Facile Preparation and Chemical Transformations of Spirocyclopropane-Annelated Heterocycles[‡]

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A productive approach has been developed to spirocyclopropane-annelated 1,4-benzoxathiane **17** (85%), 1,4-benzothiazines **20**–**22** (56–88%) and 1,4-benzoxazines **25**, **26** (55–71%), through Michael additions of binucleophilic *o*-hydroxythiophenol **15**, *o*-aminothiophenols **8** and *o*-hydroxysulfanilides **23** onto methyl and *tert*-butyl 2-chloro-2-cyclopropylideneacetates (**1**-Me, **1**-*t*Bu), followed by ring closure in the intermediate of type **3** through nucleophilic substitution of the chlorine atom and, in the case of the intermediates **20**, **21** and **25**, elimination of benzenesulfinic acid. Reduction of **20a** with $LiAlH_4$ led to the hydroxymethyl derivative **28** (88%) with retention of the *N*-phenylsulfonyl group, while that of the oxazinecarboxylate **26a**-Me gave the β-amino alcohol **27** (87%). Selective reduction of the C=N double bond in **26a**-Me was achieved with $NaBH_4$ in methanol. Halogen-substituted benzoxazines **26b**,**c** were modified further by Heck coupling with various alkenes. In the presence of a catalytic amount of triphenylphosphane, only the 6-bromobenzoxazine underwent Heck coupling accompanied by ring opening of the spirocyclopropane moiety. The best yields of cross-coupling products **30d**–**i** (60–89%) retaining the spirocyclopropane ring were achieved for 6-iodobenzoxazine **26c**-Me reacting with methyl acrylate, acrolein, and methyl vinyl ketone, respectively. By treatment with morpholine in DMF, the heterocyclic esters **26b**,**c** undergo demethoxycarbonylation to form spirocyclopropane-annelated 1,4-benzoxazines **36b**,**c** in high yields (83–98%). The 1,4-benzoxazine **36b** readily adds nucleophiles such as *p*-thiocresol and hydrogen cyanide across its C=N double bond to yield compounds **37** (76%) and **38** (95%), respectively.

Introduction

Alkyl 2-chloro-2-cyclopropylideneacetates **1**, which are readily available in three steps from tetrachlorocyclopropene and ethylene,[1] are versatile building blocks for organic synthesis.[2] As has been demonstrated previously, they can be used effectively for the construction of various S-, N-, and O-containing spirocyclopropane-annelated heterocycles by 1,3-dipolar cycloadditions[3] as well as by two-step processes involving a Michael addition and an intramolecular nucleophilic substitution.[4] These esters **1** are much better Michael acceptors than any other alkyl 3,3-dialkylacrylates and even unsubstituted acrylates, which is due mainly to the release of strain upon changing the hybridization of the ring carbon atom from sp to sp^2 upon attack of a nucleophile, but to a small extent also to the chloro substituent in the α-position. In the case of a bidentate nucleophile **2**, ring closure of the intermediate **3** through nucleophilic substitution of the chlorine atom at the newly formed sp^3-carbon center or, alternatively, nucleophilic attack on the methoxycarbonyl group (R = Me) can occur to give heterocycles of either type **4** or **5**, respectively (Scheme 1).

1,4-Benzoxazine and 1,4-benzothiazine derivatives thus obtainable with 1,2-disubstituted benzene derivatives are of great interest since similar compounds have shown Ca^{2+} antagonist[5] and aldose reductase inhibitory activities.[6]

The previously reported[4a] reactions of **1**-Me with 2-aminoethanethiol, catechol, 2-aminophenol, and 2-aminothiophenol were all conducted in two-phase systems under phase-transfer catalysis (PTC), and the yields did not exceed 45%. We engaged ourselves, therefore, in a project to develop better conditions for the synthesis of spirocyclopro-

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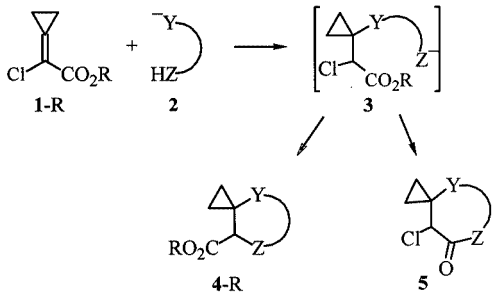


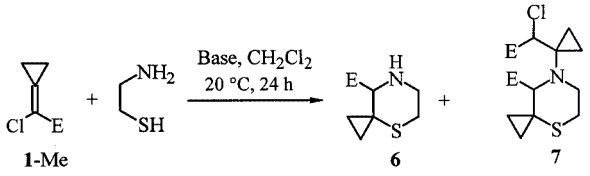
Scheme 1. Two possibilities to obtain heterocycles from 2-chloro-2-cyclopropylideneacetates **1**-R and a binucleophile **2**

pane-annelated 1,4-benzoxazines, 1,4-benzoxathianes, and 1,4-benzothiazines from 2-chloro-2-cyclopropylideneacetates **1** and 1,2-disubstituted binucleophilic benzene derivatives and to study possible modifications of the resulting heterocycles.

Results and Discussion

Preparation of Heterocycles

Most of the previous cocyclizations of **1**-Me with binucleophiles were conducted in the presence of excess potassium hydroxide and dibenzo[18]crown-6 as a phase-transfer catalyst in dichloromethane.[4a] Under these conditions, however, the methoxycarbonyl group may also be attacked, and this may be one of the reasons for the low yields obtained previously for the six-membered ring products. In addition, products with an unprotected N−H fragment in the molecule may undergo yet another Michael addition onto a second molecule of **1**-Me. For instance, 2-aminoethanethiol in the presence of potassium carbonate as a base reacted with **1**-Me to give the tetrahydro[1,4]thiazine derivative **6** in only 20% yield, and its further adduct **7** (a mixture of two diastereoisomers) was isolated in 14% yield. A similar product distribution was obtained under homogeneous conditions with triethylamine as a base (Scheme 2).



Base	Yield of **6** (%)	Yield of **7** (%)
K_2CO_3, 18-crown-6	20	14
Et_3N	27	16

Scheme 2. Cocyclization of methyl 2-chloro-2-cyclopropylideneacetate (**1**-Me) with 2-aminoethanethiol; E = CO_2Me

The structure of the amino ester **6** was confirmed by X-ray structural analysis.[7] The compound itself was obtained as an oil, but after several months of storage of its solution in $CDCl_3$, crystals of the unusual hemihydrochloride **6**·0.5HCl·0.25H_2O had precipitated and were analyzed (Figure 1).

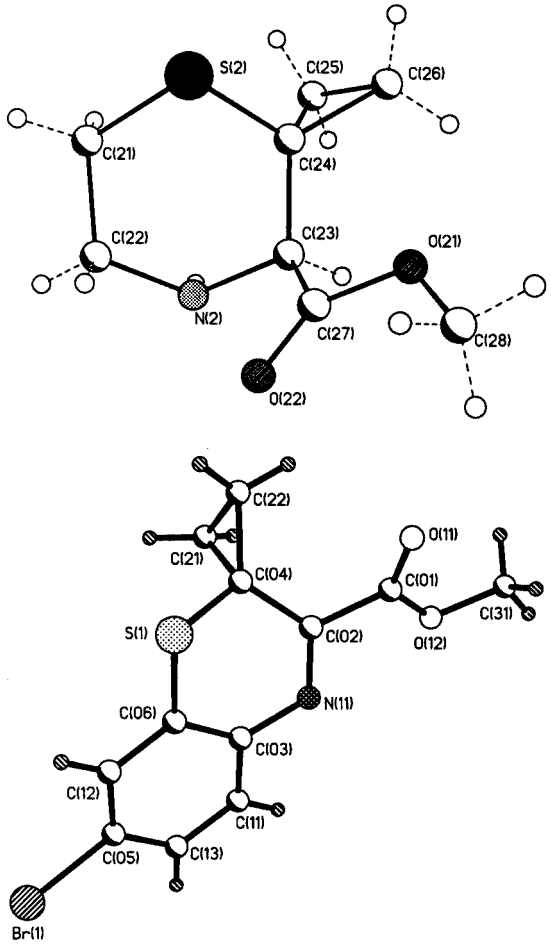
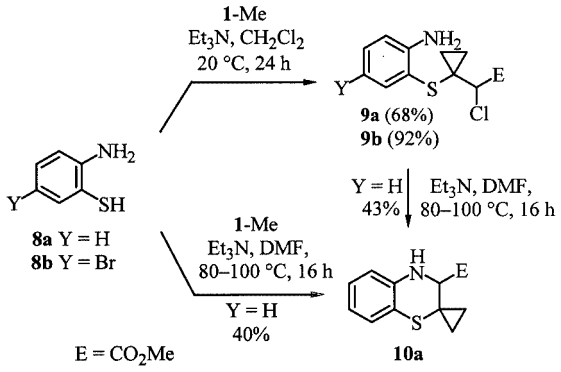


Figure 1. Molecular structures of methyl 3′,4′,5′,6′-tetrahydrospiro(cyclopropane-1,2′-[2*H*][1,4]thiazine)-3′-carboxylate (**6**) (obtained as **6**·0.5HCl·0.25H_2O) and methyl 7-bromospiro([2*H*]-[1,4]benzothiazine-2,1′-cyclopropane)-3-carboxylate (**22b**) in the crystals[7]

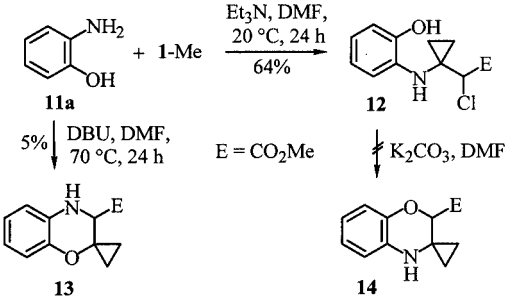
The treatment of **1**-Me with 2-aminothiophenol (**8a**) in the presence of KOH under PTC conditions in dichloromethane gave the 1,4-benzothiazine derivative **10a** in 46% yield.[4a] The reaction of 2-aminophenol (**11a**) with **1**-Me in the presence of K_2CO_3 under PTC conditions gave the corresponding 1,4-benzoxazine derivative **14** in 40% yield.[4a] In the presence of triethylamine at ambient temperature, **1**-Me reacted smoothly with **8a** and its bromo-substituted analog **8b** to give the open-chain Michael adducts **9a** and **9b** in 68 and 92% yields, respectively. When the reaction of **8a** with **1**-Me was carried out at 100 °C in DMF, however, only the benzothiazine **10a** (40%) was isolated along with several unidentified minor by-products (Scheme 3). Under these conditions, the open-chain intermediate **9a** could also be cyclized to **10a**, but the yield (43%) was not improved. The cyclization did not occur in refluxing THF.

In the presence of triethylamine in DMF, **1**-Me reacted with 2-aminophenol (**11a**) at its NH_2 group to yield mainly the open-chain adduct **12** (Scheme 4). Usually *O*-alkylation of phenols requires strong bases, yet in this case treatment



Scheme 3. Reaction of methyl 2-chloro-2-cyclopropylideneacetate (**1**-Me) with 2-aminothiophenols **8a**,**b** under various conditions

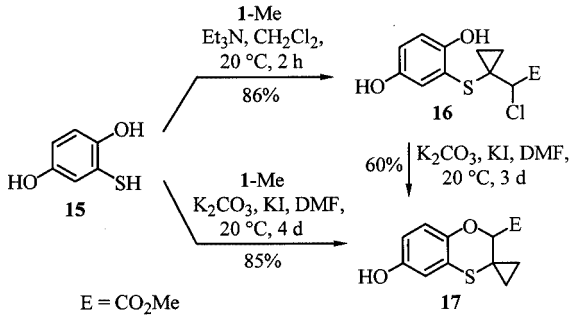
of **1**-Me with **11a** in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in DMF at 70 °C gave only the unexpected 1,4-benzoxazine derivative **13** in very low yield and in impure form along with many unidentified by-products. An attempt to cyclize **12** to **14** by treatment with K_2CO_3 and KI in DMF gave also a complex mixture of products that could not be separated.



Scheme 4. Reaction of methyl 2-chloro-2-cyclopropylideneacetate (**1**-Me) with 2-aminophenol (**11a**) under various conditions

The cocyclization of 2-chloro-2-cyclopropylideneacetates **1**-R with *o*-mercaptophenols is a route to 2,3-dihydro-1,4-benzoxathiane derivatives. With triethylamine in dichloromethane at ambient temperature, **1**-Me reacted with mercaptohydroquinone (**15**) also to yield the open-chain adduct **16**. With K_2CO_3/KI in DMF, however, the heterocycle **17** was obtained in 85% yield. Under the same conditions, the initial Michael adduct **16** could be cyclized to **17** in 60% yield (Scheme 5).

To avoid the complications arising from an unprotected N−H fragment in the heterocycles of type **10**, the open-chain adducts **9a**,**b** were converted into the sulfonamides **18a**,**b**/**19a** (Scheme 6). Treatment of **18a** with K_2CO_3/KI in DMF afforded the cyclic sulfonamide **20a** in 77% yield, while the bromo-substituted analogue **18b** gave predominantly the α-imino ester **22b** (45%), after elimination of benzenesulfinic acid, along with **20b** (14%). When the reaction of **18a** was performed at a higher temperature (85 instead of 70 °C) and for a longer time (4 instead of 2 h) the yield of **22a** increased to 88%. The structure of compound **22b** was confirmed by an X-ray analysis (Figure 1).[7]

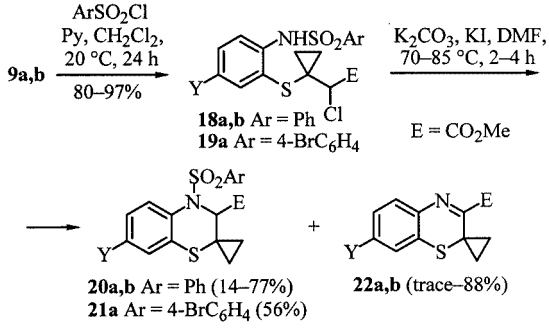


Scheme 5. Reaction of methyl 2-chloro-2-cyclopropylideneacetate (**1**-Me) with mercaptohydroquinone (**15**) under various conditions

Table 1. Sulfonamides **18a**,**b**, **19a** and 1,4-benzothiazines **20a**,**b**, **21a** and **22a**,**b** obtained from **9a**,**b**

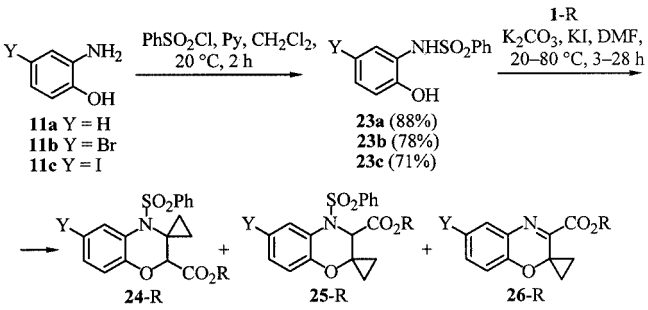
9	Y	Ar	**18**/**19** (%)	Temp. [°C]/ Time [h]	**20**/**21** (%)	**22** (%)
a	H	Ph	**18a** (80)	70/2	**20a** (77)	**22a** (trace)
				85/4	**20a** (0)	**22a** (88)
b	Br	Ph	**18b** (97)	70/2	**20a** (14)	**22b** (45)
a	H	4-BrC_6H_4	**19a** (81)	70/2	**21a** (56)	**22a**[a]

[a] Yield not determined.



