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Generation of 6*H*-benzo[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxides *via* a palladium-catalyzed reaction of 2-(2-alkynyl)benzenesulfonamide†

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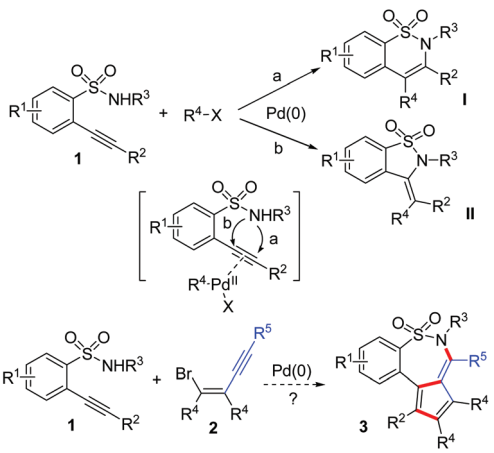
An efficient approach for the assembly of 6*H*-benzo[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxides *via* a palladium-catalyzed tandem reaction of 2-(2-alkynyl)benzenesulfonamide with 2-alkynylvinyl bromide is reported. This transformation proceeds smoothly through a double carbopalladation with high efficiency.

1. Introduction

Using small molecule modulators for the systematic perturbation of gene products has been a hot research area in the interdisciplinary research field of chemical biology as well as in the pharmaceutical industry.[1] Therefore, libraries of novel drug-like small molecules with maximized molecular diversity are of high demand.[2] In the past decade, the strategy of diversity-oriented synthesis developed by Schreiber has been widely used for the construction of natural product-like compounds in the studies of chemical genetics.[3] For example, Park and coworkers reported the diversity-oriented synthesis of some molecular frameworks with a privileged substructure, which displayed enhanced selectivity and specificity towards multiple biological assay systems as small molecule modulators for specific biological targets.[4] Among the methods developed, tandem reactions have been utilized as an efficient approach for the introduction of molecular complexity.[5]

We are interested in the synthesis of nitrogen-containing heterocycles *via* tandem reactions. We have recognized that 2-(2-alkynyl)benzenesulfonamide **1** would be a useful building block for reaction development. Usually, 2-(2-alkynyl)benzenesulfonamide **1** reacts with an aryl/alkenyl halide in the presence of Pd(0) to afford compound **I** (6-*endo* cyclization, path a) or **II** (5-*exo* cyclization, path b). However, we envisioned that a core of benzo[*f*][1,2]thiazepine dioxide would be formed if 2-alkynylvinyl bromide **2** was used as the coupling partner (Scheme 1). The presence of the alkynyl moiety in 2-alkynylvinyl bromide **2** would allow an alternative pathway in the reaction with 2-(2-alkynyl)benzenesulfonamide **1**.

As a privileged scaffold, the core of benzo[*f*][1,2]thiazepine dioxide has attracted much attention. For instance, Tianeptine (trade-names: Stablon, Coaxil, Tatinol) is a drug used for treating major depressive episodes.[6] Compounds such as the human immunodeficiency virus protease inhibitor,[7a] calcium sensing receptor agonists,[7b] and the farnesyltransferase inhibitor[7c] which contain the benzo[*f*][1,2]thiazepine dioxide skeleton show remarkable biological activities. As part of a program for synthesising natural product-like compounds for different biological applications, we are interested in benzo[*f*][1,2]thiazepine dioxide derivatives. Although methods exist for the synthesis of benzo[*f*][1,2]thiazepine dioxide derivatives,[7a,b,8] the methods usually suffer from harsh reaction conditions, multi-



Scheme 1 Palladium-catalyzed reaction of 2-(2-alkynyl)benzenesulfonamide **1** with an aryl/alkenyl halide.

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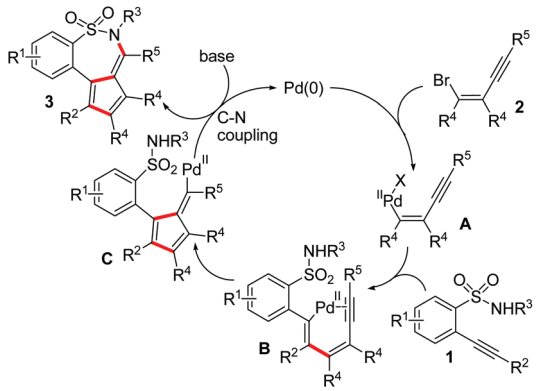
†Electronic supplementary information (ESI) available: Experimental procedure, characterization data, ^{1}H and ^{13}C NMR spectra of compounds **3**, and a CIF file of compound **3a**. CCDC 892027. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2dt32452k



Scheme 2 A proposed route for the palladium-catalyzed reaction of 2-(2-alkynyl)benzenesulfonamide **1** with 2-alkynylvinyl bromide **2**.

