SYNTHESIS OF NEW PYRIDAZINO ANELLATED HETEROCYCLES *VIA* INVERSE-ELECTRON-DEMAND DIELS-ALDER REACTIONS ON CYCLIC KETENE-*S,N*-ACETALS[1]

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Abstract - Bicyclic ketene-*S,N*-acetals were synthesized and their reactivity as electron-rich dienophiles was investigated employing electron-deficient azadienes. A series of new condensed pyridazines was obtained.

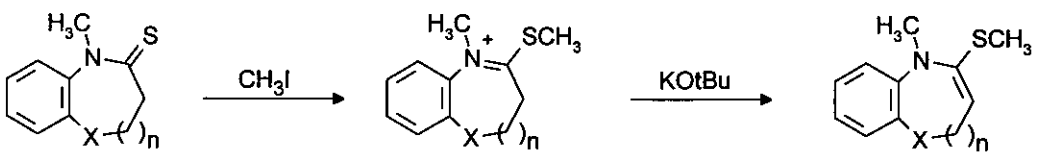
The utilization of inverse-electron-demand ($LUMO_{diene}$-controlled) Diels-Alder reactions of electron-rich dienophiles with π-electron-deficient *N*-heteroaromatics has become a well-established synthetic tool and thus continues to attract considerable interest.[2] The use of enol ethers,[3] *N,N*-dimethylhydrazones,[4] ketene-*O,N*-acetals,[5-6] ketene aminals[7-9] and ketene-*S,N*-acetals,[10] whose reactivity arise from their enamine character as dienophiles has been demonstrated. In the course of a program aimed at the investigation of cycloaddition reactions on bicyclic ketene-*S,N*-acetals, we became interested in the synthesis of 2,5-dihydro-4-

[†] Dedicated to Prof. Dr. Drs. h. c. H. Oelschläger with best wishes on the occasion of his 75th birthday.

methylthio-1,5-benzothiazepine (**7**) and 4-methyl-3-methylthio-4*H*-1,4-benzothiazine (**8**) and their ability to undergo [4+2] cycloaddition reactions with 3,6-bis(trifluoromethyl)-1,2,4,5-tetrazine[11] (**10**), dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate[12] (**11**) and phthalazine in order to construct higher anellated ring systems.

Ketene-*S,N*-acetals were prepared from lactams by Gompper's method.[13] Thus, *N*-methylation of lactams was carried out using phase transfer catalyst (PTC) (n-$Bu_4N^+Cl^-$). Subsequent sulfurization with Lawesson reagent (for benzothiazepine, benzoxazine) or P_2S_5 (for benzothiazine) afforded *N*-methylthiolactams (**1-3**).[14-16] *S*-Methylation of **1-3** with iodomethane yielded in quarternary salts (**4-6**), which were dehydroiodinated with a base (potassium *tert*-butoxide) to give the ketene-*S,N*-acetals (**7-8**). Because of the very low yield of the methoiodide (**6**) (2%) no further reaction with this compound was carried out.

