Synthesis of Benzo[*b*][1,4]thiazepines by the Reaction of 3-Aryl-1-(3-coumarinyl)propen-1-ones with 2-Aminothiophenol [1]

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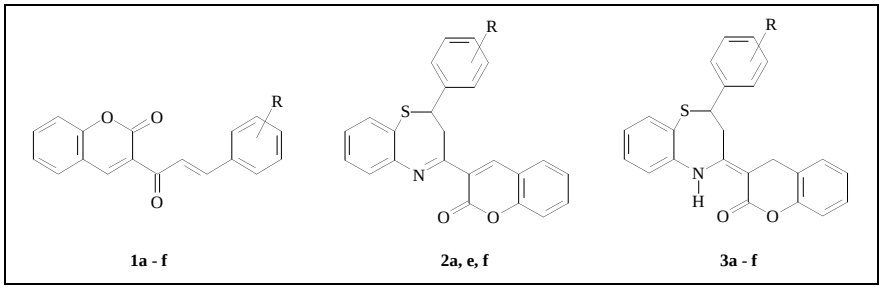
Dedicated to Professor Dr. Waldemar Adam on the occasion of his 70th birthday



3-(2-Aryl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)chromen-2-ones (**2a, e, f**) and (*Z*)-3-(2,3-dihydro-2-arylbenzo[*b*][1,4]thiazepin-4(5*H*)-ylidene)chroman-2-ones (**3a-f**) have been synthesized by the reaction of 3-aryl-1-(3-coumarinyl)propen-1-ones (**1a-f**) with 2-aminothiophenol in a hot mixture of toluene and acetic acid. Structures of all new compounds and their complete ^{1}H and ^{13}C assignments were achieved applying different one- and two-dimensional nmr experiments in combination with various spectroscopic techniques.

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INTRODUCTION

Natural, semisynthetic and synthetic coumarins [2,3] are important coumarin derivatives in drug research. As a consequence, numerous coumarin type compounds have been synthesized, some of them served as versatile intermediates for the synthesis of various heterocyclic ring systems. 3-Cinnamoyl coumarins [4-10] obtained by the reaction of 3-acetylcoumarins with aromatic aldehydes proved to be especially convenient starting materials for this purpose. 3-Cinnamoyl coumarins have been used for the synthesis of *e.g*. pyridine, pyrazoline and isoxazoline derivatives [4-10]. 1,5-Benzodiazepines and 1,5-benzothiazepines possessing a coumarin moiety have also been synthesized by the reaction of various coumarinylchalcones with 1,2-phenylenediamine and 2-aminothiophenol [11-13].

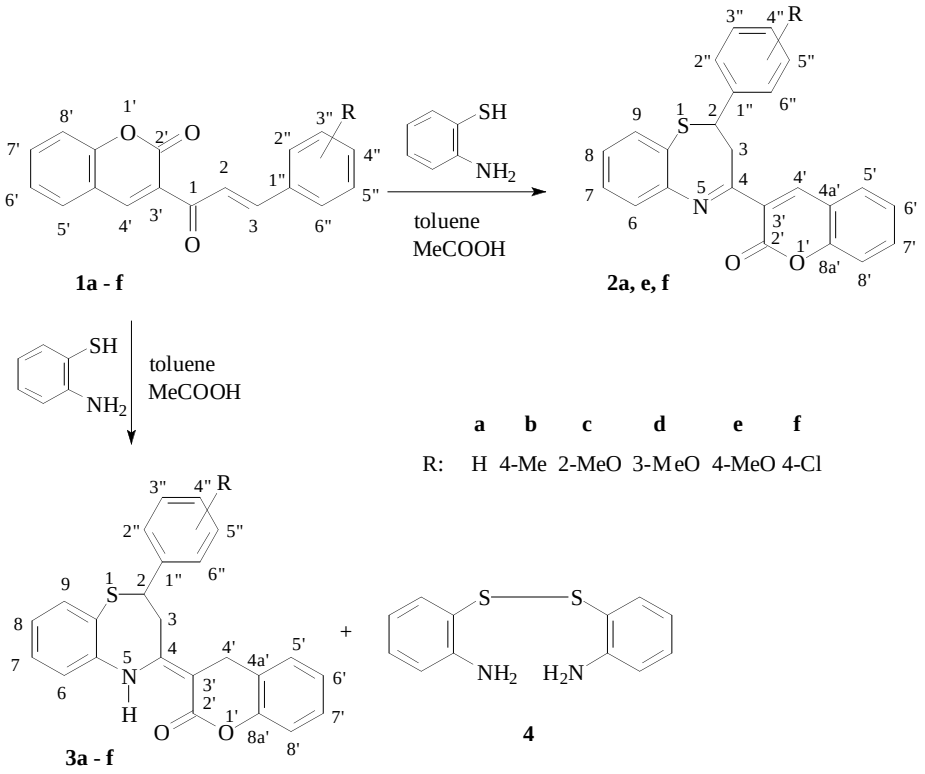
Synthesis of 2,3-dihydro-1,5-benzothiazepines (termed also as benzo[*b*][1,4]thiazepine derivatives) by the reaction of α,β-unsaturated ketones with 2-aminothiophenol is well known in the literature [14-36]. As a continuation of our studies on the preparation of 2,4-disubstituted 2,3-dihydro-1,5-benzothiazepines, in this paper we report on the synthesis of hitherto unknown benzo[*b*][1,4]thiazepine derivatives by the reaction of 3-aryl-1-(3-coumarinyl)propen-1-ones and 2-aminothiophenol.

