Benzothiazines in Synthesis: A Route to Chiral Cyclobutanes

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Dedicated to Professor Lutz F. Tietze on the occasion of his 65th birthday

Abstract: Using enantiomerically pure benzothiazines as templates, enantiomerically pure cyclobutanes were prepared. Such compounds are potentially interesting synthetic intermediates. The sequence developed for the preparation of these compounds, as well as some of their chemistry, is described.

Key words: benzothiazines, enantiomerically pure, cyclobutanes, stereoselective, metalation

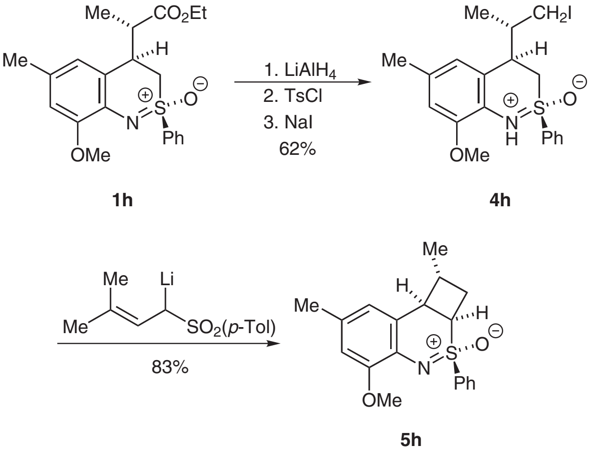
Due to their high degree of ring strain, the use of cyclobutanes as synthetic intermediates has flourished over the last 30 years.[1–5] There are four main synthetic strategies for the creation of these four-membered-ring systems: [2+2] cycloadditions, cyclization of acyclic precursors, ring expansion of cyclopropanes, and ring contraction of cyclopentanes.[1–5] The utility of cyclobutanes in synthesis makes their preparation both of interest and importance, and the synthesis of enantiomerically pure cyclobutanes leads to useful starting materials from which other chiral, nonracemic products can be formed.

We recently published the synthesis of pseudopteroxazole conducted using benzothiazine chemistry that we have developed.[6,7] During the course of that synthesis we had occasion to attempt the reactions shown in Schemes 1 and 2. Rather than serve as nucleophiles, the organometallic reagents acted as bases, deprotonating the starting benzothiazines, which then cyclized intramolecularly to afford the cyclobutanes **5h** and **5a**. We subsequently undertook a broader study of this process. This report details our results.

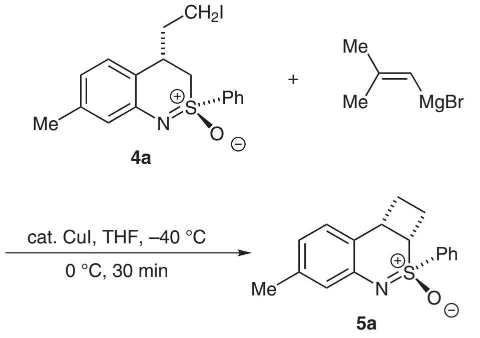
We found that treatment of **4a** with potassium hydride afforded **5a** in 83% yield, while bases such as *n*-butyllithium and lithium hexamethyldisilazide did not afford this product and led to recovery of starting material. The reasons for this are not clear.

As this process seemed a simple one for the synthesis of substituted, enantiomerically pure cyclobutanes, we decided to explore the scope of the reaction. Starting materials for the ring closure were prepared from the corresponding esters, as illustrated for **1g** in Scheme 3.

The basic procedure for cyclization consisted of treating iodides **4** with 1.5 equivalents of potassium hydride at –78 °C and allowing the reaction to warm to room temperature overnight. Examples are shown in Table 1.



Scheme 1



Scheme 2

The metalation of sulfoximines is of current interest[8] and we thus conducted a small study of the metalation of cyclobutane **5g** and trapping of the resultant anion with electrophiles. The results are illustrated in Table 2. As has been the case for other benzothiazines that we have metalated, the procedure consisted simply of treating **5g** with *n*-butyllithium for 60 minutes at –78 °C, followed by addition of an electrophile. Noteworthy and unfortunate is that diastereocontrol in the reaction with aldehydes was poor; however, diastereomeric pairs **6c/6d** and **6e/6f** could be separated by chromatography. When chlorodiphenylphosphine or chlorodicyclohexylphosphine was used as an electrophile, the products oxidized rather quickly and were isolated and characterized as the corresponding phosphine oxides **6i** and **6j**, respectively.

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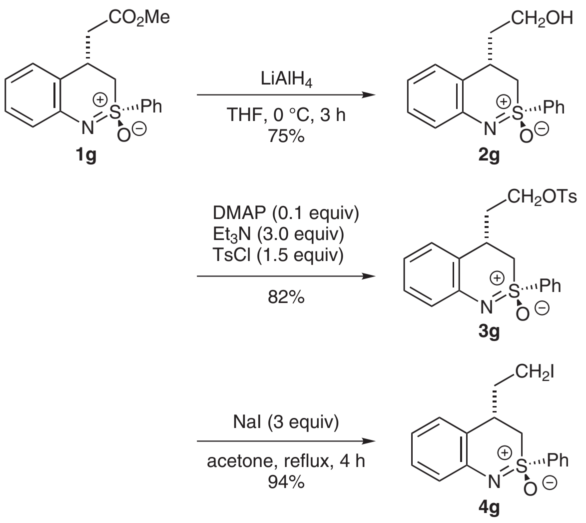


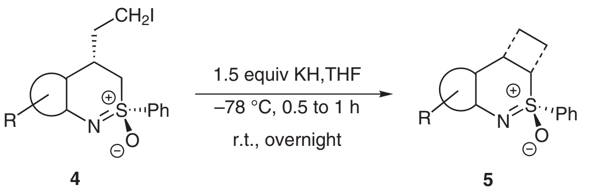
Scheme 3

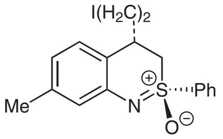
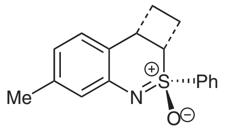
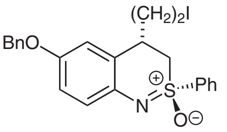
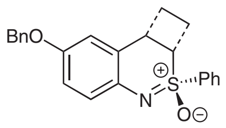
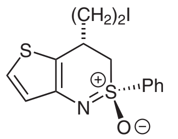
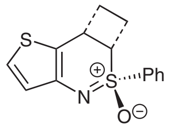
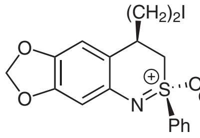
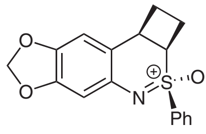
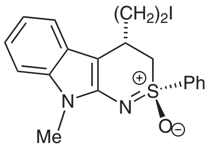
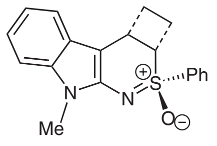
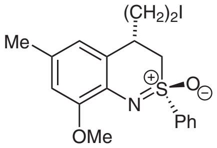
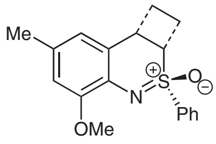
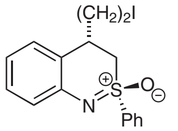
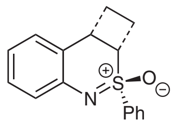
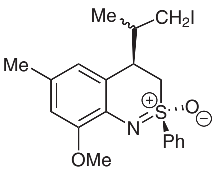
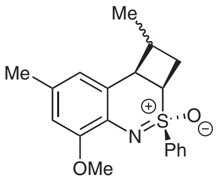
When diphenyl disulfide was used as an electrophile, **6a** could be isolated in high yield; however, **6a** was not stable and decomposed in deuterated chloroform and other mildly acidic media to afford two new products, **7** and **8**, in moderate yield as single stereoisomers (Scheme 4). The structure of **7** was assigned on the basis of NOESY and HMBC data. In Figure 1a, the correlations of C-5 and H-4 and C-5 and H-3 (HMBC) indicate that the phenylsulfanyl group is located on C-1. The NOESYcorrelations of H-12 (or H-16) and H-9 indicate that they are close in space. In Figure 1b, the correlation of H-21 (or H-19) and H-4 is shown and suggests that H-4 and the phenylsulfanyl group are *cis* to each other. The structural assignment was ultimately confirmed by X-ray crystal structure analysis of **7**.[9] The second product, **8**, possessed an exchangeable proton as determined by examining the proton NMR and IR spectra. The presence of two olefinic quaternary carbons and two monosubstituted benzene rings led us to the structure shown.

A reasonable rationalization for the formation of **7** and **8** consists of initial protonation of **6a** followed by ring opening to form the thiocarbenium ion **10** (Scheme 5). Cyclization with the sulfinamide nitrogen as the nucleophile produces **7**, while E1 elimination affords **8**. Interestingly, the oxidation of **7** to the corresponding sulfoxide with *m*-chloroperoxybenzoic acid (Scheme 6) proceeded with complete diastereoselectivity, as evidenced by ^{1}H NMR data. However, the relative stereochemistry was not established.

In summary, we have developed a simple route to enantiomerically pure cyclobutanes based on an intramolecular cyclization of iodoethyl-substituted benzothiazines (cyclic sulfoximines). The successful metalation and electrophilic trapping of one such cyclobutane has been demonstrated. Further studies will involve taking advantage of the ring strain of the cyclobutane to obtain enantiomerically pure compounds of greater complexity.

Table 1 Cyclization Reactions of Iodoethyl-Substituted Benzothiazines To Form Cyclobutanes

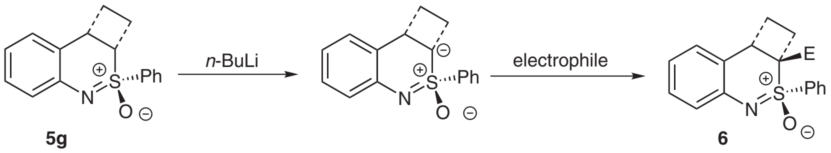


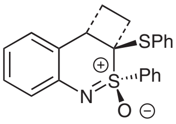
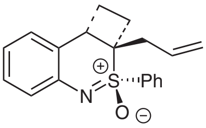
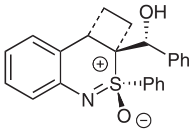
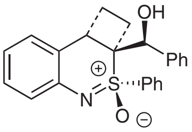
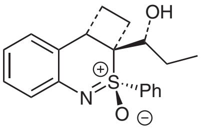
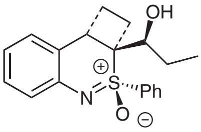
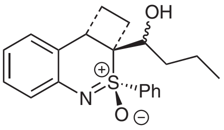
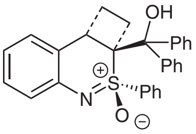
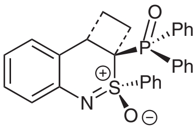
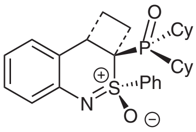
Starting Material	Product	Yield (%)
 **4a**	 **5a**	83
 **4b**	 **5b**	84
 **4c**	 **5c**	58
 **4d**	 **5d**	64
 **4e**	 **5e**	71[a]
 **4f**	 **5f**	78
 **4g**	 **5g**	88[a]
 **4h**	 **5h**	96[b]

[a] X-ray crystal structure obtained.[9]

[b] Diastereomeric ratio = 2.6:1.