Scheme 6. Synthesis of sulfonamides **18a**,**b**, **19a** and their heterocyclizations to 1,4-benzothiazine derivatives **20a**,**b**, **21a** and **22a**,**b** (for details see Table 1)

The sulfonamides **23a**−**c** derived from 2-aminophenol (**11a**) and its 4-bromo (**11b**) and 4-iodo (**11c**) derivatives, upon their reactions with chlorocyclopropylideneacetates **1**-



Scheme 7. Cocyclization of 2-chloro-2-cyclopropylideneacetates **1**-R with sulfonamides **23a**−**c** to form 1,4-benzoxazine derivatives **24**-R to **26**-R (for details see Table 2)

Table 2. Cocyclizations of *N*-(2-hydroxy-5-Y-phenyl)benzenesulfonamides **23a**−**c** with methyl (**1**-Me) and *tert*-butyl 2-chloro-2-cyclopropylideneacetate (**1**-*t*Bu) in DMF at 80 °C for 3 h

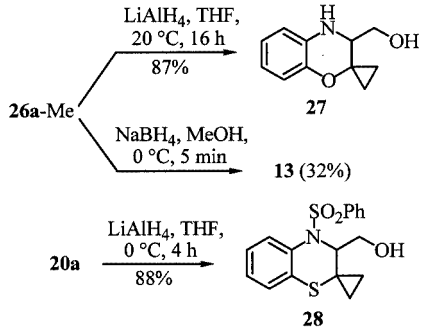
23	Y	R	**24**-Me (%)	**24**-*t*Bu (%)	**25**-Me (%)	**25**-*t*Bu (%)	**26**-Me (%)	**26**-*t*Bu (%)
a[a]	H	Me	**24a**[b]	–	**25a** (22)	–	**26a** (21)	–
a	H	Me	**24a** (11)	–	**25a** (0)	–	**26a** (71)	–
b	Br	Me	**24b** (3)	–	**25b** (0)	–	**26b** (71)	–
b	Br	*t*Bu	–	**24b** (0)	–	**25b** (5)	–	**26b** (55)
c	I	Me	**24c**[b]	–	**25c**[b]	–	**26c** (65)	–

[a] At ambient temperature for 28 h. [b] Yield not determined.

Me or **1**-*t*Bu gave up to three products from two regioisomeric modes of attack (Scheme 7). Products **25**-R and **26**-R, resulting from *O*-attack of **23** on **1**-R, predominated in all cases, and among these two types of products, compounds **26**-R, formed by additional elimination of benzenesulfinic acid, were always the major ones (Table 2), at least when the reactions were carried out at 80 °C. When **1**-Me was treated with **23a** at ambient temperature for 28 h under otherwise identical conditions, the cocyclization product **25a**-Me was isolated in 22% yield along with **26a**-Me (21%).

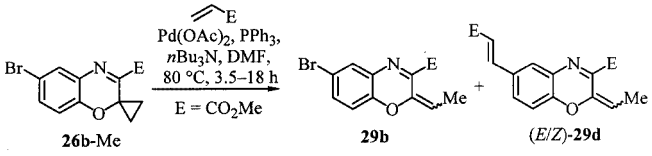
Transformations of the New Heterocycles

The C=N double bonds in the 1,4-benzoxazines **26** and 1,4-benzothiazines **22** could be reduced selectively by treatment with $NaBH_4$ in methanol, whereas treatment with $LiAlH_4$ in THF led to reduction of both the C=N and methoxycarbonyl groups. Upon reduction of **20a** under the same conditions, the *N*-benzenesulfonyl group remained unchanged, and the hydroxylmethyl derivative **28** was obtained in 88% yield (Scheme 8).



Scheme 8. Synthesis of hydroxymethyl derivatives **27** and **28** by reduction of esters **26a**-Me and **20a**

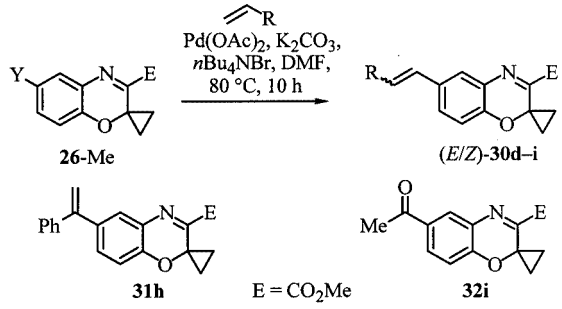
All attempts to perform Heck coupling[8] reactions with the 7-bromo-1,4-benzothiazine derivatives **20b** and **22b** failed. The treatment of methyl 6-bromo-1,4-benzoxazine-3-carboxylate **26b**-Me with methyl acrylate in the presence of a typical palladium catalyst cocktail for Heck reactions[8] [$Pd(OAc)_2$, PPh_3 and nBu_3N] in DMF at 80 °C led to opening of the spirocyclopropane ring. After 3.5 h, the uncoupled product **29b** predominated, while after 18 h the ring-opened coupling products (*Z*)-**29d** and (*E*)-**29d** were obtained in 71 and 4% yields, respectively (Scheme 9). The configuration of the double bond in compound (*Z*)-**29d** was assigned on the basis of the observed strong nuclear Overhauser effect (NOE) between the methoxycarbonyl group at C-3 and the methine proton in the 2D-NOESY NMR spectrum. The uncoupled ring-opened product **29b** was obtained as a single diastereoisomer. Like the major coupling product (*Z*)-**29d**, most probably **29b** has a (*Z*) configuration, but this stereochemistry was not verified by NMR spectroscopy.



Time [h]	**29b** (%)	(*Z*)-**29d** (%)	(*E*)-**29d** (%)
3.5	50	37	not determined
18	0	71	4

Scheme 9. Attempted Heck coupling reaction of 6-bromo-1,4-benzoxazine derivative **26b**-Me with methyl acrylate (for details see Table 3)

Under the same conditions, but without added triphenylphosphane, no reaction was observed after 18 h. Under the modified conditions according to Jeffery[9] [$Pd(OAc)_2$, K_2CO_3, nBu_4NBr, no triphenylphosphane] in DMF at 80 °C, complete conversion was observed after 72 h, but only 30% of the coupling product **30d** was isolated; apparently most of the starting material had decomposed. After only 18 h under these conditions, 57% of **26b**-Me was recovered unchanged, while 10% of **30d** was obtained (Scheme 10, Table 3).



Scheme 10. Heck reactions of 6-halo-1,4-benzoxazine-3-carboxylates **26b**,**c**-Me with alkenes (for details see Table 3)

Table 3. Products **30d**−**i**, **31h** and **32i** of Heck reactions of 6-halo-1,4-benzoxazine-3-carboxylates **26b**,**c**-Me with alkenes

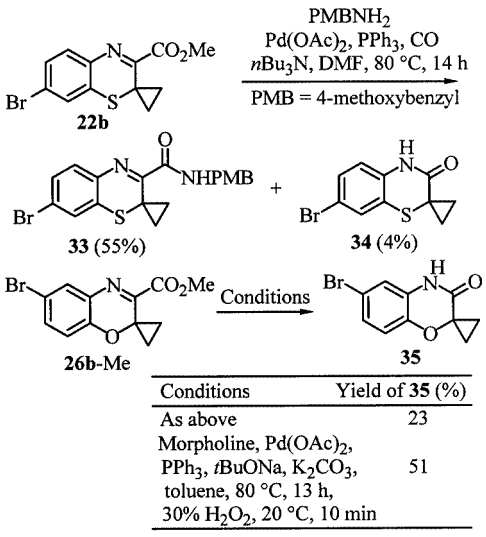
Entry	Y	R	**30** (%)	(*E*/*Z*) ratio[a]	**31**/**32** (%)
d[b]	Br	CO_2Me	≤30	>96:4	0
d	I	CO_2Me	86	>96:4	0
e	I	CHO	89	>96:4	0
f	I	COMe	72	>96:4	0
g	I	CN	87[c]	2.7:1	0
h	I	Ph	75	>96:4	8
i	I	OEt	60	3:1	35[d]

[a] According to NMR spectra. [b] nBu_3N was used instead nBu_4NBr. [c] 31% of pure (*E*)-**30g** was isolated. [d] Isolated as the hydrolysis product **32i**.

Under the same Jeffery conditions, however, the more-reactive 6-iodo-1,4-benzoxazine-3-carboxylate **26c**-Me, could be coupled with methyl acrylate and other typical Heck coupling partners to give the 6-substituted 2-spirocyclopropanated 1,4-benzoxazine derivatives **30d**−**i** in yields ranging from 60 to 89% (Scheme 10). In all these cases the (*E*) isomers were the only products, except for the coupling of acrylonitrile, which gave a mixture of (*E*)-**30g** (which could be isolated) and (*Z*)-**30g** in a ratio of 2.7:1. In addition to 75% of (*E*)-**30h**, 8% of the α-coupling product **31h** was obtained from **26c**-Me and styrene. In the reaction with ethyl vinyl ether, the isolated products were 60% of a 3:1 mixture of (*E*)- and (*Z*)-**30i**, as well as 35% of the methyl ketone **32i** arising from hydrolysis of the α-coupling product. This lack of regioselectivity in Heck couplings with vinyl ethers is well known.[10]

Several attempts to bring about palladium-catalyzed aminocarbonylation and amination reactions of the 7-bromo-1,4-benzothiazine **22b** and 6-bromo-1,4-benzoxazine **26b**-Me derivatives under established conditions were not met with success. Treatment of **22b** with 4-methoxybenzylamine ($PMBNH_2$) and CO in the presence of $Pd(OAc)_2$, PPh_3, and nBu_3N in DMF at 80 °C for 14 h led mainly to the 4-methoxybenzylamide **33** (55%), along with 4% of the 1,4-benzothiazin-3-one derivative **34** arising from **22b** by demethoxycarbonylation and subsequent oxidation. Under the same conditions, the 1,4-benzoxazine derivative **26b**-Me gave the 1,4-benzoxazin-3-one derivative **35** in 23% yield (Scheme 11). The same product was formed in 51% yield upon treatment of **26b**-Me with morpholine under conditions as optimized for aminations of haloarenes [$Pd(OAc)_2$, PPh_3, *t*BuONa, K_2CO_3 in toluene, 80 °C, 30% H_2O_2, 20 °C, 10 min].[11]

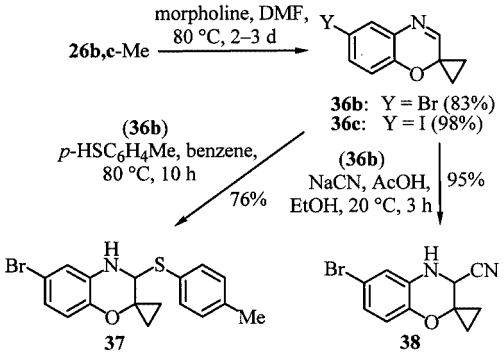
In a control experiment the 1,4-benzoxazine derivatives **26b**,**c**-Me were heated with morpholine without a catalyst in anhydrous DMF under nitrogen. Surprisingly, this procedure led to demethoxycarbonylation to give the spirocyclopropane-annelated 1,4-benzoxazine derivatives **36b**,**c** in excellent yields (83 and 98%, respectively) (Scheme 12). When this reaction of **26b**-Me was carried out in the presence of air, about 10% of **35** was detected as a byproduct according to the NMR spectrum. While the demethoxycarbonylation of **26b**,**c** most probably occurs by nucleophilic



Conditions	Yield of **35** (%)
As above	23
Morpholine, $Pd(OAc)_2$, PPh_3, *t*BuONa, K_2CO_3, toluene, 80 °C, 13 h, 30% H_2O_2, 20 °C, 10 min	51

Scheme 11. Attempted palladium-catalyzed aminocarbonylation and amination reactions of 7-bromo-1,4-benzothiazinecarboxylate **22b** and 6-bromo-1,4-benzoxazinecarboxylate **26b**-Me

attack of morpholine on the ester's methyl group, the amides **34** and **35** must be formed by addition of water onto the C=N double bond in the resulting benzoxazines, and subsequent oxidation.



Scheme 12. Demethoxycarbonylation of 1,4-benzoxazine derivatives **26b**,**c** and nucleophilic additions to the spirocyclopropane-annelated 1,4-benzoxazine moiety in the product **36b**

Facile addition of nucleophiles onto the imine moiety in **36b** does indeed occur, as was proved in reactions with *p*-thiocresol and hydrogen cyanide providing the adducts **37** and **38** in good to excellent yields (76 and 95%, respectively). Hydrolysis of the carbonitrile **38** offers itself as a better route to 3,4-dihydro-1,4-benzoxazinecarboxylate derivatives of type **13**, which are available only in poor yields by direct cocyclization of alkyl 2-chloro-2-cyclopropylideneacetates with *o*-aminophenol **11**.

Experimental Section

General: ^1H NMR spectra were recorded with a Bruker AM 250 spectrometer (250 MHz) at ambient temperature in $CDCl_3$ or [D_6]DMSO, using residual $CHCl_3$ (δ = 7.26 ppm) and [D_5]DMSO

(δ = 2.49 ppm) as internal standards. Chemical shifts (δ) are quoted in ppm and coupling constants (*J*) are given in Hz to the nearest 0.1 Hz. The following abbreviations are used for the signal multiplicities: s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet), and br (broad). ^{13}C NMR spectra were recorded with a Bruker AM 250 spectrometer (62.9 MHz) at ambient temperature in $CDCl_3$ or [D_6]DMSO, with $CDCl_3$ (δ = 77.00 ppm) and [D_6]DMSO (δ = 39.70 ppm) as internal standards. Multiplicities were determined by the DEPT 135 pulse sequence and are given as follows: + = CH or CH_3, − = CH_2, C_{quat} = quaternary carbon atom. 2D-NOESY NMR spectra were recorded with a Bruker AMX 300 spectrometer at 300 MHz. Infrared spectra were recorded with a Bruker FT-IR spectrometer IFS 66. Mass spectra were recorded with a Finnigan MAT 95 spectrometer using electron-impact ionization at 70 eV. High-resolution mass spectra (HRMS) were obtained with a Varian MAT 311 spectrometer using preselected-ion peak matching at $R \approx 10000$ to be within ±2 ppm of the exact masses. Elemental analyses were performed by the Mikroanalytisches Laboratorium im Institut für Organische Chemie, Universität Göttingen. M.p.: Büchi 510 capillary melting point apparatus, uncorrected values. Preparative column chromatography: Merck silica gel 60 (0.063−0.200 mm). All solvents used for reactions were dried according to procedures commonly used. Unless specified otherwise, solutions of $NaHCO_3$ and NaCl were saturated aqueous solutions. Methyl 2-chloro-2-cyclopropylideneacetate (**1**-Me)[1] and *tert*-butyl 2-chloro-2-cyclopropylideneacetate (**1**-*t*Bu),[4a] 2-amino-5-bromothiophenol (**8b**),[12] 2-amino-5-bromophenol (**11b**),[13] 2-amino-5-iodophenol (**11c**),[14] mercaptohydroquinone (**15**),[15] and 2′-hydroxybenzenesulfanilide (**23a**)[16] were prepared according to published methods. All other chemicals were used as commercially available.

