JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

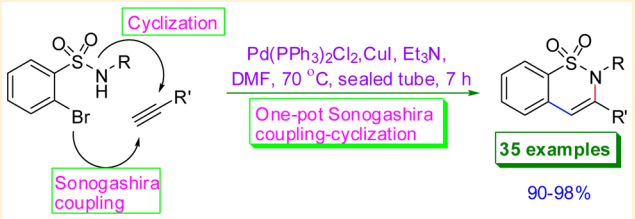
One-Pot Sonogashira Coupling−Cyclization toward Regioselective Synthesis of Benzosultams

Sudarshan Debnath and Shovan Mondal*

Department of Chemistry, Visva-Bharati University, Santiniketan 731235, India

Supporting Information

ABSTRACT: A one-pot method for the Sonogashira coupling and cyclization of 2-bromobenzenesulfonamides and terminal alkynes is presented. This method allows access to a variety of substituted benzosultams regioselectively in excellent yields. The reasons for regioselectivity are interpreted through density functional theory (DFT) studies.



INTRODUCTION

Benzosultams are pivotal structures that are found to be generously utilized in many drugs.[1] Compounds privileged with benzosultam core manifest a wide spectrum of bioactivities, such as antiviral, antimicrobial, antileukemic, anticancer, enzyme inhibition, etc.[2] Among the benzosultams, benzothiazine dioxide derivatives have been found to show resourceful inhibitory properties against a variety of enzymes. For example, Oxicams (e.g., Ampiroxicam **1**, Figure 1)[3] are a large family of

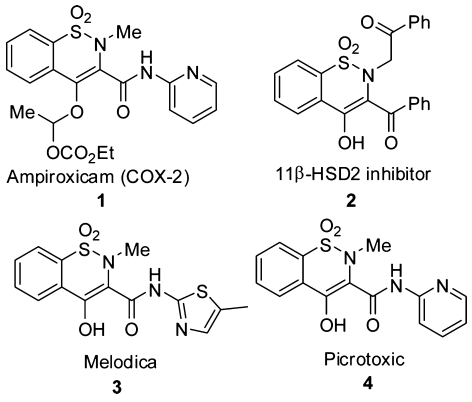


Figure 1. Biologically active benzosultams.

nonsteroidal anti-inflammatory agents. 11β-Hydroxysteroid dehydrogenase type 1 (11β-HSD1) is an endoplasmic reticulum-associated enzyme that acts as a NADPH dependent reductase and is able to convert inactive cortisone to the active glucocorticoid cortisol.[4] Benzothiazine dioxide derivative **2**, i.e., benzosultam **2** (Figure 1) has been found to show active inhibitory property against 11β-HSD1.[5] Moreover, benzothiazine dioxide derivatives have strong inhibitory properties against HIV integrand,[6] Calpain I[7] etc.

In contrast to the importance, only limited synthetic approaches toward the benzosultams have been reported.[8−10] For instance, Che et al. reported a series of benzothiazine dioxides formed by Au(PPh_3)OTf-catalyzed cycloisomerization of terminal alkenes (eq 1, Scheme 1).[11] Murakami and co-workers reported the synthesis of benzothiazine dioxide derivatives by exploiting a rhodium-catalyzed rearrangement reaction of *N*-arenesulfonylazetidin-3-ols. Mechanistically, this reaction involves the C−C bond cleavage by β-carbon elimination and C−H bond cleavage by a 1,5-rhodium shift (eq 2, Scheme 1).[12] Pal and co-workers gave a preliminary approach to the synthesis of benzothiazine dioxide derivatives by a Sonogashira coupling and a subsequent internal cyclization by the presence of an Ag(I) salt (eq 3, Scheme 1).[13] In our continuous effort on the synthesis of sultams and sultones,[14] our present aim is to develop a new, efficient and divergent route for the synthesis of benzothiazine dioxide derivatives. The results are reported here.

RESULTS AND DISCUSSION

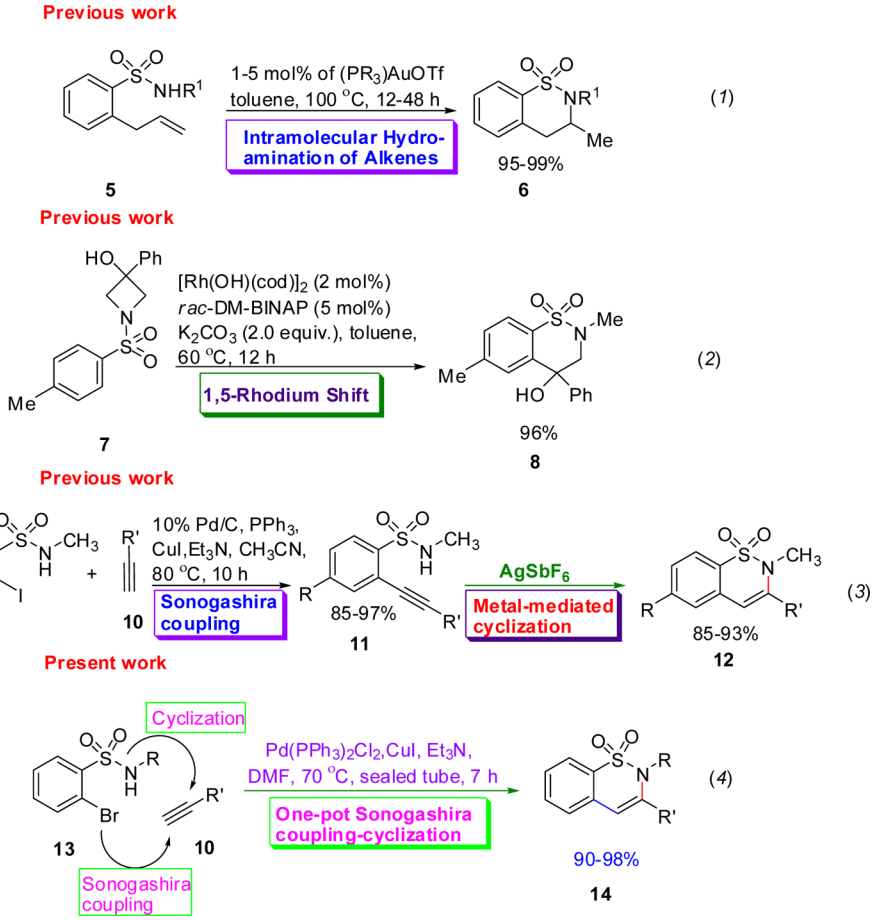
The required precursors for our present study **13a−g** were synthesized in excellent yields by the condensation reaction between 2-bromobenzenesulfonyl chloride **15** and different substituted anilines **16** in pyridine at 80 °C for 1 h (Scheme 2). Versatile aromatic and aliphatic acetylenes (**10a−i**) with electron donating, withdrawing and neutral groups were taken for the synthesis of various substituted benzothiazine dioxide derivatives (Figure 2).