Scheme 1



1 X=S n=1
2 X=S n=0
3 X=O n=0

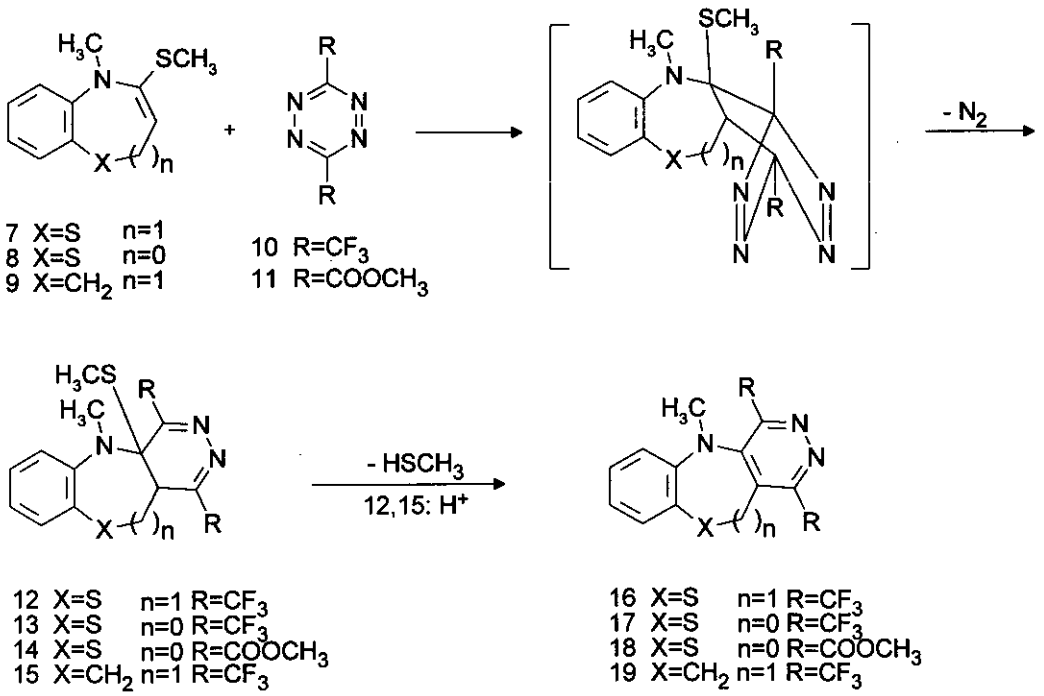
4 X=S n=1
5 X=S n=0
6 X=O n=0

7 X=S n=1
8 X=S n=0

Ketene-*S,N*-acetals (**7**, **8** and **9**)[17] were treated with phthalazine as the azadiene first. Since no conversion could be observed, we chose the more reactive and readily available 3,6-bis(trifluoromethyl)-1,2,4,5-tetrazine (**10**) and dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate (**11**). Especially the extremely reactive diene (**10**) has been shown in numerous examples, in particular by Seitz and coworkers, to be a very useful precursor for a wide variety of pyridazine

derivatives.[18-28] Reaction of the seven-membered derivatives (**7** and **9**) with **10** yielded compounds (**12**) and (**15**) (resulting from loss of N_2 from an intermediate cycloaddition adduct), which could be converted into **16** and **19** under loss of methanethiol by refluxing in toluene with catalytic amounts of *p*TSA. The corresponding intermediates (**13**) and (**14**) from the thiazine (**8**) with both tetrazines (**10**, **11**) could not be isolated. They aromatized spontaneously to give **17** and **18** in one step.

Scheme 2

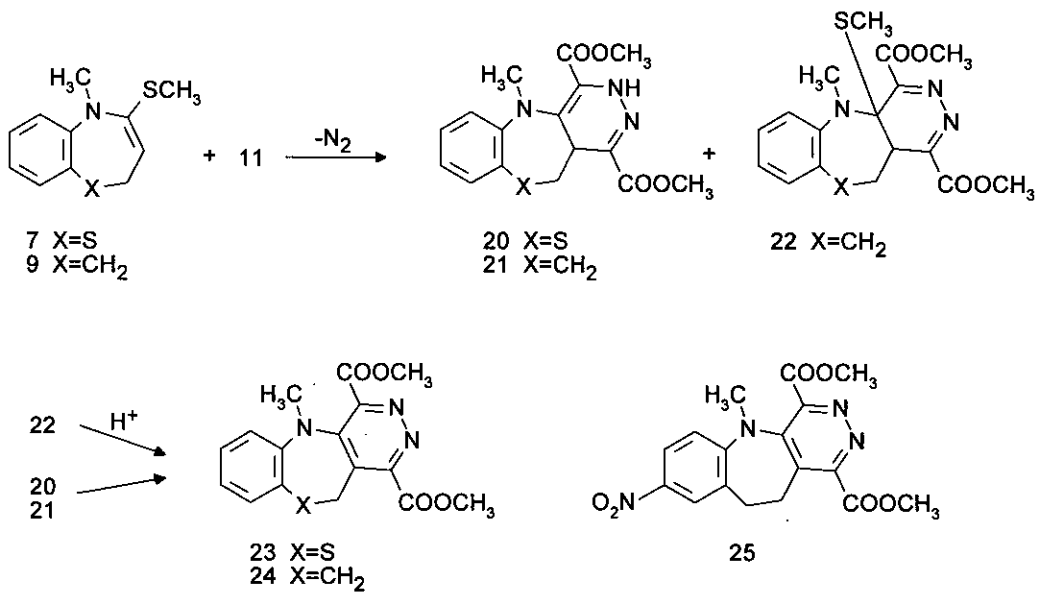


Interestingly, from the reaction of the azepine (**9**) with **11** additionally to the expected product (**22**) the dihydro derivative (**21**) could be isolated as a minor product, whereas reaction of the thiazepine (**7**) gave the dihydro derivative (**20**) exclusively. In **20**, one of the two additional hydrogen atoms could be easily identified as a NH (by D_2O exchange), the other proton appears as a triplet (δ=2.33 ppm) with a coupling constant of 11.3 Hz. Maybe the eliminated

methanethiol acts as a reducting agent as assumed, but reduction takes place as an initial step, since **23** with methanethiol did not lead to any reaction back (maybe due to the aromatic pyridazine ring).

