

## N-Unsubstituted Sulfenamides by Electrophilic Amination of Mercapto Compounds

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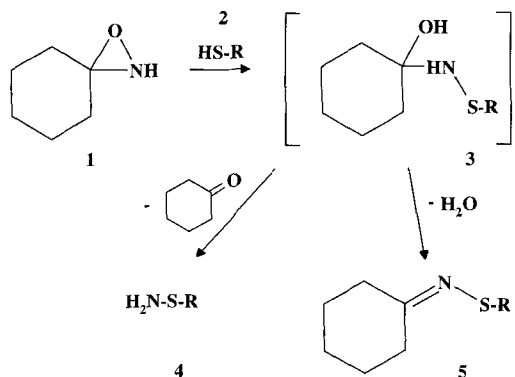
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**Abstract.** Potential mercapto compounds derived from electron deficient heterocycles as 2- and 4-thiouracils, pyridines and pyridine-1-oxide are aminated by the oxaziridine **1** to new sulfenamides (**6**, **9**, **11** and **15** or the isothiazolo-pyridine **14**) which add to phenylisocyanates forming sulfenylureas (**7**, **10**,

**12** and **16**). Several other mercapto compounds gave disulfides. Attempts of oxidation of the sulfenamides and the sulfenylureas were unsuccessful. The methylmercapto compound **19** after amination was hydrolyzed to the sulfoxide **20**.

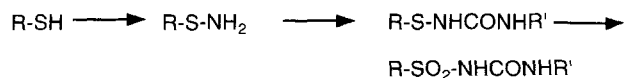
1-Oxa-2-azaspiro[2.5]octane ("3,3-pentamethyleneoxaziridine") **1** is a widely useful  $\text{NH}_2^+$ -equivalent [1]. The systematic investigation of the synthetic potential of **1** revealed a variety of stabilizing reactions of the primary adduct **3** of (potential) mercapto compounds **2** to the oxaziridine **1**.



Scheme 1

Conventional preparations of sulfenamides by substitution [2] or *via* sulfenylchlorides [3] give only unsatisfying yields. The formation of the S–N-bond by elec-

trophilic amination with **1** followed by addition of the resulting sulfenamide to an isocyanate and oxydation of the sulfur function could open an alternative route to sulfonylurea derivatives:

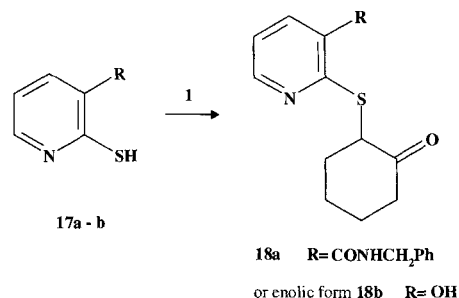


Scheme 2

If there are no other stabilizing reactions of the primary adduct **3** (as in polyfunctional nucleophiles, e.g. acylthioureas [4] or 3-unsubstituted 2-thiouracils [5]), the sulfenamides **4** can be obtained as stable final products. Whereas simple 2-thiouracils give 5a-amino-5a,6,7,8,9,9a-hexahydro-4*H*-pyrimido[2,1-*b*]benzothiazol-4-ones *via* rearrangement of the corresponding intermediate **3** [5], *N*<sup>3</sup>-substituted 2-mercaptoquinazoline-4-ones ("blocked" 2-thiouracils) yield the sulfenamides **6**. 4-Thiouracils are converted exclusively and in excellent yields into the sulfenamides **9**. The sulfenamides **6** and **9** add to isocyanates forming the new sulfenylureas **7** and **10**. The benzylation of **6a** to **8a** was demonstrated.

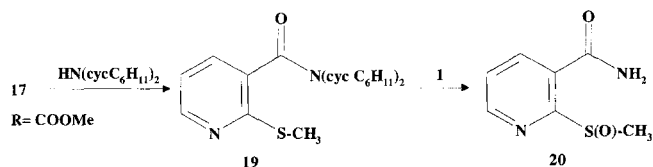


Other 2-mercaptopyridines, as 2-mercaptopyridine 17a and 3-hydroxy-2-mercaptopyridine 17b obviously are aminated at the mercapto group. Via a cyclohexylidenthioimide rearrangement (details of the mechanism see [5]) and hydrolysis the cyclohexylthiopyridines 18a and 18b are formed. In DMSO- $d_6$  they show different  $^{13}\text{C}$  NMR spectra of the cyclohexyl part indicating different tautomeric forms.