The optimization of the reaction of **13a** to **14aa** was conducted and is presented in Table 1. Among the palladium catalysts, Pd(PPh_3)$_2$$Cl_2$ gave the best result rather than Pd_2dba_3 or Pd−C. The solvent screening revealed that DMF was the most appropriate solvent. The smooth Sonogashira coupling and cyclization occurred when the reaction was carried out under pressure, i.e., in sealed tube (entry 4, Table 1). It is very interesting to note that this reaction works well in gram-scale synthesis also. Upon treatment of compound **13a** (1 g, 2.80 mmol) with Phenylacetylene (345 mg, 3.36 mmol) under the

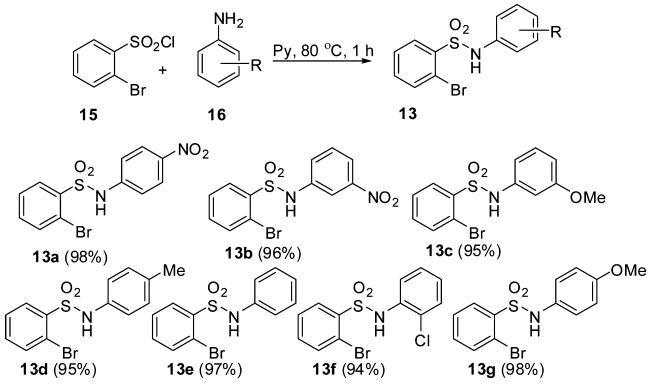
Received: February 5, 2015
Published: March 24, 2015

DOI: 10.1021/acs.joc.5b00274
J. Org. Chem. 2015, 80, 3940−3948

Scheme 1. Some Synthetic Approaches to Benzosultams (Benzothiazine Dioxide Derivatives)



Scheme 2. Synthesis of Starting Materials 13a–g



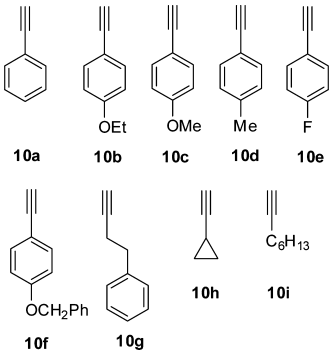


Figure 2. Various acetylenes taken for the synthesis of benzosultams.

optimized condition afforded compound **14aa** (1 g, 98%) as the only product.

The sole product got after treatment of compound **13a** with the optimized conditions showed one singlet aromatic proton at δ 7.15 along with other 13 aromatic protons in proton NMR and in carbon NMR there was no peak found for acetylinic carbons. From this result it is confirmed that the product got from **13a** is a cyclized one and the HRMS value of the synthesized compound came as 401.0574, which also well matched with the theoretical value of cyclized product 401.0572 for $[M + Na]^+$. Now the question is whether the regioselective product formed is **14aa** or **14aa′**. If the cyclization passed through 6-*endo-dig* mode, then **14aa** would be formed, and if the cyclization went through 5-*exo-dig* mode, then **14aa′** would be formed (Scheme 3).

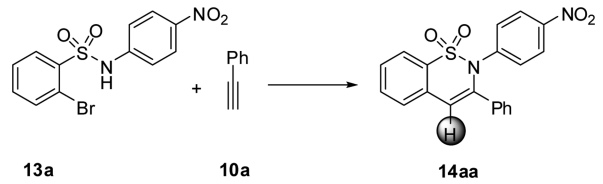
Finally, the structure was confirmed by X-ray data, and it showed that the structure of the product got from **13a** was **14aa** not **14aa′** (Figure 3).[15]

Now to find out the reasons of the selectivity observed in this cyclization, the energies of both the transition states (6-*endo-dig* and 5-*exo-dig*) were calculated by DFT. Coordinates of optimized geometry are given in Supporting Information.

For 6-*endo-dig* mode of cyclization the reaction passed through lower activation energy barrier (3 kcal/mol) compared to that of 5-*exo-dig* mode (Figure 4). This is the probable reason for the formation of benzosultum **14aa** as the only product in the reaction between **13a** and **10a**. Now for

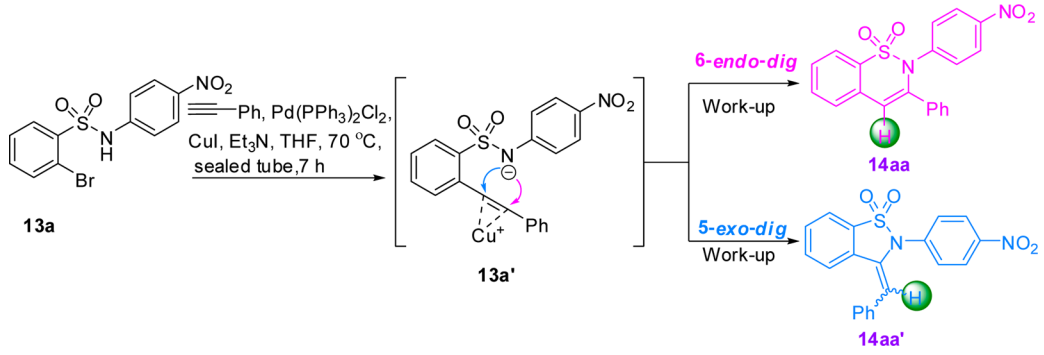
DOI: 10.1021/acs.joc.5b00274
J. Org. Chem. 2015, 80, 3940−3948

Table 1. Optimization of Conditions



entry	catalytic system	solvent:base (2:1)	time (h)	conditions	yield (%)
1	5 mol % $Pd(PPh_3)_2Cl_2$, 5 mol % CuI	$THF:Et_3N$	36	room temperature	trace
2	5 mol % $Pd(PPh_3)_2Cl_2$, 12 mol % CuI	$THF:Et_3N$	12	reflux	70
3	5 mol % $Pd(PPh_3)_2Cl_2$, 12 mol % CuI	$DMF:Et_3N$	12	100 °C	75
4	**5 mol % $Pd(PPh_3)_2Cl_2$, 12 mol % CuI**	**$DMF:Et_3N$**	**7**	**70 °C in sealed tube**	**98**
5	3 mol % $Pd(PPh_3)_2Cl_2$, 12 mol % CuI	$DMF:Et_3N$	7	70 °C in sealed tube	93
6	2.5 mol % Pd_2dba_3, 15 mol % PPh_3, 5 mol % CuI	$THF:Et_3N$	12	reflux	20
7	2 mol % Pd−C (10%), 2.5 mol % PPh_3, 5 mol % CuI	$THF:Et_3N$	8	reflux	no reaction
8	5 mol % $Pd(PPh_3)_2Cl_2$, 12 mol % CuI	$DMF:Et_3N$	7	70 °C	50

Scheme 3. Different Mode of Cyclizations



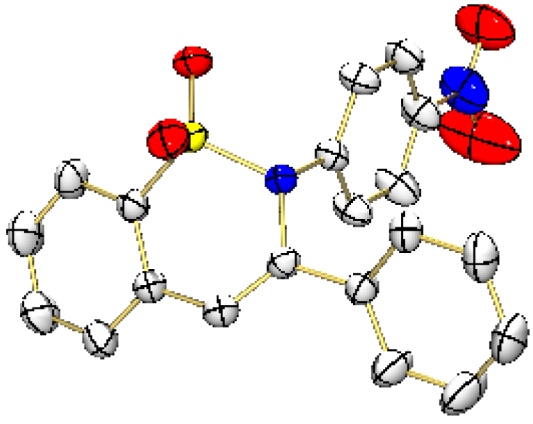


Figure 3. Ortep diagrams of benzosultam **14aa** (the thermal ellipsoids are drawn at the 50% probability level).

confirmation of formation of intermediate **13a′**, we performed the reaction with N-Me substituent **13h** under our optimized condition and we were able to separate **15**,[13] which on treatment with CuI at refluxing DMF afforded the sultam **16**[13] in 90% yield (Scheme 4). From this observation it is quite sure that reaction of **13a** to **14aa** must be gone through the intermediate **13a′**.

