One-pot synthesis of benzothiazolines and napthathiazolines *via* cascade *ortho*-lithiation, cyclisation and elimination of *N*-arylsulfonyl lactams†‡

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ortho-Lithiation of cyclic aryl sulfonamides in the presence of phosphoryl chloride provides a very simple entry to fused polycyclic sultams (benzothiazolines and naphthathiazolines).

Introduction

Sulfonamides have found many important applications in organic synthesis including as protecting groups,[1] chiral auxiliaries[2] and directed metallation groups (DMGs).[3] In addition, the sulfonamide functionality is present in many biologically active compounds where it can function as a stable amide equivalent.[4,5] In particular, cyclic sulfonamides (sultams), of which there are many variations, are well documented in the literature. For example 3,5-diamino-1,2,6-thiadiazine-1,1-dioxide derivatives **1** possess anti-parasitic activity,[4] 1,2-benzisothiazolinone-1,1-dioxides **2** (saccharin derivatives) exhibit, among other properties, human leukocyte elastase inhibitory[6] and anti-fungal[5] activity and 1,2-benzisothiazine-1,1-dioxides such as the oxicams, *e.g.* piroxicam **3** are known for their anti-inflammatory properties,[7] Fig. 1.

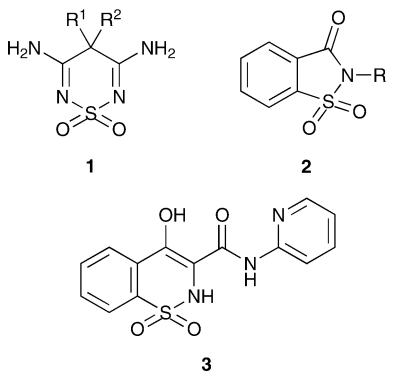
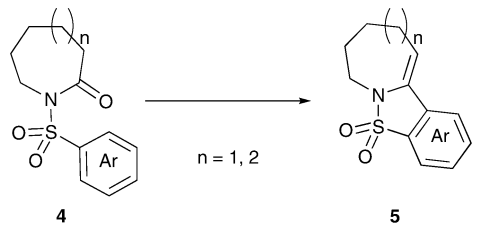


Fig. 1 Selected examples of cyclic sulfonamides.

Reflecting these diverse roles, there have been many methods described for the synthesis of sultams. These include Diels–Alder cycloadditions,[8] radical cyclisations,[9] intramolecular Heck couplings,[10] ring closing metathasis,[11] aziridination of iminoiodinanes[12] and *N*-chloramine sulfonamides,[13] *ortho*-lithiation (DMG) strategies[14] and lithiation of *o*-tolyl sulfonamides.[15,16]

Surprisingly, there have only been a limited number of methods describing the synthesis of fused amido sultams.[15] In this paper we report the synthesis of fused benzo- and napthathiazoline-1,1-dioxide heterocyclic ring systems **5** *via* a sequence involving *ortho*-lithiation–cyclisation–elimination reactions of readily prepared *N*-arylsulfonyl lactams **4**, Fig. 2

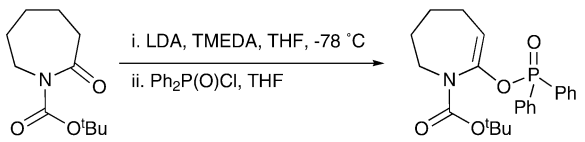


4 5

Fig. 2

Results and discussion

As part of a program aimed at exploring new electrophilic partners for cross coupling reactions,[17] we have developed an efficient protocol for the preparation of phosphonites, *e.g.* **7**, involving treatment of a THF solution of *N*-Boc caprolactam **6** and TMEDA with LDA and trapping of the resultant anion with diphenylphosphonic chloride, Scheme 1.



