

Ring Transformations of Bicyclic Cycloalka[d]- to the Isomeric Cycloalka[c]isothiazolium Salts and their Oxidation to ω -(2-Aryl-1,1,3-trioxo-2,3-dihydro-1*H*-isothiazol-4-yl)-alkanoic Acids

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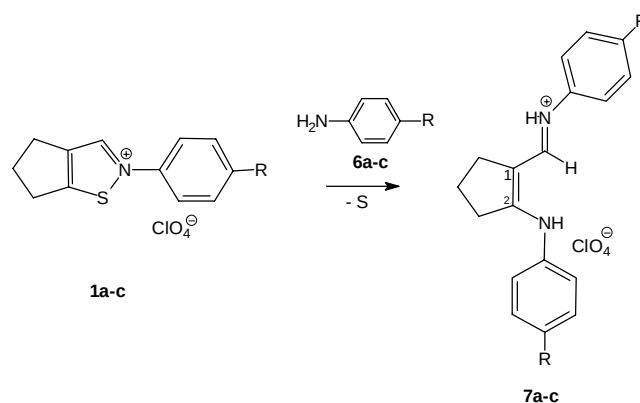
Abstract. The synthesis of tetrahydro-2,1-benzisothiazolium salts **8** and cyclohepta[c] isothiazolium salts **11** by ring transformation of bicyclic isothiazolium perchlorates **2**, **3** is described and the by-products **9**, **10** and **12** are characterized.

Oxidation of the bicyclic salts **8** and **11** results in a new route to obtain ω -(2-aryl-1,1,3-trioxo-2,3-dihydro-1*H*-isothiazol-4-yl)-alkanoic acids **17** and **18** by Criegee-type-rearrangement.

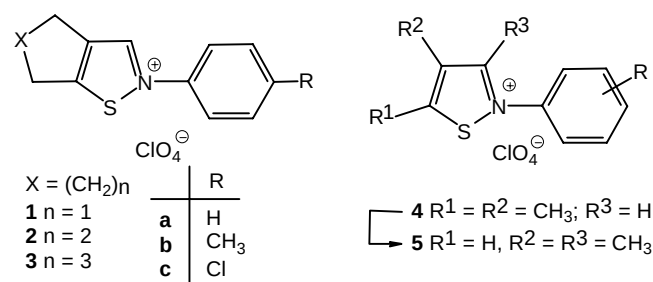
In the last years isothiazole 1,1-dioxides have received increased interest as chiral auxiliaries in asymmetric syntheses since Oppolzer's discovery of camphor sultam [1, 2]. Furthermore camphersulfonyl-oxaziridines [3] and oxaziridines of toluene-2, α -sultame type [4, 5] have acquired remarkable importance as asymmetric oxidants. In parallel to our experiments regarding the oxidation of 2-arylisothiazolium salts **2** we found the relation between donor and acceptor functionality on the substituents R and the function of these substituents on stereochemical aspects on the formation of *rac*-*cis*/*trans*-3-hydroperoxy-4,5,6,7-tetrahydrotoluene-2, α -sultams and sultams, which are oxidizing agents [6, 7]. Recently, we have demonstrated the accessibility of monocyclic chiral 3-alkyl-3-hydroperoxy-sultams and 4-methyl-isothiazol-3(2*H*)-one 1,1-dioxides by oxidation of isothiazolium salts **5**, which is alkyl substituted at the 3-position. The latter was prepared by a novel ring transformation under sulfur migration of isothiazolium salts **4** [8]. The goal of this paper is to extend the method reported previously [8] in order to obtain bicyclic isothiazolium salts and their oxidation to sultams.

Results

The starting materials, which are the bicyclic isothiazolium salts **1–3**, were prepared according to our reported synthesis by cyclocondensation of 2-thiocyanato-cycloalkene-1-carbaldehydes with anilines **6a–c** and perchloric acid [9]. The salts **1** and **3** are new compounds and were firstly synthesized in our laboratory.



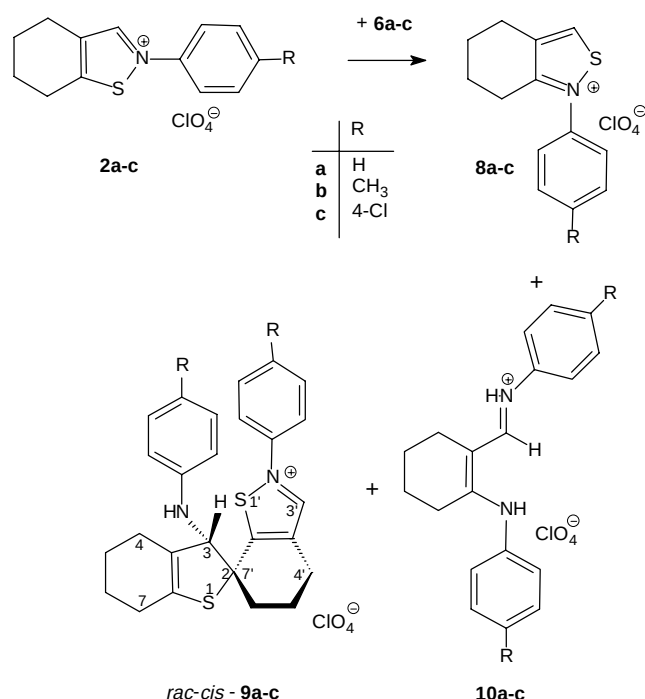
Scheme 1 Ring opening of bicyclic salts **1a–c** with anilines **6a–c** to vinamidines **7a–c**



The isothiazolium salts **1–3** possess the capability to react with the substituted anilines **6a–c** in order to prepare the isomeric isothiazolium salts by ring transformation. Depending on the ring size of the isothiazolium salts **1–3** different products were obtained in the reaction mixture (scheme 1–3). Several substituents were chosen (R = H, CH₃, Cl) for examination of the influence between electron-donating and electron-withdrawing substituents.

