

## Synthesis of Schiff Bases and Oxazolidines from 2-Amino-4-phenylthiazole

S. E. Sadigova, A. M. Magerramov, and M. A. Allakhverdiev

Baku State University, ul. Z. Khalilova 23, Baku, Az1048, Azerbaidjan  
e-mail: s\_sevinj@mail.ru

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**Abstract**—Reactions of 2-amino-4-phenylthiazole with aromatic aldehydes gave the corresponding Schiff bases which were reduced with sodium tetrahydridoborate to amines. Reactions of the Schiff bases with 2-methyloxirane, 2-chloromethyloxirane, and 2-phenoxy-methyloxirane led to the formation of 2,5-disubstituted 3-(4-phenylthiazol-2-yl)oxazolidines.

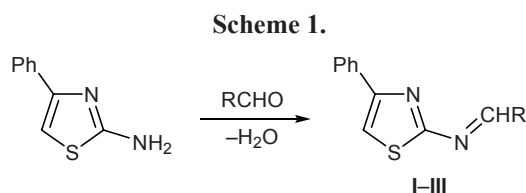
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Schiff bases derived from 2-amino-4-arylthiazoles [1] are important for analytical chemistry and chemotherapy [2–4]. In particular, these compounds are used for the concentration and photometric determination of some transition metals. It is known that reactions of various amines with aldehydes give rise to a new C=N bond. We synthesized Schiff bases **I–III** by reaction of 2-amino-4-phenylthiazole with benzaldehyde, salicylaldehyde, and 2-hydroxynaphthalene-1-carbaldehyde (Scheme 1). Schiff bases **II** and **III** were reduced with

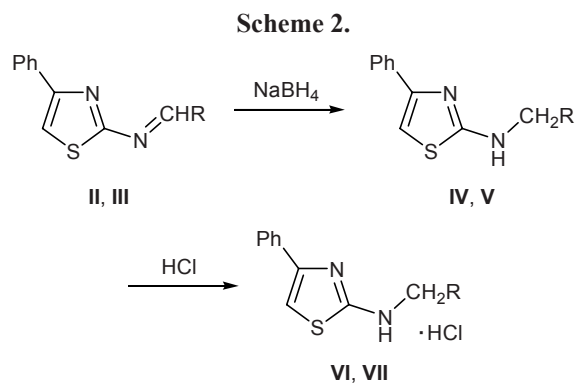
sodium tetrahydridoborate under mild conditions to 2-(2-hydroxybenzylamino)- and 2-(2-hydroxynaphthalen-1-ylmethylamino)-4-phenylthiazoles **IV** and **V**, respectively, and compounds **IV** and **V** were converted into the corresponding hydrochlorides **VI** and **VII** by treatment with hydrogen chloride (Scheme 2).

The IR spectra of Schiff bases **I–III** resembled those of initial 2-amino-4-phenylthiazole with the difference that a broad band appeared at about 3450 cm<sup>-1</sup> in the spectra of **II** and **III** due to OH group involved in intramolecular hydrogen bond with the N=CH fragment. No absorption typical of primary amino group was observed. The OH proton signal appeared in the <sup>1</sup>H NMR spectra of **II** and **III** at δ 3.25 ppm, and the N=CH proton resonated in the region δ 7.85–7.90 ppm. Four nonequivalent protons in the 2-hydroxyphenyl fragment of **II** gave a multiplet at δ 7.2–7.5 ppm.

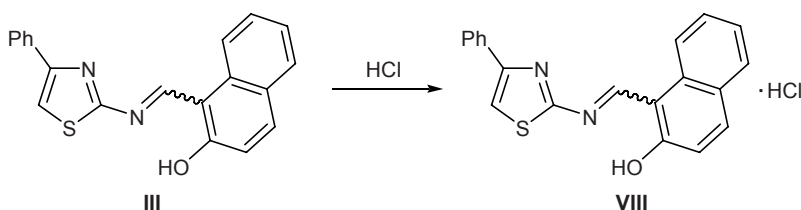
The UV spectra of Schiff bases **II** and **III** sharply differed from those of their hydrogenated derivatives **IV** and **V**. Compound **II** displayed absorption maxima at λ 208 and 278 nm due to electron transitions in the aromatic ring, and the long-wave absorption maximum (λ 385 nm) was assigned to π–π\* transition in the conjugated azomethine fragment. No band in the region of λ 385 nm was present in the UV spectrum of **IV**. Insofar as the benzene rings in molecule **IV** are not conjugated, the spectrum of **IV** contained two maxima at λ 260 and 282 nm instead of one maximum at λ 278 nm as in the spectrum of **II**; these maxima are likely to belong to the 4-phenyl and hydroxyphenyl rings, respectively.



