

Regioselective Oxidation and Halogenation of 2-(Arylsulfonylimino)- and 2-(Arylsulfinylimino)-4-thiazolines¹⁾

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Dedicated to Professor R. Gompper (Munich) on the Occasion of his 70th Birthday

Abstract. The synthesis of 4-thiazoline 2-iminium sulfinates (**3**) is described. From the salts **3** and NBS the 2-(arylsulfonylimino)-4-thiazolines (**4**) were formed, which have also been prepared by oxidation of 2-(arylsulfonylimino)-4-thiazolines (**5**) and by reaction of the arylsulfonyl chlorides (**6**) with 2-imino-4-thiazolines (**2**). The treatment of **5** with NBS (or NIS)

in dry solvents results in 2-(arylsulfonylimino)-5-bromo (or iodo)-4-thiazolines (**7**); in the presence of NaHCO₃ 2-(arylsulfonylimino)-5-bromo-4-thiazolines (**8**) are formed. 2-(Arylsulfonylimino)-4-thiazolines (**10**) have also been halogenated in the same manner with NBS or NIS to give the products (**11**).

In connection with the aim to obtain 2-(arylsulfonylimino)-heterocycles we have recently reported the synthesis of 2-(arylsulfonylimino)-4-thiazolines **5** by the reaction of 2-imino-4-thiazoline-hydrochlorides **2**·HCl (existing as 4-thiazoline 2-iminium chlorides) with arylsulfonyl chlorides as well as by the reaction of *N*-arylsulfonylsuccinimides with 2-imino-4-thiazolines **2**. We have also shown that the treatment of 2-(arylsulfonylimino)-4-thiazolines **5** with *m*-chloroperbenzoic acid (*m*-CPBA) results in 2-(arylsulfinylimino)-4-thiazolines **10**. These substances were also synthesized by the reaction of sulfinyl chlorides with compounds **2** [1].

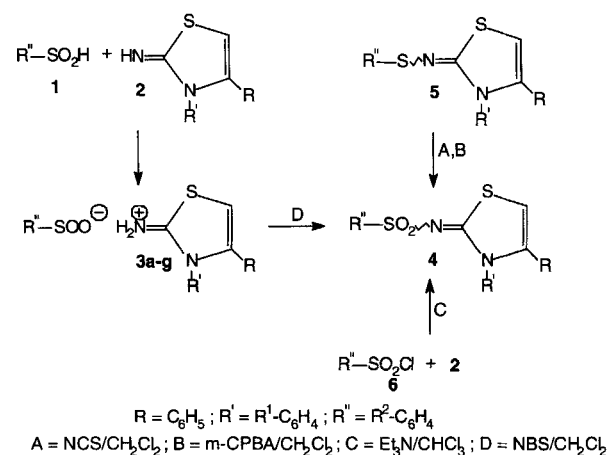
As previously discussed, both methods have disadvantages. The reaction with sulfinyl chlorides requires fairly strong conditions and often results in low yields and side reactions. The chemoselective oxidation with *m*-CPBA to the respective compounds **10** proved to be difficult. The result depends extremely on the reaction conditions and gives only moderate yields. On the other hand, the mixture TiCl₃/H₂O₂, which selectively oxidizes sulfides to sulfoxides [2], gives only the corresponding sulfonyl compounds **4**.

N-Halogensuccinimides (NHS) are well known oxidizing reagents reported to convert sulfenamides into sulfinamides in high yields without formation of inconvenient by-products [3].

In this paper we report on the results of attempts to oxidize 2-(arylsulfonylimino)-4-thiazolines **5** with NHS to the corresponding 2-(arylsulfinylimino)-4-thiazolines **10**.

