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One-pot syntheses of dihydro benzo[*b*][1,4]thiazepines and -diazepines via coupling–isomerization–cyclocondensation sequences

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Dedicated to Professor Dr. Klaus Theodor Wanner on the occasion of his 50th birthday

Abstract—2,4-Di(hetero)aryl substituted 2,3-dihydro benzo[*b*][1,4]heteroazepines **7** and **9** (hetero = S, NH) can be readily synthesized in a one-pot process initiated by a coupling–isomerization sequence of an electron poor (hetero)aryl halide **4** and a terminal propargyl alcohol **5** subsequently followed by a cyclocondensation with 2-mercapto or 2-amino anilines **6** or **8**, respectively. In addition, the structures were established unambiguously by an X-ray structure analysis of **9b**.

1. Introduction

Sequential transformations and multicomponent reactions are steadily gaining a considerable academic, economic and ecological interest since they address very fundamental principles of synthetic efficiency and reaction design.[1] Mastering unusual combinations of elementary organic reactions under similar conditions is the major conceptual challenge in engineering novel types of sequences. Transition metal catalyzed reactions with exceptionally mild reaction conditions are of a paramount benefit if they can be directed in a domino fashion generating a suitable reactive functionality en route.[2] Additionally, the prospect of extending one-pot sequences into combinatorial and solid phase syntheses[1c,3] promises manifold opportunities for developing novel lead structures of pharmaceuticals, catalysts and even novel molecule based materials. As part of our program designed to develop new multicomponent methodologies initiated by transition metal catalyzed CC-bond formation, we have recently discovered and developed an new mode of alkyne activation by a detouring outcome of the Sonogashira coupling, that is, a coupling–isomerization reaction (CIR).[4] Conceptually, the cross-coupling reaction of an electron deficient halide with a terminal alkyne not only activates the newly formed internal triple bond towards Michael-type additions, but also stimulates the propargyl position, for example, towards an alkyne–allene isomerization (Scheme 1).

In particular, the Sonogashira coupling of electron poor halides with 1-(hetero)aryl propargyl alcohols furnishes chalcones in good to excellent yields. With this new enone synthesis in hand and based upon the inherent bifunctional electrophilicity of the in situ generated Michael acceptor as a pivotal point, we have disclosed novel three- and four-component syntheses of various heterocycles in the sense of sequential one-pot reactions (Scheme 2).[4–8h] Here, we report a facile one-pot synthesis of 2,4-di(hetero)aryl substituted 2,3-dihydro benzo[*b*][1,4]diazepines and thiazepines based upon a CIR sequence with a subsequent cyclocondensation with 2-amino or 2-mercapto anilines.

2. Results and discussion

Dihydro benzodiazepines **1** and **2** (Fig. 1) constitute an important class of psychopharmaca.[9] In particular, derivatives of dihydro benzo[*b*][1,4]diazepines **2** have aroused considerable interest as CNS active anticonvulsant drugs,[10] but also as in vitro non-nucleoside inhibitors of HIV-1 reverse transcriptase.[11]

Besides these compounds, also the dihydro 1,4-benzothiazepines **3** (Fig. 1) have become increasingly interesting since they show anti-fungal, anti-bacterial,[12] anti-feedant,[13]

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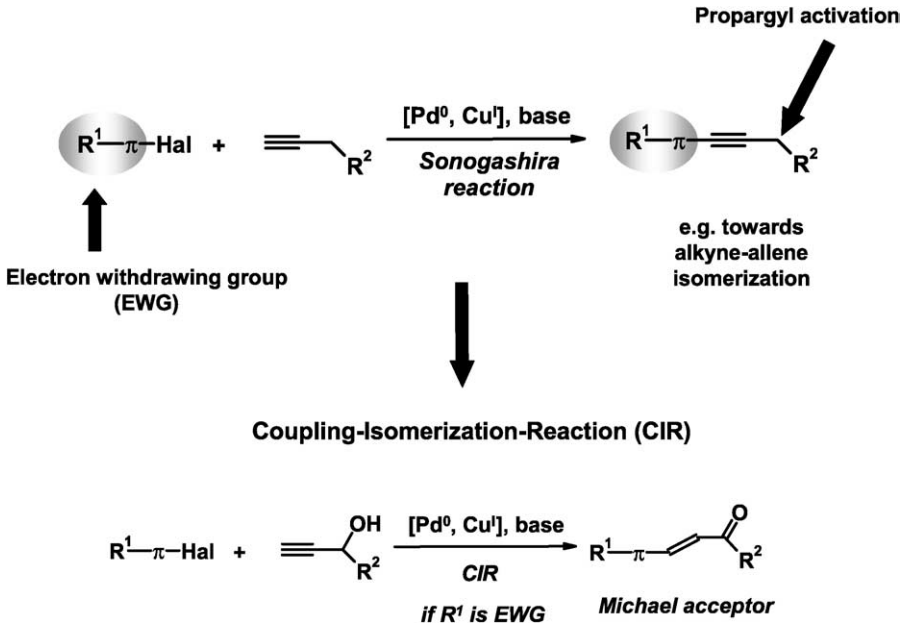


Scheme 1. The coupling–isomerization-reaction (CIR) as a new mode of alkyne activation by cross-coupling.

anti-inflammatory, analgesic,[14] and anti-convulsant[15] activity. Furthermore, they can be oxidized to 1,4-benzothiazepines under mild conditions.[16]

Our new CIR-chalcone synthesis (vide supra) opens a straightforward convergent and modular access to 2,3-dihydro benzo[*b*][1,4]heteroazepines in a one-pot fashion. Thus, upon reacting electron poor (hetero)aryl halides **4** and 1-phenyl propynol (**5a**) under the reaction conditions of the Sonogashira coupling in boiling mixture of triethylamine and THF and the subsequent addition of 2-amino thiophenols **6** as suitable 1,4-dinucleophilic component and acetic acid, the beige to yellow 2,3-dihydro benzo[*b*][1,4]thiaazepines **7** were isolated in 38–85% yield (Scheme 3).