Scheme 6

In a curious reaction sequence 2-mercaptopyridine methyl ester 17 (R = COOMe) and dicyclohexylamine give 2-methylmercaptopyridine dicyclohexylamide 19. By the action of the oxaziridine 1 the compound 19 is converted to 2-methylsulfoxynicotinic acid amide 20 (cleavage of the amide group by ammonia from the decomposition of 1 and oxidation of the thioether group). The structures 19 and 20 are in accordance with spectral and microanalytical data. Thus, the NMR signals of the methyl group ( $^1\text{H}/^{13}\text{C}$  ppm in DMSO- $d_6$ ) are typical for methyl thioethers (19: 2.33/13.6) and sulfoxides (20: 3.15/37.5), resp. Probably, in analogy to the formation of 14 the sulfur is aminated and the sulfenamide group displaces the dicyclohexylamine, followed by a hydrolytic ring cleavage of the resulting (unstable) methylsulfenium intermediate. Thus, the oxygen is not transferred directly by the oxaziridine 1.



Scheme 7

Unfortunately, all attempts of a selective oxidation of the sulfenamides and sulfenylureas described above gave no results of preparative value. Either unchanged starting material, the corresponding disulfides or desulfurization products (2-pyridones) were the only identified compounds.

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## Experimental

Analytical instruments used see ref. [5]. All new compounds gave elemental analyses in accordance with the calculated values.

### 2-Aminothioquinazoline-4-ones 6 and 4-Aminothiouraciles 9; general procedure 1 (details and analytical data see tables 2–5):

2.0 mmol of the 2-mercaptoquinazoline-4-one (6, SH instead of SNH<sub>2</sub>) or the 4-mercaptouracile (9, SH instead of SNH<sub>2</sub>), dissolved in a minimum amount of DMF, are added without cooling to a stirred solution of the oxaziridine 1 in toluene [1]. After few seconds the yellow colour of the starting material disappears, and the title compounds begin to crystallize from the reaction mixture (9) or the reaction mixture is evaporated *in vacuo* and the remainder is crystallized by scratching or addition of heptane or ether (6).

For a quantitative determination, 0.5 mmol of the sulfenamide is dissolved in glacial acetic acid and treated with an excess of aqueous potassium iodide solution. The iodine liberated is titrated with thiosulfate solution. 100% purity requires 5.00 ml of 0.2N thiosulfate solution. Recrystallized samples of the sulfenamides 6 and 9 show a purity of 96–101%. After titration the starting mercapto compound can be recovered by filtration. The iodometric titration does not give reproducible results with allylic derivatives as 6a.

### Preparation of sulfenyl ureas (7, 10, 12 and 16); general procedure 2 (details and analytical data see tables 2–5)

5 mmol of the sulfenamide, 5 ml dried dioxane (7, 10) or toluene (12) and 5.1 mmol of the corresponding isocyanate are refluxed for 15 min (12) or one hour (7, 10). The solvent is evaporated *in vacuo*. The remainder is collected or brought to crystallization by scratching with ether and recrystallized.

### 3-Allyl-2-benzoylaminothio-4-oxoquinazoline 8a (analytical data see tables 2–3)

0.3 g (2.1 mmol) benzoylchloride are added to a stirred and ice cooled solution of 0.47 g (2 mmol) 6a in 5 ml dry pyridine. After one hour at 0 °C and two hours at 20 °C the reaction mixture is shaken with cold water and chloroform. The chloroform layer is washed with water, dried and evaporated. The remaining oil crystallizes on scratching with ethanol; 0.35 g 8a (52%), *m.p.* 168 °C (EtOH); C<sub>18</sub>H<sub>15</sub>N<sub>3</sub>OS (337.39).