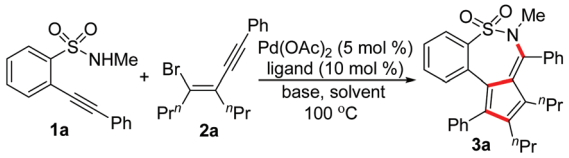
steps, and scope limitations. Thus, it is highly desirable to develop a novel route for the efficient assembly of benzo[*f*][1,2]-thiazepine dioxide derivatives.

Recently, a highly selective palladium-catalyzed intramolecular or intermolecular double carbopalladation for the formation of molecular complexity has been developed.[9] Encouraged by this result, we hypothesized that benzo[*f*][1,2]thiazepine dioxide derivatives could be generated through a palladium-catalyzed reaction of 2-(2-alkynyl)benzenesulfonamide **1** with 2-alkynylvinyl bromide **2**. The proposed synthetic route is present in Scheme 2. We envisioned that an oxidative addition of Pd(0) to 2-alkynylvinyl bromide **2** would occur first to generate a Pd(II) species **A**, which might undergo coordination to the triple bond of 2-(2-alkynyl)benzenesulfonamide **1** to afford intermediate **B**. Further intramolecular insertion of a triple bond would happen to produce intermediate **C**, which would then provide the expected benzo[*f*][1,2]thiazepine dioxide **3** *via* a C–N coupling. During the reaction process, three bonds would be formed. Additionally, complexity and diversity could be incorporated with high efficiency. We believed that the hypothesis presented in Scheme 2 was feasible although theoretically there are several possible competitive pathways, such as direct C–N coupling and direct cyclization of 2-(2-alkynyl)-benzenesulfonamide **1** under the palladium catalysis (Scheme 1).

2. Results and discussion

Initially, a model reaction of 2-(2-alkynyl)benzenesulfonamide **1a** with 2-alkynylvinyl bromide **2a** in the presence of $Pd(OAc)_2$ (5 mol%) was studied (Table 1). A trace amount of product was detected when the reaction took place in the presence of PCy_3 (10 mol%) and NaOMe in 1,4-dioxane at 100 °C (Table 1, entry 1). A similar outcome was seen when the base was changed to Cs_2CO_3, *t*-BuONa, K_3PO_4, Na_2CO_3, KOAc, NaOAc, or CsOAc (Table 1, entries 2–8). The expected benzo[*f*][1,2]-thiazepine dioxide **3a** was obtained and isolated in 48% yield when potassium carbonate was added as the base (Table 1, entry 9). The structure of compound **3a** was unambiguously

Table 1 Initial studies for the palladium-catalyzed reaction of *N*-methyl-2-(2-phenylethynyl)benzenesulfonamide **1a** with 2-alkynylvinyl bromide **2a**[a]



Entry	Ligand	Base	Solvent	Yield[b] (%)
1	PCy_3	NaOMe	1,4-Dioxane	Trace
2	PCy_3	Cs_2CO_3	1,4-Dioxane	Trace
3	PCy_3	*t*-BuONa	1,4-Dioxane	Trace
4	PCy_3	K_3PO_4	1,4-Dioxane	Trace
5	PCy_3	Na_2CO_3	1,4-Dioxane	Trace
6	PCy_3	KOAc	1,4-Dioxane	Trace
7	PCy_3	NaOAc	1,4-Dioxane	Trace
8	PCy_3	CsOAc	1,4-Dioxane	Trace
9	PCy_3	K_2CO_3	1,4-Dioxane	48
10	Xantphos	K_2CO_3	1,4-Dioxane	46
11	X-phos	K_2CO_3	1,4-Dioxane	54
12	PPh_3	K_2CO_3	1,4-Dioxane	60
13	DPPF	K_2CO_3	1,4-Dioxane	62
14	DPPP	K_2CO_3	1,4-Dioxane	85
15	S-Phos	K_2CO_3	1,4-Dioxane	30
16	DPPM	K_2CO_3	1,4-Dioxane	57
17	DPPE	K_2CO_3	1,4-Dioxane	73
18	DPPB	K_2CO_3	1,4-Dioxane	77
19	BINAP	K_2CO_3	1,4-Dioxane	55
20	DPEphos	K_2CO_3	1,4-Dioxane	70
21	DPPP	K_2CO_3	DMF	Trace
22	DPPP	K_2CO_3	Toluene	64