Likewise, the addition of *ortho*-phenylene diamine (**8**) after the CIR of electron poor (hetero)aryl halides **4** and 1-aryl propynol **5** furnishes the beige to yellow 2,3-dihydro benzo[*b*][1,4]diazepines **9** in 39–79% yield (Scheme 4).

The structures of the benzothiazepines **7** and benzodiazepines **9** were unambiguously assigned by ^{1}H, ^{13}C, COSY, and NOESY NMR experiments. As a consequence of the Michael addition–cyclocondensation of the amino thiophenols and *o*-phenylene diamine to the transient enone functionality three distinct aliphatic proton resonances, a methine and two diastereotopic methylene protons, appear most characteristically in the ^{1}H spectra as splitting patterns (doublets of doublets) of ABM spin systems. Therefore, due to the characteristic geminal and vicinal coupling constants (^{2}J=12.3–13.9 Hz, ^{3}J=4.3–4.9 Hz, ^{3}J=6.8–9.6 Hz) the signals at δ 2.72–3.29 and δ

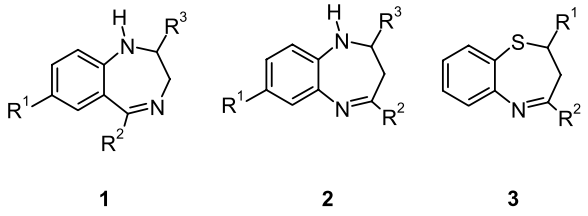
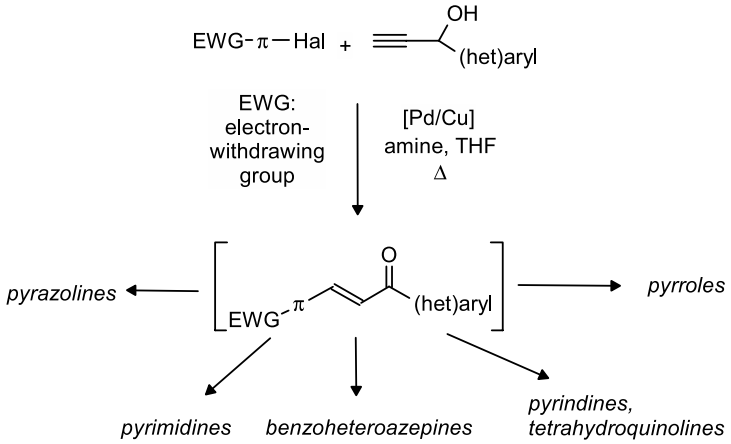
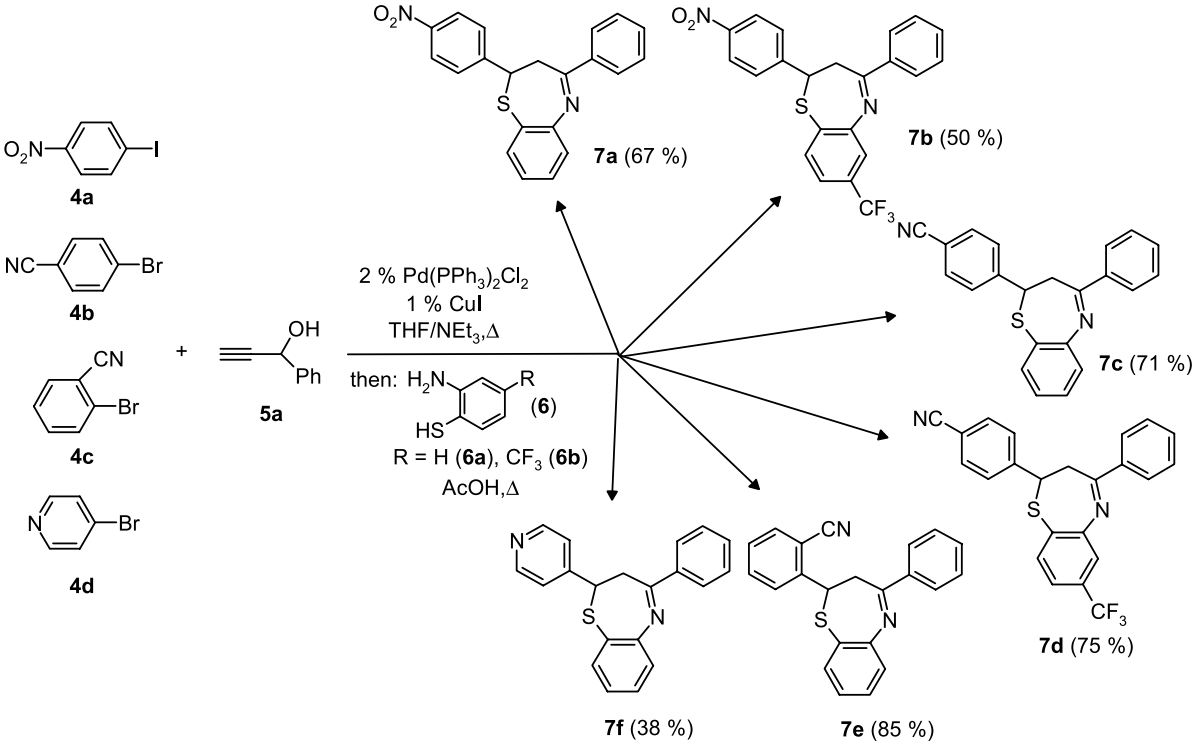


Figure 1.