After standardization of the synthesis of benzothiazine dioxide **14aa**, we made a number of benzothiazine dioxide derivatives **14aa**−**14ga** (35 examples) (Figure 5) to make the method very wide and general.

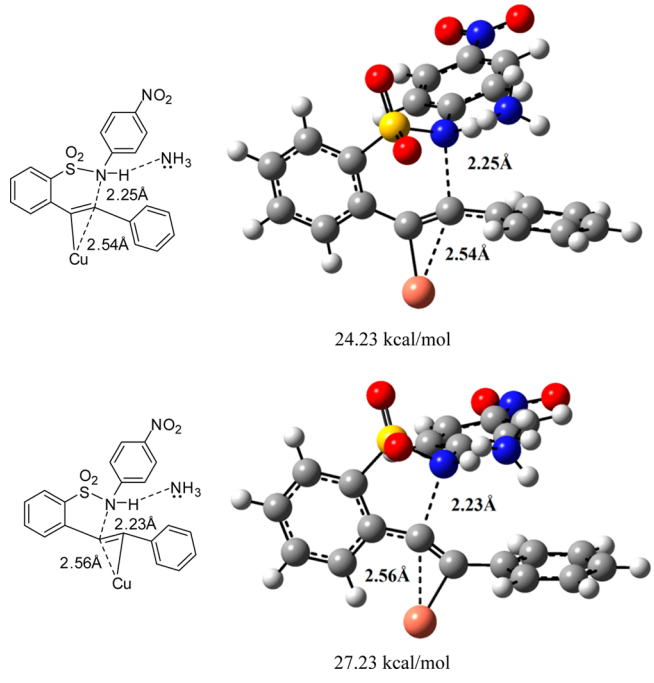
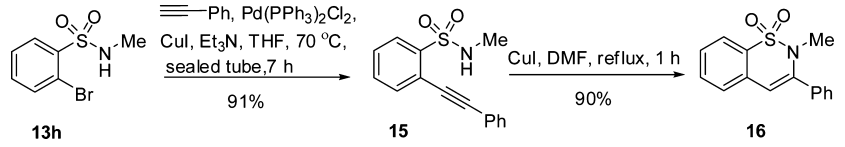


Figure 4. Optimized geometries of transition states for different modes of cyclizations (ethyl group of triethylamine is replaced by hydrogen to reduce computational time).

The single crystal XRD analysis for benzosultams **14bi**,[16] **14ch**,[17] **14db**[18] had also been done for further confirmation of structures (Figure 6).

DOI: 10.1021/acs.joc.5b00274
J. Org. Chem. 2015, 80, 3940−3948

Scheme 4. Isolation of Sonogashira Product



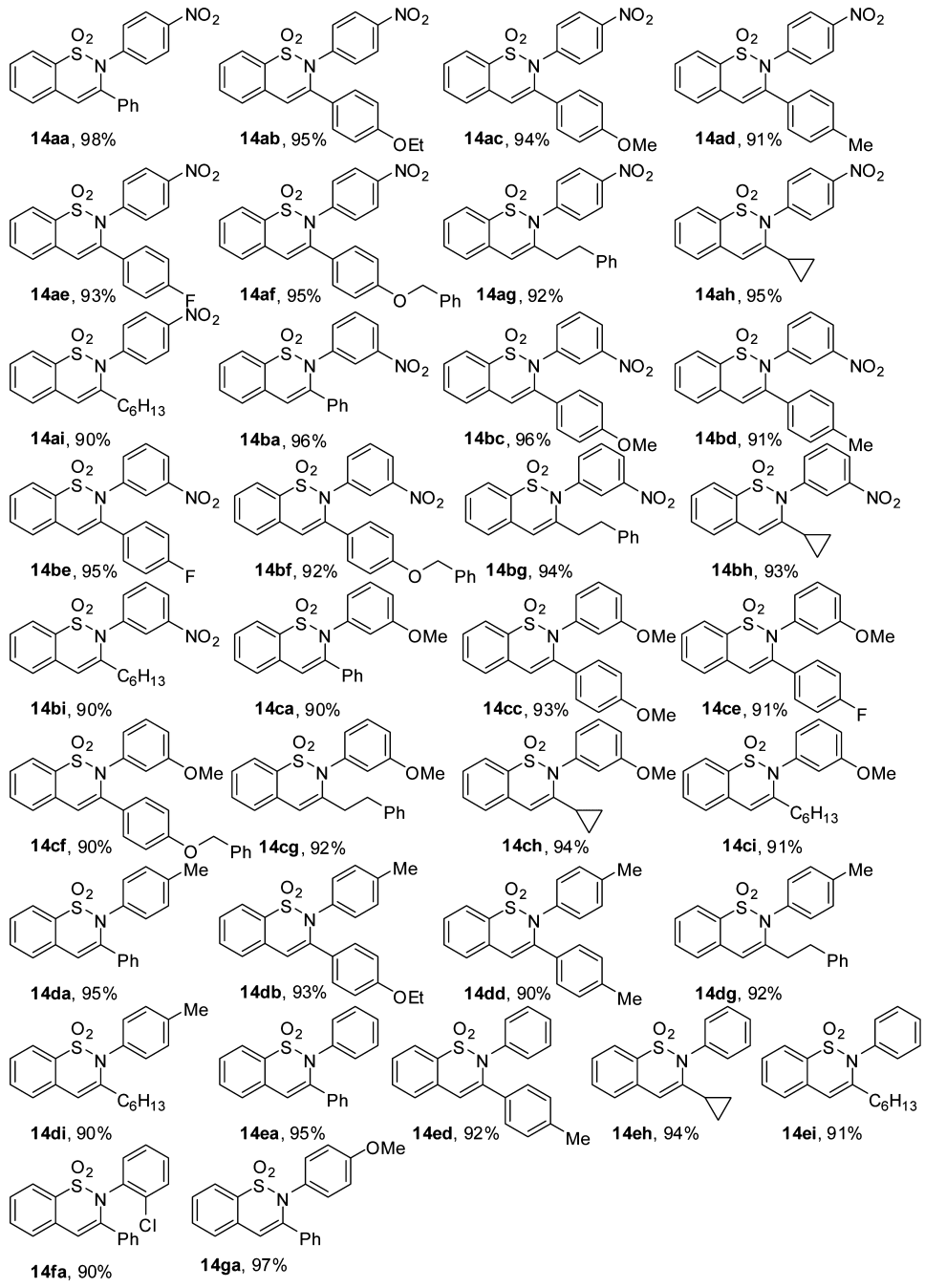


Figure 5. Summarized results of benzosultams.