### 2-Aminothio-3-methoxycarbonylpyridine 11a

7.3 g (43 mmol) 2-mercaptopyridine methyl ester 17 (R = COOMe) in a small amount of DMF and a solution of 64 mmol 1 in toluene are stirred. The temperature raises to 30 °C

**Table 2** 4-Oxoquinazolines **6**, **7** and **8** (general procedures 1 and 2) and their mass spectra

Compd.	formula	mol. wt.	yield (%)	<i>m.p.</i> (°C)/solvent	MS [ <i>m/e</i> (relative intensity)]
<b>6a</b>	C <sub>11</sub> H <sub>11</sub> N <sub>3</sub> OS	233.30	68	92/heptane 122/AcOEt <sup>a)</sup>	233 (26); 162 (100), 203 (63), 204 (52), 145 (32), 90 (32)
<b>6b</b>	C <sub>12</sub> H <sub>15</sub> N <sub>3</sub> OS	249.33	97	62–64/hexane	249 (40); 233 (100), 145 (55), 162 (41), 179 (35), 90 (27)
<b>6c</b>	C <sub>14</sub> H <sub>11</sub> N <sub>3</sub> OS	269.32	71	168/EtOH	269 (100); 77 (97), 236 (86), 221 (83), 90 (48), 48 (35)
<b>6d</b>	C <sub>16</sub> H <sub>15</sub> N <sub>3</sub> OS	297.39	70	214–215/EtOH	297 (29); 120 (100), 77 (30), 90 (24), 48 (20), 119 (17)
<b>7a</b>	C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> OS	352.41	78	183–184/ <i>i</i> PrOH	352 (5); 93 (100), 192 (92), 203 (87), 217 (51), 119 (55)
<b>7c</b>	C <sub>21</sub> H <sub>16</sub> N <sub>3</sub> OS	388.44	60	223–235/MeCN	388 (2); 296 (100), 253 (94), 312 (51), 221 (50), 77 (44)
<b>8a</b>	C <sub>18</sub> H <sub>15</sub> N <sub>3</sub> OS	337.39	52	168/ <i>i</i> PrOH	337 (0.3); 105 (100), 51 (87), 52 (73), 77 (69), 201(61)

<sup>a)</sup> polymorphism.

**Table 3** <sup>13</sup>C (first line) and <sup>1</sup>H (second line) NMR spectra of the compounds **6**, **7** and **8**

Compd.	C2	C4	C4a	C5	C6	C7	C8	C8a	R
<b>6a</b>	163.1 –	160.2 –	118.5 –	126.5 8.10m	134.6 7.82m	125.5 7.45m	125.8 7.60m	147.1 –	44.2/131.3/117.5 <sup>a)</sup> 4.55m/5.90m/5.15m; SNH <sub>2</sub> 4.32s
<b>6b</b>	162.9 –	160.4 –	118.6 –	126.4 8.06m	134.5 7.81m	125.5 7.44m	125.7 7.64m	147.0 –	42.2/29.7/19.5/13.4 <sup>b)</sup> 3.87t/1.1–1.9m, 4H/ 0.93t <sup>b)</sup> ; SNH <sub>2</sub> 4.06s
<b>6c</b>	163.5 –	160.5 –	119.3 –	126.6 8.11m	134.2 7.85m	125.6 7.49m	125.9 7.65m	147.4 –	134.8/129.4/129.1/ 130.0 <sup>c)</sup> ; 7.4–7.9m, 2H/7.57m, 3H; SNH <sub>2</sub> 4.12s
<b>6d</b>	163.6 –	159.6 –	118.9 –	126.8 8.14m	135.2 7.88m	125.8 7.38m	126.0 7.69m	147.7 –	136.2/136.2/128.7/ 130.1 <sup>c)</sup> ; CH <sub>3</sub> 17.0 7.28d, 2H/7.50t, 1H; CH <sub>3</sub> 2.04s; SNH <sub>2</sub> 4.20s
<b>7a</b>	157.9	160.2	117.9	126.5	134.8	126.0	126.0	146.8	44.6/131.1/118.1 <sup>a)</sup> ; 154.5/139.2/118.8/ 128.7/122.5 <sup>d)</sup>
<b>7c</b>	158.2	160.5	118.8	126.6	134.9	126.1	126.1	147.2	R:133.8/129.3/129.6/ 130.4 <sup>c)</sup> ; 154.4/139.2/118.7/ 128.7/122.4 <sup>d)</sup>
<b>8a</b>	156.5 –	160.7 –	118.7 –	126.5 7.4m	134.8	126.1	126.1	146.7 –	44.8/131.1/117.9 <sup>a)</sup> ; 168.8/133.5/128.1/ 128.5/132.2 <sup>d)</sup> 4.69d/5.8–6.2m/5.1– 5.4m <sup>a)</sup> ; 7.2–7.9m, 5H; NH 10.2s