Because 2-aryl-5,6-dihydro-4*H*-cyclopenta[*d*]isothiazolium perchlorates **1** (*n* = 1) are allowed to react with substituted anilines **6a–c** in methanol, vinamidines **7a–c** can be easily obtained in quantitative yield (95–99%) as the main product in a sufficient purity (scheme 1). Vinamidines are formed by reaction of 2-chloro-cyclopentene-1-carbaldehyd and anilines according to previous reported procedures [10, 11].

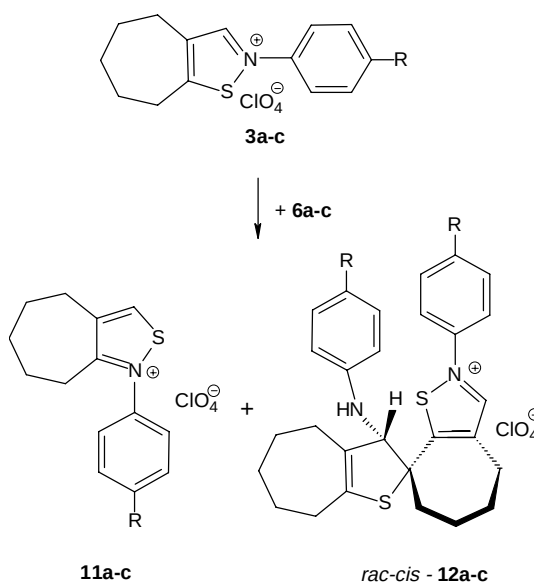
Isomerization of 2-aryl-4,5,6,7-tetrahydro-1,2-benzisothiazolium perchlorates **2a–c** (*n* = 2) results in 1-aryl-4,5,6,7-tetrahydro-2,1-benzisothiazolium perchlorates **8a–c** while the vinamidines **10a–c** (5–13%) and spirocyclic salts **9a–c** (5–31%) are only by-products (scheme 2).



Scheme 2 Isomerization of 4,5,6,7-tetrahydro-1,2-benzisothiazolium perchlorates **2a–c** to 1-aryl-2,1-benzisothiazolium salts **8a–c**, spirocyclic salts **9a–c** and vinamidines **10a–c**

The substituent R at the aryl position importantly influences the isomerization yield. Thus, it was shown that by use of unsubstituted as well as electron-donating anilines **6a,b** (R = H, CH₃) reasonable yields of isomeric salts **8a,b** could be obtained (33–64%). On the other hand the use of electron-withdrawing substituted 4-chloro-aniline **6c** only results in traces of the isomeric salt **8c** (2%), which was confirmed in the reaction mixture by NMR spectroscopy. This tendency excellently correlates with the results we previously reported for isomerization of monocyclic isothiazolium salts [8].

In comparison to these results the ring transformation works well for the 2-aryl-5,6,7,8-tetrahydro-4*H*-cyclohepta[*d*]isothiazolium perchlorates **3a–c** (*n* = 3). The isomeric cyclohepta[*c*]isothiazolium perchlorates **11a,b** are the main products while spirocyclic salts **12a–c** are found in significant lower yields as by-products (1–8%) (scheme 3). In contrast to the former mentioned results of isomerization the reaction mixture contained no vinamidines in our experiments. The substituent R at the aryl position responsibly influences the yields of **11a–c** in the same direction as observed for reaction of the salts **2a–c**. Thus the products **11a,b** (R = H, CH₃) are obtained in excellent yields (81–89%), whereas the acceptor substituted salt **11c** (R = Cl) is only formed in poor yield (4%). **11c** was not isolated but detected by spectroscopic methods.



Scheme 3 Isomerization of cyclohepta[*d*]isothiazolium perchlorates **3a–c** to the bicyclic salts **11a–c** and spiro salts **12a–c**

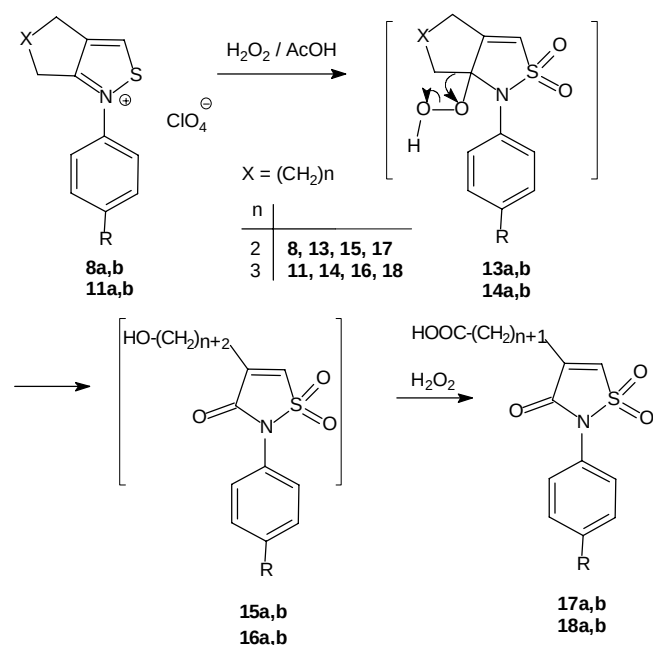
The mechanism of the ring transformation can be explained by a nucleophilic attack of aniline at the carbon atom in 5-position of **2** and **3**. Sulfur migration and a subsequent ring closure results in **8** and **11** [8]. Vinamidines **10** are obtained as by-products, which are attributed to a loss of sulfur from either the salts **2** or an intermediate. Vinamidines **7a–c** are the main-products (98–99%) in the case of reaction of **1a–c** with anilines **6a–c**. Spirocyclic salts *rac-cis*-**9** are known as the reaction products of an dimerization between two molecules of the isothiazolium salts **2** in the presence of a base [12]. Therefore, the reaction of salts **2**, **3** with anilines **6** leads in the same time to spiro salts **9**, **12** by dimerization as a side-reaction.