Reaction of Methyl 2-Chloro-2-cyclopropylideneacetate (1-Me) with 2-Aminoethanethiol Hydrochloride: A mixture of **1**-Me (382 mg, 2.61 mmol), 2-aminoethanethiol hydrochloride (304 mg, 2.67 mmol) and triethylamine (0.5 mL) in dichloromethane (10 mL) was stirred at ambient temperature for 24 h, diluted with diethyl ether, washed with $NaHCO_3$ and NaCl solutions, dried with $MgSO_4$, and concentrated. The residue was subjected to chromatography on silica gel (60 g), eluting with hexane/diethyl ether and then methanol/diethyl ether (0 → 0.15) to yield **6** (132 mg, 27%) and **7** (70 mg, 16%), respectively.

Methyl 3′,4′,5′,6′-Tetrahydrospiro(cyclopropane-1,2′-[2*H*][1,4]thiazine)-3′-carboxylate (6): A colorless oil, R_f = 0.31 (diethyl ether/methanol, 9:1). For the IR and ^{1}H NMR spectra see ref.[4a] ^{13}C NMR ($CDCl_3$): δ = 13.7 (−, C-2), 15.3 (−, C-3), 22.8 (C_{quat}, C-1), 28.9 (−, C-6′), 43.8 (−, C-5′), 51.6 (+, OCH_3), 63.6 (+, C-3′), 171.4 (C_{quat}, CO) ppm. For the X-ray crystal structure analysis of **6** see ref.[7]

Methyl 4′-{1-[Chloro(methoxycarbonyl)methyl]cyclopropyl}-3′,4′,5′,6′-tetrahydrospiro(cyclopropane-1,2′-[2*H*][1,4]thiazine)-3′-carboxylate (7): A light-yellow oil, R_f = 0.54 (diethyl ether/hexane, 2:1). ^{1}H NMR ($CDCl_3$): δ = 0.65−1.25 (m, 8 H, *c*Pr-H), 2.65−3.00 (m, 4 H, 5′,6′-H), 3.75 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 4.24 (s, 1 H), 4.34 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.8 (−, *c*Pr-C), 14.9 (−, *c*Pr-C), 15.36 (−, *c*Pr-C), 15.39 (−, *c*Pr-C), 16.2 (−, *c*Pr-C), 16.3 (−, *c*Pr-C), 28.2 (C_{quat}, C-1), 33.9 (−, C-6′), 41.6 (C_{quat}, C-1′′), 45.47 (−, C-5′), 45.51 (−, C-5′), 52.9 (+, OCH_3), 63.1 (+), 63.66 (+), 63.68 (+), 168.4 (C_{quat}, CO), 168.8 (C_{quat}, CO) ppm. Two diastereoisomers, ratio ca. 1:1. MS (EI): *m*/*z* (%) = 335/333 (8/20) [M^+], 304/302 (4/13) [$M^+ - CH_3O$], 209/207 (20/54), 192/190 (36/100), 171 (47), 140 (38), 108 (58), 59 (48). $C_{14}H_{20}ClNO_4S$ (333.8): calcd. 333.0801, correct HRMS.

Methyl 2-[1-(2-Aminophenylthio)cyclopropyl]-2-chloroacetate (9a): A solution of **1**-Me (1.016 g, 6.93 mmol) in dichloromethane (5 mL) was added to a solution of 2-aminothiophenol (**8a**) (882 mg, 7.05 mmol) and triethylamine (0.5 mL) in dichloromethane (10 mL) under nitrogen, and the mixture was stirred for 24 h at ambient temperature. The reaction mixture was concentrated, and the residue was recrystallized from hexane/dichloromethane at −60 °C to give **9a** (1.277 g, 68%) as a light-yellow solid. M.p. 73−75 °C. R_f = 0.47 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 1.15−1.35 (m, 4 H, *c*Pr-H), 3.72 (s, 3 H, CH_3O), 4.42 (br s, 2 H, NH_2), 4.49 (s, 1 H, CHCl), 6.67−6.76 (m, 2 H), 7.14 (m, 1 H), 7.39 (dd, *J* = 7.6, 1.7 Hz, 1 H). ^{13}C NMR ($CDCl_3$): δ = 13.8 (−, C-2′), 14.0 (−, C-3′), 31.0 (C_{quat}, C-1′), 52.8 (+, CH_3O), 61.5 (+, C-2), 115.2 (C_{quat}), 115.3 (+), 118.3 (+), 130.6 (+), 136.8 (+), 149.0 (C_{quat}), 168.5 (C_{quat}, CO). MS (EI): *m*/*z* (%) = 273/271 (37/100) [M^+], 236 (13) [$M^+ - Cl$], 204 (57) [$M^+ - Cl - CH_4O$], 202 (17), 176 (64), 162 (52), 125 (34), 124 (63), 106 (54), 80 (37). $C_{12}H_{14}ClNO_2S$ (271.8): calcd. 271.0433, correct HRMS; calcd. C 53.04, H 5.19, N 5.15; found C 52.96, H 5.16, N 5.16.

Methyl 2-[1-(2-Amino-5-bromophenylthio)cyclopropyl]-2-chloroacetate (9b): A solution of **1**-Me (395 mg, 2.69 mmol) in dichloromethane (5 mL) was added to a solution of 2-amino-5-bromothiophenol (**8b**) (418 mg, 2.05 mmol) and triethylamine (0.5 mL) in dichloromethane (10 mL) under nitrogen. After 1 h, the reaction mixture was concentrated and the residue was purified by column chromatography on silica gel (60 g), eluting with diethyl ether/hexane (0:1→1:1) to give **9b** (662 mg, 92%) as a yellowish oil which crystallized rapidly. M.p. 72−73 °C. R_f = 0.30 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 1.16−1.38 (m, 4 H, *c*Pr-H), 3.72 (s, 3 H, CH_3O), 4.39 (s, 1 H, CHCl), 4.40 (br s, 2 H, NH_2), 6.60 (d, *J* = 8.6 Hz, 1 H, 3′-H), 7.22 (dd, *J* = 8.6, 2.4 Hz, 1 H, 4′-H), 7.48 (d, *J* = 2.4 Hz, 1 H, 6′-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.4 (−, C-2′), 14.8 (−, C-3′), 31.4 (C_{quat}, C-1′), 53.0 (+, CH_3O), 62.1 (+, C-2), 109.0 (C_{quat}), 116.7 (+), 117.2 (C_{quat}), 133.3 (+), 138.3 (+), 148.2 (C_{quat}), 168.4 (C_{quat}, CO) ppm. MS (EI): *m*/*z* (%) = 353/351/349 (29/100/74) [M^+], 316/314 (9/6) [$M^+ - Cl$], 284/282 (17/26) [$M^+ - Cl - CH_3O$], 244/242/240 (14/48/35), 204/202 (57/60), 186/184 (37/37), 123 (77). $C_{12}H_{13}BrClNO_2S$ (350.7): calcd. 348.9539, correct HRMS; calcd. C 41.10, H 3.74, N 3.99; found C 41.13, H 3.72, N 3.59.

Methyl 3,4-Dihydrospiro([2*H*][1,4]benzothiazine-2,1′-cyclopropane)-3-carboxylate (10a): **1**-Me (358 mg, 2.44 mmol) was added to a solution of 2-aminothiophenol (**8a**) (335 mg, 2.68 mmol) and triethylamine (1 mL) in anhydrous DMF (5 mL). The mixture was stirred for 15 h at 100 °C, cooled to room temp., poured into $NaHCO_3$ solution (20 mL), and then extracted with dichloromethane. The combined organic extracts were washed twice with water and once with NaCl solution, dried with $MgSO_4$, and concentrated. The residue was purified by column chromatography on silica gel (60 g), eluting with diethyl ether/hexane (0:1→3:2) to yield **10a** (228 mg, 40%) as a red oil. R_f = 0.35 (diethyl ether/hexane, 2:1). ^{1}H NMR ($CDCl_3$, compare with ref.[4]): δ = 0.82−1.25 (m, 4 H, *c*Pr-H), 3.29 (s, 1 H, CHN), 3.65 (s, 3 H, CH_3O), 4.60 (br s, 1 H, NH), 6.52 (m, 2 H), 6.83 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.6 (−, C-2′), 16.7 (−, C-3′), 21.0 (C_{quat}, C-1′), 51.4 (+, CH_3O), 60.4 (+, C-3), 114.7 (+), 115.1 (C_{quat}), 117.1 (+), 125.0 (+), 126.6 (+), 139.5 (C_{quat}), 170.7 (C_{quat}, CO) ppm. MS (EI) (compare with ref.[4a]): *m*/*z* (%) = 235 (48) [M^+], 176 (100) [$M^+ - COOCH_3$].

Methyl 2-Chloro-2-[1-(2-hydroxyanilino)cyclopropyl]acetate (12): A solution of **1**-Me (300 mg, 2.05 mmol) in DMF (5 mL) was added to a solution of 2-aminophenol (**11a**) (225 mg, 2.06 mmol) and triethylamine (0.5 mL) in DMF (10 mL), and then the mixture was

stirred for 24 h at ambient temperature, poured into water (50 mL), and extracted with dichloromethane. The combined organic phases were washed with water and NaCl solution, dried with $MgSO_4$, and concentrated. The residue was chromatographed on silica gel (60 g), eluting with diethyl ether/hexane (0:1 → 1:1) to give **12** (335 mg, 64%) as a reddish oil, which rapidly became dark upon standing in air. R_f = 0.34 (diethyl ether/hexane, 1:1). IR (film): $\tilde{\nu}$ = 3421 cm^{-1} (br, OH, NH), 2954, 1734 (CO), 1611, 1513, 1438, 1270, 1197, 1171, 1103, 1016, 912, 744. ^1H NMR ($CDCl_3$): δ = 1.00−1.06 (m, 3 H, *c*Pr-H), 1.28−1.39 (m, 1 H, *c*Pr-H), 3.75 (s, 3 H, CH_3O), 4.58 (s, 1 H, CHCl), 5.8 (br s, 2 H, NH + OH), 6.40−6.97 (m, 4 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.6 (−, C-2′), 14.6 (−, C-3′), 37.2 (C_{quat}, C-1′), 53.1 (+, CH_3O), 60.9 (+, C-2), 113.0 (+), 114.8 (+), 118.6 (+), 120.9 (+), 133.6 (C_{quat}), 143.5 (C_{quat}), 169.2 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 257/255 (4/13) [M^+], 240/238 (3/8) [M^+ − OH], 220 (53) [M^+ − Cl], 188 (94) [M^+ − Cl − CH_3OH], 160 (29), 148 (44), 146 (100). $C_{12}H_{14}ClNO_3$ (255.7): calcd. 255.0662, correct HRMS.

Methyl 3,4-Dihydrospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate (13): A solution of **1**-Me (296 mg, 2.02 mmol) in DMF (5 mL) was added to a solution of **11a** (220 mg, 2.02 mmol) and DBU (0.31 mL, 2.1 mmol) in DMF (10 mL). The mixture was stirred at 70−80 °C for 24 h under nitrogen, cooled, poured into water (50 mL), and extracted with dichloromethane. The organic phases were washed three times with water and with NaCl solution, dried with $MgSO_4$, and concentrated. The residue was subjected to chromatography on silica gel (60 g), eluting with diethyl ether/hexane (0:1 → 1:1) to give **13** (20 mg, 4.5%) as a light-yellow oil which crystallized slowly. M.p. 59−61 °C. R_f = 0.19 (diethyl ether/hexane, 1:1). ^1H NMR ($CDCl_3$): δ = 0.72−0.82 (m, 1 H, *c*Pr-H), 0.96−1.17 (m, 2 H, *c*Pr-H), 1.21−1.32 (m, 1 H, *c*Pr-H), 3.62 (s, 3 H, CH_3O), 3.77 (s, 1 H, CHN), 4.43 (br s, 1 H, NH), 6.69−6.90 (m, 4 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.0 (−, C-2′), 12.6 (−, C-3′), 52.5 (+, CH_3O), 58.2 (+, C-3), 59.5 (C_{quat}, C-1′), 115.7 (+), 116.9 (+), 119.0 (+), 122.1 (+), 132.5 (C_{quat}), 144.0 (C_{quat}), 171.6 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 219 (37) [M^+], 160 (100) [M^+ − $COOCH_3$], 132 (9) [M^+ − $COOCH_3$ − C_2H_4]. $C_{12}H_{13}NO_3$ (219.2): calcd. 219.0895, correct HRMS.

Methyl 2-Chloro-2-[1-(2,5-dihydroxyphenylthio)cyclopropyl]acetate (16): A solution of **1**-Me (321 mg, 2.19 mmol) in dichloromethane (5 mL) was added under nitrogen to a stirred solution of mercaptohydroquinone (**15**) (311 mg, 2.19 mmol) and triethylamine (0.5 mL) in dichloromethane (10 mL), the mixture was stirred for an additional 2 h at ambient temperature, and then concentrated. The residue was subjected to chromatography on silica gel (60 g), eluting with diethyl ether/hexane to give nearly pure **16** (547 mg, 86%) as a reddish oil. R_f = 0.54 (ether). ^1H NMR ($CDCl_3$): δ = 1.10−1.30 (m, 4 H, *c*Pr-H), 3.70 (s, 3 H, CH_3O), 4.29 (s, 1 H, CHCl), 6.70 (br s, 1 H, OH), 6.80 (s, 2 H), 6.97 (s, 1 H), 7.11 (br s, 1 H, OH) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.0 (−, C-2′), 15.1 (−, C-3′), 30.7 (C_{quat}, C-1′), 53.2 (+, CH_3O), 62.2 (+, C-2), 116.0 (+), 117.1 (+), 118.7 (+), 121.5 (C_{quat}), 149.0 (C_{quat}), 150.4 (C_{quat}), 169.0 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 290/288 (37/100) [M^+], 253 (49) [M^+ − Cl], 221 (61) [M^+ − Cl − CH_3OH], 193 (52), 181 (44) [M^+ − $CHClCOOCH_3$], 141 (50) [$C_6H_5O_2S^+$].

