Iminium Carbonic Acid Derivative Salts. X [1]. Synthesis of *N,S*-Containing Heterobicycles from *N*-Protected 2-Methylthio-1,3-thiazinium and 2-Methylthiothiazolium Salts. Part 2. Reaction of *N*-Protected 2-Methylthio-1,3-thiazinium and 2-Methylthiothiazolium Salts with vinylogous CH-Acidic Compounds

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Dedicated to Professor Dr. W. Fleischhacker, Wien on the occasion of his 65th birthday.

N-Boc-protected 2-methylthio-1,3-thiazinium **3** and 2-methylthiothiazolium salts **4,7** obtained from the corresponding 1,3-thiazine-2-thiones and thiazolidine-2-thiones by the action of methyl iodide or trimethyloxonium tetrafluoroborate were reacted with vinylogous CH-acidic compounds forming ketene *N,S*-acetals **5,6,8,9**. The protection group was removed with trifluoroacetic acid whereupon the desired cyclisation to pyrido[2,1-*b*]-1,3-thiazines **10** and thiazolo[3,2-*b*]pyridines **11,12** took place.

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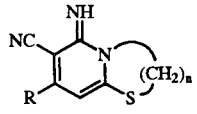
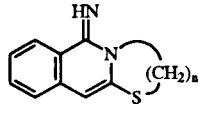
In the preceeding paper [1] we described the transformation of *N*-Boc-protected 1,3-thiazine-2-thiones and thiazolidine-2-thiones into the corresponding 2-methylthio-1,3-thiazinium and 2-methylthiothiazolium salts by methyl iodide or trimethyloxonium tetrafluoroborate. This activated species were reacted with simple CH-acidic compounds forming ketene *N,S*-acetals. Deprotection of the ring nitrogen was successful with trifluoroacetic acid yielding the *N*-unsubstituted ketene *N,S*-acetals. With this sequence of reactions we had established the necessary methology for our ultimate goal, the synthesis of heterobicyclic systems described with general formulas **1** and **2**.

Scheme 1



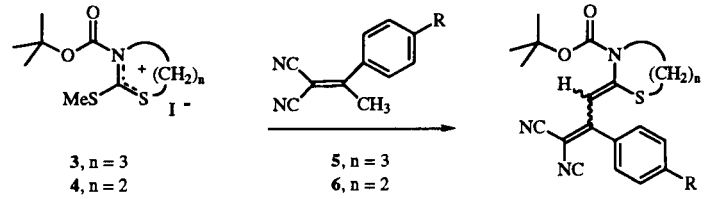
1



2 n = 2,3

Our special interest in this class of compounds is due to the variety of interesting pharmacological activities reported for structural similar thiazolo[3,2-*a*]pyrimidines [2] as well as thiazolopyrimidinium- and pyrimidinothiazinium salts [3]. So we followed our established scheme and reacted the activated intermediates, the 2-methylthiol1,3-thiazinium **3** and 2-methylthiothiazolium iodides **4**, with a number of vinylogous CH-acidic compounds, obtaining the vinyl substituted ketene *N,S*-acetals **5,6**. The nmr-spectra revealed that these acetals were formed as an inseparable mixture of cis/trans isomers where the ratio of the two isomers were strongly dependent on the substitution pattern of the CH-acidic compounds. When 5-methyl-2-methylthiothiazolium salts **7** were employed as activated species an additional type of isomerism occurred. The condensation products were obtained as a chromatographically separable mixture of the tautomeric exo methylene **8** and exo methyl ketene *N,S*-acetals **9**, the latter in some cases in such small amounts that complete analytic characterization was impossible.

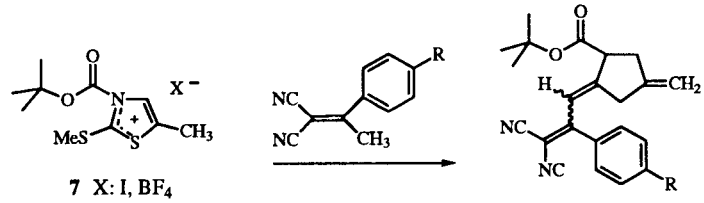
Scheme 2



3, n = 3
4, n = 2

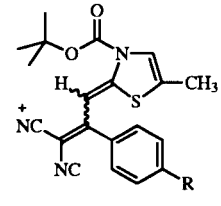
5, n = 3
6, n = 2

5	n	R	**6**	n	R
a,	3	H	**a**,	2	H
b,	3	CH_3	**b**,	2	CH_3
c,	3	Br	**c**,	2	OCH_3
d,	3	Cl	**d**,	2	Cl
e,	3	NO_2			