We have found that a cooled solution of *N*-chlorosuccinimide (NCS) as reported by Haake [3], affords the

initial substances **5** only. However, the reaction of NCS with **5** over 4 days at 25 °C results in 2-(arylsulfonylimino)-4-thiazolines **4** (Scheme 1, Method A). These substances have also been prepared in yields of 16–48% by the reaction of salts **3** with 1 equiv. *N*-bromosuccinimide (NBS) (Scheme 1, Method D). The salts **3** were produced within 10 min by the reaction of the corresponding sulfinic acid **1** with 2-imino-4-thiazolines **2** in dioxane. The oxidation of **5** with *m*-CPBA in dichloromethane (Method B) or with H₂O₂ in acetic acid [4,5]



Scheme 1

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at 70–90 °C gives **4** in high purity. Undoubtedly, the less inexpensive and simplest method for the preparation of these compounds is the direct reaction of **2** with arylsulfonyl chlorides **6** (Scheme 1, Method C).

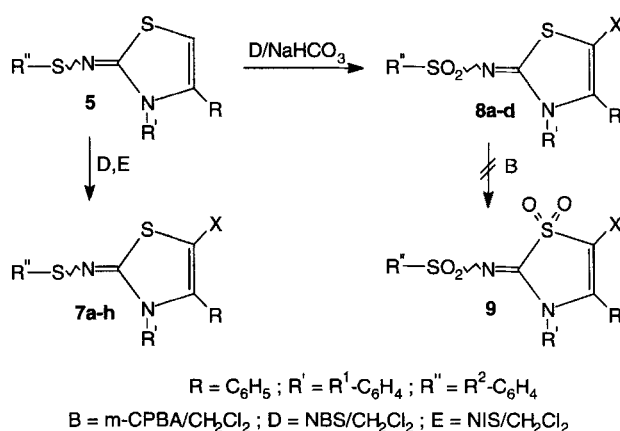
The structures of the compounds **3** and **4** are proved by microanalytical, ^{13}C NMR, ^1H NMR and mass spectral data. In the IR spectra of **3** the S=O frequency is found between $\nu = 1023\text{--}1007\text{ cm}^{-1}$, the NH_2^+ stretching of the $\text{C}=\text{NH}_2^+$ group around $\nu = 3104\text{--}3060\text{ cm}^{-1}$. This is in accordance with the literature [6]. The respective mass spectra show the molecular ion peak of the 2-imino-4-thiazolines **2** as the base peak. In accordance with the investigation of similar compounds [7], we believe that the antisymmetric SO_2 stretching mode of **4** is located between $\nu_{\text{as}} = 1304\text{--}1276\text{ cm}^{-1}$. Experimental data of the products **3** and **4** are given in table 1 and 2, respectively.

Some laboratories have introduced the use of catalysts in conjunction with NBS [8], and have applied these reagents to brominations of aromatic [9–14] and carbonyl substances [8, 15]. Additionally, NBS is a versatile synthetic reagent widely used to oxidize primary and secondary alcohols to aldehydes and ketones, respectively [16]. Nevertheless, the use of NBS as oxidizing agent for S,N-systems is unknown to our experience.

Using similar reaction conditions to those employed for NCS, compounds **5** were treated with NBS or NIS at room temperature during 2 days in dry dichloromethane without any catalytic agent. After evaporation of the solvent under reduced pressure pure regioselectively monohalogenated products **7** were isolated (Scheme 2, Methods D and E). When the reaction was run as

above but with the addition of NaHCO_3 the products obtained were 2-(arylsulfonylimino)-5-bromo-4-thiazolines **8**, which have been also rapidly synthesized by the reaction of **4** with NBS. Oxidation of **8** with *m*-CPBA to form compounds **9** was impossible.

2-(Arylsulfonylimino)-4-thiazolines **10** have also been brominated in the same manner and gave 2-(arylsulfonylimino)-5-bromo-4-thiazolines **11** in yields of 51–63 %. We found this method applicable for the synthesis of 2-(arylsulfonylimino)-5-iodo-4-thiazolines **11a,b** when **10** was treated with *N*-iodosuccinimide (NIS) for 2 days at 25° C in dichloromethane (Scheme 3, Table



Scheme 2

5). The products **7** (Table 3), **8** (Table 4) and **11** (Table 5) were checked for purity by mass spectrometry. The ^{13}C NMR, ^1H NMR, IR spectra and elemental analysis are in agreement with these structures. Additional proof for the structures are given by X-ray crystallography of **4b**, **7b** and **11h** (for **7b** and **11h** see Fig.1 and Fig.2, resp.). The observed bond lengths and angles do not show any remarkable specialities. However, there is an intermolecular contact between a chlorine and a bromine atom of 3.5892(17) Å in the solid of **7b**, which is just below the sum of the van der Waals radii of 3.60 Å.

