Iminium Carbonic Acid Derivative Salts. XI [1]. Synthesis of *N,S*-Containing Heterobicycles from *N*-Protected 2-Methylthio-1,3-thiazinium and 2-Methylthiothiazolium Salts. Part 3. Reaction of *N*-Protected 2-Methylthio-1,3-thiazinium and 2-Methylthiothiazolium Salts with 3-Amino-2-cyano-3-arylacrylonitriles

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Dedicated to Professor Dr. E. Mutschler, Frankfurt/Main on occasion of his 65th birthday.

N-Boc-protected 2-methylthio-1,3-thiazinium **1** and 2-methylthiothiazolium iodides **2, 3** obtained from the corresponding 3,4,5,6-tetrahydro-2*H*-1,3-thiazine-2-thiones and thiazolidine-2-thiones by the action of methyl iodide were reacted with 3-amino-2-cyano-3-arylacrylonitriles forming the cyclic isothioureas **5-7**. The protection group was removed with trifluoroacetic acid whereupon the desired cyclisation to 3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazines **8a-c, 8a'-c'** and thiazolo[3,2-*b*]pyrimidines **9a,b, 9a',b', 10a,b** took place.

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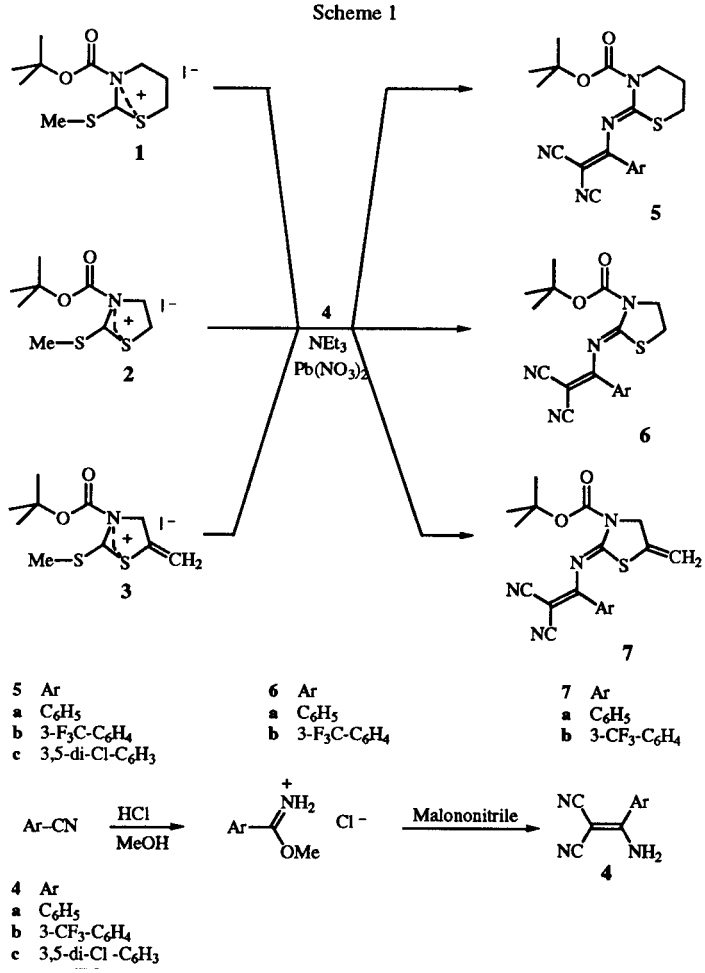
In the preceeding two papers [1,2] we described the transformation of *N*-Boc protected 3,4,5,6-tetrahydro-2*H*-1,3-thiazine-2-thiones and thiazolidine-2-thiones into the corresponding 2-methylthio-3,4,5,6-tetrahydro-1,3-thiazinium and 2-methylthiothiazolium salts by methyl iodide or trimethyloxonium tetrafluoroborate. This activated species were reacted with simple or vinylogous CH-acidic compounds forming cyclic ketene *N,S*-acetals. Deprotection of the ring nitrogen was successful with trifluoroacetic acid yielding the *N*-unsubstituted ketene *N,S*-acetals or the products of a spontaneous cyclisation when the formation of a 6-membered ring was possible. Those heterobicycles are of special interest because of the variety of interesting pharmacological activities reported for structurally similar thiazolo[3,2-*a*]pyrimidines as well as thiazolopyrimidinium- and pyrimidinothiazinium salts [3].