Methyl 3,4-Dihydro-6-hydroxyspiro([2*H*][1,4]benzoxathiine-3,1′-cyclopropane)-2-carboxylate (17): K_2CO_3 (276 mg, 2.00 mmol) was added under nitrogen to a stirred solution of **15** (266 mg, 1.87 mmol), **1**-Me (275 mg, 1.88 mmol) and KI (30 mg) in DMF (15 mL). The mixture was stirred for 4 d at ambient temperature, diluted with dichloromethane, washed with water and with NaCl solution, dried with $MgSO_4$, and then concentrated. The residue was subjected to chromatography on silica gel (60 g), eluting with diethyl ether/hexane (0:1→2:1) to give **17** (400 mg, 85%) as a colorless solid. M.p. 140−141 °C. R_f = 0.32 (diethyl ether/hexane, 2:1). IR (KBr): $\tilde{\nu}$ = 3428, 3403, 3073, 3005, 2956, 2919, 1739, 1718, 1617, 1489, 1437, 1350, 1313, 1278, 1224, 1188, 1089 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.98−1.20 (m, 3 H, *c*Pr-H), 1.32−1.41 (m, 1 H, *c*Pr-H), 3.80 (s, 3 H, CH_3O), 4.21 (s, 1 H, 2-H), 5.65 (s, 1 H, OH), 6.39 (d, *J* = 2.7 Hz, 1 H, 5-H), 6.48 (dd, *J* = 8.8, 2.7 Hz, 1 H, 7-H), 6.80 (d, *J* = 8.8 Hz, 1 H, 8-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.7 (−, C-2′), 17.1 (−, C-3′), 21.6 (C_{quat}, C-1′), 52.8 (+, CH_3O), 79.5 (+, C-2), 113.6 (+), 114.0 (+), 117.9 (C_{quat}), 118.7 (+), 143.8 (C_{quat}), 149.8 (C_{quat}), 169.7 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 252 (100) [M^+], 193 (56) [M^+ − $COOCH_3$], 166 (63). $C_{12}H_{12}O_4S$ (252.2): calcd. 252.0456, correct HRMS; calcd. C 57.13, H 4.79; found C 57.01, H 4.87.

General Procedure for the Preparation of Compounds 18a,b, 19a (GP1): A solution of benzenesulfonyl chloride in dichloromethane (5 mL) was added to a solution of **9** and pyridine (1 mL) in dichloromethane (10 mL). The reaction mixture was stirred for 20 h at ambient temperature, diluted with dichloromethane, washed twice with 5% HCl, once each with both water and NaCl solution, dried with $MgSO_4$ and then concentrated. The residue was crystallized from hexane/CH_2Cl_2 at −20 °C (**18a**, **19a**) or subjected to chromatography on silica gel (**18b**).

Methyl 2-Chloro-2-(1-{2-[(phenylsulfonyl)amino]phenylthio}cyclopropyl)acetate (18a): From **9a** (645 mg, 2.37 mmol) and benzenesulfonyl chloride (402 mg, 2.28 mmol) according to **GP1**, **18a** (753 mg, 80%) was isolated as a colorless solid. M.p. 121−122 °C. R_f = 0.35 (diethyl ether/hexane, 1:1). IR (KBr): $\tilde{\nu}$ = 3239, 3064, 3019, 2971, 2956, 1743, 1700, 1589, 1484, 1449, 1402, 1323, 1275, 1184, 1157, 1090, 926 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.12−1.38 (m, 4 H, *c*Pr-H), 3.82 (s, 3 H, CH_3O), 4.15 (s, 1 H, CHCl), 7.09 (dt, *J* = 7.6, 1.3 Hz, 1 H), 7.29−7.66 (m, 6 H), 7.82 (m, 2 H), 8.03 (br s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.9 (−, C-2′), 15.5 (−, C-3′), 31.2 (C_{quat}, C-1′), 53.3 (+, CH_3O), 62.4 (+, C-2), 121.3 (+), 123.4 (C_{quat}), 125.0 (+), 127.1 (+, 2 C), 128.8 (+, 2 C), 130.4 (+), 132.9 (+), 135.8 (+), 138.7 (C_{quat}), 138.9 (C_{quat}), 168.3 (C_{quat}, CO) ppm. MS (EI): *m*/*z* (%) = 413/411 (33/75) [M^+], 376 (60) [M^+ − Cl], 344 (38) [M^+ − Cl − CH_3OH], 270 (16), 235 (52), 234 (100), 220 (29), 175 (35), 174 (29), 163 (64), 162 (84), 124 (21), 77 (44). $C_{18}H_{18}ClNO_4S_2$ (411.9): calcd. 411.0365, correct HRMS; calcd. C 52.48, H 4.40, N 3.40; found C 52.56, H 4.59, N 3.24.

Methyl 2-(1-{5-Bromo-2-[(phenylsulfonyl)amino]phenylthio}cyclopropyl)-2-chloroacetate (18b): From **9b** (650 mg, 1.85 mmol) and benzenesulfonyl chloride (332 mg, 1.88 mmol), according to **GP1** with chromatography on silica gel (60 g), eluting with diethyl ether/hexane (0:1→1:1), **18b** (878 mg, 97%) was isolated as a colorless glass. R_f = 0.26 (diethyl ether/hexane, 1:1). ^1H NMR ($CDCl_3$): δ = 1.06−1.34 (m, 4 H, *c*Pr-H), 3.73 (s, 3 H, CH_3O), 4.06 (s, 1 H, CHCl), 7.32−7.54 (m, 6 H), 7.71−7.79 (m, 2 H), 8.02 (br s, 1 H, NH). ^{13}C NMR ($CDCl_3$): δ = 14.7 (−, C-2′), 16.4 (−, C-3′), 31.3 (C_{quat}, C-1′), 53.3 (+, CH_3O), 63.6 (+, C-2), 117.5 (C_{quat}), 123.2 (+), 126.4 (C_{quat}), 126.9 (+, 2 C), 128.8 (+, 2 C), 132.9 (+), 133.0 (+), 137.3 (+), 137.5 (C_{quat}), 138.5 (C_{quat}), 168.0 (C_{quat}, CO) ppm. MS (EI): *m*/*z* (%) = 493/491/489 (34/100/73) [M^+], 456/454 (42/37) [M^+ − Cl], 424/422 (15/13) [M^+ − Cl − CH_3OH], 315/314/313/312 (27/60/24/56), 243/242/241/240 (44/58/42/53), 77 (61). $C_{18}H_{17}BrClNO_4S_2$ (490.8): calcd. 488.9471, correct HRMS.

Methyl 2-[1-(2-{[(4-Bromophenyl)sulfonyl]amino}phenylthio)cyclopropyl]-2-chloroacetate (19a): From **9a** (584 mg, 2.15 mmol) with 4-bromobenzenesulfonyl chloride (660 mg, 2.58 mmol), according to

GP1, **19a** (855 mg, 81%) was isolated as a colorless solid. M.p. 113−115 °C. R_f = 0.32 (diethyl ether/hexane, 1:1). IR (KBr): $\tilde{\nu}$ = 3240, 3066, 3007, 2981, 2955, 1743, 1700, 1653, 1576, 1485, 1407, 1327, 1158, 931 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 1.10−1.40 (m, 4 H, *c*Pr-H), 3.79 (s, 3 H, CH_3O), 4.10 (s, 1 H, CHCl), 7.08 (dt, *J* = 7.8, 1.5 Hz, 1 H), 7.32 (dt, *J* = 7.8, 1.5 Hz, 1 H), 7.44−7.67 (m, 6 H), 8.08 (br s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.3 (−, C-2′), 16.0 (−, C-3′), 31.4 (C_{quat}, C-1′), 53.4 (+, CH_3O), 62.0 (+, C-2), 121.8 (+), 124.1 (C_{quat}), 125.4 (+), 128.0 (C_{quat}), 128.8 (+, 2 C), 130.5 (+), 132.1 (+, 2 C), 135.9 (+), 138.1 (C_{quat}), 138.4 (C_{quat}), 168.4 (C_{quat}, CO) ppm. MS (EI): *m*/*z* (%) = 493/491/489 (17/52/37) [M^+], 456/454 (38/34) [M^+ − Cl], 424/422 (22/21) [M^+ − Cl − CH_3OH], 270 (14), 235 (52), 234 (94) [M^+ − Cl − $BrC_6H_4SO_2$], 202 (29), 175 (40), 163 (77), 162 (100). $C_{18}H_{17}BrClNO_4S_2$ (490.8): calcd. 488.9471, correct HRMS; calcd. C 44.05, H 3.49, N 2.85; found C 44.04, H 3.57, N 2.58.

General Procedure for the Preparation of Compounds 20−22 (GP2): A mixture of **18** or **19**, K_2CO_3, KI (50 mg) and DMF (10 mL) was stirred at 70 °C for 2 h, cooled, diluted with dichloromethane, washed repeatedly with water and once with NaCl solution, dried with $MgSO_4$, and then concentrated. The residue was crystallized from hexane/dichloromethane.

Methyl 4-(Phenylsulfonyl)-3,4-dihydrospiro([2*H*][1,4]benzothiazine-2,1′-cyclopropane)-3-carboxylate (20a): From **18a** (726 mg, 1.76 mmol) and K_2CO_3 (365 mg, 2.64 mmol) according to **GP2**, **20a** (507 mg, 77%) was obtained as a colorless solid. M.p. 143−144 °C. R_f = 0.37 (diethyl ether/hexane, 1:1). IR (KBr): $\tilde{\nu}$ = 3096, 3000, 2957, 1751, 1479, 1451, 1436, 1326, 1202, 1161, 1086, 1072 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.84−0.98 (m, 2 H, *c*Pr-H), 1.13−1.33 (m, 2 H, *c*Pr-H), 3.71 (s, 3 H, CH_3O), 5.07 (s, 1 H, 3-H), 7.02−7.16 (m, 3 H), 7.40−7.62 (m, 4 H), 7.71−7.76 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.9 (−, C-2′), 15.7 (−, C-3′), 24.9 (C_{quat}, C-1′), 52.6 (+, CH_3O), 64.5 (+, C-3), 125.3 (+), 125.6 (+), 126.0 (+), 127.0 (+, 2 C), 127.4 (+), 128.3 (C_{quat}), 128.8 (+, 2 C), 132.8 (+), 133.6 (C_{quat}), 139.8 (C_{quat}), 168.2 (C_{quat}, CO) ppm. MS (EI): *m*/*z* (%) = 375 (73) [M^+], 316 (20) [M^+ − $COOCH_3$], 234 (91) [M^+ − $C_6H_5SO_2$], 175 (100) [M^+ − $C_6H_5SO_2$ − $COOCH_3$], 174 (62) [M^+ − $C_6H_5SO_2H$ − $COOCH_3$]. $C_{18}H_{17}NO_4S_2$ (375.5): calcd. 375.0599, correct HRMS; calcd. C 57.58, H 4.56, N 3.73; found C 57.53, H 4.51, N 3.63.

Methyl Spiro([2*H*][1,4]benzothiazine-2,1′-cyclopropane)-3-carboxylate (22a): A mixture of **18a** (733 mg, 1.78 mmol), K_2CO_3 (622 mg, 4.50 mmol), KI (50 mg) and DMF (15 mL) was stirred at 80−85 °C for 4 h, cooled, diluted with dichloromethane, washed repeatedly with water and once with NaCl solution, dried with $MgSO_4$ and concentrated to give pure **22a** (364 mg, 88%) as a yellow oil. R_f = 0.32 (diethyl ether/hexane, 1:2). ^1H NMR ($CDCl_3$): δ = 1.06 and 1.58 (AA′XX′, 4 H, *c*Pr-H), 3.87 (s, 3 H, CH_3O), 7.18−7.26 (m, 3 H), 7.48−7.56 (m, 1 H). ^{13}C NMR ($CDCl_3$): δ = 16.6 (−, 2 C, C-2′,3′), 17.1 (C_{quat}, C-1′), 52.7 (+, CH_3O), 126.4 (C_{quat}), 126.6 (+), 126.8 (+), 128.7 (+), 128.8 (+), 141.3 (C_{quat}), 154.7 (C_{quat}, C=N), 163.1 (C_{quat}, CO). MS (EI): *m*/*z* (%) = 233 (62) [M^+], 218 (3) [M^+ − CH_3], 201 (5) [M^+ − CH_3OH], 174 (25), 173 (100). $C_{12}H_{11}NO_2S$ (233.3): calcd. 233.0510, correct HRMS.

Methyl 7-Bromo-4-(phenylsulfonyl)-3,4-dihydrospiro([2*H*][1,4]benzothiazine-2,1′-cyclopropane)-3-carboxylate (20b) and Methyl 7-Bromospiro([2*H*][1,4]benzothiazine-2,1′-cyclopropane)-3-carboxylate (22b): From **18b** (870 mg, 1.77 mmol) and K_2CO_3 (370 mg, 2.68 mmol), according to **GP2**, **20b** (110 mg, 14%) was obtained as a colorless solid. M.p. 171−172 °C. R_f = 0.32 (diethyl ether/hexane, 1:1). IR (KBr): $\tilde{\nu}$ = 3097, 3005, 2957, 1775, 1700, 1653, 1473, 1450, 1437, 1323, 1202, 1161, 1086 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.84−0.98 (m, 2 H, *c*Pr-H), 1.17−1.31 (m, 2 H, *c*Pr-H), 3.73 (s, 3 H, CH_3O), 5.03 (s, 1 H, 3-H), 7.12−7.22 (m, 2 H), 7.40−7.62 (m, 4 H), 7.72−7.78 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.9 (−, C-2′), 16.1 (−, C-3′), 24.9 (C_{quat}, C-1′), 52.9 (+, CH_3O), 64.3 (+, C-3), 118.6 (C_{quat}), 127.1 (+, 2 C), 127.2 (+), 128.7 (+), 129.1 (+, 2 C), 129.7 (+), 130.4 (C_{quat}), 132.9 (C_{quat}), 133.2 (+), 139.8 (C_{quat}), 168.1 (C_{quat}, CO) ppm. MS (EI): *m*/*z* (%) = 455/453 (72/66) [M^+], 396/394 (16/14) [M^+ − $COOCH_3$], 314/312 (100/97) [M^+ − $C_6H_5SO_2$], 255/253 (82/85) [M^+ − $C_6H_5SO_3$ − $COOCH_3$], 254/252 (55/42) [M^+ − $C_6H_5SO_2H$ − $COOCH_3$]. $C_{18}H_{16}BrNO_4S_2$ (454.4): calcd. 452.9704, correct HRMS; calcd. C 47.58, H 3.55, N 3.08; found C 47.40, H 3.61, N 2.89. The mother liquor from the crystallization of **20b** was concentrated and the residue was recrystallized from hexane/diethyl ether to yield **22b** (250 mg, 45%) as yellow crystals. M.p. 108−109 °C. R_f = 0.33 (diethyl ether/hexane, 1:1). ^1H NMR ($CDCl_3$): δ = 1.08 and 1.62 (AA′XX′, 4 H, *c*Pr-H), 3.86 (s, 3 H, CH_3O), 7.32−7.43 (m, 3 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.8 (−, 2 C, C-2′,3′), 17.2 (C_{quat}, C-1′), 53.0 (+, CH_3O), 122.4 (C_{quat}), 128.6 (C_{quat}), 129.4 (+), 129.9 (+), 130.1 (+), 140.4 (C_{quat}), 155.1 (C_{quat}, C=N), 163.0 (C_{quat}, CO) ppm. MS (EI): *m*/*z* (%) = 313/311 (53/52) [M^+], 281/279 (9/9) [M^+ − CH_3OH], 254/252 (18/18), 253/251 (100/95), 172 (18). $C_{12}H_{10}BrNO_2S$ (312.2): calcd. 310.9615, correct HRMS. For the X-ray crystal structure analysis of **22b** see ref.[7]