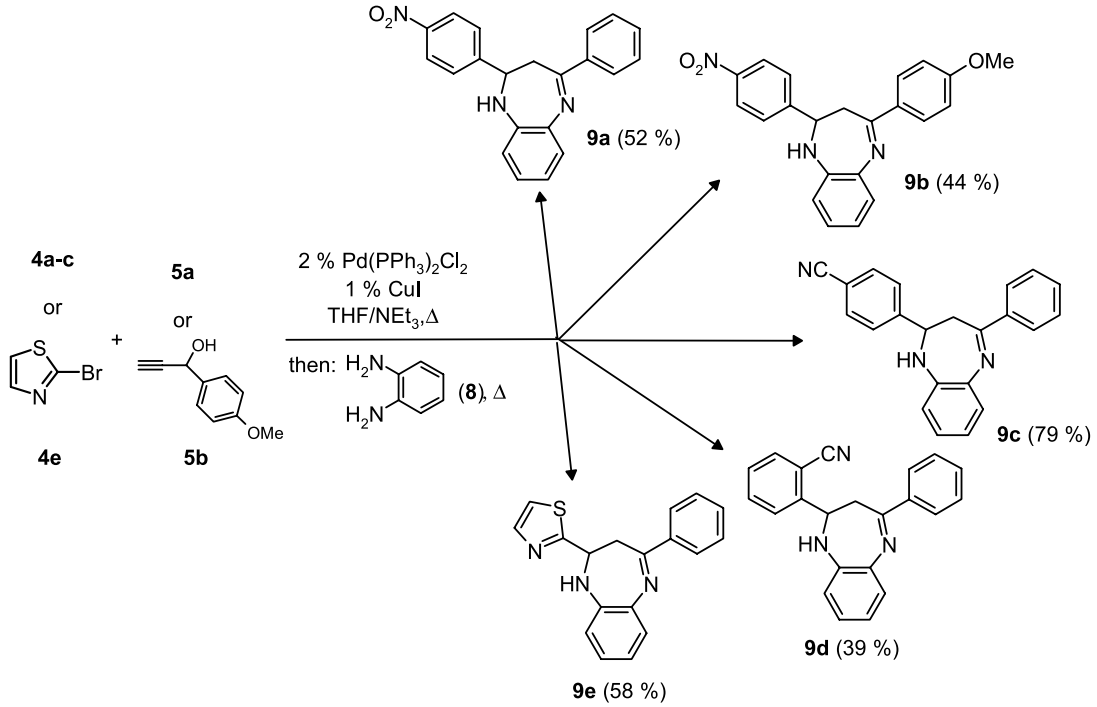
Scheme 2. One-pot syntheses of heterocycles based upon a CIR sequence.



Scheme 3. One-pot threecomponent synthesis of 2,3-dihydro benzo[*b*][1,4]thiazepines **7**.

2.90–3.50 can be assigned to the diastereotopic methylene protons. Conformation analyses applying the Karplus correlation of coupling constants and dihedral angles suggests that the thi- or diazepine core of the bicyclic molecules only displays low conformational flexibility. Furthermore, the appearance of vicinal coupling constants (^3J=4.3–4.9 Hz, ^3J=6.5–9.6 Hz) for the signals at δ 4.24–5.84 completes the assignment of the methine resonances. Furthermore, the signals of the (hetero)aromatic and aliphatic protons can be detected with expected chemical shifts.

Most indicatively, in the carbon NMR spectra the quaternary carbonyl resonances of the imine carbon nuclei are found between δ 158.1–170.3. The methine and methylene carbon nuclei resulting from the Michael



Scheme 4. One-pot threecomponent synthesis of 2,3-dihydro benzo[*b*][1,4]diazepines **9**.

addition appear at δ 57.4–73.3 and δ 35.1–37.4, respectively.

Another strong spectroscopic support of benzoheteroazepine formation can be derived from the mass spectra, revealing that a benzyl and an α-cleavage (with respect to the imine group) furnish the by far most dominant fragment ($[M\text{-Acc-}\pi\text{-CH}{=}CH_2]^+$). In the IR spectra typical CN-valence vibrations of imines are found between 1604 and 1635 cm^{-1}.

Furthermore, the structure of benzodiazepines **9** was unambiguously corroborated by an X-ray crystal structure analysis (Fig. 2) of compound **9b**.[17] The imine functionality is almost fully conjugated with the anisyl substitutent and the annealed benzo ring as clearly supported by dihedral angles of 14.0° (C21–C16–C8–N2) and 2.3° (N2–C7–C6–H6). Interestingly, the seven-membered ring adopts a chair/twist conformation as indicated by the angle (33.2°) between the plane formed by C1–C8–C9 and the annealed benzo ring.

Although, several attempts were tested to expand the scope of this facile coupling–condensation sequence to aliphatic heteroazepines no satisfying results were obtained. Conformationally flexible dinucleophiles like ethylene diamine or cysteine methylester give rise to a complex mixture of products, some of them are definitely aldol cleavage products as detected by mass spectrometry and proton NMR analysis. Structurally rigid aliphatic diamines such as (*R*,*R*)-1,2-diamino cyclohexane react in analogy to *ortho*-phenylene diamine according to NMR and mass spectrometry of the crude product furnishing a single diastereomer, however, upon purification (column chromatography or recrystallization from reasonably polar solvents) solvolysis lead to the isolation of the chalcone precursor. Hence, at this point the coupling–condensation sequence to heteroazepines is restricted to the formation of benzo derivatives.