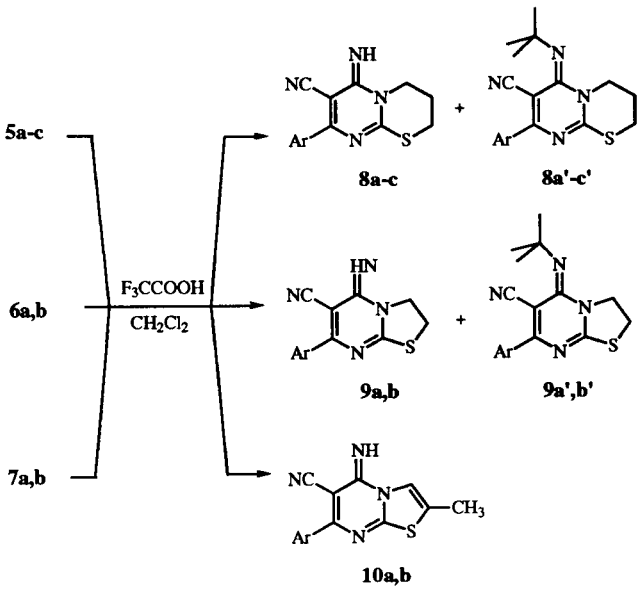
In the last paper of this series we wish to report the successful application of 2-methylthio-3,4,5,6-tetrahydro-1,3-thiazinium **1** and 2-methylthiothiazolium iodides **2, 3** in the reaction with 3-amino-2-cyano-3-arylacrylonitriles **4** yielding the cyclic isothioureas **5-7**. The 3-amino-2-cyano-3-arylacrylonitriles **4** were obtained according to the literature [4] from malonodinitrile and iminoester chlorides which in turn were obtained by the action of gaseous hydrogen chloride on the corresponding arylnitriles in dry methanol. Compounds **4b** and **c** were previously unknown in literature.

On removal of the Boc protecting group a spontanous cyclisation of **5-7** occured forming the desired 3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazines **8** and thiazolo[3,2-*b*]pyrimidines **9,10**. In the case of **8** and **9** the product of the reaction of isobutylene formed during the cleavage of the Boc group with the imino function was isolated in smaller amounts along with the *N*-unsubstituted product. With the example of **9a** we could show that the hydrolysis of the imino as well as the nitrile function in **9a** can be accomplished using 60% sulfuric acid under reflux.

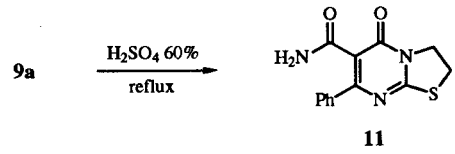
Scheme 1



Scheme 2



8	Ar	9	Ar	10	Ar
a a'	C_6H_5	a a'	C_6H_5	a	C_6H_5
b b'	3-F_3C-C_6H_4-	b b'	3-F_3C-C_6H_4	b	3-CF_3-C_6H_4
c c'	3,5 di-Cl-C_6H_3				



EXPERIMENTAL

Instrumental equipment and chromatographic conditions were those already described [1].

Preparation for 3-Amino-2-cyano-3-arylacrylonitriles **4**.

Compounds **4a-c** were prepared by a modified version of the literature method [4]; 1.5 g of gaseous hydrogen chloride were bubbled into a solution of 40 mmoles of the appropriate benzonitrile and 80 mmoles (2.6 g) of methanol in 20 ml of toluene at 5-10°. After stirring for 20 hours at room temperature the white solid was filtered, dissolved in 30 ml of methanol and with cooling brought to *p*H 7-8.5 by addition of triethylamine. After addition of 40 mmoles (2.7 g) of malononitrile the mixture was refluxed for 2 hours. After cooling it was poured on ice. The white precipitate was collected and recrystallized from ethanol. The properties of **4a** were in accordance with data from literature [4].

3-Amino-2-cyano-3-(3-trifluoromethylphenyl)acrylonitrile **4b**.