6 7

Scheme 1

However, subjecting the *N*-tosyl caprolactam **4a** to these conditions afforded a new non-phosphorus containing product (44%) accompanied by smaller amounts of the desired phosphonite **8a** (15%) and recovered starting material, Scheme 2. Analysis of the ^{1}H NMR spectra indicated only three aromatic protons (δ (ppm) = 7.29, d; 7.41, s; 7.64, d) together with a new olefinic signal at δ = 5.78 ppm (t, J = 7 Hz). Moreover, this last signal showed NOESY and HMBC correlations with the proton signal at δ = 7.41 ppm and a quaternary carbon signal at δ = 132.4 ppm respectively. Combined with a molecular ion at MH$^+$ of m/z = 250.0896, this suggested the unusual fused sultam **5a**. Ultimate confirmation of

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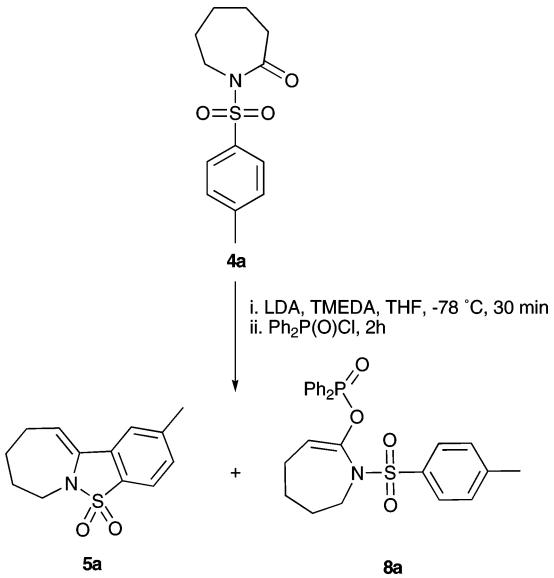
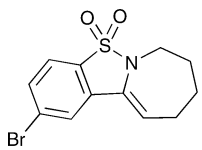
† Electronic supplementary information (ESI) available: Characterisation data for compounds **4b–4h**, **5d**, **5e**, **5g**, **8d**, **8e** and **8g**. See DOI: 10.1039/b708967h

‡ CCDC reference number 650785. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b708967h



Scheme 2

this structure was subsequently realised when the bromo derivative **5f**, which showed similar NMR correlations, provided crystals suitable for an X-ray structure determination, Fig. 3.‡



5f

Surprisingly, the Cambridge Crystallographic Database (Ver. 5.28, Nov. 2006) does not contain any structures of fused sultams. However, the geometrical parameters of **5f** are close to the expected values. The 7-membered ring is disordered over two positions. Within the crystal, **5f** stacks to form slightly bent columns with antiparallel arrangement of the molecules. Aromatic rings of adjacent molecules are partially overlapped with the shortest interatomic distance C7 · · · C7′ (1 − *x*, *y*, 0.5 − *z*) being 3.192 Å. The molecules are also linked together by a 3-D network of CH · · · O and CH · · · Br interactions.

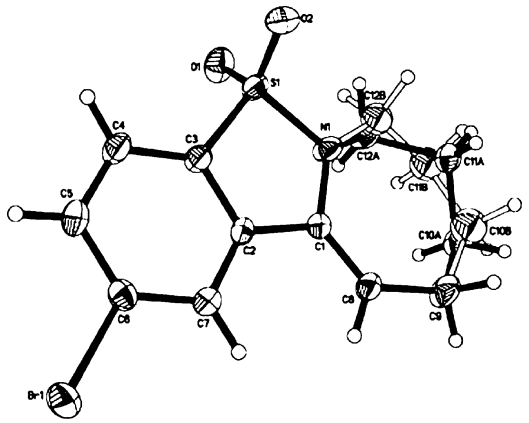
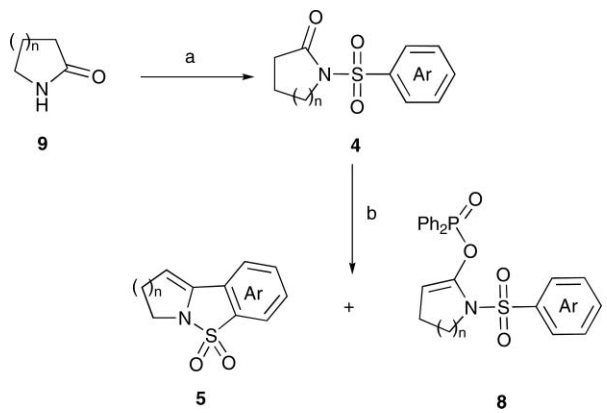


Fig. 3 X-Ray molecular structure of **5f** (50% displacement ellipsoids).