Table 2 Metalation and Trapping of **5g**



Electrophile	Product(s)		Yield (%)
$(PhS)_2$	 **6a**		93[a]
$CH_2{=}CHCH_2Br$	 **6b**		57
PhCHO	 **6c**	 **6d**	96[b]
CH_3CH_2CHO	 **6e**	 **6f**	81[c]
$CH_3(CH_2)_2CHO$	 **6g**		86[d]
Ph_2CO	 **6h**		99
Ph_2PCl	 **6i**		86[e]
Cy_2PCl	 **6j**		50[f]

[a] X-ray crystal structure obtained.[9]

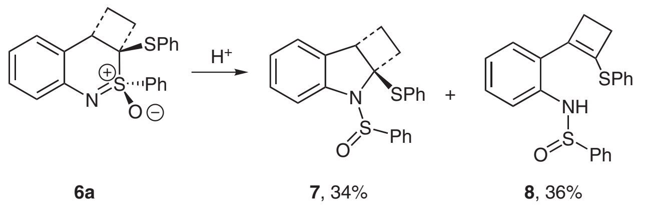
[b] Diastereomers separated, ratio **6c**/**6d** = 1.4–1.6:1.

[c] Diastereomers separated, ratio **6e**/**6f** = 1.3–1.5:1.

[d] Diastereomers separated, ratio = 1.4:1.

[e] Initial product oxidized with H_2O_2.

[f] Initial product oxidized by air.



Scheme 4

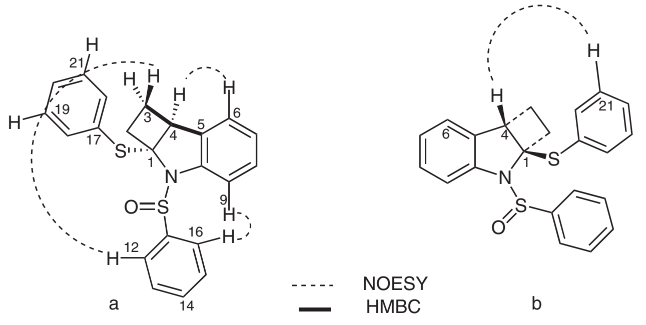
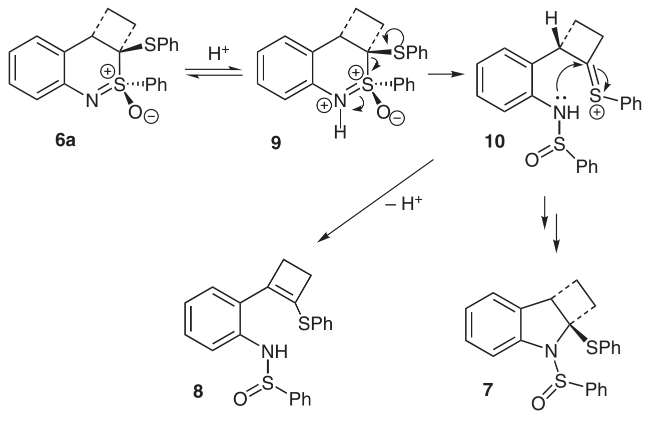
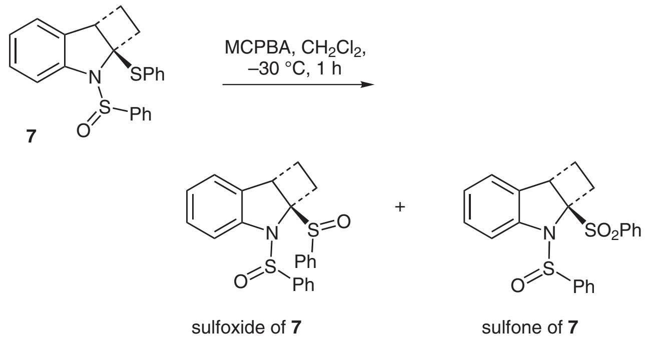


Figure 1 HMBC and NOESY correlations seen in compound **7**



Scheme 5 Proposed mechanism for the formation of **7** and **8**



Scheme 6

All reactions were carried out under an atmosphere of nitrogen in flame-dried glassware. THF was distilled over sodium/benzophenone before use. Toluene and CH_2Cl_2 were distilled over CaH_2. Chromatographic separations were carried out using Sorbent standard silica gel (230–400 mesh). Analytical TLC was performed on Sigma–Aldrich silica gel TLC plates containing UV indicator. Melting points were measured with a Fisher–Johns melting point apparatus. IR spectra were recorded (film) on a Perkin Elmer 1600 series FT-IR spectrometer. Optical rotations were measured on a Jasco DIP-370 digital polarimeter. ^{1}H NMR spectra were recorded on a Bruker ARX-250 (250 MHz), DRX-300 (300 MHz), or DRX-500 (500 MHz) spectrometer and the chemical shifts (δ) are reported in ppm relative to tetramethylsilane (TMS: δ = 0.0). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, ddd = doublet of doublet of doublets), coupling constants (Hz), and integration. ^{13}C NMR spectra were recorded on a Bruker ARX-250 (62.5 MHz), DRX-300 (75 MHz), or DRX-500 (125 MHz) spectrometer with complete proton decoupling. Chemical shifts (δ) are reported in ppm from TMS with the solvent resonance as the internal standard ($CDCl_3$: δ = 77.0). HRMS were recorded with a Bruker 12 Tesla Apex-Qe FTICR-MS with an Apollo II ion source.

Alcohol 2g; Typical Procedure for the Preparation of Alcohols 2

To ester **1g** (1.059 g, 3.363 mmol) in THF (9 mL) at 0 °C, $LiAlH_4$ (380.9 mg, 10.09 mmol) was added carefully. The mixture was stirred for another 3 h before the reaction was quenched with H_2O (386 μL), 15% aq NaOH (386 μL), and H_2O (1.2 mL). After stirring for 30 min at r.t., the mixture was filtered through Celite® and dried ($MgSO_4$). Chromatography (EtOAc–hexanes, 7:3) gave **2g** as a pale-yellow semisolid; yield: 724 mg (75%).

$[\alpha]_D^{25}$ –0.4 (*c* 1.0, $CHCl_3$).

IR (film): 3367, 3056, 3007, 2958, 2921, 2876, 1589, 1565, 1479, 1446, 1405, 1295, 1262, 1213, 1111, 1046 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (dd, *J* = 1.5, 7.2 Hz, 2 H), 7.66 (tt, *J* = 2.0, 7.2 Hz, 1 H), 7.57 (t, *J* = 7.8 Hz, 2 H), 7.21 (t, *J* = 7.2 Hz, 2 H), 7.13 (dd, *J* = 1.2, 7.8 Hz, 1 H), 6.93 (td, *J* = 1.5, 7.5 Hz, 1 H), 3.73 (t, *J* = 5.1 Hz, 2 H), 3.63 (dd, *J* = 4.5, 11.7 Hz, 1 H), 3.58–3.50 (m, 1 H), 3.08 (dd, *J* = 7.5, 12.0 Hz, 1 H), 2.43 (qd, *J* = 6.0, 12.0 Hz, 1 H), 2.00–1.80 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 145.0, 139.1, 133.8, 129.4, 128.9, 125.8, 125.3, 124.0, 120.8, 59.8, 52.5, 34.1, 31.6.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{16}H_{18}NO_2S$: 288.1053; found: 288.1055.

2b

Yield: 80%; pale-yellow semisolid.

$[\alpha]_D^{25}$ –13.9 (*c* 3.2, $CHCl_3$).

IR (film): 3371, 3064, 3027, 3007, 2925, 2872, 1610, 1573, 1483, 1442, 1417, 1381, 1283, 1221, 1099, 1021 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.04 (dd, *J* = 7.7, 1.4 Hz, 2 H), 7.63 (t, *J* = 7.6 Hz, 1 H), 7.54 (t, *J* = 7.6 Hz, 2 H), 7.45–7.26 (m, 5 H), 7.03 (d, *J* = 8.5 Hz, 1 H), 6.90–6.84 (dd, *J* = 2.3, 7.1 Hz, 1 H), 6.83 (d, *J* = 2.3 Hz, 1 H), 5.02 (s, 2 H), 3.70–3.40 (m, 4 H), 3.08 (dd, *J* = 10.1, 12.2 Hz, 1 H), 2.23 (qd, *J* = 5.1, 11.8 Hz, 1 H), 1.96 (s, 1 H), 1.82 (qd, *J* = 5.5, 11.5 Hz, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.2, 139.3, 138.4, 137.3, 133.7, 129.3, 128.8, 128.5, 127.8, 127.5, 126.4, 124.5, 114.4, 113.6, 70.6, 59.7, 52.6, 34.2, 32.0.

HRMS: *m/z* [M + H – H_2O]$^+$ calcd for $C_{23}H_{22}NO_2S$: 376.1366; found: 376.1369.

2c

Yield: 71%; pale-yellow semisolid.

$[\alpha]_D^{25}$ +6.8 (*c* 3.1, $CHCl_3$).

IR (film): 3350, 3097, 3064, 2925, 2872, 1581, 1520, 1442, 1377, 1238, 1107 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.10 (td, *J* = 1.5, 7.1 Hz, 2 H), 7.71 (tt, *J* = 1.3, 7.5 Hz, 1 H), 7.60 (tt, *J* = 1.1, 7.8 Hz, 2 H), 7.12 (dd, *J* = 1.0, 5.3 Hz, 1 H), 6.85 (d, *J* = 5.2 Hz, 1 H), 3.86 (dd, *J* = 5.0, 9.0 Hz, 2 H), 3.82–3.72 (m, 1 H), 3.62 (dd, *J* = 4. 8, 11.6 Hz, 1 H), 2.74 (dd, *J* = 11.7, 13.7 Hz, 1 H), 2.45–2.25 (m, 1 H), 2.10–1.85 (m, 1 H), 1.70 (t, *J* = 3.9 Hz, 1 H).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 142.8, 136.7, 134.2, 129.4, 129.3, 125.5, 121.6, 115.3, 60.2, 51.4, 37.7, 30.1.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{14}H_{16}NO_2S_2$: 294.0617; found: 294.0618.

