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Regio- and Stereoselective Synthesis of Benzo-δ-sultams by Palladium-Catalyzed Hydrocarbonation of Alkynes

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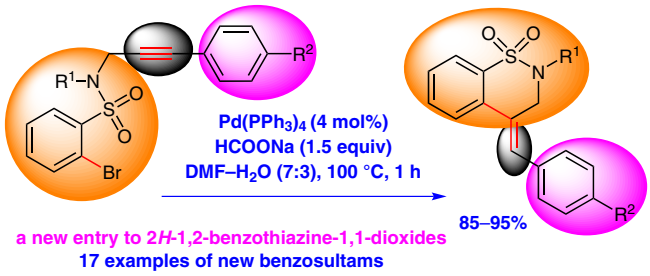

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Abstract An efficient method for the synthesis of benzo-δ-sultams [(4*Z*)-4-benzylidene-2-(arylmethyl)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-dioxides] via palladium(0)-catalyzed hydrocarbonation of alkynes is presented. This method allows regioselective access to a variety of substituted benzosultams in excellent yields under mild conditions. The stereochemistry of the exocyclic double bond of the benzosultam derivatives is confirmed by single-crystal X-ray diffraction.

Keywords benzosultams, hydrocarbonation, regioselectivity, DFT study

Compounds having a benzosultam core moiety are an important class of heterocycles due to their wide and diverse bioactivity.[1] They show antimicrobial, antiviral, anticancer, antileukemic, anti-HIV, and other promising activities.[2] For example, compound **1** (Figure 1) acts as an 11β-hydroxysteroid dehydrogenase type 1 (11β-HSD1) enzyme inhibitor;[3] 11β-HSD1 is an endoplasmic reticulum-associated enzyme that acts as a NADPH dependent reductase, which converts inactive cortisone into the active glucocorticoid cortisol.[4] Oxicams, such as ampiroxicam (**2**), are used as nonsteroidal anti-inflammatory drugs.[5] Compound **3** and several other benzosultams exhibit potential anti-HIV activity.[1a,6,7] Moreover, benzothiazine dioxide derivatives have strong inhibitory property against Calpain I.[8,9]

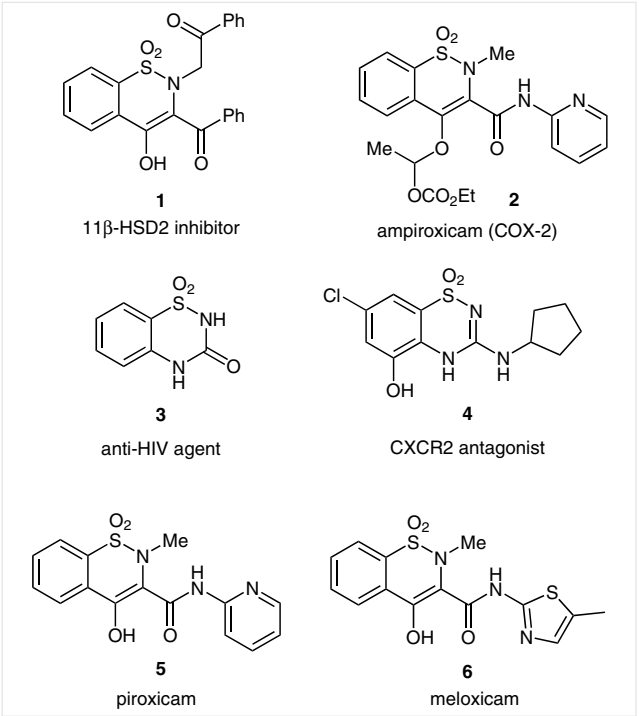


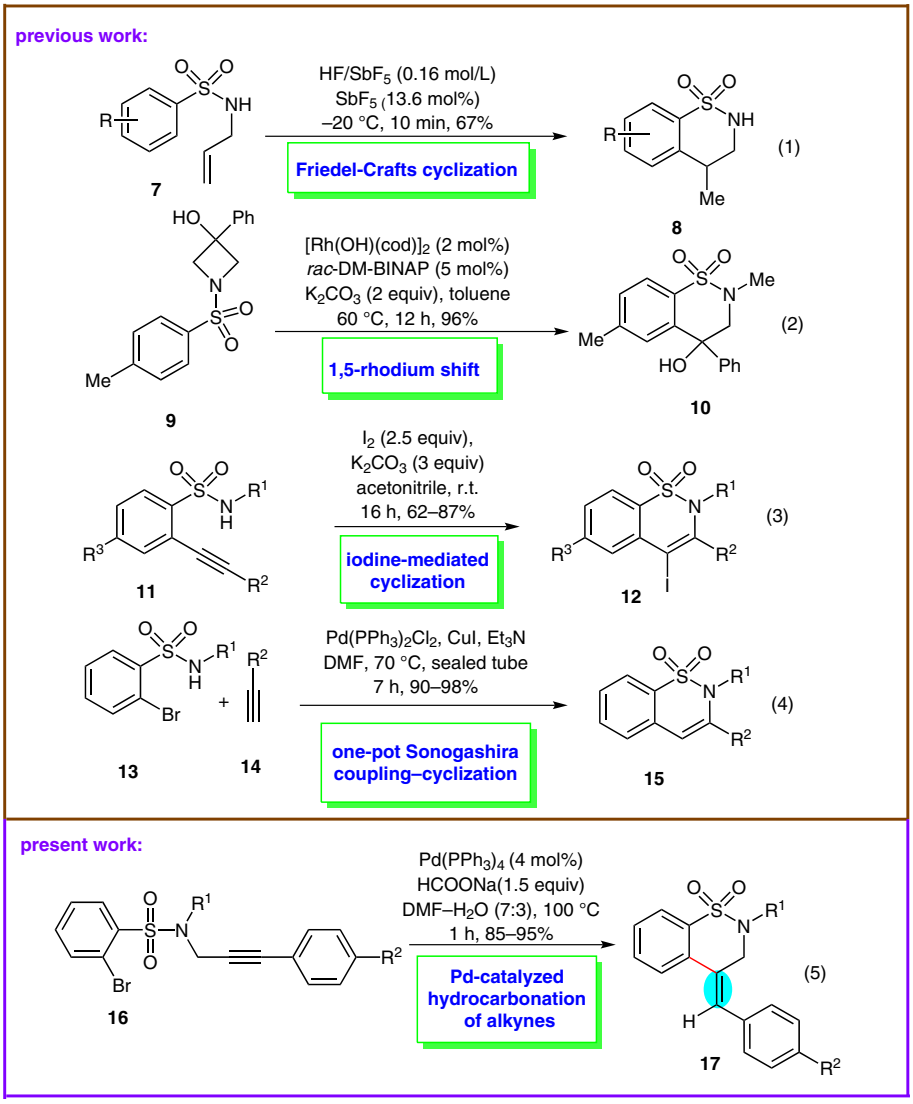
Figure 1 Biologically active benzothiazine dioxide derivatives

Due to the importance of benzothiazine dioxides among benzosultams, extensive attempts have been made to develop new and efficient routes for their synthesis. For example, Thibaudeau and co-workers reported an acid-catalyzed Friedel–Crafts cyclization process (Scheme 1, eq. 1) for the synthesis of benzothiazine dioxide derivatives.[10] Murakami and co-workers presented a synthetic route to benzothiazine dioxide derivatives by the rhodium-catalyzed rearrangement reaction of *N*-arylsulfonylazetidin-3-ols (Scheme 1, eq. 2).[11] Pal and co-workers accessed benzothiazine dioxide derivatives by N–C coupling through iodine-mediated cyclization (Scheme 1, eq. 3).[12] In our previous work we reported a one-pot synthetic strategy for the synthesis of a series of benzothiazine dioxide by Sonogashira coupling–cyclization (Scheme 1, eq. 4).[13] Beside these publications, there are few other reports on the synthesis of benzosultams.[14] Among the previously reported synthetic

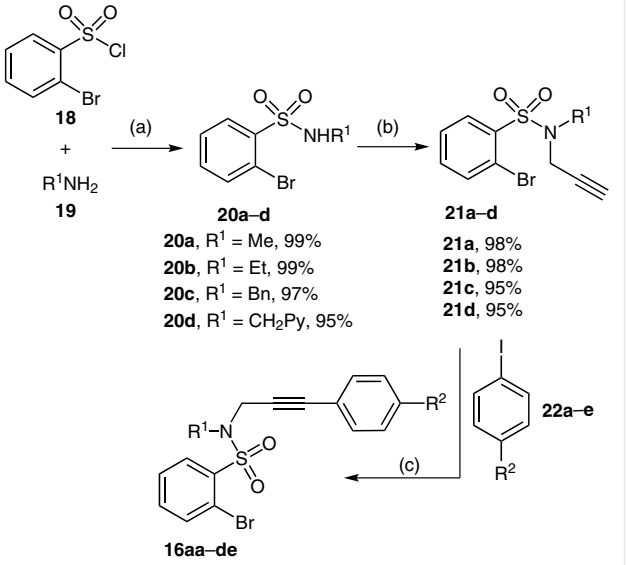
strategies, most approaches lead to benzothiazine dioxide derivatives with varying substitution at the 3-position, but few reports are available in the literature for the synthesis of benzothiazine dioxide derivatives with substitution at the 4-position. In our continued efforts in sultam and sultone chemistry,[1a,13,15] our present endeavor examines the regio- and stereoselective synthesis of benzothiazine dioxide derivatives with substitution at 4-position by palladium-catalyzed hydrocarbonation of alkynes (Scheme 1, eq. 5). Herein we report our results.

As depicted in Scheme 2, the required precursors **16aa–de** were prepared by propargylation of sulfonamides **20a–d** followed by selective intermolecular Sonogashira coupling[16] with different iodobenzenes **22a–e**. The sulfonamides **20a–d** were synthesized from commercially available 2-bromobenzenesulfonyl chloride (**18**) by reaction with various aliphatic amines **19**.

