.84 H 4.97 N 8.64 O 24.67 S 9.88

Found: C 51.86 H 5.17 N 8.65 O 24.64 S 9.97.

2-(4-Methylbenzoylamino)-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (8b)

Yield 33%; *m.p.* 165–170 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3350 m, 1661 s (CO), 1296 s (SO₂), 1165 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ϵ) = 242.0 (4.18).

$C_{15}H_{18}N_2O_5S$ (338.38)

Calcd.: C 53.24 H 5.36 N 8.28 O 23.64 S 9.48

Found: C 53.00 H 5.12 N 8.42 O 23.91 S 9.56.

2-(2-Chlorobenzoylamino)-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (8c)

Yield 10%; *m.p.* 151–154 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3407 s, 1684 s (CO), 1308 s (SO₂), 1170 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ϵ) = 208.0 (4.25).

$C_{14}H_{15}ClN_2O_5S$ Calcd.: C 46.86 H 4.21 N 7.81

(358.76) Found: C 46.74 H 4.28 N 7.99.

2-(3-Chlorobenzoylamino)-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (8d)

Yield 32%; *m.p.* 227–231 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3410 s, 1680 s (CO), 1290 s (SO₂), 1160 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ϵ) = 230.0 (4.00).

– ¹H NMR (acetone-*d*₆): δ/ppm = 11.45 (s, 1H, OOH); 10.11 (s, 1H, NH); 7.99 (s, 1H, *o*-H); 7.94 (m, 1H, *p*-H); 7.70, 7.60 (m, 2H, *o/m*-H); 5.75 (s, 1H, 3-H); 2.42 (m, 4H, 2CH₂), 1.81 (m, 4H, 2CH₂). – ¹³C NMR (acetone-*d*₆): δ/ppm = 169.4 (CO); 142.3 (C-7a); 136.9 (*m*-C); 135.8 (C-3a); 135.0 (*i*-C); 133.8, 132.1, 129.3, 127.9 (4CH arom.); 94.4 (C-3); 24.0, 22.3, 22.2, 19.9 (4CH₂).

$C_{14}H_{15}ClN_2O_5S$ Calcd.: C 46.86 H 4.21 N 7.81

(358.79) Found: C 46.76 H 4.38 N 7.79.

2-(4-Chlorobenzoylamino)-3-hydroperoxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (8e)

Yield 58%; *m.p.* 171–175 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3320 m, 1680 s (CO), 1290 m (SO₂), 1160 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ϵ) = 242.0 (4.26).

$C_{14}H_{15}ClN_2O_5S$ (358.79)

Calcd.: C 46.86 H 4.21 N 7.81 O 22.30 S 8.93

Found: C 46.73 H 4.49 N 7.79 O 22.33 S 8.94.

3-Hydroperoxy-(2-nitrobenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (8f)

Yield 32%; *m.p.* 180–188 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3410 s, 3310 s, 1670 s (CO), 1530 s (NO₂), 1340 s (NO₂), 1290 s (SO₂), 1166 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ϵ) = 290.0 (4.49).

$C_{14}H_{15}N_3O_7S$ (369.35)

Calcd.: C 45.52 H 4.09 N 11.38 O 30.33 S 8.68

Found: C 45.27 H 4.03 N 11.64 O 30.45 S 8.81.

3-Hydroperoxy-2-(3-nitrobenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (8g)

Yield 35%; *m.p.* 161–165 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3420 s, 3230 s, 1660 s (CO), 1530 s (NO₂), 1340 s (NO₂), 1300 s (SO₂), 1190 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ϵ) = 216.5 (4.63); 258.0 (4.19).

$C_{14}H_{15}N_3O_7S$ (369.35)

Calcd.: C 45.53 H 4.09 N 11.38 O 30.33 S 8.68

Found: C 45.45 H 4.22 N 11.52 O 30.40 S 8.78.

3-Hydroperoxy-2-(4-nitrobenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (8h)

Yield 32%; *m.p.* 184–188 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3410 s, 3310 s, 1670 s (CO), 1530 s (NO₂), 1350 s (NO₂), 1290 s (SO₂), 1166 s (SO₂). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 290.0 (4.49).