2d

Yield: 70%; pale-yellow semisolid.

[α]$_D^{25}$ –17.7 (*c* 0.5, CHCl$_3$).

IR (film): 3399, 3056, 3003, 2884, 1650, 1479, 1417, 1230, 1033 cm^{-1}.

^{1}H NMR (250 MHz, CDCl$_3$): δ = 8.06 (td, *J* = 1.1, 6.9 Hz, 2 H), 7.67 (td, *J* = 1.2, 7.5 Hz, 1 H), 7.58 (td, *J* = 1.1, 7.3 Hz, 2 H), 6.69 (dd, *J* = 1.8, 3.0 Hz, 2 H), 5.90 (dd, *J* = 1.4, 3.9 Hz, 1 H), 3.72 (q, *J* = 5.9 Hz, 2 H), 3.60 (dd, *J* = 4.5, 12.8 Hz, 1 H), 3.53–3.40 (m, 1 H), 3.15 (dd, *J* = 9.6, 12.8 Hz, 1 H), 2.23 (qd, *J* = 6.1, 14.2 Hz, 1 H), 1.83 (qd, *J* = 7.6, 14.0 Hz, 1 H), 1.50 (s, 1 H).

^{13}C NMR (62.5 MHz, CDCl$_3$): δ = 147.3, 142.1, 139.5, 139.3, 133.7, 129.4, 128.8, 117.7, 106.1, 105.6, 100.9, 76.5, 60.0, 53.4, 34.6, 32.1.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{18}NO_4S$: 332.0951; found: 332.0949.

2e

Yield: 83%; pale-yellow semisolid.

[α]$_D^{25}$ –40.4 (*c* 3.2, CHCl$_3$).

IR (film): 3416, 3052, 2999, 2917, 2864, 1961, 1900, 1818, 1716, 1614, 1577, 1471, 1442, 1409, 1356, 1225, 1131, 1103, 1013 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.08 (d, *J* = 7.6 Hz, 2 H), 7.69 (t, *J* = 7.2 Hz, 1 H), 7.59 (t, *J* = 7.4 Hz, 2 H), 7.41 (dd, *J* = 3.2, 8.2 Hz, 1 H), 7.20 (dd, *J* = 5.3, 6.8 Hz, 1 H), 7.10–6.90 (m, 2 H), 4.00–3.70 (m, 3 H), 3.67 (s, 3 H), 3.56 (dd, *J* = 5.3, 12.1 Hz, 1 H), 3.08 (t, *J* = 11.8 Hz, 1 H), 2.60–2.38 (m, 1 H), 2.02 (qd, *J* = 6.8, 13.6 Hz, 1 H), 1.74 (s, 1 H).

^{13}C NMR (62.5 MHz, CDCl$_3$): δ = 142.8, 137.1, 134.3, 133.8, 129.5, 129.0, 126.0, 119.3, 118.3, 117.1, 108.3, 88.3, 60.3, 53.0, 35.3, 29.3, 27.6.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{20}N_2O_2SNa$: 363.1138; found: 363.1143.

2f

Yield: 81%; pale-yellow semisolid.

[α]$_D^{25}$ +23.0 (*c* 4.3, CHCl$_3$).

IR (film): 3416, 3056, 2991, 2925, 2872, 2831, 1609, 1569, 1462, 1417, 1328, 1258, 1193, 1156 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.05 (d, *J* = 8.0 Hz, 2 H), 7.61 (t, *J* = 7.2 Hz, 1 H), 7.52 (t, *J* = 7.6 Hz, 2 H), 6.68 (s, 1 H), 6.62 (s, 1 H), 3.87 (s, 3 H), 3.63 (s, 2 H), 3.57 (dd, *J* = 4.5, 13.0 Hz, 1 H), 3.50–3.37 (m, 1 H), 3.12 (t, *J* = 10.8 Hz, 1 H), 2.31 (s, 3 H), 2.24 (qd, *J* = 6.0, 12.9 Hz, 1 H), 1.85–1.70 (qd, *J* = 6.8, 13.6 Hz, 1 H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 152.2, 139.5, 133.5, 131.4, 130.1, 129.2, 128.9, 126.5, 118.7, 111.3, 107.4, 59.7, 55.9, 53.1, 34.3, 32.0, 21.3.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{22}NO_3S$: 332.1315; found: 332.1314.

Tosylate 3g; Typical Procedure for the Preparation of Tosylates 3

To alcohol **2g** (445.7 mg, 1.552 mmol) in CH_2Cl_2 (16 mL) in a 25-mL round-bottomed flask at 0 °C, DMAP (19.1 mg, 0.156 mmol), Et_3N (0.652 mL, 473.6 mg, 4.680 mmol), and TsCl (446.1 mg, 2.340 mmol) were added. After the mixture was stirred at r.t. overnight, TLC showed that no starting materials remained. The solvent was removed; chromatography (EtOAc–hexanes, 4:6) gave **3g** as a pale-yellow semisolid; yield: 560 mg (82%).

[α]$_D^{25}$ +12.3 (*c* 1.9, CHCl$_3$).

IR (film): 3056, 3027, 2958, 2921, 2856, 1593, 1478, 1442, 1356, 1274, 1176 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.04 (dd, *J* = 1.5, 7.4 Hz, 2 H), 7.74 (d, *J* = 8.1 Hz, 2 H), 7.67 (tt, *J* = 1.5, 7.5 Hz, 1 H), 7.58 (t, *J* = 7.2 Hz, 2 H), 7.33 (d, *J* = 7.8 Hz, 2 H), 7.21 (m, 1 H), 7.11 (dd, *J* = 1.2, 7.8 Hz, 1 H), 6.94 (d, *J* = 6.3 Hz, 1 H), 6.85 (dt, *J* = 1.2, 7.5 Hz, 1 H), 4.03 (t, *J* = 6.0 Hz, 2 H), 3.48 (dd, *J* = 4.8, 12.3 Hz, 1 H), 3.44–3.35 (m, 1 H), 3.17 (dd, *J* = 7.8, 12.0 Hz, 1 H), 2.45 (s, 3 H), 2.31 (qd, *J* = 6.6, 12.6 Hz, 1 H), 1.96 (qd, *J* = 6.3, 12.6 Hz, 1 H).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 145.1, 144.7, 139.1, 133.9, 132.5, 130.0, 129.5, 128.7, 128.7, 127.8, 126.2, 124.4, 124.0, 121.0, 67.2, 31.9, 31.1, 21.6.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{23}H_{24}NO_4S_2$: 442.1141; found: 442.1135.

3a

Yield: 82%; white semisolid.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.01 (dd, *J* = 1.3, 7.4 Hz, 2 H), 7.72 (d, *J* = 8.2 Hz, 2 H), 7.64 (t, *J* = 7.4 Hz, 1 H), 7.55 (t, *J* = 8.0 Hz, 2 H), 7.31 (d, *J* = 8.2 Hz, 2 H), 6.93 (s, 1 H), 6.82 (d, *J* = 7.8 Hz, 1 H), 6.65 (dd, *J* = 1.0, 7.7 Hz, 1 H), 4.10–3.92 (m, 2 H), 3.50–3.33 (m, 2 H), 3.12 (dd, *J* = 8.7, 12.7 Hz, 1 H), 2.42 (s, 3 H), 2.35–2.22 (m, 4 H), 1.91 (qd, *J* = 6.8, 13.8 Hz, 1 H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 144.9, 144.3, 139.0, 138.3, 133.7, 132.3, 129.8, 129.3, 128.5, 127.7, 125.9, 124.8, 121.6, 120.8, 67.2, 52.7, 31.3, 31.0, 21.4, 20.9.

Anal. Calcd for $C_{24}H_{25}NO_4S_2$: C, 63.27; H, 5.53; N, 3.07. Found: C, 63.12; H, 5.41; N, 3.14.

3b

Yield: 74%; pale-yellow semisolid.

IR (film): 3064, 3032, 2958, 2921, 2868, 1601, 1565, 1479, 1442, 1360, 1274, 1225, 1189, 1172 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.05 (td, *J* = 1.0, 7.1 Hz, 2 H), 7.73 (td, *J* = 1.3, 8.3 Hz, 2 H), 7.67 (tt, *J* = 1.3, 7.4 Hz, 1 H), 7.58 (tt, *J* = 7.1, 1.5 Hz, 2 H), 7.50–7.25 (m, 7 H), 7.04 (d, *J* = 8.7 Hz, 1 H), 6.87 (dd, *J* = 2.9, 8.7 Hz, 1 H), 6.67 (d, *J* = 2.8 Hz, 1 H), 5.01 (s, 2 H), 4.10–3.90 (m, 2 H), 3.46 (dd, *J* = 4.7, 10.3 Hz, 1 H), 3.50–3.32 (m, 1 H), 3.19 (dd, *J* = 7.9, 12.5 Hz, 1 H), 2.40 (s, 3 H), 2.27 (qd, *J* = 5.6, 11.5 Hz, 1 H), 1.94 (qd, *J* = 5.5, 11.9 Hz, 1 H).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 153.4, 145.1, 139.3, 138.1, 137.2, 133.8, 132.6, 130.0, 129.5, 128.8, 128.6, 127.9, 127.8, 127.5, 125.1, 125.1, 114.9, 113.8, 70.6, 67.2, 53.2, 32.4, 31.2, 21.6.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{30}H_{30}NO_5S_2$: 548.1560; found: 548.1563.

3c

Yield: 89%; pale-yellow semisolid.

[α]$_D^{25}$ –9.6 (*c* 9.1, CHCl$_3$).

IR (film): 3060, 3023, 2962, 2921, 2860, 1597, 1520, 1442, 1381, 1352, 1242, 1172, 1107 cm^{-1}.

^{1}H NMR (250 MHz, CDCl$_3$): δ = 8.10–8.00 (m, 2 H), 7.80–7.65 (m, 3 H), 7.65–7.50 (m, 2 H), 7.33 (d, *J* = 6.6 Hz, 2 H), 7.08 (dd, *J* = 2.0, 5.2 Hz, 1 H), 6.80 (dd, *J* = 3.2, 5.2 Hz, 1 H), 4.20 (dt, *J* = 3.0, 6.2 Hz, 2 H), 3.78–3.55 (m, 1 H), 3.36 (td, *J* = 4.6, 11.5 Hz, 1 H), 2.63 (td, *J* = 2.7, 11.6 Hz, 1 H), 2.42 (d, *J* = 2.6 Hz, 3 H), 2.45–2.25 (m, 1 H), 2.20–1.90 (m, 1 H).