The scope and limitations of this process were then examined varying both the lactam ring and sulfonyl group, Scheme 3 and Table 1. Each substrate **4** was prepared in variable but unoptimised yields (33–80%) by metallation of the parent lactam with *n*-BuLi and subsequent reaction with the appropriate sulfonyl chloride. Cyclisation of both *N*-tosyl pyrrolidinone **4b** and *N*-tosyl piperidinone **4c** were unsuccessful, entries 2 and 3. With the exception of 3-nitrophenylsulfonamide **4h**, entry 12, which failed to provide any products, all the other sulfonamide analogues



Scheme 3 *Reagents and conditions*: (a) i. *n*-BuLi, THF; ii. $ArSO_2Cl$; (b) i. LDA, TMEDA, THF, −78 °C, 30 min; ii. $Ph_2P(O)Cl$, 2 h.

Table 1 Formation of cyclic sultams **5** by sequential *ortho*-lithiation, cyclisation and elimination

Entry	*n*	Ar	Yield **5** (%)	Yield **8** (%)	Recovered **4** (%)
1	3	4-Me–C_6H_4 **4a**	41	15	0–50
2	1	4-Me-C_6H_4 **4b**	0	0	43
3	2	4-Me-C_6H_4 **4c**	Trace	30	32
4	4	4-Me-C_6H_4 **4d**	18	24	0–16
5[a]	3	4-Me-C_6H_4 **4a**	44	14	0
6[b]	3	4-Me-C_6H_4 **4a**	11	0	15
7[c]	3	4-Me-C_6H_4 **4a**	0	0	100
8[d]	3	4-Me-C_6H_4 **4a**	0	73	0
9	3	1-Napthyl **4e**	26	17	41
10	3	4-Br-C_6H_4 **4f**	46	0	0
11	3	3-MeO-C_6H_4 **4g**	32[e]	23	0
12	3	4-NO_2–C_6H_4 **4h**	0	0	50–100

[a] No TMEDA present. [b] $Ph_2P(O)Cl$ replaced with TMSCl. [c] No $Ph_2P(O)Cl$ present. [d] LDA–TMEDA replaced with NaHMDS. [e] Mixture of two regioisomeric sultams (4 : 1).

examined followed a similar profile, providing mainly the fused sultam accompanied by smaller quantities of the phosphonite and recovered starting materials, with the exception of the 8-membered ring which gave a higher proportion of the phosphonite, entry 4. Attempts to enhance the yields through the use of alternative bases (BuLi, LHMDS) and other additives (DMPU, HMPA) and higher reaction temperatures provided no significant benefit.

The formation of the sultam can be explained when the powerful directing metallating properties of the sulfonamide group are taken into account.[3] We speculate that the reaction proceeds *via* initial *ortho*-lithiation of the aryl sulfonamide. The resulting carbanion then attacks the lactam carbonyl group activated by co-ordination to the phosphorus centre. The presence of the phosphorus reagent is essential, as experiments undertaken in the absence of phosphoryl chloride and simply quenched with water, entry 7, afforded only recovered starting sulfonamide **4a**. Replacement of phosphoryl chloride by trimethylsilyl chloride also afforded the desired sultam **5a** although in greatly reduced yield of 11%, entry 6.