This compound was obtained as a white powder, 5.0 g (53%), mp 162-163°; ir (potassium bromide): ν 3370, 3340, 3220, 2220, 2200, 1660 cm^{-1}; ^{1}H-nmr ([D_6]-acetone): δ 8.24, 8.07 (2s, 2H), 8.04-7.79 (m, 3H), 7.84-7.80 (m, 1H); ^{13}C-nmr ([D_6]-acetone): δ 171.4, 134.4, 133.1, 131.4, 130.8, 129.4, 129.4, 126.0, 124.8, 116.5, 115.2, 52.6; ms: m/z 237 (100, M^+), 218 (15), 172 (61).

Anal. Calcd. for $C_{11}H_6F_3N_3$ (237.18): C, 55.50; H, 2.55; N, 17.72. Found: C, 55.59; H, 2.69; N, 17.44

3-Amino-2-cyano-3-(3,5-dichlorophenyl)acrylonitrile **4c**.

This compound was obtained as white crystals after recrystallization from ethanol, 4.8 g (50%), mp 215°; ir (potassium bromide): ν 3360, 3340, 3220, 2220, 2210, 1660 cm^{-1}; ^{1}H-nmr ([D_6]-acetone): δ 8.06 (bs, 2H), 7.75-7.74 and 7.72-7.71 (m, 3H); ^{13}C-nmr ([D_6]-acetone): δ 169.9, 136.6, 136.0, 132.3, 127.9, 116.2, 114.9, 53.1; ms: m/z 238 (12, M^+), 237 (100), 174 (36), 172 (51).

Anal. Calcd. for $C_{10}H_5Cl_2N_3$ (238.08): C, 50.45; H, 2.12; N, 17.65. Found: C, 50.30; H, 2.21; N, 17.47.

General Procedure for the Condensation of the 2-Methylthio-3,4,5,6-tetrahydro-1,3-thiazinium and -thiazolium Iodides **1-3** with 3-Amino-2-cyano-3-arylacrylonnitriles **4**.

To a solution of equimolar quantities of the 2-methylthio-3,4,5,6-tetrahydro-1,3-thiazinium and -thiazolium iodides **1-3** and the 3-amino-2-cyano-3-arylacrylonitriles **4** in 30 ml of dry dichloromethane were added 2 equivalents of triethylamine and 1.5 equivalents of lead(II)nitrate under 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-(2,2-Dicyano-1-phenylvinylimino)-3,4,5,6-tetrahydro-1,3-thiazine-3-carboxylate **5a**.

This compound was obtained after 3 hours reflux by column chromatography, first with dichloromethane/ethyl acetate 9:1, second with ethyl acetate/cyclohexane 2:3; after evaporation of the solvents the residue was crystallized with ether as a white powder, 0.35 g (14%), mp 100-101°, ir (potassium bromide): ν 2220, 1730, 1620, 1600 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 7.78-7.76 (m, 2H), 7.54-7.44 (m, 3H), 3.89 (t, 2H), 3.03 (t, 2H), 2.19-2.16 (m, 2H), 1.55 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 173.2, 157.5, 151.2, 132.5, 128.9-128.7, 115.0, 114.4, 84.6, 65.0, 44.5, 28.1, 27.5, 23.4; ms: m/z 368 (3, M^+), 268 (100), 267 (53), 253 (34).

Anal. Calcd. for $C_{19}H_{20}N_4O_2S$ (368.46): C, 61.94; H, 5.47; N, 15.21; S, 8.70. Found: C, 61.79; H, 5.44; N, 15.19; S, 8.59.

tert-Butyl 2-[2,2-Dicyano-1-(3-trifluoromethylphenyl)vinylimino]-3,4,5,6-tetrahydro-1,3-thiazine-3-carboxylate **5b**.

This compound was obtained after 4 hours reflux by column chromatography with dichloromethane/ethyl acetate 4:1 and recrystallization with ethanol/petrol ether as yellow crystals, 1.0 g (36%), mp 117°; ir (potassium bromide): ν 2220, 1730, 1610, 1560 cm^{-1}; ^{1}H-nmr (deuteriochloroform): δ 8.01-7.97 (m, 2H), 7.79-7.78 (m, 1H), 7.63-7.06 (m, 1H), 3.94-3.90 (m, 2H), 3.06 (t, 2H), 2.23-2.18 (m, 2H), 1.55 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 171.3, 158.7, 151.0, 133.7, 131.9, 131.1, 129.4, 128.8, 128.7, 123.5, 114.5, 114.0, 85.0, 66.0, 44.7, 28.1, 27.7, 23.5; ms: m/z 436 (0.7, M^+), 337 (20), 336 (100), 335 (42), 321 (56).