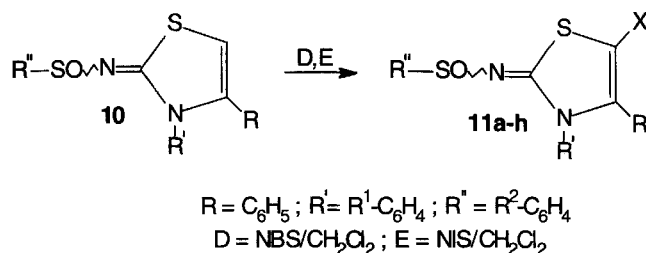
We would like to thank the BASF AG, Ludwigshafen, for financial support.

Table 1 Yields of 4-Thiazoline-2-iminium sulfinates (**3a–g**)

3	R^1	R^2	Yield (%)
a	H	H	91
b	H	4- CH_3	64
c	3-Cl	H	61
d	4-Cl	H	97
e	4- OCH_3	H	93
f	4- NO_2	H	79
g	4- NO_2	4- CH_3	95

Table 2 Data of 2-(Arylsulfonylimino)-4-thiazolines (**4a–f**)

4	R^1	R^2	Method				Yield (%)	m.p. (°C)
			A	B	C	D		
a	H	H	17	82	73	16	205–206	
b	H	4- CH_3	–	–	–	48	217–218	
c	4-Cl	H	–	–	–	36	249–250	
d	4-Cl	4-Cl	–	63	75	–	270–272	
e	4-F	4-Cl	29	67	58	–	253–256	
f	4- OCH_3	H	–	–	–	18	250–251	



Scheme 3

Table 3 Data of 2-(Arylsulfonylimino)-5-bromo(or iodo)-4-thiazolines (**7a-h**)

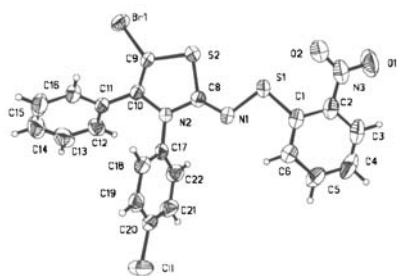
7	R ¹	R ²	X	Yield (%)	m.p. °C
a	3-Cl	2-NO ₂	Br	46	177–178
b	4-Cl	2-NO ₂	Br	63	186–187
c	4-F	H	Br	51	163–165
d	4-F	4-Cl	Br	27	195–196
e	4-OCH ₃	2-NO ₂	Br	57	186–189
f	4-NO ₂	4-Cl	Br	47	153–155
g	4-NO ₂	2-NO ₂	Br	76	170–172
h	4-Cl	2,4-(NO ₂) ₂	I	63	230–232

Table 4 Data of 2-(Arylsulfonylimino)-5-bromo-4-thiazolines (**8a-d**)

	R ¹	R ²	X	Yield (%)	m.p. °C
a	H	H	Br	60	194–195
b	3-Cl	H	Br	93	235–236
c	4-Cl	H	Br	79	230–233
d	4-OCH ₃	H	Br	81	190–191

Table 5 Data of 2-(Arylsulfonylimino)-5-bromo(or iodo)-4-thiazolines (**11a-h**)