<sup>a)</sup> NCH<sub>2</sub>/CH=CH<sub>2</sub>; <sup>b)</sup> NCH<sub>2</sub>/CH<sub>2</sub>/CH<sub>2</sub>/CH<sub>3</sub>; <sup>c)</sup> C1/C2,6/C3,5/C4; <sup>d)</sup> CO/C1/C2,6/C3,5/C4.

and the yellow color of the starting material disappears. After one hour some precipitated bis-(3-methoxycarbonylpyridin-2-yl)-disulfide (1.08 g, 15%; *m.p.* 191–193 °C after recrystallisation from ethanol) is removed by suction. The filtrate is evaporated *in vacuo*. The residue is treated with ether and yields **11a**; 4.12 g (52%); *m.p.* 137–138 °C (from methanol); C<sub>7</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>S (184.22). – <sup>1</sup>H NMR: δ OMe 3.81s (3H), H4 8.11d (1H), H5 7.16t (1H), H6 8.65d (1H). – <sup>13</sup>C NMR: δ C2 168.8, C3 120.0, C4 138.4, C5 118.8, C6 152.5, CO 165.0,

OMe 52.3. – MS (70 eV): 184 (M<sup>+</sup>, 70 %), 78 (53 %), 153 (36 %), 48 (28 %), 50 (25 %), 47 (23 %).

#### 2-Aminothio-6-methoxy-3-nitropyridine **11b**

1.56 g (8.4 mmol) 2-mercapto-6-methoxy-3-nitropyridine (*m.p.* 74–75 °C) and a solution of 13 mmol **1** in toluene are stirred. After few seconds the starting material dissolves and **11b** precipitates; 1.0 g, 59%; *m.p.* 192 °C (EtOH); C<sub>6</sub>H<sub>7</sub>N<sub>3</sub>O<sub>3</sub>S (202.21). – <sup>1</sup>H NMR: δ OMe 3.34s (3H), H4 8.11 AB (*J* = 8.8

**Table 4** 4-Aminothiouraciles **9** and 4-phenylaminocarbonylaminothiouraciles **10** (general procedures 1 and 2) and their mass spectra

Compd.	formula	mol. wt.	yield (%)	<i>m.p.</i> (°C)/solvent	mass spectra ( <i>m/e</i> [relative intensity])
<b>9a</b>	C <sub>4</sub> H <sub>5</sub> N <sub>3</sub> OS	143.17	98	160/EtOH	143 (7); 58 (100), 45 (66), 128 (60), 57 (56), 52 (42)
<b>9b</b>	C <sub>5</sub> H <sub>7</sub> N <sub>3</sub> OS	157.20	87	196–197/EtOH	157 (100); 140 (76), 141 (60), 54 (57), 81 (56), 82 (35)
<b>9c</b>	C <sub>6</sub> H <sub>9</sub> N <sub>3</sub> OS	171.23	95	191/EtOH	171(45); 153 (100), 155 (48), 154 (34), 86 (15), 127 (13)
<b>9d</b>	C <sub>7</sub> H <sub>11</sub> N <sub>3</sub> OS	185.26	93	181/EtOH	185 (45); 153 (100), 169 (70), 185 (45), 167 (31), 113 (29)
<b>9e</b>	C <sub>7</sub> H <sub>11</sub> N <sub>3</sub> OS	185.26	82	193–194/EtOH	185 (43); 153 (100), 167 (82), 169 (43), 168 (23), 170 (20)
<b>9f</b>	C <sub>8</sub> H <sub>13</sub> N <sub>3</sub> OS	199.28	71	172/EtOH	53 (100); 183 (43), 113 (31), 199 (24), 81 (24), 86 (19)
<b>9g</b>	C <sub>9</sub> H <sub>15</sub> N <sub>3</sub> OS	213.31	93	167–168/EtOH	213 (47); 153 (100), 197 (52), 113 (29), 141 (23), 165 (21)
<b>9h</b>	C <sub>10</sub> H <sub>17</sub> N <sub>3</sub> OS	227.34	86	172/EtOH	227 (28); 153 (100), 211 (45), 113 (36), 179 (35), 141 (26)
<b>9i</b>	C <sub>12</sub> H <sub>21</sub> N <sub>3</sub> OS	255.39	81	182/EtOH	55 (18); 153 (100), 207 (99), 239 (50), 81 (46), 141 (41)
<b>10b</b>	C <sub>12</sub> H <sub>12</sub> N <sub>4</sub> O <sub>2</sub> S	276.33	56	198/DMSO/H <sub>2</sub> O	276 (0.2); 93 (100), 119 (43), 142 (32), 91 (30), 222 (7)
<b>10c</b>	C <sub>13</sub> H <sub>14</sub> N <sub>4</sub> O <sub>2</sub> S	290.35	66	190–192/DMF/EtOH/H <sub>2</sub> O	290 (0.4); 93 (100), 119 (77), 64 (56), 155 (48), 91 (47)