C₁₄H₁₅N₃O₇S (369.32)

Calcd.: C 45.53 H 4.09 N 11.38 O 30.33 S 8.67

Found: C 45.27 H 4.03 N 11.54 O 30.45 S 8.81.

3-Hydroperoxy-2-(3-trifluoromethylbenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (8i)

Yield 30%; *m.p.* 151–154 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3400 s, 3230 s, 1685 s (CO), 1334 s (SO₂), 1166 s (SO₂). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 290.0 (4.49). – ¹H NMR (acetone-d₆): δ/ppm = 11.32 (s, 1H, OOH); 10.25 (s, 1H, NH); 8.31 (s, 1H, o-H); 8.26 (m, 1H, p-H); 8.01 (m, 1H, o-H); 7.83 (m, 1H, m-H); 2.42 (m, 4H, 2CH₂); 1.81 (m, 4H, 2CH₂). – ¹³C NMR (acetone-d₆): δ/ppm = 168.8 (CO); 142.2 (C-7a); 137.0 (C-3a); 134.0 (i-C); 133.3; 132.0; 131.6 (q, *J* = 32, 6 Hz, C–CF₃); 130.8; 126.1; 125.4 (q, *J* = 273, 5 Hz, CF₃); 94.2 (C-3); 24.0, 22.3, 22.2, 19.9 (4CH₂). – MS (*m/z*, %) = 374 (M⁺–H₂O, 5); 358 (2); 173 (100); 145 (60); 79 (35).

C₁₅H₁₅F₃N₃O₄S Calcd.: C 45.91 H 3.85 N 7.14

(392.35) Found: C 46.05 H 4.05 N 7.29.

1-Benzoylamino-8a-hydroperoxy-1,5,6,7,8,8a-hexahydro-4H-cyclohepta[c]-isothiazole 2,2-dioxides 9a,g,h

H₂O₂ (5 ml, 30%) was added to a stirred suspension of 5 (1.68 mmol) in AcOH (8 ml) at room temperature. After 8 h the formed 1,1-dioxide 9 was filtrated and recrystallized from EtOH.

1-Benzoylamino-8a-hydroperoxy-1,5,6,7,8,8a-hexahydro-4H-cyclohepta[c]-isothiazole 2,2-dioxide (9a)

Yield 48%; *m.p.* 138–142 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3302 s, 1678 s (CO), 1521 m, 1305 s (SO₂), 1186 s (SO₂). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 227.0 (4.06). – ¹H NMR (acetone-d₆): δ/ppm = 12.15 (s, 1H, OOH); 10.24 (s, 1H, NH); 8.06 (d, 2H, o-H, *J* = 6.8 Hz); 7.67 (m, 1H, p-H); 7.58 (m, 2H, m-H); 7.04 (s, 1H, 3-H); 2.85 (m, 4H, 2CH₂); 1.73 (m, 4H, 2CH₂); 1.53 (m, 2H, CH₂). – ¹³C NMR (acetone-d₆): δ/ppm = 171.9 (CO); 155.3 (C-3); 134.6 (p-C); 130.3 (m-C); 129.6 (o-C); 124.7 (C-3a); 101.1 (C-8a); 32.6, 31.2, 28.9, 24.4 (4CH₂). – MS (*m/z*, %) = 322 (M⁺–16, 0.3); 304 (M⁺–H₂O, 0.6); 136 (15); 123 (23); 105 (100); 77 (57).

C₁₅H₁₈N₂O₅S (338.38)

Calcd.: C 53.24 H 5.36 N 8.28 O 23.64 S 9.48

Found: C 53.19 H 5.56 N 8.25 O 23.60 S 9.35.