Methyl 4-[(4-Bromophenyl)sulfonyl]-3,4-dihydrospiro([2*H*][1,4]benzothiazine-2,1′-cyclopropane)-3-carboxylate (21a): From **19a** (832 mg, 1.70 mmol) and K_2CO_3 (250 mg, 1.81 mmol), according to **GP2**, **21a** (435 mg, 56%) was obtained as a colorless solid. M.p. 98−99 °C. R_f = 0.44 (diethyl ether/hexane, 1:1). IR (KBr): $\tilde{\nu}$ = 3083, 3001, 2953, 1756, 1575, 1478, 1439, 1348, 1207, 1159, 1093, 1068, 873 cm^{-1}. ^1H NMR ($CDCl_3$): δ = 0.83−0.99 (m, 2 H, *c*Pr-H), 1.09−1.18 (m, 1 H, *c*Pr-H), 1.23−1.32 (m, 1 H, *c*Pr-H), 3.73 (s, 3 H, CH_3O), 5.06 (s, 1 H, 3-H), 7.05−7.18 (m, 3 H), 7.57 (s, 4 H, 4-BrC_6H_4), 7.56−7.63 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.2 (−, C-2′), 15.5 (−, C-3′), 25.4 (C_{quat}, C-1′), 52.8 (+, CH_3O), 65.1 (+, C-3), 125.8 (+), 126.0 (+), 126.5 (+), 127.8 (+), 128.0 (C_{quat}), 128.7 (+, 2 C), 129.1 (C_{quat}), 132.2 (+, 2 C), 133.6 (C_{quat}), 138.9 (C_{quat}), 168.2 (C_{quat}, CO) ppm. MS (EI): *m*/*z* (%) = 455/453 (40/39) [M^+], 396/394 (11/10) [M^+ − $COOCH_3$], 234 (90) [M^+ − $BrC_6H_4SO_2$], 175 (100) [M^+ − $BrC_6H_5SO_2$ − $COOCH_3$], 174 (48) [M^+ − $BrC_6H_4SO_2H$ − $COOCH_3$]. $C_{18}H_{16}BrNO_4S_2$ (454.4): calcd. 452.9704, correct HRMS; calcd. C 47.58, H 3.55, N 3.08; found C 47.48, H 3.63, N 2.87. The mother solution contained **22a** and some **21a**. The yield of **22a** was not determined.

Benzenesulfanilides 23a−c: These were obtained from the corresponding 2-aminophenols according to the procedure reported[17] for the synthesis of 2′-hydroxy-*p*-toluenesulfanilide, with yields as shown in Scheme 7. The new sulfanilides **23b,c** were characterized by their spectroscopic data as follows.

5′-Bromo-2′-hydroxybenzenesulfanilide (23b): Light-brown solid, m.p. 153−155 °C. IR (KBr): $\tilde{\nu}$ = 3380, 3249, 1506, 1451, 1394, 1319, 1159, 1091, 930 cm^{-1}. ^1H NMR ([D_6]DMSO): δ = 6.68 (d, *J* = 8.6 Hz, 1 H, 3′-H), 7.09 (dd, *J* = 8.6, 2.4 Hz, 1 H, 4′-H), 7.25 (d, *J* = 2.4 Hz, 1 H, 6′-H), 7.48−7.60 (m, 3 H), 7.73−7.77 (m, 2 H), 9.79 (br s, 2 H, NH, OH) ppm. ^{13}C NMR ([D_6]DMSO): δ = 109.5 (C_{quat}), 117.5 (+), 126.1 (C_{quat}), 126.9 (+), 127.0 (+), 128.9 (+), 129.3 (+), 133.0 (+), 140.5 (C_{quat}), 149.9 (C_{quat}) ppm. MS (EI): *m*/*z* (%) = 329/327 (9/9) [M^+], 188/186 (98/100) [M^+ − $C_6H_5SO_2$], 160/158 (35/37), 77 (60) [$C_6H_5^+$], 51 (49). $C_{12}H_{10}BrNO_3S$ (328.2): calcd. 326.9565, correct HRMS; calcd. C 43.92, H 3.07, N 4.27; found C 44.02, H 3.12, N 3.89.

2′-Hydroxy-5′-iodobenzenesulfanilide (23c): Yellow solid, m.p. 172−174 °C. IR (KBr): $\tilde{\nu}$ = 3362, 3235, 3063, 1590, 1498, 1432, 1385, 1326, 1287, 1162, 1118, 1089, 1072, 921 cm^{-1}. ^1H NMR ([D$_6$]DMSO): δ = 6.55 (d, *J* = 8.6 Hz, 1 H, 3′-H), 7.23 (dd, *J* = 8.6, 2.4 Hz, 1 H, 4′-H), 7.37 (d, *J* = 2.4 Hz, 1 H, 6′-H), 7.48−7.60 (m, 3 H), 7.71−7.75 (m, 2 H), 9.52 (br s, 1 H), 9.93 (br s, 1 H) ppm. ^{13}C NMR ([D$_6$]DMSO): δ = 80.2 (C_{quat}, C-5′), 118.2 (+), 126.3 (C_{quat}), 126.9 (+), 129.2 (+), 133.0 (+), 133.0 (+), 134.9 (+), 140.6 (C_{quat}), 150.7 (C_{quat}) ppm. MS (EI): *m*/*z* (%) = 375 (20) [M^+], 234 (100) [$M^+ - C_6H_5SO_2$], 206 (17), 77 (21) [$C_6H_5^+$], 51 (18). $C_{12}H_{10}INO_3S$ (375.2): calcd. 374.9426, correct HRMS; calcd. C 38.42, H 2.69, N 3.73; found C 38.59, H 2.82, N 3.40.

Methyl 4-(Phenylsulfonyl)-3,4-dihydrospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate (25a-Me): A mixture of **23a** (486 mg, 1.95 mmol), **1**-Me (288 mg, 1.96 mmol), K_2CO_3 (418 mg, 3.03 mmol), KI (50 mg), and DMF (15 mL) was stirred for 28 h at ambient temperature, then diluted with dichloromethane, washed repeatedly with water and once with NaCl solution, dried with $MgSO_4$, and concentrated. The residue was subjected to chromatography on silica gel (60 g), eluting with diethyl ether/hexane (0:1→1:2) to give **26a**-Me (87 mg, 21%) and a mixture of **24a**-Me (see below) and **25a**-Me. This mixture was recrystallized from diethyl ether to yield of **25a**-Me (153 mg, 22%) as a colorless solid. M.p. 125−126 °C. R_f = 0.21 (diethyl ether/hexane, 1:2). ^1H NMR ($CDCl_3$): δ = 0.50−0.62 (m, 1 H, *c*Pr-H), 0.72−0.84 (m, 1 H, *c*Pr-H), 1.27−1.40 (m, 2 H, *c*Pr-H), 3.76 (s, 3 H, CH_3O), 4.72 (s, 1 H, 3-H), 6.77−7.03 (m, 3 H), 7.48−7.67 (m, 4 H), 7.90−7.98 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.7 (−, C-2′), 12.7 (−, C-3′), 52.8 (+, CH_3O), 60.1 (C_{quat}, C-1′), 60.8 (+, C-3), 117.6 (+), 120.7 (+), 121.8 (+), 124.3 (C_{quat}), 124.6 (+), 127.2 (+, 2 C), 129.2 (+, 2 C), 133.3 (+), 140.2 (C_{quat}), 145.4 (C_{quat}), 168.2 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 359 (79) [M^+], 300 (29) [$M^+ - COOCH_3$], 218 (92) [$M^+ - C_6H_5SO_2$], 190 (13), 174 (18), 159 (100) [$M^+ - C_6H_5SO_2 - COOCH_3$]. $C_{18}H_{17}NO_5S$ (359.4): calcd. 359.0827, correct HRMS; calcd. C 60.16, H 4.77, N 3.90; found C 60.46, H 4.85, N 3.62.

General Procedure for the Preparation of Benzoxazines 24−26 (GP3): K_2CO_3 was added to a stirred mixture of *N*-(2-hydroxy-5-Y-phenyl)benzenesulfonamide **23**, **1**-R and KI (30 mg) in DMF (40 mL). The mixture was stirred at 80 °C for 3 h, cooled, diluted with dichloromethane, washed repeatedly with water and once with NaCl solution, dried with $MgSO_4$, and then concentrated. The residue was subjected to chromatography on silica gel (60 g), eluting with diethyl ether/hexane (0:1→1:4).

Methyl 4-(Phenylsulfonyl)-3,4-dihydrospiro([2*H*][1,4]benzoxazine-3,1′-cyclopropane)-2-carboxylate (24a-Me) and Methyl Spiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate (26a): From **23a** (497 mg, 1.99 mmol), K_2CO_3 (689 mg, 4.99 mmol), and **1**-Me (294 mg, 2.01 mmol), according to **GP3**, **24a**-Me (80 mg, 11%) and **26a**-Me (306 mg, 71%) were obtained. **24a-Me:** Colorless solid. M.p. 124−125 °C. R_f = 0.12 (diethyl ether/hexane, 1:4). ^1H NMR ($CDCl_3$): δ = 0.75−0.90 (br m, 2 H, *c*Pr-H), 1.16 (br m, 1 H, *c*Pr-H), 1.92 (br m, 1 H, *c*Pr-H), 3.71 (s, 3 H, CH_3O), 4.18 (s, 1 H, 2-H), 6.92−7.00 (m, 2 H), 7.17 (m, 1 H), 7.45−7.70 (m, 6 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.0 (−, C-2′), 13.3 (br, −, C-3′), 38.2 (C_{quat}, C-1′), 52.5 (+, CH_3O), 74.7 (br, +, C-2), 117.3 (+), 120.7 (+), 125.3 (C_{quat}), 126.7 (br, +), 127.4 (br, +, 2 C), 127.6 (+), 129.4 (+, 2 C), 133.5 (+), 138.9 (br, C_{quat}), 147.2 (C_{quat}), 167.4 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 359 (16) [M^+], 300 (2) [$M^+ - COOCH_3$], 218 (100) [$M^+ - C_6H_5SO_2$], 159 (27) [$M^+ - C_6H_5SO_2 - COOCH_3$]. $C_{18}H_{17}NO_5S$ (359.4): calcd. 359.0827, correct HRMS. **26a-Me:** Yellow solid. M.p. 52−53 °C. R_f = 0.21 (diethyl ether/hexane, 1:4). ^1H NMR ($CDCl_3$): δ = 1.22 and 1.54 (AA′XX′, 4 H, *c*Pr-H), 3.84 (s, 3 H, CH_3O), 6.71 (dd, *J* = 7.9, 1.4 Hz, 1 H), 6.96 (dt, *J* = 7.9, 1.4 Hz, 1 H), 7.14 (dt, *J* = 7.9, 1.7 Hz, 1 H), 7.43 (dd, *J* = 7.9, 1.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.9 (−, 2 C, C-2′,3′), 52.7 (+, CH_3O), 58.0 (C_{quat}, C-1′), 115.8 (+), 122.6 (+), 128.3 (+), 131.0 (+), 132.9 (C_{quat}), 147.6 (C_{quat}), 155.9 (C_{quat}, C=N), 162.0 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 217 (54) [M^+], 202 (2) [$M^+ - CH_3$], 185 (10) [$M^+ - CH_3OH$], 158 (20), 157 (100). $C_{12}H_{11}NO_3$ (217.2): calcd. 217.0738, correct HRMS; calcd. C 66.35, H 5.10, N 6.45; found 66.67, H 5.20, N 6.20.

Methyl 6-Bromo-4-(phenylsulfonyl)-3,4-dihydrospiro([2*H*][1,4]benzoxazine-3,1′-cyclopropane)-2-carboxylate (24b-Me) and Methyl 6-Bromospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate (26b-Me): From **23b** (3.54 g, 10.8 mmol), K_2CO_3 (2.07 g, 15.0 mmol), and **1**-Me (1.60 g, 10.9 mmol), according to **GP3**, **24b**-Me (140 mg, 3%) and **26b**-Me (2.27 g, 71%) were obtained. **24b-Me:** Colorless solid. M.p. 165−166 °C. R_f = 0.23 (diethyl ether/hexane, 1:1). ^1H NMR ($CDCl_3$): δ = 0.70−0.95 (br s, 2 H, *c*Pr-H), 1.10−1.22 (m, 1 H, *c*Pr-H), 1.74−2.05 (br s, 1 H, *c*Pr-H), 3.72 (s, 3 H, CH_3O), 4.12 (s, 1 H, 2-H), 6.86 (d, *J* = 8.6 Hz, 1 H, 8-H), 7.28 (dd, *J* = 8.6, 2.1 Hz, 1 H, 7-H), 7.48−7.58 (m, 2 H), 7.59−7.73 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.0 (−, C-2′), 13.3 (br, −, C-3′), 38.1 (C_{quat}, C-1′), 52.6 (+, CH_3O), 74.8 (br, +, C-2), 112.5 (C_{quat}), 118.8 (+), 126.5 (C_{quat}), 127.6 (+), 129.2 (br, C_{quat}), 129.6 (+, 4 C), 130.3 (+), 133.8 (+), 146.4 (C_{quat}), 167.1 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 439/437 (15/14) [M^+], 298/296 (96/100) [$M^+ - C_6H_5SO_2$], 238/236 (18/14), 77 (10). $C_{18}H_{16}BrNO_5S$ (438.3): calcd. C 49.33, H 3.68, N 3.20; found C 49.30, H 3.70, N 3.02. **26b-Me:** Yellow oil. R_f = 0.48 (hexane/diethyl ether, 1:1). ^1H NMR ($CDCl_3$): δ = 1.20 and 1.54 (AA′XX′, 4 H, *c*Pr-H), 3.82 (s, 3 H, CH_3O), 6.58 (d, *J* = 8.5 Hz, 1 H, 8-H), 7.23 (dd, *J* = 8.5, 2.0 Hz, 1 H, 7-H), 7.53 (d, *J* = 2.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.2 (−, 2 C, C-2′,3′), 52.8 (+, CH_3O), 58.3 (C_{quat}, C-1′), 114.2 (C_{quat}), 117.3 (+), 130.8 (+), 133.4 (+), 133.9 (C_{quat}), 146.8 (C_{quat}), 157.2 (C_{quat}, C=N), 161.8 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 297/295 (52/55) [M^+], 265/263 (31/30) [$M^+ - CH_3OH$], 237/235 (100/97), 156 (10), 128 (14). $C_{12}H_{10}BrNO_3$ (296.1): calcd. C 48.67, H 3.40, N 4.73; found C 48.85, H 3.30, N 4.60.