7 X: I, BF_4

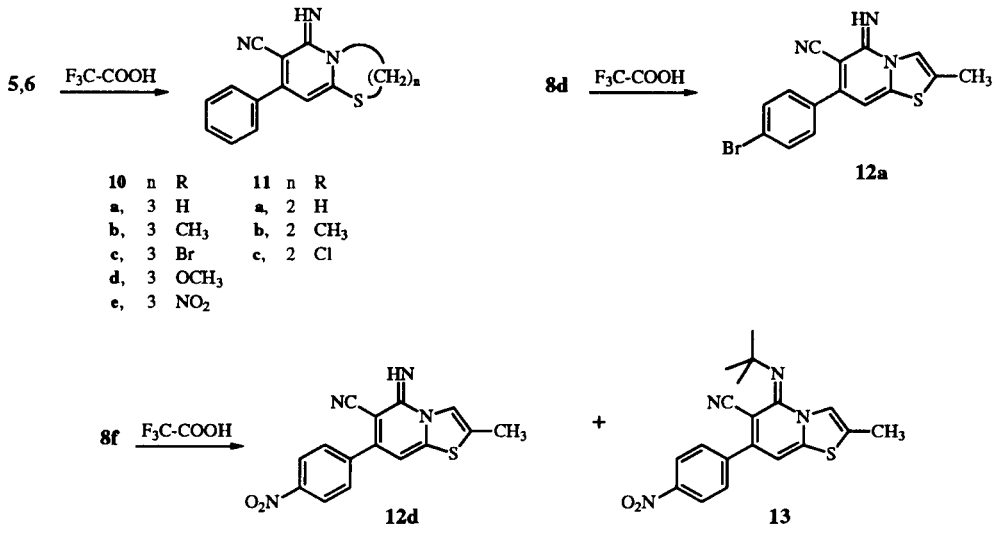
8



9

run	X	R	yield of **8**	yield of **9**
a,	I	H	20%	6%
b,	I	CH_3	18%	4%
c,	BF_4	OCH_3	62%	8%
d,	I	Br	22%	0.23%
e,	BF_4	Cl	84%	0%
f,	BF_4	NO_2	50%	0%

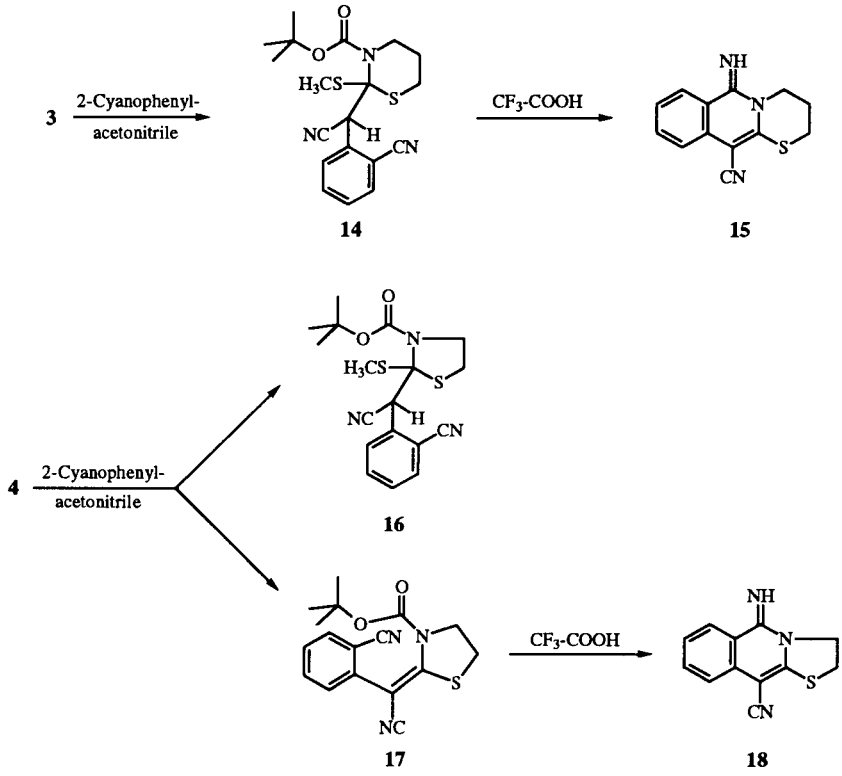
Scheme 3



The removal of the BOC-protection group with trifluoroacetic acid in dichloromethane did not yield the expected *N*-unsubstituted ketene *N,S*-acetals but the ultimately desired cyclisation products **10-12**. This heterobicycles were formed by the proton catalysed intramolecular addition of the intermediately formed NH-group of the thiazine respectively thiazolidine ring to one of the nitrile functions. From the deprotection of **8d** resulted the cyclisation product **12a**, from **8f** the cyclisation product **12b** and compound **13** as a reaction product of **12b** with isobutylen, the fragmentation product of the Boc protection group.

When phenylogous compounds are brought to reaction with the thiazinium salts **3** or the thiazolium salts **4**, for example 2-cyanophenylacetonitrile, the isolation of addition products **14** and **16** is possible. These compounds show the rare structure of dithioorthocarboxylic acid diester amides.

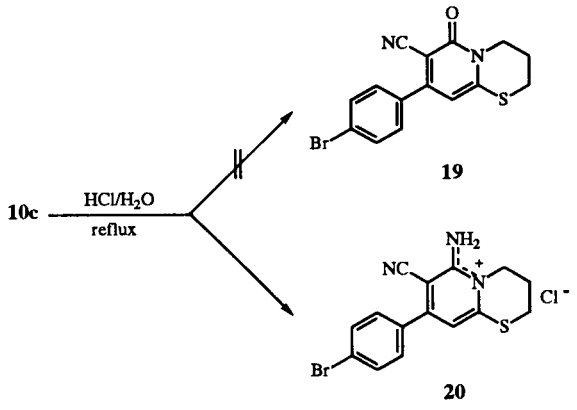
Scheme 4



The treatment of **14** with trifluoroacetic acid results in the formation of the thiazino[3,2-*b*]isoquinoline **15**. The corresponding thiazolo[3,2-*b*]isoquinoline **18** resulted from **17** after treatment with trifluoroacetic acid. Both **16** and **17** are reaction products of **4** with 2-cyanophenylacetonitrile depending upon the reaction conditions.

Attempts to hydrolyse the imino group of **10c** to an oxo group by prolonged reflux with hydrochloric acid **10c** did not form the desired hydrolysis product **19** but only the hydrochloride **20**.

Scheme 5



With our new method of synthezising our target structures we have established a convenient route to make a number of compounds available for pharmacological testing.

EXPERIMENTAL

Instrumental equipment and chromatographic conditions were those in reference [1].