[a] Reaction conditions: *N*-methyl-2-(2-phenylethynyl)benzenesulfonamide **1a** (0.3 mmol), 2-alkynylvinyl bromide **2a** (1.2 equiv., 0.36 mmol), palladium catalyst (5 mol%, 0.015 mmol), ligand (5 or 10 mol%), base (2.0 equiv., 0.6 mmol), 100 °C. [b] Isolated yield based on *N*-methyl-2-(2-phenylethynyl)benzenesulfonamide **1a**.

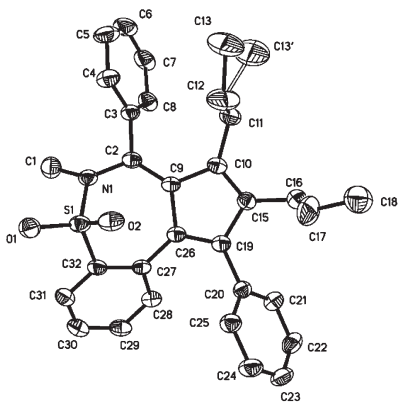


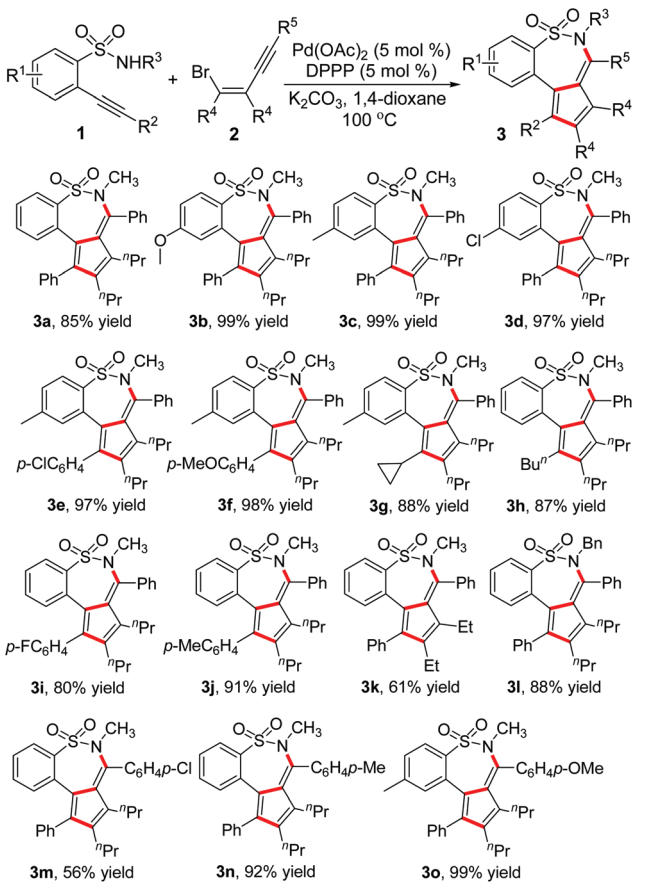
Fig. 1 X-ray ORTEP illustration of 6*H*-benzo[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxide **3a** (30% probability ellipsoids).

identified by X-ray diffraction analysis (Fig. 1, also see the ESI†). No desired product was formed in the absence of a phosphine ligand (data not shown in Table 1). Further screening of other ligands revealed that the reaction worked efficiently in the presence of DPPP, which produced the corresponding product **3a** in 85% yield (Table 1, entries 10–20).

The reaction was not successful in DMF (Table 1, entry 21). A 64% yield was obtained when the reaction was performed in toluene (Table 1, entry 22). The reaction was slower at a lower temperature (data not shown in Table 1).