For the synthesis of our target benzothiazine dioxide derivatives, i.e. benzosultams, by the palladium-catalyzed hydrocarbonation of alkynes, we initiated our investigation with substrate **16aa**, optimizing the conditions for the formation of **17aa** (Table 1). Among the palladium catalysts, $Pd(PPh_3)_4$ gave the best result rather than $Pd(PPh_3)_2Cl_2$, $Pd_2(dba)_3$, or Pd/C. The solvent screening revealed that *N*,*N*-dimethylformamide–water mixture was the most appropriate solvent. In the absence of water the reaction failed to convert **16aa** into any cyclized product; the detailed role of water was investigated in our previous work which showed that water mainly ionized the sodium formate molecule,



Scheme 1 Various approaches towards the synthesis of benzothiazine dioxide



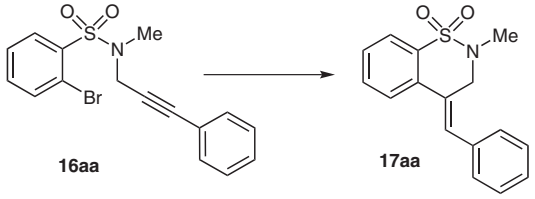
16aa, R^1 = Me, R^2 = H, 98%
16ab, R^1 = Me, R^2 = Me, 98%
16ac, R^1 = Me, R^2 = OMe, 95%
16ad, R^1 = Me, R^2 = OEt, 96%
16ae, R^1 = Me, R^2 = OBn, 95%
16ba, R^1 = Et, R^2 = H, 97%
16bb, R^1 = Et, R^2 = Me, 98%
16bc, R^1 = Et, R^2 = OMe, 96%
16bd, R^1 = Et, R^2 = OEt, 95%
16be, R^1 = Et, R^2 = OBn, 97%
16ca, R^1 = Bn, R^2 = H, 96%
16cb, R^1 = Bn, R^2 = Me, 95%
16cc, R^1 = Bn, R^2 = OMe, 97%
16cd, R^1 = Bn, R^2 = OEt, 95%
16ce, R^1 = Bn, R^2 = OBn, 96%
16da, R^1 = CH_2Py, R^2 = H, 90%
16de, R^1 = CH_2Py, R^2 = OBn, 85%

Scheme 2 Synthesis of benzosultam precursors **16aa–de**. *Reagents and conditions*: (a) EtOH, reflux, 2 h; (b) propargyl bromide (2 equiv), MEK, K_2CO_3, NaI, reflux, 4 h; (c) $Pd(PPh_3)_2Cl_2$ (5 mol%), CuI (12 mol%), Et_3N, THF, r.t., 8 h.

thereby acting as hydride ion source.[15d] The catalyst loading was also optimized and the reaction of **16aa** to **17aa** proceeded smoothly with 4 mol% $Pd(PPh_3)_4$ catalyst and was complete within one hour at 100 °C. At low catalyst loading, **16aa** was not fully converted into **17aa** in one hour. Increasing the time or temperature lead to decomposition of the product and a lower yield of compound **17aa** was obtained. Treatment of compound **16aa** (100 mg, 0.27 mmol) with $Pd(PPh_3)_4$ (4 mol%) and sodium formate (28 mg, 0.41 mmol) in *N*,*N*-dimethylformamide–water (7:3, 3 mL) under the optimized conditions afforded compound **17aa** (72 mg, 92%) as the only identified product.

The sole product obtained after treatment of compound **16aa** under the optimized conditions showed one extra aromatic proton in its ^1H NMR and in the ^{13}C NMR there was no peak found for acetylenic carbon atoms. This result confirmed that the product obtained from **16aa** was cyclized and the HRMS value of the synthesized compound was 308.0716, which also matched well with the theoretical value of cyclized product 308.0716 for $[M + Na]^+$. The remaining question concerns the regioselectivity: is the product formed (*Z*)-**17aa**, (*E*)-**17aa** or **17aa'**? If the cyclization

Table 1 Optimization of the Synthesis of Benzosultam **17aa** by Palladium-Catalyzed Hydrocarbonation of Alkynes



Entry	Catalyst[a]	Solvent	Time	Temp (°C)	Yield (%)
1	$Pd(PPh_3)_2Cl_2$ (5 mol%)[b]	DMF–H_2O (7:3)	2 h	100	trace
2	Pd/C (5 mol%)[b]	DMF–H_2O (7:3)	2 h	100	–[c]
3	$Pd_2(dba)_3$ (5 mol%)	DMF–H_2O (7:3)	2 h	100	10
4	$Pd_2(dba)_3$ (10 mol%)	DMF–H_2O (7:3)	2 h	100	15
5	$Pd_2(dba)_3$ (10 mol%)	DMF–H_2O (7:3)	4 h	120	–[d]
6	$Pd(PPh_3)_4$ (4 mol%)	DMF–H_2O (7:3)	2 h	100	88
7	**$Pd(PPh_3)_4$ (4 mol%)**	**DMF–H_2O (7:3)**	**1 h**	**100**	**92**
8	$Pd(PPh_3)_4$ (3 mol%)	DMF–H_2O (7:3)	1 h	100	84
9	$Pd(PPh_3)_4$ (4 mol%)	DMF–H_2O (7:3)	30 min	120	70
10	$Pd(PPh_3)_4$ (4 mol%)	DMF	1 h	100	–[c]

[a] In all cases HCOONa (1.5 equiv) were used.
[b] Ph_3P (15 mol%) was used as additive.
[c] No product.
[d] Complex mixture.

passed through a 7-*endo*-*dig* process then compound **17aa'** would be formed, and if the cyclization went through a 6-*exo*-*dig* mode then (*Z*)-**17aa** or (*E*)-**17aa** would be formed (Scheme 3).

Finally, the structure was confirmed by X-ray data and it showed that the structure of the product obtained from **16aa** was (*Z*)-**17aa**[17] [Figure 2 (a)].

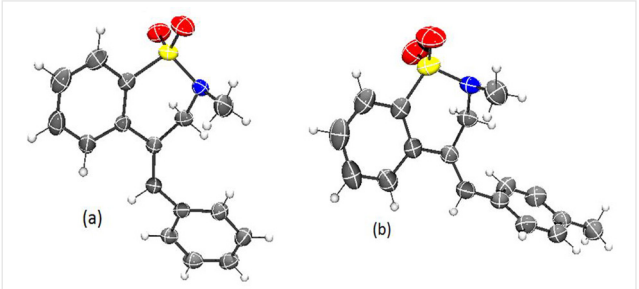
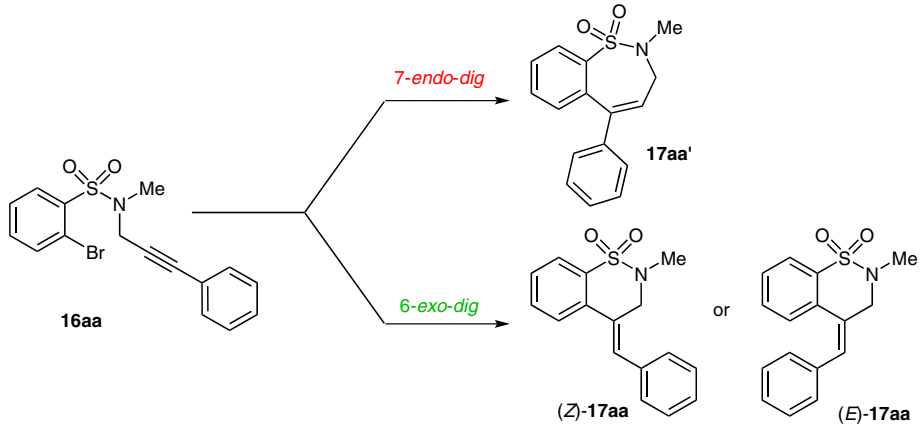


Figure 2 ORTEP diagram of benzosultams (a) **17aa** (b) **17ab** (the thermal ellipsoid are drawn at the 50% probability level)

To identify the reasons for the selectivity observed in this cyclization, the energies of both the transition states (7-*endo*-*dig* and 6-*exo*-*dig*) were calculated by DFT. Optimized geometry coordinates are given in the Supporting In-



Scheme 3 Different cyclization modes

formation. For the 6-*exo-dig* cyclization mode, the reaction passed through a lower activation energy barrier (6.38 kcal/mol) than that of the 7-*endo-dig* mode (Figure 3).

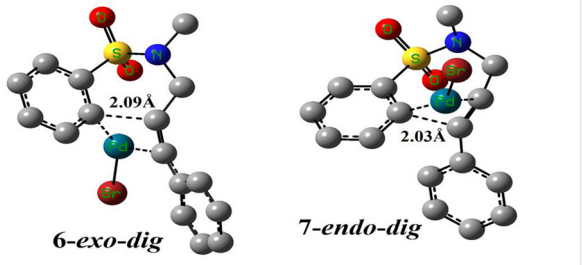


Figure 3 Optimized structure of transition states for 6-*exo-dig* and 7-*endo-dig* mode of cyclizations; hydrogen atoms are omitted for clarity

Therefore, the theoretical results of the two possible pathways are well matched with the experimental results, i.e. compound **17aa** was obtained solely from sulfonamide **16aa**. DFT calculations showed that the energy of (*E*)-**17aa** is lower than that of (*Z*)-**17aa** by 10.28 kcal/mol. A possible explanation for this may be that two distinct paths can exist for the 6-*exo-dig* cyclization: one leading to the (*Z*)-carbopalladation product and another, more energy demanding, leading to the (*E*)-carbopalladation product. When the carbon and palladium of the C–Pd bond interact with acetylenic carbon atoms from the same side, this leads to (*Z*)-**17aa**; from the opposite side, which is geometrically unfavorable, this would lead to (*E*)-**17aa**. Therefore, the formation of product (*E*)-**17aa** by this route is not possible, although it is energetically stable (Figure 4).