General Procedure for the Condensation of the 2-Methylthiothiazinium and -thiazolium Salts **3**,**4**,**7** with CH-acidic Compounds.

To a solution of equimolar quantities of the 2-methylthiothiazinium and -thiazolium salts **3**,**4**,**7** [1] and the CH-acidic compound in 30 ml of dry dichloromethane were added 2 equivalents of triethylamine and 1.5 equivalents of lead(II) nitrate with protection from moisture. The mixture was refluxed for the time indicated below. After cooling to room temperature the solids were filtered off and the filtrate evaporated *in vacuo*. The residue was treated as described below.

tert-Butyl 2-(3,3-Dicyano-2-phenylallylidene)-perhydro-1,3-thiazine-3-carboxylate **5a**.

This compound was obtained refluxing for 2 hours and chromatographic purification as yellow crystals, 1.2 g (63%), mp 131-132°; ir (potassium bromide): ν 2210, 1700, 1570 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.53-7.43 (m, 5 H*), 7.39-7.37 (m, 5H), 6.83 (s, 1H*), 6.61 (s, 1H) 3.72 (t, 2H), 2.77 (t, 2H), 2.53 (t, 2H), 2.08-2.01 (m, 2H*, 2H), 1.56 (s, 9H*), 1.38 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 169.1, 169.0, 159.9, 157.6, 152.1, 150.4, 134.3, 134.3, 131.1-128.2, 117.7, 114.3, 113.8, 83.4, 82.9, 78.7, 78.5, 43.9, 43.3, 28.1, 28.1, 26.8, 26.5, 24.0, 23.2; ms: m/z 311 (29), 308 (54), 267 (100).

Anal. Calcd. for $C_{20}H_{21}N_3O_2S$ (367.40): C, 65.37; H, 5.76; N, 11.43; S, 8.73. Found: C, 65.36; H, 5.52; N, 11.58; S, 8.77.

tert-Butyl 2-(3,3-Dicyano-2-*p*-tolylallylidene)-perhydro-1,3-thiazine-3-carboxylate **5b**.

This compound was obtained as described above. Yellow crystals recrystallized from ethanol, 1.1 g (37%), mp 134°; ir (potassium bromide): ν 2220, 1700, 1610, 1570 cm^{-1}; ^{1}H-nmr (deuteriochlorofom): δ 7.30-7.27 (m, 4H*, 4H), 6.80 (s, 1H*), 6.57 (s, 1H), 3.72 (t, 2H), 2.79-2.77 (m, 2H), 2.55 (t, 2H), 2.42 (s, 3H*), 2.37 (s, 3H), 2.08-1.71 (m, 2H*, 2H), 1.56 (s, 9H*), 1.39 (s, 9H); ms: m/z 381 (1, M^+), 325 (17), 322 (36), 281 (100).

Anal. Calcd. for $C_{21}H_{23}N_3O_2S$ (381.50): C, 66.12; H, 6.08; N, 11.01; S, 8.40. Found: C, 66.01; H, 5.93; N, 11.05; S, 8.51.

tert-Butyl 2-[2-(4-Bromophenyl)-3,3-dicyanoallylidene)-perhydro-1,3-thiazine-3-carboxylate **5c**.

This compound was obtained as described above. Yellow crystals recrystallized from ethanol, 1.0 g (57%), mp 147-148°; ir (potassium bromide): ν 2220, 1710, 1580, 1560 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.63-7.61 (m, 2H*), 7.54-7.52 (m, 2H), 7.28-7.23 (m, 2H*, 2H), 6.82 (s, 1H*), 6.58 (s, 1H), 3.74 (t, 2H*, 2H), 2.78 (t, 2H), 2.58 (t, 2H*), 2.08-1.71 (m, 2H*, 2H), 1.56, (s, 9H*), 1.38 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 167.7, 167.5, 160.3, 158.1, 152.0, 150.4, 133.2, 132.6-130.1, 125.8, 125.6, 117.2, 114.2, 114.1, 83.7, 83.1, 78.9, 78.6, 44.0, 43.5, 28.1, 26.8, 26.5, 24.1, 23.2; ms: m/z 446 (0.5, M^+), 389 (27), 388 (33), 347 (97), 345 (95).

Anal. Calcd. for $C_{20}H_{20}BrN_3O_2S$ (446.37): C, 53.82; H, 4.52; N, 9.41; S, 7.18. Found C, 53.78; H, 4.54; N, 9.48; S, 7.19.

tert-Butyl 2-[2-(4-Chlorophenyl)-3,3-dicyanoallylidene]-perhydro-1,3-thiazine-3-carboxylate **5d**.

This compound was obtained as described above. Yellow crystals recrystallized from ethanol, 0.80 g (50%), mp 113°; ir: ν 2220, 1720, 1590, 1560, 1510 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.38-7.30 (m, 4H*, 4H), 6.82 (s, 1H*), 6.59 (s, 1H), 3.74 (t, 2H*, 2H) 2.80-2.77 (m, 2H), 2.59 (t, 2H*), 2.09-1.71 (m, 2H*, 2H), 1.56 (s, 9H*), 1.39 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 167.7, 167.5, 160.2, 157.9, 152.1, 150.4, 137.5, 137.3, 132.8, 130.3-128.6, 117.3, 114.2, 114.1, 83.7, 83.1, 79.0, 78.7, 44.0, 43.5, 28.1, 26.8, 26.5, 24.1, 23.2; ms: m/z 401 (1, M^+), 303 (38), 302 (25), 301 (100).

Anal. Calcd. for $C_{20}H_{20}ClN_3O_2S$ (401.92): C, 59.77; H, 5.02; N, 10.45; S, 7.98. Found: C, 59.72; H, 5.05; N, 10.67; S, 7.99.

tert-Butyl 2-(3,3-Dicyano-2-(4-nitrophenyl)allylidene]-perhydro-1,3-thiazine-3-carboxylate **5e**.