RESULTS AND DISCUSSION

Chemistry. 3-Aryl-1-(3-coumarinyl)propen-1-ones (**1a-f**) were allowed to react with a slight excess of 2-aminothiophenol (1.2 equivalent) in hot toluene in the presence of acetic acid and a multicomponent crude reaction mixture was obtained in each case. Thin-layer chromatographic (TLC) monitoring of the reaction showed that quite a large amount of the starting materials **1a-f** remained unchanged under these reaction conditions. The expected 2,3-dihydro-1,5-benzothiazepine type compounds could be isolated only in three cases (**2a, e, f**, Scheme 1) in low yields (15-24%). Structures of compounds **2a, e, f** have been elucidated by nmr (*vide infra*), ir and mass spectroscopy (*cf*. Experimental).

If three equivalents of 2-aminothiophenol was reacted with 3-aryl-1-(3-coumarinyl)propen-1-ones (**1a-f**) under the above-mentioned reaction conditions, a complete conversion of the starting materials **1a-f** has taken place and, again, a multicomponent reaction mixture was obtained in each case. One major product and a by-product were isolated from the crude reaction mixtures

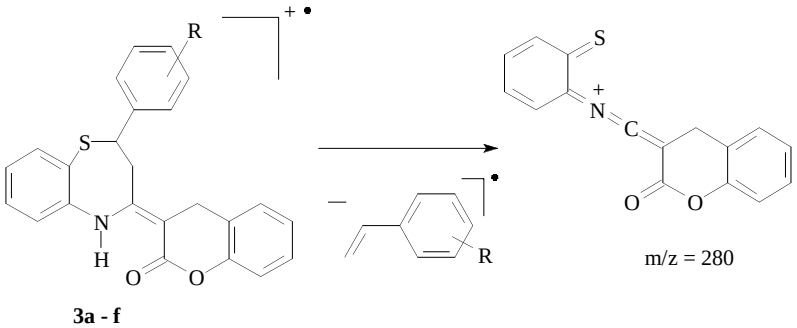
Scheme 1



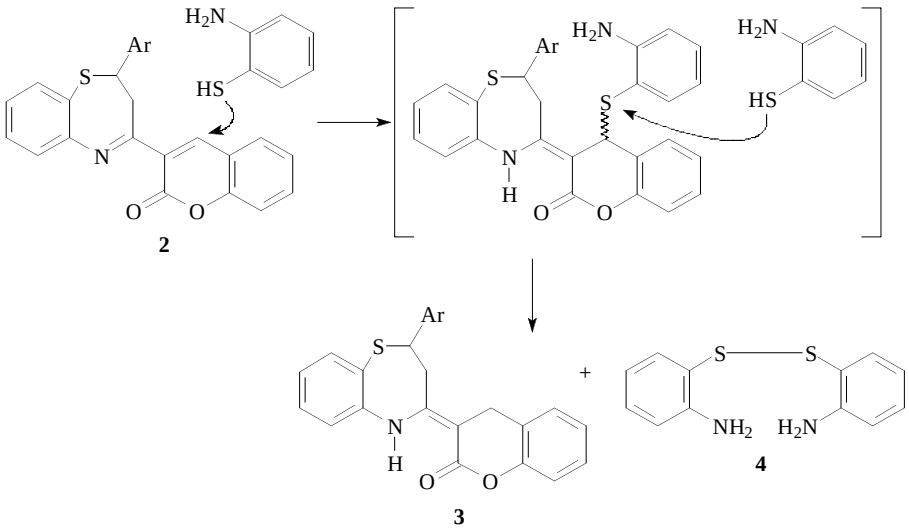
by silica gel column chromatography. Electron impact (70 eV) mass spectra of all isolated major products (**3a-f**) revealed molecular ions higher by two Daltons than those of the expected 3-(2-aryl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)chromen-2-ones (**2a-f**). Structures of the isolated major products were primarily elucidated by various nmr techniques (*vide infra*) in combination with ir, mass spectroscopic data and microanalyses (*cf.* Experimental). All these investigations unequivocally prove the formation of (*Z*)-3-(2,3-dihydro-2-arylbenzo-[*b*][1,4]thiazepin-4(5*H*)-ylidene)chroman-2-ones (**3a-f**, Scheme 1). Structures of compounds **3a-f** is corroborated by their mass spectroscopic fragmentation (Scheme 2), base peak is *m*/*z* = 280.

Together with the isolation of compounds **3a-f** as major products we have also isolated bis(2-aminophenyl) disulfide (**4**) as by-product from each crude reaction mixture. On this basis, previously we have suggested a plausible reaction mechanism for the formation of compounds **3a-f** [1]. Now, we managed to convert the 3-(2-phenyl-2,3-dihydrobenzo[*b*][1,4]thiazepin-4-yl)chromen-2-one (**2a**) into (*Z*)-3-(2,3-dihydro-2-phenylbenzo[*b*][1,4]-thiazepin-4(5*H*)-ylidene)chroman-2-one (**3a**) on treatment with 2-aminothiophenol in hot toluene in the presence of acetic acid. In this case bis(2-aminophenyl) disulfide (**4**) has also been isolated as by-product. This experimental result helps us to suggest another possible mechanism for the formation of compounds **3a-f** (*cf.* Scheme 3).