Methyl 6-Iodospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate (26c-Me): From **23c** (2.25 g, 6.00 mmol), K_2CO_3 (1.66 g, 12.0 mmol), and **1**-Me (0.89 g, 6.07 mmol), according to **GP3**, **26c**-Me (1.34 g, 65%) was obtained as a yellow solid. M.p. 72 °C. R_f = 0.48 (hexane/diethyl ether, 1:1). ^1H NMR ($CDCl_3$): δ = 1.23−1.29 (m, 2 H, *c*Pr-H), 1.56−1.62 (m, 2 H, *c*Pr-H), 3.88 (s, 3 H, CH_3O), 6.52 (d, *J* = 8.4 Hz, 1 H, 8-H), 7.47 (dd, *J* = 8.4, 2.0 Hz, 1 H, 7-H), 7.77 (d, *J* = 2.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.4 (−, 2 C, C-2′,3′), 53.0 (+, CH_3O), 58.5 (C_{quat}, C-1′), 84.1 (C_{quat}, C-6), 118.0 (+), 134.5 (C_{quat}), 136.9 (+), 139.6 (+), 147.8 (C_{quat}), 157.2 (C_{quat}, C=N), 162.0 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 343 (100) [M^+], 310 (25), 282 (95), 156 (18). $C_{12}H_{10}INO_3$ (343.1): calcd. C 42.01, H 2.94, N 4.07; found C 42.16, H 3.02, N 3.81.

***tert*-Butyl 6-Bromo-4-(phenylsulfonyl)-3,4-dihydrospiro([2*H*][1,4]-benzoxazine-2,1′-cyclopropane)-3-carboxylate (25b-*t*Bu) and *tert*-Butyl 6-Bromospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate (26b-*t*Bu):** From **23b** (660 mg, 2.01 mmol), K_2CO_3 (690 mg 5.0 mmol), and **1**-*t*Bu (374 mg, 1.98 mmol), according to **GP3**, crude **25b**-*t*Bu (50 mg, 5%) and **26b**-*t*Bu (369 mg, 55%) were obtained. **25b-*t*Bu:** Light-brown oil. R_f = 0.24 (hexane/diethyl ether, 4:1). ^1H NMR ($CDCl_3$): δ = 0.46−0.57 (m, 1 H, *c*Pr-H),

0.67−0.78 (m, 1 H, *c*Pr-H), 1.23−1.32 (m, 2 H, *c*Pr-H), 1.40 (s, 9 H, *t*Bu), 4.52 (s, 1 H, 3-H), 6.63 (d, J = 8.3 Hz, 1 H, 8-H), 7.04 (dd, J = 8.3, 2.1 Hz, 1 H, 7-H), 7.47−7.73 (m, 3 H), 7.81 (d, J = 2.1 Hz, 1 H, 5-H), 7.88 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.5 (−, C-2′), 12.7 (−, C-3′), 27.7 (+, 3 C, CH_3), 60.6 (+, C-3), 60.9 (C_{quat}, C-1′), 83.0 (C_{quat}, *t*Bu), 113.5 (C_{quat}), 118.8 (+), 123.1 (+), 125.8 (C_{quat}), 127.2 (+, 2 C), 129.3 (+, 2 C), 130.4 (+), 133.5 (+), 139.7 (C_{quat}), 144.7 (C_{quat}), 166.1 (C_{quat}, C=O) ppm. **26b-*t*Bu:** Yellow solid. M.p. 70 °C. R_f = 0.60 (hexane/diethyl ether, 4:1). ^{1}H NMR ($CDCl_3$): δ = 1.20−1.27 (m, 2 H, *c*Pr-H), 1.39−1.46 (m, 2 H, *c*Pr-H), 1.53 (s, 9 H, *t*Bu), 6.60 (d, J = 8.5 Hz, 1 H, 8-H), 7.23 (dd, J = 8.5, 2.1 Hz, 1 H, 7-H), 7.54 (d, J = 2.1 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.0 (−, 2 C, C-2′,3′), 27.8 (+, 3 C, CH_3), 58.0 (C_{quat}, C-1′), 83.9 (C_{quat}, *t*Bu), 114.2 (C_{quat}), 117.2 (+), 130.7 (+), 132.8 (+), 134.3 (C_{quat}), 146.8 (C_{quat}), 159.3 (C_{quat}, C=N), 161.0 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 339/337 (3/3) [M^+], 283/281 (63/62), 265/263 (12/11), 237/235 (44/39), 229 (17), 224/222 (10/10), 57 (100), 41 (20).

Reduction of Methyl Spiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate (26a-Me). Method A (with $LiAlH_4$). [3,4-Dihydrospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropan)-3-yl]methanol (27): A solution of **26a**-Me (510 mg, 2.35 mmol) in THF (5 mL) was added dropwise to a suspension of $LiAlH_4$ (150 mg, 3.95 mmol) in THF (20 mL) under nitrogen, then the mixture was stirred overnight and the reaction carefully quenched with water (0.15 mL), 15% NaOH (0.15 mL) and water (0.45 mL). The precipitate was filtered off and washed thoroughly with diethyl ether. The filtrate was washed with NaCl solution, dried with $MgSO_4$, and concentrated. The residue was subjected to chromatography on silica gel (60 g), eluting with diethyl ether/hexane to give **27** (391 mg, 87%) as a colorless oil. R_f = 0.24 (ether). ^{1}H NMR ($CDCl_3$): δ = 0.53−0.64 (m, 1 H, *c*Pr-H), 0.74−0.95 (m, 2 H, *c*Pr-H), 1.10−1.21 (m, 1 H, *c*Pr-H), 3.69, 3.73 and 2.98 (ABX, J_{AB} = 11.0, J_{AX} = 8.6, J_{BX} = 5.1 Hz, 3 H, α-H and 3-H), 3.96 (br s, 2 H, NH and OH), 6.68−6.88 (m, 4 H, Ar-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.7 (−, C-2′), 11.7 (−, C-3′), 52.6 (+, C-3), 58.4 (C_{quat}, C-1′), 62.3 (−, CH_2O), 116.0 (+), 116.8 (+), 118.4 (+), 121.9 (+), 132.3 (C_{quat}), 143.8 (C_{quat}) ppm. MS (EI): *m*/*z* (%) = 191 (31) [M^+], 160 (100) [$M^+ - CH_2OH$]. $C_{11}H_{13}NO_2$ (191.2): calcd. 191.0946, correct HRMS. **Method B (with $NaBH_4$):** $NaBH_4$ (40 mg, 1.1 mmol) was added over 5 min at 0 °C to a stirred solution of **26a**-Me (161 mg, 0.741 mmol) in methanol (10 mL). After another 5 min of stirring, the solution was acidified with two drops of glacial acetic acid, poured into diluted $NaHCO_3$ solution and the mixture extracted with dichloromethane. The combined organic phases were washed with NaCl solution, dried with $MgSO_4$ and concentrated. The residue was subjected to chromatography on silica gel (60 g), eluting with diethyl ether/hexane (0:1→2:1) to give **13** (52 mg, 32%), which was identified on the basis of its spectroscopic data (see above).

[4-(Phenylsulfonyl)-3,4-dihydrospiro([2*H*][1,4]benzothiazine-2,1′-cyclopropan)-3-yl]methanol (28): A solution of **20a** (462 mg, 1.23 mmol) in THF (5 mL) was added dropwise to a stirred suspension of $LiAlH_4$ (50 mg, 1.3 mmol) in THF (30 mL) that was cooled with ice. After the mixture had been stirred for an additional 4 h, it was worked up and purified by chromatography as described for compound **27** to give **28** (375 mg, 88%) as a colorless oil, which crystallized slowly. M.p. 96−98 °C. R_f = 0.52 (ether). ^{1}H NMR ($CDCl_3$): δ = 0.62 (m, 2 H, *c*Pr-H), 1.07 (m, 2 H, *c*Pr-H), 2.53 (br s, 1 H, OH), 3.52 (dd, J = 11.7, 8.9 Hz, 1 H, α-H), 3.70 (dd, J = 11.7, 4.6 Hz, 1 H, α-H), 4.21 (dd, J = 8.9, 4.6 Hz, 1 H, 3-H), 6.95−7.10 (m, 3 H), 7.39 (t, J = 8.8 Hz, 1 H), 7.50 (t, J = 8.8 Hz, 1 H), 7.60−7.74 (m, 4 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.3 (−, C-2′), 18.4 (−, C-3′), 22.4 (C_{quat}, C-1′), 61.7 (−, CH_2O), 62.0 (+, C-3), 124.8 (+), 125.9 (+), 126.3 (+), 127.2 (+), 127.5 (+, 2 C), 128.3 (C_{quat}), 128.7 (+, 2 C), 130.6 (C_{quat}), 132.7 (+), 140.3 (C_{quat}) ppm. MS (EI): *m*/*z* (%) = 347 (44) [M^+], 316 (60) [$M^+ - CH_2OH$], 206 (16) [$M^+ - C_6H_5SO_2$], 176 (100) [$M^+ - C_6H_5SO_2 - CH_2O$], 175 (79) [$M^+ - C_6H_5SO_2 - CH_2OH$], 174 (48) [$M^+ - C_6H_5SO_2 - CH_3OH$], 77 (17) [$C_6H_5^+$]. $C_{17}H_{17}NO_3S_2$ (347.5): calcd. 347.0649; found 347.0649, correct HRMS.

Palladium-Catalyzed Coupling of 6-Bromobenzoxazine 26b-Me with Methyl Acrylate: A mixture of **26b**-Me (100 mg, 0.34 mmol), methyl acrylate (0.05 mL, 0.60 mmol), nBu_3N (0.1 mL, 0.42 mmol), PPh_3 (14 mg, 0.053 mmol) and $Pd(OAc)_2$ (4 mg) in DMF (6 mL) was stirred under nitrogen at 80 °C for 3.5 h. After cooling to ambient temperature, the mixture was diluted with dichloromethane (30 mL) and washed repeatedly with water and once with NaCl solution. The organic phase was dried with $MgSO_4$ and concentrated. The residue was subjected to chromatography on silica gel (30 g) eluting with diethyl ether/hexane (0:1→1:2) to give *methyl 6-bromo-2-ethylidene[2H][1,4]benzoxazine-3-carboxylate* (**29b**) (50 mg, 50%) and *methyl (Z)-2-ethylidene-6-[(E)-2-methoxycarbonylethenyl][2H][1,4]benzoxazine-3-carboxylate* [(*Z*)-**29d**] (38 mg, 37%). **29b:** Yellow crystals. M.p. 59−60 °C. R_f = 0.22 (diethyl ether/hexane, 1:2). ^{1}H NMR ($CDCl_3$): δ = 1.79 (d, J = 7.3 Hz, 3 H, CH_3), 3.92 (s, 3 H, CH_3O), 5.73 (q, J = 7.3 Hz, 1 H, CH=), 6.73 (d, J = 8.5 Hz, 1 H, 8-H), 7.28 (dd, J = 8.5, 2.4 Hz, 1 H, 7-H), 7.50 (d, J = 2.4 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 10.3 (+, CH_3), 53.2 (+, CH_3O), 112.2 (+, CH=), 114.8 (C_{quat}), 116.3 (+), 131.5 (+), 132.4 (C_{quat}), 133.4 (+), 140.9 (C_{quat}), 146.0 (C_{quat}), 152.0 (C_{quat}, C=N), 163.4 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 297/295 (42/43) [M^+], 265/263 (15/15), 239 (30), 237/235 (98/68), 199/197 (10/10), 162 (54), 131 (100), 103 (54), 77 (42), 63 (24), 51 (28). $C_{12}H_{10}BrNO_3$ (296.2): calcd. 294.9844, correct HRMS. (*Z*)-**29d:** Yellow solid. M.p. 99−101 °C. R_f = 0.30 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 1.80 (d, J = 7.4 Hz, 3 H, CH_3), 3.77 (s, 3 H, CH_3O), 3.93 (s, 3 H, CH_3O), 5.78 (q, J = 7.4 Hz, 1 H, CH=C), 6.30 (d, J = 15.8 Hz, 1 H, MeOCOCH=), 6.84 (d, J = 8.4 Hz, 1 H, 8-H), 7.34 (dd, J = 8.4, 2.0 Hz, 1 H, 7-H), 7.55 (d, J = 2.0 Hz, 1 H, 5-H), 7.56 (d, J = 15.8 Hz, 1 H, ArCH=) ppm. ^{13}C NMR ($CDCl_3$): δ = 10.3 (+, CH_3), 51.7 (+, CH_3O), 53.3 (+, CH_3O), 112.4 (+, 2-CH=), 115.3 (+), 117.0 (+), 128.1 (+), 129.8 (C_{quat}), 131.1 (+), 131.4 (C_{quat}), 140.9 (C_{quat}), 143.2 (+, ArCH=), 148.2 (C_{quat}), 151.5 (C_{quat}, C=N), 163.4 (C_{quat}, C=O), 167.3 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 301 (100) [M^+], 270 (11) [$M^+ - OCH_3$], 242 (22) [$M^+ - COOCH_3$], 241 (97), 210 (19), 172 (12). $C_{16}H_{15}NO_5$ (301.3): calcd. 301.0950, correct HRMS. When the reaction mixture was heated at the same temperature for 18 h, (*Z*)-**29d** (73 mg, 71%) and *methyl (E)-2-ethylidene-6-[(E)-2-methoxycarbonylethenyl][2H][1,4]benzoxazine-3-carboxylate* [(*E*)-**29d**] (4 mg, 4%) were isolated. (*E*)-**29d**: Yellow oil. R_f = 0.24 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 1.77 (d, J = 7.2 Hz, 3 H, CH_3), 3.77 (s, 3 H, CH_3O), 3.93 (s, 3 H, CH_3O), 5.07 (q, J = 7.0 Hz, 1 H, CH=), 6.31 (d, J = 15.8 Hz, 1 H, MeOCOCH=), 6.81 (d, J = 8.0 Hz, 1 H, 8-H), 7.27 (dd, J = 8.0, 2.0 Hz, 1 H, 7-H), 7.42 (d, J = 2.0 Hz, 1 H, 5-H), 7.59 (d, J = 15.8 Hz, 1 H, ArCH=) ppm. ^{13}C NMR ($CDCl_3$): δ = 10.0 (+, CH_3), 51.7 (+, CH_3O), 53.3 (+, CH_3O), 110.8 (+, 2-CH=), 115.3 (+), 116.6 (+), 127.2 (+), 129.3 (+), 129.6 (C_{quat}), 132.5 (C_{quat}), 143.6 (+, ArCH=), 144.3 (C_{quat}), 148.0 (C_{quat}), 151.5 (C_{quat}, C=N), 163.4 (C_{quat},C=O), 167.3 (C_{quat}, C=O) ppm.

General Procedure for Palladium-Catalyzed Coupling Reactions of 6-Iodobenzoxazine 26c-Me with Alkenes (GP4): The alkene (0.70 mmol) and $Pd(OAc)_2$ (4 mg) were added to a stirred mixture

of **26c**-Me (103 mg, 0.30 mmol), nBu$_4$NBr (120 mg, 0.37 mmol) and K_2CO_3 (125 mg, 0.90 mmol) in DMF (6 mL) under nitrogen, and the mixture heated at 80 °C for 10 h. After cooling to ambient temperature, the mixture was filtered, diluted with dichloromethane (30 mL), and then washed repeatedly with water and once with NaCl solution. The organic phase was dried with $MgSO_4$ and concentrated. The residue was subjected to chromatography on silica gel (30 g), eluting with diethyl ether/hexane (0:1→1:2).