^{13}C NMR (62.5 MHz, CDCl$_3$): δ = 145.1, 143.0, 136.3, 134.3, 132.3, 130.0, 129.4, 129.2, 127.8, 125.5, 121.8, 113.7, 67.1, 50.5, 34.0, 29.6, 21.6.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{22}NO_4S_3$: 448.0705; found: 448.0707.

3d

Yield: 68%; pale-yellow semisolid.

$[\alpha]_D^{25}$ –29.2 (*c* 2.0, CHCl$_3$).

IR (film): 3060, 3015, 2970, 2897, 1961, 1920, 1618, 1597, 1499, 1475, 1413, 1364, 1238, 1172 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.05 (dd, *J* = 1.4, 7.3 Hz, 2 H), 7.76 (d, *J* = 8.3 Hz, 2 H), 7.69 (t, *J* = 7.3 Hz, 1 H), 7.60 (t, *J* = 7.1 Hz, 2 H), 7.35 (d, *J* = 8.0 Hz, 2 H), 6.67 (s, 1 H), 6.38 (s, 1 H), 5.90 (dd, *J* = 1.3, 4.9 Hz, 2 H), 4.10–3.90 (m, 2 H), 3.49 (q, *J* = 16.6 Hz, 1 H), 3.35–3.20 (m, 2 H), 2.46 (s, 3 H), 2.24 (qd, *J* = 5.8, 11.9 Hz, 1 H), 1.90 (qd, *J* = 5.7, 12.8 Hz, 1 H).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 147.7, 145.2, 142.2, 139.3, 139.1, 133.9, 132.5, 130.0, 129.5, 128.7, 127.9, 116.4, 106.5, 106.1, 100.9, 67.3, 54.1, 32.5, 31.6, 21.7.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{24}H_{24}NO_6S_2$: 486.1040; found: 486.1038.

3e

Yield: 83%; pale-yellow semisolid.

$[\alpha]_D^{25}$ –45.7 (*c* 0.9, CHCl$_3$).

IR (film): 3060, 2917, 2860, 1597, 1528, 1471, 1442, 1356, 1230, 1176, 1099, 1013 cm^{-1}.

^{1}H NMR (250 MHz, CDCl$_3$): δ = 8.07 (td, *J* = 1.0, 7.1 Hz, 2 H), 7.80–7.55 (m, 5 H), 7.26 (d, *J* = 8.2 Hz, 2 H), 7.18 (td, *J* = 1.4, 6.0 Hz, 2 H), 7.10–6.90 (m, 2 H), 4.22–4.05 (m, 2 H), 3.90–3.75 (m, 1 H), 3.66 (s, 3 H), 3.42 (dd, *J* = 5.5, 12.1 Hz, 1 H), 2.99 (t, *J* = 11.7 Hz, 1 H), 2.60–2.45 (m, 1 H), 2.42 (s, 3 H), 2.28–2.10 (m, 1 H).

^{13}C NMR (62.5 MHz, CDCl$_3$): δ = 144.9, 143.0, 136.8, 134.5, 133.8, 132.6, 129.9, 129.6, 129.0, 127.7, 125.6, 119.4, 118.4, 116.5, 108.3, 87.0, 68.0, 52.4, 31.9, 29.0, 27.6, 21.6.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{26}N_2O_4S_2Na$: 517.1226; found: 517.1221.

3f

Yield: 86%; pale-yellow semisolid.

$[\alpha]_D^{25}$ +31.2 (*c* 1.7, CHCl$_3$).

IR (film): 3056, 2974, 2921, 2856, 2835, 1597, 1573, 1462, 1356, 1266, 1176 cm^{-1}.

^{1}H NMR (250 MHz, CDCl$_3$): δ = 8.07 (td, *J* = 1.4, 7.1 Hz, 2 H), 7.75 (d, *J* = 8.3 Hz, 2 H), 7.66 (t, *J* = 7.2 Hz, 1 H), 7.55 (t, *J* = 7.0 Hz, 2 H), 7.33 (d, *J* = 8.0 Hz, 2 H), 6.68 (s, 1 H), 6.40 (s, 1 H), 3.98 (t, *J* = 5.8 Hz, 2 H), 3.87 (s, 3 H), 3.55–3.40 (m, 1 H), 3.40–3.20 (m, 2 H), 2.45 (s, 3 H), 2.35–2.15 (m, 4 H), 1.91 (qd, *J* = 6.3, 12.5 Hz, 1 H).

^{13}C NMR (62.5 MHz, CDCl$_3$): δ = 152.8, 145.0, 139.6, 133.7, 132.7, 131.1, 130.7, 129.9, 129.3, 128.9, 127.9, 125.2, 119.3, 111.9, 67.5, 56.0, 54.1, 32.7, 31.4, 21.6, 21.3.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{25}H_{28}NO_5S_2$: 486.1403; found: 486.1403.

3h

Yield: 84%; pale-yellow semisolid consisting of two inseparable diastereomers (dr = 1.1:1).

$[\alpha]_D^{25}$ –4.9 (*c* 1.8, CHCl$_3$).

IR (film): 3064, 2974, 2925, 1577, 1462, 1356, 1258, 1172 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.16–8.00 (t, *J* = 6.9 Hz, 2 H), 7.76 (d, *J* = 8.1 Hz, 1 H), 7.70–7.46 (m, 4 H), 7.40–7.26 (m, 2 H), 6.68 (s, 1 H), 6.49 (s, 1 H), 6.44 (s, 1 H), 4.00–3.75 (m, 5 H), 3.53 (dd, *J* = 5.4, 9.9 Hz, 1 H), 3.48–3.10 (m, 2 H), 2.70–2.47 (m, 1 H), 2.44 (s, 3 H), 2.27 (d, *J* = 8.1 Hz, 2 H), 0.99 (d, *J* = 6.9 Hz, 3 H), 0.67 (d, *J* = 6.9 Hz, 3 H).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 152.8, 152.7, 144.9, 144.8, 139.2, 139.0, 133.6, 133.6, 132.5, 132.1, 131.2, 131.1, 130.5, 130.3, 129.8, 129.8, 129.2, 129.2, 128.9, 128.9, 127.8, 127.7, 125.0, 124.9, 119.7, 119.6, 111.6, 111.5, 72.6, 71.4, 55.9, 50.7, 50.4, 38.7, 37.6, 32.2, 31.8, 21.5, 21.2, 21.2, 16.0, 12.9.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{26}H_{29}NO_5S_2Na$: 522.1379; found: 522.1375.

Iodide 4g; Typical Procedure for the Preparation of Iodides 4

To tosylate **3g** (508 mg, 1.152 mmol) in acetone (5 mL), NaI (524.7 mg, 3.500 mmol) was added. The mixture was refluxed for 4 h. The reaction mixture was filtered and the filtrate was dried (MgSO$_4$) and concentrated. Chromatography (EtOAc–hexanes, 4:6) gave **4g** as a pale-yellow semisolid; yield: 430 mg (94%).

IR (film): 3097, 3056, 3019, 3003, 2958, 2929, 2848, 1597, 1475, 1446, 1295, 1270, 1209, 1119, 1099, 1013 cm^{-1}.

^{1}H NMR (300 MHz, CDCl$_3$): δ = 8.06 (d, *J* = 7.5 Hz, 2 H), 7.66 (t, *J* = 7.5 Hz, 1 H), 7.56 (t, *J* = 7.8 Hz, 2 H), 7.23 (dt, *J* = 1.2, 7.6 Hz, 1 H), 7.16 (d, *J* = 7.2 Hz, 1 H), 7.12 (dd, *J* = 1.5, 7.6 Hz, 1 H), 6.94 (dt, *J* = 7.5, 0.9 Hz, 1 H), 3.51 (dd, *J* = 4.8, 12.0 Hz, 1 H), 3.48–3.38 (m, 1 H), 3.19 (dd, *J* = 8.4, 12.3 Hz, 1 H), 3.15–2.96 (m, 2 H), 2.49 (qd, *J* = 6.9, 14.1 Hz, 1 H), 2.07 (qd, *J* = 6.9, 14.1 Hz, 1 H).

^{13}C NMR (75 MHz, CDCl$_3$): δ = 144.6, 139.0, 133.7, 129.3, 128.5, 128.5, 126.1, 124.2, 124.0, 120.9, 52.1, 35.8, 35.4, 2.1.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{17}INOS$: 398.0070; found: 398.0070.

4a

Yield: 91%; yellow solid; mp 138–140 °C.

$[\alpha]_D^{25}$ +25.0 (*c* 0.84, CHCl$_3$).

IR (film): 3060, 2933, 2913, 2856, 1610, 1491, 1446, 1397, 1295, 1213, 1140, 1127 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.06 (dd, *J* = 1.1, 8.4 Hz, 2 H), 7.65 (t, *J* = 7.5 Hz, 1 H), 7.56 (t, *J* = 7.5 Hz, 2 H), 7.04 (d, *J* = 7.8 Hz, 1 H), 6.96 (d, *J* = 0.8 Hz, 1 H), 6.75 (dd, *J* = 1.2, 7.8 Hz, 1 H), 3.50 (dd, *J* = 4.8, 13.0 Hz, 1 H), 3.46–3.37 (m, 1 H), 3.16 (dd, *J* = 8.9, 13.0 Hz, 1 H), 3.13–3.00 (m, 2 H), 2.47 (qd, *J* = 6.8, 14.5 Hz, 1 H), 2.31 (s, 3 H), 2.06 (qd, *J* = 6.7, 14.4 Hz, 1 H).

^{13}C NMR (125 MHz, CDCl$_3$): δ = 144.4, 139.2, 138.5, 133.7, 129.3, 128.6, 126.0, 124.9, 121.8, 120.9, 52.4, 35.7, 35.6, 21.0, 2.1.

Anal. Calcd for $C_{17}H_{18}INOS$: C, 49.64; H, 4.41; N, 3.41. Found: C, 49.44; H, 4.48; N, 3.37.

4b

Yield: 85%; yellow semisolid.

$[\alpha]_D^{25}$ –1.8 (*c* 8.0, CHCl$_3$).

IR (film): 3052, 3027, 2921, 2864, 1610, 1565, 1479, 1270, 1221, 1013 cm^{-1}.