Scheme 2



Scheme 3



We suppose that first 3-(2-aryl-2,3-dihydrobenzo[*b*]-[1,4]thiazepin-4-yl)chromen-2-ones (**2**) are formed by the reaction of 3-aryl-1-(3-coumarinyl)propen-1-ones (**1**) with 2-aminothiophenol (Scheme 1). Compounds **2** react with 2-aminothiophenol to afford Mannich-adducts (Scheme 3). These intermediates react with another 2-amino-thiphenol molecule in the presence of proton catalyst to provide (*Z*)-3-(2,3-dihydro-2-arylbenzo[*b*][1,4]thiazepin-4(5*H*)-ylidene)chroman-2-ones (**3**) together with bis(2-aminophenyl) disulfide (**4**).

Nuclear Magnetic Resonance Spectroscopy. The structures of compounds (**2a, e, f** and **3a-f**) were elucidated by nmr spectroscopy using ^{1}H, ^{13}C, DEPT-135, one-dimensional selective TOCSY, one-dimensional selective NOESY, two-dimensional ^{1}H-^{13}C HSQC, ^{1}H-^{13}C HMBC, ^{1}H-^{1}H COSY and ^{1}H-^{1}H NOESY techniques, applying widely accepted strategies [37,38]. The route of the signal and structure assignments of **2a** is discussed as a representative example. Utilizing the ^{1}H and ^{1}H-^{1}H COSY spectra we identified five separated spin systems, one 1,2-disubstituted aromatic ring with S– and N–, one another 1,2-disubstituted aromatic ring with O– and C– substituents, one $-C_6H_5$ phenyl group. Furthermore, one =CH and one –CH–CH_2– moiety (see DEPT results) have also been detected. The long-range $J_{C,H}$ HMBC correlations of the isolated =CH signal at 8.80 (4'-H) resulted cross-peaks to C-4, C-2', C-8a', C-5' and C-4a' atoms (δ: 168.4, 159.8, 154.8, 129.6 and 119.0 ppm, respectively). The 4'-H/ C-5' correlation assigned δC-5' to 129.6 ppm, whereas the HSQC spectrum gave 5'-H δ: 7.71 chemical shift, serving as starting point to the ^{1}H-^{1}H COSY of 5'-H, 6'-H, 7'-H, 8'-H spin system. The 4'-H/C-4 (8.80/168.4) cross-peak revealed that the 3-coumarinyl group is attached to C-4 atom of the 2,3-dihydro-1,5-benzothiazepine moiety. A further support for this arrangement resulted from the 3-H_{trans}/C-3' (2.94/125.3) response. The value of ^{3}J(3-H_{trans},2-H) = 12.5 Hz proved the antiperiplanar position of this two hydrogen atoms which resulted from the preference of the chair conformation of the seven-membered ring with equatorial Ph at C-2 position. In addition, the 3-H_{trans}/C-1" correlation provided the assignment of the C-1" *ipso* carbon atom. Considering the signal intensities, the identification of the other signals (C-2",6", C-3",5" and C-4") of the monosubstituted phenyl ring is straightforward.

The structure determination of compounds **3a**-**f** was achieved as described for compound **2a**. The electron impact mass spectrum of **3a** revealed a molecular ion higher by two Daltons than that of compound **2a**. The ^{1}H and ^{13}C nmr spectra, beside the high similarity, exhibited some characteristic differences.

In compound **3a** there are 24 carbon atoms of 22 different types and 22 signals were assigned in its ^{13}C nmr spectrum. As a basic difference between the ^{13}C nmr spectra of substances **2a** and **3a** is the presence of an additional CH_2 group in the latter instead of a =CH moiety. In the sp^3 CH range of the ^{1}H nmr spectrum of **3a**, two AB type doublets were detected at 3.61 and 3.45 ppm assigned to the protons attached to the C-4' carbon atom. In addition, a sharp NH signal appeared at 11.47 ppm. Its high chemical shift indicates strong hydrogen bonding. The long-range $J_{C,H}$ HMBC correlations of the NH, SCH and the isolated –CH_2– hydrogen atoms (*cf.* Figure 1) provided an unambiguous assignment of the benzo-thiazepine and coumarin units. The NH/C-3' correlation proved the C-4 position of the coumarinyl moiety, whereas the NH/C-3 cross-peak revealed the presence of the thiazepine ring.

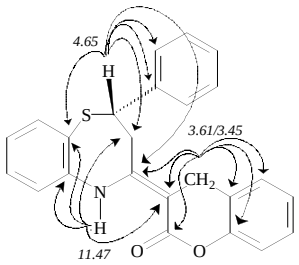


Figure 1. Characteristic HMBC correlations of the NH, 2-H and 4'-H_2 hydrogen atoms in compound **3a**.

In the NOESY spectrum a cross-peak (4.65/3.45) was detected between 2-H_{ax} and one of the doublet signal of the separated –CH_2– group. This steric proximity (*ca.* 3 Å, see the double arrows) is possible only in the chair conformation of the seven-membered thiazepine ring, where the configuration of the exo $\Delta^{4,3'}$ double bond is *Z*.