Table 2 summarizes the results for the palladium-catalyzed reaction of 2-(2-alkynyl)benzenesulfonamides **1** with 2-alkynylvinyl bromides **2** under the optimized conditions (5 mol% of $Pd(OAc)_2$, 5 mol% of DPPP, 2.0 equiv. of K_2CO_3, 1,4-dioxane, 100 °C). The double carbopalladation was found to be highly efficient, and a range of 6*H*-benzo[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxides **3** was obtained in good to excellent yields. Different functional groups were compatible under the standard conditions. 2-(2-Alkynyl)benzenesulfonamides **1** with various substituents (electron-donating and electron-withdrawing groups) on the aromatic ring were all good partners in the transformation. Reactions involving 2-(2-alkynyl)benzenesulfonamides **1** with aryl or alkyl groups attached on the triple bond all worked well to produce the desired products **3**. For some cases, the quantitative yields were obtained. Additionally, 2-alkynylvinyl bromides **2** were workable during the reaction process.

Table 2 Synthesis of 6*H*-benzo[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxides **3** *via* a palladium-catalyzed reaction of 2-(2-alkynyl)benzenesulfonamide **1** with 2-alkynylvinyl bromide **2**[a]



[a] Isolated yield based on 2-(2-alkynyl)benzenesulfonamide **1**.

3. Conclusion

In conclusion, we have described an efficient approach for the preparation of 6*H*-benzo[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxides *via* a palladium-catalyzed tandem reaction of 2-(2-alkynyl)benzenesulfonamide with 2-alkynylvinyl bromide. The reaction proceeds efficiently with the formation of three bonds in a one-pot procedure. A double carbopalladation is believed to be the key step during the reaction process. The construction of a library of novel drug-like small molecules with maximized molecular diversity is ongoing in our laboratory.

4. Experimental section

General procedure of the synthesis of 6*H*-benzo[*f*]cyclopenta[*d*]-[1,2]thiazepine 5,5-dioxides **3** *via* a palladium-catalyzed reaction of 2-(2-alkynyl)benzenesulfonamide **1** with 2-alkynylvinyl bromide **2**: 2-(2-alkynyl)benzenesulfonamide **1** (0.30 mmol) was added to a mixture of $Pd(OAc)_2$ (5 mol%), DPPP (5 mol%), K_2CO_3 (0.60 mmol), and 2-alkynylvinyl bromide **2** (0.36 mmol) in 1,4-dioxane (2.0 mL). The mixture was stirred at 100 °C. After completion of the reaction as indicated by TLC (~12 hours), the mixture was cooled and diluted using EtOAc (10 mL), washed with saturated brine (2 × 10 mL), and dried using anhydrous Na_2SO_4. Evaporation of the solvent followed by purification on silica gel provided the product **3**.

6-Methyl-7,10-diphenyl-8,9-dipropyl-6*H*-benzo[*f*]cyclopenta[*d*]-[1,2]thiazepine 5,5-dioxide (3a)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.43 (t, J = 7.3 Hz, 3H), 0.73 (t, J = 6.9 Hz, 3H), 1.13–1.26 (m, 4H), 1.43–1.56 (m, 1H), 1.87–1.92 (m, 1H), 2.16–2.24 (m, 1H), 2.29–2.36 (m, 2H), 2.68 (s, 3H), 7.02 (d, J = 7.8 Hz, 2H), 7.09 (t, J = 7.8 Hz, 1H), 7.18–7.25 (m, 4H), 7.39–7.44 (m, 3H), 7.50–7.56 (m, 2H), 7.77 (d, J = 6.4 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.5, 23.5, 25.5, 28.5, 29.0, 36.9, 125.3, 126.3, 127.0, 127.6, 128.3, 128.5, 128.8, 130.0, 130.6, 131.5, 133.2, 133.7, 134.0, 136.4, 136.0, 137.8, 142.6, 146.1, 146.5; HRMS (ESI) calcd for $C_{31}H_{31}NO_2S$: 504.1968 (M + Na^+), found: 504.1970.

2-Methoxy-6-methyl-7,10-diphenyl-8,9-dipropyl-6*H*-benzo[*f*]-cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3b)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.43 (t, J = 6.9 Hz, 3H), 0.73 (t, J = 7.3 Hz, 3H), 1.14–1.27 (m, 4H), 1.48–1.53 (m, 1H), 1.91–1.96 (m, 1H), 2.20–2.26 (m, 1H), 2.30–2.36 (m, 1H), 2.70 (s, 3H), 3.25 (s, 3H), 6.50 (s, 1H), 6.71 (d, J = 8.2 Hz, 2H), 7.26–7.54 (m, 9H), 7.80 (d, J = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 14.5, 23.6, 25.6, 28.5, 29.0, 36.9, 55.1, 113.6, 116.7, 126.9, 127.6, 128.2, 128.3, 128.7, 128.8, 130.1, 130.6, 132.8, 133.7, 134.1, 135.8, 136.5, 138.4, 142.3, 146.0, 147.1, 161.6; HRMS (ESI) calcd for $C_{32}H_{33}NO_3S$: 534.2073 (M + Na^+), found: 534.2077.