In conclusion, we have disclosed a straightforward convergent and modular one-pot synthesis of 2,3-dihydro benzo[*b*][1,4]thiazepines **7** and 2,3-dihydro benzo[*b*][1,4]diazepines **9** based upon a CIR–cyclocondensation sequence of electron poor (hetero)aryl halides, 1-aryl propargyl alcohols, and 2-mercapto anilines or *ortho*-phenylene diamine, respectively. Further studies to enhance molecular diversity in pharmaceutically interesting targets and extension to a combinatorial approach to 2,3-dihydro benzo[*b*][1,4]heteroazepines are currently under investigation.

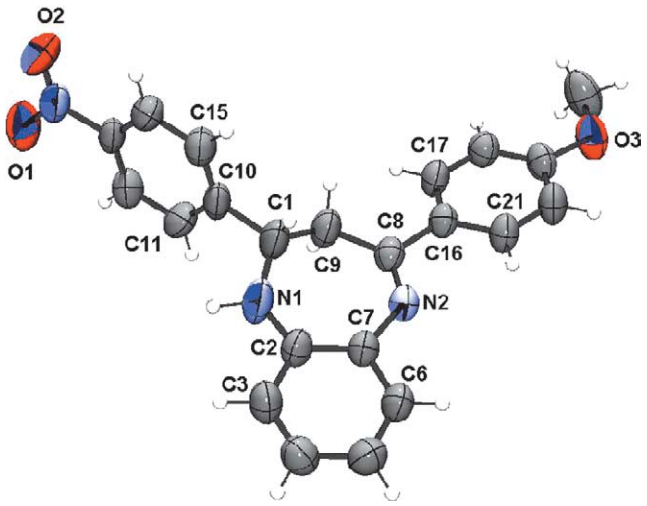


Figure 2. ORTEP-plot of benzodiazepine **9b**.

3. Experimental

All reactions involving water-sensitive compounds were carried out in oven-dried Schlenk glassware under a nitrogen atmosphere. The solvents were dried according to standard procedures[18] and were distilled prior to use. Column chromatography: silica gel 60 M (mesh 230–400) Macherey-Nagel or aluminium oxide 5016 A basic Fluka. Thin layer chromatography (TLC): silica gel layered aluminium foil (60 F_{254} Merck, Darmstadt) or aluminum oxide layered aluminium foil (60 F_{254} Merck, Darmstadt). Melting points (uncorrected): Büchi Melting Point B-540. The aryl propynols **5** were synthesized according to literature procedures.[19] Electron-poor (hetero)aryl halides **4**, 2-mercapto anilines **6** and *ortho*-phenylene diamine (**8**) were purchased from ACROS or Merck and used without further purification. ^1H and ^{13}C NMR spectra: Bruker ARX250, Bruker DRX 300, Bruker ARX 300, Varian VXR 400S, Bruker DRX500 or Bruker AC300 with $CDCl_3$ as a solvent. The assignments of quaternary C, CH, CH_2 and CH_3 was made on the basis of DEPT spectra. IR: Bruker Vector 22 FT-IR or Perkin Elmer Models Lambda 16. UV/VIS: Hewlett Packard HP8452 A. MS: Finnigan MAT 90, MAT 95 Q, Jeol JMS-700 and Finnigan TSQ 700. Elemental analyses were carried out in the microanalytical laboratories of Department Chemie der Universität München and the Organisch-Chemisches Institut der Universität Heidelberg.

3.1. General procedure for the one-pot synthesis of benzodiazepines and benzothiazepines

A magnetically stirred solution of 1.00 mmol of halogen compound **4**, 1.05 mmol of propargyl alcohol **5**, 14 mg (0.02 mmol) of $Pd(PPh_3)_2Cl_2$, and 2 mg (0.01 mmol) of CuI in 5 mL of degassed triethylamine under nitrogen was heated to reflux temperature for 16 h (for experimental details see Table 1). After cooling to room temperature a solution of 1.1 mmol of a 2-amino thiophenol **6** and 1.6 mL of acetic acid or 1.1 mmol of *o*-phenylene diamine (**8**) were added and the reaction mixture was heated to reflux temperature for the times indicated. After cooling 15 mL of diethylether was added and the mixture was filtered (for benzodiazepines **9**). Then, the solvents were removed from the filtrate in vacuo. For benzothiazepines **7** the reaction mixture was poured into a saturated aqueous solution of potassium carbonate. The aqueous phase was extracted with diethylether and the combined organic layers were dried with anhydrous sodium sulfate and filtered. The solvents were removed in vacuo. Crude **7** and **9** were chromatographed on silica gel and/or recrystallized to give the analytically pure benzothiazepines **7** or benzodiazepines **9**.

Table 1. Experimental details of the one-pot synthesis of 2,3-dihydro benzo[*b*][1,4]thiazepines **7** and 2,3-dihydro benzo[*b*][1,4]diazepines **9**