1-(3-Nitrobenzoylamino)-8a-hydroperoxy-1,5,6,7,8,8a-hexahydro-4H-cyclohepta[c]-isothiazole 2,2-dioxide (9g)

Yield 41%; *m.p.* 145–148 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1691 s (CO), 1531 s (NO₂), 1353 s (NO₂), 1302 s (SO₂), 1186 s (SO₂). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 214.0 (4.30); 258.5 (3.77). – ¹H NMR (acetone-d₆): δ/ppm = 11.86 (s, 1H, OOH); 10.63 (s, 1H, NH); 8.86 (s, 1H, o-H); 8.54 (m, 1H, p-H); 8.47 (m, 1H, o-H); 7.92 (m, 1H, m-H); 7.80 (s, 1H, 3-H); 2.89 (m, 4H, 2CH₂); 1.71 (m, 4H, 2CH₂); 1.54 (m, 2H, CH₂). – ¹³C NMR (acetone-d₆): δ/ppm = 169.8 (CO); 155.5 (C-3); 149.9 (m-C); 135.8 (i-C); 132.1; 129.1; 124.8 (C-3a); 124.3;

124.2; 101.2 (C-8a); 31.6, 28.9, 24.4, 24.0, 19.6 (5CH₂). – MS (*m/z*, %) = 349 (M⁺–H₂O, 5); 330 (7); 167 (30); 150 (47); 135 (100); 121 (23); 104 (29); 76 (28).

C₁₅H₁₇N₃O₇S (383.38)

Calcd.: C 46.99 H 4.47 N 10.96 O 29.22 S 8.36

Found: C 46.74 H 4.58 N 10.76 O 29.10 S 8.06.

1-(4-Nitrobenzoylamino)-8a-hydroperoxy-1,5,6,7,8,8a-hexahydro-cyclohepta[c]-isothiazole 2,2-dioxide (9h)

Yield 25%; *m.p.* 143–145 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1698 s (CO), 1605 m, 1543 s (NO₂), 1428 m, 1350 s (NO₂), 1314 s (SO₂), 1293 s (SO₂). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 202.0 (4.39); 259.0 (4.46).

C₁₅H₁₇N₃O₇S (383.38)

Calcd.: C 46.99 H 4.47 N 10.96 O 29.22 S 8.36

Found: C 46.79 H 4.55 N 10.78 O 29.20 S 8.16.

2-Benzoylamino-3-hydroxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide 10a,b,d,e,g–i (General Procedure)

3-Hydroperoxyisothiazole 1,1-dioxide 8 (1 mmol) was added to a stirred solution of Na₂SO₃·7H₂O (635 mg, 2.33 mmol) in 7.5 ml H₂O at room temperature. After 8 h the formed 3-hydroxyisothiazole 1,1-dioxide 10 was collected by filtration and recrystallized from EtOH.

2-Benzoylamino-3-hydroxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (10a)

Yield 90%; *m.p.* 199–200 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3300 s, 2920 m, 1660 s (CO), 1320 s (SO₂), 1160 s (SO₂). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 228.0 (3.71). – ¹H NMR (acetone-d₆): δ/ppm = 10.55 (s, 1H, NH); 7.97 (d, 2H, *J* = 7.12 Hz); 7.48–7.66 (m 3H, *m/p*-H) 7.11 (d, 1H, OH, *J*_{AB} = 8.11 Hz); 5.60 (d, 1H, 3-H, *J*_{AB} = 8.11 Hz); 2.37 (m, 4H, 2CH₂); 1.81 (m, 4H, 2CH₂). – ¹³C NMR (acetone-d₆): δ/ppm = 168.0 (CO); 145.1 (C-7a); 134.9 (i-C); 134.6 (C-3a); 133.6 (p-C); 130.0 (m-C); 129.2 (o-C); 85.3 (C-3); 24.2, 22.4, 22.5, 19.9 (4CH₂). – MS (*m/z*, %) = 290 (M⁺–H₂O, 23); 277 (33.5); 226 (65); 214 (25); 150 (93); 141 (38.5); 105 (100); 77 (33).

C₁₄H₁₆N₂O₄S (308.35)

Calcd.: C 54.53 H 5.23 N 9.08 O 20.76 S 10.40

Found: C 54.45 H 5.06 N 9.12 O 20.34 S 10.55.