**Table 5** <sup>13</sup>C- (first line) and <sup>1</sup>H- (second line) NMR spectra of the compounds **9** and **10**

Comp.	C2	C4 (SNH <sub>2</sub> )	C5	C6 (H6)	R
<b>9a</b>	149.8 –	190.3 4.27s	111.3 6.57 <sup>a</sup> )	140.5 7.74 <sup>a</sup> )	–
<b>9b</b>	155.0 –	182.8 3.7br.s	116.1 –	139.9 7.36s	12.3 1.85s
<b>9c</b>	155 <sup>b</sup> ) –	182 <sup>b</sup> ) 3.44	117.5 –	146.6 7.37s	18.4/11.8 2.20q, 1.04t
<b>9d</b>	154.2 –	182.6 3.8br.s	111.5 –	140.2 7.41s	28.0/21.4/13.3 2.18t/1.45sext/0.84t
<b>9e</b>	154.0 –	182.0 3.8br.s	118.2 –	138.1 7.43s	25.2/22.1 2.59sept/1.09d
<b>9f</b>	154.2 –	182.6 3.80s	111.7 –	140.1 7.39s	30.5/25.7/21.6/13.5 2.23t/1.1–1.6m, 4H, 0.90t
<b>9g</b>	154 <sup>b</sup> ) –	182 <sup>b</sup> ) 3.8br.s	112 <sup>b</sup> ) –	140.2 7.33s	30.7/26.0/25.7/20.8/13.8 2.20t/1.3br.m, 6H/0.86t
<b>9h</b>	154.2 –	182.6 3.8br.s	111.7 –	140.2 7.32s	30.8/28.3/28.1/26.0/21.9/13.8 2.19t/1.3br.m, 8H/0.85t
<b>10b</b>	154.1* –	178.1 7.9/9.1	107.0 –	141.7 7.43s	11.5; 154.4*/139.3/118.4/128.7/122.3 <sup>c</sup> ) 1.94s; 7.1–7.6m
<b>10c</b>	154.1* –	177.8 7.9/9.1	113.2 –	140.8 7.39s	19.2/13.0; 154.4*/139.3/118.4/128.6/122.2 <sup>c</sup> ) 2.28q/1.09t; 6.9–7.5br.m
<b>10f</b>	153.9* –	177.8 7.8/9.0	111.8 –	141.4 7.44s	30.6/25.7/21.6/13.5; 154.3*/139.3/118.3/128.7/122.2 <sup>c</sup> ) 2.30t/1.4br.m, /0.90t
<b>10g</b>	153.9* –	177.7 7.8/9.1	111.8 –	141.4 7.43s	30.7/28.1/25.9/21.7/13.8; 154.3*/139.2/118.3/128.7/122.2 <sup>c</sup> ) 2.28t/1.2–1.6m, 6H/0.86t;

\* assignments not clear; <sup>a</sup>) AB-system, *J*<sub>AB</sub> = 7 Hz; <sup>b</sup>) very low solubility/intensity; <sup>c</sup>) CO/NHPh C1/C2,6/C3,5/C4.

H<sub>z</sub>, 2H) H<sub>5</sub> 6.73, NH<sub>2</sub> 4.1br.s (2H). – <sup>13</sup>C NMR: δ C2 167.6, C3 133.9, C4 136.9, C5 106.8, C6 165.1, OMe 55.0. – MS (70 eV, *m/e*): 201 (M, 56%), 108 (100%), 137 (90%), 80 (83%), 64 (65%), 96 (45%), 48 (50%), 136 (36%).