In conclusion, we have successfully realized the synthesis of benzothiazine dioxide derivatives, i.e., benzosultams via the Pd-catalyzed Sonogashira coupling and cyclization. This synthetic method is an efficient and convergent route to prepare benzo-delta-sultams. This method benefits from the advantages of mild and clean conditions, high efficiency, and regioselectivity.

EXPERIMENTAL SECTION

General Information. The reactions sensitive to air or moisture were carried out under nitrogen atmosphere using dry solvents, unless otherwise noted. Column chromatography was performed on silica gel (60−120 mesh). Reaction progress was monitored by thin-layer chromatography (TLC). TLC plates were visualized with ultraviolet light (256 nm) and in an iodine chamber. IR spectra were recorded using KBr discs. Wavelengths (ν) are reported in cm^{-1}. Melting points

DOI: 10.1021/acs.joc.5b00274
J. Org. Chem. 2015, 80, 3940−3948

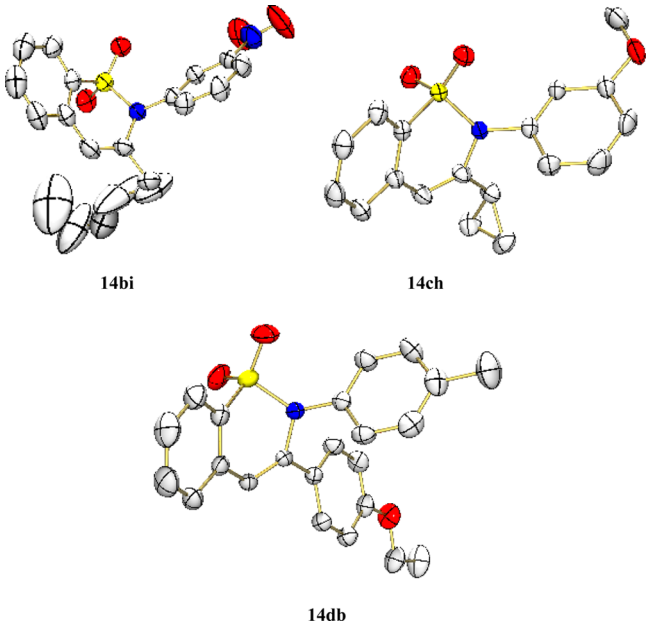


Figure 6. Ortep diagrams of benzosultams (the thermal ellipsoids are drawn at the 50% probability level).

were recorded in open capillaries and are uncorrected. HRMS were recorded on a QTOF instrument. All ^{1}H and ^{13}C NMR spectra were recorded in 400 and 100 MHz spectrometer, respectively. Chemical shifts were given in parts per million (ppm, δ) and are relative to internal $CHCl_3$ (^{1}H, δ = 7.26) and $CDCl_3$ (^{13}C, δ = 77.16). Multiplicity is indicated by one or more of the following abbreviations: s (singlet), d (doublet), t (triplet), q (quartet), pentet (p), septet (se), octet (o). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m) or broad (br). The lists of coupling constants (J) correspond to the order of multiplicity assignment and are reported in Hertz (Hz).

DFT calculations were performed with Gaussian09 program package.[19] Geometry were optimized with hybrid density functional (B3LYP) theory[20] using 6-31G(d) basis set.[21] For Cu atom LanL2DZ basis set[22] was used with LanL2 effective core potential. Frequency calculations were used to characterize the transition state and stationary points (reactants/products) as minima. Transition states were connected with corresponding reactants and products by intrinsic reaction coordinate (IRC) calculation.[23] Conductor-like polarizable continuum solvation model (CPCM) was used for solvation of stationary points and transition states.[24]

General Procedure for Preparation of 2-Bromo-*N*-arylbenzenesulfonamide Derivatives. *Preparation of 2-Bromo-N-(4-nitrophenyl)benzenesulfonamide (**13a**).* Commercially available 2-bromobenzenesulfonyl chloride (400 mg, 1.56 mmol) was heated with 4-nitroaniline (216 mg, 1.56 mmol) in the presence of pyridine (0.5 mL) at 80 °C for 1 h. The resulting reaction mixture was poured then into ice water. A white precipitate of compound **13a** (548 mg, 98%) appeared, which was filtered, dried and collected for the next step: mp 124−126 °C; IR (KBr) 3323, 1336, 1167 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.19 (dd, J = 7.8, 1.9 Hz, 1H), 8.10 (dt, J = 9.0, 1.9 Hz, 2H), 7.86 (bs, 1H), 7.70 (dd, J = 7.8, 1.3 Hz, 1H), 7.50−7.40 (m, 2H), 7.25 (dt, J = 9.0, 1.8 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.4, 141.9, 137.3, 135.6, 135.0, 132.6, 128.2, 125.5, 119.9, 119.1. Anal. Calcd for $C_{12}H_9BrN_2O_4S$: C, 40.35; H, 2.54; N, 7.84. Found: C, 40.63; H, 2.39; N, 7.69.

*Preparation of 2-Bromo-N-(3-nitrophenyl)benzenesulfonamide (**13b**).* 96% yield (537 mg), white solid: mp 134−136 °C; IR (KBr) 3267, 1336, 1169 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13 (dd, J = 7.4, 2.1 Hz, 1H), 7.99 (t, J = 2.1 Hz, 1H), 7.94−7.91 (m, 1H), 7.73−7.69 (m, 2H), 7.51−7.39 (m,4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.8, 137.3, 137.2, 135.5, 134.8, 132.5, 130.5, 128.2, 126.4, 120.1, 119.8, 115.3. Anal. Calcd for $C_{12}H_9BrN_2O_4S$: C, 40.35; H, 2.54; N, 7.84. Found: C, 40.04; H, 2.72; N, 8.01.

*Preparation of 2-Bromo-N-(3-methoxyphenyl)-benzenesulfonamide (**13c**).* 95% yield (509 mg), white solid: mp 80−82 °C; IR (KBr) 3388, 1326, 1164 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.07−8.05 (m, 1H), 7.69−7.67 (m, 1H), 7.38−7.34 (m, 2H), 7.27 (bs, 1H), 7.09 (t, J = 8.1 Hz, 1H), 6.73 (t, J = 1.7 Hz, 1H), 6.69−6.67 (m, 1H), 6.62−6.59 (m, 1H), 3.71 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.3, 137.8, 137.0, 135.2, 134.2, 132.5, 130.2, 127.9, 119.8, 113.6, 111.3, 107.3, 55.4. Anal. Calcd for $C_{13}H_{12}BrNO_3S$: C, 45.63; H, 3.53; N, 4.09. Found: C, 45.84; H, 3.70; N, 3.85.

*Preparation of 2-Bromo-N-p-tolylbenzenesulfonamide (**13d**).* 95% yield (485 mg), white solid: mp 144−146 °C; IR (KBr) 3263, 1336, 1163 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00−7.97 (m, 1H), 7.70−7.67 (m, 1H), 7.36−7.31 (m, 2H), 7.21 (bs, 1H), 7.03−6.97 (m, 4H), 2.22 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.9, 135.9, 135.1, 134.1, 133.1, 132.4, 129.9, 127.9, 122.4, 119.8, 20.9. Anal. Calcd for $C_{13}H_{12}BrNO_2S$: C, 47.86; H, 3.71; N, 4.29. Found: C, 47.98; H, 3.59; N, 4.44.