^{1}H NMR (500 MHz, CDCl$_3$): δ = 8.07 (td, *J* = 1.4, 7.1 Hz, 2 H), 7.65 (tt, *J* = 1.3, 7.2 Hz, 1 H), 7.56 (tt, *J* = 1.2, 7.0 Hz, 2 H), 7.46–7.25

(m, 5 H), 7.05 (d, *J* = 9.2 Hz, 1 H), 6.89 (dd, *J* = 2.9, 8.6 Hz, 1 H), 6.81 (d, *J* = 2.8 Hz, 1 H), 5.04 (s, 2 H), 3.50 (dd, *J* = 4.7, 12.9 Hz, 1 H), 3.44–3.30 (m, 1 H), 3.22 (dd, *J* = 8.0, 12.9 Hz, 1 H), 3.10–2.90 (m, 2 H), 2.44 (qd, *J* = 5.9, 11.9 Hz, 1 H), 2.02 (qd, *J* = 6.0, 11.8 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.3, 139.4, 138.0, 137.1, 133.7, 129.4, 128.7, 128.5, 127.9, 127.5, 125.1, 125.1, 114.9, 113.9, 70.5, 52.8, 36.5, 35.7, 2.2.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{23}H_{23}INO_2S$: 504.0489; found: 504.0485.

4c

Yield: 85%; yellow semisolid.

IR (film): 3403, 3110, 2933, 2876, 1524, 1450, 1397, 1389, 1266, 1238, 1201, 1160, 1107, 1046 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.08 (d, *J* = 8.2 Hz, 2 H), 7.69 (t, *J* = 6.9 Hz, 1 H), 7.58 (t, *J* = 7.1 Hz, 2 H), 7.11 (d, *J* = 5.2 Hz, 1 H), 6.82 (d, *J* = 5.3 Hz, 1 H), 3.80–3.60 (m, 1 H), 3.44 (dd, *J* = 4.9, 11.4 Hz, 1 H), 3.32 (td, *J* = 5.2, 9.6 Hz, 1 H), 3.17 (q, *J* = 8.2 Hz, 1 H), 2.65 (dd, *J* = 11.5, 13.0 Hz, 1 H), 2.55 (qd, *J* = 7.6, 12.8 Hz, 1 H), 2.22 (qd, *J* = 8.2, 13.9 Hz, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 142.8, 136.3, 134.2, 129.4, 129.1, 125.3, 121.8, 113.6, 50.0, 38.6, 33.3, 0.3.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{14}H_{15}INOS_2$: 403.9634; found: 403.9632.

4d

Yield: 96%; yellow semisolid.

[α]$_D^{25}$ –27.9 (*c* 7.3, $CHCl_3$).

IR (film): 3056, 2970, 2889, 2770, 1912, 1614, 1495, 1475, 1417, 1234, 1185, 1148, 1033 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.06 (td, *J* = 1.4, 7.3 Hz, 2 H), 7.66 (tt, *J* = 1.2, 7.4 Hz, 1 H), 7.58 (t, *J* = 8.0 Hz, 2 H), 6.67 (s, 1 H), 6.67 (s, 1 H), 5.90 (dd, *J* = 1.5, 6.9 Hz, 2 H), 3.52 (dd, *J* = 4.3, 12.7 Hz, 1 H), 3.36–3.30 (m, 1 H), 3.27 (dd, *J* = 7.6, 12.8 Hz, 1 H), 3.08–3.00 (m, 2 H), 2.42 (qd, *J* = 6.9, 14.0 Hz, 1 H), 1.99 (qd, *J* = 7.3, 13.7 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.5, 142.1, 139.2, 139.0, 133.7, 129.4, 128.6, 116.4, 106.4, 105.9, 100.8, 53.4, 36.4, 35.8, 2.5.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{17}H_{17}INO_3S$: 441.9968; found: 441.9966.

4e

Yield: 83%; pale-yellow semisolid.

IR (film): 3056, 2954, 2925, 2856, 1720, 1524, 1467, 1446, 1234, 1099, 1009 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10 (td, *J* = 1.0, 7.3 Hz, 2 H), 7.73 (tt, *J* = 1.1, 7.5 Hz, 1 H), 7.63 (tt, *J* = 1.7, 8.1 Hz, 2 H), 7.44–7.39 (m, 1 H), 7.24–7.19 (m, 1 H), 7.10–7.04 (m, 2 H), 3.86–3.79 (m, 1 H), 3.69 (s, 3 H), 3.48 (dd, *J* = 5.5, 12.0 Hz, 1 H), 3.25 (td, *J* = 5.1, 9.6 Hz, 1 H), 3.05 (td, *J* = 7.3, 9.4 Hz, 1 H), 2.99 (t, *J* = 11.8 Hz, 1 H), 2.75–2.66 (m, 1 H), 2.44–2.35 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.9, 137.1, 134.5, 133.8, 129.6, 129.0, 125.8, 119.6, 118.6, 116.6, 108.4, 87.1, 51.9, 37.2, 32.5, 27.7, 1.1.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{19}H_{20}IN_2OS$: 451.0336; found: 451.0340.

4f

Yield: 60%; pale-yellow semisolid.

[α]$_D^{25}$ +29.0 (*c* 3.4, $CHCl_3$).

IR (film): 3063, 2922, 2859, 2820, 1571, 1459, 1322, 1268, 1151 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.12 (d, *J* = 7.6 Hz, 2 H), 7.66 (t, *J* = 7.5 Hz, 1 H), 7.57 (t, *J* = 7.6 Hz, 2 H), 6.72 (d, *J* = 1.0 Hz, 1 H), 6.62 (s, 1 H), 3.90 (s, 3 H), 3.60–3.50 (m, 1 H), 3.40–3.30 (m, 2 H), 3.10–3.00 (m, 2 H), 2.48 (qd, *J* = 7.1, 14.1 Hz, 1 H), 2.34 (s, 3 H), 2.03 (qd, *J* = 7.1, 13.7 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 152.8, 139.7, 133.6, 131.1, 130.7, 129.3, 128.9, 125.3, 119.3, 111.9, 56.0, 53.7, 36.9, 35.8, 21.3, 2.8.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{18}H_{21}INO_2S$: 442.0332; found: 442.0333.

4h

Yield: 81%; pale-yellow semisolid consisting of two inseparable diastereoisomers (dr = 1.6:1).

IR (film): 3060, 2962, 2933, 2831, 1573, 1479, 1458, 1442, 1328, 1254, 1189, 1156, 1099, 1013, 1005 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$) (major isomer): δ = 8.20–8.10 (m, 2 H), 7.66 (tt, *J* = 1.2, 7.5 Hz, 1 H), 7.57 (tt, *J* = 1.2, 6.0 Hz, 2 H), 6.71 (s, 2 H), 3.88 (s, 3 H), 3.60 (dd, *J* = 5.7, 14.4 Hz, 1 H), 3.50–3.35 (m, 1 H), 3.20 (dd, *J* = 4.5, 9.9 Hz, 1 H), 3.15–3.00 (m, 2 H), 2.33 (s, 3 H), 2.15–2.00 (m, 1 H), 0.66 (d, *J* = 6.6 Hz, 3 H).

(minor isomer): δ = 8.20–8.10 (m, 2 H), 7.66 (tt, *J* = 1.2, 7.5 Hz, 1 H), 7.57 (tt, *J* = 1.2, 6.0 Hz, 2 H), 6.71 (s, 1 H), 6.56 (s, 1 H), 3.88 (s, 3 H), 3.50–3.35 (m, 2 H), 3.15–3.00 (m, 2 H), 2.51 (dd, *J* = 7.2, 9.9 Hz, 1 H), 2.33 (s, 3 H), 2.27–2.15 (m, 1 H), 1.00 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.9, 152.8, 139.4, 139.3, 133.6, 133.6, 131.2, 130.7, 130.5, 129.3, 129.2, 128.9, 128.8, 125.9, 125.6, 120.3, 119.9, 111.7, 111.6, 55.9, 51.5, 50.7, 42.3, 41.3, 33.1, 33.0, 21.3, 21.3, 19.4, 17.5, 16.8, 12.7.

HRMS: *m/z* [M + Na]$^+$ calcd for $C_{19}H_{22}INO_2SNa$: 478.0308; found: 478.0306.

Cyclobutane 5g; Typical Procedure for the Preparation of Cyclobutanes 5

To iodide **4g** (215 mg, 0.542 mmol) in THF (10 mL) at –78 °C, KH (30% in mineral oil; 108.3 mg, 0.812 mmol) was added. After stirring for 1 h at –78 °C, the reaction mixture was warmed to r.t. and stirred overnight. TLC showed that no starting material remained. The reaction was quenched with H_2O (10 mL) and extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (15 mL), dried ($MgSO_4$), and concentrated. Chromatography (EtOAc–hexanes, 4:6) gave **5g** as a pale-yellow solid; yield: 128 mg (88%); mp 138–141 °C.

[α]$_D^{25}$ –34.8 (*c* 1.5, $CHCl_3$).

IR (film): 3015, 2974, 2954, 2933, 1597, 1565, 1479, 1446, 1250 cm^{-1}.

^{1}H NMR (250 MHz, $CDCl_3$): δ = 8.11 (d, *J* = 7.4 Hz, 2 H), 7.67 (t, *J* = 7.2 Hz, 1 H), 7.55 (t, *J* = 7.2 Hz, 2 H), 7.15 (t, *J* = 7.4 Hz, 1 H), 7.07 (d, *J* = 7.5 Hz, 1 H), 7.03–6.80 (m, 2 H), 4.18 (q, *J* = 8.5 Hz, 1 H), 4.07 (q, *J* = 8.4 Hz, 1 H), 2.65 (qd, *J* = 8.6, 8.6 Hz, 1 H), 2.35 (qd, *J* = 8.4, 8.4 Hz, 1 H), 2.30–1.80 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 142.5, 134.7, 133.6, 129.1, 128.4, 127.8, 125.3, 125.2, 121.7, 54.5, 37.4, 29.5, 23.5.

HRMS: *m/z* [M + H]$^+$ calcd for $C_{16}H_{16}NOS$: 270.0947; found: 270.0949.

5a

Yield: 83%; yellow solid; mp 85–86 °C.

[α]$_D^{25}$ –24.2 (*c* 2.5, $CHCl_3$).

IR (film): 3060, 3032, 2954, 2921, 2856, 1724, 1610, 1565, 1495, 1442, 1405, 1291, 1270, 1205, 1156, 1119, 1099, 1074, 1037 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): δ = 8.13 (dt, *J* = 1.6, 6.9 Hz, 2 H), 7.69 (tt, *J* = 1.5, 7.1 Hz, 1 H), 7.60 (tt, *J* = 1.6, 7.5 Hz, 2 H), 6.94 (s, 1 H), 6.88 (d, *J* = 7.7 Hz, 1 H), 6.77 (dd, *J* = 1.1, 7.7 Hz, 1 H), 4.19 (q, *J* = 8.7 Hz, 1 H), 4.13–4.02 (m, 1 H), 2.77–2.56 (m, 1 H), 2.49–2.34 (m, 1 H), 2.31 (s, 3 H), 2.13–1.91 (m, 2 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 142.2, 137.8, 135.0, 133.7, 129.3, 129.1, 128.3, 126.0, 122.9, 122.1, 54.7, 37.3, 29.6, 23.6, 21.0.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{18}NOS$: 284.1104; found: 284.1105.