#### 2-Aminothiopyridine-1-oxide **11c**

0.77 g (6.1 mmol) 2-mercapto-pyridine-1-oxide (precipitated freshly from an aqueous solution of the sodium salt by 2N

sulfuric acid) and a solution of 19 mmol **1** in toluene are stirred over night. Precipitated **11c** is separated by suction and washed with ether; 0.78 g, 90%; *m.p.* 163 °C (DMF/toluene); C<sub>5</sub>H<sub>6</sub>N<sub>2</sub>OS (142.19). – <sup>1</sup>H NMR: δ H<sub>3</sub> 7.52dd, H<sub>4</sub> 7.42dt, H<sub>5</sub> 7.14dt, H<sub>6</sub> 8.19dd; NH<sub>2</sub> 4.00s (2H). – <sup>13</sup>C NMR: δ C2 157.9, C3 125.4, C4 120.5, C5 120.1, C6 137.8. – MS (70 eV, *m/e*): 142 (M<sup>+</sup>, 50%), 78 (100%), 125 (50%), 79 (53%), 51 (30%), 98 (24%), 69 (18%).

**3-Methoxycarbonyl-2-phenylaminocarbonylaminothiopyridine 12a**

As described in the general procedure 2, 4.3 g (23.4 mmol) **11a** and 2.54 ml (23.4 mmol) phenylisocyanate give **12a**; 6.2 g (87%); *m.p.* 210–212 °C (DMF/toluene); C<sub>14</sub>H<sub>13</sub>N<sub>3</sub>O<sub>3</sub>S (303.33). – <sup>1</sup>H NMR: δ OMe 3.86s (3H), H4 8.20d (1H), H5 7.2 (superposed by Ph), H6 8.61d (1H); Ph 6.8–7.6 m (6H including H5). – <sup>13</sup>C NMR: δ NHPH C1 139.6, C2/6 128.6, C3/5 118.3, C4 121.9; CONH 155.3; MeO 52.5, COOMe 164.2; C2 165.2, C3 120.4, C4 138.6, C5 119.9, C6 152.8. – MS (70 eV, *m/e*): 303 (M<sup>+</sup>, 9%), 152 (45%), 211 (43%), 93 (39%).

**2-(4-Chlorphenylaminocarbonylaminothio)-6-methoxy-2-nitropyridine 12b**

As described in the general procedure 2, 0.2 g (1 mmol) **11b** and 0.15 g (1 mmol) 4-chlor-phenylisocyanate give **12b**; 0.3 g (85%); *m.p.* 245–255 °C (DMF/toluene); C<sub>13</sub>H<sub>11</sub>N<sub>4</sub>ClO<sub>4</sub>S (354.78). – <sup>1</sup>H NMR: δ OMe 3.36s (3H), H4 8.13 AB (*J* = 8.8 Hz, 2H) H5 6.77, 4-Cl-C<sub>6</sub>H<sub>4</sub> 7.30/7.47 (AB system, 4H). – <sup>13</sup>C NMR: δ C2/C6 165.3/162.1, C3 134.4, C4 137.2 C5 108.2; MeO 54.7; CO 155.6; 4-Cl-C<sub>6</sub>H<sub>4</sub> C1 138.6, C2/C6 120.4, C3/C5 128.8, C4 126.2. – MS (70 eV, *m/e*): 354/356 (M<sup>+</sup>, 22%/8 %), 137 (100%), 99 (80%), 127 (74%), 126 (54%), 64 (52%), 111 (47%), 185 (39%), 96 (39%), 108 (36%).

**2-(4-Chlorphenylaminocarbonylaminothio)pyridine-1-oxide 12c**

0.28 g (2 mmol) **11c** and 0.3 g (2 mmol) 4-chlor-phenylisocyanate give **12c**; 0.55 g (93%); *m.p.* 213 °C (DMF/toluene); C<sub>12</sub>H<sub>10</sub>N<sub>3</sub>ClO<sub>2</sub>S (295.75). – <sup>1</sup>H NMR: δ H3 7.48m (1H), H4/H5 7.18–7.35m (2H), H6 8.31dd (1H); 4-Cl-C<sub>6</sub>H<sub>4</sub> 7.32/7.50 (AB system, 4H), NH 9.31s/8.04s. – <sup>13</sup>C NMR: δ C2 153.5, C3 126.5, C4 121.7, C5 119.8, C6 138.0; CO 154.9; 4-Cl-C<sub>6</sub>H<sub>4</sub> C1 138.5, C2/C6 120.5, C3/C5 128.7, C4 126.2. – MS (70 eV, *m/e*): 295 (M<sup>+</sup>, 0.5%), 127 (100%), 90 (60%), 78 (45%), 153 (40%), 125 (25%), 154 (15%).