Anal. Calcd. for $C_{20}H_{19}F_3N_4O_2S$ (436.45): C, 55.04; H, 4.39; N, 12.84 S, 7.35. Found: C, 54.99; H, 4.52; N, 12.58; S, 7.18.

tert-Butyl 2-[1-(3,5-Dichlorophenyl)-2,2-dicyano-vinylimino]-3,4,5,6-tetrahydro-1,3-thiazine-3-carboxylate **5c**.

This compound was obtained after 4 hours reflux by column chromatography with dichloromethane/ethyl acetate 4:1 and recrystallization with ethanol/petrol ether as yellow crystals, 0.90 g (44%), mp 134°; ir (potassium bromide): ν 2220, 1740,

1570, 1550, 1530 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.62-7.61 (m, 2H), 7.51-7.50 (m, 1H), 3.93-3.90 (t, 2H), 3.08 (t, 2H), 2.22-2.19 (m, 2H), 1.56 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 169.9, 158.9, 150.9, 135.6, 135.5, 132.0, 128.9, 114.1, 113.7, 85.1, 66.3, 44.7, 28.1, 27.7, 23.5; ms: m/z 338 (64), 337 (51), 336 (93), 335 (54), 323 (37), 321 (55).

Anal. Calcd. for $C_{19}H_{18}Cl_2N_4O_2S$ (437.35): C, 52.18; H, 4.15; N, 12.81; S, 7.32. Found: C, 52.07; H, 4.16; N, 12.79; S, 7.38.

tert-Butyl 2-(2,2-Dicyano-1-phenylvinylimino)thiazolidine-3-carboxylate **6a**.

This compound was obtained after 3 hours reflux by column chromatography first with dichloromethane, than with ethyl acetate/cyclohexane 2:3. Recrystallization from ethanol/petrol ether yielded yellow crystals, 1.30 g (37%), mp 94°; ir (potassium bromide): ν 2230, 1750, 1720, 1620, 1590, 1580 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.74-7.72 (m, 2H), 7.54-7.44 (m, 3H), 4.19 (t, 2H), 3.20 (t, 2H), 1.57 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 175.7, 156.9, 148.9, 132.6-128.7, 132.2, 114.5, 113.6, 84.6, 67.3, 50.3, 28.0, 26.7; ms: m/z 354 (1.5, M^+), 254 (100), 253 (86).

Anal. Calcd. for $C_{18}H_{18}N_4O_2S$ (354.43): C, 61.00; H, 5.12; N, 15.81; S, 9.05. Found: C, 61.18; H, 5.19; N, 15.60; S, 9.09.

tert-Butyl 2-[2,2-Dicyano-1-(3-trifluoromethylphenyl)vinylimino]thiazolidine-3-carboxylate **6b.**

This compound was obtained after 3.5 hours reflux by column chromatography with dichloromethane/ethyl acetate 9:1 and recrystallization with ethanol as white crystals, 2.0 g (47%), mp 126°; ir (potassium bromide): ν 2220, 1710, 1640, 1520 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.98-7.95 (m, 2H), 7.80-7.78 (m, 1H), 7.64-7.59 (m, 1H), 4.23 (t, 2H), 3.25 (t, 2H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 173.9, 157.4, 148.9, 133.4, 131.8, 131.5, 129.5, 129.0, 125.7, 123.5, 114.0, 113.2, 85.1, 68.4, 50.6, 28.1, 26.8; ms: m/z 422 (1.7, M^+), 322 (100).

Anal. Calcd. for $C_{19}H_{17}F_3N_4O_2S$ (422.43): C, 54.02; H, 4.06; N, 13.28; S, 7.59. Found: C, 54.13; H, 4.15; N, 12.99; S, 7.36.

tert-Butyl 2-(2,2-Dicyano-1-phenylvinylimino)-5-methylenthiazolidine-3-carboxylate **7a**.