This compound was obtained as described above as a yellow powder, 1.80 g (39%), mp 142°; ir ν 2210, 1710, 1545, 1520 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 8.35-8.24 (m, 2H*, 2H), 7.58-7.55 (m, 2H*, 2H), 6.90 (s, 1H*), 6.66 (s, 1H), 3.76 (t, 2H*, 2H), 2.80 (t, 2H), 2.58 (t, 2H*), 2.11-2.05 (m, 2H*, 2H), 1.57 (s, 9H*), 1.38 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 166.2, 165.8, 161.2, 151.8, 150.3, 149.2, 148.9, 141.0, 140.9, 129.7-123.3, 116.3, 113.7, 113.5, 113.1, 113.0, 84.1, 83.5, 80.1, 79.0, 44.1, 43.5, 28.1, 26.9, 26.4, 24.1, 23.1; ms: m/z 412 (2, M^+), 356 (15), 312 (51).

Anal. Calcd. for $C_{20}H_{20}N_4O_4S$ (412.47): C, 58.24; H, 4.89; N, 13.58; S, 7.77. Found: C, 58.23; H, 4.86; N, 13.64; S, 7.61.

tert-Butyl 2-(3,3-Dicyano-2-phenylallylidene)-thiazolidine-3-carboxylate **6a**.

This compound was obtained as described above after 3 hours of heating and 12 hours at 20°. Yellow crystals recrystallized from ethanol, 1.2 g (50%), mp 171°; ir (potassium bromide): ν 2220, 1710 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.74 (s, 1H), 7.53-7.46 (m, 3H), 7.31-7.28 (m, 2H), 4.06 (t, 2H), 2.81 (t, 2H), 1.60 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 171.6, 158.9, 150.4, 134.3, 131.0, 128.9, 115.0, 114.3, 104.3, 85.2, 75.8, 52.0, 27.8, 25.2; ms: m/z 353 (0.6, M^+), 252 (100).

Anal. Calcd. for $C_{19}H_{19}N_3O_2S$ (353.45): C, 64.57; H, 5.42; N, 11.89; S, 9.07. Found: C, 64.27; H, 5.41; N, 11.91; S, 9.07.

tert-Butyl 2-(3,3-Dicyano-2-*p*-tolylallylidene)-thiazolidine-3-carboxylate **6b**.

This compound was obtained like that above after chromatographic purification as yellow crystals, 2.1 g (88%), mp 171°; ir (potassium bromide): ν 2220, 1715, 1620, 1530, 1490, cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.73 (s, 1H), 7.28-7.17 (m, 4H), 4.05 (t, 2H), 2.81 (t, 2H), 2.24 (s, 3H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 172.1, 158.9, 150.4, 141.7, 131.3, 130.0-128.8, 115.3, 114.5, 104.7, 85.0, 75.2, 52.0, 28.1, 27.7, 21.6; ms: m/z 367 (0.3, M^+), 267 (87), 266 (100).

Anal. Calcd. for $C_{20}H_{21}N_3O_2S$ (367.47): C, 65.37; H, 5.76; N, 11.43; S, 8.73. Found: C, 65.29; H, 5.69; N, 11.51; S, 8.74.

tert-Butyl 2-(3,3-Dicyano-2-*p*-methoxyphenylallylidene)-thiazolidine-3-carboxylate **6c**.

This compound was obtained by the same procedure as yellow crystals, recrystallized from ethanol, 1.8 g (72%), mp 171°; ir (potassium bromide): ν 2220, 1600, 1580, 1550, 1510 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.70 (s, 1H), 7.27-7.24 (m, 2H), 7.00-6.97 (m, 2H), 4.06 (t, 2H), 3.87 (s, 3H), 2.83 (t, 2H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 171.8, 162.3 158.4, 150.4, 130.9, 126.2, 115.4, 114.6; ms: m/z 383 (0.3, M^+), 283 (80), 282 (100).

Anal. Calcd. for $C_{20}H_{21}N_3O_3S$ (383.47): C, 62.64; H, 5.52; N, 10.96; S, 8.36. Found: C, 62.67, H, 5.53; N, 10.99; S, 8.30.

tert-Butyl 2-[2-(4-Chlorophenyl)-3,3-dicyanoallylidene]thiazolidine-3-carboxylate **6d**.

This compound was obtained following the foregoing procedure as yellow crystals, 3.2 g (94%), mp 177°; ir (potassium bromide): ν 2220, 1710, 1530, 1500, 1480 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.73 (s, 1H), 7.47-7.45 (m, 2H), 7.26-7.24 (m, 2H), 4.07 (t, 2H), 2.85 (t, 2H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 170.3, 159.2, 150.3, 137.5, 132.7, 130.3-129.7, 114.9, 114.1, 104.4, 85.3, 75.7, 52.1, 28.1, 27.7; ms: m/z 387 (3, M^+), 331 (13), 287 (95), 286 (100).

Anal. Calcd. for $C_{19}H_{18}ClN_3O_2S$ (387.89): C, 58.83; H, 4.68; N, 10.83; S, 8.27. Found: C, 59.08; H, 4.53; N, 10.70; S, 8.20.

Reactions of *tert*-butyl 5-methyl-2-methylthiothiazolium iodide **7** with 2-cyano-3-aryl-2-butenenitriles following the foregoing procedure result in a mixture of compounds **8** and **9** which have been separated by crystallization and column chromatography.

tert-Butyl 2-(3,3-Dicyano-2-phenylallylidene)-5-methylene-thiazole-3-carboxylate **8a**.