Aryl halide **4**	Propargyl alcohol **5**	Aniline **6/8**	THF (mL)	NEt_3 (mL)	Time (h)	Yield
249 mg (1.00 mmol) of **4a**	139 mg (1.05 mmol) of **5a**	137 mg (1.09 mmol) of **6a**	6.0	3.5	20	242 mg (67%) of **7a**
249 mg (1.00 mmol) of **4a**	139 mg (1.05 mmol) of **5a**	253 mg (1.10 mmol) of **6b**[a]	6.0	3.5	24	242 mg (50%) of **7b**
182 mg (1.00 mmol) of **4b**	139 mg (1.05 mmol) of **5a**	137 mg (1.09 mmol) of **6a**	6.0	3.5	14	241 mg (71%) of **7c**
182 mg (1.00 mmol) of **4b**	139 mg (1.05 mmol) of **5a**	253 mg (1.10 mmol) of **6b**[a]	6.0	3.5	24	307 mg (75%) of **7d**
182 mg (1.00 mmol) of **4c**	139 mg (1.05 mmol) of **5a**	137 mg (1.09 mmol) of **6a**	6.0	3.5	24	289 mg (85%) of **7e**
195 mg (1.00 mmol) of **4d**[b]	139 mg (1.05 mmol) of **5a**	137 mg (1.09 mmol) of **6a**	6.0	3.5	8.5	120 mg (38%) of **7f**
249 mg (1.00 mmol) of **4a**	139 mg (1.05 mmol) of **5a**	119 mg (1.10 mmol) of **8**	6.0	3.0	24	269 mg (52%) of **9a**
249 mg (1.00 mmol) of **4a**	162 mg (1.05 mmol) of **5b**	119 mg (1.10 mmol) of **8**	10	5.0	23	163 mg (44%) of **9b**
182 mg (1.00 mmol) of **4b**	139 mg (1.05 mmol) of **5a**	119 mg (1.10 mmol) of **8**	3.0	2.0	36	254 mg (79%) of **9c**
182 mg (1.00 mmol) of **4c**	139 mg (1.05 mmol) of **5a**	119 mg (1.10 mmol) of **8**	10	5.0	16	125 mg (39%) of **9d**
164 mg (1.00 mmol) of **4e**	139 mg (1.05 mmol) of **5a**	119 mg (1.10 mmol) of **8**	3.0	2.0	36	177 mg (58%) of **9e**

[a] As **3b** hydrochloride.
[b] As **1d** hydrochloride.

3.1.1. 2-(4-Nitro-phenyl)-4-phenyl-2,3-dihydro-benzo[*b*][1,4]thiazepine (7a). According to the standard procedure and after chromatography on silica gel (petrolether/ethyl acetate 4:1) and after recrystallization from ethanol **7a** was isolated as pale yellow needles, mp 185 °C (181 °C).[20] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.09 (m, 1H), 3.40 (dd, J=4.9, 12.8 Hz, 1H), 5.04 (dd, J=4.8, 12.5 Hz, 1H), 7.26–7.20 (m, 1H), 7.62–7.45 (m, 8H), 8.18 (d, J=8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 37.3 (CH_2), 59.2 (CH), 122.3 ($C_{quat.}$), 124.2 (CH), 124.2 ($C_{quat.}$), 125.9 (CH), 126.4 (CH), 127.0 (CH), 127.9 (CH), 129.1 (CH), 130.6 (CH), 132.2 (CH), 135.1 (CH), 136.2 ($C_{quat.}$), 147.4 ($C_{quat.}$), 150.4 ($C_{quat.}$), 169.8 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)): 360 (M^+, 7), 224 (14), 211 ($M^+ - O_2NC_6H_4CHCH_2$, 100). IR (KBr): $\tilde{\nu}$ 1608 cm^{-1}, 1596, 1574, 1517, 1452, 1348, 1320, 1245, 1214, 1110, 1024, 856, 827, 787, 748, 700, 689, 613, 484. UV/Vis ($CHCl_3$): λ_{max} (ε) 264 nm (25,800), 322 (8000). Anal. calcd for $C_{21}H_{16}N_2O_2S$ (360.5): C 69.77, H 4.48, N 7.77, S 8.90. Found: C 69.78, H 4.45, N 7.73, S 8.78.

3.1.2. 2-(4-Nitro-phenyl)-4-phenyl-7-trifluoromethyl-2,3-dihydro-benzo[*b*][1,4]thiazepine (7b). According to the standard procedure and after chromatography on silica gel (petrolether/ethyl acetate 1:1) and after recrystallization from ethanol **7a** was isolated as a colorless solid, mp 166–167 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.13 (m, 1H), 3.50 (dd, J=4.9, 13.1 Hz, 1H), 5.14 (dd, J=4.3, 12.3 Hz, 1H), 7.46 (d, J=9.1 Hz, 2H), 7.50–7.66 (m, 4H), 7.74–7.85 (m, 2H), 8.12–8.17 (m, 2H), 8.23 (d, J=9.1 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 36.8 (CH_2), 59.5 (CH), 121.9 (q, J_{CF}=3.5 Hz, CH), 122.7 (q, J_{CF}=3.8 Hz, CH), 124.3 (CH), 126.3 (q, J=271.1 Hz $C_{quat.}$), 127.0 (CH), 127.5 (CH), 128.1 ($C_{quat.}$), 128.5 ($C_{quat.}$), 128.6 ($C_{quat.}$), 128.9 ($C_{quat.}$), 129.0 (CH), 131.9 (CH), 135.7 (q, J=29.1 Hz $C_{quat.}$), 135.3 (CH), 147.5 ($C_{quat.}$), 169.5 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)): 428 (M^+, 8), 292 (19), 279 ($M^+ - O_2NC_6H_4CHCH_2$, 100). IR (KBr): $\tilde{\nu}$ 1614 cm^{-1}, 1576, 1522, 1407, 1348, 1331, 1256, 1201, 1169, 1131, 1084, 901, 700. UV/Vis ($CHCl_3$): λ_{max} (ε) 268 (27,700) nm. Anal. calcd for $C_{22}H_{15}F_3N_2O_2S$ (428.5): C 61.68, H 3.53, N 6.54. Found: C 61.40, H 3.67, N 6.40.