**3-Oxo-1,2-thiazolo[4,5-*b*]pyridine (14)**

1.82 g (10 mmol) 2-dimethyl-aminocarbonyl-2-mercapto-pyridine **13**, 15 mmol **1** in toluene, 25 g ice and 5 ml 2N NaOH are shaken in separatory funnel for 20 min. The aqueous phase is acidified with concentrated hydrochloric acid, the precipitated product is washed with water.; 1.00 g (66%) **14**, *m.p.* 246–246.5 °C (DMF/EtOH 1:1); C<sub>6</sub>H<sub>4</sub>N<sub>2</sub>OS (152.18). – <sup>1</sup>H NMR: δ Py H4 8.32m, H5 7.51m, H6 8.82m; NH 11.9br.s. – <sup>13</sup>C NMR: δ Py C2 162.9, C3 118.4, C4 133.0, C5 120.2, C6 152.4; CO 167.7. – MS (70 eV, *m/e*): 152 (M<sup>+</sup>, 100%), 97 (40%), 78 (37%), 77 (22%), 70 (22%), 124 (13%).

**Sodium salt of 2-aminothionicotinic acid tetrahydrate (15)**

A crystalline precipitate from the alkaline reaction mixture of the preparation of **14** is isolated and recrystallized from EtOH; 0.9 g (34%) **15**, *m.p.* > 360 °C. The acidified aqueous phase yields 0.4 g (26%) **14**. Warming of crude **15** with acetic acid for 1 min. gives **14** (68% yield); C<sub>6</sub>H<sub>13</sub>N<sub>2</sub>NaO<sub>6</sub>S (263.24). – <sup>1</sup>H NMR: δ Py H4 8.08m, H5 7.19m, H6 8.51m. – <sup>13</sup>C NMR: δ Py C2 171.0\*, C3 123.2, C4 132.5, C5 117.7, C6 149.1;

CO 171.6\*. – MS (70 eV, *m/e*): 152 (100%), 64 (75%), 48 (75%), 46 (60%), 51 (50%), 47 (50%), 76 (35%), 78 (30%), 70 (30%).

**3-Oxo-2-phenylaminocarbonyl-1,2-thiazolo[4,5-*b*]pyridine (16)**

350 mg (2.29 mmol) **14**, 5 ml toluene and 320 mg (2.7 mmol) phenylisocyanate are refluxed for one hour. After cooling the separated crystals are collected; 550 mg (89%) **16**, *m.p.* 165–167 °C (EtOH); C<sub>13</sub>H<sub>9</sub>N<sub>3</sub>O<sub>2</sub>S (271.31). – <sup>1</sup>H NMR: δ Py H4 7.84m, H5 7.61m, H6 8.97m; NH 10.8br.s.; Ph H2/H6 7.59m (2H), H3/H5 7.41m (2H), H4 7.19m (1H). – <sup>13</sup>C NMR: δ Py C2 161.4, C3 118.4, C4 136.0, C5 124.9, C6 152.7, CO 163.7; CONHPh CO 156.2, Ph C1 136.7, C2/C6 120.3, C3/C5 129.3, C4 122.0. – MS (70 eV, *m/e*): 271 (M<sup>+</sup>, 6%), 152 (100%), 119 (40%), 91 (20%), 64 (14%), 98 (10%), 78 (10%).