5b

Yield: 84%; yellow semisolid.

$[\alpha]_D^{25}$ –42.9 (*c* 0.9, $CHCl_3$).

IR (film): 3060, 3032, 2942, 2852, 1605, 1483, 1262, 1221, 1099, 1033 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.12 (td, *J* = 1.1, 7.1 Hz, 2 H), 7.67 (t, *J* = 7.3 Hz, 1 H), 7.58 (t, *J* = 7.0 Hz, 2 H), 7.45–7.25 (m, 5 H), 7.02 (d, *J* = 8.7 Hz, 1 H), 6.84 (dd, *J* = 2.9, 8.7 Hz, 1 H), 6.62 (d, *J* = 2.9 Hz, 1 H), 5.02 (s, 2 H), 4.25–4.10 (q, *J* = 8.5 Hz, 1 H), 4.10–3.90 (m, 1 H), 2.80–2.55 (m, 1 H), 2.50–2.25 (m, 1 H), 2.15–1.80 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 153.9, 137.3, 136.0, 134.9, 133.7, 129.4, 129.2, 128.5, 127.8, 127.5, 126.3, 126.1, 114.9, 114.8, 70.5, 54.6, 37.9, 29.5, 23.6.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{23}H_{22}NO_2S$: 376.1366; found: 376.1364.

5c

Yield: 58%; yellow semisolid.

IR (film): 3085, 3068, 2958, 2921, 1532, 1450, 1381, 1377, 1242, 1180, 1099, 1050 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.11 (td, *J* = 1.2, 6.1 Hz, 2 H), 7.69 (t, *J* = 7.3 Hz, 1 H), 7.59 (t, *J* = 7.0 Hz, 2 H), 7.16 (d, *J* = 5.4 Hz, 1 H), 6.81 (d, *J* = 5.3 Hz, 1 H), 4.23–4.06 (m, 2 H), 2.80–2.45 (m, 2 H), 2.07 (t, *J* = 8.4 Hz, 1 H), 1.97–1.80 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.9, 134.4, 130.0, 129.6, 129.3, 125.9, 122.9, 116.2, 53.5, 35.8, 30.0, 24.1.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{14}H_{14}NOS_2$: 276.0511; found: 276.0511.

5d

Yield: 64%; yellow semisolid.

$[\alpha]_D^{25}$ +47.5 (*c* 2.2, $CHCl_3$).

IR (film): 3064, 2942, 2884, 2770, 1728, 1617, 1499, 1475, 1426, 1209, 1148, 1103, 1033 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.12 (td, *J* = 1.0, 7.1 Hz, 2 H), 7.68 (tt, *J* = 1.2, 7.4 Hz, 1 H), 7.60 (t, *J* = 8.0 Hz, 2 H), 6.64 (s, 1 H), 6.45 (s, 1 H), 5.89 (dd, *J* = 1.4, 11.0 Hz, 2 H), 4.16 (q, *J* = 8.0 Hz, 1 H), 4.05–3.97 (m, 1 H), 2.65 (qd, *J* = 8.5, 10.5 Hz, 1 H), 2.36 (dqd, *J* = 0.9, 9.5, 11.3 Hz, 1 H), 2.10–1.93 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 147.2, 142.7, 136.9, 134.7, 133.7, 129.3, 129.2, 117.6, 107.6, 106.6, 100.8, 54.8, 37.8, 29.5, 23.5.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{17}H_{16}NO_3S$: 314.0845; found: 314.0848.

5e

Yield: 71%; yellow solid; mp 200–202 °C.

$[\alpha]_D^{25}$ –125.9 (*c* 1.5, $CHCl_3$).

IR (film): 3072, 3052, 2999, 2958, 2913, 1540, 1471, 1438, 1225, 1189, 1099, 1037 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.13 (td, *J* = 1.5, 7.2 Hz, 2 H), 7.70 (tt, *J* = 1.2, 7.5 Hz, 1 H), 7.61 (t, *J* = 8.0 Hz, 2 H), 7.30–7.18 (m, 2 H), 7.10–7.02 (m, 2 H), 4.32–4.25 (m, 1 H), 4.17 (td, *J* = 8.0, 10.2 Hz, 1 H), 3.71 (s, 3 H), 2.65–2.56 (m, 1 H), 2.44 (qd, *J* = 10.5, 10.9 Hz, 1 H), 2.03 (t, *J* = 9.8 Hz, 1 H), 1.88–1.80 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.8, 134.5, 134.1, 134.1, 129.5, 129.3, 126.1, 119.1, 118.7, 115.7, 108.2, 88.4, 54.2, 33.6, 27.6, 27.3, 24.7.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{19}N_2OS$: 323.1213; found: 323.1220.

5f

Yield: 78%; pale-yellow solid; mp 192–194 °C.

$[\alpha]_D^{25}$ –33.3 (*c* 1.4, $CHCl_3$).

IR (film): 3060, 2995, 2966, 2942, 1573, 1471, 1446, 1336, 1217, 1180, 1148, 1091, 1025 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.17 (td, *J* = 1.5, 8.0 Hz, 2 H), 7.66 (tt, *J* = 1.5, 7.5 Hz, 1 H), 7.57 (t, *J* = 2.0, 8.5 Hz, 2 H), 6.63 (d, *J* = 1.5 Hz, 1 H), 6.44 (d, *J* = 1.0 Hz, 1 H), 4.17 (q, *J* = 8.0 Hz, 1 H), 4.10–4.02 (m, 1 H), 3.89 (s, 3 H), 2.66 (qd, *J* = 8.5, 9.0 Hz, 1 H), 2.41 (dqd, *J* = 1.5, 9.0, 12.0 Hz, 1 H), 2.29 (s, 3 H), 2.12–2.04 (m, 1 H), 2.04–1.94 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.0, 135.0, 133.6, 131.2, 129.6, 129.3, 129.0, 125.9, 120.8, 111.0, 56.1, 54.9, 37.6, 29.5, 23.6, 21.2.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{20}NO_2S$: 314.1209; found: 314.1210.

5h

Yield: 96%; pale-yellow solid consisting of two diastereomers (dr = 2.6:1).

IR (film): 3089, 3060, 2938, 2860, 2831, 2827, 1610, 1569, 1462, 1446, 1328, 1266, 1234, 1217, 1180, 1095, 1029, 1013 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 7.5 Hz, 2 H), 8.15 (dd, *J* = 2.0, 7.5 Hz, 2 H), 7.67–7.60 (m, 2 H), 7.60–7.50 (m, 4 H), 6.63 (d, *J* = 1.0 Hz, 1 H), 6.62 (d, *J* = 1.0 Hz, 1 H), 6.42 (s, 1 H), 6.30 (s, 1 H), 4.25–4.17 (m, 1 H), 4.15–4.05 (m, 2 H), 3.88 (s, 3 H), 3.87 (s, 3 H), 3.55–3.47 (m, 1 H), 2.97–2.83 (m, 1 H), 2.62–2.50 (m, 1 H), 2.29 (s, 3 H), 2.27 (s, 3 H), 2.11–2.03 (m, 1 H), 2.03–1.95 (m, 1 H), 1.81 (s, 1 H), 1.75–1.65 (m, 1 H), 1.22 (d, *J* = 7.0 Hz, 3 H), 0.73 (d, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 153.2, 153.0, 134.8, 134.8, 133.5, 133.4, 131.2, 130.1, 130.1, 129.5, 129.4, 129.0, 128.9, 128.9, 126.9, 126.2, 122.8, 121.1, 120.3, 111.3, 110.9, 56.0, 55.9, 55.1, 52.0, 45.3, 41.3, 37.4, 33.1, 32.1, 30.2, 21.2, 21.2, 21.0, 17.7.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{21}NO_2SNa$: 350.1185; found: 350.1190.

6a; Typical Procedure for the Alkylation of Cyclobutane 5g

To a soln of cyclobutane **5g** (181.1 mg, 0.672 mmol) in THF (8.5 mL) at –78 °C, 2.2 M *n*-BuLi in hexanes (458 μL, 1.000 mmol) was added dropwise. After stirring for 45 min, a soln of diphenyl disulfide (234 mg, 1.075 mmol) in THF (3.5 mL) was added dropwise. The mixture was stirred for another 3 h before the reaction was quenched with H_2O (5 mL). The mixture was extracted with EtOAc (3 × 10 mL) and the organic layer was washed with H_2O (10 mL), dried (Na_2SO_4), and concentrated. The crude product was purified by fast flash chromatography (EtOAc–hexanes, 2:8, 4:6), which afforded **6a** as a white solid; yield: 232.3 mg (93%); mp 139–141 °C.

IR (film): 3064, 2991, 2946, 1597, 1569, 1475, 1442, 1266, 1246, 1230, 1205, 1115 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.25 (dd, *J* = 1.5, 7.5 Hz, 2 H), 7.73 (t, *J* = 7.5 Hz, 1 H), 7.61 (dt, *J* = 1.0, 7.5 Hz, 4 H), 7.35 (tt, *J* = 1.6, 7.5 Hz, 1 H), 7.31 (tt, *J* = 7.5, 1.5 Hz, 2 H), 7.16 (dt, *J* = 1.0, 7.5 Hz, 1 H), 7.11 (dd, *J* = 1.0, 7.5 Hz, 1 H), 6.92 (td, *J* = 1.0, 7.5 Hz, 1 H), 6.85 (dd, *J* = 1.0, 7.5 Hz, 1 H), 3.85–3.79 (m, 1 H), 2.88–2.74 (m, 2 H), 2.08–2.00 (m, 1 H), 1.95–1.85 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.8, 135.6, 134.0, 132.8, 130.8, 130.4, 129.2, 128.9, 128.9, 128.3, 128.2, 127.4, 125.7, 122.1, 70.2, 45.0, 31.5, 27.9.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{22}H_{19}NOS_2Na$: 400.0800; found: 400.0798.

6b
Yield: 57%; pale-yellow semisolid.

$[\alpha]_D^{25}$ –80.5 (*c* 1.6, $CHCl_3$).

IR (film): 3060, 2978, 2946, 2852, 1634, 1597, 1564, 1479, 1442, 1262, 1238, 1197 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.13 (d, *J* = 8 Hz, 2 H), 7.69 (t, *J* = 7.5 Hz, 1 H), 7.60 (t, *J* = 8 Hz, 2 H), 7.18 (dt, *J* = 2.0, 7.5 Hz, 2 H), 7.11 (dt, *J* = 2.0, 7.5 Hz, 1 H), 7.05–6.90 (m, 2 H), 5.95–5.80 (m, 1 H), 5.26 (d, *J* = 17.0 Hz, 1 H), 5.20 (d, *J* = 10.0 Hz, 1 H), 3.73 (s, 1 H), 2.87 (dd, *J* = 7.0, 14.5 Hz, 1 H), 2.65–2.59 (m, 2 H), 2.58–2.46 (m, 1 H), 2.06–1.95 (m, 1 H), 1.94–1.83 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.3, 133.7, 133.3, 131.5, 130.5, 128.9, 128.0, 128.0, 127.5, 125.4, 122.0, 120.1, 63.6, 42.3, 39.6, 27.0, 26.4.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{19}H_{19}NOSNa$: 332.1080; found: 332.1083.

