Synthesis Z. Dong et al. Paper

A Tandem Sulfonylation and Knoevenagel Condensation for the Preparation of Sulfocoumarin-3-carboxylates

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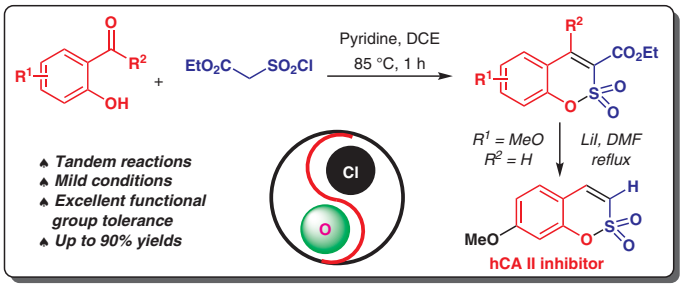

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Abstract Sulfocoumarins are key structural motifs in several bioactive molecules. Herein, we describe a simple, one-pot procedure for the synthesis of structurally diverse sulfonocoumarin-3-carboxylates by heating 2-hydroxyaryl aldehydes with an active sulfonyl chloride in the presence of pyridine. The process tolerates numerous functional groups including alkoxy, alkyl, halogen, nitro, and even nucleophilic phenolic hydroxy. Additionally, reactions of 2-hydroxyaryl ketones and 2-methylaminoaryl aldehydes give 4-substituted sulfocoumarins and 1-aza-2-sulfocoumarins, respectively. A gram-scale synthesis and further derivatizations are also reported. The ester group is easily removed via Happer's decarboxylation.

Key words sulfocoumarin-3-carboxylates, tandem reactions, sulfonylation, Knoevenagel condensation, salicylaldehyde

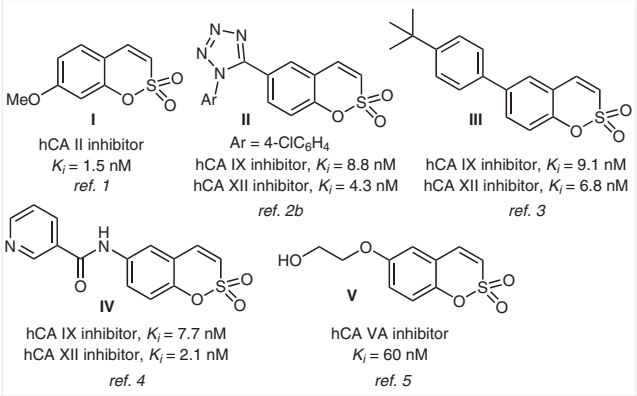


Figure 1 Representative bioactive sulfocoumarins reported by Supuran's group

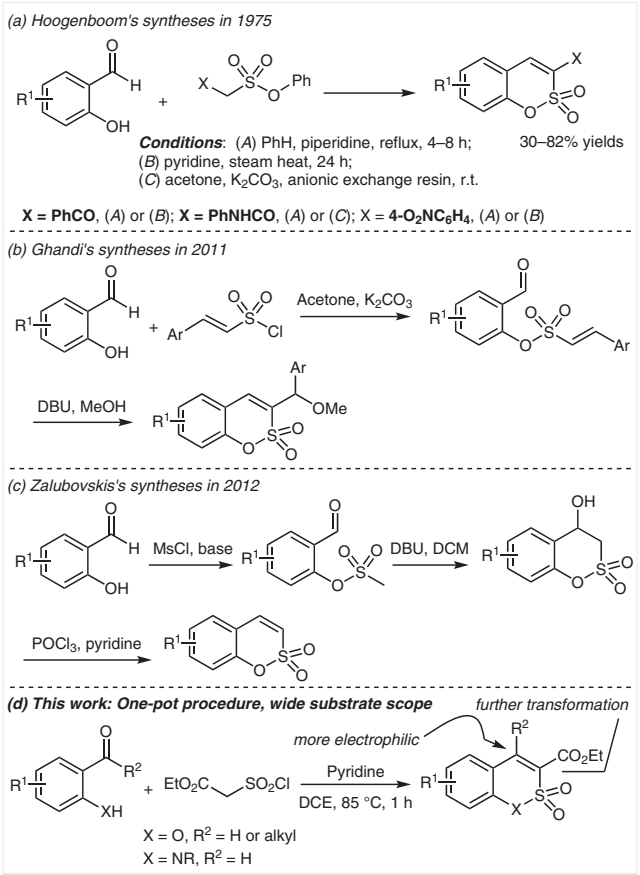
Sulfocoumarins, the sulfonyl analogues of coumarins, have been demonstrated as potent and selective inhibitors of human carbonic anhydrases (hCA)[1–6] and metalloenzymes.[2] Recent work from the group of Zalubovskis and Supuran disclosed that 7-alkoxy- or 7-acyloxy-substituted sulfocoumarins were inhibitors against the most abundant and cytosolic hCA II,[1] while 6-triazolyl-,[2] 6-tetrazolyl,[3] 6-aryl-,[4] 6-amidyl-,[5] and 6-alkoxy-substituted examples[6] were inhibitors against tumor-associated hCA IX and XII. Representative bioactive sulfocoumarins reported by Supuran's group are listed in Figure 1. 7-(2-Hydroxyethyl)-substituted sulfocoumarin **V** also showed good inhibition against the mitochondrial hCA VA.[6] In organic chemistry, sulfocoumarins also act as important building blocks for the construction of valuable structures.[7]

Despite their importance, synthetic approaches toward sulfocoumarins are very limited. In 1975, Hoogenboom and co-workers synthesized *3-substituted* sulfocoumarin derivatives from different salicylaldehydes and α-substituted methanesulfonates via a transesterification and condensation sequence (Scheme 1a).[8] The conditions were dependent on the substituent effect of not only the sulfonates, but also the salicylaldehydes. In 2011, Ghandi's group reported the stepwise synthesis of *3-substituted* sulfocoumarins from salicylaldehydes and alkenesulfonyl chlorides (Scheme 1b).[9] These two methods are mainly restricted by the inconvenient routes to access the sulfonyl reagents. In 2012, in response to the irreproducibility of literature procedures,[10] Zalubovskis et al. developed an efficient procedure to prepare *3,4-unsubstituted* sulfocoumarins, which

featured the mesylation of salicylaldehydes, a DBU-catalyzed aldol-type condensation, and $POCl_3$-mediated dehydration (Scheme 1c).[11] This method was widely used in the studies by Supuran and co-workers on the bioactivities of structurally diverse sulfocoumarins.[1–6] Despite these synthetic advances, new methods to conveniently construct structurally diverse sulfocoumarins are still in high demand.