After chromatographic purification this compound was isolated as yellow crystals from ethanol, 0.35 g (20%), mp 169°; ir (potassium bromide): ν 2220, 1760, 1630, 1525; 1500, 1480 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.84 (s, 1H), 7.57-7.29 (m, 5H), 5.14-5.13 (m, 1H), 4.89-4.88 (m, 1H), 4.62-4.61 (m, 2H), 1.60 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 171.1, 157.2, 149.8, 135.0, 133.7, 131.4, 129.5, 128.9, 114.7, 114.1, 105.5, 104.6, 85.5, 56.6, 28.2; ms: m/z 365 (2, M^+), 265 (100).

Anal. Calcd. for $C_{20}H_{19}N_3O_2S$ (365.45): C, 65.73; H, 5.24; N, 11.50; S, 8.77. Found: C, 65.52, H, 5.24, N, 11.52; S, 8.75.

tert-Butyl 2-(3,3-Dicyano-2-phenylallylidene)-5-methyl-2,3-dihydro-thiazole-3-carboxylate **9a**.

This compound was isolated from the foregoing run by chromatography. Orange crystals were obtained 0.11 g (6%), mp 143°; ir (potassium bromide): ν 2210, 1750, 1640, 1500, 1470 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.76 (s, 1H), 7.55-7.52 (m, 3H), 7.27-7.26 (m, 2H), 6.92 (s, 1H), 1.92 (s, 3H), 1.65 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 169.0, 159.9, 148.2, 134.4, 131.0, 130.3, 128.2, 121.8, 119.1, 116.2, 115.5, 100.6, 87.6, 70.3, 28.0, 12.1; ms: m/z 306 (4), 265 (100).

Anal. Calcd. for $C_{20}H_{19}N_3O_2S$ (365.45): C, 65.73; H, 5.24; N, 11.50; S, 8.77. Found: C, 65.59; H, 5.26; N, 11.26; S, 8.94.

tert-Butyl 2-(3,3-Dicyano-2-*p*-tolylallylidene)-5-methylenethiazolidine-3-carboxylate **8b**.

This compound was obtained like before after 4.5 hours heating and chromatographic purification as yellow crystals, 0.27 g (18%), mp 159-161°; ir (potassium bromide): ν 2210, 1720, 1630, 1610, 1525 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.81 (s, 1H), 7.31-7.29 (m, 2H), 7.20-7.18 (m, 2H), 5.14-5.13 (m, 1H), 4.89-4.88 (m, 1H), 4.62-4.61 (m, 2H), 2.45 (s, 3H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 171.4, 157.0, 149.8, 142.1, 135.1, 130.7, 130.2, 128.9, 115.0, 114.2, 105.4, 104.7, 85.3, 76.2, 56.6, 28.1; ms: m/z 320 (22), 279 (100).

Anal. Calcd. for $C_{21}H_{21}N_3O_2S$ (379.50): C, 66.46; H, 5.58; N, 11.07; S, 8.45. Found: C, 66.18; H, 5.52; N, 11.25; S, 8.57.

tert-Butyl 2-(3,3-Dicyano-2-*p*-methoxyphenylallylidene)-5-methylenethiazolidine-3-carboxylate **8c**.

This compound was obtained like before after 4.5 hours heating and chromatographic purification as yellow crystals recrystallized from ethanol, 0.8 g (62%), mp 156°; ir (potassium bromide): ν 2210, 1720, 1630, 1605, 1530, 1480 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.79 (s, 1H), 7.28-7.25 (m, 2H), 7.01-6.99 (m, 2H), 5.15-5.14 (m, 1H), 4.92-4.91 (m, 1H), 4.62 (t, 2H), 3.89 (s, 3H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 171.2, 162.5, 156.9, 149.8, 135.1, 131.0, 125.5, 115.2, 114.9, 114.4, 105.4, 104.8, 85.2, 75.6, 56.6, 55.5, 28.1; ms: m/z 383 (0.5, M^+), 296 (100).

Anal. Calcd. for $C_{21}H_{21}N_3O_3S$ (395.13): C, 63.78; H, 5.35; N, 10.63; S, 8.11; Found: C, 64.03; H, 5.44; N, 10.45; S, 8.21.

tert-Butyl 2-[2-(4-Bromophenyl)-3,3-dicyanoallylidene]-5-methylene-2,3-dihydrothiazole-3-carboxylate **8d**.

This compound was obtained following the foregoing procedures as yellow crystals, 0.48 g (22%), mp 240° dec; ir: ν 2220, 1730, 1630, 1590, 1530; ^{1}H-nmr (deuteriochloroform): δ 7.84 (s, 1H), 7.66-7.64 (m, 2H), 7.20-7.18 (m, 2H), 5.18-5.17 (m, 1H), 4.97-4.86 (m, 1H), 4.64 (t, 2H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 170.3, 157.9, 150.3, 135.0, 133.4, 133.1, 131.1, 126.9, 115.2, 114.4, 106.6, 104.7, 86.2, 76.5, 56.3, 28.7; ms: m/z 386 (14), 345 (100).

Anal. Calcd. for $C_{20}H_{18}BrN_3O_2S$ (444.35): C, 54.06; H, 4.08; N, 9.46; S, 7.22. Found: C, 53.96; H, 4.06; N, 9.41; S, 7.12.

tert-Butyl 2-[2-(4-Chlorophenyl)-3,3-dicyanoallylidene]-5-methylenethiazolidine-3-carboxylate **8e**.