**3-Benzylaminocarbonyl-2-(2-oxocyclohexylthio)pyridine (18a)**

0.57 g (2.34 mmol) **17a** and 3.5 mmol **1** in toluene (see general procedure 1) give after scratching with petroleum ether 0.65 g (82%) **18a**, *m.p.* 120–122 °C, after recrystallization from EtOH 139–140 °C; C<sub>19</sub>H<sub>20</sub>N<sub>2</sub>O<sub>2</sub>S (340.44). – <sup>1</sup>H NMR: δ Py H4 7.84m, H5 7.19m, H6 8.46m; NH 9.08t; CH<sub>2</sub> 4.45d (2H) Ph 7.2–7.4m (5H); cyclohex SCH 4.72m, H3–H6 1.2–2.4m (8H). – <sup>13</sup>C NMR: δ Py C2 156.1, C3 118.9, C4 135.3, C5 126.7, C6 149.7, CONH 166.0; CH<sub>2</sub>Ph CH<sub>2</sub> 42.5, Ph C1 139.0, C2/C6 128.2, C3/C5 129.2, C4 129.6; cyclohex C1 52.4, C2 205.9, C3 41.2, C4 26.8, C5 24.5, C6 33.9. – MS (70 eV, *m/e*): 340 (M<sup>+</sup>, 18%), 323 (100%), 91 (32%), 324 (23%), 106 (18%), 197(14%), 213 (13%).

**3-Hydroxy-2-(2-hydroxycyclohexenylthio)-pyridine (18b)**

0.63 g (5 mmol) **17b**, 15 g of crushed ice, 2.5 ml (5 mmol) 2N NaOH and 7.5 mmol **1** in toluene (see general procedure 1) are shaken for 10 min. The aqueous layer is separated, acidified with concentrated HCl, evaporated and dried under reduced pressure. The residue is extracted with ethanol, filtered from NaCl and treated with ether giving 0.7 g (63%) **18b**, *m.p.* 190–195 °C (from toluene/DMF); C<sub>11</sub>H<sub>13</sub>N<sub>2</sub>O<sub>2</sub>S (223.30). – <sup>1</sup>H NMR: δ Py H4 7.92m, H5 7.72m, H6 8.49m; OH 12.9; CH<sub>2</sub> 2.03m (4 H)/1.59m (4 H). – <sup>13</sup>C NMR: δ Py C2 152.3, C3 153.2, C4 104.0, C5 129.0, C6 143.3; cyclohex C1 50.7, C2 153.2, C3 38.8, C4 20.6, C5 19.7, C6 23.5. – MS (70 eV, *m/e*): 223 (M<sup>+</sup>, 30%), 206 (60%), 162 (30%), 128 (30%), 127 (100%), 96 (65%), 83 (40%), 55 (30%).

**3-Dicyclohexylaminocarbonyl-2-methylthio-pyridine (19)**

0.85 g (5 mmol) 2-mercaptocotinic acid methylester **17** (R = COOMe) and 1.08 g (6 mmol) dicyclohexylamine are heated at 150 °C for 10 min. The TLC indicates complete conversion. The product is washed with ether leaving 1.45 g (87%) **19**, *m.p.* 168–170 °C (from *n*-heptane); C<sub>19</sub>H<sub>28</sub>N<sub>2</sub>O<sub>2</sub>S (332.52). – <sup>1</sup>H NMR: δ Py H4 8.05m, H5 7.10m, H6 8.44m; CH<sub>2</sub> 1.0–2.1m (20 H), CH 3.08t (2 H); SCH<sub>3</sub> 2.33s (3 H). – <sup>13</sup>C NMR: δ Py C2 159.5, C3 132.0, C4 137.0, C5 117.9, C6 148.5; CO 167.9; SCH<sub>3</sub> 13.6; cyclohex C1 51.8, C2/C6 29.0/24.1, C3/C5 24.1/24.1, C4 24.9. – MS (70 eV, *m/e*): 133 (100%), 106 (14%), 78 (78%), 77 (68 %).

**3-Aminocarbonyl-2-methylsulfinyl-pyridine (20)**

1.45 g (4.36 mmol) **19** in 4 ml DMF and 7 mmol **1** in toluene (see general procedure 1) give after stirring overnight 0.5 g (62%) **20**, *m.p.* 164–165 °C (from EtOH); C<sub>7</sub>H<sub>8</sub>N<sub>2</sub>O<sub>2</sub>S (184.22). – <sup>1</sup>H NMR: δ Py H4 8.34m, H5 7.76m, H6 8.74m; NH<sub>2</sub> 5.61s; CH<sub>3</sub> 3.15s. – <sup>13</sup>C NMR: δ Py C2 152.4, C3 132.8, C4 140.3, C5 127.8, C6 151.5, CO 166.3; CH<sub>3</sub> 37.5. – MS (70 eV, *m/e*): 184 (M<sup>+</sup>, 10%), 183 (20%), 169 (100%), 152 (65%), 151 (75%), 138 (85%), 136 (30%), 124 (75%), 123 (50%), 122 (45%), 79 (85%).

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