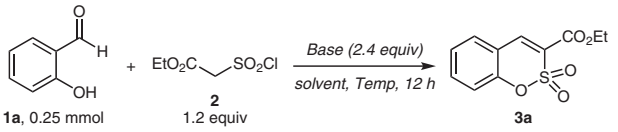
Over the past five years, our group has investigated the chemistry of the sulfonyl moiety. We improved the synthetic methods for the preparation of alkanesulfonyl chlorides,[12] and used them in mechanistic and stereochemical studies on sulfa-Staudinger (sulfene-imine) cycloadditions.[13] Our work on sulfonyl chlorides has also supported our studies on the selectivity of C–H functionalizations of diazosulfonamides.[14] During these studies, we found that the active sulfonyl chlorides could react with 2-hydroxy- or 2-aminobenzaldehydes to give the corresponding six-membered products in a one-pot fashion (Scheme 1d). The reaction can be used to prepare not only 3- or 4-substituted sulfocoumarins (X = O), but benzoazacycles (X = NR). Herein, we present our synthetic studies on sulfocoumarin-3-carboxylates and their nitrogen analogues. The introduction of the ester group significantly improves the electrophilicity of the sp^2 C4 carbon, and will allow potential transformations at the ester group, enabling future structural modifications.

The reaction between salicylaldehyde (**1a**) and ethyl chlorosulfonylacetate (**2**) was used to perform the optimization (Table 1). Solvent screening with Et_3N (2.4 equiv) as the base revealed 1,2-dichloroethane (DCE) as the optimum (entries 1–9). Nucleophilic solvents such as ethanol and water gave no or a trace amount of the desired product, respectively (entries 8 and 9), because they reacted with the sulfonyl chloride. When 1.2 equivalents of Et_3N was used, only a trace amount of product was observed by TLC. Optimization of the base was performed next. Inorganic bases such as potassium carbonate and cesium carbonate gave only trace and 5% yields, respectively, probably due to their poor solubility in 1,2-dichloroethane (entries 10 and 11). Strong organic bases, for example, DMAP, $^iPr_2NEt$, DABCO, imidazole (Imid), *N*-methylimidazole (*N*-Me-Imid), and 1,1,3,3-tetramethylguanidine (TMG) gave yields ranging from trace to 25% (entries 12–18). However, the weak organic bases quinoline and pyridine gave 54% and 56% yields, respectively (entries 19 and 20). Different substituted pyridines were also tested. 4-Methylpyridine (4-Me-Py) and 2,6-dimethylpyridine (2,6-diMe-Py) gave moderate yields of 39% and 48% (entries 21 and 22), while 2,6-di-*tert*-butylpyridine (2,6-di^{t}Bu-Py) gave only a poor 6% yield (entry 23). The presence of fluorine or chlorine atoms at the 2-position of the pyridine ring completely inhibited the reactions (entries 24–28). Thus, pyridine was the most suitable base. Furthermore, heating at 85 °C for 1 hour gave the highest yield of 79% (entry 29). Prolonging the heating time gave almost the same yields (75–78%) (entries 30–32).



Scheme 1 Previous synthetic approaches toward sulfocoumarins and this work

Table 1 Optimization of the Reaction Conditions



Entry	Solvent[a]	Base (pK_a)[b]	Temp (°C)	Yield (%)[c]
1	PhMe	Et_3N (10.68)[15]	25	17
2	THF	Et_3N	25	22
3	MeCN	Et_3N	25	12
4	DCM	Et_3N	25	12
5	DCE	Et_3N	25	25
6	EtOAc	Et_3N	25	16
7	$CHCl_3$	Et_3N	25	19
8	H_2O	Et_3N	25	trace[d]
9	EtOH	Et_3N	25	trace

Table 1 (continued)

Entry	Solvent[a]	Base (pK_a)[b]	Temp (°C)	Yield (%)[c]
10	DCE	K_2CO_3	25	trace
11	DCE	Cs_2CO_3	25	5
12	DCE	DMAP (9.87)[15]	25	6
13	DCE	$^{i}Pr_2NEt$ (10.75)[16]	25	10
14	DCE	DBU (11.6)[15]	25	25
15	DCE	DABCO (8.72)[15]	25	25
16	DCE	Imid (7.03)[15]	25	20
17	DCE	*N*-Me-Imid (7.12)[15]	25	trace
18	DCE	TMG (13.6)[17]	25	13
19	DCE	quinoline (4.85)[18]	25	54
20	DCE	Py (5.37)[15]	25	56
21	DCE	4-Me-Py (6.02)[18]	25	39
22	DCE	2,6-diMe-Py (6.70)[17]	25	48
23	DCE	2,6-di^{t}Bu-Py (3.58)[18]	25	6
24	DCE	4-Me-2-F-Py	25	trace
25	DCE	6-Me-2-F-Py	25	trace
26	DCE	2-F-5-Cl-Py	25	trace
27	DCE	2-Cl-Py (0.49)[19]	25	trace
28	DCE	2,6-diCl-Py	25	trace
29[e]	**DCE**	**Py**	**85**	**79**
30[f]	DCE	Py	85	78
31[g]	DCE	Py	85	75
32[h]	DCE	Py	85	75

[a] With the exception of water, all solvents were anhydrous.
[b] The pK_a of the base (B) was recorded by measuring its conjugate acid (BH^+), see the cited references for details.
[c] Yield of isolated product.
[d] TLC indicated no product.
[e] Reaction time = 1 h.
[f] Reaction time = 2 h.
[g] Reaction time = 4 h.
[h] Reaction time = 8 h.

As shown in Table 1 (entries 5 and 12–28), the basicity and nucleophilicity of the organic bases affected the yield of sulfocoumarin **3a**. The best yield was obtained at pK_a = 5.37, with greater or smaller values leading to decreased yields of **3a** to different degrees (see Figure S1 in the Supporting Information). An irregular yield–MCA (methyl cation affinity)[20] correlation was observed (see Figure S2 and Table S1 in the Supporting Information). Probably, the yield of sulfocoumarin **3a** was controlled by both the basicity and nucleophilicity of the added organic base. The basicity should be strong enough to dehydrochlorinate sulfonyl chloride **2** to generate sulfene **B**,[21] while the nucleophilicity should be weak enough to not interrupt the nucleophilic addition of salicylaldehyde (**1a**) (pK_a = 7.95)[22] to the sulfene (see Scheme S1 in the Supporting Information).