6c
Yield: 60%; white solid; mp 84–86 °C.

$[\alpha]_D^{25}$ –68.9 (*c* 1.3, $CHCl_3$).

IR (film): 3448, 3060, 3007, 2950, 1597, 1577, 1479, 1442, 1262, 1238, 1168, 1111, 1095 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 7.5 Hz, 2 H), 7.76 (t, *J* = 7.5 Hz, 1 H), 7.65 (t, *J* = 7.5 Hz, 2 H), 7.44–7.38 (m, 2 H), 7.38–7.33 (m, 3 H), 7.21 (dt, *J* = 1.5, 7.0 Hz, 1 H), 7.13 (d, *J* = 7.5 Hz, 1 H), 7.03 (dd, *J* = 1.5, 7.5 Hz, 1 H), 7.00 (dt, *J* = 1.0, 7.5 Hz, 1 H), 5.14 (d, *J* = 1.0 Hz, 1 H), 4.59 (d, *J* = 1.5 Hz, 1 H), 4.30–4.22 (m, 1 H), 2.40–2.30 (m, 1 H), 1.76–1.62 (m, 2 H), 1.60–1.48 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.4, 138.0, 134.2, 131.9, 130.5, 129.3, 128.5, 128.4, 128.2, 128.1, 127.9, 127.7, 125.7, 122.7, 73.5, 67.7, 37.5, 26.9, 25.5.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{21}NO_2SNa$: 398.1185; found: 398.1183.

6d
Yield: 36%; white semisolid.

$[\alpha]_D^{25}$ +0.9 (*c* 0.2, $CHCl_3$).

IR (film): 3334, 3060, 2999, 2950, 1597, 1475, 1446, 1262, 1242, 1197 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 7.91 (dd, *J* = 1.0, 8.0 Hz, 2 H), 7.58 (t, *J* = 7.5 Hz, 1 H), 7.44 (t, *J* = 7.5 Hz, 2 H), 7.40–7.32 (m, 5 H), 7.25–7.18 (m, 1 H), 7.13 (d, *J* = 8.0 Hz, 1 H), 6.95 (d, *J* = 4.0 Hz, 2 H), 5.43 (d, *J* = 7.0 Hz, 1 H), 3.72 (dd, *J* = 7.0, 9.0 Hz, 1 H), 3.17 (d, *J* = 7.0 Hz, 1 H), 2.53–2.42 (m, 1 H), 2.28–2.15 (m, 2 H), 2.01–1.90 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.8, 139.4, 134.9, 133.3, 130.4, 128.5, 128.5, 128.3, 128.1, 127.7, 127.4, 127.2, 125.4, 122.3, 76.0, 73.3, 43.1, 25.4, 24.3.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{23}H_{21}NO_2SNa$: 398.1185; found: 398.1187.

6e
Yield: 45%; white solid; mp 165–167 °C.

IR (film): 3473, 3452, 3064, 2987, 2950, 2938, 2921, 1593, 1479, 1450, 1267, 1246, 1180, 1115, 1091 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.18 (dd, *J* = 1.0, 8.0 Hz, 2 H), 7.72 (tt, *J* = 1.0, 8.0 Hz, 1 H), 7.63 (t, *J* = 8.0 Hz, 2 H), 7.20 (dt, *J* = 1.0, 7.5 Hz, 1 H), 7.12 (dd, *J* = 1.0, 7.5 Hz, 1 H), 7.06–6.92 (m, 2 H), 4.15 (t, *J* = 2.0 Hz, 1 H), 4.09 (t, *J* = 8.0 Hz, 1 H), 3.93 (td, *J* = 2.0, 11.0 Hz, 1 H), 2.55–2.38 (m, 2 H), 2.10–2.00 (m, 1 H), 1.90–1.76 (m, 2 H), 1.76–1.65 (m, 1 H), 1.11 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.6, 134.0, 132.4, 130.5, 129.2, 128.1, 128.0, 127.8, 125.6, 122.6, 73.1, 68.3, 37.8, 27.4, 25.4, 23.9, 11.0.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{22}NO_2S$: 328.1366; found: 328.1369.

6f
Yield: 36%; pale-yellow semisolid.

IR (film): 3340, 3064, 2962, 2933, 2872, 1597, 1573, 1483, 1446, 1270, 1238, 1201, 1172, 1111, 1013 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.18 (d, *J* = 7.5 Hz, 2 H), 7.68 (t, *J* = 7.5 Hz, 1 H), 7.59 (t, *J* = 7.5 Hz, 2 H), 7.19 (t, *J* = 7.0 Hz, 1 H), 7.09 (d, *J* = 7.5 Hz, 1 H), 7.02 (d, *J* = 7.0 Hz, 1 H), 6.95 (t, *J* = 7.5 Hz, 1 H), 4.02 (t, *J* = 8.0 Hz, 1 H), 3.80 (t, *J* = 10.0 Hz, 1 H), 3.23 (d, *J* = 10.5 Hz, 1 H), 2.60–2.34 (m, 2 H), 2.32–2.20 (m, 1 H), 2.10–1.90 (m, 1 H), 1.70–1.55 (m, 1 H), 1.50–1.30 (m, 1 H), 1.00 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.0, 135.3, 133.8, 130.5, 129.0, 128.3, 127.7, 127.6, 125.2, 122.5, 79.5, 71.3, 43.3, 25.8, 25.3, 11.7.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{22}NO_2S$: 328.1366; found: 328.1368.

6g, Isomer A
Yield: 51%; pale-yellow solid; mp 142–144 °C.

$[\alpha]_D^{25}$ –17.2 (*c* 2.7, $CHCl_3$).

IR (film): 3477, 3064, 2958, 2925, 2864, 1475, 1446, 1262, 1176, 1111, 1095, 1013 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 8.17 (dd, *J* = 1.0, 8.5 Hz, 2 H), 7.72 (tt, *J* = 1.0, 7.5 Hz, 1 H), 7.63 (t, *J* = 7.5 Hz, 2 H), 7.20 (dd, *J* = 1.0, 7.5 Hz, 1 H), 7.19 (td, *J* = 1.5, 7.5 Hz, 1 H), 7.00 (dd, *J* = 1.5, 7.5 Hz, 1 H), 6.96 (dt, *J* = 1.0, 7.5 Hz, 1 H), 4.14–4.12 (t, *J* = 7.0 Hz, 1 H), 4.11–4.07 (m, 1 H), 4.03 (td, *J* = 2.0, 10.5 Hz, 1 H), 2.54–2.38 (m, 2 H), 2.04 (qd, *J* = 5.5, 11.5 Hz, 1 H), 1.88–1.71 (m, 3 H), 1.59–1.51 (m, 1 H), 1.45–1.34 (m, 1 H), 0.96 (t, *J* = 7.5 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.6, 134.0, 132.4, 130.5, 129.2, 128.2, 128.1, 127.8, 125.6, 122.6, 71.4, 68.3, 37.8, 33.0, 27.4, 25.4, 19.6, 14.0.

HRMS: *m*/*z* $[M + Na]^+$ calcd for $C_{20}H_{23}NO_2SNa$: 364.1342; found: 364.1340.

6g, Isomer B
Yield: 35%; pale-yellow solid; mp 137–139 °C.

$[\alpha]_D^{25}$ –35.1 (*c* 1.7, $CHCl_3$).

IR (film): 3473, 3060, 2958, 2868, 1479, 1446, 1262, 1242, 1197, 1168, 1111, 1091 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.19 (dd, *J* = 1.0, 8.0 Hz, 2 H), 7.69 (tt, *J* = 1.0, 7.5 Hz, 1 H), 7.61 (t, *J* = 7.5 Hz, 2 H), 7.20 (td, *J* = 1.5, 7.5 Hz, 1 H), 7.09 (dd, *J* = 1.0, 7.5 Hz, 1 H), 7.02 (dd, *J* = 1.5, 7.5 Hz, 1 H), 6.97 (td, *J* = 1.5, 7.5 Hz, 1 H), 4.02 (t, *J* = 8.0 Hz, 1 H), 3.90 (td, *J* = 1.5, 10.5 Hz, 1 H), 3.22 (d, *J* = 11.0 Hz, 1 H), 2.52–2.44 (m, 1 H), 2.43–2.35 (m, 1 H), 2.31–2.23 (m, 1 H), 1.98 (dtd, *J* = 1.0, 8.0, 12.5 Hz, 1 H), 1.72–1.56 (m, 2 H), 1.34–1.24 (m, 2 H), 0.88 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.1, 135.4, 133.8, 130.6, 129.0, 128.4, 127.8, 127.6, 125.3, 122.5, 77.6, 71.4, 43.4, 34.4, 25.8, 25.7, 20.1, 13.8.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{20}H_{23}NO_2SNa$: 364.1342; found: 364.1345.

6h

Yield: 100%; white solid; mp 209–211 °C.

$[\alpha]_D^{25}$ –181.8 (*c* 2.5, $CHCl_3$).

IR (film): 3424, 3085, 3056, 3011, 2974, 2946, 1822, 1601, 1573, 1495, 1483, 1446, 1389, 1266, 1242, 1168, 1111, 1090, 1025, 993 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.68 (d, *J* = 7.5 Hz, 2 H), 7.60 (t, *J* = 7.5 Hz, 1 H), 7.48 (s, 2 H), 7.40–7.32 (m, 5 H), 7.32–7.17 (m, 4 H), 7.15–6.98 (m, 5 H), 5.68 (s, 1 H), 4.24 (t, *J* = 9.0 Hz, 1 H), 2.83 (td, *J* = 9.5, 13.5 Hz, 1 H), 2.63 (ddd, *J* = 4.5, 10.0, 13.5 Hz, 1 H), 2.24 (dq, *J* = 10.0, 10.0 Hz, 1 H), 1.69 (dq, *J* = 4.5, 11.0 Hz, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.3, 142.4, 141.6, 134.5, 133.4, 131.0, 129.3, 128.6, 128.5, 128.3, 127.8, 127.4, 127.2, 126.7, 125.3, 122.7, 81.0, 80.1, 42.3, 27.6, 25.2.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{25}NO_2SNa$: 474.1498; found: 474.1498.