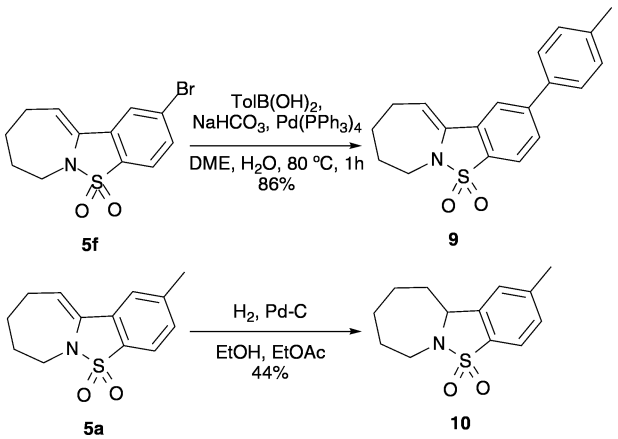
The competing formation of the phosphinite can arise either from direct metallation or from the initial aryl carbanion functioning as a base to generate the enolate through either lateral or intermolecular proton abstraction.[18] The latter is favoured as increasing the concentration of the reaction leads to higher levels of phosphinite formation (**4a** 0.08 M, **5a** : **8a** 3 : 1; 0.16 M, 1 : 1; 0.32 M, 1 : 1.6). The alternative possibility of initial enolate formation cannot be ruled out although metallation with NaHMDS, which does not lead to *ortho*-metallation, affords only phosphinite and no sultam, entry 8. Moreover, isolating a pure sample of the phosphinite and re-subjecting this to the deprotonation conditions, either in the presence or absence of diphenylphosphoryl chloride, failed to provide any evidence for sultam formation and led to efficient recovery of the phosphinite. The failure of smaller lactam rings to undergo sultam formation is attributed to the increased level of ring strain in the transition state leading to preferential lateral metallation and phosphinite formation.[19]

Conclusion

In conclusion, *ortho*-lithiation of cyclic aryl sulfonamides in the presence of phosphoryl chloride provides a very simple entry to fused polycyclic sultams that are not easy to prepare by more standard methods. Moreover, further functionalisation of these products is straightforward. For example, Suzuki–Miyaura reaction of bromosultam **5f** affords biphenyl derivative **9** in excellent yield (86%) whilst conversion of the methyl analogue **5a** to the saturated sultam **10** is easily achieved by simple hydrogenation, Scheme 4.

Experimental

All reactions were carried out under an argon atmosphere unless otherwise stated. Solvents were purified following established protocols. Petrol refers to petroleum spirit boiling in the 40–60 °C range. Ether refers to diethyl ether. Commercially available reagents were used as received unless otherwise stated. Flash column chromatography was performed according to the method of Still *et al.* using 200–400 mesh silica gel.[20] Yields refer to isolated yields of products of greater than 95% purity as determined by



Scheme 4

^{1}H and ^{13}C NMR spectroscopy or elemental analysis (Durham University Microanalytical Laboratory).

Melting points were determined using Gallenkamp melting point apparatus and are uncorrected. Infrared spectra were recorded as thin films between KBr plates (liquids) or using an ATR attachment (golden gate apparatus) on a Perkin-Elmer FT-IR 1600 spectrometer. Unless otherwise stated ^{1}H NMR spectra were recorded in $CDCl_3$ on either a Varian Mercury 200, Varian Unity-300, Mercury-400 or Varian Inova-500 and are reported as follows: chemical shift δ (ppm) (number of protons, multiplicity, coupling constant J (Hz), assignment). Residual protic solvent $CHCl_3$ (δ_H = 7.26 ppm) was used as the internal reference. ^{13}C NMR spectra were recorded at 101 MHz or 126 MHz on a Mercury-400 or Varian Inova-500 respectively, using the central resonance of $CDCl_3$ (δ_C = 77.0 ppm) as the internal reference. All chemical shifts are quoted in parts per million relative to tetramethylsilane (δ_H = 0.00 ppm) and coupling constants are given in Hertz to the nearest Hz. All ^{13}C spectra were proton decoupled. Assignment of spectra was carried out using DEPT, COSY, HSQC, HMBC and NOESY experiments. Low-resolution electrospray mass spectra (ES) were obtained on a Micromass LCT mass spectrometer or a Thermo-Finnigan LTQ. High-resolution mass spectra (ES) were obtained on a Thermo-Finnigan LTQFT mass spectrometer in Durham. Characterisation data for compounds **4b–4h**, **5d**, **5e**, **5g**, **8d**, **8e** and **8g** can be found in the ESI.†

General method for *N*-alkylsulfonyl protection of lactams

To a cold (0 °C) solution of lactam (0.34 M, 1.0 eq.) in dry THF was added a solution of *n*-BuLi (1.6 M, 1.1 eq.) *via* a syringe and the reaction mixture was stirred at 0 °C for 1 h (white precipitate (salt) forms). To this was added a cold (0 °C) solution of arylsulfonyl chloride (1.0 M, 1.3 eq.) in dry THF *via* cannula. The reaction mixture was stirred at 0 °C and followed by TLC or LCMS until all the starting material was consumed. The reaction was warmed to room temperature and concentrated *in vacuo*, the crude material was taken into DCM, washed with water (3×), dried over $MgSO_4$ and concentrated under reduced pressure.