2,6-Dimethyl-7,10-diphenyl-8,9-dipropyl-6*H*-benzo[*f*]-cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3c)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.42 (t, J = 7.3 Hz, 3H), 0.72 (t, J = 7.3 Hz, 3H), 1.11–1.27 (m, 4H), 1.47–1.52 (m, 1H), 1.87–1.93 (m, 1H), 1.97 (s, 3H), 2.18–2.26 (m, 1H), 2.29–2.36 (m, 1H), 2.67 (s, 3H), 6.78 (s, 1H), 6.99 (d, J = 7.8 Hz, 2H), 7.23–7.52 (m, 9H), 7.77 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.5, 21.3, 23.6, 25.5, 28.5, 29.0, 36.8, 126.2, 126.4 126.9, 127.6, 128.2, 128.4, 128.8, 130.0, 130.5, 133.2, 133.6, 133.7, 133.9, 134.4, 136.5, 138.0, 142.0, 142.5, 145.9, 146.5; HRMS (ESI) calcd for $C_{32}H_{33}NO_2S$: 518.2124 (M + Na^+), found: 518.2142.

2-Chloro-6-methyl-7,10-diphenyl-8,9-dipropyl-6*H*-benzo[*f*]-cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3d)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.43 (t, J = 7.3 Hz, 3H), 0.74 (t, J = 7.3 Hz, 3H), 1.10–1.29 (m, 4H), 1.48–1.54 (m, 1H), 1.89–1.94 (m, 1H), 2.18–2.27 (m, 1H), 2.28–2.36 (m, 1H), 2.69 (s, 3H), 6.94 (s, 1H), 7.14 (d, J = 8.2 Hz, 2H), 7.30 (d, J = 6.4 Hz, 2H), 7.40–7.41 (m, 3H), 7.52–7.54 (m, 2H), 7.74–7.76 (m, 1H), 7.81 (d, J = 8.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.5, 23.5, 25.5, 28.4, 29.0, 36.9, 125.6, 126.1 127.4, 127.7, 128.4, 128.7, 128.9, 129.9, 130.7, 133.1, 133.3, 133.7, 134.6, 134.8, 135.6, 136.1, 137.2, 137.8, 142.7, 146.7, 147.3; HRMS (ESI) calcd for $C_{31}H_{30}ClNO_2S$: 538.1578 (M + Na^+), found: 538.1569.

10-(4-Chlorophenyl)-2,6-dimethyl-7-phenyl-8,9-dipropyl-6*H*-benzo[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3e)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.42 (t, J = 6.9 Hz, 3H), 0.74 (t, J = 7.3 Hz, 3H), 1.09–1.25 (m, 4H), 1.42–1.53 (m, 1H), 1.85–1.92 (m, 1H), 2.03 (s, 3H), 2.17–2.24 (m, 1H), 2.26–2.34 (m, 1H), 2.67 (s, 3H), 6.78 (s, 1H), 7.02 (d, J = 7.8 Hz, 2H), 7.25–7.39 (m, 5H), 7.49–7.54 (m, 2H),7.74–7.79 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.5, 21.4, 23.6, 25.5, 28.5, 29.0, 36.9, 126.4, 126.5 128.0, 128.3, 128.6, 128.9, 130.0, 130.6, 132.7, 133.4, 133.7, 133.9, 134.0, 134.3, 136.3, 136.6, 141.9, 142.2, 144.3 147.1; HRMS (ESI) calcd for $C_{32}H_{32}ClNO_2S$: 552.1734 (M + Na^+), found: 552.1734.