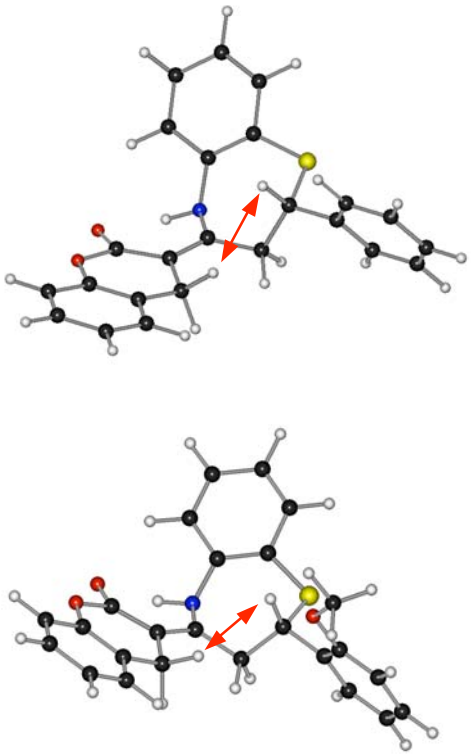


Figure 2. Stereo structures of compounds **3a** and **3c**.

The ^3J(3-H_{trans},2-H) = 10.9 Hz value is in accordance with the antiperiplanar arrangement of these hydrogen atoms. The results of the semiempirical PM3 calculations (HyperChem 7.0) also supported this stereo structure (Figure 2). In the case of the boat conformation of the thiazepine ring the 2-H/4'-H distance is higher by 4.5 Å. According to the NOESY results in compound **3c** in the preferred conformation the 2"-OCH_3 group is interestingly coplanar with 2–H bond (*cf.* Figure 2). Due to this spatial arrangement the γ-gauche effect of the 2"-OCH_3 substituent results in a characteristic 6 ppm upfield shift on δC-2, moreover other small changes in the ^{1}H and ^{13}C chemical shifts of the spatial neighbouring nuclei (*cf.* Experimental).

In conclusion, an unprecedented formation of new type of 2,3-dihydro-1,5-benzothiazepines with an exocyclic double bond at position 4 has been achieved in our present study. Although the yields of compounds **3a-f** are only medium (39-59%), these results seem to be valuable contribution to the chemistry of the 2,3-dihydro-1,5-benzothiazepines. 1,5-Benzothiazepines with an exocyclic double bond has been mentioned as a possible tautomeric form in the case of such compounds obtained by the reaction of α,β-unsaturated ketones derived from dehydroacetic acid and 2-aminothiophenol [35].

EXPERIMENTAL

Melting points were measured with a Kofler hot-stage apparatus and are uncorrected. The nmr spectra were recorded on BRUKER Avance DRX-500 and Bruker Avance 500 MHz spectrometers. Chemical shifts were determined on δ-scale. For structure elucidation and ^{1}H/^{13}C nmr signal assignment one-dimensional ^{1}H, ^{13}C, APT, DEPT-135, selective 1D-NOESY, selective 1D-ROESY and two-dimensional gradient selected ^{1}H,^{1}H-COSY, ^{1}H,^{13}C-HSQC, ^{1}H,^{13}C-HSQC, ^{1}H,^{13}C-HMBC, ^{1}H,^{1}H-NOESY and ^{1}H,^{1}H-ROESY spectra were run. Pulse programs were taken from the Bruker software library. Ir (KBr) spectra were recorded with Perkin-Elmer 16 PC spectrometer. Mass spectra were obtained with a VG Trio-2 instrument. Elemental analyses were obtained with a Carlo-Erbo 1106 apparatus. Thin layer chromatography (TLC) was performed with Merck silica gel (60 F_{254}) foils with toluene: ethyl acetate (4:1 v/v) as eluent. Starting materials **1a-f** were synthesized by known procedures [4-10].

General Procedure for the Synthesis of 3-(2-Aryl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)chromen-2-ones 2a, e, f. A mixture of the appropriate 3-aryl-1-(3-coumarinyl)propen-1-one (**1a, e, f**, 5.0 mmoles), 2-aminothiophenol (6.0 mmoles), toluene (50 ml) and acetic acid (5.0 ml) was heated at reflux for 6 h, and then the solvent was evaporated under reduced pressure. Compounds **2a, e, f** (Scheme 1) were isolated from the residue by silica gel column chromatography with toluene: ethyl acetate (4:1 v/v) as eluent and recrystallized from methanol.

3-(2-Phenyl-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl)chromen-2-one (2a) [29]. This compound was isolated as white needles in 22% yield, mp 202-203° (recrystallized from methanol); ^{1}H nmr (500 MHz, $CDCl_3$): δ 5.37 (dd, *J* = 12.5, 4.9 Hz, 1H, 2-H), 2.94 (t, *J* = 12.5 Hz, 1H, 3-H_{trans}), 3.62 (dd, *J* = 12.5, 4.9 Hz, 1H, 3-H_{cis}), 7.36 (d, 1H, 6-H), 7.51 (t, 1H, 7-H), 7.23 (t, 1H, 8-H), 7.69 (d, 1H, 9-H), 8.80 (s, 1H 4'-H), 7.71 (d, 1H, 5'-H), 7.37 (t, 1H, 6'-H), 7.65 (t, 1H, 7'-H), 7.42 (d, 1H, 8'-H), 7.36 (dm, 2H, 2",6"-H), 7.30 (t, 2H, 3",5"-H), 7.25 (t, 1H, 4"-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 60.5 (d, C-2), 39.7 (t, C-3), 168.4 (s, C-4), 150.3 (s, C-5a), 125.5 (d, C-6), 129.8 (d, C-7), 126.3 (d, C-8), 135.3 (d, C-9), 124.3 (s, C-9a), 159.8 (s, C-2'), 125.3 (s, C-3'), 145.3 (d, C-4'), 119.0 (s, C-4a'), 129.6 (d, C-5'), 125.0 (d, C-6'), 133.4 (d, C-7'), 116.6 (d, C-8'), 154.8 (s, C-8a'),

144.1 (s, C-1"), 126.2 (2xd, C-2",6"), 128.7 (2xd, C-3",5"), 127.7 (d, C-4"); ir (KBr): cm^{-1} 1724, 1610, 1565, 1453, 1217, 1165, 986, 763, 698; ms: m/z 383 (M^+, 5), 350 (5), 279 (100), 251 (28). *Anal*. Cald. for $C_{24}H_{17}NO_2S$: C, 75.18; H, 4.47; N, 3.65. Found: C, 75.27; H, 4.51; N, 3.59.