**I**, R = Ph; **II**, R = 2-HOC<sub>6</sub>H<sub>4</sub>; **III**, R = 2-HOC<sub>10</sub>H<sub>6</sub>.

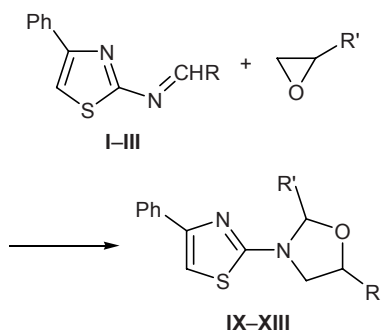


Scheme 3.



2-(2-(4-Phenyl-1,3-thiazol-2-yl)iminomethyl)phenol (**III**) was converted into hydrochloride **VIII** (Scheme 3). Schiff bases **I–III** reacted with 2-methyloxirane, 2-chloromethyloxirane, and 2-phenoxymethyloxirane in carbon tetrachloride in the presence of  $\text{SnCl}_4$  to give 2,5-disubstituted 3-(4-phenylthiazol-2-yl)oxazolidines **IX–XIII** (Scheme 4).

Scheme 4.



**IX**, R = 2-HOC<sub>10</sub>H<sub>6</sub>, R' = Me; **X**, R = Ph, R' = ClCH<sub>2</sub>; **XI**, R = 2-HOC<sub>10</sub>H<sub>6</sub>, R' = ClCH<sub>2</sub>; **XII**, R = 2-HOC<sub>6</sub>H<sub>4</sub>, R' = PhOCH<sub>2</sub>; **XIII**, R = 2-HOC<sub>10</sub>H<sub>6</sub>, R' = PhOCH<sub>2</sub>.

## EXPERIMENTAL

The IR spectra (700–3700  $\text{cm}^{-1}$ ) were recorded on a Specord 75IR spectrometer from samples prepared as thin films or dispersed in mineral oil. The <sup>1</sup>H NMR spectra were measured from solutions in DMSO-*d*<sub>6</sub> on a Varian VXR-400S spectrometer (400 MHz) relative to TMS as internal reference. Analytical thin-layer chromatography was performed on Silufol UV-254 plates using propan-2-ol–heptane (1 : 1) as eluent; spots were visualized by treatment with iodine vapor.

**N-Benzylidene-4-phenyl-1,3-thiazol-2-amine (I).** A mixture of 5.3 g (0.05 mol) of benzaldehyde and 8.8 g (0.05 mol) of 2-amino-4-phenylthiazole was vigorously stirred for 30 min and poured into 15 ml of ethanol. After several minutes, the colorless crystalline product was filtered off. Yield 9.4 g (71%), mp 155–156°C, *R*<sub>f</sub> 0.74. Found, %: C 72.61; H 4.73; N 10.75; S 12.02. C<sub>16</sub>H<sub>12</sub>N<sub>2</sub>S. Calculated, %: C 72.80; H 4.58; N 10.60; S 12.12.

**2-(4-Phenyl-1,3-thiazol-2-yliminomethyl)phenol (II)** was synthesized in a similar way. Yield 11.21 g (86%), mp 143°C. Found, %: C 68.76; H 4.13; N 9.74; S 11.28. C<sub>16</sub>H<sub>12</sub>N<sub>2</sub>OS. Calculated, %: C 68.55; H 4.32; N 9.99; S 11.44.

**1-(4-Phenyl-1,3-thiazol-2-yliminomethyl)naphthalen-2-ol (III).** A solution of 4.4 g (0.025 mol) of 2-amino-4-phenylthiazole in 15 ml of ethanol was added to 4.3 g (0.025 mol) of 2-hydroxynaphthalene-1-carbaldehyde in 12 ml of ethanol, and the mixture was stirred for 3 h at 75°C. After cooling to room temperature, the precipitate was filtered off. Yield 5.1 g (74%), mp 156–157°C. Found, %: C 72.52; H 4.43; N 8.78; S 9.51. C<sub>20</sub>H<sub>14</sub>N<sub>2</sub>OS. Calculated, %: C 72.70; H 4.30; N 8.50; S 9.70.

**2-(4-Phenyl-1,3-thiazol-2-ylaminomethyl)phenol (IV).** Compound **II**, 5.6 g (0.02 mol), was dispersed in 30 ml of ethanol under stirring at 30–40°C, sodium tetrahydridoborate was added until the mixture turned white, and the mixture was stirred for 30 min, diluted with 100 ml of water, and acidified to pH 7.5. The colorless precipitate was filtered off and recrystallized from benzene. Yield 3.9 g (70%), mp 155°C. Found, %: C 67.93; H 5.14; N 9.86; S 11.49. C<sub>16</sub>H<sub>14</sub>N<sub>2</sub>OS. Calculated, %: C 68.06; H 5.00; N 9.92; S 11.36.

**1-(4-Phenyl-1,3-thiazol-2-ylaminomethyl)naphthalen-2-ol (V)** was synthesized in a similar way. Yield 4.5 g (68%), mp 171–172°C. Found, %: C 72.41; H 4.63; N 8.27; S 9.79. C<sub>20</sub>H<sub>16</sub>N<sub>2</sub>OS. Calculated, %: C 72.26; H 4.85; N 8.43; S 9.65.