The structures of all compounds prepared are confirmed by their spectroscopic data and elemental analysis. The isomeric salts **8** and **11** exhibit characteristic

signals at about 9,27–9,35 ppm, 2,86–2,95 ppm and 2,74–2,83 ppm in ^1H NMR spectra. The first set of signals can be attributed to the proton in 3-position of the isothiazole ring, the second and third one to the methylene groups of the cycloalkene ring. A characteristic feature of the salts **8**, **11** are the ^{13}C NMR signals of the isothiazole moiety at 168–173 ppm (C-5), 150–151 ppm (CH-3) and 132–134 ppm (C-4). In the IR spectra of **8**, **11** the characteristic signals of the O–Cl–O absorption bands is found as an intense signal at about 1090–1117 cm^{-1} . Electrospray ionization mass spectra which are taken from **1a**, **3b** and **8b**, show the expected molecular ion peaks of the cations.

The vinamidines **7** and **10** exhibit characteristic signals in ^1H NMR spectra at 11,60 ppm (NH), 10,60 ppm (NH) and 8,90 ppm (CH=N), whereas the spirocyclic salts **9**, **12** can be identified by their typical ^1H NMR signals at 9,30 ppm (3'-H), and two doublets at 4,40 ppm (3-H) and 5,80 ppm (NH). The typical signals in the ^{13}C NMR spectra of **12** are 66,8 ppm for C-2/8', a doublet of the C-3 atoms at 82 ppm and a further one of the C-3' at 153 ppm.

The isomeric isothiazolium salts **8a,b** and **11a,b** are valuable starting compounds for the preparation of bicyclic 3-hydroperoxy-isothiazole-1,1-dioxides **13**, **14**. The oxidation of the mentioned salts was performed by heating the salts **8**, **11** in acetic acid with an excess of hydrogen peroxide (30%) for several hours. Surprisingly ω -(2-aryl-1,1,3-trioxo-2,3-dihydro-1*H*-isothiazol-4-yl)-alkanoic acids **17a,b**, **18a,b** are isolated as products in mostly good yields (38–43%). The formation of these



Scheme 4 Oxidation of bicyclic isothiazolium salts **8** and **11** via instable hydroperoxides **13**, **14** to ω -(2-aryl-1,1,3-trioxo-2,3-dihydro-1*H*-isothiazol-4-yl)-alkanoic acids **17**, **18**

carboxylic acids **17**, **18** can be attributed to a criegee-type rearrangement of initially formed hydroperoxides **13**, **14** followed by a subsequent oxidation of the non-isolable alkanols obtained **15**, **16** (scheme 4). Only in one case the hydroperoxid **13a** could be isolated in low yield (2%) by applying slight oxidation conditions at low temperature.

The structure of ω -(2-aryl-1,1,3-trioxo-2,3-dihydro-1*H*-isothiazol-4-yl)-alkanoic acids **17a,b**, **18a,b** follows from the spectroscopic data. Thus, characteristic signals at 1182–1185 cm^{-1} , 1327–1334 cm^{-1} , 1705–1713 cm^{-1} , and 1730–1740 cm^{-1} were found in the IR spectra. Whereas the first and second set of signals are related to the symmetrical and asymmetrical SO₂ absorption of the SO₂ moiety, the third one can be attributed to the carboxyl group and the last one to the carbonyl group. Another typical signals of this compounds are found in the ^{13}C NMR at 178–179 ppm (COOH) and at 160–161 ppm (C=O). Additionally, the structure of these compounds is confirmed by mass spectroscopic analysis, where a molecular ion peak with high intensity was found. The comparison of various spectroscopic data of the sultams **17** and **18** with those of typical isothiazole-3(2*H*) on 1,1-dioxides supports the structure of **17** and **18**.

Conclusion

In summary, the bicyclic isothiazolium salts **2** and **3** react with anilines **6** to form isomeric salts **8** and **11**. By-products are spirocyclic salts *rac*-*cis* **9** and *rac*-*cis* **12** and vinamidines **10a–c**. In the case of salts **1** only ring opening products, the vinamidines **7a–c**, are obtained. Furthermore a new efficient route to alkanolic acids **17** and **18** has been found through oxidation of the bicyclic salts **8** and **11**.

Experimental

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

Bicyclic 2-Aryl-cycloalka[*d*]isothiazolium Perchlorates 1–3 (General Procedure)

The salts **1–3** were prepared according ref. [9]. The isothiazolium perchlorates **2a–c** were described in [9, 12].

2-Phenyl-5,6-dihydro-4*H*-cyclopenta[*d*]isothiazolium perchlorate (**1a**)

Yield 92%; *m.p.* 155–158 °C (ethanol) beige crystals. – IR

(KBr): $\nu/\text{cm}^{-1} = 1096$ s (O–Cl–O). – UV (CH_3CN): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 224.5 (3.78); 247.0 (3.72); 297.0 (3.94). – ^1H NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 9.39$ (s, 1H, CH=N); 7.81–7.76 (m, 2H, *o*-H); 7.68–7.63 (m, 3H, *m/p*-H); 3.32 (t, 2H, CH_2); 2.97 (t, 2H, CH_2); 2.47 (q, 2H, CH_2). – ^{13}C NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 178.2$ (C-6a); 151.5 (C-3); 144.7 (C-3a); 138.5 (*i*-C); 131.8 (*p*-CH); 131.4 (*m*-CH); 124.4 (*o*-CH); 33.6; 29.0; 27.3 (3CH_2).

$\text{C}_{12}\text{H}_{12}\text{ClNO}_4\text{S}$ Calcd.: C 47.76 H 4.01 N 4.64 S 10.63 (301.73) Found: C 47.75 H 4.14 N 4.71 S 10.44.

2-(4-Methylphenyl)-5,6-dihydro-4H-cyclopenta[d]isothiazolium perchlorate (1b)

Yield 31%; *m.p.* 139–141 °C (ethanol) beige crystals. – IR (KBr): $\nu/\text{cm}^{-1} = 1119$ s (O–Cl–O). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 218.0 (3.95); 254.0 (3.76); 305.5 (4.01).

$\text{C}_{13}\text{H}_{14}\text{ClNO}_4\text{S}$ (315.75).

2-(4-Chlorophenyl)-5,6-dihydro-4H-cyclopenta[d]isothiazolium perchlorate (1c)

Yield 41%; *m.p.* 115–120 °C (ethanol), beige crystals. – IR (KBr): $\nu/\text{cm}^{-1} = 1112$ s (O–Cl–O). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 222.5 (3.93); 253.0 (3.69); 303.5 (9.91).