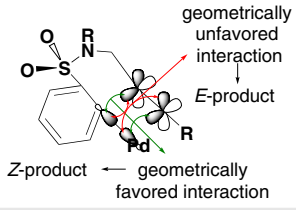


Figure 4 Geometrically favored and unfavored interactions in the 6-*exo-dig* mode of cyclization

After standardization of the synthesis of benzothiazine dioxide **17aa**, we prepared 17 examples of benzothiazine dioxide derivatives (**17aa**–**de**; Figure 5) to explore the scope of the reaction.

The single-crystal X-ray diffraction analysis for benzosultams **17ab**[18] was also obtained to further confirm the structure [Figure 2 (b)].

In summary, an efficient route is achieved for the synthesis of benzothiazine dioxide derivatives, i.e. benzosultams, based on the palladium-catalyzed hydrocarbonation of alkynes. This synthetic method is an efficient and convergent route for the preparation of benzo-δ-sultams and it should become widely acceptable to the synthetic organic community due to its mildness, high efficiency, and regioselectivity. The possible reasons for the regioselectivity of the palladium-catalyzed hydrocarbonation of alkynes and stereoselectivity of the exocyclic double bond in the synthesized compounds are explained by density functional theory calculations. The structure of benzothiazine dioxide derivatives were also confirmed by single-crystal X-ray diffraction data.

The reactions sensitive to air or moisture were carried out under a N_2 atmosphere using dry solvents, unless otherwise noted. Column chromatography was performed on silica gel (60–120 mesh); petroleum ether = PE. Reaction progress was monitored by TLC. TLC plates were visualized with UV light (256 nm) and in an iodine chamber. IR spectra were recorded using KBr discs. Melting points were recorded in open capillaries and are uncorrected.

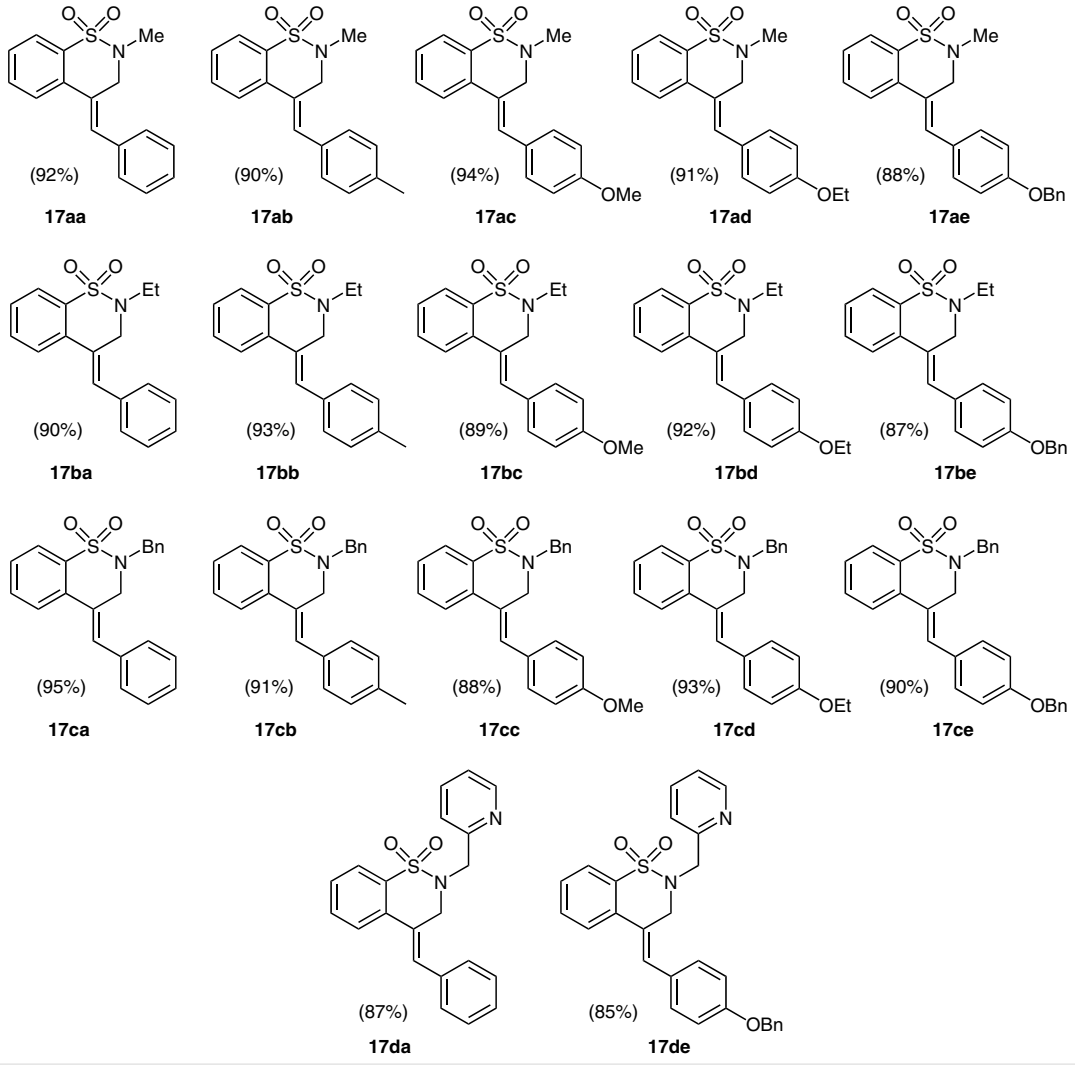


Figure 5 Summarized results of benzosultams

HRMS were recorded on a QTOF instrument. All ^{1}H and ^{13}C NMR spectra were recorded in 400 and 100 MHz spectrometer, respectively, relative to internal $CHCl_3$ (^{1}H, δ = 7.26) and $CDCl_3$ (^{13}C NMR, δ = 77.16).

2-Bromo-*N*-methylbenzenesulfonamide (20a); Typical Procedure

To a solution of commercially available 2-bromobenzenesulfonyl chloride (**18**, 500 mg, 1.96 mmol) in EtOH (20 mL), $MeNH_2$ (0.7 mL, 7.83 mmol) was added and the mixture was refluxed for 2 h. The residual solvent was evaporated under reduced pressure and the crude product obtained was purified by column chromatography (10% EtOAc–PE) to afford **20a**[12] (484 mg, 99%) as a white solid; mp 99–101 °C; R_f = 0.20 (10% EtOAc–PE).

2-Bromo-*N*-ethylbenzenesulfonamide (20b)

Prepared following the typical procedure for **20a** using **18** (500 mg, 1.96 mmol), EtOH (20 mL), and $EtNH_2$ (0.7 mL, 7.83 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **20b** (512 mg, 99%) as a white solid; mp 90–92 °C; R_f = 0.25 (10% EtOAc–PE).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (dd, *J* = 8.0, 2.0 Hz, 1 H), 7.72 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.48–7.38 (m, 2 H), 5.15 (br s, 1 H), 2.99–2.92 (m, 2 H), 1.08 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.9, 135.1, 133.8, 131.7, 127.9, 119.7, 38.5, 15.0.

Anal. Calcd for $C_8H_{10}BrNO_2S$: C, 36.38; H, 3.82; N, 5.30. Found: C, 36.69; H, 3.96; N, 5.03.

***N*-Benzyl-2-bromobenzenesulfonamide (20c)**

Prepared following the typical procedure for **20a** using **18** (500 mg, 1.96 mmol), EtOH (20 mL), and $BnNH_2$ (315 mg, 2.93 mmol). The product was purified by column chromatography (5% EtOAc–PE) to yield **20c** (619 mg, 97%) as a white solid; mp 94–96 °C; R_f = 0.30 (10% EtOAc–PE).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (dd, *J* = 7.8, 1.9 Hz, 1 H), 7.69 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.45 (td, *J* = 7.5, 1.3 Hz, 1 H), 7.39 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.27–7.17 (m, 5 H), 5.42 (t, *J* = 5.6 Hz, 1 H), 4.10 (d, *J* = 6.2 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.0, 135.8, 135.1, 133.8, 131.8, 128.8, 128.1, 128.1, 128.0, 119.8, 47.7.

Anal. Calcd for $C_{13}H_{12}BrNO_2S$: C, 47.86; H, 3.71; N, 4.29. Found: C, 48.13; H, 3.50; N, 4.43.

2-Bromo-*N*-(pyridin-2-ylmethyl)benzenesulfonamide (20d)

Prepared following the typical procedure for **20a** using **18** (200 mg, 0.78 mmol), EtOH (10 mL), and pyridin-2-ylmethanamine (127 mg, 1.17 mmol). The product was purified by column chromatography (30% EtOAc–PE) to yield **20d** (233 mg, 95%) as a white solid; mp 110–112 °C; R_f = 0.30 (30% EtOAc–PE).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48–8.44 (m, 1 H), 8.13–8.10 (m, 1 H), 7.66–7.62 (m, 1 H), 7.59–7.54 (m, 1 H), 7.44–7.39 (m, 1 H), 7.36–7.32 (m, 1 H), 7.16–7.12 (m, 2 H), 6.45–6.43 (m, 1 H), 4.23 (d, *J* = 5.4 Hz, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 154.7, 149.3, 138.8, 136.8, 135.2, 133.7, 131.7, 127.7, 122.8, 121.9, 120.2, 48.0.

Anal. Calcd for $C_{12}H_{11}BrN_2O_2S$: C, 44.05; H, 3.39; N, 8.56. Found: C, 44.34; H, 3.21; N, 8.45.

2-Bromo-*N*-methyl-*N*-(prop-2-ynyl)benzenesulfonamide (21a); Typical Procedure

To a solution of **20a** (400 mg, 1.60 mmol) in MEK (10 mL), K_2CO_3 (1.10 g, 7.99 mmol) and a catalytic amount of NaI (5 mg) were added. Then propargyl bromide (0.28 mL, 3.20 mmol) was added and the mixture was refluxed for 4 h. The residual solvent was evaporated under reduced pressure and the crude product obtained was purified by column chromatography (10% EtOAc–PE) to afford **21a** (452 mg, 98%) as a colorless gummy liquid; R_f = 0.25 (10% EtOAc–PE).