This compound was obtained following the foregoing procedures after chromatographic purification as yellow crystals, 1.3 g (84%), mp 170°; ir (potassium bromide): ν 2220, 1730, 1630, 1600, 1530, 1500 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.87 (s, 1H), 7.50-7.48 (m, 2H), 7.27-7.25 (m, 2H), 5.18-5.17 (m, 1H), 4.96-4.93 (m, 1H), 4.65-4.63 (t, 2H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 169.7, 157.6, 149.7, 137.8, 134.4, 132.1, 130.4, 129.9, 114.6, 113.8, 106.1, 104.1, 85.5, 76.3, 56.7, 28.1; ms: m/z 399 (0.2, M^+), 301 (37), 300 (27), 299 (100).

Anal. Calcd. for $C_{20}H_{18}ClN_3O_2S$ (399.89): C, 60.07; H, 4.54; N, 10.51; S, 8.02. Found: C, 60.13; H, 4.71; N,10.52; S, 8.00.

tert-Butyl 2-[3,3-Dicyano-2-(4-nitrophenyl)allylidene]-5-methylenethiazolidine-3-carboxylate **8f**.

This compound was obtained according to the foregoing procedures as orange crystals recrystallized from ethanol/dichloromethane, 0.90 g (50%), mp 170° dec; ir (potassium bromide): ν 2220, 1730, 1630, 1605, 1530, 1505 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 8.38-7.36 (m, 2H), 7.94 (s, 1H), 7.27-7.25 (m, 2H), 5.21-5.20 (m, 1H), 4.96-4.95 (m, 1H), 4.67 (t, 2H), 1.60 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 168.2, 157.9, 149.6, 140.3, 133.7, 130.3, 124.6, 114.2, 113.4, 106.7, 103.6, 85.9, 76.9, 56.8, 28.1; ms: m/z 410 (0.4, M^+), 310 (31), 280 (16).

Anal. Calcd. for $C_{20}H_{18}N_4O_4S$ (410.45): C, 58.53, H, 4.42; N, 13.65; S, 7.81. Found: C, 58.48; H, 4.42; N, 13.55; S, 7.83.

General Procedure for the Deprotection of the *N*-Boc-ketene *N,S*-Acetals **5,6,8,17**.

The *N*-protected ketene *N,S*-acetals **5,6,8,17** were dissolved in 10 ml for one mmole of a 1:1 mixture of trifluoroacetic acid and dichloromethane and stirred at room temperature for 1 hour. The reaction mixture was extracted with (2 x 30 ml) dried over sodium sulfate and evaporated *in vacuo*. The residue was further treated as stated below.

6-Imino-8-phenyl-2,3,4,6-tetrahydropyrido[2,1-*b*]-1,3-thiazine-7-carbonitrile **10a**.

This compound was obtained after crystallization from ether, chromatographic purification and recrystallization from ethanol as yellow crystals, 0.18 g (62%), mp 175-176°; ir (potassium bromide): ν 3320, 2200, 1590 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.54-7.43 (m, 5H), 6.83 (s, 1H), 5.86 (s, 1H), 4.20-4.17 (m, 2H), 3.11 (t, 2H), 2.34-2.28 (m, 2H); ^{13}C-nmr (deuteriochloroform): δ 158.5, 153.7, 150.9, 136.3, 130.3, 127.7, 117.7, 102.5, 93.5, 43.4, 26.6, 23.6; ms: m/z 267 (100, M^+), 252 (85).

Anal. Calcd. for $C_{15}H_{13}N_3S$ (267.35): C, 67.39; H, 4.90; N, 15.72; S, 11.99. Found: C, 67.18; H, 4.98; N, 15.52; S, 11.70.

6-Imino-8-*p*-tolyl-2,3,4,6,-tetrahydropyrido-[2,1-*b*]-1,3-thiazine-7-carbonitrile **10b**.

This compound was isolated following the procedure described above as orange yellow crystals, 0.18 g (64%), mp 170-171°; ir (potassium bromide): ν 3320, 2200, 1590 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.45-7.41 (m, 2H), 7.27-7.24 (m, 2H), 6.79 (bs, 1H), 5.85 (s, 1H), 4.19-4.16 (m, 2H), 3.10 (t, 2H), 2.39 (s, 3H) 2.34-2.28 (m, 2H); ms: m/z 281 (100, M^+), 266 (85).

Anal. Calcd. for $C_{16}H_{15}N_3S$ (281.38): C, 68.29; H, 5.37; N, 14.93; S, 11.39. Found: C, 68.02, H, 5.21; N, 15.01; S, 11.29.

8-(4-Bromophenyl)-6-imino-2,3,4,6-tetrahydropyrido-[2,1-*b*]-1,3-thiazine-7-carbonitrile **10c**.

This compound was obtained like above as orange yellow crystals, 0.24 g (76%), mp 201-202°; ir (potassium bromide): ν 3300, 2200, 1600 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.62-7.57 (m, 2H), 7.42-7.38 (m, 2H), 6.86 (s, 1H), 5.80 (s, 1H), 4.20-4.17 (m, 2H), 3.13 (t, 2H), 2.35-2.29 (m, 2H); ^{13}C-nmr (deuteriochloroform): δ 158.2, 152.4, 151.4, 135.2, 132.1-129.3, 124.6, 117.5, 102.0, 93.4, 43.5, 26.7, 23.5; ms: m/z 346 (32, M^+), 347 (100), 332 (85), 330 (80).

6-Imino-8-(4-methoxyphenyl)-2,3,4,6-tetrahydropyrido[2,1-*b*]-1,3-thiazine-7-carbonitrile **10d**.

This compound was obtained like above as orange yellow crystals, 0.16 g (67%), mp 163-164°; ir (potassium bromide): ν 3310, 2200, 1600, 1540 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.53-7.49 (m, 2H), 6.98-6.95 (m, 2H), 6.87 (s, 1H), 5.85 (s, 1H), 4.19-4.17 (m, 2H), 3.84 (s, 3H), 3.11 (t, 2H), 2.34-2.28 (m, 2H); ^{13}C-nmr (deuteriochloroform): δ 161.2, 158.6, 153.2, 150.4, 128.4, 129.3, 118.1, 114.2, 102.4, 92.9, 55.4, 43.3, 26.6, 23.7; ms: m/z 297 (100, M^+), 282 (87), 264 (51).