Analogously to **12** and **15**, compound (**22**) was converted into the elimination product (**24**). Oxidation reaction of **20** and **21** with DDQ or nitrous gas led to the elimination products (**23**) and (**24**), whereas with excess of nitrous gas **25** was formed. By means of nuclear Overhauser enhancement (NOE) difference spectroscopy, we could establish the structure of **25** as the 8-nitro derivative.

Scheme 3



7 X=S
9 X=CH_2

20 X=S
21 X=CH_2

22 X=CH_2

23 X=S
24 X=CH_2

25

EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. ^{1}H-Nmr and ^{13}C-nmr spectra were recorded on a Varian Unityplus 300 (300 MHz; 75 MHz) spectrometer (TMS as internal reference, δ values in ppm). Mass spectra were obtained with a

Hewlett-Packard 5970 and a Shimadzu GC/MS QP 1000 spectrometers, ir spectra with a Perkin-Elmer 1600 FTIR (KBr pellets). Analytical tlc was performed on silica gel F254 plates, psc on silica gel F254s plates. Column chromatography was done on Merck silica gel 60, 0.063-0.200 mm. Evaporation refers to evaporation under reduced pressure, and drying of solutions refers to the use of anhydrous sodium sulfate.

General procedure for the synthesis of compounds (4) and (5)

To a solution of 2 mmol of the *N*-methylthiolactam (**1** or **2**) in 20 ml of dry ether iodomethane (852 mg, 6 mmol) was added and the reaction mixture was stirred at room temperature for 72 h. The resulting precipitate was collected by filtration and washed with dry ether. Without further purification the resulting solids were used for the next step.

2,3-Dihydro-5-methyl-4-methylthio-1,5-benzothiazepinium iodide (4)

Prepared from 418 mg **1**. Yield: 337 mg (48%) of **4**, mp 159°C. Anal. Calcd for $C_{11}H_{14}NIS_2$: C, 37.61; H, 4.02; N, 3.99. Found: C, 37.73; H, 3.86; N, 3.92. Ir (cm^{-1}): 2949, 2906, 1525, 1460. ^{1}H-Nmr (DMSO-d_6): δ: 7.56-6.99 (m, 4H, aromat. H), 3.15-3.11 (m, 2H, SCH_2), 2.92-2.87 (m, 2H, CH_2), 2.92 (s, 3H, NCH_3), 2.32 (s, 3H, SCH_3).

4-Methyl-3-methylthio-2*H*-1,4-benzothiazinium iodid (5)

Prepared from 390 mg **2**. Yield: 236 mg (35%) of **5**, mp 146-147°C. Anal. Calcd for $C_{10}H_{12}NIS_2$: C, 35.62; H, 3.59; N, 4.15. Found: C, 35.32; H, 3.48; N, 4.07. Ir (cm^{-1}): 2970, 2901, 1577, 1526. ^{1}H-Nmr (DMSO-d_6): δ: 7.47-7.09 (m, 4H, aromat. H), 3.58 (s, 2H, SCH_2), 3.41 (s, 3H, NCH_3), 2.58 (s, 3H, SCH_3). ^{13}C-Nmr (DMSO-d_6): δ: 165.2 (C-3), 140.0 (C-8a), 127.9, 127.3, 123.2, 118.0 (4 $CH_{aromat.}$), 122.5 (C-4a), 31.6 (NCH_3), 30.3 (C-2), 21.5 (SCH_3).

General procedure for the synthesis of compounds (7) and (8)

To a solution of **4** or **5** (2 mmol) in 30 ml of dry ether potassium *tert*-butoxide (269 mg, 2.4 mmol) was added and the mixture was refluxed with stirring at 50°C for 3 h under argon

atmosphere. The solids were filtered off and the solvent evaporated. Without further purification the resulting instable oils were used for the next step.