IR (KBr): 3279, 2343, 1153, 1011 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11 (dd, *J* = 7.8, 1.8 Hz, 1 H), 7.74 (dd, *J* = 7.7, 1.2 Hz, 1 H), 7.45 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.38 (td, *J* = 7.8, 1.9 Hz, 1 H), 4.14 (d, *J* = 2.4 Hz, 2 H), 2.94 (s, 3 H), 2.23 (t, *J* = 2.4 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.2, 135.8, 133.8, 132.4, 127.6, 120.7, 77.3, 73.7, 39.6, 34.4.

Anal. Calcd for $C_{10}H_{10}BrNO_2S$: C, 41.68; H, 3.50; N, 4.86. Found: C, 41.39; H, 3.69; N, 4.98.

2-Bromo-*N*-ethyl-*N*-(prop-2-ynyl)benzenesulfonamide (21b)

Prepared following the typical procedure for **21a** using **20b** (400 mg, 1.51 mmol), MEK (10 mL), NaI (5 mg), and propargyl bromide (0.27 mL, 3.03 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **21b** (448 mg, 98%) as a colorless gummy liquid; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 3280, 2338, 1161, 1027 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.12 (dd, *J* = 7.7, 1.7 Hz, 1 H), 7.72 (dt, *J* = 7.8, 1.3 Hz, 1 H), 7.43 (td, *J* = 7.5, 1.4 Hz, 1 H), 7.37 (td, *J* = 7.6, 1.9 Hz, 1 H), 4.20 (d, *J* = 2.5 Hz, 2 H), 3.44 (q, *J* = 7.2 Hz, 2 H), 2.20 (t, *J* = 2.4 Hz, 1 H), 1.14 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.1, 135.7, 133.7, 132.2, 127.6, 120.6, 77.6, 73.3, 41.7, 35.8, 13.1.

Anal. Calcd for $C_{11}H_{12}BrNO_2S$: C, 43.72; H, 4.00; N, 4.64. Found: C, 44.07; H, 3.88; N, 4.41.

***N*-Benzyl-2-bromo-*N*-(prop-2-ynyl)benzenesulfonamide (21c)**

Prepared following the typical procedure for **21a** using **20c** (400 mg, 1.23 mmol), MEK (10 mL), NaI (5 mg), and propargyl bromide (0.22 mL, 2.45 mmol). The product was purified by column chromatography (5% EtOAc–PE) to yield **21c** (424 mg, 95%) as a colorless gummy liquid; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 3282, 2343, 1151, 1050 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (dd, *J* = 7.7, 1.9 Hz, 1 H), 7.77 (dd, *J* = 7.6, 1.4 Hz, 1 H), 7.48–7.39 (m, 2 H), 7.34–7.26 (m, 5 H), 4.59 (s, 2 H), 3.99 (d, *J* = 2.4 Hz, 2 H), 2.19 (t, *J* = 2.5 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.1, 135.8, 135.0, 133.9, 132.4, 128.9, 128.8, 128.2, 127.7, 120.8, 77.0, 73.8, 50.7, 35.7.

Anal. Calcd for $C_{16}H_{14}BrNO_2S$: C, 52.76; H, 3.87; N, 3.85. Found: C, 52.94; H, 4.04; N, 3.69.

2-Bromo-*N*-(prop-2-ynyl)-*N*-(pyridin-2-ylmethyl)benzenesulfonamide (21d)

Prepared following the typical procedure for **21a** using **20d** (200 mg, 0.61 mmol), MEK (10 mL), NaI (5 mg), and propargyl bromide (0.11 mL, 1.22 mmol). The product was purified by column chromatography (20% EtOAc–PE) to yield **21d** (212 mg, 95%) as a reddish gummy liquid; R_f = 0.35 (30% EtOAc–PE).

IR (KBr): 3282, 2346, 1153, 1054 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.54–8.52 (m, 1 H), 8.17 (dd, *J* = 7.8, 1.8 Hz, 1 H), 7.74 (dd, *J* = 7.8, 1.4 Hz, 1 H), 7.66 (td, *J* = 7.6, 1.7 Hz, 1 H), 7.47–7.37 (m, 3 H), 7.21–7.17 (m, 1 H), 4.80 (s, 2 H), 4.16 (d, *J* = 2.4 Hz, 2 H), 2.13 (t, *J* = 2.5 Hz, 1 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.2, 149.6, 139.1, 137.1, 135.8, 133.9, 132.4, 127.7, 122.8, 122.5, 120.8, 76.9, 73.8, 52.8, 37.0.

Anal. Calcd for $C_{15}H_{13}BrN_2O_2S$: C, 49.33; H, 3.59; N, 7.67. Found: C, 49.57; H, 3.70; N, 7.54.

2-Bromo-*N*-methyl-*N*-(3-phenylprop-2-ynyl)benzenesulfonamide (16aa); Typical Procedure

N_2 gas was bubbled through a solution of **21a** (100 mg, 0.35 mmol) and Et_3N (1 mL) in anhyd THF (3 mL) for 10 min. Then catalyst $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%) and co-catalyst CuI (8 mg, 12 mol%) were added to the mixture and it was stirred for a further 10 min. Iodobenzene (78 mg, 0.38 mmol) was then added and the mixture was stirred for 8 h at r.t. under N_2. Most of the solvent and Et_3N were removed under reduced pressure and the residue was subjected to chromatography (silica gel, 10% EtOAc–PE) to afford **16aa** (124 mg, 98%) as a colorless gummy liquid; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 2350, 2235, 1165, 1014 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (dd, *J* = 7.9, 1.8 Hz, 1 H), 7.73 (dd, *J* = 7.7, 1.1 Hz, 1 H), 7.44 (td, *J* = 7.6, 1.1 Hz, 1 H), 7.36 (td, *J* = 7.6, 1.7 Hz, 1 H), 7.31–7.27 (m, 5 H), 4.36 (s, 2 H), 3.03 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.5, 135.9, 133.7, 132.5, 131.8, 128.7, 128.4, 127.6, 122.4, 120.7, 85.6, 82.4, 40.5, 34.7.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{16}H_{14}BrNNaO_2S$: 385.9821/387.9801; found: 385.9824/387.9803.

2-Bromo-*N*-methyl-*N*-(3-*p*-tolylprop-2-ynyl)benzenesulfonamide (16ab)

Prepared following the typical procedure for **16aa** using **21a** (100 mg, 0.35 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%), co-catalyst CuI (8 mg, 12 mol%), and 1-iodo-4-methylbenzene (83 mg, 0.38 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **16ab** (128 mg, 98%) as a reddish gummy liquid; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 2344, 2230, 1160, 1012 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (dd, J = 7.9, 1.8 Hz, 1 H), 7.72 (dd, J = 7.8, 1.1 Hz, 1 H), 7.43 (td, J = 7.5, 1.1 Hz, 1 H), 7.35 (td, J = 7.8, 1.8 Hz, 1 H), 7.19 (d, J = 8.1 Hz, 2 H), 7.08 (d, J = 8.0 Hz, 2 H), 4.35 (s, 2 H), 3.03 (s, 3 H), 2.33 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.8, 138.5, 135.9, 133.7, 132.5, 131.7, 129.1, 127.6, 120.8, 85.7, 81.7, 40.5, 34.7, 21.6.

Anal. Calcd for $C_{17}H_{16}BrNO_2S$: C, 53.98; H, 4.26; N, 3.70. Found: C, 54.29; H, 4.43; N, 3.42.

2-Bromo-*N*-[3-(4-methoxyphenyl)prop-2-ynyl]-*N*-methylbenzenesulfonamide (16ac)

Prepared following the typical procedure for **16aa** using **21a** (100 mg, 0.35 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%), co-catalyst CuI (8 mg, 12 mol%), and 1-iodo-4-methoxybenzene (89 mg, 0.38 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **16ac** (130 mg, 95%) as a reddish gummy liquid; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 2343, 2229, 1163, 1017 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (dd, J = 7.8, 1.7 Hz, 1 H), 7.72 (dd, J = 7.8, 1.4 Hz, 1 H), 7.43 (td, J = 7.6, 1.3 Hz, 1 H), 7.36 (td, J = 7.7, 1.8 Hz, 1 H), 7.25–7.22 (m, 2 H), 6.80 (dt, J = 8.9, 2.2 Hz, 2 H), 4.34 (s, 2 H), 3.80 (s, 3 H), 3.03 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 138.6, 135.9, 133.7, 133.3, 132.5, 127.6, 120.8, 114.5, 114.0, 85.5, 81.0, 55.4, 40.6, 34.7.

Anal. Calcd for $C_{17}H_{16}BrNO_3S$: C, 51.79; H, 4.09; N, 3.55. Found: C, 51.60; H, 4.21; N, 3.82.

2-Bromo-*N*-[3-(4-ethoxyphenyl)prop-2-ynyl]-*N*-methylbenzenesulfonamide (16ad)

Prepared following the typical procedure for **16aa** using **21a** (100 mg, 0.35 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%), co-catalyst CuI (8 mg, 12 mol%), and 1-ethoxy-4-iodobenzene (95 mg, 0.38 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **16ad** (136 mg, 96%) as a reddish gummy liquid; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 2344, 2226, 1167, 1021 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (dd, J = 7.8, 1.7 Hz, 1 H), 7.72 (dd, J = 7.8, 1.2 Hz, 1 H), 7.43 (td, J = 7.6, 1.2 Hz, 1 H), 7.35 (td, J = 7.8, 1.8 Hz, 1 H), 7.22 (dt, J = 8.8, 2.0 Hz, 2 H), 6.79 (dt, J = 8.8, 2.0 Hz, 2 H), 4.34 (s, 2 H), 4.02 (q, J = 7.0 Hz, 2 H), 3.02 (s, 3 H), 1.40 (t, J = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 138.6, 135.9, 133.7, 133.3, 132.4, 127.6, 120.8, 114.5, 114.3, 85.6, 80.9, 63.7, 40.6, 34.7, 14.9.