3-[2-(4-Methoxyphenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]chromen-2-one (2e). This substance was obtained as white plates in 15% yield, mp 140-141° (recrystallized from methanol); ^{1}H nmr (500 MHz, $CDCl_3$): δ 5.34 (dd, *J* = 12.5, 4.9 Hz, 1H, 2-H), 2.91 (t, *J* = 12.5 Hz, 1H, 3-H_{trans}), 3.57 (dd, *J* = 12.5, 4.9 Hz, 1H, 3-H_{cis}), 7.35 (d, 1H, 6-H), 7.50 (t, 1H, 7-H), 7.21 (t, 1H, 8-H), 7.67 (d, 1H, 9-H), 8.75 (s, 1H, 4'-H), 7.70 (d, 1H, 5'-H), 7.36 (t, 1H, 6'-H), 7.64 (t, 1H, 7'-H), 7.41 (d, 1H, 8'-H), 7.26 (dm, 2H, 2",6"-H), 6.82 (dm, 2H, 3",5"-H), 3.78 (s, 3H, 4"-OCH_3); ^{13}C nmr (125 MHz, $CDCl_3$): δ 60.1 (d, C-2), 39.8 (t, C-3), 168.2 (s, C-4), 150.4 (s, C-5a), 125.4 (d, C-6), 129.7 (d, C-7), 126.2 (d, C-8), 135.3 (d, C-9), 124.2 (s, C-9a), 159.8 (s, C-2'), 125.6 (s, C-3'), 145.1 (d, C-4'), 119.0 (s, C-4a'), 129.5 (d, C-5'), 124.9 (d, C-6'), 133.3 (d, C-7'), 116.6 (d, C-8'), 154.7 (s, C-8a'), 136.5 (s, C-1"), 127.3 (2xd, C-2",6"), 113.9 (2xd, C-3",5"), 159.0 (s, C-4"), 55.3 (q, 4"-OCH_3); ir (KBr): cm^{-1} 1724, 1608, 1558, 1510, 1453, 1256, 1176, 1033, 983, 8.32, 759; ms: m/z 413 (M^+, 2), 279 (17), 251 (10), 134 (100). *Anal*. Calcd. for $C_{25}H_{19}NO_3S$: C, 72.63; H, 4.63; N 3.39. Found: C, 72.69; H, 4.68; N 3.32.

3-[2-(4-Chlorophenyl)-2,3-dihydro-benzo[*b*][1,4]thiazepin-4-yl]chromen-2-one (2f). This compound was prepared as white needles in 24% yield, mp 182-183° (recrystallized from methanol); ^{1}H nmr (500 MHz, $CDCl_3$): δ 5.37(dd, *J* = 12.5, 4.9 Hz, 1H, 2-H), 2.85 (t, *J* = 12.5 Hz, 1H, 3-H_{trans}), 3.57 (dd, *J* = 12.5, 4.9 Hz, 1H, 3-H_{cis}), 7.37 (d, 1H, 6-H), 7.51 (t, 1H, 7-H), 7.23 (t, 1H, 8-H), 7.67 (d, 1H, 9-H), 8.82 (s, 1H, 4'-H), 7.72 (d, 1H, 5'-H), 7.37 (t, 1H, 6'-H), 7.65 (t, 1H, 7'-H), 7.41 (d, 1H, 8'-H), 7.29 (dm, 2H, 2",6"-H), 7.26 (dm, 2H, 3",5"-H); ^{13}C nmr (125 MHz, $CDCl_3$): δ 59.6 (d, C-2), 39.7 (t, C-3), 168.0 (s, C-4), 150.1 (s, C-5a), 125.5 (d, C-6), 130.0 (d, C-7), 126.4 (d, C-8), 135.3 (d, C-9), 123.9 (s, C-9a), 159.9 (s, C-2'), 125.0 (s, C-3'), 145.4 (d, C-4'), 118.9 (s, C-4a'), 129.7 (d, C-5'), 125.0 (d, C-6'), 133.0 (d, C-7'), 116.6 (d, C-8'), 154.8 (s, C-8a'), 142.6 (s, C-1"), 127.6 (2xd, C-2",6"), 128.8 (2xd, C-3",5"), 133.3 (s, C-4"); ir (KBr): cm^{-1} 1720, 1607, 1558, 1489, 1453, 1273, 1206, 1090, 983, 761; ms: m/z 417 (M^+, 2), 384 (2), 279 (100), 251 (24). *Anal*. Calcd. for $C_{24}H_{16}ClNO_2S$: C, 68.98; H, 3.86; N 3.35. Found: C, 68.89; H, 3.90, N, 3.30.