10-(4-Methoxyphenyl)-2,6-dimethyl-7-phenyl-8,9-dipropyl-6*H*-benzo[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3f)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.42 (t, J = 7.4 Hz, 3H), 0.74 (t, J = 7.3 Hz, 3H), 1.10–1.25 (m, 4H), 1.47–1.54 (m, 1H), 1.86–1.92 (m, 1H), 2.01 (s, 3H), 2.18–2.25 (m, 1H), 2.29–2.38 (m, 1H), 2.66 (s, 3H), 6.83 (s, 1H), 6.99 (d, J = 7.8 Hz, 2H), 7.35–7.42 (m, 2H), 7.47–7.53 (m, 2H), 7.75–7.78 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 14.6, 21.5, 23.6, 25.5, 28.6, 29.0, 36.8, 55.3, 113.9, 126.2, 126.4 127.3, 128.2, 128.8, 130.0, 130.1, 130.5, 133.3, 133.6, 133.7, 133.8, 133.9, 134.3, 136.6, 136.6, 142.0, 142.7, 145.6 146.2, 158.7; HRMS (ESI) calcd for $C_{33}H_{35}NO_3S$: 548.2230 (M + Na^+), found: 548.2239.

10-Cyclopropyl-2,6-dimethyl-7-phenyl-8,9-dipropyl-6*H*-benzo[*f*]-cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3g)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ −1.20 to −0.15 (m, 1H), 0.37 (t, J = 7.3 Hz, 3H), 0.40–0.45 (m, 1H), 0.60–0.66 (m, 1H), 0.92–1.77 (m, 6H), 1.47–1.54 (m, 2H), 1.66–1.80 (m, 3H), 2.32–2.40 (m, 1H), 2.45 (s, 3H), 2.50–2.58 (m, 1H), 2.60 (s, 3H), 7.16 (d, J = 7.8 Hz, 2H), 7.33–7.36 (m, 2H), 7.47 (d, J = 6.9 Hz, 2H), 7.65–7.69 (m, 2H), 7.8 (d, J = 7.8 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 7.8, 10.1, 10.5, 14.1, 14.8, 21.7, 24.0, 25.3, 28.5, 28.8, 36.6, 126.1, 126.4, 127.3, 128.0, 128.8, 130.0, 130.1, 132.4, 133.0, 133.3, 133.4, 134.1, 136.8, 141.7, 144.5, 144.7, 146.0; HRMS (ESI) calcd for $C_{29}H_{33}NO_2S$: 482.2124 (M + Na^+), found: 482.2132.

10-Butyl-6-methyl-7-phenyl-8,9-dipropyl-6*H*-benzo[*f*]-cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3h)

Dark red oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.39 (t, J = 6.9 Hz, 3H) 0.90 (t, J = 7.3 Hz, 3H), 0.98 (t, J = 7.3 Hz, 3H), 1.05–1.12 (m, 2H), 1.36–1.42 (m, 2H), 1.49–1.58 (m, 5H), 1.76–1.82 (m, 1H), 2.30 (t, J = 7.8 Hz, 2H), 2.44–2.49 (m, 2H), 2.61 (s, 3H), 7.34–7.36 (m, 3H), 7.47–7.60 (m, 4H), 7.71 (d, J = 6.0 Hz, 1H), 7.96 (d, J = 8.4 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.7, 14.0, 14.7, 22.8, 24.2, 25.2, 26.9, 28.3, 28.7, 32.3, 36.4, 125.5, 126.6, 126.7, 127.9, 128.6, 129.8, 130.1, 131.2, 132.0, 133.3, 133.4, 133.7, 134.3, 136.3, 136.5, 142.8, 144.0, 146.1; HRMS (ESI) calcd for $C_{29}H_{35}NO_2S$: 500.2020 (M + K^+), found: 500.2001.

10-(4-Fluorophenyl)-6-methyl-7-phenyl-8,9-dipropyl-6*H*-benzo-[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3i)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.42 (t, J = 6.9 Hz, 3H), 0.73 (t, J = 6.8 Hz, 3H), 1.12–1.25 (m, 4H), 1.47–1.54 (m, 1H), 1.86–1.90 (m, 1H), 2.03 (s, 3H), 2.20–2.24 (m, 1H), 2.28–2.34 (m, 1H), 2.68 (s, 3H), 7.00 (d, J = 7.8 Hz, 2H), 7.12 (t, J = 7.8 Hz, 2H), 7.22 (t, J = 7.3 Hz, 2H), 7.36–7.55 (m, 5H), 7.76 (d, J = 5.5 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.5, 23.5, 25.5, 28.6, 29.0, 36.9, 115.5 (d, $^2J_{CF}$ = 21.0 Hz); 125.7, 126.4 127.8, 128.3, 128.9, 130.0, 130.7, 131.5, 131.7, 133.0, 133.5, 133.6, 133.8 (d, $^3J_{CF}$ = 8.6 Hz), 136.3, 136.7, 142.2, 144.8, 146.8, 162.0 (d, $^1J_{CF}$ = 245.0 Hz); HRMS (ESI) calcd for $C_{31}H_{30}FNO_2S$: 522.1873 (M + Na^+), found: 522.1874.