This compound was obtained after 3 hours reflux by column chromatography first with dichloromethane/ethyl acetate 9:1, than with ethyl acetate/cyclohexane 1:4. The first fraction yielded **7a**, the second fraction **10a**.

Compound **7a** was recrystallized from ethanol/petrol ether to a yellow powder, 0.24 g (5%), mp 108°; ir (potassium bromide): ν 3220, 2240, 2220, 1750, 1650, 1620, 1580 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.77-7.53 (m, 5H), 5.33-5.32 (m, 1H), 5.14-5.13 (m, 1H), 4.76-4.74 (m, 2H), 1.58 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 175.2, 167.4, 154.9, 148.9, 133.1-131.9, 114.4, 113.4, 108.3, 85.1, 68.1, 55.6, 28.1; ms: m/z 266 (4), 195 (15), 169 (23), 57 (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, 62.07; H, 4.89; N, 15.41, S, 8.58.

5-Imino-2-methyl-7-phenyl-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carbonitrile **10a**.

This compound was isolated from the foregoing run after evaporation of the second fraction, yellow-green crystals from ethanol, 50 mg (1.4%), mp 199°; ir (potassium bromide): ν 3320, 2210, 1610, 1530 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.94-7.91 (m, 2H), 7.88 (s, 1H), 7.54-7.47 (m, 3H), 7.33 (bs, 1H), 2.45 (s, 3H); ^{13}C-nmr (deuteriochloroforrn): δ 164.9, 162.7, 152.5, 135.8, 131.3, 128.6, 128.6, 125.7, 119.3, 116.8, 87.8, 13.3; ms: m/z 266 (100, M^+), 240 (14), 201 (29).

Anal. Calcd. for $C_{14}H_{10}N_4S$ (266.32): C, 63.14; H, 3.78; N, 21.04; S, 12.04. Found: C, 63.10, H, 3.59, N, 20.83; S, 11.88.

tert-Butyl 2-[2,2-Dicyano-1-(3-trifluoromethylphenyl)vinylimino]-5-methylenethiazolidine-3-carboxylate **7b.**

This compound was obtained after 3 hours reflux by column chromatography with dichloromethane/ethyl acetate 9:1 from the first fractions; from the later fractions **10b** could be isolated. Compound **7b** was a yellowish powder, 0.30 g (11%), mp 105°; ir (potassium bromide): ν 2230, 1750, 1630, 1620 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.98-7.95 (m, 2H), 7.82-7.80 (m, 1H), 7.66-7.62 (m, 1H), 5.39-5.38 (m, 1H), 5.20-5.19 (m, 1H), 4.80-4.79 (m, 2H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 173.3, 155.2, 148.1, 133.0, 131.8, 131.7, 131.5, 129.6, 129.2, 125.7, 123.4, 113.8, 112.9, 108.8, 85.4, 69.1, 55.8, 28.1; ms: m/z 434 (1.4, M^+), 334 (100).

Anal. Calcd. for $C_{20}H_{17}F_3N_4O_2S$ (434.44): C, 55.29; H, 3.94; N, 12.90; S, 7.38. Found: C, 55.49; H, 3.98; N, 12.83; S, 7.55.

5-Imino-2-methyl-7-(3-trifluoromethylphenyl)-5*H*-thiazolo-[3,2-*a*]pyrimidine-6-carbonitrile **10b**.

This compound was isolated from the foregoing run as yellow-green crystals from ethanol, 35 mg (1.7%), mp 189°; ir (potassium bromide): ν 3310, 2210, 1620, 1520 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 8.18-8.15 (m, 2H), 7.91 (s, 1H), 7.79-7.77 (m, 1H), 7.65-7.62 (m, 1H), 7.41 (bs, 1H), 2.49 (s, 3H); ^{13}C-nmr (deuteriochloroform): δ 165.2, 161.0, 152.1, 136.6, 131.4, 129.2, 127.8, 126.2, 125.8, 123.7, 119.5, 116.3, 88.2, 13.4, ms: m/z 334 (100, M^+), 308 (12), 269 (24).