With optimized conditions in hand, different 2-hydroxybenzaldehydes were reacted with sulfonyl chloride **2** to deliver sulfocoumarin-3-carboxylates **3** (Table 2). 4-Methoxy- (**1b**) and 5-methoxysalicylaldehyde (**1c**) were converted into the corresponding sulfocoumarins **3b** and **3c** in 77% and 66% yields, respectively (entries 2 and 3). However, the reaction of 3,5-di-*tert*-butylsalicylaldehyde (**1d**) only gave a 31% yield of the desired product **3d** (entry 4), possibly due to the large steric hindrance of the 3-*tert*-butyl groups. The sulfonylation of 3-hydroxy-2-naphthaldehyde (**1e**) and subsequent condensation occurred readily, delivering sulfocoumarin-3-carboxylate **3e** in 75% yield (entry 5). 5-Fluoro- (**1f**), 3-fluoro- (**1g**), and 6-fluoro- (**1h**) salicylaldehydes were converted into sulfocoumarins **3f**, **3g**, and **3h** in 90%, 70%, and 53% yields, respectively (entries 6–8). 6-Chloro- and 6-bromo-sulfocoumarins **3i** and **3j** were isolated in 61% and 66% yields, respectively, from the corresponding salicylaldehydes **1i** and **1j** (entries 9 and 10). 3,5-Dibromosalicylaldehyde (**1k**) and its iodo counterpart **1l** readily underwent the tandem reaction to produce sulfocoumarins **3k** and **3l** in 50% and 51% yields, respectively (entries 11 and 12). The presence of a nitro group *para* to the hydroxy group of the aldehyde facilitated the formation of sulfocoumarins, as demonstrated by the reactions of **1m** and **1n** (entries 13 and 14). In these two cases, 84% and 85% yields were obtained. 2,4-Dihydroxybenzaldehyde, with two free hydroxy groups, selectively underwent the 2-sulfonylation and subsequent condensation to give 7-hydroxysulfocoumarin-3-carboxylate **3o** in 61% yield (entry 15), even though the amount of sulfonyl chloride and pyridine had been doubled. Sulfonylation of the 4-hydroxy group also occurred to give the 4-sulfonylated aldehyde in 8% yield. Our present method provides a direct access to 7-hydroxysulfocoumarins, without protection and deprotection manipulations. In Supuran's report on the synthesis of 7-hydroxysulfocoumarin using the method of Zalubovskis, tedious protection and deprotection manipulations were required.[6]

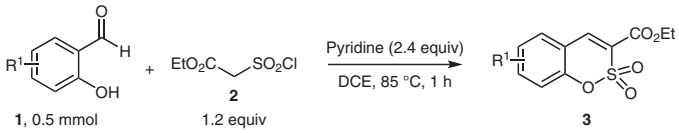
Generally, in the reactions of different 2-hydroxybenzaldehydes, sterically large substituents *ortho* to the hydroxy or formyl group of **1** resulted in decreased yields of the sulfocoumarins (entries 4, 11 and 12), because they to some extent inhibit either the sulfonylation or Knoevenagel condensation step. However, the presence of electron-withdrawing substituents at C-5 gave rise to high yields of the corresponding sulfocoumarins (entries 6, 13 and 14), possibly because of the increased acidity of the hydroxy group and facile deprotonation to form nucleophilic phenoxide anions.

Other sulfonyl chlorides, for example, ethanesulfonyl chloride and phenylmethanesulfonyl chloride, did not undergo the tandem reaction under the standard conditions

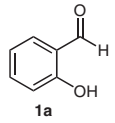
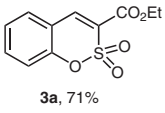
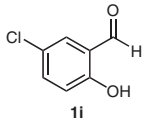
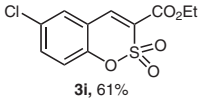
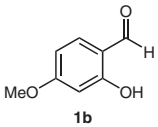
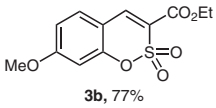
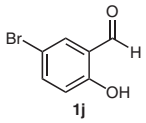
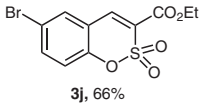
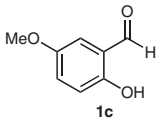
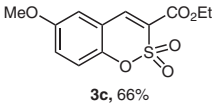
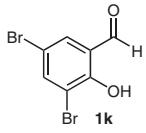
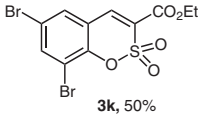
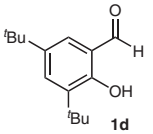
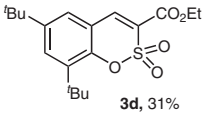
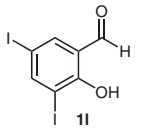
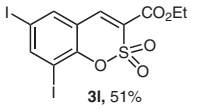
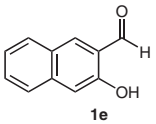
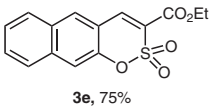
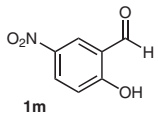
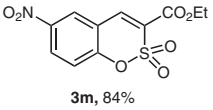
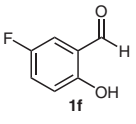
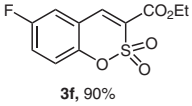
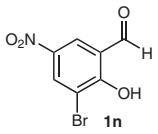
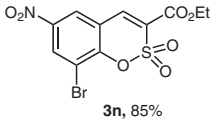
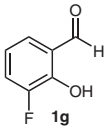
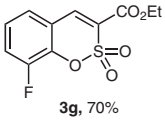
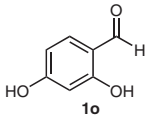
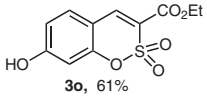
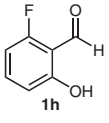
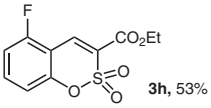
to afford the corresponding sulfocoumarin derivatives. Switching to stronger bases such as triethylamine also failed.