General Method for the Preparation of (*Z*)-3-(2,3-Dihydro-2-arylbenzo[*b*][1,4]thiazepin-4(5*H*)ylidene)chroman-2-ones 3a-f. A mixture of the respective 3-aryl-1-(3-coumarinyl)propen-1-one (**1a-f**, 5.0 mmoles), 2-aminothiophenol (15.0 mmoles), toluene (50 ml) and acetic acid (5.0 ml) were treated as described for the synthesis of compounds **2a,e,f** to afford benzothiazepines **3a-f** on column chromatography (Scheme 1).

(*Z*)-3-(2,3-Dihydro-2-phenylbenzo[*b*][1,4]thiazepin-4(5*H*)-ylidene)chroman-2-one (3a). This compound was isolated as white needles in 46% yield, mp 185-186° (recrystallized from methanol); ^{1}H nmr (500 MHz, $CDCl_3$): δ 4.65 (dd, *J* = 10.9, 5.0 Hz, 1H, 2-H), 2.74 (dd, *J* = 13.7, 10.9 Hz, 1H, 3-H_{trans}), 2.91 (dd, *J* = 13.7, 5.0 Hz, 1H, 3-H_{cis}), 7.12 (d, 1H, 6-H), 7.33 (t, 1H, 7-H), 7.10 (t, 1H, 8-H), 7.48 (d, 1H, 9-H), 3.45 (d, *J* = 18.6 Hz, 1H, 4'-H_a), 3.61 (d, *J* = 18.6 Hz, 1H, 4'-H_b), 6.96 (d, 1H, 5'-H), 6.95 (t, 1H, 6'-H), 7.09 (t, 1H, 7'-H), 6.91 (d, 1H, 8'-H), 7.23 (dm, 2H, 2",6"-H), 7.22 (t, 2H, 3",5"-H), 7.19 (t, 1H, 4"-H), 11.47 (s, 1H, NH); ^{13}C nmr (125 MHz, $CDCl_3$): δ 53.2 (d, C-2), 35.9 (t, C-3), 159.3 (s, C-4), 141.6 (s, C-5a), 123.5 (d, C-6), 130.1 (d, C-7), 125.9 (d, C-8), 135.3 (d, C-9), 125.7 (s, C-9a), 166.4 (s, C-2'), 84.6 (s, C-3'), 26.8 (t, C-4'), 120.3 (s, C-4a'), 127.9 (d, C-5'), 123.6 (d, C-6'), 127.5 (d, C-7'), 116.1 (d, C-8'), 150.5 (s, C-8a'), 142.8 (s, C-1"), 126.2 (2xd, C-2",6"), 128.6 (2xd, C-3",5"), 127.8 (d, C-4"); ir (KBr): cm^{-1} 3412, 1665, 1582, 1491, 1456, 1332, 1229, 1186, 1164, 1118, 987, 760, 698; ms: m/z 385 (M^+, 22), 352 (7), 280 (100), 236 (27). *Anal*. Calcd. for $C_{24}H_{19}NO_2S$: C, 74.79; H, 4.97; N, 3.63. Found: C, 74.92; H, 5.03; N, 3.54.

(*Z*)-3-[2,3-Dihydro-2-(4-methylphenyl)benzo[*b*][1,4]thiazepin-4(5*H*)-ylidene]chroman-2-one (3b). This substance was prepared as white plates in 51% yield, mp 180-181° (recrystallized from methanol); ^{1}H nmr (500 MHz, $CDCl_3$): δ 4.74 (dd, *J* = 10.5, 4.6 Hz, 1H, 2-H), 2.84 (dd, *J* = 13.7, 10.5 Hz, 1H, 3-H_{trans}), 3.00 (dd, *J* = 13.7, 4.6 Hz, 1H, 3-H_{cis}), 7.22 (d, 1H, 6-H), 7.42 (t, 1H, 7-H), 7.19 (t, 1H, 8-H), 7.59 (d, 1H, 9-H), 3.56 (d, *J* = 18.3 Hz, 1H, 4'-H_a), 3.71 (d, *J* = 18.3 Hz, 1H, 4'-H_b), 7.04 (d, 1H, 5'-H), 7.04 (t, 1H, 6'-H), 7.21 (t, 1H, 7'-H), 7.05 (d, 1H, 8'-H), 7.24 (dm, 2H, 2",6"-H), 7.13 (dm, 2H, 3",5"-H), 2.35 (s, 3H, 4"-CH_3), 11.62 (s, 1H, NH); ^{13}C nmr (125 MHz, $CDCl_3$): δ 53.2 (d, C-2), 36.1 (t, C-3), 159.1 (s, C-4), 142.2 (s, C-5a), 123.9 (d, C-6), 130.2 (d, C-7), 125.9 (d, C-8), 135.6 (d, C-9), 126.1 (s, C-9a), 166.3 (s, C-2'), 84.9 (s, C-3'), 27.3 (t, C-4'), 120.7 (s, C-4a'), 128.1 (d, C-5'), 123.7 (d, C-6'), 127.7 (d, C-7'), 116.6 (d, C-8'), 151.0 (s, C-8a'), 140.1 (s, C-1"), 126.4 (2xd, C-2",6"), 129.5 (2xd, C-3",5"), 137.9 (s, C-4"), 21.1 (q, 4"-CH_3); ir (KBr): cm^{-1} 3408, 1667, 1583, 1559, 1492, 1455, 1333, 1230, 1186, 1166, 1104, 990, 755, 633; ms: m/z 399 (M^+, 17), 366 (8), 280 (100), 236 (17). *Anal*. Calcd. for $C_{25}H_{21}NO_2S$: C, 75.17; H, 5.30; N, 3.50. Found: C, 75.26; H, 5.26; N, 3.57.