Methyl (*E*)-6-(2-Methoxycarbonylethenyl)spiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate [(*E*)-30d]: From **26c**-Me and methyl acrylate, according to **GP4**, (*E*)-**30d** (78 mg, 86%) was obtained as a yellow solid. M.p. 102−103 °C. R_f = 0.36 (diethyl ether/hexane, 1:2). ^{1}H NMR ($CDCl_3$): δ = 1.21−1.26 (m, 2 H, *c*Pr-H), 1.56−1.61 (m, 2 H, *c*Pr-H), 3.75 (s, 3 H, CH_3O), 3.84 (s, 3 H, CH_3O), 6.22 (d, J = 16.0 Hz, 1 H, MeOCOCH=), 6.71 (d, J = 8.5 Hz, 1 H, 8-H), 7.32 (dd, J = 8.5, 1.9 Hz, 1 H, 7-H), 7.57 (d, J = 16.0 Hz, 1 H, ArCH=), 7.60 (d, J = 1.9 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.6 (−, 2 C, C-2′,3′), 51.7 (+, CH_3O), 53.1 (+, CH_3O), 58.9 (C_{quat}, C-1′), 116.4 (+), 116.8 (+), 127.8 (+), 129.4 (C_{quat}), 131.2 (+), 132.9 (C_{quat}), 143.5 (+, ArCH=), 149.6 (C_{quat}), 157.0 (C_{quat}, C=N), 162.0 (C_{quat}, C=O), 167.4 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 301 (97) [M^+], 270 (14), 242 (21) [$M^+ - COOCH_3$], 241 (100), 210 (22). $C_{16}H_{15}NO_5$ (301.3): calcd. 301.0950, correct HRMS. When the bromo derivative **26b**-Me and nBu$_3$N were used instead of **26c**-Me and nBu$_4$NBr, the compound (*E*)-**30d** was isolated with a yield of only 30%.

Methyl (*E*)-6-(2-Formylethenyl)spiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate [(*E*)-30e]: From **26c**-Me and acrolein, according to **GP4**, (*E*)-**30e** (72 mg, 89%) was obtained as a yellow solid. M.p. 140 °C. R_f = 0.26 (diethyl ether/hexane, 1:2). ^{1}H NMR ($CDCl_3$): δ = 1.25−1.32 (m, 2 H, *c*Pr-H), 1.62−1.69 (m, 2 H, *c*Pr-H), 3.89 (s, 3 H, CH_3O), 6.60 (dd, J = 15.9, 7.6 Hz, 1 H, C*H*CHO), 6.78 (d, J = 8.1 Hz, 1 H, 8-H), 7.41 (dd, J = 8.1, 2.1 Hz, 1 H, 7-H), 7.38 (d, J = 15.9 Hz, 1 H, ArCH=), 7.66 (d, J = 2.1 Hz, 1 H, 5-H), 9.78 (d, J = 7.6 Hz, 1 H, CHO) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.8 (−, 2 C, C-2′,3′), 53.0 (+, CH_3O), 59.1 (C_{quat}, C-1′), 116.7 (+), 127.7 (+), 128.4 (+), 129.0 (C_{quat}), 131.5 (+), 133.0 (C_{quat}), 150.4 (C_{quat}), 151.4 (+, ArCH=), 157.3 (C_{quat}, C=N), 161.9 (C_{quat}, C=O), 193.4 (+, CHO) ppm. MS (EI): *m*/*z* (%) = 271 (100) [M^+], 211 (42), 183 (13). $C_{15}H_{13}NO_4$ (271.3): calcd. 271.0844, correct HRMS.

Methyl (*E*)-6-(3-Oxobut-1-enyl)spiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate [(*E*)-30f]: From **26c**-Me and methyl vinyl ketone, according to **GP4**, (*E*)-**30f** (62 mg, 72%) was obtained as a yellow oil. R_f = 0.23 (diethyl ether/hexane, 1:2). ^{1}H NMR ($CDCl_3$): δ = 1.20−1.27 (m, 2 H, *c*Pr-H), 1.55−1.62 (m, 2 H, *c*Pr-H), 2.32 (s, 3 H, Ac), 3.85 (s, 3 H, CH_3O), 6.57 (d, J = 16.1 Hz, 1 H, AcCH=), 6.72 (d, J = 8.3 Hz, 1 H, 8-H), 7.34 (dd, J = 8.3, 2.0 Hz, 1 H, 7-H), 7.38 (d, J = 16.1 Hz, 1 H, ArCH=), 7.61 (d, J = 2.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.6 (−, 2 C, C-2′,3′), 27.6 (+, Ac), 53.0 (+, CH_3O), 58.8 (C_{quat}, C-1′), 116.4 (+), 126.0 (+), 127.9 (+), 129.3 (C_{quat}), 131.3 (+), 132.8 (C_{quat}), 142.0 (+, ArCH=), 149.6 (C_{quat}), 156.9 (C_{quat}, C=N), 161.9 (C_{quat}, *C*OOMe), 198.0 (C_{quat}, Me*C*=O) ppm. MS (EI): *m*/*z* (%) = 285 (100) [M^+], 270 (13) [$M^+ - CH_3$], 238 (11), 225 (40), 210 (33), 143 (10). $C_{16}H_{15}NO_4$ (285.3): calcd. 285.1001, correct HRMS.

Methyl (*E*)- and (*Z*)-6-(2-Cyanoethenyl)spiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylates [(*E*)- and (*Z*)-30g]: From **26c**-Me and acrylonitrile, according to **GP4**, a mixture of (*E*)- and (*Z*)-**30g** (70 mg, 87%) in a ratio of 2.7:1 (according to the NMR spectra) was obtained. After chromatography on silica gel (*E*)-**30g** (25 mg, 31%) was isolated. The isomer (*Z*)-**30g** was not isolated as a pure substance. (*E*)-**30g:** Yellow solid. M.p. 103−104 °C. R_f = 0.38 (diethyl ether/hexane, 1:2). ^{1}H NMR ($CDCl_3$): δ = 1.25−1.32 (m, 2 H, *c*Pr-H), 1.61−1.68 (m, 2 H, *c*Pr-H), 3.89 (s, 3 H, CH_3O), 5.75 (d, J = 16.8 Hz, 1 H, NCCH=), 6.76 (d, J = 8.4 Hz, 1 H, 8-H), 7.28 (dd, J = 8.4, 2.2 Hz, 1 H, 7-H), 7.30 (d, J = 16.8 Hz, 1 H, ArCH=), 7.56 (d, J = 2.2 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.8 (−, 2 C, C-2′,3′), 53.1 (+, CH_3O), 59.1 (C_{quat}, C-1′), 95.1 (+, NC*C*H=), 116.6 (+), 118.2 (C_{quat}, C≡N), 126.9 (+), 128.4 (C_{quat}), 130.6 (+), 132.9 (C_{quat}), 149.1 (+, ArCH), 150.2 (C_{quat}), 157.4 (C_{quat}, C=N), 161.8 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 268 (56) [M^+], 236 (8), 208 (100). $C_{15}H_{12}N_2O_3$ (268.3): calcd. C 67.16, H 4.51, N 10.44; found C 67.32, H 4.72, N 10.54. (*Z*)-**30g:** R_f = 0.30 (diethyl ether/hexane, 1:2). ^{1}H NMR ($CDCl_3$): δ = 1.23−1.30 (m, 2 H, *c*Pr-H), 1.57−1.65 (m, 2 H, *c*Pr-H), 3.88 (s, 3 H, CH_3O), 5.37 (d, J = 16.8 Hz, 1 H, NC*C*H=), 6.78 (d, J = 8.4 Hz, 1 H, 8-H), 7.01 (d, J = 16.8 Hz, 1 H, ArCH=), 7.71 (d, J = 2.2 Hz, 1 H, 5-H), 7.82 (dd, J = 8.4, 2.2 Hz, 1 H, 7-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.6 (−, 2 C, C-2′,3′), 52.9 (+, CH_3O), 58.9 (C_{quat}, C-1′), 93.8 (+, NC*C*H=), 116.5 (+), 117.3 (C_{quat}, C≡N), 128.5 (C_{quat}), 129.9 (+), 131.1 (+), 132.7 (C_{quat}), 147.1 (+, ArCH=), 149.9 (C_{quat}), 157.0 (C_{quat}, C=N), 161.9 (C_{quat}, C=O) ppm.

Methyl (*E*)-6-(2-Phenylethenyl)spiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate [(*E*)-30h] and Methyl 6-(1-Phenylethenyl)spiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate (31h): From **26c**-Me and styrene, according to **GP4**, (*E*)-**30h** (72 mg, 75%) and **31h** (8 mg, 8%) were obtained. (*E*)-**30h:** Yellow solid. M.p. 75−76 °C. R_f = 0.38 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 1.24−1.31 (m, 2 H, *c*Pr-H), 1.58−1.66 (m, 2 H, *c*Pr-H), 3.88 (s, 3 H, CH_3O), 6.73 (d, J = 8.2 Hz, 1 H, 8-H), 7.02 (s, 2 H, PhC*H*=C*H*), 7.21−7.29 (m, 1 H), 7.30−7.39 (m, 3 H), 7.48 (m, 2 H), 7.66 (d, J = 2.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.2 (−, 2 C, C-2′,3′), 52.8 (+, CH_3O), 58.5 (C_{quat}, C-1′), 116.0 (+), 126.0 (+), 126.3 (+, 2 C), 127.1 (+), 127.5 (+), 128.0 (+), 128.6 (+), 129.3 (+), 132.4 (C_{quat}), 133.0 (C_{quat}), 137.0 (C_{quat}), 147.2 (C_{quat}), 156.3 (C_{quat}, C=N), 162.1 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 319 (100) [M^+], 259 (37), 165 (16). $C_{20}H_{17}NO_3$ (319.4): calcd. 319.1208, correct HRMS. **31h:** Yellow oil. R_f = 0.31 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 1.24−1.32 (m, 2 H, *c*Pr-H), 1.57−1.65 (m, 2 H, *c*Pr-H), 3.87 (s, 3 H, CH_3O), 5.35 (d, J = 1.2 Hz, 1 H, C=CH_2), 5.44 (d, J = 1.2 Hz, 1 H, C=CH_2), 6.72 (d, J = 8.4 Hz, 1 H, 8-H), 7.23 (dd, J = 8.4, 2.2 Hz, 1 H, 7-H), 7.33 (br. s, 5 H), 7.47 (d, J = 2.2 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.3 (−, 2 C, C-2′,3′), 52.9 (+, CH_3O), 58.4 (C_{quat}, C-1′), 113.8 (−, =CH_2), 115.6 (+), 127.8 (+), 128.2 (+), 128.3 (+, 3 C), 130.8 (+), 132.6 (C_{quat}), 136.4 (C_{quat}), 141.2 (C_{quat}), 147.5 (C_{quat}), 148.8 (C_{quat}), 159.8 (C_{quat}, C=N), 162.3 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 319 (100) [M^+], 259 (82), 165 (18). $C_{20}H_{17}NO_3$ (319.4): calcd. 319.1208, correct HRMS.

Methyl (*E*/*Z*)-6-(2-Ethoxyethenyl)spiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate [(*E*/*Z*)-30i] and Methyl 6-Acetylspiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carboxylate (32i): **26c**-Me and ethyl vinyl ether gave, according to **GP4**, a mixture of (*E*)- and (*Z*)-**30i** (52 mg, 60%) in a ratio of 3:1 (according to the NMR spectra), and **32i** (27 mg, 35%). (*E*/*Z*)-**30i:** Yellow oil. R_f = 0.38 (diethyl ether/hexane, 1:1). MS (EI): *m*/*z* (%) = 287 (100) [M^+], 227 (24), 199 (17), 185 (12), 170 (14), 158 (10). $C_{16}H_{17}NO_4$ (287.3): calcd. 287.1157, correct HRMS. (*E*)-**30i:** ^{1}H NMR ($CDCl_3$): δ = 1.20−1.27 (m, 2 H, *c*Pr-H), 1.32 (t, J = 7.1 Hz, 3 H, CH_3), 1.53−1.60 (m, 2 H, *c*Pr-H), 3.87 (q, J = 7.1 Hz, 2 H, OCH_2), 3.88 (s, 3 H, CH_3O), 5.76 (d, J = 13.0 Hz, 1 H, ArCH=), 6.65 (d, J =

7.8 Hz, 1 H, 8-H), 6.90 (d, J = 13.0 Hz, 1 H, OCH=), 7.03 (dd, J = 7.8, 2.1 Hz, 1 H, 7-H), 7.36 (d, J = 2.1 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.8 (+, CH_3), 15.1 (−, 2 C, C-2′,3′), 52.9 (+, CH_3O), 58.2 (C_{quat}, C-1′), 65.5 (−, OCH_2), 104.7 (+, ArCH=), 115.9 (+), 124.3 (+), 128.0 (+), 131.6 (C_{quat}), 133.1 (C_{quat}), 145.7 (C_{quat}), 147.5 (+, OCH=), 156.2 (C_{quat}, C=N), 162.3 (C_{quat}, C=O) ppm. (*Z*)-**30i:** ^{1}H NMR ($CDCl_3$): δ = 1.19−1.27 (m, 2 H, *c*Pr-H), 1.35 (t, J = 7.1 Hz, 3 H, CH_3), 1.52−1.60 (m, 2 H, *c*Pr-H), 3.88 (s, 3 H, CH_3O), 3.96 (q, J = 7.1 Hz, 2 H, OCH_2), 5.14 (d, J = 6.8 Hz, 1 H, ArCH=), 6.16 (d, J = 6.8 Hz, 1 H, OCH=), 6.67 (d, J = 8.2 Hz, 1 H, 8-H), 7.43 (dd, J = 8.2, 2.1 Hz, 1 H, 7-H), 7.74 (d, J = 2.1 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.9 (−, 2 C, C-2′,3′), 15.5 (+, CH_3), 52.9 (+, CH_3O), 58.1 (C_{quat}, C-1′), 69.1 (−, OCH_2) 104.1 (+, ArCH=), 115.5 (+), 124.3 (+), 130.9 (+), 131.3 (C_{quat}), 132.8 (C_{quat}), 145.6 (C_{quat}), 146.0 (+, OCH=), 155.9 (C_{quat}, C=N), 161.1 (C_{quat}, C=O) ppm. **32i:** Yellow oil. R_f = 0.27 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 1.23−1.30 (m, 2 H, *c*Pr-H), 1.60−1.67 (m, 2 H, *c*Pr-H), 2.53 (s, 3 H, CH_3), 3.87 (s, 3 H, CH_3O), 6.78 (d, J = 8.7 Hz, 1 H, 8-H), 7.85 (dd, J = 8.7, 2.0 Hz, 1 H, 7-H), 8.02 (d, J = 2.0 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.8 (−, 2 C, C-2′,3′), 26.4 (+, CH_3), 53.0 (+, CH_3O), 59.1 (C_{quat}, C-1′), 116.1 (+), 129.4 (+), 131.4 (+), 132.0 (C_{quat}), 132.2 (C_{quat}), 151.9 (C_{quat}), 156.8 (C_{quat}, C=N), 161.8 (C_{quat}, *C*OOMe), 196.0 (C_{quat}, Me*C*O) ppm. MS (EI): *m*/*z* (%) = 259 (100) [M^+], 244 (17) [$M^+ - CH_3$], 227 (11), 199 (56), 184 (58). $C_{14}H_{13}NO_4$ (259.3): calcd. C 64.86, H 5.05, N 5.40; found C 64.65, H 5.15, N 5.44.