2,5-Dihydro-5-methyl-4-methylthio-1,5-benzothiazepine (7)

Prepared from 702 mg **4**. Ms: m/z (rel. int.) 224 (M^+ +1, 97%), 223 (M^+, 52%), 176 (M^+ -SCH_3, 100%), 109 (32%). ^{1}H-Nmr ($CDCl_3$): δ: 7.56-6.82 (m, 4H, aromat. H), 5.60 (t, 1H, CH J=6.4 Hz), 3.59 (d, 2H, CH_2, J=6.4 Hz), 3.06 (s, 3H, NCH_3), 2.10 (s, 3H, SCH_3). ^{13}C-Nmr ($CDCl_3$): δ: 146.2 (C-5a), 129.5 (C-9a), 129.8, 126.4, 123.4, 121.6 (4 $CH_{aromat.}$), 115.6 (C-3), 39.4 (NCH_3), 29.1 (C-2), 15.7 (SCH_3).

4-Methyl-3-methylthio-4*H*-1,4-benzothiazine (8)

Prepared from 674 mg **5**. Ms: m/z (rel. int.) 209 (M^+, 100%), 194 (M^+ -CH_3, 75%), 162 (M^+ -SCH_3, 100%). ^{1}H-Nmr ($CDCl_3$): δ: 7.04-6.67 (m, 4H, aromat. H), 4.86 (s, 1H, CH), 3.30 (s, 3H, NCH_3), 2.17 (s, 3H, SCH_3). ^{13}C-Nmr ($CDCl_3$): δ: 146.4 (C-3), 142.9 (C-4a), 127.0, 126.6, 126.6, 123.5 (4 $CH_{aromat.}$), 125.2 (C-8a), 113.7 (C-2), 35.1 (NCH_3), 17.6 (SCH_3).

General procedure for the synthesis of compounds (12, 15, 17, 18 and 20-22)

A solution of crude **7**, **8** or **9**[17] (2 mmol) and the tetrazine (**10**) or (**11**) (2 mmol) in 20 ml of dry toluene was heated with stirring at 100°C for 30 min under argon atmosphere. The volatile components were removed and the residue was purified by column chromatography.

4a,5,11,11a-Tetrahydro-5-methyl-4a-methylthio-1,4-bis(trifluoromethyl)pyridazino[4,5-*c*]-[1,5]benzothiazepine (12)

Prepared from crude **7** (from 702 mg, 2 mmol **4**) and 436 mg of **10**. Eluent: toluene/ethyl acetate 20:1. After recrystallization from diluted ethanol 545 mg (66%, calcd from **4**) of **12** were obtained as yellow needles, mp 149-150°C. Anal. Calcd for $C_{15}H_{13}N_3F_6S_2$: C, 43.58; H, 3.17; N, 10.16. Found: C, 43.30; H, 3.04; N, 9.76. Ms: m/z (rel. int.) 413 (M^+, 16%), 366 (M^+ -SCH_3, 100%), 351 (M^+ -SCH_3, -CH_3, 56%), 338 (82%), 160 ($C_6H_4SCH_2CHCN^+$, 25%), 109 (58%). Ir (cm^{-1}): 1544, 1393, 1290, 1199, 1151. ^{1}H-Nmr ($CDCl_3$): δ: 7.64-7.27 (m, 4H, aromat. H), 3.72-

3.67 (m, 3H, NCH_3), 3.12-3.05 (m, 1H, SCH_2), 2.25-2.19 (m, 1H, SCH_2), 2.64 (t, 1H, CH, J=11.3 Hz), 2.05 (s, 3H, SCH_3). ^{13}C-Nmr ($CDCl_3$) δ: 152.1-122.0 (7 C_{qu}), 136.5, 131.6, 128.5, 123.2 (4 $CH_{aromat.}$), 43.2 (C-11a), 34.6 (SCH_2), 34.1 (NCH_3), 13.3 (SCH_3).