*Preparation of 2-Bromo-N-phenylbenzenesulfonamide (**13e**).* 97% yield (474 mg), white solid: mp 129−131 °C; IR (KBr) 3286, 1331, 1165 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.04−8.01 (m, 1H), 7.71−7.68 (m, 1H), 7.38−7.34 (m, 2H), 7.23−7.19 (m, 3H), 7.14−7.11 (m, 2H), 7.09−7.06 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 137.9, 135.8, 135.1, 134.2, 132.4, 129.5, 127.9, 125.9, 121.8, 119.8. Anal. Calcd for $C_{12}H_{10}BrNO_2S$: C, 46.17; H, 3.23; N, 4.49. Found: C, 46.40; H, 3.38; N, 4.34.

*Preparation of 2-Bromo-N-(2-chlorophenyl)benzenesulfonamide (**13f**).* 94% yield (510 mg), white solid: mp 95−97 °C; IR (KBr) 3338, 1417,1116 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.13 (dd, J = 7.4, 2.1 Hz, 1H), 7.70 (dd, J = 7.3, 1.7 Hz, 1H), 7.64 (brs, 1H), 7.53 (dd, J = 8.2, 1.3 Hz, 1H), 7.44−7.37 (m, 2H), 7.28 (dd, J = 8.0, 1.4 Hz, 1H), 7.15 (td, J = 7.9, 1.3 Hz, 1H), 6.98 (td, J = 7.7, 1.4 Hz, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 138.0, 135.6, 134.5, 133.2, 132.3, 129.8, 127.9, 127.8, 125.4, 123.9, 120.4, 120.2. Anal. Calcd for $C_{12}H_9BrClNO_2S$: C, 41.58; H, 2.62; N, 4.04. Found: C, 41.77; H, 2.46; N, 4.18.

*Preparation of 2-Bromo-N-(4-methoxyphenyl)-benzenesulfonamide (**13g**).* 98% yield (525 mg), white solid: mp 111−113 °C; IR (KBr) 3280, 1265, 1157 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.91 (d, J = 5.2 Hz, 1H), 7.71 (d, J = 6.0 Hz, 1H), 7.42−7.28 (m, 2H), 7.12−6.90 (m, 3H), 6.71 (d, J = 8.0 Hz, 2H), 3.70 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.1, 137.8, 134.9, 133.9, 132.3, 128.0, 127.8, 125.4, 119.6, 114.4, 55.3. Anal. Calcd for $C_{13}H_{12}BrNO_3S$: C, 45.63; H, 3.53; N, 4.09. Found: C, 45.49; H, 3.42; N, 4.27.

General Procedure for Preparation of Benzothiazine Dioxide Derivatives. *Preparation of 2-(4-Nitrophenyl)-3-phenyl-2H-1,2-benzothiazine 1,1-dioxide (**14aa**).* The solution of compound **13a** (70 mg, 0.20 mmol) in anhydrous DMF (2 mL) and Et_3N (1 mL) was bubbled through nitrogen gas for 10 min. $Pd(PPh_3)_2Cl_2$ (7 mg, 5 mol %) and CuI (4.5 mg, 12 mol %) were then added to this solution, which was stirred for further 5 min. Phenylacetylene (24 mg, 0.23 mmol) was then added to this reaction mixture, which was heated at 70 °C for 7 h in a sealed tube. The reaction 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 on silica gel to yield compound **14aa** (73 mg, 98%) as a white solid: mp 169−171 °C; IR (KBr) 1598, 1350, 1176 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.06 (d, J = 8.9 Hz, 2H), 7.84 (d, J = 7.8 Hz, 1H), 7.70 (t, J = 7.8 Hz, 1H), 7.64−7.62 (m, 3H), 7.55 (t, J = 7.7 Hz, 1H), 7.34−7.29 (m, 5H), 7.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.3, 143.0, 142.2, 134.3, 133.1, 132.6, 132.4, 130.1, 129.1, 128.4, 127.8, 127.6, 127.5, 124.4, 123.3, 115.6; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.1, 130.2, 129.2, 128.4, 127.8, 127.6, 127.5, 124.4, 123.3, 115.6; HRMS (ES^+) MNa^+, found 401.0574. $C_{20}H_{14}N_2NaO_4S$ requires 401.0572.

*Preparation of 3-(4-Ethoxyphenyl)-2-(4-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ab**).* 95% yield (79 mg), white solid: mp

DOI: 10.1021/acs.joc.5b00274
J. Org. Chem. 2015, 80, 3940−3948

177−179 °C; IR (KBr) 1598, 1348, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.07−8.04 (m, 2H), 7.81 (d, J = 7.8 Hz, 1H), 7.68 (td, J = 7.6, 0.9 Hz, 1H), 7.59 (d, J = 7.6 Hz, 1H), 7.55−7.49 (m, 3H), 7.30−7.26 (m, 2H), 7.06 (s, 1H), 6.82 (d, J = 8.7 Hz, 2H), 3.98 (q, J = 7.0 Hz, 2H), 1.38 (t, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.5, 146.2, 143.2, 142.1, 133.1, 132.9, 132.0, 129.2, 128.7, 128.2, 127.5, 126.5, 124.3, 123.2, 115.0, 113.9, 63.7, 14.8; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.1, 129.2, 128.7, 128.2, 127.5, 124.3, 123.2, 115.0, 113.9, 63.7, 14.8. Anal. Calcd for $C_{22}H_{18}N_2O_5S$: C, 62.55; H, 4.29; N, 6.63. Found: C, 62.74; H, 4.16; N, 6.75.

*Preparation of 3-(4-Methoxyphenyl)-2-(4-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ac**).* 94% yield (75 mg), white solid: mp 187−189 °C; IR (KBr) 1596, 1350, 1176 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.06 (dd, J = 7.0, 2.0 Hz, 2H), 7.82 (d, J = 7.9 Hz, 1H), 7.68 (td, J = 7.5, 0.8 Hz, 1H), 7.60 (d, J = 7.4 Hz, 1H), 7.56−7.49 (m, 3H), 7.30−7.26 (m, 2H), 7.06 (s, 1H), 7.84 (dd, J = 6.9, 1.8 Hz, 2H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.1, 146.2, 143.2, 142.0, 133.1, 132.9, 132.1, 129.2, 128.7, 128.2, 127.5, 126.8, 124.3, 123.3, 114.6, 114.0, 55.5; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.1, 129.2, 128.7, 128.2, 127.5, 124.3, 123.3, 114.6, 114.0, 55.5. Anal. Calcd for $C_{21}H_{16}N_2O_5S$: C, 61.76; H, 3.95; N, 6.86. Found: C, 61.58; H, 4.12; N, 6.95.

*Preparation of 3-(4-Methylphenyl)-2-(4-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ad**).* 91% yield (70 mg), white solid: mp 202−204 °C; IR (KBr) 1598, 1346, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.05 (d, J = 9.0 Hz, 2H), 7.82 (d, J = 7.8 Hz, 1H), 7.68 (t, J = 7.4 Hz, 1H), 7.61 (d, J = 7.6 Hz, 1H), 7.55−7.49 (m, 3H), 7.29 (d, J = 9.0 Hz, 2H), 7.13 (superimposed d, J = 8.2 Hz, 2H), 7.11 (superimposed s, 1H), 2.30 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.2, 143.1, 142.2, 140.5, 133.1, 132.8, 132.2, 131.5, 129.9, 128.9, 128.3, 127.7, 127.5, 124.3, 123.2, 114.8, 21.4; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.1, 129.9, 128.9, 128.3, 127.7, 127.5, 124.3, 123.2, 114.8, 21.4. Anal. Calcd for $C_{21}H_{16}N_2O_4S$: C, 64.27; H, 4.11; N, 7.14. Found: C, 64.48; H, 4.26; N, 6.95.