Anal. Calcd. for $C_{16}H_{15}N_3OS$ (297.38): C, 64.16; H, 5.08; N, 14.13; S, 10.78. Found: C, 64.66; H, 5.04; N, 14.05; S, 10.78.

6-Imino-8-(4-nitrophenyl)-2,3,4,6-tetrahydropyrido[2,1-*b*]-1,3-thiazine-7-carbonitrile **10e**.

This compound was obtained as before as orange crystals, 0.44 g (73%), mp 261°; ir (potassium bromide): ν 3310, 2200, 1585, 1520 cm^{-1}; ^{1}H-nmr ([D_6]-DMSO): δ 8.34-8.32 (m, 2H), 7.84-7.82 (m, 2H), 6.81 (s, 1H), 6.02 (s, 1H), 4.06 (m, 2H), 3.21 (t, 2H), 2.27-2.21 (m, 2H); ^{13}C-nmr ([D_6]-DMSO): δ 151.0, 148.2, 142.3, 129.3, 123.7, 117.3, 100.9, 54.8, 43.3, 26.1, 22.6; ms: m/z 312 (100, M^+), 297 (98), 282 (18), 279 (48).

Anal. Calcd. for $C_{15}H_{12}N_4O_2S$ (312.32): C, 57.69; H, 3.87; N, 17.94; S, 10.27. Found: C, 57.42; H, 3.88; N, 17.81; S, 10.43.

5-Imino-7-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyridine-6-carbonitrile **11a**.

This compound was obtained as before after recrystallization from cyclohexane/toluene as yellow crystals, 0.17 g (42%), mp 176°; ir (potassium bromide): ν 3300, 2200, 1590, 1550, 1490 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.55-7.50 (m, 2H), 7.48-7.43 (m, 3H), 6.62 (bs, 1H), 5.87 (s, 1H), 4.48 (t, 2H), 3.37 (t, 2H); ^{13}C-nmr (deuteriochloroform): δ 156.3, 156.1, 154.9, 136.3, 130.2, 128.7, 127.6, 117.1, 98.0, 94.4, 51.7, 28.0; ms: m/z 253 (75, M^+), 252 (100).

Anal. Calcd. for $C_{14}H_{11}N_3S$ (253.33): C, 66.38; H, 4.38; N, 16.59; S, 12.66. Found: C, 66.40; H, 4.30; N, 16.72; S, 12.35.

5-Imino-7-*p*-tolyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyridine-6-carbonitrile **11b**.

This compound was obtained like before and crystallized from ether as yellow crystals, 0.30 g (94%), mp 166°; ir (potassium bromide): ν 3310, 2200, 1600, 1560, 1550, 1540 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.45-7.42 (m, 2H), 7.27-7.24 (m, 2H), 6.64 (bs, 1H), 5.87 (s, 1H), 4.49-4.44 (m, 2H), 3.49-3.44 (m, 2H), 2.40 (s, 3H); ^{13}C-nmr (deuteriochloroform): δ 156.4, 156.3, 154.7, 140.7, 133.5, 129.5, 117.4, 98.0, 94.0, 51.8, 28.0, 21.4; ms: m/z 267 (70, M^+), 266 (100).

Anal. Calcd. for $C_{15}H_{13}N_3S$ (267.35): C, 67.39; H, 4.90; N, 15.72; S, 11.99. Found: C, 67.13; H, 4.84; N, 15.72; S, 11.70.

7-(4-Chlorophenyl)-5-imino-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyridine-6-carbonitrile **11c**.

This compound was obtained like before as a yellow powder, 0.10 g (23%), mp 227°; ir (potassium bromide): ν 3300, 2200, 1600, 1560, 1490 cm^{-1}; ^{1}H-nmr ([D$_6$]-DMSO): δ 7.58 (s, 4H), 6.61 (s, 1H), 6.11 (s, 1H), 4.34 (t, 2H), 3.57 (t, 2H); ^{13}C-nmr (deuteriochloroform): δ 156.0, 155.4, 155.1, 136.5, 134.8, 129.2, 129.1, 116.9, 97.7, 94.4, 51.9, 28.1; ms: m/z 287 (74, M$^+$), 286 (100).

Anal. Calcd. for $C_{14}H_{10}ClN_3S$ (287.77): C, 58.43; H, 3.50; N, 14.60; S, 11.14. Found: C, 58.66; H, 3.62; N, 14.51; S, 11.27.

7-(4-Bromophenyl)-5-imino-2-methyl-5*H*-thiazolo[3,2-*a*]pyridine-6-carbonitrile **12a**.

This compound was obtained from **8d** following the foregoing procedure as yellow crystals recrystallized from ethanol, 0.12 g (71%), mp 259-260°; ir (potassium bromide): ν 3310, 2200, 1600, 1540, 1490 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 8.05 (s, 1H), 7.61-7.59 (m, 2H), 7.45-7.43 (m, 2H), 6.22 (s, 1H), 2.45 (s, 3H); ^{13}C-nmr (deuteriochloroform): δ 154.7, 153.4, 151.4, 135.9, 132.1, 129.5, 125.8, 124.5, 122.3, 117.8, 96.2, 89.1, 13.0; ms: m/z 344 (38, M$^+$), 345 (100), 343 (98).

Anal. Calcd. for $C_{15}H_{10}BrN_3S$ (344.24): C, 52.34; H, 2.93; N, 12.21; S, 9.31. Found: C, 52.16; H, 2.97; N, 12.24; S, 9.26.