5,10,11,11a-Tetrahydro-5-methyl-4a-methylthio-1,4-bis(trifluoromethyl)-4a*H*-pyridazino-[4,5-*b*][1]benzazepine (15)

Prepared from 410 mg of **9** and 436 mg of **10**. Eluent: light petroleum/ethyl acetate/ triethylamine 9:1:1). After recrystallization from diluted ethanol 648 mg (82%) of **15** were obtained as yellow needles, mp 149°C. Anal. Calcd for $C_{16}H_{15}N_3F_6S$: C, 48.61; H, 3.82; N, 10.63. Found: C, 48.59; H, 3.53; N, 10.56. Ms: m/z (rel. int.) 395 (M^+, 12%), 348 (M^+ -SCH_3, 100%), 320 (38%). Ir (cm^{-1}): 1545, 1394, 1186, 1160. ^{1}H-Nmr ($CDCl_3$): δ: 7.44-7.15 (m, 4H, aromat. H), 3.74-3.67 (m, 3H, NCH_3), 2.55-2.50 (m, 2H, CH_2-10), 2.11-2.03 (m, 1H, CH), 2.02 (s, 3H, SCH_3), 1.88-1.77 (m, 2H, CH_2-11). ^{13}C-Nmr ($CDCl_3$): δ: 151.4-115.5 (7 C_{qu}), 129.6, 128.8, 128.2, 122.2 (4 $CH_{aromat.}$), 42.3 (C-11a), 33.4 (NCH_3), 30.5 (C-10), 28.6 (C-11), 13.2 (SCH_3).

10-Methyl-1,4-bis(trifluoromethyl)-10*H*-pyridazino[4,5-*b*][1,4]benzothiazine (17)

Prepared from crude **8** (from 674 mg, 2 mmol **5**) and 436 mg of **10**. Eluent: toluene. After *recrystallization from diluted* ethanol 391 mg (51%, calcd from **5**) of **17** were obtained as yellow needles, mp 114-115°C. Anal. Calcd for $C_{13}H_7N_3F_6S$: C, 44.45; H, 2.01; N, 11.96. Found: C, 44.75; H, 1.82; N, 11.74. Ms: m/z (rel. int.) 351 (M^+, 100%), 336 (M^+ -CH_3, 88%), 146 ($C_6H_4SCCN^+$, 12%). Ir (cm^{-1}): 1449, 1408, 1174, 1131. ^{1}H-Nmr ($CDCl_3$): δ: 7.35-7.04 (m, 4H, aromat. H), 3.61 (s, 3H, NCH_3). ^{13}C-Nmr: ($CDCl_3$): δ: 145.2-119.2 (8 C_{qu}), 129.3, 127.6, 126.0, 118.4 (4 $CH_{aromat.}$), 41.1 (NCH_3).

Dimethyl 10-methyl-10*H*-pyridazino[4,5-*b*][1,4]benzothiazine-1,4-dicarboxylate (18)

Prepared from crude **8** (from 674 mg, 2 mmol **5**) and 396 mg of **11**. Eluent: toluene/ethyl acetate 6:4. After recrystallization from ethanol 245 mg (37%, calcd from **5**) of **18** were obtained

as orange needles, mp 186°C. Anal. Calcd for $C_{15}H_{13}N_3O_4S$: C, 54.37; H, 3.95; N, 12.68. Found: C, 54.26; H, 3.76; N, 12.53. Ms: m/z (rel. int.) 332 (M^+ +1, 100%), 331 (M^+, 91%), 272 (M^+ -$COOCH_3$, 38%). Ir (cm^{-1}): 1726 (C=O), 1704 (C=O). ^{1}H-Nmr ($CDCl_3$): δ: 7.30-6.81 (m, 4H, aromat. H), 4.07 (s, 3H, OCH_3), 4.06 (s, 3H, OCH_3), 3.24 (s, 3H, NCH_3). ^{13}C-Nmr ($CDCl_3$): δ: 165.4 (C=O), 164.4 (C=O), 144.8, 143.8, 142.5, 141.3, 136.1, 121.4 (6 C_{qu}), 128.6, 127.2, 125.0, 116.8 (4 $CH_{aromat.}$), 53.6 (OCH_3), 53.3 (OCH_3), 39.1 (NCH_3).

Dimethyl 3,5,11,11a-tetrahydro-5-methylpyridazino[4,5-*c*][1,5]benzothiazepin-1,4-dicarboxylate (20)