$\text{C}_{12}\text{H}_{11}\text{Cl}_2\text{NO}_4\text{S}$ (336.17).

2-Phenyl-5,6,7,8-tetrahydro-4H-cyclohepta[d]isothiazolium perchlorate (3a)

Yield 98%; *m.p.* 204–206 °C (ethanol) colorless crystals. – IR (KBr): $\nu/\text{cm}^{-1} = 1100$ s (O–Cl–O). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 253.5 (3.85); 296.5 (3.98). – ^1H NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 9.48$ (s, 1H, CH=N); 7.81 (m, 2H, *o*-H); 7.67 (m, 3H, *m/p*-H); 3.35 (t, 2H, CH_2); 2.92 (t, 2H, CH_2); 1.89 (m, 2H, CH_2); 1.70 (m, 4H, 2CH_2). – ^{13}C NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 174.2$ (C-8a); 156.7 (C-3); 141.2 (C-3a); 137.6 (*i*-C); 132.0 (*p*-CH); 131.5 (*m*-CH); 124.1 (*o*-CH); 31.8; 28.5; 27.9; 27.1; 26.9 (5CH_2).

$\text{C}_{14}\text{H}_{16}\text{ClNO}_4\text{S}$ Calcd.: C 50.99 H 4.89 N 4.25 S 9.72 (329.81) Found: C 50.51 H 4.77 N 4.15 S 9.81.

2-(4-Methylphenyl)-5,6,7,8-tetrahydro-4H-cyclohepta[d]isothiazolium perchlorate (3b)

Yield 85%; *m.p.* 150–151 °C (ethanol) colorless crystals. – IR (KBr): $\nu/\text{cm}^{-1} = 1096$ s (O–Cl–O). – UV (CH_3CN): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 201.5 (4.13); 257.0 (3.71); 302.5 (3.89). – ^1H NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 9.46$ (s, 1H, CH=N); 7.72 (d, 2H, $J_{\text{AB}} = 8.6$ Hz, *o*-H); 7.50 (d, 2H, $J_{\text{AB}} = 8.6$ Hz, *m*-H); 3.35 (t, 2H, CH_2); 2.94 (t, 2H, CH_2); 2.43 (s, 3H, CH_3); 1.93 (m, 2H, CH_2); 1.73 (m, 4H, 2CH_2). – ^{13}C NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 172.9$ (C-8a); 155.8 (C-3); 137.1 (C-3a); 142.7 (*p*-C); 123.4 (*o*-CH); 131.7 (*m*-CH); 134.3 (*i*-C); 31.2; 27.8; 27.2; 26.5; 26.3; (5CH_2); 20.9 (*p*- CH_3).

$\text{C}_{15}\text{H}_{18}\text{ClNO}_4\text{S}$ Calcd.: C 52.40 H 5.28 N 4.07 S 8.32 (343.80) Found: C 52.30 H 5.18 N 4.06 S 8.79.

2-(4-Chlorophenyl)-5,6,7,8-tetrahydro-4H-cyclohepta[d]isothiazolium perchlorate (3c)

Yield 67%; *m.p.* 128–129 °C (ethanol) colorless crystals. – IR (KBr): $\nu/\text{cm}^{-1} = 1090$ s (O–Cl–O). – UV (CH_3CN): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 217.5 (4.14); 254.0 (3.88); 296.1 (4.01). – ^1H NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 9.45$ (s, 1H, CH=N); 7.84 (d, 2H, $J_{\text{AB}} = 9.0$ Hz, *o*-H); 7.76 (d, 2H, $J_{\text{AB}} = 9.0$ Hz, *m*-H); 3.34 (t, 2H, CH_2); 2.91 (t, 2H, CH_2); 1.88 (m, 2H, CH_2); 1.69 (m,

4H, 2CH_2).

$\text{C}_{14}\text{H}_{15}\text{Cl}_2\text{NO}_4\text{S}$ Calcd.: C 46.16 H 4.15 N 3.85 S 8.80 (364.22) Found: C 45.95 H 4.25 N 3.79 S 8.68.

Isomeric Bicyclic 1-Aryl-cycloalka[c]isothiazolium Perchlorates 8a,b and 11a,b (General Procedure)

The isomeric isothiazolium salts **8** and **11** were prepared according ref. [8]. 3 mmol 2-aryl-isothiazolium perchlorate **2** or **3** and 3 mmol aniline **4** were dissolved by stirring and gentle heating in 30 ml methanol. The reaction mixture is stirred at 50 °C for 8 hours, while the by-products **9** and **12** are precipitated as a yellow powder, which can be separated. After removing the solvent up to 4–6 ml, 25–30 ml of ether are carefully added. After scratching and standing at 0–5 °C the perchlorates **8** and **11** are precipitated as microcrystalline powders, which are filtered off, washed with ether and purified by recrystallization from ethanol/ether. The remaining solution contains the vinamidines **7** and **10**.

1-Phenyl-4,5,6,7-tetrahydro-2,1-benzisothiazolium perchlorate (8a)

Yield 33%; *m.p.* 185–188 °C (ethanol/ether) beige needles. – IR (KBr): $\nu/\text{cm}^{-1} = 1090$ s (O–Cl–O). – UV (CH_3CN): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 242.0 (4.09); 302.0 (3.78). – ^1H NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 9.35$ (s, 1H, CH=N); 7.71–7.70 (m, 5H); 2.86 (t, 2H, CH_2); 2.74 (t, 2H, CH_2); 1.79 (m, 4H, CH_2). – ^{13}C NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 168.5$ (C-7a); 150.9 (C-3); 134.9 (*i*-C); 133.7 (C-3a); 131.5 (*p*-CH); 130.2 (*m*-CH); 126.6 (*o*-CH); 26.8; 24.2; 20.7; 20.6 (4CH_2).

$\text{C}_{13}\text{H}_{14}\text{ClNO}_4\text{S}$ Calcd.: C 49.45 H 4.47 N 4.44 S 10.15 (315.77) Found: C 49.61 H 4.40 N 4.50 S 10.46.