*Preparation of 3-(4-Fluorophenyl)-2-(4-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ae**).* 93% yield (72 mg), white solid: mp 181−183 °C; IR (KBr) 1598, 1348, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.09−8.05 (m, 2H), 7.83 (d, J = 7.7 Hz, 1H), 7.70 (td, J = 7.6, 1.0 Hz, 1H), 7.63−7.60 (m, 3H), 7.55 (td, J = 7.6, 1.0 Hz, 1H), 7.30−7.27 (m, 2H), 7.10 (s, 1H), 7.03 (t, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.7 (d, J = 249.5 Hz), 146.4, 142.8, 141.2, 133.2, 132.5, 132.3, 130.6, 129.7 (d, J = 8.6 Hz), 129.3, 128.4, 127.5, 124.4, 123.3, 116.4 (d, J = 21.9 Hz), 115.6; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.2, 129.7, 129.3, 128.4, 127.5, 124.4, 123.3, 116.4, 115.6. Anal. Calcd for $C_{20}H_{13}FN_2O_4S$: C, 60.60; H, 3.31; N, 7.07. Found: C, 60.39; H, 3.19; N, 7.24.

*Preparation of 3-(4-Benzyloxyphenyl)-2-(4-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14af**).* 95% yield (90 mg), white solid: mp 155−157 °C; IR (KBr) 1599, 1348, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.06 (d, J = 8.9 Hz, 2H), 7.82 (d, J = 7.7 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.61−7.50 (m, 4H), 7.38−7.27 (m, 7H), 7.06 (s, 1H), 7.91 (d, J = 8.6 Hz, 2H), 5.02 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.3, 146.3, 143.2, 142.0, 136.4, 133.1, 132.9, 132.1, 129.3, 128.8, 128.3, 128.2, 127.6, 127.5, 127.0, 124.4, 123.3, 115.4, 114.1, 70.3; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.1, 129.3, 128.8, 128.3, 128.2, 127.6, 127.5, 124.4, 123.3, 115.4, 114.1, 70.3. Anal. Calcd for $C_{27}H_{20}N_2O_5S$: C, 66.93; H, 4.16; N, 5.78. Found: C, 67.21; H, 3.99; N, 5.62.

*Preparation of 2-(4-Nitrophenyl)-3-(2-phenylethyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ag**).* 92% yield (73 mg), white solid: mp 110−112 °C; IR (KBr) 1596, 1348, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.21 (d, J = 8.8 Hz, 2H), 7.79 (d, J = 7.8 Hz, 1H), 7.63 (t, J = 7.4 Hz, 1H), 7.49 (t, J = 7.6 Hz, 1H), 7.43 (d, J = 7.8 Hz, 1H), 7.30−7.24 (m, 4H), 7.21−7.17 (m, 1H), 7.10 (d, J = 7.1 Hz, 2H), 6.59 (s, 1H), 2.91 (t, J = 7.6 Hz, 2H), 2.58 (t, J = 7.6 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.9, 142.1, 141.7, 140.1, 132.9, 132.3, 131.9, 128.7, 128.6, 128.2, 127.8, 126.5, 124.6, 122.8, 115.1, 36.2, 33.9; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.9, 128.7, 128.6, 128.2, 127.8, 126.5, 124.6, 122.8, 115.1, 36.2, 33.9. Anal. Calcd for $C_{22}H_{18}N_2O_4S$: C, 65.01; H, 4.46; N, 6.89. Found: C, 65.16; H, 4.35; N, 6.72.

*Preparation of 3-Cyclopropyl-2-(4-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ah**).* 95% yield (64 mg), white solid: mp 97−99 °C; IR (KBr) 1606, 1344, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.22 (d, J = 8.9 Hz, 2H), 7.76 (d, J = 7.8 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.46−7.40 (m, 4H), 6.48 (s, 1H), 1.51−1.44 (m, 1H), 0.80−0.77 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.9, 144.9, 142.2, 132.8, 132.6, 131.7, 128.6, 128.1, 127.4, 124.5, 122.7, 110.8, 15.3, 8.6; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.8, 128.6, 128.1, 127.5, 124.4, 122.7, 110.8, 15.4, 8.6. Anal. Calcd for $C_{17}H_{14}N_2O_4S$: C, 59.64; H, 4.12; N, 8.18. Found: C, 59.42; H, 4.34; N, 7.95.

*Preparation of 3-Hexyl-2-(4-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ai**).* 90% yield (68 mg), red gummy liquid: IR (KBr) 1610, 1350, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.21 (d, J = 8.8 Hz, 2H), 7.76 (d, J = 7.7 Hz, 1H), 7.61 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 9.1 Hz, 2H), 7.33 (d, J = 8.9 Hz, 2H), 6.63 (s, 1H), 2.27 (t, J = 7.4 Hz, 2H), 1.55 (p, J = 7.3 Hz, 2H), 1.33−1.20 (m, 6H), 0.84 (t, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.8, 143.1, 141.7, 132.8, 132.4, 131.7, 128.4, 128.2, 127.6, 124.5, 122.6, 114.6, 34.0, 31.5, 28.3, 27.4, 22.5, 14.1; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.8, 128.4, 128.2, 127.6, 124.5, 122.6, 114.6, 34.0, 31.5, 28.3, 27.4, 22.5, 14.1. Anal. Calcd for $C_{20}H_{22}N_2O_4S$: C, 62.16; H, 5.74; N, 7.25. Found: C, 62.00; H, 5.61; N, 7.44.

*Preparation of 2-(3-Nitrophenyl)-3-phenyl-2H-1,2-benzothiazine 1,1-dioxide (**14ba**).* 96% yield (71 mg), white solid: mp 207−209 °C; IR (KBr) 1614, 1348, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.99 (d, J = 7.4 Hz, 1H), 7.84−7.82 (m, 2H), 7.73−7.62 (m, 5H), 7.55 (t, J = 7.5 Hz, 1H), 7.43 (t, J = 8.2 Hz, 1H), 7.34−7.30 (m, 3H), 7.15 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.4, 142.2, 138.6, 134.2, 133.5, 133.1, 132.6, 132.1, 130.1, 129.7, 129.2, 129.1, 128.5, 127.8, 123.2, 122.5, 121.6, 115.6; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.5, 133.1, 130.1, 129.7, 129.2, 129.1, 128.5, 127.8, 123.2, 122.5, 121.6, 115.6. Anal. Calcd for $C_{20}H_{14}N_2O_4S$: C, 63.48; H, 3.73; N, 7.40. Found: C, 63.73; H, 3.87; N, 7.17.