6-Methyl-7-phenyl-8,9-dipropyl-10-(*p*-tolyl)-6*H*-benzo[*f*]-cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3j)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.43 (t, J = 7.4 Hz, 3H), 0.74 (t, J = 7.3 Hz, 3H), 1.12–1.27 (m, 4H), 1.49–1.56 (m, 1H), 1.87–1.95 (m, 1H), 2.18–2.24 (m, 1H), 2.30–2.35 (m, 4H), 2.67 (s, 3H), 7.05–7.12 (m, 5H), 7.20 (t, J = 7.8 Hz, 2H), 7.37–7.44 (m, 2H), 7.76–7.54 (m, 2H), 7.77 (d, J = 6.0 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 14.6, 21.4, 23.6, 25.5, 28.5, 29.0, 36.9, 125.4, 126.3 127.4, 128.2, 128.8, 129.2, 130.0, 130.5, 131.6, 133.4, 133.7, 134.2, 134.7, 136.4, 136.5, 136.6, 142.8, 146.1, 146.2; HRMS (ESI) calcd for $C_{32}H_{33}NO_2S$: 518.2124 (M + Na^+), found: 518.2117.

8,9-Diethyl-6-methyl-7,10-diphenyl-6*H*-benzo[*f*]cyclopenta[*d*]-[1,2]thiazepine 5,5-dioxide (3k)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.70 (t, J = 7.4 Hz, 3H), 0.80 (t, J = 6.9 Hz, 3H), 1.60–1.65 (m, 1H), 1.95–2.00 (m, 1H), 2.26–2.38 (m, 2H), 2.68 (s, 3H), 7.02 (d, J = 7.8 Hz, 2H), 7.09 (t, J = 7.3 Hz, 1H), 7.18–7.25 (m, 4H), 7.38–7.44 (m, 3H), 7.51 (d, J = 7.3 Hz, 2H), 7.79 (d, J = 7.8 Hz, 1H), 7.90 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.8, 16.7, 19.3, 19.6, 36.9, 125.6, 126.3, 127.0, 127.6, 128.2, 128.5, 128.8, 129.9, 130.6, 131.6, 132.9, 133.6, 133.7, 134.0, 134.9, 136.5, 137.7, 143.8, 146.1, 146.4; HRMS (ESI) calcd for $C_{29}H_{27}NO_2S$: 476.1655 (M + Na^+), found: 476.1655.

6-Benzyl-7,10-diphenyl-8,9-dipropyl-6*H*-benzo[*f*]cyclopenta[*d*]-[1,2]thiazepine 5,5-dioxide (3l)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.43 (t, J = 7.3 Hz, 3H), 0.73 (t, J = 6.8 Hz, 3H), 1.13–1.28 (m, 4H), 1.42–1.49 (m, 1H), 1.84–1.91 (m, 1H), 2.18–2.24 (m, 1H), 2.29–2.38 (m, 1H), 4.31 (d, J = 16.0 Hz, 2H), 4.82 (d, J = 16.0 Hz, 2H), 6.45 (d, J = 7.8, 2), 6.80 (t, J = 6.8 Hz, 2H), 6.86–6.91 (m, 5H), 7.22–7.26 (m, 2H), 7.32–7.33 (m, 3H), 7.50–7.55 (m, 3H), 7.77 (d, J = 6.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 14.6, 23.6, 25.6, 28.5, 29.1, 53.3, 125.5, 126.9 127.2, 127.8, 127.9, 128.2, 128.3, 128.4, 128.6, 130.0, 130.4, 131.1, 133.2, 133.5, 133.7, 133.8, 133.9, 135.3, 136.0, 137.9, 139.2, 142.3, 145.7, 146.1; HRMS (ESI) calcd for $C_{37}H_{35}NO_2S$: 580.2281 (M + Na^+), found: 580.2281.