Anal. Calcd. for $C_{15}H_9F_3N_4S$ (334.32): C, 53.89, H, 2.71; N, 16.76; S, 9.60. Found: C, 54.10; H, 2.53; N, 16.53; S, 9.82.

General Procedure for the Deprotection of the Cyclic *N*-Boc-isothioureas **5-7**.

The *N*-protected cyclic isothioureas **5-7** were dissolved in 10 ml per one mmole of a 1:1 mixture of trifluorocetic acid and dichloromethane and stirred for 1 hour at room temperature. The reaction mixture was extracted with water (2 x 30 ml) dried over sodium sulfate and evaporated *in vacuo*. The residue was further treated as stated below.

6-Imino-8-phenyl-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]-thiazine-7-carbonitrile **8a**.

The residue was purified by column chromatography with dichloromethane/ethyl acetate 1:1, yielding **8a'**; eluation of the column with methanol led to **8a** as yellow crystals, 0.10 g (50%), mp 194-195°; ir (potassium bromide): ν 2200, 1590, 1560, 1530, 1500 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.96-7.90 (m, 2H), 7.52- 7.43 (m, 3H), 7.26 (s, 1H), 4.19-4.16 (m, 2H), 3.19 (t, 2H), 2.38-2.32 (m, 2H); ^{13}C-nmr (deuteriochloroform): δ 163.4, 161.6, 155.7, 135.1, 131.4-128.5, 116.6, 90.6, 43.8, 27.9, 22.4; ms: m/z 268 (100, M^+), 253 (56), 235 (64).

Anal. Calcd. for $C_{14}H_{12}N_4S$ (268.34): C, 62.66; H, 4.51; N, 20.88; S, 11.95. Found: C, 62.33; H, 4.54; N, 20.96; S, 11.74.

6-*tert*-Butylimino-8-phenyl-3,4-dihydro-2*H*,6*H*-pyrimido-[2,1-*b*][1,3]thiazine-7-carbonitrile **8a'**.

The compound resulted from the foregoing run as a yellow powder, 30 mg (14%), mp 150-152°; ir (potassium bromide): ν

2200, 1650, 1530 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.76-7.74 (m, 2H), 7.44-7.42 (m, 3H), 3.95-3.92 (m, 2H), 3.09 (t, 2H), 2.32-2.26 (m, 2H), 1.50 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 167.0, 165.1, 138.7, 136.6, 130.7, 129.1, 128.2, 121.0, 85.9, 53.6, 44.2, 31.6, 27.7, 23.4; ms: m/z 325 (1, M^+), 323 (11), 309 (100).

Anal. Calcd. for $C_{18}H_{20}N_4S$ (324.45): C, 66.64; H, 6.21 N, 17.27; S, 9.88. Found: C, 66.48; H, 6.09; N, 17.11; S, 9.92.

6-Imino-8-(3-trifluoromethylphenyl)-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazine-7-carbonitrile **8b**.

The residue was separated by column chromatography with dichloromethane/ethyl acetate 1:1 giving a first fraction containing **8b'** and a second fraction containing **8b**; recrystallization from ethanol gave yellow crystals, 0.26 g (68%), mp 156°; ir (potassium bromide): ν 3300, 2220, 1620 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 8.15-8.11 (m, 2H), 7.78-7.75 (m, 1H), 762-7.58 (m, 1H), 7.35 (bs, 1H), 4.20-4.17, (m, 2H), 3.24-3.21 (m, 2H), 2.41-2.35 (m, 2H); ^{13}C-nmr (deuteriochloroform): δ 164.2, 160.1, 155.4, 136.0, 131.7, 131.3, 129.1, 127.9, 125.6, 123.8, 116.1, 91.1, 43.9, 28.0, 22.4; ms: m/z 336 (100, M^+), 335 (57), 322 (14), 321 (77).

Anal. Calcd. for $C_{15}H_{11}F_3N_4S$ (336.34): C, 53.57; H, 3.30; N, 16.66; S, 9.53. Found: C, 53.72; H, 3.35; N, 16.52; S, 9.70.

6-*tert*-Butylimino-8-(3-trifluoromethylphenyl)-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazine-7-carbonitrile **8b'**.