Prepared from crude **7** (from 702 mg, 2 mmol **4**) and 396 mg of **11**. Eluent: toluene/ethyl acetate 6:4. After recrystallization from methanol 321 mg (46%, calcd from **4**) of **20** were obtained as yellow crystals, mp 188°C. Anal. Calcd for $C_{16}H_{17}N_3O_4S$: C, 55.32; H, 4.93; N, 12.10. Found: C, 55.14; H, 4.82; N, 11.82. Ms: m/z (rel. int.) 347 (M^+, 26%), 288 (M^+ -$COOCH_3$, 100%). Ir (cm^{-1}): 3310 (N-H), 1691 (C=O). ^{1}H-Nmr ($CDCl_3$): δ: 9.02 (br s, 1H, exchangeable, NH), 7.55-6.93 (m, 4H, aromat. H), 4.55-4.49 (m, 1H, CH_2), 3.96 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 3.33 (s, 3H, NCH_3), 3.31-3.25 (m, 1H, CH_2), 2.33 (t, 1H, CH, J=11.3 Hz). ^{13}C-Nmr ($CDCl_3$): δ: 164.4 (C=O), 160.6 (C=O), 148.8, 134.4, 123.5, 122.9, 108.8 (5 C_{qu}), 137.8, 130.7, 123.5, 118.0 (4 $CH_{aromat.}$), 52.4 (OCH_3), 52.2 (OCH_3), 44.1 (C-11a), 37.2 (NCH_3), 35.0 (C-10).

Dimethyl 5,10,11,11a-tetrahydro-5-methyl-3*H*-pyridazino[4,5-*b*][1]benzazepine-1,4-dicarboxylate (21) and **Dimethyl 5,10,11,11a-tetrahydro-5-methyl-4a-methylthio-4a*H*-pyridazino[4,5-*b*][1]benzazepine-1,4-dicarboxylate (22)**

The residue from 410 mg of **9** and 396 mg of **11** was seperated by column chromatography (toluene/ethyl acetate 4:6). After recrystallization from methanol 227 mg (35%) of **21** as yellow crystals, mp 193°C and 355 mg (47%) of **22** as yellow crystals, mp 165°C were obtained. **21**: Anal. Calcd for $C_{17}H_{19}N_3O_4$: C, 62.00; H, 5.81; N, 12.76. Found: C, 61.84; H, 5.90; N, 12.55. Ms: m/z (rel. int.) 329 (M^+, 84%), 270 (M^+ -$COOCH_3$, 100%), 210 (13%). Ir (cm^{-1}): 3328 (N-H),

1691 (C=O). ^{1}H-Nmr ($CDCl_3$): δ: 8.59 (br s, 1H, exchangeable, NH), 7.27-6.94 (m, 4H, aromat. H), 4.25-4.19 (m, 1H, CH_2CH_2CH), 3.91 (s, 3H, OCH_3), 3.80 (s, 3H, OCH_3), 3.38-3.20 (m, 1H, CH_2CH_2CH), 3.31 (s, 3H, NCH_3), 2.28-2.22 (m, 1H, CH_2CH_2CH), 2.10-1.95 (m, 1H, CH_2CH_2CH), 1.70-1.59 (m, 1H, CH_2CH_2CH). ^{13}C-Nmr ($CDCl_3$): δ: 164.7 (C=O), 160.3 (C=O), 144.9, 135.7, 132.1, 125.2, 108.4 (5 C_{qu}), 130.8, 127.8, 122.9, 116.8 (4 $CH_{aromat.}$), 52.1 (OCH_3), 51.9 (OCH_3), 43.1 (C-11a), 35.4 (NCH_3), 31.8 (CH_2), 28.0 (CH_2). **22**: Anal. Calcd for $C_{18}H_{21}N_3O_4S$: C, 57.58; H, 5.64; N, 11.19. Found: C, 57.37; H, 5.51; N, 10.98. Ms: m/z (rel. int.) 376 (M^+ +1, 45%), 375 (M^+, 18%), 328 (M^+ -SCH_3, 77%), 300 (100%), 182 (41%), 143 ($C_6H_4CH_2CH_2CHCN^+$, 26%), 114 (98%). Ir (cm^{-1}): 1735 (C=O), 1701 (C=O). ^{1}H-Nmr ($CDCl_3$): δ: 7.40-7.15 (m, 4H, aromat. H), 3.98 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 3.51 (s, 3H, NCH_3), 2.52-2.42 (m, 3H, CH_2-10, CH), 2.15 (s, 3H, SCH_3), 1.93-1.65 (m, 2H, CH_2-11). ^{13}C-Nmr ($CDCl_3$): δ: 169.4 (C=O), 165.8 (C=O), 152.0, 140.5, 136.2, 119.5 (4 C_{qu}), 129.6, 128.4, 127.7, 122.0 (4 $CH_{aromat.}$), 68.8 (C-4a), 52.8 (OCH_3), 52.1 (OCH_3), 43.2 (C-11a), 34.6 (NCH_3), 30.1 (CH_2), 28.9 (CH_2), 13.4 (SCH_3).