1-(4-Methylphenyl)-4,5,6,7-tetrahydro-2,1-benzisothiazolium perchlorate (8b)

Yield 64%; *m.p.* 197–199 °C (ethanol/ether) yellow needles. – IR (KBr): $\nu/\text{cm}^{-1} = 1100$ s (O–Cl–O). – UV (CH_3CN): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 243.0 (4.20); 308.5 (3.85). – ^1H NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 9.35$ (s, 1H, CH=N); 7.71 (d, $J_{\text{AB}} = 8.3$ Hz, *o*-H); 7.22 (d, $J_{\text{AB}} = 8.3$ Hz, *m*-H); 2.86 (t, 2H, CH_2); 2.74 (t, 2H, CH_2); 2.32 (s, 3H, *p*- CH_3); 1.79 (m, 4H, CH_2).

$\text{C}_{14}\text{H}_{16}\text{ClNO}_4\text{S}$ Calcd.: C 50.99 H 4.89 N 4.25 S 9.72 (329.78) Found: C 50.79 H 4.75 N 4.09 S 9.84.

1-Phenyl-5,6,7,8-tetrahydro-4H-cyclohepta[c]isothiazolium perchlorate (11a)

Yield 81%; *m.p.* 162–165 °C (ethanol/ether) yellow powder. – IR (KBr): $\nu/\text{cm}^{-1} = 1092$ s (O–Cl–O). – UV (CH_3CN): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 209.0 (3.82); 272.5 (3.80). – ^1H NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 9.29$ (s, 1H, CH=N); 7.71–7.69 (m, 5H); 2.95 (t, 2H, CH_2); 2.83 (t, 2H, CH_2); 1.85 (m, 2H, CH_2); 1.69 (m, 4H, 2CH_2). – ^{13}C NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} = 172.7$ (C-8a); 150.1 (C-3); 139.3 (*i*-C); 134.9 (C-3a); 131.7 (*p*-CH); 130. (*m*-CH); 127.1 (*o*-CH); 30.7; 30.2; 28.3; 26.5; 24.3 (5CH_2). $\text{C}_{14}\text{H}_{16}\text{ClNO}_4\text{S}$ Calcd.: C 50.99 H 4.89 N 4.25 S 9.72 (329.78) Found: C 50.61 H 4.87 N 4.41 S 9.94.

1-(4-Methylphenyl)-5,6,7,8-tetrahydro-4H-cyclohepta[c]isothiazolium perchlorate (11b)

Yield 89%; *m.p.* 112–114 °C (ethanol/ether) yellow powder. – IR (KBr): $\nu/\text{cm}^{-1} = 1117$ s (O–Cl–O). – UV (CH_3CN): $\lambda_{\text{max}}/\text{nm}$ ($\lg \epsilon$) = 270.0 (4.01). – ^1H NMR ($\text{DMSO}-d_6$): $\delta/\text{ppm} =$

9.27 (s, 1H, CH=N); 7.60 (d, J_{AB} = 8.4 Hz, *o*-H); 7.50 (d, J_{AB} = 8.4 Hz, *m*-H); 2.96 (t, 2H, CH₂); 2.85 (t, 2H, CH₂); 2.44 (s, 3H, *p*-CH₃); 1.84 (m, 2H, CH₂); 1.70 (m, 4H, 2 CH₂). – ¹³C NMR (DMSO-*d*₆): δ /ppm = 172.9 (C-8a); 150.1 (C-3); 139.5 (*i*-C); 132.7 (C-3a); 142.1 (*p*-C); 130.8 (*m*-CH); 127.0 (*o*-CH); 30.9; 30.4; 28.6; 26.7; 24.6 (5CH₂); 21.0 (*p*-CH₃).
C₁₅H₁₈ClNO₄S Calcd.: C 52.40 H 5.28 N 4.07 S 8.32 (343.80) Found: C 52.30 H 5.18 N 4.06 S 8.79.

(2-Arylamino-cycloalkenylmethylene)-aryl-ammonium Perchlorates **7a–c**, **10a–c**

The vinamidines **7a–c** are the main products of the reaction of the perchlorates **1a–c** with substituted anilines **6a–c**. The vinamidines **10a–c** are obtained as by-products at the synthesis of the salts **8a–c**. The vinamidines **7a** and **10a** are described in ref. [10] as chlorides.

(2-Phenylamino-cyclopent-1-enylmethylene)-phenyl-ammonium perchlorate (**7a**)

Yield 98%; *m.p.* 220–222 °C (ethanol) yellow crystals. – IR (KBr): ν /cm^{–1} = 1111 s (O–Cl–O). – UV (CH₃CN): $\lambda_{\max}$ /nm (lg ϵ) = 243.5 (4.01); 398.0 (4.45).
C₁₈H₁₉ClN₂O₄ Calcd.: C 59.59 H 5.28 N 7.72 Cl 9.77 (362.80) Found: C 59.42 H 5.19 N 7.84 Cl 9.68.

4-Methylphenyl-[2-(4-methylphenylamino)-cyclopent-1-enylmethylene]-ammonium perchlorate (**7b**)

Yield 95%; *m.p.* 195–198 °C (ethanol) yellow crystals. – IR (KBr): ν /cm^{–1} = 1114 s (O–Cl–O). – UV (CH₃CN): $\lambda_{\max}$ /nm (lg ϵ) = 245.5 (4.10); 405.0 (4.59). – ¹H NMR (DMSO-*d*₆): δ /ppm = 11.63 (bs, 1H, NH); 10.60 (d, 1H, NH); 8.98 (d, 1H, CH=N); 7.42–7.28 (m, 8H, arom.); 2.91 (t, 2H, CH₂); 2.69 (t, 2H, CH₂); 2.36 (s, 3H, *p*-CH₃); 2.33 (s, 3H, *p*-CH₃); 1.97 (m, 2H, CH₂). – ¹³C NMR (DMSO-*d*₆): δ /ppm = 179.2 (C-2); 144.3 (C-1'); 137.5; 137.3; 135.6; 135.2; 130.4; 130.3; 129.9; 118.1; 106.6 (C-1); 28.9; 28.8; 27.3.
C₂₀H₂₃ClN₂O₄ Calcd.: C 61.45 H 5.93 N 7.17 Cl 9.07 (390.85) Found: C 61.34 H 5.80 N 7.10 Cl 8.91.