3-Hydroxy-2-(4-methylbenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (10b)

Yield 76%; *m.p.* 180–183 °C (ethanol). – IR (KBr): ν/cm^{-1} = 3300 s, 2920 m, 1660 s (CO), 1500 m, 1320 s, 1300 s (SO₂), 1160 s (SO₂). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 235.5 (4.11).

C₁₅H₁₈N₂O₄S (322.38)

Calcd.: C 55.88 H 5.63 N 8.69 O 19.85 S 9.95

Found: C 55.85 H 5.54 N 8.76 O 19.55 S 10.04.

2-(3-Chlorobenzoylamino)-3-hydroxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (10d)

Yield 91%; *m.p.* 184–186 °C (ethanol). – IR (KBr): ν/cm^{-1} = 2940 m, 1680 s (CO), 1305 s (SO₂), 1160 s (SO₂). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 230.5 (3.98). – ¹H NMR (acetone-d₆): δ/ppm = 9.67 (s, 1H, NH); 7.96 (s, 1H, o-H); 7.90 (d, 1H, p-H, *J* = 7.50 Hz); 7.64 (d, 1H, o-H, *J* = 8.20 Hz); 7.54 (t, 1H, m-H); 5.68 (d, 1H, 3-H); 2.40 (m, 4H, 2CH₂); 1.7 (m,

4H, 2CH₂). – ¹³C NMR (acetone-d₆): δ/ppm = 166.7 (CO); 145.3 (C-7a); 136.2 (*m*-C); 135.6 (*i*-C); 134.2 (C-3a); 127.7; 129.2; 131.9; 133.5 (4CH, arom.); 24.2, 22.5, 22.4, 19.9 (4CH₂). – MS (*m/z*, %) = 324 (M⁺ – H₂O, 3); 139 (100); 111 (90); 91 (25); 77 (45); 65 (25).

C₁₄H₁₅ClN₂O₄S Calcd.: C 49.06 H 4.41 N 8.17 O 18.67 (342.76) Found: C 48.98 H 4.64 N 8.27 O 18.99.

2-(4-Chlorobenzoylamino)-3-hydroxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (10e)

Yield 52%; *m.p.* 192–195 °C (ethanol). – IR (KBr): ν/cm^{–1} = 3300 m, 1670 s (CO), 1320 s (SO₂), 1170 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ε) = 238.0 (3.79).

C₁₄H₁₅ClN₂O₄S Calcd.: C 49.05 H 4.41 N 8.17 O 18.67 (342.79) Found: C 48.88 H 4.53 N 8.07 O 18.77.

3-Hydroxy-2-(3-nitrobenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (10g)

Yield 75%; *m.p.* 190–191 °C (ethanol). – IR (KBr): ν/cm^{–1} = 1677 s (CO), 1530 s (NO₂), 1353 s (NO₂), 1314 s (SO₂); 1165 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ε) = 248. (4.11).

C₁₄H₁₅N₃O₆S (353.35) Calcd.: C 47.59 H 4.28 N 11.89 O 27.17 S 9.07 Found: C 47.79 H 3.99 N 11.73 O 27.30 S 9.29.

3-Hydroxy-2-(4-nitrobenzoylamino)-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (10h)

Yield 73%; *m.p.* 204–208 °C (ethanol). – IR (KBr): ν/cm^{–1} = 3280 s, 2930 m, 1670 s (CO), 1600 m, 1520 s (NO₂), 1340 m (NO₂), 1300 s (SO₂); 1160 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ε) = 261.0 (3.80).

C₁₄H₁₅N₃O₆S (353.35) Calcd.: C 47.59 H 4.28 N 11.89 O 27.17 S 9.07 Found: C 47.67 H 4.29 N 11.83 O 27.22 S 9.09.

3-Hydroxy-2-(3-trifluoromethylbenzoylamino)-3-hydroxy-2,3,4,5,6,7-hexahydro-1,2-benzisothiazole 1,1-dioxide (10i)

Yield 78%; *m.p.* 199–201 °C (ethanol). – IR (KBr): ν/cm^{–1} = 1668 s (CO), 1317 s (SO₂); 1166 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ε) = 222.0 (4.07).