6i

To a soln of cyclobutane **5g** (29.2 mg, 0.108 mmol) in THF (2 mL) at –78 °C, 2.2 M *n*-BuLi in hexanes (64 μL, 0.141 mmol) was added dropwise. After 1 h, Ph_2PCl (36.6 mg, 29.8 μL, 0.163 mmol) was added dropwise. The mixture was stirred for another 3 h before H_2O_2 (500 μL) was added. The reaction was stirred for another 5 min before it was quenched with H_2O (2 mL). The mixture was extracted with EtOAc (3 × 2 mL). The organic layers were washed with brine (5 mL), dried (Na_2SO_4), and concentrated. Chromatography (EtOAc–hexanes, 2:8) gave **6i** as a white solid; yield: 43.5 mg (86%); mp 243–245 °C.

$[\alpha]_D^{25}$ –6.1 (*c* 5.5, $CHCl_3$).

IR (film): 3060, 2978, 2856, 2071, 1965, 1908, 1818, 1601, 1479, 1438, 1266, 1242, 1189, 1115, 1091, 1009 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.98 (d, *J* = 7.5 Hz, 1 H), 7.95 (d, *J* = 7.5 Hz, 1 H), 7.65 (d, *J* = 7.5 Hz, 1 H), 7.62 (d, *J* = 7.5 Hz, 1 H), 7.52–7.48 (m, 5 H), 7.42–7.32 (m, 6 H), 7.24 (dt, *J* = 1.0, 7.5 Hz, 1 H), 7.15 (d, *J* = 7.5 Hz, 1 H), 6.88 (t, *J* = 7.5 Hz, 1 H), 6.73 (d, *J* = 6.5 Hz, 1 H), 4.29 (td, *J* = 9.0, 13.5 Hz, 1 H), 3.39 (m, 1 H), 2.65 (dq, *J* = 9.5, 9.5 Hz, 1 H), 2.35–2.25 (m, 1 H), 2.00–2.15 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.0, 134.1, 133.6, 133.1, 133.0, 132.6, 132.6, 132.2, 132.2, 132.0, 132.0, 131.9, 131.1, 130.3, 129.0, 129.0, 128.6, 128.3, 128.2, 128.2, 128.1, 127.2, 126.6, 125.6, 122.5, 70.7, 70.3, 42.0, 26.7, 26.6, 25.1.

^{31}P NMR (101.25 MHz, $CDCl_3$): δ = 32.3.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{24}NO_2PSNa$: 492.1158; found: 492.1154.

6j

Yield: 50%; white solid; mp 127–129 °C.

$[\alpha]_D^{25}$ –29.7 (*c* 1.1, $CHCl_3$).

IR (film): 3064, 2929, 2852, 1483, 1442, 1270, 1246, 1189, 1152, 1115, 1013 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.19 (d, *J* = 8.0 Hz, 2 H), 7.74 (t, *J* = 7.5 Hz, 1 H), 7.65 (t, *J* = 8.0 Hz, 2 H), 7.23 (dt, *J* = 2.0, 7.5 Hz, 1 H), 7.11 (d, *J* = 7.5 Hz, 1 H), 7.02 (dd, *J* = 1.0, 7.5 Hz, 1 H), 6.95 (dt, *J* = 1.0, 7.5 Hz, 1 H), 4.53 (q, *J* = 9.5 Hz, 1 H), 3.28–3.12 (qd, *J* = 10.5, 11.0 Hz, 1 H), 2.87–2.72 (qd, *J* = 10.5, 10.5 Hz, 1 H), 2.39–2.26 (q, *J* = 9.5 Hz, 1 H), 2.20–0.80 (m, 22 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.3, 135.9, 134.2, 130.2, 129.1, 128.9, 127.2, 126.7, 125.0, 122.5, 71.5, 71.2, 41.0, 38.9, 38.4, 36.6, 36.1, 28.4, 28.3, 27.6, 27.6, 27.4, 27.3, 26.9, 26.9, 26.8, 26.8, 26.5, 26.5, 26.4, 26.3, 26.2, 26.1, 26.0, 25.9, 25.5.

^{31}P NMR (101.25 MHz, $CDCl_3$): δ = 54.1.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{36}NO_2PSNa$: 504.2097; found: 504.2096.

7 and 8

To starting material **6a** (360 mg, 0.966 mmol) in $CHCl_3$ (20 mL) at r.t., PTSA (9.2 mg, 0.0483 mmol) was added. After 15 min, the reaction was quenched with H_2O (10 mL) and sat. $NaHCO_3$ soln (5 mL). The mixture was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were washed with brine (15 mL), dried (Na_2SO_4), and concentrated. Chromatography (EtOAc–hexanes, 2:8) gave **7** as a yellow semisolid [yield: 123.7 mg (34%)] and **8** as a yellow semisolid [yield: 128.7 mg (36%)].

7

$[\alpha]_D^{25}$ –200.4 (*c* 0.5, $CHCl_3$).

IR (film): 3289, 3056, 2987, 2942, 2361, 2333, 1601, 1581, 1471, 1454, 1438, 1225, 1176, 1095, 1058 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.78 (td, *J* = 1.5, 7.5 Hz, 2 H), 7.58–7.53 (m, 2 H), 7.51 (t, *J* = 8.0 Hz, 2 H), 7.47 (t, *J* = 7.0 Hz, 1 H), 7.16–7.08 (m, 3 H), 6.84 (d, *J* = 7.5 Hz, 1 H), 6.76 (t, *J* = 7.5 Hz, 1 H), 6.66 (t, *J* = 7.5 Hz, 1 H), 6.52 (d, *J* = 8.0 Hz, 1 H), 3.98 (dd, *J* = 6.3, 8.3 Hz, 1 H), 2.87–2.67 (m, 3 H), 2.15–2.06 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 145.1, 142.9, 134.4, 132.7, 130.8, 130.7, 129.3, 128.5, 128.3, 127.1, 126.3, 123.8, 121.8, 112.8, 80.2, 49.5, 36.8, 25.8.

HRMS: *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{19}NOS_2Na$: 400.0800; found: 400.0800.

8

IR (film): 3346, 3183, 3060, 2958, 2917, 2835, 1585, 1479, 1475, 1442, 1291, 1262, 1242, 1225, 1091, 1062 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.80–7.73 (m, 2 H), 7.67 (s, 1 H), 7.52 (dd, *J* = 1.0, 7.5 Hz, 1 H), 7.35 (dd, *J* = 3.0, 3.0 Hz, 3 H), 7.27–7.20 (m, 5 H), 7.11 (dd, *J* = 2.5, 6.0 Hz, 2 H), 7.04 (t, *J* = 7.5 Hz, 1 H), 2.85–2.75 (m, 2 H), 2.53–2.44 (m, 2 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 144.2, 143.1, 138.0, 131.8, 131.2, 129.3, 129.0, 129.0, 128.8, 128.6, 127.4, 125.3, 124.9, 122.8, 117.9, 30.2, 29.2.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{22}H_{20}NOS_2$: 378.0980; found: 378.0981.

Sulfoxide and Sulfone of 7

To starting material **7** (9.6 mg, 0.0254 mmol) in CH_2Cl_2 (1.2 mL) at –30 °C, 50–60% MCPBA (16.8 mg, 0.0534 mmol) was added dropwise. The reaction was stirred for another 1 h before H_2O (1 mL) was added. The mixture was extracted with CH_2Cl_2 (3 × 2 mL). The combined organic layers were washed with brine (5 mL), dried

(Na_2SO_4), and concentrated. Chromatography (EtOAc–hexanes, 2:8, 3:7, 4:6) gave a yellow, solid sulfone [yield: 3.7 mg (36%)] and a sulfoxide [yield: 5.2 mg (52%)].

Sulfone of 7
Mp 100–102 °C.

IR (film): 3387, 3064, 2999, 2950, 1601, 1577, 1462, 1454, 1442, 1303, 1225, 1148, 1107, 927 cm^{-1}.

^1H NMR (250 MHz, $CDCl_3$): $\delta = 8.07$ (d, $J = 7.1$ Hz, 2 H), 7.69 (dd, $J = 2.0, 7.7$ Hz, 2 H), 7.52–7.40 (m, 3 H), 7.35–7.25 (m, 3 H), 6.69 (dd, $J = 1.7, 6.3$ Hz, 1 H), 6.54 (dt, $J = 1.6, 6.8$ Hz, 2 H), 6.47 (d, $J = 8.7$ Hz, 1 H), 4.16 (t, $J = 7.9$ Hz, 1 H), 3.68 (td, $J = 10.3, 12.9$ Hz, 1 H), 2.80–2.50 (m, 2 H), 2.30–2.00 (m, 1 H).

^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta = 145.5$, 141.9, 134.1, 133.9, 131.2, 130.6, 130.2, 129.2, 128.5, 127.1, 126.2, 123.2, 122.4, 113.8, 86.1, 45.4, 27.4, 24.5.

HRMS: m/z $[M + Na]^+$ calcd for $C_{22}H_{19}NO_3S_2Na$: 432.0699; found: 432.0700.

Sulfoxide of 7
IR (film): 3052, 2991, 2938, 2852, 1597, 1471, 1458, 1438, 1221, 1099, 1086, 1042 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): $\delta = 7.80$ (dd, $J = 1.0, 8.0$ Hz, 2 H), 7.76 (dd, $J = 1.5, 7.0$ Hz, 2 H), 7.57 (t, $J = 7.5$ Hz, 2 H), 7.52 (t, $J = 7.5$ Hz, 1 H), 7.18–7.10 (m, 3 H), 6.66 (t, $J = 7.5$ Hz, 1 H), 6.54 (t, $J = 8.5$ Hz, 2 H), 6.50 (dt, $J = 1.0, 7.0$ Hz, 1 H), 3.99 (t, $J = 8.0$ Hz, 1 H), 3.45 (td, $J = 10.0, 13.0$ Hz, 1 H), 2.71 (ddd, $J = 3.0, 8.5, 12.0$ Hz, 1 H), 2.63–2.53 (q, $J = 11.0$ Hz, 1 H), 2.23–2.13 (m, 1 H).

^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 131.6$, 131.0, 129.5, 128.0, 127.0, 126.3, 125.8, 123.5, 122.4, 113.2, 88.4, 40.6, 27.4, 25.2.

HRMS: m/z $[M + Na]^+$ calcd for $C_{22}H_{19}NO_2S_2Na$: 416.0749; found: 416.0753.

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(9) Crystallographic data (excluding structure factors) for some structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 658446 (**5e**), 658447 (**5g**), 672249 (**6a**), 658448 (**6c**), 658567 (**6e**), 658449 (**7**), and 658450 (sulfone of **7**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [Fax: +44(1223)336033; E-mail: deposit@ccdc.cam.ac.uk].