Anal. Calcd for $C_{18}H_{18}BrNO_3S$: C, 52.95; H, 4.44; N, 3.43. Found: C, 52.72; H, 4.28; N, 3.72.

N-{3-[4-(Benzyloxy)phenyl]prop-2-ynyl}-2-bromo-*N*-methylbenzenesulfonamide (16ae)

Prepared following the typical procedure for **16aa** using **21a** (100 mg, 0.35 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%), co-catalyst CuI (8 mg, 12 mol%), and 1-(benzyloxy)-4-iodobenzene (118 mg, 0.38 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **16ae** (155 mg, 95%) as a reddish gummy liquid; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 2343, 2229, 1163, 1015 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.14 (dd, J = 7.9, 1.7 Hz, 1 H), 7.72 (dd, J = 7.9, 1.2 Hz, 1 H), 7.45–7.33 (m, 7 H), 7.24 (dt, J = 8.8, 1.8 Hz, 2 H), 6.88 (dt, J = 8.8, 1.9 Hz, 2 H), 5.05 (s, 2 H), 4.35 (s, 2 H), 3.03 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 138.4, 136.6, 135.8, 133.7, 133.3, 132.4, 128.7, 128.2, 127.6, 127.5, 120.7, 114.9, 114.7, 85.4, 81.0, 70.1, 40.5, 34.7.

Anal. Calcd for $C_{23}H_{20}BrNO_3S$: C, 58.73; H, 4.29; N, 2.98. Found: C, 58.96; H, 4.48; N, 2.80.

2-Bromo-*N*-ethyl-*N*-(3-phenylprop-2-ynyl)benzenesulfonamide (16ba)

Prepared following the typical procedure for **16aa** using **21b** (100 mg, 0.33 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%), co-catalyst CuI (7 mg, 12 mol%), and iodobenzene (74 mg, 0.36 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **16ba** (121 mg, 97%) as a colorless gummy liquid; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 2232, 1161, 1024 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (dd, J = 7.8, 1.6 Hz, 1 H), 7.71 (dd, J = 7.9, 1.3 Hz, 1 H), 7.43 (td, J = 7.5, 1.1 Hz, 1 H), 7.37–7.26 (m, 6 H), 4.42 (s, 2 H), 3.54 (q, J = 7.2 Hz, 2 H), 1.22 (t, J = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.4, 135.8, 133.6, 132.3, 131.8, 128.6, 128.4, 127.6, 122.5, 120.7, 85.1, 82.8, 42.1, 36.7, 13.4.

Anal. Calcd for $C_{17}H_{16}BrNO_2S$: C, 53.98; H, 4.26; N, 3.70. Found: C, 54.24; H, 4.07; N, 3.65.

2-Bromo-*N*-ethyl-*N*-(3-*p*-tolylprop-2-ynyl)benzenesulfonamide (16bb)

Prepared following the typical procedure for **16aa** using **21b** (100 mg, 0.33 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%), co-catalyst CuI (7 mg, 12 mol%), and 1-iodo-4-methylbenzene (79 mg, 0.36 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **16bb** (127 mg, 98%) as a colorless gummy liquid; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 2227, 1165, 1026 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16 (dd, J = 7.9, 1.8 Hz, 1 H), 7.71 (dd, J = 7.8, 1.2 Hz, 1 H), 7.42 (td, J = 7.6, 1.4 Hz, 1 H), 7.34 (td, J = 7.5, 1.9 Hz, 1 H), 7.20–7.17 (m, 2 H), 7.09–7.07 (m, 2 H), 4.41 (s, 2 H), 3.54 (q, J = 7.1 Hz, 2 H), 2.33 (s, 3 H), 1.22 (t, J = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.4, 138.8, 135.8, 133.6, 132.3, 131.7, 129.1, 127.6, 120.7, 119.4, 85.3, 82.1, 42.0, 36.7, 21.6, 13.4.

HRMS (ESI$^+$): m/z [M + Na]$^+$ calcd for $C_{18}H_{18}BrNNaO_2S$: 414.0134/416.0114; found: 414.0138/416.0116.

2-Bromo-*N*-ethyl-*N*-[3-(4-methoxyphenyl)prop-2-ynyl]benzenesulfonamide (16bc)

Prepared following the typical procedure for **16aa** using **21b** (100 mg, 0.33 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%), co-catalyst CuI (7 mg, 12 mol%), and 1-iodo-4-methoxyben-

zene (85 mg, 0.36 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **16bc** (130 mg, 96%) as a reddish gummy liquid; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 2345, 2227, 1161, 1027 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.15 (dd, *J* = 7.9, 1.8 Hz, 1 H), 7.71 (dd, *J* = 7.9, 1.1 Hz, 1 H), 7.42 (td, *J* = 8.0, 1.0 Hz, 1 H), 7.34 (td, *J* = 7.8, 1.9 Hz, 1 H), 7.23 (dt, *J* = 8.9, 2.1 Hz, 2 H), 6.80 (dt, *J* = 8.9, 2.0 Hz, 2 H), 4.40 (s, 2 H), 3.80 (s, 3 H), 3.53 (q, *J* = 7.1 Hz, 2 H), 1.1 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 139.4, 135.8, 133.5, 133.3, 132.3, 127.6, 120.7, 114.6, 114.0, 85.0, 81.4, 55.4, 42.0, 36.7, 13.4.

Anal. Calcd for $C_{18}H_{18}BrNO_3S$: C, 52.95; H, 4.44; N, 3.43. Found: C, 52.77; H, 4.30; N, 3.64.

2-Bromo-*N*-[3-(4-ethoxyphenyl)prop-2-ynyl]-*N*-ethylbenzenesulfonamide (16bd)

Prepared following the typical procedure for **16aa** using **21b** (100 mg, 0.33 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%), co-catalyst CuI (7 mg, 12 mol%), and 1-ethoxy-4-iodobenzene (90 mg, 0.36 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **16bd** (133 mg, 95%) as a reddish gummy liquid; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 2343, 2225, 1161, 1029 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.15 (dd, *J* = 7.9, 1.8 Hz, 1 H), 7.71 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.42 (td, *J* = 7.6, 1.4 Hz, 1 H), 7.34 (td, *J* = 7.6, 1.6 Hz, 1 H), 7.21 (dt, *J* = 8.7, 2.0 Hz, 2 H), 6.78 (dt, *J* = 8.8, 2.0 Hz, 2 H), 4.39 (s, 2 H), 4.01 (q, *J* = 7.0 Hz, 2 H), 3.53 (q, *J* = 7.1 Hz, 2 H), 1.40 (t, *J* = 7.0 Hz, 3 H), 1.21 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 139.4, 135.7, 133.5, 133.3, 132.2, 127.6, 120.7, 114.5, 114.3, 85.1, 81.3, 63.7, 42.0, 36.7, 14.9, 13.4.

Anal. Calcd for $C_{19}H_{20}BrNO_3S$: C, 54.03; H, 4.77; N, 3.32. Found: C, 54.33; H, 4.54; N, 3.49.

N-{3-[4-(Benzyloxy)phenyl]prop-2-ynyl}-2-bromo-*N*-ethylbenzenesulfonamide (16be)

Prepared following the typical procedure for **16aa** using **21b** (100 mg, 0.33 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (12 mg, 5 mol%), co-catalyst CuI (7 mg, 12 mol%), and 1-(benzyloxy)-4-iodobenzene (113 mg, 0.36 mmol). The product was purified by column chromatography (10% EtOAc–PE) to yield **16be** (155 mg, 97%) as a reddish gummy liquid; R_f = 0.40 (10% EtOAc–PE).

IR (KBr): 2344, 2225, 1160, 1019 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (dd, *J* = 7.8, 1.7 Hz, 1 H), 7.71 (dd, *J* = 7.9, 1.2 Hz, 1 H), 7.44–7.32 (m, 7 H), 7.23 (td, *J* = 8.8, 1.9 Hz, 2 H), 6.88 (td, *J* = 8.8, 2.0 Hz, 2 H), 5.05 (s, 2 H), 4.40 (s, 2 H), 3.52 (q, *J* = 7.1 Hz, 2 H), 1.21 (t, *J* = 7.1 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 139.4, 136.6, 135.7, 133.5, 133.3, 132.3, 128.8, 128.3, 127.6, 120.7, 114.9, 114.8, 85.0, 81.5, 70.2, 42.0, 36.7, 13.4.

Anal. Calcd for $C_{24}H_{22}BrNO_3S$: C, 59.51; H, 4.58; N, 2.89. Found: C, 59.26; H, 4.74; N, 2.76.

N-Benzyl-2-bromo-*N*-(3-phenylprop-2-ynyl)benzenesulfonamide (16ca)

Prepared following the typical procedure for **16aa** using **21c** (100 mg, 0.27 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (10 mg, 5 mol%), co-catalyst CuI (6 mg, 12 mol%), and iodobenzene (62 mg, 0.30 mmol). The product was purified by column chromatography (5% EtOAc–PE) to yield **16ca** (116 mg, 96%) as a reddish gummy liquid; R_f = 0.40 (10% EtOAc–PE).

IR (KBr): 2344, 2230, 1150, 1051 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (dd, *J* = 7.8, 1.6 Hz, 1 H), 7.74 (dd, *J* = 7.9, 1.2 Hz, 1 H), 7.44 (td, *J* = 7.6, 1.1 Hz, 1 H), 7.39–7.25 (m, 11 H), 4.69 (s, 2 H), 4.20 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.3, 135.8, 135.4, 133.8, 132.5, 131.8, 128.9, 128.9, 128.7, 128.4, 128.2, 127.7, 122.4, 120.9, 85.6, 82.3, 51.2, 36.6.

Anal. Calcd for $C_{22}H_{18}BrNO_2S$: C, 60.01; H, 4.12; N, 3.18. Found: C, 60.29; H, 4.25; N, 2.99.