4-Chlorophenyl-[2-(4-chlorophenylamino)-cyclopent-1-enylmethylene]-ammonium perchlorate (**7c**)

Yield 46%; *m.p.* 213–216 °C (ethanol) yellow crystals. – IR (KBr): ν /cm^{–1} = 1096 s (O–Cl–O). – UV (CH₃CN): $\lambda_{\max}$ /nm (lg ϵ) = 246.0 (4.20); 405.5 (4.63).
C₁₈H₁₇Cl₃N₂O₄ Calcd.: C 50.07 H 3.97 N 6.48 Cl 24.64 (431.70) Found: C 50.91 H 3.72 N 6.63 Cl 24.44.

(2-Phenylamino-cyclohex-1-enylmethylene)-phenyl-ammonium perchlorate (**10a**)

Yield 13%; *m.p.* 143–145 °C (ethanol) yellow crystals. – IR (KBr): ν /cm^{–1} = 1111 s (O–Cl–O). – UV (CH₃CN): $\lambda_{\max}$ /nm (lg ϵ) = 243.5 (4.20); 400.0 (4.58). – ¹H NMR (DMSO-*d*₆): δ /ppm = 11.79 (bs, 1H, NH); 10.60 (d, 1H, NH); 8.78 (d, 1H, CH=N); 7.63–7.21 (m, 10H, arom.); 2.63 (m, 2H, CH₂); 2.50 (m, 2H, CH₂); 1.72 (m, 4H, CH₂). – ¹³C NMR (DMSO-*d*₆): δ /ppm = 174.5 (C-2); 147.6 (C-1'); 139.7; 136.9; 129.5; 129.4; 127.7; 125.6; 125.5; 118.4; 103.4; 29.9; 23.6; 21.6; 20.9; (4CH₂).
C₁₉H₂₁ClN₂O₄S Calcd.: C 60.55 H 5.61 N 7.43 Cl 9.40 (376.83) Found: C 60.75 H 5.73 N 7.21 Cl 9.32.

4-Methylphenyl-[2-(4'-methylphenylamino)-cyclohex-1-enylmethylene]-ammonium perchlorate (**10b**)

Yield 11%; *m.p.* 153–154 °C (ethanol) yellow crystals. – IR (KBr): ν /cm^{–1} = 1135 s (O–Cl–O). – UV (CH₃CN): $\lambda_{\max}$ /nm (lg ϵ) = 246.0 (4.14); 405.0 (4.56). – ¹H NMR (DMSO-*d*₆): δ /ppm = 11.35 (bs, 1H, NH); 10.38 (d, 1H, NH); 8.57 (d, 1H, CH=N); 7.40–7.16 (m, 8H, arom.); 2.50 (m, 2H, CH₂); 2.43 (m, 2H, CH₂); 1.62 (m, 4H, CH₂). – ¹³C NMR (DMSO-*d*₆): δ /ppm = 174.1 (C-2); 147.2 (C-1'); 137.4; 137.3; 134.9; 129.9; 129.8; 125.5; 118.2; 102.8; 29.8; 23.5; 21.6; 20.9; (4CH₂); 20.6 (*p*-CH₃); 20.4 (*p*-CH₃).
C₂₁H₂₅ClN₂O₄S Calcd.: C 62.29 H 6.22 N 6.92 Cl 8.75 (445.73) Found: C 62.15 H 6.35 N 6.71 Cl 8.61.

4-Chlorophenyl-[2-(4'-chlorophenylamino)-cyclohex-1-enylmethylene]-ammonium perchlorate (**10c**)

Yield 5%; *m.p.* 167–168 °C (ethanol) orange crystals. – IR (KBr): ν /cm^{–1} = 1114 s (O–Cl–O). – UV (CH₃CN): $\lambda_{\max}$ /nm (lg ϵ) = 245.5 (4.30); 400.5 (4.35). – ¹H NMR (DMSO-*d*₆): δ /ppm = 11.55 (bs, 1H, NH); 10.57 (d, 1H, NH); 8.65 (d, 1H, CH=N); 7.58–7.13 (m, 8H, arom.); 2.63 (m, 2H, CH₂); 2.51 (m, 2H, CH₂); 1.72 (m, 4H, CH₂). – ¹³C NMR (DMSO-*d*₆): δ /ppm = 175.3 (C-2); 147.47 (C-1'); 138.6; 135.7; 129.5; 129.4; 127.4; 122.2; 119.9; 117.2; 104.2; 29.8; 23.6; 21.6; 20.9; (4CH₂); 20.6 (CH₃); 20.4 (CH₃).
C₁₉H₁₉Cl₃N₂O₄ Calcd.: C 51.19 H 4.29 N 6.28 Cl 23.86 (445.73) Found: C 51.23 H 4.17 N 6.31 Cl 23.99.

Spirocyclic Isothiazolium Perchlorates **9a–c**, **12a–c** (General Procedure)

The spirocyclic isothiazolium perchlorates **9a–c** and **12a–c** are obtained as by-products at the synthesis of the isomeric salts **8a–c**, **11a–c** (method A). Otherwise these compounds are available by dimerization of **2a–c** and **3a–c** (method B), see ref [12]. **9a–c** are described (method B) in [12].

Method B: 0.4 mmol of isothiazolium perchlorate **3a–c** were dissolved in 1.8 ml methanol by stirring and heating on a water bath (70 °C). To the warm reaction mixture 3 drops of dicyclohexylamine were slowly added, while the clear solution is becoming red. The reaction mixture is stirred on the water bath for 2–5 minutes. After this another 2 drops of dicyclohexylamine are added and the reaction mixture is stirred at room temperature, until the perchlorates **12a–c** are precipitated as a fluffy, yellow solid. The precipitate is filtered off and washed with ether. Further purification of **12a–c** is achieved by recrystallisation from ethanol.