(*Z*)-3-[2,3-Dihydro-2-(2-Methoxyphenyl)benzo[*b*][1,4]thiazepin-4(5*H*)-ylidene]chroman-2-one (3c). This compound was obtained as white plates in 52% yield, mp 176-177° (recrystallized from methanol); ^{1}H nmr (500 MHz, $CDCl_3$): δ 5.23 (dd, *J* = 12.0, 4.6 Hz, 1H, 2-H), 2.67 (dd, *J* = 13.6, 12.0 Hz, 1H, 3-H_{trans}), 3.06 (dd, *J* = 13.6, 4.6 Hz, 1H, 3-H_{cis}), 7.22 (d, 1H, 6-H), 7.41 (t, 1H, 7-H), 7.20 (t, 1H, 8-H), 7.67 (d, 1H, 9-H), 3.76 (d, *J* = 18.4 Hz, 1H, 4'-H_a), 3.92 (d, *J* = 18.4 Hz, 1H, 4'-H_b), 7.12 (d, 1H, 5'-H), 7.08 (t, 1H, 6'-H), 7.23 (t, 1H, 7'-H), 7.07 (d, 1H, 8'-H), 6.93 (d, 1H, 3"-H), 7.28 (t, 1H, 4"-H), 6.94 (t, 1H, 5"-H), 7.50 (d, 1H, 6"-H), 3.95 (s, 3H, 2"-OCH_3), 11.58 (s, 1H, NH); ^{13}C nmr (125 MHz, $CDCl_3$): δ 46.7 (d, C-2), 34.9 (t, C-3), 159.9 (s, C-4), 142.3 (s, C-5a), 123.7 (d, C-6), 130.0 (d, C-7), 125.9 (d, C-8), 135.8 (d, C-9), 126.1 (s, C-9a), 166.3 (s, C-2'), 84.6 (s, C-3'), 27.0 (t, C-4'), 121.0 (s, C-4a'), 128.0 (d, C-5'), 123.7 (d, C-6'), 127.7 (d, C-7'), 116.7 (d, C-8'), 151.1 (s, C-8a'), 134.1 (s, C-1"), 155.4 (d, C-2"), 110.4 (d, C-3"), 128.8 (d, C-4"), 120.9 (d, C-5"), 127.1 (d, C-6"), 55.5 (q, 2"-OCH_3); ir (KBr): cm^{-1} 3442, 1665, 1583, 1558, 1457, 1335, 1238, 1187, 1168, 1105, 986, 752, 692; ms: m/z 415 (M^+, 15), 382 (6), 280 (100), 236 (31). *Anal*. Calcd. for $C_{25}H_{21}NO_3S$: C, 72.27; H, 5.10; N, 3.37. Found: C, 72.36; H, 5.04; N, 3.44.

(*Z*)-3-[2,3-Dihydro-2-(3-methoxyphenyl)benzo[*b*][1,4]thiazepin-4(5*H*)-ylidene]chroman-2-one (3d). This material was obtained as white plates in 39% yield, mp 166-167° (recrystallized from methanol); ^{1}H nmr (500 MHz, $CDCl_3$): δ 4.72 (dd, *J* = 10.7, 5.0 Hz, 1H, 2-H), 2.84 (dd, *J* = 13.8, 10.7 Hz, 1H, 3-H_{trans}), 3.02 (dd, *J* = 13.8, 5.0 Hz, 1H, 3-H_{cis}), 7.23 (d, 1H, 6-H), 7.43 (t, 1H, 7-H), 7.20 (t, 1H, 8-H), 7.60 (d, 1H, 9-H), 3.59 (d, *J* = 18.1 Hz, 1H, 4'-H_a), 3.73 (d, *J* = 18.1 Hz, 1H, 4'-H_b), 7.06

(d, 1H, 5'-H), 7.07 (t, 1H, 6'-H), 7.22 (t, 1H, 7'-H), 7.05 (d, 1H, 8'-H), 6.92 (s, 1H, 2"-H), 6.84 (d, 1H, 4"-H), 7.26 (t, 1H, 5"-H), 6.91 (d, 1H, 6"-H), 3.75 (s, 3H, 3"-OCH_3), 11.61 (s, 1H, NH); ^{13}C nmr (125 MHz, $CDCl_3$): δ 53.4 (d, C-2), 36.1 (t, C-3), 159.0 (s, C-4), 142.2 (s, C-5a), 123.8 (d, C-6), 130.3 (d, C-7), 126.0 (d, C-8), 135.6 (d, C-9), 126.1 (s, C-9a), 166.3 (s, C-2'), 85.0 (s, C-3'), 27.3 (t, C-4'), 120.6 (s, C-4a'), 128.1 (d, C-5'), 123.7 (d, C-6'), 127.8 (d, C-7'), 116.6 (d, C-8'), 151.0 (s, C-8a'), 144.6 (s, C-1"), 112.4 (d, C-2"), 159.9 (d, C-3"), 113.3 (d, C-4"), 129.9 (d, C-5"), 118.7 (d, C-6"), 55.2 (q, 3"-OCH_3); ir (KBr): cm^{-1} 3426, 1655, 1597, 1560, 1465, 1332, 1268, 1228, 1184, 1117, 985, 759, 698; ms: m/z 415 (M^+, 11), 382 (6), 280 (100), 236 (11). *Anal.* Calcd. for $C_{25}H_{21}NO_3S$: C, 72.27; H, 5.10; N, 3.37. Found: C, 72.19; H, 5.15; N 3.31.