N-Benzyl-2-bromo-*N*-(3-*p*-tolylprop-2-ynyl)benzenesulfonamide (16cb)

Prepared following the typical procedure for **16aa** using **21c** (100 mg, 0.27 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (10 mg, 5 mol%), co-catalyst CuI (6 mg, 12 mol%), and 1-iodo-4-methylbenzene (66 mg, 0.30 mmol). The product was purified by column chromatography (5% EtOAc–PE) to yield **16cb** (118 mg, 95%) as a reddish gummy liquid; R_f = 0.40 (10% EtOAc–PE).

IR (KBr): 2339, 2227, 1150, 1050 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (dd, *J* = 7.9, 1.7 Hz, 1 H), 7.74 (dd, *J* = 7.7, 1.1 Hz, 1 H), 7.44 (td, *J* = 7.6, 1.0 Hz, 1 H), 7.38–7.28 (m, 6 H), 7.17 (d, *J* = 8.0 Hz, 2 H), 7.09 (d, *J* = 8.0 Hz, 2 H), 4.69 (s, 2 H), 4.19 (s, 2 H), 2.35 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 139.4, 138.9, 135.8, 135.5, 133.7, 132.5, 131.7, 129.1, 128.9, 128.9, 128.2, 127.7, 120.9, 119.3, 85.8, 81.5, 51.2, 36.7, 21.6.

Anal. Calcd for $C_{23}H_{20}BrNO_2S$: C, 60.80; H, 4.44; N, 3.08. Found: C, 61.02; H, 4.28; N, 3.32.

N-Benzyl-2-bromo-*N*-[3-(4-methoxyphenyl)prop-2-ynyl]benzenesulfonamide (16cc)

Prepared following the typical procedure for **16aa** using **21c** (100 mg, 0.27 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (10 mg, 5 mol%), co-catalyst CuI (6 mg, 12 mol%), and 1-iodo-4-methoxybenzene (71 mg, 0.30 mmol). The product was purified by column chromatography (5% EtOAc–PE) to yield **16cc** (125 mg, 97%) as a colorless gummy liquid; R_f = 0.40 (10% EtOAc–PE).

IR (KBr): 2341, 2225, 1153, 1041 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (dd, *J* = 7.9, 1.8 Hz, 1 H), 7.74 (dd, *J* = 7.7, 1.1 Hz, 1 H), 7.44 (td, *J* =7.6, 1.3 Hz, 1 H), 7.38–7.29 (m, 6 H), 7.21 (dt, *J* = 8.9, 2.0 Hz, 2 H), 6.81 (dt, *J* = 8.9, 2.0 Hz, 2 H), 4.68 (s, 2 H), 4.18 (s, 2 H), 3.81 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.9, 139.4, 135.8, 135.5, 133.7, 133.3, 132.5, 128.9, 128.8, 128.2, 127.7, 120.9, 114.5, 114.0, 85.6, 80.8, 55.4, 51.1, 36.7.

Anal. Calcd for $C_{23}H_{20}BrNO_3S$: C, 58.73; H, 4.29; N, 2.98. Found: C, 58.47; H, 4.42; N, 3.15.

N-Benzyl-2-bromo-*N*-[3-(4-ethoxyphenyl)prop-2-ynyl]benzenesulfonamide (16cd)

Prepared following the typical procedure for **16aa** using **21c** (100 mg, 0.27 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (10 mg, 5 mol%), co-catalyst CuI (6 mg, 12 mol%), and 1-ethoxy-4-iodobenzene

(75 mg, 0.30 mmol). The product was purified by column chromatography (5% EtOAc–PE) to yield **16cd** (126 mg, 95%) as a colorless gummy liquid; R_f = 0.40 (10% EtOAc–PE).

IR (KBr): 2343, 2225, 1147, 1047 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (dd, *J* = 7.8, 1.6 Hz, 1 H), 7.74 (dd, *J* = 7.8, 1.1 Hz, 1 H), 7.44 (td, *J* = 7.6, 1.3 Hz, 1 H), 7.38–7.29 (m, 6 H), 7.20 (dt, *J* = 8.9, 2.0 Hz, 2 H), 6.80 (dt, *J* = 8.8, 2.1 Hz, 2 H), 4.69 (s, 2 H), 4.05 (s, 2 H), 4.02 (q, *J* = 7.0 Hz, 2 H), 1.42 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.3, 139.3, 135.7, 135.5, 133.7, 133.2, 132.4, 128.8, 128.8, 128.2, 127.7, 120.8, 114.5, 114.2, 85.7, 80.7, 63.7, 51.1, 36.7, 29.8, 14.9.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{22}BrNNaO_3S$: 506.0396/508.0376; found: 506.0400/508.0373.

N-Benzyl-*N*-{3-{4-(benzyloxy)phenyl]prop-2-ynyl}-2-bromobenzenesulfonamide (16ce)

Prepared following the typical procedure for **16aa** using **21c** (100 mg, 0.27 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (10 mg, 5 mol%), co-catalyst CuI (6 mg, 12 mol%), and 1-(benzyloxy)-4-iodobenzene (94 mg, 0.30 mmol). The product was purified by column chromatography (5% EtOAc–PE) to yield **16ce** (144 mg, 96%) as a reddish gummy liquid; R_f = 0.50 (10% EtOAc–PE).

IR (KBr): 2345, 2226, 1150, 1028 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.20 (dd, *J* = 7.9, 1.6 Hz, 1 H), 7.74 (dd, *J* = 7.7, 1.1 Hz, 1 H), 7.46–7.29 (m, 12 H), 7.21 (td, *J* = 8.8, 1.9 Hz, 2 H), 6.89 (td, *J* = 8.7, 2.0 Hz, 2 H), 5.07 (s, 2 H), 4.68 (s, 2 H), 4.18 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 139.3, 136.6, 135.7, 135.5, 133.7, 133.3, 132.5, 128.9, 128.8, 128.8, 128.3, 128.2, 127.7, 127.6, 120.8, 114.9, 114.8, 85.5, 80.9, 70.2, 51.1, 36.7.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{29}H_{24}BrNNaO_3S$: 568.0552/570.0532; found: 568.0557, 570.0535.

2-Bromo-*N*-(3-phenylprop-2-ynyl)-*N*-(pyridin-2-ylmethyl)benzenesulfonamide (16da)

Prepared following the typical procedure for **16aa** using **21d** (100 mg, 0.27 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (10 mg, 5 mol%), co-catalyst CuI (6 mg, 12 mol%), and iodobenzene (61 mg, 0.30 mmol). The product was purified by column chromatography (20% EtOAc–PE) to yield **16da** (109 mg, 90%) as a reddish gummy liquid; R_f = 0.40 (30% EtOAc–PE).

IR (KBr): 2345, 2230, 1154, 1083 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.56–8.53 (m, 1 H), 8.21 (dd, *J* = 8.0, 1.6 Hz, 1 H), 7.72–7.66 (m, 2 H), 7.51 (d, *J* = 7.8 Hz, 1 H), 7.43 (td, *J* = 7.6, 1.2 Hz, 1 H), 7.34 (td, *J* = 7.7, 1.8 Hz, 1 H), 7.29–7.18 (m, 6 H), 4.90 (s, 2 H), 4.36 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 156.6, 149.5, 149.3, 137.1, 135.7, 133.8, 132.6, 131.8, 128.6, 128.3, 127.7, 122.8, 122.3, 122.3, 120.8, 85.5, 82.2, 53.3, 37.9.

Anal. Calcd for $C_{21}H_{17}BrN_2O_2S$: C, 57.15; H, 3.88; N, 6.35. Found: C, 57.35; H, 3.71; N, 6.24.

N-{3-[4-(Benzyloxy)phenyl]prop-2-ynyl}-2-bromo-*N*-(pyridin-2-ylmethyl)benzenesulfonamide (16de)

Prepared following the typical procedure for **16aa** using **21d** (100 mg, 0.27 mmol), Et_3N (1 mL), anhyd THF (3 mL), $Pd(PPh_3)_2Cl_2$ (10 mg, 5 mol%), co-catalyst CuI (6 mg, 12 mol%), and 1-(benzyloxy)-4-iodobenzene (93 mg, 0.30 mmol). The product was purified by column chromatography (20% EtOAc–PE) to yield **16de** (127 mg, 85%) as a reddish gummy liquid; R_f = 0.45 (30% EtOAc–PE).

IR (KBr): 2345, 2227, 1157, 1006 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.55–8.53 (m, 1 H), 8.20 (dd, *J* = 7.9, 1.6 Hz, 1 H), 7.72–7.67 (m, 2 H), 7.51 (d, *J* = 7.9 Hz, 1 H), 7.45–7.31 (m, 7 H), 7.22–7.18 (m, 1 H), 7.15 (dt, *J* = 8.8, 1.9 Hz, 2 H), 6.85 (dt, *J* = 8.8, 1.9 Hz, 2 H), 5.05 (s, 2 H), 4.90 (s, 2 H), 4.33 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 156.7, 149.5, 139.3, 137.1, 135.7, 133.7, 133.3, 132.5, 128.8, 128.3, 127.7, 127.6, 122.8, 122.3, 120.8, 114.8, 114.7, 85.4, 80.8, 70.2, 53.3, 38.0.

Anal. Calcd for $C_{28}H_{23}BrN_2O_3S$: C, 61.43; H, 4.23; N, 5.12. Found: C, 61.66; H, 4.36; N, 4.98.

(4*Z*)-4-Benzylidene-2-methyl-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17aa); Typical Procedure

To a mixture of **16aa** (100 mg, 0.27 mmol) and sodium formate (28 mg, 0.41 mmol) in DMF–H_2O (7:3, 3 mL), $Pd(PPh_3)_4$ (13 mg, 4 mol%) was added and the mixture was heated at 100 °C for 1 h. The mixture was cooled, H_2O (10 mL) was added, and it was extracted with EtOAc (3 × 10 mL). The combined EtOAc extracts were washed with H_2O (4 × 10 mL) and brine (10 mL), and dried (Na_2SO_4). The solvent was distilled off to furnish a viscous mass that was purified by column chromatography (silica gel, 10% EtOAc–PE) to give **17aa** (72 mg, 92%) as a white solid; mp 131–133 °C; R_f = 0.25 (10% EtOAc–PE).