N-[(4′-Methylphenyl)sulfonyl]-2-oxoazepane 4a

Purification by flash chromatography (1: 15%, 2: 25%, 3: 35% ethyl acetate–pet. ether) afforded the desired product as a white

solid (1.10 g, 4.12 mmol, 46%). Mp 117–120 °C. Found; C, 58.11; H, 6.28; N, 4.92%; calc. for $C_{13}H_{17}NO_3S$; C, 58.40; H, 6.41; N, 5.24%. ν_{max} (KBr) 2941, 2861, 1697 (NC=O), 1597, 1353 (SO_2), 1168 (SO_2), 1123, 1088, 813, 549, 535 cm^{-1}. δ_H (500 MHz, $CDCl_3$) 1.64–1.76 (4H, m, 4-H_2, 5-H_2), 1.81 (2H, m, 6-H_2), 2.41 (3H, s, 4′-CH_3), 2.53 (2H, t, $J = 6$ Hz, 3-H_2), 4.01 (2H, t, $J = 5$ Hz, 7-H_2), 7.29 (2H, d, $J = 9$ Hz, 3′-*H*, 5′-*H*), 7.87 (2H, d, $J = 9$ Hz, 2′-*H*, 6′-*H*). δ_C (125 MHz, $CDCl_3$) 21.9 (4′-*C*H_3), 23.2 (*C*-4), 29.4 (C5), 29.6 (*C*-6), 39.0 (*C*-3), 46.7 (*C*-7), 128.8 (*C*-2′), 129.5 (*C*-3′), 136.8 (*C*-4′), 144.7 (*C*-1′), 175.1 (*C*-2). *m/z* (ES^+) 268.0 (MH^+).

General method for cyclisation of *N*-alkylsulfonyl protected lactams

To a cold solution (0.08 M, −78 °C) of *N*-sulfonyl lactam (1 eq.) and *N*,*N*,*N*′,*N*′-tetramethyl-1,2-ethylenediamine (TMEDA, 1.3 eq.) in dry THF was added a cold solution of lithium diisopropylamide (LDA, 1.3 eq.) *via* cannula. The resulting reaction mixture was stirred at −78 °C for 2 h after which time a cold solution (0.2 M, −78 °C) of diphenylphosphonic chloride (1.2 eq.) in dry THF was added *via* cannula. The reaction mixture was stirred at −78 °C for 1 h then warmed to room temperature and quenched with NH_4Cl (aq.). The mixture was concentrated *in vacuo* and the aqueous layer was extracted with ethyl acetate. The organic phase was washed with $NaHCO_3$ (aq.) then brine, dried over $MgSO_4$ and concentrated *in vacuo* affording crude material.