This process was not limited to 2-hydroxybenzaldehydes, as 2-hydroxyacetophenone (**1p**) also underwent the cyclization to afford 4-methylsulfocoumarin-3-carboxylate **3p** in 39% yield under the standard conditions (Scheme 2, a). The low reaction rate was probably due to the slow con-

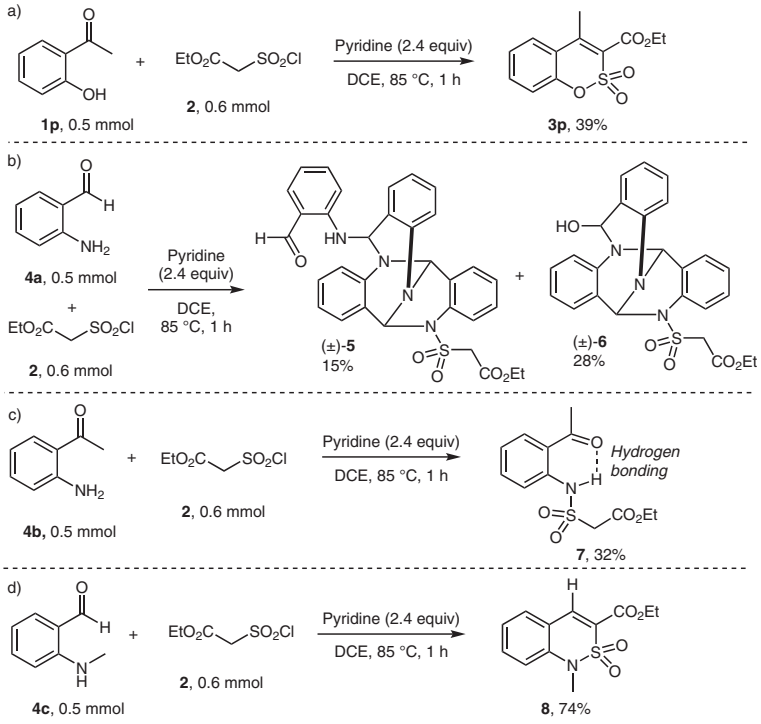
Table 2 Synthesis of Structurally Diverse Sulfocoumarin-3-carboxylates from 2-Hydroxy Aryl Aldehydes[a]



1, 0.5 mmol + **2** 1.2 equiv → **3**

Entry	Substrate	Product	Entry	Substrate	Product
1	 **1a**	 **3a**, 71%	9	 **1i**	 **3i**, 61%
2	 **1b**	 **3b**, 77%	10	 **1j**	 **3j**, 66%
3	 **1c**	 **3c**, 66%	11	 **1k**	 **3k**, 50%
4	 **1d**	 **3d**, 31%	12	 **1l**	 **3l**, 51%
5	 **1e**	 **3e**, 75%	13	 **1m**	 **3m**, 84%
6	 **1f**	 **3f**, 90%	14	 **1n**	 **3n**, 85%
7	 **1g**	 **3g**, 70%	15[b]	 **1o**	 **3o**, 61%
8	 **1h**	 **3h**, 53%			

[a] Yields of isolated products after column chromatography on silica gel.
[b] The amounts of sulfonyl chloride **2** and pyridine were doubled.



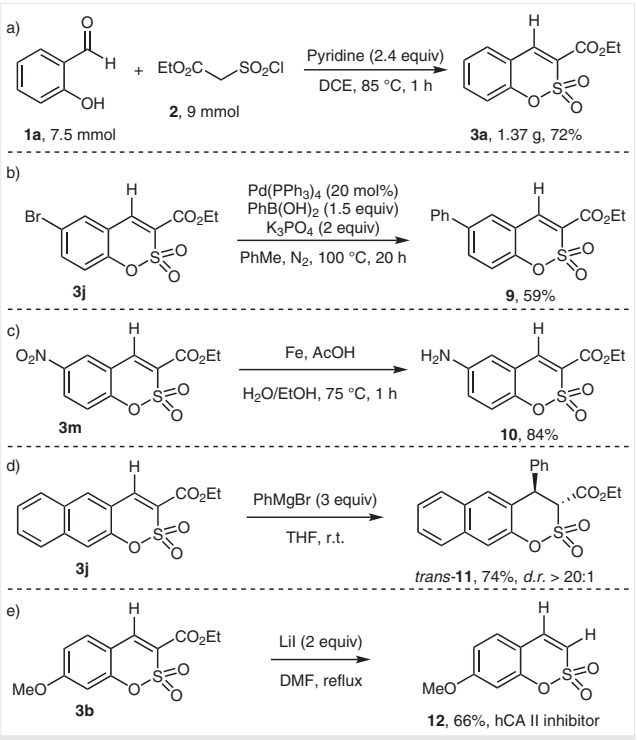
Scheme 2 Reactions of 2-hydroxyacetophenone (**1p**), 2-aminobenzaldehyde (**4a**), 2-aminoacetophenone (**4b**), and 2-methylaminobenzaldehyde (**4c**)

densation between the active methylene and the ketone moiety. To our surprise, the reaction of 2-aminobenzaldehyde (**4a**) delivered tetramer **5** and trimer **6** in 15% and 28% yield, respectively (Scheme 2, b). Such types of products had been occasionally observed by several groups.[23] The reaction of 2-aminoacetophenone (**4b**) stopped at the sulfonylation step, giving the corresponding sulfonamide **7** in 32% yield (Scheme 2, c). Most likely, it was either the intramolecular hydrogen bonding between the N–H and C=O groups or the electronic and steric factors of the ketone moiety that prevented the condensation. Gratifyingly, when 2-methylaminobenzaldehyde (**4c**) was submitted to the standard conditions, the desired ring-closed product, cyclic alkenesulfonamide **8**, was isolated in 74% yield (Scheme 2, d).

In a gram-scale preparation, sulfocoumarin **3a** was obtained in 72% yield (1.37 g) (Scheme 3, a). Palladium-catalyzed Suzuki coupling of **3j** with phenylboronic acid gave **9** in 59% yield (Scheme 3, b), while reduction of the nitro group in **3m** delivered amine **10** in 84% yield (Scheme 3, c). The ester groups were tolerated in the two derivations described above. Reduction of the ester group in **3j** with $NaBH_4$ or $LiAlH_4$ failed. No reaction occurred with $NaBH_4$, while $LiAlH_4$ gave unidentifiable mixtures. However, the reaction of **3j** with PhMgBr delivered the 1,4-addition product **11** in 74% yield (Scheme 3, d). Decarboxylation of **3b** by refluxing in aqueous NaOH solution[24] or by reflux in aqueous AcOH/HCl solution failed.[25] Finally, using Happer's decarboxylation procedure,[26] **3b** was directly converted into hCA II inhibitor **12** in 66% yield in only one step (Scheme 3, e).