C₁₅H₁₅F₃N₂O₄S Calcd.: C 47.87 H 4.02 N 7.44 (376.35) Found: C 47.79 H 4.19 N 7.34.

2-Benzoylamino-4,5,6,7-tetrahydro-1,2-benzisothiazole-3(2H)-on 1,1-dioxides 11a,b,d,h

Hydroperoxide **8** (1 mmol) was refluxed for 2 hours in 5 ml ethanol. Colourless crystals were obtained and recrystallized from ethanol.

2-(Benzoylamino)-4,5,6,7-tetrahydro-1,2-benzisothiazole-3(2H)-on 1,1-dioxide (11a)

Yield 25%; *m.p.* 215–218 °C (ethanol). – IR (KBr): ν/cm^{–1} = 3250 m, 1760 m (CO), 1650 m (CO), 1290 s (SO₂), 1160 s (SO₂).

C₁₄H₁₄N₂O₄S (306.33) Calcd.: C 54.89 H 4.61 N 9.14 O 20.89 S 10.47 Found: C 54.78 H 4.55 N 9.11 O 21.00 S 10.61.

2-(4-Methylbenzoylamino)-4,5,6,7-tetrahydro-1,2-benzisothiazole-3(2H)-on 1,1-dioxide (11b)

Yield 20%; *m.p.* 245–248 °C (ethanol). – IR (KBr): ν/cm^{–1} =

3270 m, 1760 m (CO), 1680 s (CO), 1530 m, 1340 s, 1270 s (SO₂), 1180 m (SO₂).

C₁₅H₁₆N₂O₄S Calcd.: C 56.24 H 5.03 N 8.74 (320.33) Found: C 56.46 H 5.05 N 8.53.

2-(3-Chlorobenzoylamino)-4,5,6,7-tetrahydro-1,2-benzisothiazole-3(2H)-on 1,1-dioxide (11d)

Yield 23%; *m.p.* 288–289 °C (ethanol). – IR (KBr): ν/cm^{–1} = 3250 m, 1680 m (CO), 1640 s (CO), 1290 s (SO₂), 1160 s (SO₂). – UV (ethanol): λ_{max}/nm (lg ε) = 226.0 (3.74). – ¹H NMR (acetone-d₆): δ/ppm = 9.90 (s, 1H, NH); 7.97 (s, 1H, *o*-H); 7.94 (d, 1H, *p*-H, *J* = 7.68 Hz); 7.65 (d, 1H, *o*-H, *J* = 8.90 Hz); 7.57 (m, 1H, *m*-H). 2.40 (m, 4H, 2CH₂), 1.85 (m 4H, 2CH₂). – ¹³C NMR (acetone-d₆): δ/ppm = 164.9 (CO); 165.3 (C-3); 159.3 (C-7a); 142.9 (*m*-C); 133.7 (C-3a); 132.9 (*i*-C); 132.1; 131.0; 127.6; 126.6 (4CH, arom.). – MS (*m/z*, %) = 314 (M⁺, 2); 139 (100); 111 (40); 75 (15).

C₁₄H₁₃ClN₂O₄S (340.77) Calcd.: C 49.34 H 3.85 N 8.22 O 18.78 S 9.41 Found: C 49.15 H 3.74 N 8.48 O 18.66 S 9.33.

2-(4-Nitrobenzoylamino)-4,5,6,7-tetrahydro-1,2-benzisothiazole-3(2H)-on 1,1-dioxide (11h)

Yield 20%; *m.p.* 246–248 °C (ethanol). – IR (KBr): ν/cm^{–1} = 3280 m, 1760 m (CO), 1680 s (CO), 1530 m (NO₂), 1350 s (NO₂), 1270 s (SO₂), 1180 s (SO₂). – ¹H NMR (acetone-d₆): δ/ppm = 11.75 (s, 1H, NH); 8.28 (m, 4H_{Ar}); 1.79 (m, 4H, 2CH₂).

C₁₄H₁₃N₃O₆S (351.33) Calcd.: C 47.86 H 3.73 N 11.96 Found: C 47.72 H 4.02 N 11.61.

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