1,2,3,4-Tetrahydro-7-methylazepino[1,2-b][1,2]benzothiazole-10,10-dioxide 5a

Purification by flash chromatography (15% ethyl acetate–dichloromethane) afforded the title compound as a white solid (0.19 g, 0.76 mmol, 41%) and phosphonite (0.13 g, 0.28 mmol, 15%). Mp 112–114 °C. ν_{max} (KBr) 2936, 1666, 1610, 1464, 1305, 1178, 1146, 1061, 941 cm^{-1}. δ_H (500 MHz, $CDCl_3$) 1.79 (2H, m, 3-H_2), 1.98 (2H, m, 2-H_2), 2.42 (5H, m, 4-H_2, 7-CH_3), 3.57 (2H, t, $J = 6$ Hz, 1-H_2), 5.78 (1H, t, $J = 7$ Hz, 5-*H*), 7.29 (1H, d, $J = 8$ Hz, 8-*H*), 7.41 (1H, s, 6-*H*), 7.64 (1H, d, $J = 8$ Hz, 9-*H*). δ_C (125 MHz, $CDCl_3$) 22.2 (7-*C*H_3), 27.0 (*C*-3), 27.3 (*C*-4), 28.9 (*C*-2), 45.3 (*C*-1), 106.3 (*C*-5), 120.8 (*C*-6), 121.1 (*C*-9), 128.9 (*C*-9a), 130.6 (*C*-8), 132.4 (*C*-5b), 135.9 (*C*-5a), 144.1 (*C*-7). *m/z* (ES^+) 249.6 (MH^+), HRMS (ES) found MH^+ 250.0896, $C_{13}H_{16}NO_2S$ requires M^+ 250.0896.

1,2,3,4-Tetrahydro-7-bromoazepino[1,2-b][1,2]benzothiazole-10,10-dioxide 5f

Purification by flash chromatography (1: 15% ethyl acetate–cyclohexane, 2: 30% ethyl acetate–cyclohexane) afforded the title compound as a white solid (0.219 g, 0.70 mmol, 46%). Mp 199–200 °C. Found; C, 46.25; H, 3.96; N, 4.38%; calc. for $C_{12}H_{12}NO_2SBr$; C, 45.87; H, 3.85; N, 4.38%. ν_{max} (KBr) 2939, 2866, 1661, 1589, 1572, 1455, 1418, 1309, 1229, 1177, 1143, 1073, 1055 cm^{-1}. δ_H (400 MHz, $CDCl_3$) 1.79 (2H, quint., $J = 6$ Hz, 3-H_2), 1.98 (2H, m, 2-H_2), 2.44 (2H, q, $J = 6$ Hz, 4-H_2), 3.58 (2H, m, 1-H_2), 5.79 (1H, t, $J = 6$ Hz, 5-*H*), 7.58–7.68 (2H, m, 8-*H*, 9-*H*), 7.76 (1H, s, 6-*H*). δ_C (100 MHz, $CDCl_3$) 26.9 (*C*-4), 27.4 (*C*-3), 28.8 (*C*-2), 45.4 (*C*-1), 108.2 (*C*-5), 122.8 (*C*-9), 123.9 (*C*-6), 128.0 (Ar*C*), 130.3 (Ar*C*), 132.6 (*C*-8), 134.0 (*C*-5b), 134.7 (*C*-5a). *m/z* (ES^+) 314.2 [MH^+ (Br^{79})], 316.2 [MH^+ (Br^{81})].

Crystal data for 5f. $C_{12}H_{12}BrNO_2S$, $M = 314.20$, orthorhombic, space group *Pbcn*, $a = 16.5525(3)$, $b = 10.1393(2)$, $c = 14.0826(3)$ Å, $U = 2363.5(1)$ $Å^3$, $F(000) = 1264$, $Z = 8$, $D_c = 1.766$ Mg m^{-3}, $\mu = 3.643$ mm^{-1} (Mo-Kα, $\lambda = 0.71073$ Å), $T = 120(1)$K. 30330 reflections were collected on a Bruker SMART CCD 6000 diffractometer (ω-scan, 0.3° per frame) yielding 3450 unique data ($R_{int} = 0.0259$). The SADABS absorption correction has been applied. The structure was solved by direct methods and refined by full-matrix least squares on F^2 for all data using SHELXTL software.[21] All non-hydrogen atoms (except the disordered ones) were refined with anisotropic displacement parameters, H-atoms were located on the difference map and refined isotropically. Final w*R*2 (F^2) = 0.0724 for all data (190 refined parameters), conventional $R(F) = 0.0285$ for 3450 reflections with $I \geq 2\sigma(I)$, GOF = 1.145. Crystallographic data for the structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC 650785.