In conclusion, a one-pot procedure for the synthesis of sulfonocoumarin-3-carboxylates has been established by heating 2-hydroxyaryl aldehydes with ethyl chlorosulfonylacetate in the presence of pyridine. The procedure consists of two reactions, namely sulfonylation of phenolic hydroxy groups and subsequent intramolecular Knoevenagel condensation. A number of structurally diverse products are easily prepared. Functional groups such as alkoxy, alkyl, halogen, nitro, and even nucleophilically active phenolic hydroxy, are well tolerated. In addition, 2-hydroxyaryl ketones and 2-(alkylamino)aryl aldehydes also serve as good materials for the synthesis of 4-substituted sulfocoumarin and 1-aza-2-sulfocoumarin derivatives, respectively. In combination with Happer's decarboxylation procedure, our report also provides an efficient route to bioactive sulfocoumarins.

Toluene and tetrahydrofuran were dried by refluxing over sodium with diphenyl ketone as an indicator. Acetonitrile, dichloromethane, 1,2-dichloroethane, and ethyl acetate were dried by refluxing over calcium hydride. Chloroform was dried over $MgSO_4$ overnight. Ethanol was dried by refluxing over magnesium powder. All the solvents were freshly distilled prior to use. Ethyl chlorosulfonylacetate (**2**) was prepared according to our published procedures.[13b–e,14a] The other



Scheme 3 A gram-scale synthesis of **3a** and further derivatizations of sulfocoumarin-3-carboxylates **3b**,**j**,**m**

chemicals used are commercially available. TLC analyses were performed on Yantai Chemical Co., Ltd. silica gel GF_{254} plates with combinations of petroleum ether (PE) and ethyl acetate (EA) as the eluent, and the plates were visualized with UV light. Products were purified by column chromatography using Qingdao Ocean Chemical Co., Ltd. silica gel (200–300 mesh). Melting points were obtained on a Yanaco MP-500 melting point apparatus and are uncorrected. IR spectra were recorded on a Bruker FT-IR spectrometer on KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 400 MHz spectrometer as $CDCl_3$ solutions with TMS as an internal standard. HRMS data were obtained using a Agilent LC/MS TOF mass spectrometer.

Sulfocoumarin-3-carboxylates; General Procedure

To a heavy-walled reaction tube containing a magnetic stir bar were sequentially added 2-hydroxyaryl aldehyde **1** (0.5 mmol), 1,2-dichloroethane (3 mL), pyridine (98 µL, 1.2 mmol), and sulfonyl chloride **2** (112 mg, 0.6 mmol, dropwise addition). The resulting solution quickly turned brown in color. The tube was quickly sealed with a screw cap and placed in a preheated (85 °C) oil bath. After stirring for 1 h, the mixture was cooled to room temperature and washed with 2 M HCl (8 mL) to remove the pyridine. The aqueous phase was washed with dichloromethane (5 mL). The combined organic phase was washed with saturated $NaHCO_3$ solution (15 mL), dried over Na_2SO_4, and concentrated under vacuum. The residue was submitted to column chromatography over silica gel with PE/EtOAc as eluent to afford the pure products **3**.

Ethyl Benzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3a)

Yield: 85 mg (71%); white solid; mp 111–113 °C; R_f = 0.40 (PE/EtOAc = 3:1, v/v).

IR (film): 1716, 1567, 1449, 1376, 1332, 1179, 1013, 970, 755, 720 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (s, 1 H), 7.62–7.31 (m, 4 H, ArH), 4.45 (q, *J* = 8.0 Hz, 2 H), 1.42 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.8, 152.5, 142.2, 134.5, 131.1, 127.6, 126.34, 118.9, 118.9, 63.1, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{11}O_5S$: 255.0322; found: 255.0326.

Ethyl 7-Methoxybenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3b)

Yield: 109 mg (77%); white solid; mp 167–169 °C; R_f = 0.35 (PE/EtOAc = 5:1, v/v).

IR (film): 1715, 1596, 1446, 1368, 1324, 1277, 1180, 1102, 826, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (s, 1 H), 7.47–6.79 (m, 3 H, ArH), 4.42 (q, *J* = 8.0 Hz, 2 H), 3.90 (s, 3 H), 1.41 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 164.8, 160.1, 154.4, 142.5, 132.5, 123.8, 113.5, 111.9, 103.8, 62.8, 56.2, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{13}O_6S$: 285.0427; found: 285.0429.

Ethyl 6-Methoxybenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3c)

Yield: 94 mg (66%); light yellow solid; mp 118–120 °C; R_f = 0.15 (PE/EtOAc = 5:1, v/v).

IR (film): 1719, 1615, 1491, 1375, 1275, 1127, 856, 751 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (s, 1 H), 7.26–7.00 (m, 3 H, ArH), 4.45 (q, *J* = 8.0 Hz, 2 H), 3.85 (s, 3 H), 1.42 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.8, 157.3, 146.3, 142.2, 128.0, 120.7, 119.9, 119.4, 114.2, 63.1, 56.0, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{13}O_6S$: 285.0427; found: 285.0428.

Ethyl 6,8-Di-*tert*-butylbenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3d)

Yield: 57 mg (31%); white solids; mp 110–112 °C; R_f = 0.60 (PE/EtOAc = 5:1, v/v).

IR (film): 1726, 1614, 1583, 1468, 1383, 1252, 855, 756, 732 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (s, 1 H), 7.63–7.37 (m, 2 H, ArH), 4.44 (q, *J* = 8.0 Hz, 2 H), 1.48 (s, 9 H), 1.42 (t, *J* = 8.0 Hz, 3 H), 1.34 (s, 9 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.0, 149.6, 148.9, 143.8, 139.9, 129.8, 126.5, 126.1, 119.3, 62.9, 35.2, 34.8, 31.2, 30.0, 29.3, 14.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{19}H_{27}O_5S$: 367.1574; found: 367.1577.

Ethyl Naphtho[2,3-*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3e)

Yield: 114 mg (75%); yellow solid; mp 169–171 °C; R_f = 0.50 (PE/EtOAc = 3:1, v/v).