The compound resulted from the foregoing run as yellow crystals from ethanol, 41 mg (11%), mp 138°; ir (potassium bromide): ν 2200, 1660, 1620, 1580 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.99-7.95 (m, 2H), 7.70-7.69 (m, 1H), 7.56-7.55 (m, 1H), 3.95-3.92 (m, 2H), 3.11 (t, 2H), 2.33-2.27 (m, 2H), 1.50 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 165.8, 165.5, 138.1, 137.4, 132.4, 130.8, 128.7, 127.3, 127.3, 123.9, 120.6, 86.4, 53.7, 44.3, 31.7, 27.7, 23.5; ms: m/z 392 (5, M^+), 377 (100).

Anal. Calcd. for $C_{19}H_{19}F_3N_4S$ (392.44): C, 58.12; H, 4.88; N, 14.28; S, 8.17. Found: C, 58.03; H, 4.72; N, 14.32; S, 8.23.

6-Imino-8-(3,5-dichlorophenyl)-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazine-7-carbonitrile **8c**.

The residue was separated by column chromatography with dichloromethane/ethyl acetate 1:1; the first fraction contained **8c'**, the last fraction **8c**. After recrystallization from ethanol, yellow-green crystals were obtained, 0.17 g (66%), mp 176°; ir: ν 3320, 2220, 1600, 1570, 1530 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.81-7.75 (m, 2H), 7.49-7.48 (m, 1H), 7.37 (bs, 1H), 4.19-4.16 (m, 2H), 3.22 (t, 2H), 2.39-2.36 (m, 2H); ^{13}C-nmr (deuteriochloroform): δ 164.3, 158.8, 155.1, 138.0, 135.4, 131.2, 126.9, 115.7, 91.2, 44.0, 28.0, 22.4; ms: m/z 337 (69, M^+), 339 (20), 336 (100).

Anal. Calcd. for $C_{14}H_{10}Cl_2N_4S$ (337.23): C, 49.86; H, 2.99; N, 16.61; S, 9.51. Found C, 49.74; H, 3.01; N, 16.38; S, 9.48.

6-*tert*-Butylimino-8-(3,5-dichlorophenyl)-3,4-dihydro-2*H*,6*H*-pyrimido[2,1-*b*][1,3]thiazine-7-carbonitrile **8c'**.

The compound resulted from the foregoing run as yellow crystals from ethanol, 30 mg (10%), mp 178°; ir (potassium bromide): ν 2200, 1650, 1530 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.60-7.59 (m, 2H), 7.44-7.43 (m, 1H), 3.94-3.92 (m, 2H), 3.13-3.10 (m, 2H), 2.33-2.28 (m, 2H), 1.59 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 165.8, 164.2, 139.5, 137.9, 135.0, 130.5, 120.1, 86.5, 53.8, 44.3, 31.6, 27.7, 23.3; ms: m/z 381 (14), 380 (14), 379 (69), 377 (100).

Anal. Calcd. for $C_{18}H_{18}Cl_2N_4S$ (393.34): C, 54.97; H, 4.61; N, 14.24; S, 8.15. Found: C, 54.78; H, 4.49; N, 14.28; S, 8.24.

5-Imino-7-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carbonitrile **9a**.

The residue was separated by column chromatography with dichloromethane/ethyl acetate 1:1 yielding **9a'**; elution with ethyl acetate yielded **9a**, yellow crystals from ethanol, 0.23 g (44%), mp 193°; ir (potassium bromide): ν 3300, 2210, 1610, 1595, 1540 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.92-7.90 (m, 2H), 7.53-7.45 (m, 3H), 7.17 (s, 1H), 4.52 (t, 2H), 3.52 (t, 2H); ^{13}C-nmr (deuteriochloroform): δ 168.6, 164.4, 153.7, 135.2, 131.6-128.6, 116.1, 91.5, 49.9, 26.0; ms: m/z 254 (100, M^+), 255 (19), 253 (98), 226 (15).

Anal. Calcd. for $C_{13}H_{10}N_4S$ (254.31): C, 61.40; H, 3.96; N, 22.03; S, 12.61. Found: C, 61.43; H, 3.93; N, 22.14; S, 12.96.

5-*tert*-Butylimino-7-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]-pyrimidine-carbonitrile **9a'**.