3.1.3. 2-(4-Cyanophenyl)-4-phenyl-2,3-dihydro-benzo[*b*][1,4]thiazepine (7c). According to the standard procedure and after chromatography on silica gel (petrolether/ethyl acetate 4:1) and after recrystallization from ethanol **7c** was isolated as pale yellow needles, mp 192–193 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.03 (m, 1H), 3.30 (dd, J=4.9, 12.9 Hz, 1H), 4.97 (dd, J=7.7, 12.6 Hz, 1H), 7.16 (dt, J=1.4, 7.5 Hz, 1H), 7.32 (dd, J=1.9, 7.8 Hz, 1H), 7.41 (d, J=8.3 Hz, 2H), 7.61–7.46 (m, 7H), 8.04 (dd, J=1.4, 7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 36.7 (CH_2), 59.4 (CH), 111.3 ($C_{quat.}$), 118.3 ($C_{quat.}$), 121.6 ($C_{quat.}$), 125.2 (CH), 125.3 (CH), 126.6 (CH), 127.1 (CH), 128.6 (CH), 130.0 (CH), 131.0 (CH), 132.4 (CH), 134.7 (CH), 137.1 ($C_{quat.}$), 148.6 ($C_{quat.}$), 152.2 ($C_{quat.}$), 168.1 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)): 340 (M^+, 8), 211 ($M^+ - NCC_6H_4CHCH_2$, 100), 108 ($C_6H_4S^+$, 15). IR (KBr): $\tilde{\nu}$ 3054 cm^{-1}, 2229, 1609, 1574, 1500, 1452, 1434, 1414, 1324, 1246, 1214, 1182, 1110, 1064, 1020, 834, 792, 761, 694, 563, 484, 454. UV/Vis ($CHCl_3$): λ_{max} (ε) 244 nm (28,700). Anal. calcd for $C_{22}H_{16}N_2S$ (340.5): C 77.62, H 4.74, N 8.23, S 9.42. Found: C 77.48, H 4.76, N 8.26, S 9.52.

3.1.4. 2-(4-Cyanophenyl)-4-phenyl-7-trifluoromethyl-2,3-dihydro-benzo[*b*][1,4]thiazepine (7d). According to the standard procedure and after triturating with ethanol and after recrystallization from ethanol **7d** was isolated as a colorless solid, mp 178–179 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.08 (m, 1H), 3.45 (dd, J=4.7, 12.9 Hz, 1H), 5.05 (dd, J=4.6, 12.4 Hz, 1H), 7.39–7.48 (m, 3H), 7.55–7.65 (m, 5H), 7.72–7.78 (m, 2H), 8.12 (d, J=7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 37.3 (CH_2), 59.6 (CH), 112.6 ($C_{quat.}$), 119.2 ($C_{quat.}$), 122.4 (q, J=3.7 Hz, CH), 123.0 (q, J=3.7 Hz, CH), 126.3 (q, J=271.1 Hz $C_{quat.}$), 127.7 (CH), 128.1 (CH), 129.0 (CH), 132.5 (CH), 133.4 ($C_{quat.}$), 133.5 (CH), 133.6 (q, J=29.1 Hz $C_{quat.}$), 136.2 (CH), 137.6 ($C_{quat.}$), 149.1 ($C_{quat.}$), 153.6 ($C_{quat.}$), 170.3 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)): 408 (M^+, 5), 292 (16), 279 ($M^+ - NCC_6H_4CHCH_2$, 100), IR (KBr): $\tilde{\nu}$ 3062 cm^{-1}, 2230, 1611, 1576, 1502, 1452, 1407, 1331, 1304, 1256, 1202, 1169, 1125, 1082, 1021, 899, 830, 769, 755, 690, 563. UV/Vis ($CHCl_3$): λ_{max} (ε) 242 nm (25,200), 266 (21,200). Anal. calcd for $C_{23}H_{15}F_3N_2S$ (408.4): C 67.64, H 3.70, N 6.86. Found: C 67.62, H 3.42, N 6.84.

3.1.5. 2-(2-Cyanophenyl)-4-phenyl-2,3-dihydro-benzo[*b*][1,4]thiazepine (7e). According to the standard procedure and after triturating with ethanol and after recrystallization from ethanol **7e** was isolated as a beige solid, mp 183–184 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.95 (m, 1H), 3.44 (dd, J=4.9, 12.9 Hz, 1H), 5.49 (dd, J=4.9, 12.5 Hz, 1H), 7.17–7.23 (m, 1H), 7.34–7.41 (m, 2H), 7.48–7.58 (m, 5H), 7.62–7.70 (m, 2H), 7.77 (d, J=8.0 Hz, 1H),

8.19–8.22 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 37.4 (CH_2), 57.4 (CH), 109.9 ($C_{quat.}$), 117.4 ($C_{quat.}$), 122.4 ($C_{quat.}$), 125.8 (CH), 125.9 (CH), 127.4 (CH), 127.8 (CH), 128.2 (CH), 129.0 (CH), 130.3 (CH), 131.8 (CH), 132.7 (CH), 133.5 (CH), 135.0 (CH), 136.6 ($C_{quat.}$), 147.4 ($C_{quat.}$), 151.7 ($C_{quat.}$), 168.9 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)) 340 (M^+, 17), 338 (M^+-H_2, 17), 236 (M^+-H_2–$NCC_6H_4^+$, 11), 224 (97), 211 ($M^+-NCC_6H_4CHCH_2$, 100), 108 ($C_6H_4S^+$, 10). IR (KBr): $\tilde{\nu}$ 3053 cm^{-1}, 2220, 1612, 1598, 1575, 1478, 1451, 1320, 1259, 1244, 1214, 1064, 1024, 834, 796, 760, 744, 688, 559, 475. UV/Vis ($CHCl_3$): λ_{max} (ε) 264 nm (18,200), 336 (4500). Anal. calcd for $C_{22}H_{16}N_2S$ (340.4): C 77.62, H 4.74, N 8.23, S 9.42. Found: C 77.45, H 4.81, N 8.17, S 9.49.