IR (film): 1716, 1622, 1567, 1516, 1454, 1379, 1273, 819, 749 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.86 (s, 1 H), 8.24–7.42 (m, 6 H, ArH), 4.50 (q, *J* = 8.0 Hz, 2 H), 1.46 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.2, 152.8, 138.4, 136.2, 131.0, 130.2, 129.5, 129.4, 125.0, 126.1, 121.9, 117.6, 113.2, 63.2, 14.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{15}H_{13}O_5S$: 305.0478; found: 305.0471.

Ethyl 6-Fluorobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3f)

Yield: 122 mg (90%); white solid; mp 112–114 °C; R_f = 0.50 (PE/EtOAc = 5:1, v/v).

IR (film): 1720, 1619, 1579, 1480, 1381, 1261, 751 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (s, 1 H), 7.32–7.28 (m, 3 H, ArH), 4.46 (q, *J* = 8.0 Hz, 2 H), 1.43 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.6 (d, J_{C-F} = 247.8 Hz), 159.5, 148.4 (d, J_{C-F} = 2.7 Hz), 141.0 (d, J_{C-F} = 2.6 Hz), 128.8, 121.3 (d, J_{C-F} = 24.2 Hz), 120.7 (d, J_{C-F} = 8.4 Hz), 119.9 (d, J_{C-F} = 8.9 Hz), 116.8 (d, J_{C-F} = 24.6 Hz), 63.3, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}FO_5S$: 273.0227; found: 273.0232.

Ethyl 8-Fluorobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3g)

Yield: 95 mg (70%); white solid; mp 138–140 °C; R_f = 0.35 (PE/EtOAc = 5:1, v/v).

IR (film): 1721, 1608, 1476, 1385, 1365, 1265, 765 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.07 (s, 1 H), 7.43–7.30 (m, 3 H, ArH), 4.46 (q, *J* = 8.0 Hz, 2 H), 1.43 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.4, 150.9 (d, J_{C-F} = 254.9 Hz), 141.5 (d, J_{C-F} = 3.2 Hz), 140.3 (d, J_{C-F} = 13.2 Hz), 128.6, 126.5 (d, J_{C-F} = 6.8 Hz), 126.0 (d, J_{C-F} = 3.8 Hz), 121.5 (d, J_{C-F} = 17.7 Hz), 120.7, 63.4, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}FO_5S$: 273.0227; found: 273.0226.

Ethyl 5-Fluorobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3h)

Yield: 72 mg (53%); white solid; mp 108–110 °C; R_f = 0.30 (PE/EtOAc = 5:1, v/v).

IR (film): 1724, 1614, 1472, 1385, 1275, 1184, 1068, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (s, 1 H), 7.61–7.08 (m, 3 H, ArH), 4.46 (q, *J* = 8.0 Hz, 2 H), 1.43 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.11 (d, J_{C-F} = 260.8 Hz), 159.4, 152.6 (d, J_{C-F} = 4.1 Hz), 135.3 (d, J_{C-F} = 10.3 Hz), 135.0 (d, J_{C-F} = 4.9 Hz), 127.9 (d, J_{C-F} = 2.0 Hz), 114.7 (d, J_{C-F} = 3.8 Hz), 112.9 (d, J_{C-F} = 20.4 Hz), 109.1 (d, J_{C-F} = 17.3 Hz), 63.3, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}FO_5S$: 273.0227; found: 273.0222.

Ethyl 6-Chlorobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3i)

Yield: 88 mg (61%); white solid; mp 159–160 °C; R_f = 0.40 (PE/EtOAc = 5:1, v/v).

IR (film): 1722, 1616, 1563, 1383, 1277, 1218, 1183, 751 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (s, 1 H), 7.55–7.29 (m, 3 H, ArH), 4.46 (q, *J* = 8.0 Hz, 2 H), 1.42 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.4, 150.1, 140.8, 134.1, 131.8, 130.2, 128.7, 120.3, 120.0, 63.3, 14.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}ClO_5S$: 288.9932; found: 288.9933.

Ethyl 6-Bromobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3j)

Yield: 110 mg (66%); light brown solid; mp 170–171 °C; R_f = 0.45 (PE/EtOAc = 5:1, v/v).

IR (film): 1718, 1598, 1486, 1378, 1276, 1180, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.98 (s, 1 H), 7.69–7.20 (m, 3 H, ArH), 4.46 (q, *J* = 8.0 Hz, 2 H), 1.42 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.4, 151.3, 140.7, 137.0, 133.2, 128.7, 120.6, 120.4, 119.1, 63.4, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}BrO_5S$: 332.9427; found: 332.9428.

Ethyl 6,8-Dibromobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3k)

Yield: 104 mg (50%); white solid; mp 149–151 °C; R_f = 0.50 (PE/EtOAc = 5:1, v/v).

IR (film): 1715, 1612, 1549, 1442, 1381, 1276, 1172, 865, 755 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.95 (s, 1 H), 7.93 (s, 1 H), 7.65 (s, 1 H), 4.46 (q, *J* = 8.0 Hz, 2 H), 1.43 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.0, 148.6, 140.3, 139.7, 132.2, 129.4, 121.3, 119.1, 113.9, 63.6, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_9Br_2O_5S$: 410.8532; found: 410.8531.

Ethyl 6,8-Diiodobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3l)

Yield: 129 mg (51%); white solid; mp 190–192 °C; R_f = 0.50 (PE/EtOAc = 5:1, v/v).

IR (film): 1716, 1613, 1387, 1276, 1173, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (s, 1 H), 7.89 (s, 1 H), 7.82 (s, 1 H), 4.46 (q, *J* = 8.0 Hz, 2 H), 1.42 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.1, 152.1, 150.9, 140.3, 139.1, 129.2, 121.1, 89.9, 87.4, 63.5, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_9I_2O_5S$: 506.8255; found: 506.8253.

Ethyl 6-Nitrobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3m)

Yield: 125 mg (84%); yellow solid; mp 193–195 °C; R_f = 0.45 (PE/EtOAc = 5:1, v/v).

IR (film): 1716, 1614, 1575, 1384, 1347, 1265, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.51–8.46 (m, 2 H, ArH), 8.14 (s, 1 H), 7.51–7.48 (m, 1 H, ArH), 4.49 (q, *J* = 8.0 Hz, 2 H), 1.44 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.9, 155.9, 145.3, 140.1, 129.7, 128.9, 126.7, 120.2, 119.1, 63.8, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{10}NO_7S$: 300.0172; found: 300.0174.