7-(4-Chlorophenyl)-6-methyl-10-phenyl-8,9-dipropyl-6*H*-benzo-[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3m)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.47 (t, J = 6.9 Hz, 3H), 0.72 (t, J = 7.3 Hz, 3H), 1.11–1.28 (m, 4H), 1.51–1.59 (m, 1H), 1.91–1.97 (m, 1H), 2.18–2.24 (m, 1H), 2.28–2.34 (m, 1H), 2.66 (s, 3H), 7.00 (d, J = 7.8 Hz, 2H), 7.09 (t, J = 7.8 Hz, 1H), 7.18–7.38 (m, 7H), 7.52 (d, J = 8.2 Hz, 1H), 7.71 (d, J = 8.2 Hz, 1H), 7.89 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.5, 23.5, 25.4, 28.5, 29.0, 36.9, 125.7, 126.4, 127.1, 127.6, 128.6, 129.2, 131.3, 131.6, 133.2, 133.6, 133.7, 133.8, 134.8, 134.9, 136.4, 136.9, 137.6, 143.2, 144.9, 146.4; HRMS (ESI) calcd for $C_{31}H_{30}ClNO_2S$: 538.1578 (M + Na^+), found: 538.1572.

6-Methyl-10-phenyl-8,9-dipropyl-7-(*p*-tolyl)-6*H*-benzo[*f*]-cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3n)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.45 (t, J = 6.8 Hz, 3H), 0.73 (t, J = 7.3 Hz, 3H), 1.13–1.27 (m, 4H), 1.55–1.61 (m, 1H), 1.90–1.98 (m, 1H), 2.19–2.26 (m, 1H), 2.30–2.38 (m, 1H), 2.45 (s, 3H), 2.69 (s, 3H), 7.01 (d, J = 7.8 Hz, 2H), 7.08 (t, J = 7.4 Hz, 1H), 7.14–7.26 (m, 4H), 7.31–7.36 (m, 3H), 7.65 (d, J = 7.8 Hz, 1H), 7.80 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.2, 14.5, 21.6, 23.6, 25.5, 28.5, 29.0, 37.0, 125.4, 126.3, 126.9, 127.5, 128.5, 128.9, 129.6, 129.9, 131.5, 132.9, 133.5, 133.7, 133.8, 134.1, 136.6, 138.0, 141.0, 142.3, 145.8, 146.9; HRMS (ESI) calcd for $C_{32}H_{33}NO_2S$: 518.2124 (M + Na^+), found: 518.2127.

7-(4-Methoxyphenyl)-2,6-dimethyl-10-phenyl-8,9-dipropyl-6*H*-benzo[*f*]cyclopenta[*d*][1,2]thiazepine 5,5-dioxide (3o)

Dark red solid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.47 (t, J = 6.8 Hz, 3H), 0.73 (t, J = 7.3 Hz, 3H), 1.12–1.25 (m, 4H), 1.56–1.63 (m, 1H), 1.96–2.22 (m, 4H), 2.20–2.26 (m, 1H), 2.30–2.36 (m, 1H), 2.68 (s, 3H), 6.77 (s, 1H), 6.89 (d, J = 8.2 Hz, 1H), 6.98 (d, J = 7.8 Hz, 1H), 7.05 (d, J = 8.2 Hz, 1H), 7.23–7.35 (m, 6H), 7.68 (d, J = 8.2 Hz, 1H), 7.77 (d, J = 7.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 14.3, 14.6, 21.3, 23.7, 25.4, 28.5, 29.0, 37.0, 55.6, 113.4, 114.6, 126.1, 126.4, 126.8, 127.5, 128.3, 128.6, 130.2, 131.5, 132.5, 133.7, 133.8, 134.3, 135.6, 138.1, 141.9, 142.0, 145.4, 146.8; HRMS (ESI) calcd for $C_{33}H_{35}NO_3S$: 548.2230 (M + Na^+), found: 548.2230.

Crystal data for 3a

$C_{31}H_{31}NO_2S$, M_r = 481.63, monoclinic, space group $P2_1/n$, a = 10.517(4), b = 13.401(5), c = 18.699(7) Å, β = 90.737(5)°, V = 2635.2(18) Å^3, Z = 4, D_c = 1.903 g cm^{-1}, μ = 0.151 mm^{-1}, F_{000} = 1024, GOF = 0.920. A total of 10 715 reflections were collected, 4631 of which were unique (R_{int} = 0.0638). R_1/wR_2 = 0.0482/0.1377 for 323 parameters and 4631 reflections ($I > 2\sigma(I)$).

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