7-Bromo-*N*-(4-methoxybenzyl)spiro([2*H*][1,4]benzothiazine-2,1′-cyclopropane)-3-carboxamide (33) and 7-Bromospiro([2*H*][1,4]benzothiazine-2,1′-cyclopropan)-3(4*H*)-one (34): $Pd(OAc)_2$ (4 mg) was added under nitrogen to a stirred solution of **22b** (200 mg, 0.64 mmol), 4-methoxybenzylamine (96 mg, 0.70 mmol), PPh_3 (14 mg, 0.053 mmol) and nBu_3N (130 mg, 0.71 mmol) in DMF (3 mL). The nitrogen was replaced with carbon monoxide by three freeze-pump-thaw cycles, and then the mixture was heated at 80 °C and 1 atm of CO pressure for 14 h with stirring. After cooling to ambient temperature, the mixture was diluted with diethyl ether, filtered, and washed with 10% HCl, water and NaCl solution. The diethyl ether phase was dried with $MgSO_4$, concentrated and the residue separated by column chromatography on silica gel (50 g), eluting with diethyl ether/hexane (0:1→1:4) to give recovered **22b** (53 mg, 26%), **33** (147 mg, 55%) and **34** (6 mg, 4%). **33:** Yellow solid. M.p. 112−114 °C. R_f = 0.28 (diethyl ether/hexane, 1:2). ^{1}H NMR ($CDCl_3$): δ = 1.03−1.10 (m, 2 H, *c*Pr-H), 2.00−2.07 (m, 2 H, *c*Pr-H), 3.80 (s, 3 H, CH_3O), 4.43 (d, J = 7.0 Hz, 2 H, CH_2N), 6.89 (m, 2 H, 3′′,5′′-H), 7.20−7.37 (m, 5 H), 7.71 (br s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.8 (−, 2 C, C-2′,3′), 17.1 (C_{quat}, C-1′), 42.9 (−, NCH_2), 55.3 (+, CH_3O), 114.1 (+, 2 C), 122.2 (C_{quat}), 129.18 (+, 2 C), 129.22 (+), 129.3 (C_{quat}), 129.6 (+), 129.71 (+), 129.73 (C_{quat}), 140.1 (C_{quat}), 155.8 (C_{quat}) 158.4 (C_{quat}, C=N), 162.5 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 418/416 (13/13) [M^+], 121 (100) [$C_7H_6OCH_3^+$]. $C_{19}H_{17}BrN_2O_2S$ (417.4): calcd. 416.0194, correct HRMS. **34:** Light-yellow oil. R_f = 0.15 (diethyl ether/hexane, 1:2). ^{1}H NMR ($CDCl_3$): δ = 1.00−1.08 (m, 2 H, *c*Pr-H), 1.58−1.66 (m, 2 H, *c*Pr-H), 6.72 (d, J = 8.0 Hz, 1 H, 5-H), 7.28 (dd, J = 8.0, 1.7 Hz, 1 H, 6-H), 7.37 (d, J = 1.7 Hz, 1 H, 8-H), 8.77 (br. s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 16.3 (−, 2 C, C-2′,3′), 21.3 (C_{quat}, C-1′), 116.0 (C_{quat}), 118.0 (+), 122.5 (C_{quat}), 129.9 (+), 130.1 (+), 135.3 (C_{quat}), 170.1 (C_{quat}, C=O) ppm.

6-Bromospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropan)-3(4*H*)-one (35): Morpholine (110 mg, 1.26 mmol) and $Pd(OAc)_2$ (4 mg) were added under nitrogen to a stirred suspension of **26b**-Me (300 mg, 1.01 mmol), *t*BuONa (192 mg, 2.00 mmol), K_2CO_3 (276 mg, 2.00 mmol) and PPh_3 (14 mg, 0.053 mmol) in toluene (5 mL). The reaction mixture was stirred at 80 °C for 13 h, cooled to ambient temperature, diluted with diethyl ether (20 mL), filtered, and then stirred for 10 min with 30% H_2O_2 (10 mL). The diethyl ether phase was washed with water, saturated $FeSO_4$ solution, then again with water, and NaCl solution, dried with $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (40 g), eluting with diethyl ether/hexane (0:1→1:2) to yield **35** (130 mg, 51%) as colorless needles, which were recrystallized from diethyl ether/hexane. M.p. 174−175 °C. R_f = 0.20 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 1.22−1.30 (m, 2 H, *c*Pr-H), 1.42−1.50 (m, 2 H, *c*Pr-H), 6.72 (d, J = 8.4 Hz, 1 H, 8-H), 6.97 (d, J = 2.0 Hz, 1 H, 5-H), 7.05 (dd, J = 8.0, 2.0 Hz, 1 H, 7-H), 9.42 (br s, 1 H, NH) ppm. ^{13}C NMR ($CDCl_3$): δ = 14.4 (−, 2 C, C-2′,3′), 61.2 (C_{quat}, C-1′), 114.7 (C_{quat}), 118.1 (+), 118.3 (+), 126.5 (+), 128.2 (C_{quat}), 142.9 (C_{quat}), 169.6 (C_{quat}, C=O) ppm. MS (EI): *m*/*z* (%) = 255/253 (98/100) [M^+], 228/226 (25/40), 224 (15). $C_{10}H_8BrNO_2$ (254.1): calcd. C 47.27, H 3.17, N 5.51; found C 47.05, H 3.22, N 5.73. When the compound **26b**-Me was treated with 4-methoxybenzylamine under conditions used for the preparation of the 1,4-benzothiazine derivatives **33** and **34**, the product **35** was isolated with a yield of 23% along with 63% of recovered **26b**-Me.

General Procedure for the Demethoxycarbonylation of 26b,c (GP5): A solution of **26** and morpholine in DMF (5 mL) was heated at 80 °C for 2−3 d under nitrogen. After cooling to ambient temperature, the solution was diluted with dichloromethane (20 mL) and washed repeatedly with water and once with NaCl solution. The dichloromethane phase was dried with $MgSO_4$, concentrated and the residue purified by chromatography on silica gel (20 g), eluting with diethyl ether/hexane (0:1→1:0).

6-Bromospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane) (36b): From **26b**-Me (200 mg, 0.68 mmol) and morpholine (60 mg, 0.69 mmol), after heating for 3 d according to **GP5**, **36b** (134 mg, 83%) was isolated as a colorless solid. M.p. 75 °C. R_f = 0.23 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 0.97−1.05 (m, 2 H, *c*Pr-H), 1.25−1.32 (m, 2 H, *c*Pr-H), 6.56 (d, J = 8.6 Hz, 1 H, 8-H), 7.17 (s, 1 H, CH=N), 7.19 (dd, J = 8.6, 2.5 Hz, 1 H, 7-H), 7.40 (d, J = 2.5 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.0 (−, 2 C, C-2′,3′), 59.0 (C_{quat}, C-1′), 113.8 (C_{quat}), 117.2 (+), 130.0 (+), 131.7 (+), 133.8 (C_{quat}), 146.4 (C_{quat}), 162.7 (+, CH=N) ppm. MS (EI): *m*/*z* (%) = 239/237 (94/100) [M^+], 236 (35), 130 (19), 75 (10). $C_{10}H_8BrNO$ (238.2): calcd. C 50.45, H 3.39, N 5.88; found C 50.21, H 3.49, N 6.09.

6-Iodospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane) (36c): From **26c**-Me (100 mg, 0.29 mmol) and morpholine (50 mg, 0.57 mmol), after heating for 2 d according to **GP5**, **36c** (81 mg, 98%) was isolated as a colorless oil. R_f = 0.26 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 0.97−1.04 (m, 2 H, *c*Pr-H), 1.25−1.32 (m, 2 H, *c*Pr-H), 6.43 (d, J = 8.4 Hz, 1 H, 8-H), 7.15 (s, 1 H, CH=N), 7.37 (dd, J = 8.4, 2.2 Hz, 1 H, 7-H), 7.57 (d, J = 2.2 Hz, 1 H, 5-H) ppm. ^{13}C NMR ($CDCl_3$): δ = 15.0 (−, 2 C, C-2′,3′), 59.0 (C_{quat}, C-1′), 83.5 (C_{quat}, C-6), 117.8 (+), 134.1 (C_{quat}), 135.8 (+), 137.7 (+), 147.3 (C_{quat}), 162.5 (+, CH=N) ppm. MS (EI): *m*/*z* (%) = 285 (37) [M^+], 142 (100). $C_{10}H_8INO$ (285.1): calcd. C 42.13, H 2.83, N 4.91; found C 42.17, H 2.91, N 4.69.

6-Bromo-3-[(4-methylphenyl)thio]-3,4-dihydrospiro([2*H*][1,4]-benzoxazine-2,1′-cyclopropane) (37): A solution of **36b** (100 mg, 0.42 mmol) and 4-methylthiophenol (55 mg, 0.44 mmol) in anhydrous benzene (6 mL) was heated for 10 h under reflux. After cool-

ing to ambient temperature and evaporation of the solvent, the residue was purified by chromatography on silica gel (20 g) eluting with diethyl ether/hexane (0:1 → 1:0) to give **37** (115 mg, 76%) as a light-yellow solid. M.p. 99−100 °C. R_f = 0.52 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 0.65−0.75 (m, 1 H, *c*Pr-H), 0.90−1.15 (m, 2 H, *c*Pr-H), 1.22−1.32 (m, 1 H, *c*Pr-H), 2.35 (s, 3 H, CH_3), 4.25 (br s, 1 H, 3-H), 4.45 (br s, 1 H, NH), 6.63 (d, *J* = 8.0 Hz, 1 H, 8-H), 6.67 (br s, 1 H, 5-H), 6.84 (m, 1 H, 7-H), 7.16−7.22 (m, 2 H), 7.35−7.41 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.5 (br, −, C-2′), 14.7 (br, −, C-3′), 21.2 (+, CH_3), 60.9 (C_{quat}, C-1′), 65.6 (br, +, C-3), 113.7 (C_{quat}), 118.3 (+), 122.4 (+), 128.8 (C_{quat}), 129.8 (+), 130.1 (+, 2 C), 131.8 (br, C_{quat}), 135.3 (+, 2 C), 138.8 (C_{quat}), 143.1 (br, C_{quat}) ppm. MS (EI): *m*/*z* (%) = 363/361 [M^+], 246 (16), 239/237 (100/96) [$M^+ - CH_3C_6H_4SH$], 222 (29), 130 (15), 124 (70), 91 (93), 77 (12), 63 (10). $C_{17}H_{16}BrNOS$ (362.3): calcd. 361.0136, correct HRMS.

6-Bromo-3,4-dihydrospiro([2*H*][1,4]benzoxazine-2,1′-cyclopropane)-3-carbonitrile (38): Acetic acid (0.03 mL) was added to a stirred solution of **36b** (50 mg, 0.21 mmol) and NaCN (11 mg, 0.22 mmol) in anhydrous ethanol (10 mL). The mixture was stirred for 3 h at ambient temperature, diluted with dichloromethane (20 mL), then washed with water and NaCl solution. The organic phase was concentrated, and the residue purified by chromatography on silica gel (20 g), eluting with diethyl ether/hexane (0:1→1:0) to give **38** (53 mg, 95%) as a light-yellow solid. M.p. 151−152 °C. R_f = 0.10 (diethyl ether/hexane, 1:1). ^{1}H NMR ($CDCl_3$): δ = 0.72−0.81 (m, 1 H, *c*Pr-H), 0.99−1.17 (m, 2 H, *c*Pr-H), 1.29−1.39 (m, 1 H, *c*Pr-H), 3.83 (d, *J* = 3.1 Hz, 1 H, 3-H), 4.51 (br s, 1 H, NH), 6.67 (d, *J* = 8.2 Hz, 1 H, 8-H), 6.83−6.69 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 10.5 (−, C-2′), 13.3 (−, C-3′), 47.5 (+, C-3), 59.8 (C_{quat}, C-1′), 114.4 (C_{quat}), 117.4 (C_{quat}, CN), 118.4 (+), 118.8 (+), 123.1 (+), 131.3 (C_{quat}), 142.4 (C_{quat}) ppm. MS (EI): *m*/*z* (%) = 266/264 (100/100) [M^+], 251/249 (34/38), 240/238 (18/32) [$M^+ -$ CN], 226/224 (78/78), 200/198 (15/16), 185 (10), 157 (12), 145 (10), 130 (10), 102 (10), 78 (23). $C_{11}H_9BrN_2O$ (265.1): calcd. 263.9898, correct HRMS.

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[7] Colorless crystals (m.p. 75−77 °C) with the composition of **6**·0.5HCl·0.25H_2O had formed from the amino acid ester **6** after 4 months of storage of its $CDCl_3$ solution at ambient temperature. The yellow crystals of **22b** (m.p. 108−109 °C) were obtained by crystallization from a hexane/diethyl ether solution. Both crystals were measured with a Stoe−Siemens AED four-circle diffractometer using graphite-monochromated Mo-K_α radiation, λ = 71.073 pm. The structure solutions and refinements on F^2 were performed by direct methods with the SHELXS-97 and SHELXL-97 programs. The hydrogen atoms were located in a difference-Fourier map and refined as riding groups with the 1.2-fold isotropic displacement parameter of the corresponding C atom. **6**·0.5HCl·0.25H_2O: $C_{32}H_{56}Cl_2N_4O_9S_4$ (839.95), crystal size 0.40 × 0.30 × 0.30 mm, triclinic, *a* = 1165.2(2), *b* = 1352.6(3), *c* = 1421.8(3) pm; α = 90.08(3), β = 112.33(3), γ = 98.88(3)°, *V* = 2.0435(7) nm^3, *Z* = 2, space group $P\bar{1}$, *T* = 133(2) K, ρ = 1.365 Mg/m^3, intensities measured: 21962 (2.24° ≤ θ ≤ 24.71°), independent: 6833 (R_{int} = 0.0189), 496 parameters refined, R_1 = 0.0304, wR_2 (all data) = 0.0706, *Gof* = 1.041, maximum and minimum residual electron density 411 and −297 e nm^{-3}. **22b**: $C_{12}H_{10}BrNO_2S$ (312.18), crystal size 0.30 × 0.20 × 0.15 mm, triclinic, *a* = 723.78(14), *b* = 818.55(16), *c* = 1083.0(2) pm; α = 85.23(3), β = 87.18(3), γ = 68.40(3)°, *V* = 0.5944(2) nm^3, *Z* = 2, space group $P\bar{1}$, *T* = 133(2) K, ρ = 1.744 Mg/m^3, intensities measured: 7288 (1.89° ≤ θ ≤ 26.50°), independent: 2447 (R_{int} = 0.0373), 155 parameters refined, R_1 = 0.0331, wR_2 (all data) = 0.0817, *Gof* = 1.044, maximum and minimum residual electron density 931 and −1088 e nm^{-3}. CCDC-176186 (**6**) and -176187 (**22b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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