Ethyl 8-Bromo-6-nitrobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3n)

Yield: 161 mg (85%); light brown solid; mp 185–186 °C; R_f = 0.35 (PE/EtOAc = 5:1, v/v).

IR (film): 1724, 1609, 1543, 1391, 1275, 1212, 749 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = = 8.67 (d, *J* = 1.6 Hz, 1 H), 8.46 (d, *J* = 1.6 Hz, 1 H), 8.13 (s, 1 H), 4.50 (q, *J* = 8.0 Hz, 2 H), 1.45 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 158.6, 153.3, 145.0, 139.9, 132.1, 130.1, 124.9, 112.0, 113.9, 64.0, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_9BrNO_7S$: 377.9278; found: 377.9283.

Ethyl 7-Hydroxybenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3o)

Yield: 83 mg (61%); light brown solid; mp 196–198 °C; R_f = 0.60 (PE/EtOAc = 1:1, v/v).

IR (film): 1719, 1598, 1508, 1447, 1371, 1214, 750 cm^{-1}.

^{1}H NMR (400 MHz, acetone-d_6): δ = 10.00 (s, 1 H), 8.12 (s, 1 H), 7.64–6.71 (m, 3 H, ArH), 4.44 (q, *J* = 8.0 Hz, 2 H), 1.22 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, acetone-d_6): δ = 164.6, 160.7, 155.3, 143.8, 134.6, 124.1, 115.3, 115.2, 112.2, 106.2, 106.1, 63.0, 14.4.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{11}O_6S$: 271.0271; found: 271.0276.

Ethyl 4-Methylbenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (3p)

Yield: 52 mg (39%); white solid; mp 87–88 °C; R_f = 0.35 (PE/EtOAc = 5:1, v/v).

IR (film): 1719, 1596, 1561, 1449, 1377, 1241, 1178, 762 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71–7.29 (m, 4 H, ArH), 4.44 (q, *J* = 8.0 Hz, 2 H), 2.64 (s, 3 H), 1.42 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.5, 150.4, 149.5, 133.5, 127.6, 127.1, 126.3, 121.8, 119.5, 62.9, 16.7, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{13}O_5S$: 269.0478; found: 269.0469.

Ethyl 2-({13-[(2-Formylphenyl)amino]-6*H*,13*H*-6,12-[1,2]benzenoquinazolino[3,4-*a*]quinazolin-7(11b*H*)-yl}sulfonyl)acetate (5)

Yield: 11 mg (15%); yellow solid; mp 138–140 °C; R_f = 0.7 (PE/EtOAc = 3:1, v/v).

IR (film): 2930, 2826, 1717, 1698, 1653, 1521, 1508, 1374, 1275, 1030, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 9.97 (s, 1 H), 9.05 (d, *J* = 4.6 Hz, 1 H), 7.87–7.63 (m, 4 H), 7.45–6.93 (m, 12 H), 6.39 (s, 1 H), 5.80 (d, *J* = 4.7 Hz, 1 H), 5.75 (s, 1 H), 4.60 (d, *J* = 13.8 Hz, 1 H), 4.27–4.14 (m, 2 H), 4.09 (d, *J* = 13.8 Hz, 1 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 194.7, 162.5, 148.7, 143.5, 143.0, 136.8, 136.0, 133.8, 130.0, 129.8, 129.3, 129.2, 129.1, 128.2, 126.9, 126.6, 125.7, 124.7, 124.5, 123.1, 119.8, 117.6, 113.4, 73.2, 73.1, 62.9, 62.5, 56.7, 29.7, 14.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{32}H_{29}N_4O_5S$: 581.1854; found: 581.1862.

Ethyl 2-[(13-Hydroxy-6*H*,13*H*-6,12-[1,2]benzenoquinazolino[3,4-*a*]quinazolin-7(11b*H*)-yl)sulfonyl]acetate (6)

Yield: 22 mg (28%); yellow solid; mp 175–178 °C; R_f = 0.2 (PE/EtOAc = 3:1, v/v).

IR (film): 1740, 1605, 1484, 1455, 1366, 1275, 1156, 1053, 1029, 762 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.71 (d, *J* = 7.9 Hz, 1 H), 7.52–6.95 (m, 11 H), 6.36 (s, 1 H), 5.77 (s, 1 H), 5.71 (s, 1 H), 4.57 (d, *J* = 13.8 Hz, 1 H), 4.24–4.15 (m, 2 H), 4.10 (d, *J* = 13.8 Hz, 1 H), 3.26 (s, 1 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.5, 143.0, 141.8, 133.9, 129.9, 129.8, 129.6, 129.5, 129.0, 127.9, 127.3, 126.6, 125.3, 125.0, 124.7, 124.4, 124.1, 85.8, 72.6, 63.0, 62.5, 56.7, 14.0.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{24}N_3O_5S$: 478.1431; found: 478.1435.

Ethyl 2-[*N*-(2-Acetylphenyl)sulfamoyl]acetate (7)

Yield: 43 mg (32%); brownish oil; R_f = 0.20 (PE/EtOAc = 5:1, v/v).

IR (film): 1741 (br), 1652, 1603, 1578, 1396, 1276, 1154, 750 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 11.64 (s, 1 H), 7.97–7.18 (m, 4 H, ArH), 4.15 (q, *J* = 8.0 Hz, 2 H), 4.08 (s, 2 H), 2.69 (s, 3 H), 1.24 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 202.4, 162.4, 139.8, 135.3, 132.3, 123.2, 122.3, 117.9, 62.5, 55.6, 28.2, 13.9.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{16}NO_5S$: 286.0744; found: 286.0747.

Ethyl 1-Methyl-1*H*-benzo[*c*][1,2]thiazine-3-carboxylate 2,2-Dioxide (8)

Yield: 99 mg (74%); yellow solid; mp 96–98 °C; R_f = 0.20 (PE/EtOAc = 5:1, v/v).

IR (film): 1719, 1613, 1562, 1455, 1368, 1335, 1211, 1151, 762 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (s, 1 H), 7.61-7.54 (m, 2 H, ArH), 7.24-7.17 (m, 2 H, ArH), 4.44 (q, *J* = 8.0 Hz, 2 H), 3.54 (s, 3 H), 1.42 (t, *J* = 8.0 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.4, 142.3, 142.2, 133.8, 132.0, 126.2, 123.1, 119.6, 116.3, 62.6, 30.7, 14.2.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{12}H_{14}NO_4S$: 268.0638; found: 268.0647.