3.1.6. 4-Phenyl-2-(4-pyridyl)-2,3-dihydro-benzo[*b*][1,4]thiazepine (7f). According to the standard procedure and after chromatography on silica gel (petrolether/ethyl acetate 4:1) and after recrystallization from ethanol **7f** was isolated as brown resin. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.72 (dd, J=9.5, 13.7 Hz, 1H), 2.90 (dd, J=5.4, 13.8 Hz, 1H), 4.24 (dd, J=5.4, 9.6 Hz, 1H), 7.09–7.11 (m, 2H), 7.18–7.59 (m, 7H), 7.80–8.11 (m, 2H), 8.56 (br, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 36.3 (CH_2), 73.3 (CH), 119.8 ($C_{quat.}$), 127.3 (CH), 127.8 (CH), 128.3 (CH), 128.5 (CH), 129.1 (CH), 129.2 (CH), 129.7 (CH), 131.5 (CH), 137.3 ($C_{quat.}$), 143.0 ($C_{quat.}$), 147.6 ($C_{quat.}$), 149.0 (CH), 158.1 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)) 316 (M^+, 2), 224 (100). EI HRMS (70eV, *m/z*) calcd for $C_{20}H_{16}N_2S$: 316.1034, found: 316.1047. IR (KBr): $\tilde{\nu}$ 2924 cm^{-1}, 1635, 1597, 1467, 1445, 1375, 1254, 1218, 1179, 1072, 992, 761, 690. UV/Vis ($CHCl_3$): λ_{max} (ε) 260 (15,800).

3.1.7. 2-(4-Nitrophenyl)-4-phenyl-2,3-dihydro-benzo[*b*][1,4]diazepine (9a). According to the standard procedure and after chromatography on silica gel (petrolether/ethyl acetate 5:1) and after recrystallization from ethanol **9a** was isolated as orange crystals, mp 189–190 °C (189–190 °C).[21] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.10 (dd, J=7.1, 13.5 Hz, 1H), 3.23 (dd, J=4.4, 13.5 Hz, 1H), 3.78 (br, 1H, NH), 5.41 (dd, J=4.4, 7.0 Hz, 1H), 6.84–6.87 (m, 1H), 7.07–7.11 (m, 2H), 7.29–7.38 (m, 4H), 7.61 (d, J=8.6 Hz, 2H), 7.70–7.73 (m, 2H), 8.14 (d, J=8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 36.6 (CH_2), 70.5 (CH), 120.7 (CH), 122.2 (CH), 124.0 (CH), 126.7 (CH), 126.8 (CH), 127.1 (CH), 128.4 (CH), 128.7 (CH), 130.4 (CH), 137.7 ($C_{quat.}$), 138.7 ($C_{quat.}$), 139.8 ($C_{quat.}$), 147.5 ($C_{quat.}$), 151.5 ($C_{quat.}$), 166.8 ($C_{quat.}$).

3.1.8. 4-(4-Methoxyphenyl)-2-(4-nitrophenyl)-2,3-dihydro-benzo[*b*][1,4]diazepine (9b). According to the standard procedure and after chromatography on silica gel (petrolether/ethyl acetate 3:1) and after recrystallization from ethanol **9b** was isolated as a yellow solid, mp 186–187 °C (186–187 °C).[22] ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.05 (dd, J=6.8, 13.5 Hz, 1H), 3.19 (dd, J=4.7, 13.5 Hz, 1H), 3.82 (s, 3H), 5.40 (dd, J=4.7, 6.5 Hz, 1H), 6.82 (d, J=8.9 Hz, 2H), 6.83–6.86 (m, 1H), 7.05–7.09 (m, 2H), 7.31–7.34 (m, 1H), 7.62 (d, J=8.7 Hz, 2H), 7.67 (d, J=8.9 Hz, 2H), 8.15 (d, J=8.7 Hz, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 36.2 (CH_2), 55.4 (CH_3), 70.7 (CH), 113.3 ($C_{quat.}$), 113.7 (CH), 120.8 (CH), 122.3 (CH), 124.0 (CH), 126.2 (CH), 127.1 (CH), 128.5 (CH), 128.6 (CH), 131.3 ($C_{quat.}$), 137.6 ($C_{quat.}$), 147.5 ($C_{quat.}$), 151.6 ($C_{quat.}$), 161.6 ($C_{quat.}$), 166.3 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)): 373 (M^+, 85), 358 (M^+-CH_3, 45), 266 ($M^+-C_6H_4OMe$, 20), 224 ($M^+-O_2NC_6H_4CHCH_2$, 100), 209 ($C_6H_4N{=}CC_6H_4OMe^+$, 24), 181 (24), 133 ($MeOC_6H_4CCH_2^+$, 32), 119 ($MeOC_6H_4C^+$, 19), 77 (Ph^+, 13). IR (KBr): $\tilde{\nu}$ 3372 cm^{-1}, 3071, 2836, 1604, 1570, 1514, 1479, 1417, 1346, 1288, 1251, 1175, 1108, 1038, 855, 833, 756, 699, 628, 531. UV/Vis ($CHCl_3$): λ_{max} (ε) 275 nm (26,200), 351 (8800). Anal. calcd for $C_{22}H_{19}N_3O_3$ (373.4): C 70.76, H 5.13, N 11.25. Found: C 70.58, H 5.19, N 11.40.