**2-(4-Phenyl-1,3-thiazol-2-ylaminomethyl)phenol hydrochloride (VI).** Dry hydrogen chloride was passed through a solution of 2.8 g (0.01 mol) of compound **IV** in isopropyl alcohol cooled to 0°C. The colorless precipitate was filtered off, washed with several portions of anhydrous diethyl ether, and recrystallized from ethanol. Yield 3.0 g (93%), mp 177–178°C. Found, %: C 60.35; H 4.57; N 8.92; S 10.26. C<sub>16</sub>H<sub>15</sub>ClN<sub>2</sub>OS. Calculated, %: C 60.28; H 4.74; N 8.79; S 10.06.

Compounds **VII** and **VIII** were obtained in a similar way.

**1-(4-Phenyl-1,3-thiazol-2-ylaminomethyl)naphthalen-2-ol hydrochloride (VII).** Yield 3.3 g (90%), mp 193–194°C. Found, %: C 65.47; H 4.53; N 7.68; S 8.37.  $C_{20}H_{17}ClN_2OS$ . Calculated, %: C 65.12; H 4.65; N 7.59; S 8.69.

**1-(4-Phenyl-1,3-thiazol-2-yliminomethyl)naphthalen-2-ol hydrochloride (VIII).** Yield 0.5 g (72%), mp 115°C. Found, %: C 65.13; H 4.32; N 7.46; S 8.81.  $C_{20}H_{15}ClN_2OS$ . Calculated, %: C 65.48; H 4.12; N 7.64; S 8.74.

**1-[5-Methyl-3-(4-phenyl-1,3-thiazol-2-yl)oxazolidin-2-yl]naphthalen-2-ol (IX).** A solution of 0.23 ml (0.002 mol) of tin(IV) chloride in 2.4 ml of carbon tetrachloride was added dropwise over a period of 1 h to a solution of 1.69 ml (0.022 mol) of 2-methyl-oxirane and 3.3 g (0.01 mol) of Schiff base III in 4 ml of carbon tetrachloride. The organic phase was dried over  $Na_2SO_4$ . Yield 2.52 g (65%), mp 85–86°C. Found, %: C 71.26; H 5.32; N 7.43; S 8.03.  $C_{23}H_{20}N_2O_2S$ . Calculated, %: C 71.11; H 5.19; N 7.21; S 8.25.

**5-Chloromethyl-2-phenyl-3-(4-phenyl-1,3-thiazol-2-yl)oxazolidine (X).** A solution of 0.23 ml (0.002 mol) of tin(IV) chloride in 5 ml of carbon tetrachloride was added dropwise over a period of 1 h to a solution of 1.69 ml (0.022 mol) of 2-chloromethyl-oxirane and 5.60 g (0.02 mol) of Schiff base I in 8 ml of carbon tetrachloride. The organic phase was dried over  $Na_2SO_4$ . Yield 5.2 g (75%), mp 78–79°C. Found, %: C 63.72; H 4.96; N 7.68; S 8.66.  $C_{19}H_{17}ClN_2OS$ . Calculated, %: C 63.95; H 4.80; N 7.85; S 8.99.

**1-[5-Chloromethyl-3-(4-phenyl-1,3-thiazol-2-yl)oxazolidin-2-yl]naphthalen-2-ol (XI)** was synthesized in a similar way. Yield 5.92 g (70%), mp 106°C.

Found, %: C 65.13; H 4.72; N 6.47; S 7.79.  $C_{23}H_{19}ClN_2O_2S$ . Calculated, %: C 65.32; H 4.53; N 6.62; S 7.58.

**2-[5-Phenoxymethyl-3-(4-phenyl-1,3-thiazol-2-yl)oxazolidin-2-yl]phenol (XII).** A solution of 0.23 ml (0.002 mol) of tin(IV) chloride in 5 ml of carbon tetrachloride was added dropwise over a period of 1 h to a solution of 3.3 ml (0.022 mol) of 2-phenoxymethyl-oxirane and 5.6 g (0.02 mol) of Schiff base II in 8 ml of carbon tetrachloride. The organic phase was dried over  $Na_2SO_4$ . Yield 5.76 g (67%), mp 128–129°C. Found, %: C 69.56; H 5.37; N 6.42; S 7.66.  $C_{25}H_{22}N_2O_3S$ . Calculated, %: C 69.74; H 5.15; N 6.51; S 7.45.

**1-[5-Phenoxymethyl-3-(4-phenyl-1,3-thiazol-2-yl)oxazolidin-2-yl]naphthalen-2-ol (XIII)** was synthesized in a similar way. Yield 6.9 g (72%), mp 171–172°C. Found, %: C 72.31; H 5.18; N 5.97; S 6.79.  $C_{29}H_{24}N_2O_3S$ . Calculated, %: C 72.48; H 5.03; N 5.83; S 6.67.

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