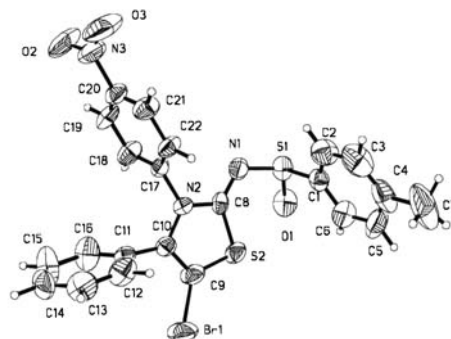
11	R ¹	R ²	X	Yield (%)	m.p. °C
a	4-Cl	H	I	41	186–188
b	4-Cl	4-CH ₃	I	74	189–191
c	4-Cl	4-CH ₃	Br	51	160–162
d	4-F	H	Br	58	175–176
e	4-F	4-Cl	Br	57	202–203
f	4-OCH ₃	4-CH ₃	Br	61	163–165
g	4-NO ₂	H	Br	51	177–179
h	4-NO ₂	4-CH ₃	Br	63	210–211

**Fig. 1** Molecular structure of **7b** (ORTEP-plot with 50% probability)

Selected bond distances [Å] and angles [°]: C(1)–S(1) 1.754(5), S(1)–N(1) 1.705(4), N(1)–C(8) 1.274(6), C(8)–S(2) 1.774(5), C(8)–N(2) 1.390(6), S(2)–C(9) 1.749(5), C(1)–S(1)–N(1) 99.90(22), S(1)–N(1)–C(8) 112.69(33)

Experimental

Melting points were determined with a micro heating stage of Boëtius (Carl Zeiss Jena) without correction. ¹H NMR and

**Fig. 2** Molecular structure of **11h** (ORTEP-plot with 50% probability)

Selected bond distances [Å] and angles [°]: C(1)–S(1) 1.814(8), S(1)–O(1) 1.497(6), S(1)–N(1) 1.665(7), N(1)–C(8) 1.292(9), C(8)–S(2) 1.768(8), C(8)–N(2) 1.362(9), C(1)–S(1)–N(1) 99.99(35), S(1)–N(1)–C(8) 120.07(59)

¹³C NMR spectra were taken with an AC 250 spectrometer (Bruker) using TMS as an internal reference and mass spectra on a AMD 402-3 spectrometer (Intectra GmbH). IR spectra were recorded on a 205FT-IR spectrophotometer. Elementary analyses were performed by a CHNS-932 LECO analyzer.

Crystal Structure Determination

Crystals of **7b** and **11h** were measured on a Siemens P4 four circle diffractometer after taking rotational photos and determining the unit cells in automatic mode. The unit cell measures found are: *a* = 10.007(1) Å, *b* = 9.158(1) Å, *c* = 23.158(1) Å, β = 90.10(1)° for **7b**, that crystallizes in P2₁/n and *a* = 25.934(4) Å, *b* = 8.043(2) Å, *c* = 21.970(4) Å, β = 104.83(1)° for **11h**, crystallizing in C2/c. The data were collected in routine ω-scan. The structures were solved by direct methods (Siemens SHELXTL, 1990, Siemens Analytical X-ray Inst. Inc.) and refined by the full-matrix least squares method of SHELXL-93 [17]. All non-hydrogen atoms were refined anisotropically. Although some hydrogen positions could be seen from the difference Fourier map, all hydrogens were put into their theoretical positions and refined using the „riding model“. The weighting scheme was calculated according to *w* = 1/[σ²(*F*_o²) + (0.0562*P*)² + 0.0000*P*] for **7b** and *w* = 1/[σ²(*F*_o²) + (0.0848*P*)² + 0.0000*P*] for **11h** with *P* = (*F*_o² + 2*F*_c²)/3 in both cases. Since the absorption coefficient μ was above 20 cm^{−1} for both data sets an empirical absorption correction was performed using the XEMP part of Siemens SHELXTL.

The reflection to parameter ratio was 2575/271 for **7b** and 2848/281 for **11h**. The weighted R2 (*w*R2, based on *F*²) was 0.1116 and 0.1927, respectively, while the conventional R1 were calculated to be 0.0414 for 2126 observed reflections of **7b** and 0.069 for 1707 observed reflections of **11h** (observation criterion: *I* > 2σ(*I*)).

Further details of the crystal structure investigations are available on request from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-76344 Eggenstein-Leopoldshafen, on quoting the depository number CSD-405120 (**7b**) and CSD-405121 (**11h**),

the names of the authors, and the journal citation. Data for **4b** may be obtained on quoting the depository number CSD-405122.