Reaction of **8f** with trifluoroacetic acid following the foregoing procedure led to a mixture of **12b** and **13** which was chromatographically separated.

7-(4-Nitrophenyl)-5-imino-2-methyl-5*H*-thiazolo[3,2-*a*]pyridine-6-carbonitrile **12b**.

This compound was obtained after recrystallization from ethanol as a red powder, 0.12 g (36%), mp 255°; ir (potassium bromide): ν 3300, 2210, 1610, 1600, 1540, 1520 cm^{-1}; ^{1}H-nmr ([D$_6$]-DMSO): δ 8.37-8.35 (m, 2H), 7.87-7.85 (m, 2H), 8.29 (s, 1H), 8.19 (s, 1H), 6.74 (s, 1H), 2.47 (s, 3H); ms: m/z 310 (100, M$^+$), 280 (15).

Anal. Calcd. for $C_{15}H_{10}N_4O_2S$ (310.33): C, 58.06; H, 3.25; N, 18.05; S, 10.33. Found: C, 57.87; H, 3.22; N, 17.85; S, 10.47.

5-*tert*-Butylimino-2-methyl-7-(4-nitrophenyl)-5*H*-thiazolo-[3,2-*a*]pyridine-6-carbonitrile **13**.

This compound was obtained as violet crystals from ethanol, 30 mg (7%), mp 228-230°; ir (potassium bromide): ν 2190, 1620, 1520 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 8.30-8.28 (m, 2H), 7.67-7.65 (m, 2H), 8.24-8.23 (s, 1H), 6.05 (s, 1H), 2.43 (s, 3H), 1.52 (s, 9H); ms: m/z 352 (18, M$^+$), 310 (100).

Anal. Calcd. for $C_{19}H_{18}N_4O_2S$ (366.44): C, 62.28; H, 4.95; N, 15.29; S, 8.75. Found: C, 61.99; H, 4.80; N, 15.07; S, 8.58.

6-Imino-2,3,4,6-tetrahydro-1,3-thiazino[3,2-*b*]isoquinoline-11-carbonitrile **15**.

This compound was obtained from **14** [1] as a yellow powder, 38 mg (27%), mp 184-186°; ir (potassium bromide): ν 3320, 2200, 1670, 1610, 1590 cm^{-1}; ^{1}H-nmr ([D$_6$]-DMSO): δ 9.18 (s, 1H), 8.22-8.20 (m, 1H), 7.63-7.60 (m, 1H), 7.39-7.35 (m, 2H), 4.17-4.14 (m, 2H), 3.25 (t, 2H), 2.26-2.22 (m, 2H); ^{13}C-nmr ([D$_6$]-DMSO): δ 156.1, 151.0, 132.0, 126.3, 126.2, 121.7, 130.3, 121.3, 116.5, 81.6, 43.1, 26.3, 23.3, ms: m/z 241 (100, M$^+$), 226 (33), 208 (60).

Anal. Calcd. for $C_{13}H_{11}N_3S$ (241.32): C, 64.70; H, 4.59; N, 17.41; S, 13.29. Found: C, 64.46; H, 4.43, N, 17.25; S, 13.05.

5-Imino-2,3-dihydro-5*H*-thiazolo[3,2-*b*]isoquinoline-10-carbonitrile **18**.

This compound was obtained from **17** [11] after recrystallization from ethanol as yellowish crystals, 0.10 g (32%), mp 191-192°; ir (potassium bromide): ν 3320, 2200, 1670, 1610, 1595, 1570, 1550 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.78-7.76 (m, 1H), 7.59-7.51 (m, 2H), 7.38-7.34 (m, 1H), 4.54 (t, 2H), 3.52 (t, 2H); ^{13}C-nmr (deuteriochloroform): δ 156.4, 154.8, 132.3, 126.5, 124.6, 123.2, 121.7, 121.1, 116.5, 80.7, 52.5, 27.9; ms: m/z 227 (100, M$^+$), 226 (92), 201 (22).

Anal. Calcd. for $C_{12}H_9N_3S$ (227.29): C, 63.41; H, 3.99; N, 18.49; S, 14.11; Found: C, 63.19; H, 3.99; N, 18.38; S, 13.86.

6-Amino-8-(4-bromophenyl)-7-cyano-2,3-dihydro-4*H*-pyrido-[2,1-*b*]-1,3-thiazinium Chloride **20**.

This compound was obtained after 9 hours heating of 150 mg (4.3 mmol) of **10c** in 10 ml of 22% hydrochloric acid by pouring into water, collecting the precipitate and recrystallization from ethanol, yellow crystals, 85 mg (57%), mp 282-284°; ir (potassium bromide): ν 3200-2800, 2220, 1650, 1600, 1590, 1540 cm^{-1}; ^{1}H nmr ([D$_6$]-DMSO): δ 9.09 (s, 2H), 7.83-7.78 (m, 2H), 7.64-7.61 (m, 2H), 7.23 (s, 1H), 4.16-4.13 (m, 2H), 3.30-3.13 (m, 2H), 2.39-2.21 (m, 2H); ^{13}C-nmr ([D$_6$]-DMSO): δ 156.4, 155.9, 153.7, 133.2, 132.0, 130.9, 124.9, 114.3, 112.1, 88.7, 48.3, 25.6, 21.7; ms: m/z 347 (100), 348 (32), 346 (43), 345 (95), 332 (81).

Anal. Calcd. for $C_{15}H_{13}BrClN_3S$ (382.71): C, 47.08; H, 3.42; N, 10.98; S, 8.38. Found: C, 46.80; H, 3.47; N, 10.71; S, 8.22.

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