*Preparation of 3-(4-Methoxyphenyl)-2-(3-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14bc**).* 96% yield (77 mg), white solid: mp 180−182 °C; IR (KBr) 1602, 1348, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.99 (dd, J = 8.1, 1.5 Hz, 1H), 7.83−7.80 (m, 2H), 7.69 (td, J = 8.0, 1.1 Hz, 1H), 7.62 (d, J = 7.7 Hz, 2H), 7.57 (d, J = 8.8 Hz, 2H), 7.51 (td, J = 7.7, 0.8 Hz, 1H), 7.43 (t, J = 8.1 Hz, 1H), 7.06 (s, 1H), 6.83 (d, J = 8.7 Hz, 2H), 3.77 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 161.0, 148.4, 142.1, 138.8, 133.5, 133.1, 132.9, 131.8, 129.7, 129.3, 128.8, 128.3, 126.7, 123.2, 122.4, 121.7, 114.6, 114.0, 55.5; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.5, 133.1, 129.7, 129.3, 128.8, 128.3, 123.2, 122.4, 121.7, 114.6, 114.0, 55.5. Anal. Calcd for $C_{21}H_{16}N_2O_5S$: C, 61.76; H, 3.95; N, 6.86. Found: C, 61.59; H, 3.74; N, 7.11.

*Preparation of 3-(4-Methylphenyl)-2-(3-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14bd**).* 91% yield (70 mg), white solid: mp 217−219 °C; IR (KBr) 1610, 1348, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.99 (dd, J = 8.1, 1.1 Hz, 1H), 7.83−7.81 (m, 2H), 7.69 (td, J = 7.8, 0.8 Hz, 1H), 7.63 (d, J = 7.9 Hz, 2H), 7.54−7.51 (m, 3H), 7.43 (t, J = 8.1 Hz, 1H), 7.13 (superimposed d, J = 8.4 Hz, 2H), 7.11 (superimposed s, 1H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.4, 142.3, 140.4, 138.8, 133.5, 133.1, 132.8, 132.0, 131.4, 129.9, 129.7, 128.9, 128.4, 127.8, 123.2, 122.4, 121.7, 114.8, 21.4; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.5, 133.1, 129.9, 129.7, 128.9, 128.4, 127.8, 123.2, 122.4, 121.7, 114.8, 21.4. Anal. Calcd for $C_{21}H_{16}N_2O_4S$: C, 64.27; H, 4.11; N, 7.14. Found: C, 64.11; H, 4.30; N, 7.24.

*Preparation of 3-(4-Fluorophenyl)-2-(3-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14be**).* 95% yield (73 mg) as a white solid: mp 200−202 °C; IR (KBr) 1606, 1350, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.01 (dd, J = 8.0, 1.0 Hz, 1H), 7.84−7.80 (m, 2H), 7.71 (t, J = 7.4 Hz, 1H), 7.65−7.61 (m, 4H), 7.55 (t, J = 7.6 Hz, 1H), 7.44 (t, J = 8.1 Hz, 1H), 7.10 (s, 1H), 7.02 (t, J = 8.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.7 (d, J = 250.5 Hz), 148.4, 141.2, 138.5, 133.4, 133.2, 132.4, 132.0, 130.4 (d, J = 2.8 Hz), 129.8, 129.7 (d, J = 8.8 Hz), 129.3, 128.5, 123.3, 122.6, 121.6, 116.4 (d, J = 21.9 Hz), 115.5; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.4, 133.2, 129.8, 129.7, 129.3, 128.5, 123.3, 122.6, 121.6, 116.4, 115.5. Anal. Calcd for

DOI: 10.1021/acs.joc.5b00274
J. Org. Chem. 2015, 80, 3940−3948

$C_{20}H_{13}FN_2O_4S$: C, 60.60; H, 3.31; N, 7.07. Found: C, 60.83; H, 3.47; N, 6.81.

*Preparation of 3-(4-Benzyloxyphenyl)-2-(3-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14bf**).* 92% yield (87 mg), white solid: mp 142−144 °C; IR (KBr) 1606, 1350, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.00 (dd, J = 8.0, 0.9 Hz, 1H), 7.82−7.80 (m, 2H), 7.69 (t, J = 7.4 Hz, 1H), 7.63−7.61 (m, 2H), 7.57 (d, J = 8.7 Hz, 2H), 7.51 (t, J = 7.6 Hz, 1H), 7.46−7.32 (m, 6H), 7.06 (s, 1H), 6.91 (d, J = 8.7 Hz, 2H), 5.01 (s, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.3, 148.4, 142.0, 138.8, 136.4, 133.5, 133.1, 132.9, 131.9, 129.7, 129.4, 128.8, 128.3, 127.6, 126.9, 123.2, 122.4, 121.6, 115.4, 114.1, 70.2; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 133.5, 133.1, 129.7, 129.3, 128.8, 128.3, 127.6, 123.2, 122.4, 121.6, 115.4, 114.1, 70.2. Anal. Calcd for $C_{27}H_{20}N_2O_5S$: C, 66.93; H, 4.16; N, 5.78. Found: C, 67.11; H, 4.29; N, 5.52.

*Preparation of 2-(3-Nitrophenyl)-3-(2-phenylethyl)-2H-1,2-benzothiazine 1,1-dioxide (**14bg**).* 94% yield (89 mg), white solid: mp 127−129 °C; IR (KBr) 1625, 1350, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.23−8.20 (m, 1H), 7.92−7.90 (m, 1H), 7.81 (d, J = 7.8 Hz, 1H), 7.66 (td, J = 7.6, 0.9 Hz, 1H), 7.62−7.56 (m, 2H), 7.51 (t, J = 7.7 Hz, 1H), 7.47 (d, J = 7.7 Hz, 1H), 7.30−7.26 (m, 2H), 7.23−7.19 (m, 1H), 7.14 (d, J = 7.0 Hz, 2H), 6.61 (s, 1H), 2.95 (t, J = 7.5 Hz, 2H), 2.60 (t, J = 7.7 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.6, 142.1, 140.1, 137.3, 134.2, 132.9, 132.3, 131.6, 130.0, 128.6, 128.6, 127.8, 126.5, 123.1, 122.7, 122.4, 114.7, 36.0, 33.9; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 134.2, 132.9, 130.0, 128.6, 128.6, 127.8, 126.5, 123.1, 122.7, 122.4, 114.7, 36.0, 33.9. Anal. Calcd for $C_{22}H_{18}N_2O_4S$: C, 65.01; H, 4.46; N, 6.89. Found: C, 64.75; H, 4.62; N, 6.81.

*Preparation of 3-Cyclopropyl-2-(3-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14bh**).* 93% yield (62 mg), white solid: mp 134−136 °C; IR (KBr) 1631, 1346, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.19 (dd, J = 8.1, 1.0 Hz, 1H), 8.01 (t, J = 2.0 Hz, 1H), 7.77 (d, J = 7.7 Hz, 1H), 7.69 (dt, J = 8.0, 0.8 Hz, 1H), 7.63−7.56 (m, 2H), 7.47−7.42 (m, 2H), 6.46 (s, 1H), 1.45 (p, J = 7.0 Hz, 1H), 0.78−0.76 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.5, 144.9, 137.7, 134.7, 132.8, 132.7, 131.5, 129.9, 128.0, 127.5, 123.2, 122.6, 110.1, 15.3, 8.4; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 134.7, 132.8, 129.9, 128.0, 127.5, 123.2, 122.6, 110.1, 15.3, 8.4. Anal. Calcd for $C_{17}H_{14}N_2O_4S$: C, 59.64; H, 4.12; N, 8.18. Found: C, 59.86; H, 3.93; N, 8.35.