IR (KBr): 1600, 1163, 1049 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.88–7.82 (m, 2 H), 7.57 (td, *J* = 7.6, 1.4 Hz, 1 H), 7.50–7.41 (m, 4 H), 7.37–7.33 (m, 1 H), 7.29–7.26 (m, 2 H), 4.67 (d, *J* = 1.3 Hz, 2 H), 2.70 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.5, 134.3, 133.3, 132.6, 131.9, 129.4, 129.1, 128.9, 128.4, 126.2, 125.6, 124.8, 52.0, 36.4.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{16}H_{15}NNaO_2S$: 308.0716; found: 308.0716.

(4*Z*)-2-Methyl-4-(4-methylbenzylidene)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17ab)

Prepared following the typical procedure for **17aa** using **16ab** (100 mg, 0.26 mmol), sodium formate (27 mg, 0.39 mmol), and $Pd(PPh_3)_4$ (12 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17ab** (71 mg, 90%) as a white solid; mp 132–134 °C; R_f = 0.25 (10% EtOAc–PE).

IR (KBr): 1590, 1160, 1047 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.80 (m, 2 H), 7.58–7.53 (m, 1 H), 7.48–7.42 (m, 2 H), 7.26–7.15 (m, 4 H), 4.67 (s, 2 H), 2.69 (s, 3 H), 2.39 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.5, 134.5, 133.2, 132.7, 132.5, 131.9, 129.6, 129.4, 128.9, 125.6, 125.4, 124.8, 52.1, 36.4, 21.4.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}NNaO_2S$: 322.0872; found: 322.0871.

(4*Z*)-4-(4-Methoxybenzylidene)-2-methyl-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17ac)

Prepared following the typical procedure for **17aa** using **16ac** (100 mg, 0.25 mmol), sodium formate (26 mg, 0.38 mmol), and $Pd(PPh_3)_4$ (12 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product

was purified by column chromatography (10% EtOAc–PE) to yield **17ac** (75 mg, 94%) as a white solid; mp 143–145 °C; R_f = 0.25 (10% EtOAc–PE).

IR (KBr): 1595, 1170, 1041 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.80 (d, *J* = 7.9 Hz, 1 H), 7.55 (td, *J* = 7.7, 1.4 Hz, 1 H), 7.47–7.42 (m, 1 H), 7.39 (s, 1 H), 7.25–7.20 (m, 2 H), 6.97–6.93 (m, 2 H), 4.68 (d, *J* = 1.1 Hz, 2 H), 3.85 (s, 3 H), 2.69 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 134.7, 132.9, 132.6, 131.6, 131.0, 128.7, 128.0, 125.5, 124.7, 124.5, 114.3, 55.5, 52.2, 36.5.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}NNaO_3S$: 338.0821; found: 338.0825.

(4*Z*)-4-(4-Ethoxybenzylidene)-2-methyl-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17ad)

Prepared following the typical procedure for **17aa** using **16ad** (100 mg, 0.24 mmol), sodium formate (25 mg, 0.37 mmol), and $Pd(PPh_3)_4$ (11 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17ad** (75 mg, 91%) as a reddish gummy liquid; R_f = 0.25 (10% EtOAc–PE).

IR (KBr): 1595, 1170, 1049 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.80 (d, *J* = 8.1 Hz, 1 H), 7.57–7.53 (m, 1 H), 7.46–7.42 (m, 1 H), 7.38 (s, 1 H), 7.23–7.19 (m, 2 H), 6.95–6.91 (m, 2 H), 4.68 (d, *J* = 1.0 Hz, 2 H), 4.08 (q, *J* = 7.0 Hz, 2 H), 2.69 (s, 3 H), 1.44 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 134.7, 133.0, 132.5, 131.7, 131.0, 128.6, 127.9, 125.5, 124.7, 124.4, 114.8, 63.7, 52.3, 36.5, 14.9.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{19}NNaO_3S$: 352.0978; found: 352.0980.

(4*Z*)-4-[4-(Benzyloxy)benzylidene]-2-methyl-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17ae)

Prepared following the typical procedure for **17aa** using **16ae** (100 mg, 0.21 mmol), sodium formate (22 mg, 0.32 mmol), and $Pd(PPh_3)_4$ (10 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17ae** (73 mg, 88%) as a white solid; mp 123–125 °C; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 1600, 1165, 1005 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.87–7.79 (m, 2 H), 7.58–7.53 (m, 1 H), 7.47–7.35 (m, 7 H), 7.26–7.22 (m, 2 H), 7.05–7.00 (m, 2 H), 5.11 (s, 2 H), 4.68 (s, 2 H), 2.70 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9, 136.7, 134.6, 133.0, 132.5, 131.5, 131.0, 128.8, 128.6, 128.3, 127.6, 125.5, 124.7, 124.5, 115.2, 70.2, 52.2, 36.5, 29.8.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{21}NNaO_3S$: 414.1134; found: 414.1134.

(4*Z*)-4-Benzylidene-2-ethyl-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17ba)

Prepared following the typical procedure for **17aa** using **16ba** (100 mg, 0.26 mmol), sodium formate (27 mg, 0.40 mmol), and $Pd(PPh_3)_4$ (12 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17ba** (71 mg, 90%) as white solid; mp 112–115 °C; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 1577, 1163, 1032 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (dd, *J* = 7.8, 1.1 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.55 (td, *J* = 7.8, 1.2 Hz, 1 H), 7.48–7.40 (m, 4 H), 7.38–7.34 (m, 1 H), 7.29 (d, *J* = 7.3 Hz, 2 H), 4.69 (d, *J* = 1.2 Hz, 2 H), 3.06 (q, *J* = 7.2 Hz, 2 H), 0.97 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.6, 134.6, 134.6, 132.5, 131.5, 129.3, 128.9, 128.9, 128.4, 126.7, 125.2, 124.9, 48.1, 43.2, 13.4.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{17}H_{17}NNaO_2S$: 322.0872; found: 322.0871.

(4*Z*)-2-Ethyl-4-(4-methylbenzylidene)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17bb)

Prepared following the typical procedure for **17aa** using **16bb** (100 mg, 0.25 mmol), sodium formate (26 mg, 0.38 mmol), and $Pd(PPh_3)_4$ (12 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17bb** (74 mg, 93%) as white solid; mp 109–111 °C; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 1614, 1159, 1028 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.86–7.77 (m, 2 H), 7.57–7.52 (m, 1 H), 7.46–7.38 (m, 2 H), 7.26–7.17 (m, 4 H), 4.69 (d, *J* = 1.0 Hz, 2 H), 3.05 (q, *J* = 7.2 Hz, 2 H), 2.39 (s, 3 H), 0.98 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.5, 134.8, 134.5, 132.7, 132.4, 131.6, 129.6, 129.3, 128.7, 125.9, 125.2, 124.8, 48.2, 43.2, 21.4, 13.4.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{19}NNaO_2S$: 336.1029; found: 336.1028.

(4*Z*)-2-Ethyl-4-(4-methoxybenzylidene)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17bc)

Prepared following the typical procedure for **17aa** using **16bc** (100 mg, 0.24 mmol), sodium formate (25 mg, 0.37 mmol), and $Pd(PPh_3)_4$ (11 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17bc** (72 mg, 89%) as white solid; mp 108–110 °C; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 1595, 1163, 1006 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (d, *J* = 7.6 Hz, 1 H), 7.77 (d, *J* = 8.0 Hz, 1 H), 7.53 (t, *J* = 7.3 Hz, 1 H), 7.43 (t, *J* = 7.5 Hz, 1 H), 7.36 (s, 1 H), 7.26–7.23 (m, 2 H), 6.95 (d, *J* = 8.5 Hz, 2 H), 4.70 (s, 2 H), 3.85 (s, 3 H), 3.05 (q, *J* = 7.1 Hz, 2 H), 0.99 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 135.0, 134.3, 132.4, 131.3, 130.9, 128.5, 128.1, 125.2, 125.1, 124.8, 114.3, 55.5, 48.3, 43.2, 13.4.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{18}H_{19}NNaO_3S$: 352.0978; found: 352.0981.

(4*Z*)-4-(4-Ethoxybenzylidene)-2-ethyl-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17bd)

Prepared following the typical procedure for **17aa** using **16bd** (100 mg, 0.24 mmol), sodium formate (24 mg, 0.35 mmol), and $Pd(PPh_3)_4$ (11 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17bd** (75 mg, 92%) as white solid; mp 97–100 °C; R_f = 0.30 (10% EtOAc–PE).

IR (KBr): 1600, 1160, 1016 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 7.84 (dd, *J* = 7.7, 1.2 Hz, 1 H), 7.77 (d, *J* = 7.9 Hz, 1 H), 7.53 (td, *J* = 7.6, 1.4 Hz, 1 H), 7.42 (td, *J* = 7.6, 0.8 Hz, 1 H), 7.35 (s, 1 H), 7.22 (d, *J* = 8.7 Hz, 2 H), 6.94 (dt, *J* = 8.7, 1.9 Hz, 2 H), 4.67 (d, *J* = 1.4 Hz, 2 H), 4.08 (q, *J* = 7.0 Hz, 2 H), 3.05 (q, *J* = 7.3 Hz, 2 H), 1.44 (t, *J* = 7.0 Hz, 3 H), 0.99 (t, *J* = 7.2 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.1, 135.0, 134.3, 132.4, 131.4, 130.9, 128.5, 128.0, 125.2, 124.9, 124.8, 114.7, 63.7, 48.2, 43.2, 14.9, 13.4.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{19}H_{21}NNaO_3S$: 366.1134; found: 366.1134.