(*Z*)-3-[2,3-Dihydro-2-(4-methoxyphenyl)benzo[*b*][1,4]thiazepin-4-(5*H*)-ylidene]chroman-2-one (3e). This compound was isolated as white plates in 59% yield, mp 161-162° (recrystallized from methanol); ^{1}H nmr (500 MHz, $CDCl_3$): δ 4.76 (dd, *J* = 10.1, 5.0 Hz, 1H, 2-H), 2.82 (dd, *J* = 13.6, 10.1 Hz, 1H, 3-H_{trans}), 2.99 (dd, *J* = 13.6, 5.0 Hz, 1H, 3-H_{cis}), 7.21 (d, 1H, 6-H), 7.42 (t, 1H, 7-H), 7.19 (t, 1H, 8-H), 7.58 (d, 1H, 9-H), 3.50 (d, *J* = 18.1 Hz, 1H, 4'-H_a), 3.69 (d, *J* = 18.1 Hz, 1H, 4'-H_b), 7.03 (d, 1H, 5'-H), 7.04 (t, 1H, 6'-H), 7.21 (t, 1H, 7'-H), 7.04 (d, 1H, 8'-H), 7.27 (dm, 2H, 2",6"-H), 6.83 (dm, 2H, 3",5"-H), 3.78 (s, 3H, 4"-OCH_3), 11.62 (s, 1H, NH); ^{13}C nmr (125 MHz, $CDCl_3$): δ 53.0 (d, C-2), 36.2 (t, C-3), 159.0 (s, C-4), 142.1 (s, C-5a), 123.7 (d, C-6), 130.1 (d, C-7), 125.9 (d, C-8), 135.5 (d, C-9), 126.1 (s, C-9a), 166.3 (s, C-2'), 84.9 (s, C-3'), 27.2 (t, C-4'), 120.7 (s, C-4a'), 128.0 (d, C-5'), 123.6 (d, C-6'), 127.7 (d, C-7'), 116.5 (d, C-8'), 151.0 (s, C-8a'), 135.0 (s, C-1"), 127.7 (2xd, C-2",6"), 114.1 (2xd, C-3",5"), 159.3 (s, C-4"), 55.3 (q, 4"-OCH_3); ir (KBr): cm^{-1} 3432, 1669, 1583, 1559, 1511, 1469, 1332, 1231, 1185, 1161, 1033, 981, 756, 640; ms: m/z 415 (M^+, 36), 382 (8), 280 (100), 236 (12). *Anal.* Cald. for $C_{25}H_{21}NO_3S$: C, 72.27; H, 5.10; N, 3.37. Found: C, 72.33; H, 5.16; N, 3.42.

(*Z*)-3-[2,3-Dihydro-2-(4-chlorophenyl)benzo[*b*][1,4]thiazepin-4-(5*H*)-ylidene]chroman-2-one (3f). This compound was obtained as pale yellow needles in 57% yield, mp 170-171° (recrystallized from methanol); ^{1}H nmr (500 MHz, $CDCl_3$): δ 4.73 (dd, *J* = 10.6, 5.1 Hz, 1H, 2-H), 2.80 (dd, *J* = 13.9, 10.6 Hz, 1H, 3-H_{trans}), 3.00 (dd, *J* = 13.9, 5.1 Hz, 1H, 3-H_{cis}), 7.24 (d, 1H, 6-H), 7.44 (t, 1H, 7-H), 7.21 (t, 1H, 8-H), 7.57 (d, 1H, 9-H), 3.56 (d, *J* = 18.0 Hz, 1H, 4'-H_a), 3.70 (d, *J* = 18.0 Hz, 1H, 4'-H_b), 7.05 (d, 1H, 5'-H), 7.06 (t, 1H, 6'-H), 7.23 (t, 1H, 7'-H), 7.06 (d, 1H, 8'-H), 7.29 (s, 2H, 2",6"-H), 7.29 (s, 2H, 3",5"-H), 11.60 (s, 1H, NH); ^{13}C nmr (125 MHz, $CDCl_3$): δ 52.7 (d, C-2), 36.0 (t, C-3), 159.5 (s, C-4), 142.2 (s, C-5a), 123.9 (d, C-6), 130.5 (d, C-7), 126.1 (d, C-8), 135.6 (d, C-9), 125.6 (s, C-9a), 166.4 (s, C-2'), 85.2 (s, C-3'), 27.3 (t, C-4'), 120.6 (s, C-4a'), 128.1 (d, C-5'), 123.9 (d, C-6'), 127.9 (d, C-7'), 116.6 (d, C-8'), 151.0 (s, C-8a'), 141.5 (s, C-1"), 127.9 (2xd, C-2",6"), 129.1 (2xd, C-3",5"), 133.9 (s, C-4"); ir (KBr): cm^{-1} 3423, 1668, 1584, 1491, 1456, 1331, 1265, 1231, 1185, 1164, 1103, 985, 758, 630; ms: m/z 419 (M^+, 13), 384 (8), 280 (100), 251 (23). *Anal.* Calcd. for $C_{24}H_{18}ClNO_2S$: C, 68.65; H, 4.32; N, 3.33. Found: C, 68.74; H, 4.28; N 3.38.

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