General procedure for the synthesis of compounds (16, 19 and 24)

To a solution of **12**, **15** or **22** (1 mmol) in 20 ml of dry toluene *p*-toluenesulfonic acid (100 mg) was added and the mixture was heated at 70°C. The solvent was evaporated and the residue purified by column chromatography.

5,11-Dihydro-5-methyl-1,4-bis(trifluoromethyl)pyridazino[4,5-c][1,5]benzothiazepine (16)

Prepared from 413 mg of **12**. Eluent: toluene. Yield 161 mg (44%) of **16** as yellow crystals, mp 109°C (diluted ethanol). Anal. Calcd for $C_{14}H_9N_3F_6S$: C, 46.03; H, 2.48; N, 11.50. Found: C, 45.82; H, 2.46; N, 11.25. Ms: m/z (rel. int.) 365 (M^+, 100%), 201 (95%), 174 (16%), 109 (26%). Ir (cm^{-1}): 1152, 1126. ^{1}H-Nmr ($CDCl_3$): δ: 7.28-6.93 (m, 4H, aromat. H), 4.48 (s, 2H, SCH_2), 3.37 (s, 3H, NCH_3). ^{13}C-Nmr ($CDCl_3$): δ: 147.0-119.1 (8 C_{qu}), 128.4, 127.3, 124.6, 123.9 (4 $CH_{aromat.}$), 43.3 (NCH_3), 25.9 (SCH_2).

10,11-Dihydro-5-methyl-1,4-bis(trifluoromethyl)-5*H*-pyridazino[4,5-*b*][1]benzazepine (19)

Prepared from 395 mg of **15**. Eluent: light petroleum/ethyl acetate 5:1. Yield 250 mg (72%) of **19**, mp 126-127°C. Anal. Calcd for $C_{15}H_{11}N_3F_6$: C, 51.88; H, 3.19; N, 12.10. Found: C, 51.66; H, 3.13; N, 11.90. Ms: m/z (rel. int.) 347 (M^+, 100%), 332 (M^+ -CH_3, 60%). Ir (cm^{-1}): 1549, 1489, 1152. ^{1}H-Nmr ($CDCl_3$): δ: 7.28-6.99 (m, 4H, aromat. H), 3.45 (s, 3H, NCH_3), 3.42-3.40 (m, 2H, CH_2), 3.18-3.14 (m, 2H, CH_2). ^{13}C-Nmr ($CDCl_3$): δ: 149.5-129.8 (6 C_{qu}), 130.6, 127.7, 124.2, 122.2 (4 $CH_{aromat.}$), 121.6 (q, CF_3, J=276.4 Hz), 121.3 (q, CF_3, J=276.4 Hz), 43.3 (NCH_3), 30.4 (CH_2), 25.4 (CH_2).

Dimethyl 10,11-dihydro-5-methyl-5*H*-pyridazino[4,5-*b*][1]benzazepine-1,4-dicarboxylate (24)

1) Prepared from 375 mg of **22**. Eluent: ethyl acetate. Yield 286 mg (88%) of **24** as an oil.

2) Prepared from **21**: To a solution of **21** (329 mg, 1 mmol) in 20 ml of dry toluene DDQ (227 mg, 1 mmol) was added and the mixture was heated at 80°C for 45 min. The solvent was evaporated and the residue partitioned between dichloromethane and water. The organic layer was dried, the solvent evaporated and the residue chromatographed on silica gel (ethyl acetate) to give 291 mg (89%) of **24** as an oil. Anal. Calcd for $C_{17}H_{17}N_3O_4$: C, 62.38; H, 5.23; N, 12.84. Found: C, 62.19; H, 5.17; N, 12.60. Ms: m/z (rel. int.) 327 (M^+, 100%), 312 (M^+ -CH_3, 66%), 296 (M^+ -OCH_3, 20%), 268 (M^+ -$COOCH_3$, 66%), 236 (51%), 208 (19%). Ir (cm^{-1}): 1735 (C=O). ^{1}H-Nmr ($CDCl_3$): δ: 7.78-7.10 (m, 4H, aromat. H), 4.12 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 3.31 (s, 3H, NCH_3), 3.18 (s, 4H, CH_2CH_2). ^{13}C-Nmr ($CDCl_3$): δ: 166.1 (C=O), 165.5 (C=O), 153.4, 148.4, 146.0, 145.9, 134.3, 130.7 (6 C_{qu}), 129.0, 127.5, 125.5, 123.0 (4 $CH_{aromat.}$), 53.5 (OCH_3), 53.2 (OCH_3), 43.0 (NCH_3), 30.2 (CH_2), 28.7 (CH_2).