4-Thiazoline-2-iminium sulfinates (**3a–g**) (General procedures)

A solution of 0.01 mol 2-imino-4-thiazoline (**2**) in 20 mL anhydrous dioxane is added to a solution of 0.01 mol sulfinic acid (**1**) in 10 mL anhydrous dioxane. The reaction mixture is stirred for 10 min. The precipitated salt **3** is filtered off, washed with dry ether, dried one day on the air and used in the next step (Method D) without purification.

2-(Arylsulfonylimino)-4-thiazolines (**4a–f**)

Method A:

A solution of 0.01 mol *N*-chlorosuccinimide in 50 mL anhydrous dichloromethane is added dropwise at 25 °C to a solution of 0.01 mol 2-(arylsulfonylimino)-4-thiazolines (**5**) in 50 mL anhydrous dichloromethane. The reaction mixture is shaken (shaking machine) for 4 d. The solvent is evaporated under reduced pressure, and the residue is recrystallized from ethanol/water.

Method B:

A solution of 0.01 mol (85%) *m*-chloroperbenzoic acid in 80 mL dry dichloromethane is added dropwise at 80 °C to a stirred solution of 0.01 mol 2-(arylsulfonylimino)-4-thiazoline (**5**) in 100 mL dry dichloromethane. Stirring is continued for 1 h, then the solution is evaporated to dryness under reduced pressure. The residue is purified by recrystallization from ethanol.

Method C:

A solution of 0.01 mol sulfonyl chloride (**6**) in 50 mL anhydrous chloroform is added dropwise at room temperature to a mixture of 0.01 mol 2-imino-4-thiazoline (**2**) and 0.01 mol triethylamine stirred in 50 mL anhydrous chloroform. After addition, the mixture is stirred 3 h, the solvent is evaporated under reduced pressure, and the residue is recrystallized from ethanol/water.

Method D:

A solution of 0.01 mol *N*-bromosuccinimide in 20 mL anhydrous dichloromethane is added to a slurry of 50 mL dichloromethane and the corresponding 4-thiazoline-2-iminium sulfinate **3** (0.01 mol). The reaction mixture is stirred at room temperature for 2 h and then filtered to remove the precipitated succinimide. The solution is evaporated to dryness under reduced pressure. The residue is purified by recrystallization from ethanol.

2-(Arylsulfonylimino)-5-bromo-4-thiazolines (**7a–g**) and 2-(Arylsulfonylimino)-5-iodo-4-thiazoline (**7h**)

Methods D and E:

A solution of 0.01 mol *N*-bromosuccinimide or *N*-iodosuccinimide in 50 mL anhydrous dichloromethane is added at room temperature to a solution of 0.01 mol 2-(arylsulfonylimino)-4-thiazoline (**5**) in 50 mL dichloromethane. The mixture is stirred for 2 d, the solvent is evaporated under reduced pressure, and the residue is recrystallized from dry ethanol.

2-(Arylsulfonylimino)-5-bromo-4-thiazolines (**8a–d**)

A solution of 0.01 mol 2-(arylsulfonylimino)-4-thiazoline (**5**) in 50 mL dry dichloromethane is added at room temperature to a mixture of a 10 mL solution of NaHCO₃ and a solution of 0.01 mol *N*-bromosuccinimide in 50 mL dichloromethane stirred at room temperature. After addition, the reaction mixture is stirred 3 h. The organic phase is dried with magnesium sulfate, filtered and evaporated to dryness under reduced pressure. The residue is purified by recrystallization from ethanol.

2-(Arylsulfonylimino)-5-bromo(or iodo)-4-thiazolines (**11a–h**)

Methods D and E:

A solution of 0.01 mol *N*-bromosuccinimide or *N*-iodosuccinimide in 50 mL anhydrous dichloromethane is added at room temperature to a solution of a 0.01 mol 2-(arylsulfonylimino)-4-thiazoline (**10**) in 50 mL dichloromethane. The mixture is stirred for 2 d, the solvent is evaporated under reduced pressure, and the residue is recrystallized from dry ethanol.

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