Spiro[3-phenylamino-2,3,5,6,7,8-hexahydro-4H-cyclohepta[b]thiophen-2,8'-2'-phenyl-5',6',7',8'-tetrahydro-4'H-cyclohepta[d]-isothiazolium perchlorate] (**12a**)

Yield 3% (method A); 50% (method B); *m.p.* 172–177 °C (ethanol). – IR (KBr): ν /cm^{–1} = 1089 s (O–Cl–O). – UV (CH₃CN): $\lambda_{\max}$ /nm (lg ϵ) = 242.0 (4.21); 300.5 (3.87). – ¹H NMR (CDCl₃): δ /ppm = 8.74 (s, 1H, CH=N); 7.55–7.10 (m, 10H, arom.); 5.78 (d, 1H, NH); 4.38 (d, 1H, 3-H); 3.21 (m, 2H, CH₂); 2.75 (t, 2H, CH₂); 2.49 (t, 2H, CH₂); 2.61–1.43 (m, 12H, 6 CH₂). – ¹³C NMR (CDCl₃): δ /ppm = 168.9 (C-8'a); 153.4 (C-3'); 142.7; 139.2; 137.4; 137.1; 130.8; 130.5; 130.1; 124.9; 123.8; 123.6; 121.2; 82.2 (C-3); 66.7 (C-2/8'); 66.7 (C-2/8').

37.8; 31.1; 30.2; 29.2; 28.9; 27.7; 26.8; 26.4; 25.1 (9CH₂).
C₂₈H₃₁ClN₂O₄S₂ Calcd.: C 60.15 H 5.59 N 5.01 S 11.47
(559.14) Found: C 59.84 H 5.40 N 5.25 S 12.08.

Spiro[3-(4-methylphenyl)-2,3,5,6,7,8-hexahydro-4H-cyclohepta[b]thiophen-2,8'-2'-(4-methylphenyl)-5',6',7',8'-tetrahydro-4'H-cyclohepta[d]-isothiazolium perchlorate] (12b)

Yield 8% (method A); 58% (method B); *m.p.* 187–190 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1097 s (O–Cl–O). – UV (CH₃CN): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 243.5 (4.24); 304.5 (3.88).

C₃₀H₃₅ClN₂O₄S₂ Calcd.: C 61.36 H 6.01 N 4.77 S 10.92
(587.18) Found: C 61.24 H 6.15 N 4.51 S 10.81.

Spiro[3-(4-chlorophenylamino)-2,3,5,6,7,8-hexahydro-4H-cyclohepta[b]thiophen-2,8'-2'-(4-chlorophenyl)-5',6',7',8'-tetrahydro-4'H-cyclohepta[d]-isothiazolium perchlorate] (12c)

Yield 1% (method A); 35% (method B); *m.p.* 178–179 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1096 s (O–Cl–O). – UV (CH₃CN): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 246.0 (4.38); 302.0 (4.03). – ¹H NMR (CDCl₃): δ/ppm = 8.65 (s, 1H, CH=N); 7.51–7.11 (m, 8H, arom.); 5.95 (d, 1H, NH); 4.41 (d, 1H, 3-H); 3.11 (m, 2H, CH₂); 2.85 (t, 2H, CH₂); 2.50 (t, 2H, CH₂); 2.63–1.42 (m, 12H, 6 CH₂). – ¹³C NMR (CDCl₃): δ/ppm = 169.5 (C-8'a); 153.3 (C-3'); 141.1; 139.6; 137.5; 137.0; 135.5; 130.4; 130.1; 127.1; 125.4; 125.3, 122.7; 81.9 (C-3); 66.8 (C-2/8'); 37.7; 31.1; 30.3; 29.1; 29.0; 27.6; 26.9; 26.2; 25.0 (9CH₂).
C₂₈H₂₉Cl₃N₂S₂O₄ Calcd.: C 53.55 H 4.65 N 4.46 S 10.21
(628.03) Found: C 53.41 H 4.76 N 4.31 S 10.01.

7a-Hydroperoxy-4,5,6,7-tetrahydrobenzo-1-phenyl-2,3-dihydro-isothiazol 1,1-dioxide (13a)

The preparation of hydroperoxid **13a** was performed like reported for monocyclic 3-hydroperoxy-isothiazol 1,1-dioxides in [8]. 1 mmol isothiazolium perchlorate **8a** is dissolved in 6 ml acetic acid and under stirring 4 ml of hydrogen peroxide is added dropwise at room temperature. The reaction mixture is stirred for 8 h at 50 °C. After removing the solvent at room temperature **13a** is obtained as colorless needles, which are filtered off and washed well with distilled water. Yield 2%; *m.p.* 86–90 °C. – IR (KBr): ν/cm^{-1} = 1166 s (SO₂), 1289 s (SO₂). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 224.5 (3.73). – ¹H NMR (CDCl₃): δ/ppm = 7.67–7.57 (m, 2H, o-H); 7.47–7.49 (m, 3H, *m/p*-H); 6.31 (s, 1H, 3-H); 2.66 (t, 2H, CH₂); 2.27 (t, 2H, CH₂), 1.87–1.81 (m, 4H, 2CH₂). – ¹³C NMR (CDCl₃): δ/ppm = 139.4 (C-3a); 131.2 (*p*-CH), 130.5 (*m*-CH); 129.8 (*o*-CH); 129.6 (*i*-C); 127(C-3); 108.8 (C-7a); 30.4; 25.4; 24.1; 22.8 (4CH₂). – MS (*m/z*, %): 281 (M⁺, 1); 263 (2); 247 (23); 183 (100); 167 (23); 154 (39); 80 (56); 77 (30); 51 (20). C₁₃H₁₅NO₄S (281.3)

ω -(2-Aryl-1,1,3-trioxo-2,3-dihydro-1H-isothiazol-4-yl)-alkanoic Acids 17a,b, 18a,b (General Procedure)

1 mmol of isothiazolium perchlorate **8a,b**, **11a,b** is diluted in 6 ml acetic acid by gentle heating. To the stirred solution 4 ml hydrogen peroxide (30%) are added slowly and the reaction mixture is stirred at 70–80 °C for 6–8 hours. After removing the solvent the remaining colorless oil is stirred up in distilled water. The alkanic acids **17a,b**, **18a,b** crystallize after a short standing time as colorless powders, which are filtered off, dried and recrystallized from ethanol.