1-Tosyl-4,5,6,7-tetrahydro-1*H*-azepin-2-yl diphenylphosphinate 8a

To a cold solution (−78 °C) of *N*-tosyl caprolactam (0.63 g, 2.36 mmol, 1 eq.) in dry THF (30 ml) was added sodium hexamethyldisilazane (NaHMDS, 2 M, 1.25 ml, 2.51 mmol, 1.2 eq.) *via* syringe. The resulting reaction mixture was stirred at −78 °C for 1 h after which time diphenylphosphonic chloride (0.48 ml, 2.51 mmol, 1.2 eq.) was added *via* syringe. The reaction mixture was stirred at −78 °C for 2 h before being warmed to room temperature and quenched with H_2O. The mixture was concentrated *in vacuo* and the aqueous layer was extracted with ethyl acetate. The organic phase was washed with brine then dried over $MgSO_4$ and concentrated *in vacuo* affording the crude material as a yellow soild. Purification on a Horizon® column chromatography system (1: 5% ethyl acetate–pet. ether, 2: 10% ethyl acetate–pet. ether) afforded the desired product as a white solid (0.80 g, 1.71 mmol, 73%). ν_{max} (KBr) 3056, 2947, 2914, 2848, 1672, 1595, 1440, 1343, 1230, 1160, 1031, 993, 953, 869 cm^{-1}. δ_H (400 MHz, $CDCl_3$) 1.34 (2H, quint., $J = 6$ Hz, 5-H_2), 1.65 (2H, quint., $J = 6$ Hz, 6-H_2), 1.85 (2H, q, $J = 6$ Hz, 4-H_2), 2.35 (3H, s, 4″-CH_3), 3.19 (2H, m, 7-H_2), 5.52 (1H, dt, $J_P = 2$ Hz, $J_H = 8$ Hz, 3-*H*), 7.07 (2H, d, $J = 8$ Hz, 3″-*H*, 5″-*H*), 7.41–7.47 (4H, m, Ar-*H*), 7.52–7.57 (2H, m, 4′-*H*), 7.67 (2H, d, $J = 8$ Hz, 2″-*H*, 6″-*H*), 7.78–7.86 (4H, m, Ar-*H*). δ_C (100 MHz, $CDCl_3$) 21.9 (4″-*C*H_3), 24.1 (*C*-5), 24.4 (*C*-4), 30.1 (*C*-6), 49.6 (*C*-7), 113.6 (*C*-3), 127.7 (*C*-2″), 128.8 (Ar*C*H), 129.9 (*C*-3″), 130.3 (Ar*C*), 131.6 (Ar*C*), 132.4 (Ar*C*H), 132.8 (*C*-4′), 138.4 (Ar*C*), 143.9 (*C*-2). δ_P (162 MHz, $CDCl_3$) 33.0. *m/z* (ES^+) 468.2 (MH^+), 490.3 (MNa^+), 956.8 ($2MNa^+$). HRMS (ES) found MH^+ 468.1398, $C_{25}H_{27}NO_4PS$ requires M^+ 468.1393; found MNa^+ 490.1214, $C_{25}H_{26}NNaO_4PS$ requires M^+ 490.1212.

1,2,3,4-Tetrahydro-7-tolylazepino[1,2-b][1,2]benzothiazole-10,10-dioxide 9

A mixture of *p*-tolylboronic acid (0.05 g, 0.37 mmol, 1 eq.), $NaHCO_3$ (0.09 g, 1.10 mmol, 3 eq.) and **5f** in a DME (7 ml)–H_2O (3 ml) mixture was degassed by 3 freeze–pump–thaw cycles. $Pd(PPh_3)_4$ (0.02 g, 0.017 mmol, 0.05 eq) was then added and the reaction mixture was heated at 80 °C for 45 min. The mixture was allowed to cool to room temperature and concentrated *in vacuo*