This compound resulted from the foregoing run, recrystallized from ethanol as yellow crystals, 80 mg (16%), mp 130°; ir (potassium bromide): ν 2200, 1640, 1530 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.74-7.72 (m, 2H), 7.45-7.43 (m, 3H), 4.36 (t, 2H), 3.36 (t, 2H), 1.47 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 170.6, 170.2, 137.7, 137.1, 131.1, 129.2, 128.5, 121.0, 88.0, 53.6, 52.2, 32.2, 25.6; ms: m/z 310 (2, M^+), 295 (100).

Anal. Calcd. for $C_{17}H_{18}N_4S$ (310.42): C, 65.77; H, 5.84; N, 18.04; S, 10.33. Found: C, 65.77; H, 5.77; N, 18.22; S, 10.58.

5-Imino-7-(3-trifluoromethylphenyl)-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carbonitrile **9b**.

The residue was separated by column chromatography with dichloromethane/ethyl acetate 1:1 yielding **9b'**; elution with ethyl acetate yielded **9b** as a yellow powder, 0.22 g (29%), mp 119-121°; ir (potassium bromide): ν 3320, 2210, 1620, 1540, 1500 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 8.15-8.11 (m, 2H), 7.78-7.77 (m, 1H), 7.62-7.59 (m, 1H), 4.54-4.50 (m, 2H), 3.56-3.52 (m, 2H); ^{13}C-nmr (deuteriochloroform): δ 169.3, 162.8, 153.3, 135.9, 131.7, 131.2, 129.2, 128.1, 128.1, 123.7, 115.7, 92.1, 50.1, 26.1; ms: m/z 322 (100, M^+), 321 (94), 264 (14).

Anal. Calcd. for $C_{14}H_9F_3N_4S$ (322.31): C, 52.17; H, 2.81; N, 17.38; S, 9.95. Found C, 52.35; H, 2.78; N, 17.13; S, 10.07.

5-*tert*-Butylimino-7-(3-trifluoromethylphenyl)-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carbonitrile **9b'**.

This compound was obtained from the foregoing run as yellow crystals, 0.21 g (23%), mp 133°; ir (potassium bromide): ν 2200, 1640, 1530 cm^{-1}; ^1H-nmr (deuteriochloroform): δ 7.98-7.93 (m, 2H), 7.72-7.71 (m, 1H), 7.59-7.55 (m, 1H), 4.38 (t, 2H), 3.39 (t, 2H), 1.46 (s, 9H); ^{13}C-nmr (deuteriochloroform): δ 170.5, 168.8, 137.5, 136.8, 132.3, 130.9, 128.8, 127.4, 127.4, 123.8, 120.3, 88.2, 53.4, 52.0, 31.9, 25.4; ms: m/z 378 (1.5, M^+), 363 (100).

Anal. Calcd. for $C_{18}H_{17}F_3N_4S$ (378.42): C, 57.13; H, 4.53; N, 14.81; S, 8.47. Found: C, 57.13; H, 4.52; N, 14.85; S, 8.68.

5-Oxo-7-phenyl-2,3-dihydro-5*H*-thiazolo[3,2-*a*]pyrimidine-6-carboxamide **11**.

A suspension of **9a** (140 mg, 0.55 mole) in 10 ml of sulfuric acid (60%) was refluxed for 2 hours. After cooling, the mixture was diluted with 50 ml of water and extracted 3 times with 30 ml of dichloromethane. The combined extracts were

dried over sodium sulfate and evaporated *in vacuo*. The solid was recrystallized from ethanol, 20 mg (13%), mp 271°; ir (potassium bromide): ν 3390, 3110, 1660, 1580 cm^{-1}, ^1H-nmr ([D_6]-DMSO): δ 7.73-7.70 (m, 2H), 7.61 (s, 1H), 7.46-7.39 (m, 3H), 7.34 (s, 1H), 4.42 (t, 2H), 3.59 (t, 2H); ^{13}C-nmr ([D_6]-DMSO): δ 166.2, 163.9, 158.5, 157.9, 137.0, 129.5, 128.1, 127.9, 117.5, 48.9, 26.1; ms: m/z 273 (27, M^+), 272 (100), 255 (20); hrms: $C_{13}H_{10}N_3O_2S$: Calcd. 273.0572; Found 273.0572.

REFERENCES AND NOTES

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