(4*Z*)-4-(4-Benzoxybenzylidene)-2-ethyl-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17be)

Prepared following the typical procedure for **17aa** using **16be** (100 mg, 0.21 mmol), sodium formate (21 mg, 0.31 mmol), and $Pd(PPh_3)_4$ (9 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17be** (73 mg, 87%) as a white solid; mp 102–105 °C; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 1590, 1160, 1019 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.77 (d, *J* = 7.8 Hz, 1 H), 7.53 (td, *J* = 7.4, 1.3 Hz, 1 H), 7.47–7.33 (m, 7 H), 7.26–7.22 (m, 2 H), 7.03 (dt, *J* = 8.8, 2.0 Hz, 2 H), 5.11 (s, 2 H), 4.70 (d, *J* = 1.4 Hz, 2 H), 3.05 (q, *J* = 7.1 Hz, 2 H), 1.00 (t, *J* = 7.3 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9, 136.7, 134.9, 134.3, 132.4, 131.2, 130.9, 128.8, 128.5, 128.4, 128.3, 127.6, 125.2, 124.8, 115.2, 70.3, 48.3, 43.3, 13.5.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{23}NNaO_3S$: 428.1291; found: 428.1290.

(4*Z*)-2-Benzyl-4-benzylidene-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17ca)

Prepared following the typical procedure for **17aa** using **16ca** (100 mg, 0.23 mmol), sodium formate (23 mg, 0.34 mmol), and $Pd(PPh_3)_4$ (10 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17ca** (78 mg, 95%) as a white solid; mp 85–88 °C; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 1586, 1162, 1101 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.92 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.84 (d, *J* = 7.9 Hz, 1 H), 7.59 (td, *J* = 7.6, 1.4 Hz, 1 H), 7.52–7.47 (m, 2 H), 7.34–7.26 (m, 3 H), 7.17–7.07 (m, 5 H), 7.04–7.01 (m, 2 H), 4.50 (d, *J* = 1.3 Hz, 2 H), 4.13 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 135.4, 134.8, 134.7, 132.6, 132.3, 129.2, 129.1, 129.0, 128.7, 128.5, 128.4, 127.9, 126.2, 125.3, 125.0, 51.9, 47.3.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{22}H_{19}NNaO_2S$: 384.1029; found: 384.1030.

(4*Z*)-2-Benzyl-4-(4-methylbenzylidene)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17cb)

Prepared following the typical procedure for **17aa** using **16cb** (100 mg, 0.22 mmol), sodium formate (22 mg, 0.33 mmol), and $Pd(PPh_3)_4$ (10 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17cb** (75 mg, 91%) as a white solid; mp 80–83 °C; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 1589, 1163, 1102 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 7.7, 1.2 Hz, 1 H), 7.82 (d, *J* = 7.9 Hz, 1 H), 7.57 (td, *J* = 7.6, 1.3 Hz, 1 H), 7.47 (td, *J* = 7.6, 0.9 Hz, 1 H), 7.43 (s, 1 H), 7.18–7.03 (m, 9 H), 4.51 (d, *J* = 1.2 Hz, 2 H), 4.13 (s, 2 H), 2.36 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 138.4, 135.0, 134.6, 132.6, 132.5, 132.4, 129.4, 129.2, 129.1, 128.8, 128.5, 127.8, 125.5, 125.3, 125.0, 51.9, 47.4, 21.4.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{21}NNaO_2S$: 398.1185; found: 398.1185.

(4*Z*)-2-Benzyl-4-(4-methoxybenzylidene)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17cc)

Prepared following the typical procedure for **17aa** using **16cc** (100 mg, 0.21 mmol), sodium formate (22 mg, 0.32 mmol), and $Pd(PPh_3)_4$ (10 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17cc** (73 mg, 88%) as a white solid; mp 99–101 °C; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 1599, 1160, 1030 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.56 (td, *J* = 7.8, 1.2 Hz, 1 H), 7.46 (td, *J* = 7.6, 0.8 Hz, 1 H), 7.39 (s, 1 H), 7.17–7.09 (m, 5 H), 7.06–7.04 (m, 2 H), 6.85 (dt, *J* = 8.8, 1.7 Hz, 2 H), 4.51 (d, *J* = 0.9 Hz, 2 H), 4.13 (s, 2 H), 3.82 (s, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.7, 135.1, 135.0, 134.4, 132.5, 132.1, 130.8, 129.1, 128.6, 128.5, 128.1, 127.9, 125.3, 124.9, 124.6, 114.2, 55.5, 51.9, 47.5.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{23}H_{21}NNaO_3S$: 414.1134; found: 414.1135.

(4*Z*)-2-Benzyl-4-(4-ethoxybenzylidene)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17cd)

Prepared following the typical procedure for **17aa** using **16cd** (100 mg, 0.21 mmol), sodium formate (21 mg, 0.31 mmol), and $Pd(PPh_3)_4$ (9 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (10% EtOAc–PE) to yield **17cd** (78 mg, 93%) as a white solid; mp 80–83 °C; R_f = 0.35 (10% EtOAc–PE).

IR (KBr): 1589, 1163, 1039 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 7.7, 1.0 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.56 (td, *J* = 7.4, 1.2 Hz, 1 H), 7.46 (td, *J* = 7.6, 0.7 Hz, 1 H), 7.39 (s, 1 H), 7.18–7.04 (m, 7 H), 6.83 (d, *J* = 8.7 Hz, 2 H), 4.51 (s, 2 H), 4.12 (s, 2 H), 4.04 (q, *J* = 7.0 Hz, 2 H), 1.43 (t, *J* = 7.0 Hz, 3 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 159.0, 135.1, 134.9, 134.3, 132.5, 132.2, 130.8, 129.1, 128.6, 128.5, 127.9, 125.2, 124.9, 124.3, 114.7, 63.7, 51.9, 47.4, 15.0.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{24}H_{23}NNaO_3S$: 428.1291; found: 428.1294.

(4*Z*)-2-Benzyl-4-(4-benzoxybenzylidene)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17ce)

Prepared following the typical procedure for **17aa** using **16ce** (100 mg, 0.18 mmol), sodium formate (19 mg, 0.27 mmol), and $Pd(PPh_3)_4$ (8 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (5% EtOAc–PE) to yield **17ce** (77 mg, 90%) as a white solid; mp 119–121 °C; R_f = 0.40 (10% EtOAc–PE).

IR (KBr): 1599, 1167, 1037 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.90 (dd, *J* = 7.8, 1.3 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.57 (td, *J* = 7.7, 1.4 Hz, 1 H), 7.49–7.35 (m, 7 H), 7.15–7.03 (m, 7 H), 6.92 (dt, *J* = 8.8, 1.8 Hz, 2 H), 5.09 (s, 2 H), 4.50 (d, *J* = 1.1 Hz, 2 H), 4.13 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.9, 136.8, 135.1, 134.9, 134.4, 132.5, 132.0, 130.8, 129.1, 128.8, 128.6, 128.5, 128.3, 128.3, 127.9, 127.5, 125.3, 124.9, 124.6, 115.1, 70.2, 51.9, 47.4.

HRMS (ESI$^+$): *m*/*z* [M + H]$^+$ calcd for $C_{29}H_{26}NO_3S$: 468.1628; found: 468.1630.

(4*Z*)-4-Benzylidene-2-(pyridin-2-ylmethyl)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17da)

Prepared following the typical procedure for **17aa** using **16da** (100 mg, 0.23 mmol), sodium formate (23 mg, 0.34 mmol), and $Pd(PPh_3)_4$ (10 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (20% EtOAc–PE) to yield **17da** (71 mg, 87%) as a reddish gummy liquid; R_f = 0.30 (30% EtOAc–PE).

IR (KBr): 1587, 1163, 1082 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 4.4 Hz, 1 H), 7.90 (d, *J* = 7.5 Hz, 1 H), 7.80 (d, *J* = 8.0 Hz, 1 H), 7.60–7.52 (m, 2 H), 7.48 (t, *J* = 7.6 Hz, 1 H), 7.41 (s, 1 H), 7.37–7.23 (m, 4 H), 7.18 (d, *J* = 7.2 Hz, 2 H), 7.10–7.07 (m, 1 H), 4.63 (d, *J* = 0.6 Hz, 2 H), 4.31 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 155.8, 149.2, 136.8, 135.5, 134.9, 134.5, 132.7, 132.1, 129.3, 128.8, 128.6, 128.2, 126.3, 125.2, 122.8, 122.7, 54.2, 49.1.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{21}H_{18}N_2NaO_2S$: 385.0981; found: 385.0983.

(4*Z*)-4-(4-Benzoxybenzylidene)-2-(pyridin-2-ylmethyl)-3,4-dihydro-2*H*-1,2-benzothiazine 1,1-Dioxide (17de)

Prepared following the typical procedure for **17aa** using **16de** (100 mg, 0.18 mmol), sodium formate (19 mg, 0.27 mmol), and $Pd(PPh_3)_4$ (8 mg, 4 mol%) in DMF–H_2O (7:3, 3 mL) at 100 °C for 1 h. The product was purified by column chromatography (20% EtOAc–PE) to yield **17de** (73 mg, 85%) as a reddish gummy liquid; R_f = 0.40 (30% EtOAc–PE).

IR (KBr): 1598, 1163, 1017 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.35–8.32 (m, 1 H), 7.88 (dd, *J* = 7.8, 1.2 Hz, 1 H), 7.77 (d, *J* = 7.9 Hz, 1 H), 7.58–7.52 (m, 2 H), 7.47–7.32 (m, 8 H), 7.16–7.11 (m, 2 H), 7.10–7.06 (m, 1 H), 6.91 (dt, *J* = 8.7, 1.9 Hz, 2 H), 5.07 (s, 2 H), 4.64 (d, *J* = 1.3 Hz, 2 H), 4.29 (s, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 158.6, 155.7, 149.1, 136.7, 136.6, 135.2, 134.1, 132.5, 131.6, 130.8, 128.7, 128.3, 128.2, 128.1, 127.4, 125.0, 124.6, 122.7, 122.6, 114.8, 70.0, 54.1, 49.3.

HRMS (ESI$^+$): *m*/*z* [M + Na]$^+$ calcd for $C_{28}H_{24}N_2NaO_3S$: 491.1400; found: 491.1402.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1561288.

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