Ethyl 6-Phenylbenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (9)

To a dry reaction tube were sequentially added **3j** (31 mg, 0.1 mmol), phenylboronic acid (18 mg, 0.15 mmol), K_3PO_4 (43 mg, 0.2 mmol), and $Pd(PPh_3)_4$ (7 mg, 0.02 mmol). The tube was evacuated and back filled with nitrogen (3 times). Next, dry toluene (1.5 ml) was added and the mixture was heated at 100 °C for 20 h. After cooling, the mixture was filtered through a pad of Celite, the solvent removed and the residue purified by column chromatography over silica gel to give the title product.

Yield: 18 mg (59%); yellow solid; mp 134–136 °C; R_f = 0.4 (PE/EtOAc = 1:1, v/v).

IR (film): 1719, 1613, 1576, 1479, 1380, 1251, 1174, 834, 764, 719 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.13 (s, 1 H), 7.79 (dd, *J* = 8.5, 2.2 Hz, 1 H), 7.73 (d, *J* = 2.2 Hz, 1 H), 7.57–7.52 (m, 2 H), 7.52–7.46 (m, 2 H), 7.45–7.36 (m, 2 H), 4.46 (q, *J* = 7.1 Hz, 2 H), 1.43 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 159.8, 151.7, 142.3, 140.0, 138.5, 133.2, 129.3, 129.2, 128.4, 127.9, 127.1, 119.3, 115.3, 63.2, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{15}O_5S$: 331.0635; found: 331.0640.

Ethyl 6-Aminobenzo[*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (10)

To a reaction tube were sequentially added **3m** (8 mg, 0.027 mmol) and Fe powder (9 mg, 0.16 mmol). The tube was evacuated and backfilled with nitrogen (3 times). H_2O (67 µL), AcOH (1 µL) and EtOH (44 µL) were added and the resulting mixture was stirred at 75 °C for 1 h. Following extraction with EtOAc, the organic phase was washed with saturated $NaHCO_3$ solution and dried over Na_2SO_4. Removal of the solvent and subsequent purification of the residue by column chromatography over silica gel gave the title product.

Yield: 6 mg (84%); yellow solid; mp 159–161 °C; R_f = 0.4 (PE/EtOAc = 1:1, v/v).

IR (film): 3384, 2918, 1716, 1161, 1576, 1491, 1368, 1244, 1167, 859, 823, 770 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.93 (s, 1 H), 7.10 (d, *J* = 8.8 Hz, 1 H), 6.85 (dd, *J* = 8.8, 2.8 Hz, 1 H), 6.76 (d, *J* = 2.8 Hz, 1 H), 4.43 (q, *J* = 7.1 Hz, 2 H), 3.83 (br s, 2 H), 1.41 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 160.1, 144.9, 144.7, 142.5, 127.8, 120.7, 119.7, 119.4, 115.1, 63.0, 14.1.

HRMS (ESI): *m*/*z* [M + H]$^+$ calcd for $C_{11}H_{12}NO_5S$: 270.0431; found: 270.0434.

Ethyl (3,4-*trans*)-4-Phenyl-3,4-dihydronaphtho[2,3-*e*][1,2]oxathiine-3-carboxylate 2,2-Dioxide (11)

To a dry reaction tube was added **3j** (30 mg, 0.1 mmol) and the tube was evacuated and backfilled with nitrogen (3 times). Dry THF (1.5 mL) was added via a syringe, followed by the slow addition of PhMgBr (0.3 mmol, 0.3 mL, 1 mol/L) at room temperature. The mixture was stirred overnight. H_2O was added and the mixture was extracted with EtOAc (3 × 5 mL). After drying over Na_2SO_4, the organic phase was concentrated under vacuum. Subsequent purification of the residue by column chromatography over silica gel afforded **11**.

Yield: 28 mg (74%); white solid; mp 156–158 °C; R_f = 0.5 (PE/EtOAc = 10:1, v/v).

IR (film): 1741, 1621, 1597, 1512, 1494, 1457, 1381, 1291, 1192, 1176, 1154, 1037, 935, 850, 751, 703 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 8.9 Hz, 1 H), 7.81 (d, *J* = 8.1 Hz, 1 H), 7.62 (d, *J* = 8.5 Hz, 1 H), 7.43–7.36 (m, 1 H), 7.35–7.21 (m, 5 H), 7.19–7.12 (m, 2 H), 5.70 (d, *J* = 8.0 Hz, 1 H), 4.61 (d, *J* = 8.0 Hz, 1 H), 4.41–4.25 (m, 2 H), 1.29 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 163.5, 149.2, 141.2, 132.2, 131.1, 131.0, 129.4, 128.9, 128.0, 127.8, 127.4, 125.8, 124.9, 118.5, 118.3, 68.0, 63.6, 45.7, 14.0.

HRMS (ESI): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{18}NaO_5S$: 405.0767; found: 405.0749.

7-Methoxybenzo[*e*][1,2]oxathiine 2,2-Dioxide (12)

To a dry reaction tube were added **3b** (28 mg, 0.1 mmol) and LiI (27 mg, 0.2 mmol). The tube was evacuated and backfilled with nitrogen (3 times), followed by addition of dry DMF (1.0 mL) via a syringe. The tube was heated at 180 °C for 5 h. Upon cooling to room temperature, H_2O (15 mL) and 2 M HCl (2 mL) were added. After extraction with EtOAc (3 × 10 mL), drying over Na_2SO_4, and concentration under vacuum, the residue was purified by column chromatography over silica gel to afford **12**.

Yield: 14 mg (66%); white solid; mp 103–105 °C (Lit.[1] 111–112 °C); R_f = 0.6 (PE/EtOAc = 10:1, v/v).

^1H NMR (400 MHz, $CDCl_3$): δ = 7.32 (d, *J* = 8.6 Hz, 1 H), 7.19 (d, *J* = 10.2 Hz, 1 H), 6.83 (dd, *J* = 8.5, 2.3 Hz, 1 H), 6.78 (d, *J* = 2.3 Hz, 1 H), 6.62 (d, *J* = 10.2 Hz, 1 H), 3.87 (s, 3 H).

^{13}C NMR (101 MHz, $CDCl_3$): δ = 162.8, 153.1, 135.9, 130.4, 118.8, 112.8, 112.1, 104.0, 55.9.

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