and the aqueous layer was extracted with ethyl acetate. The organic phase was washed with H_2O then brine, dried over $MgSO_4$ and concentrated *in vacuo* affording crude material. Purification by flash chromatography (10% ethyl acetate–pet. ether) afforded the title compound as an off-white solid (0.102 g, 0.31 mmol, 86%). Mp >130 °C (sinters and decomposes). ν_{max} (KBr) 2940, 2920, 1622, 1393, 1291, 1173, 1142, 1067, 1005, 973, 829, 805, 701 cm^{-1}. δ_H (500 MHz, $CDCl_3$) 1.83 (2H, quint., $J = 6$ Hz, 3-H_2), 2.01 (2H, m, 2-H_2), 2.43 (3H, s, 4′-CH_3), 2.48 (2H, s, $J = 6$ Hz, 4-H_2), 3.63 (2H, m, 1-H_2), 5.90 (1H, t, $J = 6$ Hz, 5-*H*), 7.30 (2H, d, $J = 8$ Hz, 3′-*H*), 7.50 (2H, d, $J = 8$ Hz, 2′-*H*), 7.68 (1H, dd, $J_1 = 9$ Hz, $J_2 = 1$ Hz, 8-*H*), 7.77 (1H, d, $J = 1$ Hz, 6-*H*), 7.82 (1H, d, $J = 9$ Hz, 9-*H*). δ_C (125 MHz, $CDCl_3$) 21.4 (4′-*C*H_3), 27.0 (*C*-3), 27.3 (*C*-4), 28.9 (*C*-2), 45.3 (*C*-1), 106.7 (*C*-5), 118.9 (*C*-6), 121.7 (*C*-9), 127.5 (*C*-2′), 128.6 (*C*-8), 129.8 (*C*-7), 130.0 (*C*-3′), 132.8 (*C*-5b), 136.0 (*C*-5a), 136.8 (*C*-1′), 138.9 (*C*-4′), 146.6 (*C*-9a). *m/z* (ES^+) 326.1 (MNa^+), 389.1 ($MNaMeCN^+$). HRMS (ES) found MH^+ 326.1208, $C_{19}H_{20}NO_2S$ requires M^+ 326.1209.

1,2,3,4,5-Quintahydro-7-methylazepino[1,2-b][1,2]benzothiazole-10,10-dioxide 10

A solution of **5a** (0.05 g, 0.20 mmol, 1 eq.) in EtOH (1 ml, 0.2 M) was added *via* cannula to a flask containing 10% Pd/C (7.5 mg, 15% w/w). The flask was placed under an atmosphere of H_2 and the reaction mixture was stirred at room temperature overnight. The flask was flushed with argon and the suspension was filtered through a pad of Celite and washed through with EtOAc; the organics were concentrated *in vacuo* affording crude material. Purification by flash chromatography (20% ethyl acetate–pet. ether) afforded the title compound as a white solid (0.022 g, 0.088 mmol, 44%). Mp 113–115 °C. ν_{max} (KBr) 2934, 2856, 1610, 1464, 1305, 1178, 1146, 1061, 941 cm^{-1}. δ_H (500 MHz, $CDCl_3$) 1.57–1.90 (6H, m), 2.08 (1H, m, 2-H*H*), 2.28 (1H, m, 5-H*H*), 2.45 (3H, s, 7-*CH*$_3$), 3.29 (1H, ddd, $J_1 = 12$ Hz, $J_2 = 8$ Hz, $J_3 = 4$ Hz, 1-H*H*), 3.68 (1H, ddd, $J_1 = 12$ Hz, $J_2 = 8$ Hz, $J_3 = 4$ Hz, 1-*H*H), 4.47 (1H, dd, $J_1 = 10$ Hz, $J_2 = 3$ Hz, 5a-*H*), 7.16 (1H, s, 6-*H*), 7.31 (1H, d, $J = 8$ Hz, 8-*H*), 7.66 (1H, d, $J = 8$ Hz, 9-*H*). δ_C (125 MHz, $CDCl_3$) 22.1 (7-*C*H_3), 27.1, 27.6 (2 × CH_2), 27.7 (*C*-2), 36.3 (*C*-5), 42.5 (*C*-1), 62.3 (*C*-5a), 121.1 (*C*-9), 124.3 (*C*-6), 130.3 (*C*-8), 132.0 (*C*-9a), 139.2 (*C*-5b), 143.9 (*C*-7). *m/z* (ES^+) 252.0 (MH^+), 503.1 ($2MH^+$), 525.1 ($2MNa^+$). HRMS (ES) found MH^+ 252.1060, $C_{13}H_{17}NO_2S$ requires M^+ 252.1858.

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