4-(2-Phenyl-1,1,3-trioxo-2,3-dihydro-1H-isothiazol-4-yl)-butanoic acid (17a)

Yield 39%; *m.p.* 103–106 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1185 s (SO₂), 1327 s (SO₂), 1713 s (COOH), 1740 s (C=O). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 219.0 (4.11). – ¹H NMR (CDCl₃): δ/ppm = 7.50–7.46 (m, 5H, arom. H); 7.16 (s, 1H, 5-H); 2.66 (t, 2H, CH₂); 2.52 (t, 2H, CH₂), 2.01 (t, 2H, CH₂). – ¹³C NMR (CDCl₃): δ/ppm = 178.6 (COOH); 160.2 (C=O); 144.5 (C-4); 131.8 (C-5)*, 130.7 (*p*-CH)*; 130.6 (*m*-CH); 129.3 (*i*-C); 128.7 (*o*-CH); 33.5; 26.0; 22.4 (3CH₂). – MS (*m/z*, %): 295 (M⁺, 100); 277 (16); 263 (35); 250 (8); 236 (21); 223 (4); 212 (14); 196 (5); 185 (21); 170 (18); 159 (10); 117 (7).

C₁₃H₁₃NO₅S Calcd.: C 52.87 H 4.43 N 4.74 S 10.86
(295.3) Found: C 52.71 H 4.54 N 4.85 S 10.63.

4-[2-(4-Methylphenyl)-1,1,3-trioxo-2,3-dihydro-1H-isothiazol-4-yl]-butanoic acid (17b)

Yield 8%; *m.p.* 116–120 °C (ethanol). – IR (KBr): ν/cm^{-1} = 1185 s (SO₂), 1330 s (SO₂), 1710 s (COOH), 1735 s (C=O). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 219.0 (4.12). – ¹H NMR (CDCl₃): δ/ppm = 7.30–7.29 (m, 4H, arom. H); 7.17 (s, 1H, 5-H); 2.64 (t, 2H, CH₂); 2.49 (t, 2H, CH₂), 2.39 (s, 3H, *p*-CH₃); 1.98 (t, 2H, CH₂). – ¹³C NMR (CDCl₃): δ/ppm = 178.8 (COOH); 160.4 (C=O); 144.5 (C-4)*; 140.9 (*p*-C)*; 131.8 (C-5); 131.2 (*m*-CH); 128.7 (*o*-CH); 126.4 (*i*-C); 33.5, 25.9; 22.2 (3CH₂); 22.1 (*p*-CH₃).

C₁₄H₁₅NO₅S Calcd.: C 54.36 H 4.89 N 4.53 S 10.37
(309.3) Found: C 54.21 H 4.72 N 4.68 S 10.20.

4-(2-Phenyl-1,1,3-trioxo-2,3-dihydro-1H-isothiazol-4-yl)-pentanoic acid (18a)

Yield 38%; *m.p.* 143–144 °C. – IR (KBr): ν/cm^{-1} = 1182 s (SO₂), 1333 s (SO₂), 1706 s (COOH), 1730 s (C=O). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 218.5 (3.98). – ¹H NMR (CDCl₃): δ/ppm = 7.57–7.42 (m, 5H, arom. H); 7.17 (s, 1H, 5-H); 2.59 (t, 2H, CH₂); 2.44 (t, 2H, CH₂), 1.73 (m, 4H, 2CH₂). – ¹³C NMR (CDCl₃): δ/ppm = 179.5 (COOH); 160.6 (C=O); 144.9 (C-4); 131.4 (C-5)*; 130.5 (*p*-CH)*; 130.4 (*m*-CH); 129.2 (*i*-C); 128.5 (*o*-CH); 33.6, 26.4; 26.0; 24.2 (4CH₂). – MS (*m/z*, %) = 309 (M⁺, 80); 291 (8); 250 (52); 238 (15); 223 (12); 198 (22); 186 (19); 172 (20); 159 (21); 144 (10); 130 (31); 119 (98); 92 (100); 77 (71); 64 (49); 52 (40); 38 (57).

C₁₄H₁₅NO₅S Calcd.: C 54.36 H 4.89 N 4.53 S 10.37
(309.3) Found: C 54.48 H 4.66 N 4.75 S 10.15.

4-[2-(4-Methylphenyl)-1,1,3-trioxo-2,3-dihydro-1H-isothiazol-4-yl]pentanoic acid (18b)

Yield 43%; *m.p.* 118–122 °C. – IR (KBr): ν/cm^{-1} = 1184 s (SO₂), 1334 s (SO₂), 1705 s (COOH), 1739 s (C=O). – UV (ethanol): $\lambda_{\text{max}}/\text{nm}$ (lg ϵ) = 219.5 (4.15). – ¹H NMR (CDCl₃): δ/ppm = 7.28–7.27 (m, 4H, arom. H); 7.21 (s, 1H, 5-H); 2.55 (t, 2H, CH₂); 2.43 (t, 2H, CH₂), 2.37 (s, 3H, *p*-CH₃); 1.70 (m, 4H, 2CH₂). – ¹³C NMR (CDCl₃): δ/ppm = 179.0 (COOH); 160.5 (C=O); 145.0 (C-4)*; 140.8 (*p*-C)*; 131.5 (C-5); 131.6 (*m*-CH); 128.6 (*o*-CH); 124.0 (*i*-C); 33.8, 26.8; 26.5; 25.1 (4CH₂); 21.8 (*p*-CH₃). – MS (*m/z*, %) = 323 (M⁺, 30); 305 (2); 291 (48); 264 (11); 250 (5); 226 (5); 212 (10); 198 (14); 186 (9); 172 (9); 156 (12); 144 (13); 133 (40); 117 (100); 107

¹) carbon atoms marked with * could be exchanged

(60); 91 (43); 77 (35); 65 (32); 52 (24); 40 (38).

$C_{15}H_{17}NO_5S$ Calcd.: C 55.72 H 5.30 N 4.33 S 9.92
(323.3) Found: C 55.91 H 5.43 N 4.24 S 9.99.

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