3.1.9. 2-(4-Cyanophenyl)-4-phenyl-2,3-dihydro-benzo[*b*][1,4]diazepine (9c). According to the standard procedure and after chromatography on silica gel (petrolether/ethyl acetate 3:1) and after recrystallization from isopropanol **9c** was isolated as a beige solid, mp 183 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.06 (dd, J=7.2, 13.4 Hz, 1H), 3.20 (dd, J=4.4, 13.4 Hz, 1H), 3.74 (br, 1H), 5.34 (dd, J=4.4, 7.2 Hz, 1H), 6.82–6.85 (m, 1H), 7.03–7.11 (m, 2H), 7.29–7.41 (m, 4H), 7.52–7.59 (m, 4H), 7.68–7.71 (m, 2H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 36.7 (CH_2), 70.6 (CH), 111.7 ($C_{quat.}$), 118.6 ($C_{quat.}$), 120.6 (CH), 122.0 (CH), 126.6 (CH), 126.8 (CH), 126.9 (CH), 128.4 (CH), 128.9 (CH), 130.4 (CH), 132.6 (CH), 137.7 ($C_{quat.}$), 138.7 ($C_{quat.}$), 149.6 ($C_{quat.}$), 155.9 ($C_{quat.}$), 166.9 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)): 323 (M^+, 62), 308 (M^+-NH, 23), 246 ($M^+-C_6H_5$, 29), 221 ($M^+-NCC_6H_4$, 28), 194 ($M^+-NCC_6H_4CHCH_2$, 100). IR (KBr): $\tilde{\nu}$ 3058 cm^{-1}, 2227, 1608, 1498, 1475, 1448, 1350, 1330, 1298, 1249, 1230, 1113, 1099, 833, 761, 693, 566. UV/Vis ($CHCl_3$): λ_{max} (ε) 242 nm (23,022), 260 (19,200), 362 (4800). Anal. calcd for $C_{22}H_{17}N_3$ (323.4): C 81.71, H 5.30, N 12.99. Found: C 81.42, H 5.24, N 12.83.

3.1.10. 2-(2-Cyanophenyl)-4-phenyl-2,3-dihydro-benzo[*b*][1,4]diazepine (9d). According to the standard procedure and after chromatography on silica gel (petrolether/ethyl acetate 4:1) and after recrystallization from ethanol **9d** was isolated as a yellow orange solid, mp 161–163 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 3.19 (dd, J=6.4, 13.5 Hz, 1H), 3.27 (dd, J=4.6, 13.5 Hz, 1H), 3.81 (br, 1H, NH), 5.84 (m, 1H), 6.89 (d, J=6.8 Hz, 1H), 7.04–7.12 (m, 2H), 7.26–7.36 (m, 5H), 7.42–7.47 (m, 1H), 7.63 (d, J=7.6 Hz, 1H), 7.72 (d, J=6.8 Hz, 2H), 7.87 (d, J=8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 35.7 (CH_2), 68.6 (CH), 109.7 ($C_{quat.}$), 117.3 ($C_{quat.}$), 120.7 (CH), 122.0 (CH), 126.6 (CH), 126.8 (CH), 127.4 (CH), 128.1 (CH), 128.3 (CH), 128.9 (CH), 130.2 (CH), 132.9 (CH), 133.2 (CH), 138.0 ($C_{quat.}$), 138.7 ($C_{quat.}$), 139.7 ($C_{quat.}$), 148.4 ($C_{quat.}$), 166.9 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)): 323 (M^+, 25), 320 (M^+-H_2–H, 100), 308 (M^+-NH, 14), 246 (M^+-Ph, 22), 219 ($M^+-C_6H_4N_2$, 57), 194 ($M^+-NCC_6H_4CHCH_2$, 53). IR (KBr): $\tilde{\nu}$ 3064 cm^{-1}, 2222, 1612, 1573, 1478, 1448, 1335, 1264, 1108, 858, 764, 693, 528. UV/Vis ($CHCl_3$): λ_{max} (ε) 263 nm (20,300), 362 (27,900). Anal. calcd for $C_{22}H_{17}N_3$ (323.4): C 81.71, H 5.30, N 12.99. Found: C 81.71, H 5.31, N 12.88.

3.1.11. 4-Phenyl-2-(2-thiazolyl)-2,3-dihydro-benzo[*b*][1,4]diazepine (9e). According to the standard procedure and after chromatography on silica gel (petrolether/ethyl acetate 2:1) and after crystallization from isopropanol **9e** was isolated as yellow resin. ^{1}H NMR ($CDCl_3$,

300 MHz): δ 3.29 (dd, J=4.8, 13.9 Hz, 1H), 3.30 (dd, J=5.7, 13.4 Hz, 1H), 5.67–5.71 (m, 1H), 6.87–6.90 (m, 1H), 7.03–7.13 (m, 3H), 7.25–7.34 (m, 4H), 7.70–7.75 (m, 3H). ^{13}C NMR ($CDCl_3$, 75 MHz): δ 35.1 (CH_2), 69.5 (CH), 119.1 (CH), 121.0 (CH), 122.5 (CH), 126.1 (CH), 126.6 (CH), 128.0 (CH), 128.1 (CH), 130.0 (CH), 136.7 ($C_{quat.}$), 138.4 ($C_{quat.}$), 140.6 ($C_{quat.}$), 142.6 (CH), 167.1 ($C_{quat.}$), 175.1 ($C_{quat.}$). EI MS (70 eV, *m/z* (%)): 305 (M^+, 96), 303 ($M^+ - H_2$, 30), 228 ($M^+ - C_6H_5$, 20), 221 (M^+ − thiazolyl, 35) 194 (M^+ − thiazolylCHCH$_2$, 100), 179 ($C_6H_5C{=}NC_6H_4^+$, 22), 84 (thiazolyl$^+$, 69), 77 ($C_6H_5^+$, 14). EI HRMS (70eV, *m/z*) calcd for $C_{18}H_{15}N_3S$: 305.0993, found: 305.0988. IR (KBr): $\tilde{\nu}$ 3057 cm^{-1}, 1609, 1569, 1496, 1473, 1445, 1345, 1314, 1293, 1256, 1226, 1180, 1139, 1111, 1054, 769, 753, 729, 691. UV/Vis ($CHCl_3$): λ_{max} (ε) 254 nm (18,500), 352 (5200). Anal. calcd for $C_{18}H_{15}N_3S$ (305.4): C 70.79, H 4.95, N 13.76, S 10.50. Found: C 70.47, H 5.21, N 12.97, S 10.19.

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