Dimethyl 5,11-dihydro-5-methylpyridazino[4,5-*c*][1,5]benzothiazepine-1,4-dicarboxylate (23)

To a solution of **20** (347 mg, 1 mmol) in 20 ml of dry toluene DDQ (227 mg, 1 mmol) was added and the mixture was heated at 80°C for 2 h. After work-up as described above (compound **24**, *method 2*) and recrystallization from methanol 293 mg (85%) of **23** as orange-yellow needles, mp 138°C are obtained. Anal. Calcd for $C_{16}H_{15}N_3O_4S$: C, 55.64; H, 4.38; N, 12.17. Found: C, 55.37; H, 4.16; N, 12.09. Ms: m/z (rel. int.) 345 (M^+, 42%), 286 (M^+ -$COOCH_3$, 100%), 226 (11%), 109 (14%). Ir (cm^{-1}): 1727 (C=O). ^{1}H-Nmr ($CDCl_3$): δ: 7.31-7.03 (m, 4H, aromat. H), 4.43 (s, 2H, SCH_2), 4.11 (s, 3H, OCH_3), 4.04 (s, 3H, OCH_3), 3.25 (s, 3H, NCH_3). ^{13}C-Nmr ($CDCl_3$): δ: 165.3 (C=O), 164.9 (C=O), 150.4, 150.4, 145.9, 144.8, 133.9, 128.9 (6 C_{qu}), 130.0, 127.8, 125.1, 123.9 (4 $CH_{aromat.}$), 53.5 (OCH_3), 53.3 (OCH_3), 43.6 (NCH_3), 29.3 (CH_2).

Dimethyl 10,11-dihydro-5-methyl-8-nitro-5*H*-pyridazino[4,5-*b*][1]benzazepine-1,4-dicarboxylate (25)

At ambient temperature nitrous gas was bubbled through a solution of **21** (329 mg, 1 mmol) in 20 ml of dry toluene. The solvent was evaporated to yield 270 mg (38%) of **25**, mp 205-206°C (dichloromethane/ethanol 1.5:1). Preparation of nitrous gas: To 125 ml of concentrated hydrochloric acid 200 ml of a 6N sodium nitrite solution was added and the resulting gas was bubbled into the reaction vessel *via* argon flow. Anal. Calcd for $C_{17}H_{16}N_4O_6$: C, 54.84; H, 4.33; N, 15.05. Found: C, 54.63; H, 4.26; N, 14.96. Ms: m/z (rel. int.) 372 (M^+, 80%), 357 (M^+ -CH_3, 100%), 313 (M^+ -$COOCH_3$, 65%), 253 (32%). Ir (cm^{-1}): 1725 (C=O). ^{1}H-Nmr ($CDCl_3$): δ: 8.10 (1H, A-part of an ABM-system, J_{AB}=9.2 Hz, J_{AM}=2.8 Hz, shows NOE on irradiation at 7.27 ppm, H-7), 8.02 (1H, M-part of an ABM-system, J_{AM}=2.8 Hz, shows NOE on irradiation at 3.29 ppm, H-9), 7.27 (1H, B-part of an ABM-system, J_{AB}=9.2 Hz, shows NOE on irradiation at 8.10 ppm and at 3.35 ppm, H-6), 4.11 (s, 3H, $COOCH_3$-4), 4.08 (s, 3H, shows NOE on irradiation at 3.35 ppm, $COOCH_3$-1), 3.43-3.40 (m, 2H, CH_2-11), 3.35 (s, 3H, shows NOE on irradiation at 7.27

ppm, NCH_3), 3.30-3.28 (m, 2H, shows NOE on irradiation at 8.02 ppm, CH_2-10). ^{13}C-Nmr ($CDCl_3$): δ: 165.2 (C=O), 164.9 (C=O), 152.4, 150.0, 149.3, 146.8, 142.2, 136.0, 130.2 (7 C_{qu}), 126.2, 122.9, 120.0 (3 $CH_{aromat.}$), 53.8 (OCH_3), 53.4 (OCH_3), 42.2 (NCH_3), 32.0 (CH_2), 25.8 (CH_2).

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