*Preparation of 3-Hexyl-2-(3-nitrophenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14bi**).* 90% yield (68 mg), white solid: mp 99−101 °C; IR (KBr) 1633, 1350, 1176 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.20−8.17 (m, 1H), 7.91 (t, J = 2.0 Hz, 1H), 7.76 (d, J = 7.5 Hz, 1H), 7.65−7.61 (m, 2H), 7.58 (t, J = 8.0 Hz, 1H), 7.47 (t, J = 7.6 Hz, 2H), 6.62 (s, 1H), 2.26 (t, J = 7.4 Hz, 2H), 1.56 (p, J = 7.4 Hz, 2H), 1.34−1.20 (m, 6H), 0.84 (t, J = 7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.6, 143.2, 137.4, 134.2, 132.8, 132.5, 131.6, 130.0, 128.4, 127.7, 123.1, 122.6, 122.5, 114.2, 34.0, 31.5, 28.3, 27.4, 22.5, 14.1; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 134.2, 132.8, 130.0, 128.4, 127.7, 123.1, 122.6, 122.5, 114.2, 34.0, 31.5, 28.3, 27.4, 22.5, 14.1. Anal. Calcd for $C_{20}H_{22}N_2O_4S$: C, 62.16; H, 5.74; N, 7.25. Found: C, 61.87; H, 6.00; N, 7.37.

*Preparation of 2-(3-Methoxyphenyl)-3-phenyl-2H-1,2-benzothiazine 1,1-dioxide (**14ca**).* 90% yield (67 mg), white solid: mp 156−158 °C; IR (KBr) 1596, 1344, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.83 (d, J = 7.7 Hz, 1H), 7.69−7.64 (m, 3H), 7.59 (d, J = 7.5 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.34−7.28 (m, 3H), 7.08 (t, J = 8.3 Hz, 1H), 7.05 (s, 1H), 6.74−6.67 (m, 3H), 3.69 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.8, 143.2, 138.4, 135.0, 133.0, 132.6, 132.1, 129.6, 129.4, 128.8, 128.7, 128.1, 127.9, 123.3, 119.8, 114.3, 113.6, 113.3, 55.5; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.6, 129.6, 129.4, 128.8, 128.7, 128.1, 127.9, 123.3, 119.8, 114.3, 113.6, 113.3, 55.5. Anal. Calcd for $C_{21}H_{17}NO_3S$: C, 69.40; H, 4.71; N, 3.85. Found: C, 69.56; H, 4.83; N, 3.74.

*Preparation of 2-(3-Methoxyphenyl)-3-(4-methoxyphenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14cc**).* 93% yield (75 mg), white solid: mp 145−147 °C; IR (KBr) 1598, 1348, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.81 (d, J = 7.8 Hz, 1H), 7.65−7.55 (m, 4H), 7.47 (t, J = 8.8 Hz, 1H), 7.08 (t, J = 7.9 Hz, 1H), 6.96 (s, 1H), 6.82 (d, J = 8.8 Hz, 2H), 6.72−6.66 (m, 3H), 3.77 (s, 3H), 3.69 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.7, 159.8, 143.1, 138.6, 133.3, 132.6, 131.9, 129.4, 129.3, 128.3, 127.8, 127.6, 123.3, 119.8, 114.2, 113.6, 113.2, 112.9, 55.5, 55.4; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.6, 129.4, 129.3, 128.3, 127.8, 123.3, 119.8, 114.2, 113.6, 113.2, 112.9, 55.5, 55.4. Anal. Calcd for $C_{22}H_{19}NO_4S$: C, 67.16; H, 4.87; N, 3.56. Found: C, 67.31; H, 5.00; N, 3.34.

*Preparation of 3-(4-Fluorophenyl)-2-(3-methoxyphenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ce**).* 91% yield (71 mg), white solid: mp 148−150 °C; IR (KBr) 1596, 1346, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.83 (d, J = 7.8 Hz, 1H), 7.68−7.63 (m, 3H), 7.57 (d, J = 7.6 Hz, 1H), 7.51 (t, J = 7.8 Hz, 1H), 7.09 (t, J = 8.1 Hz, 1H), 7.02−6.98 (m, 3H), 6.71−6.68 (m, 2H), 6.65−6.64 (m, 1H), 3.69 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 163.5 (d, J = 248.0 Hz), 159.9, 142.2, 138.2, 132.9, 132.7, 132.0, 131.2 (d, J = 3.1 Hz), 129.7 (d, J = 8.7 Hz), 129.6, 128.8, 128.0, 123.3, 119.8, 115.9 (d, J = 21.8 Hz), 114.2, 113.7, 113.3, 55.5; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.7, 129.7, 129.5, 128.8, 128.0, 123.3, 119.8, 115.9, 114.2, 113.7, 113.3, 55.5. Anal. Calcd for $C_{21}H_{16}FNO_3S$: C, 66.13; H, 4.23; N, 3.67. Found: C, 65.94; H, 4.06; N, 3.89.

*Preparation of 3-(4-Benzyloxyphenyl)-2-(3-methoxyphenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14cf**).* 90% yield (86 mg), white solid: mp 141−143 °C; IR (KBr) 1596, 1344, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.81 (d, J = 7.7 Hz, 1H), 7.66−7.60 (m, 3H), 7.56 (d, J = 7.6 Hz, 1H), 7.47 (t, J = 7.4 Hz, 1H), 7.44−7.29 (m, 5H), 7.09 (t, J = 8.0 Hz, 1H), 6.97 (s, 1H), 6.91 (d, J = 8.6 Hz, 2H), 6.74−6.67 (m, 3H), 5.01 (s, 2H), 3.69 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.0, 159.8, 143.0, 138.5, 136.6, 133.3, 132.6, 131.8, 129.4, 129.3, 128.7, 128.3, 128.3, 127.9, 127.8, 127.7, 123.2, 119.8, 115.1, 113.6, 113.2, 113.0, 70.2, 55.5; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.6, 129.4, 129.3, 128.7, 128.3, 128.3, 127.9, 127.7, 123.2, 119.8, 115.1, 113.6, 113.2, 113.0, 70.2, 55.5. Anal. Calcd for $C_{28}H_{23}NO_4S$: C, 71.62; H, 4.94; N, 2.98. Found: C, 71.36; H, 5.07; N, 3.15.

*Preparation of 2-(3-Methoxyphenyl)-3-(2-phenylethyl)-2H-1,2-benzothiazine 1,1-dioxide (**14cg**).* 92% yield (74 mg), red gummy liquid: IR (KBr) 1596, 1346, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.81 (d, J = 7.8 Hz, 1H), 7.59 (td, J = 7.6, 0.9 Hz, 1H), 7.45 (t, J = 7.5 Hz, 1H), 7.39 (d, J = 7.8 Hz, 1H), 7.30−7.23 (m, 3H), 7.18 (d, J = 7.2 Hz, 1H), 7.10 (d, J = 7.1 Hz, 2H), 6.90 (dd, J = 8.1, 1.9 Hz, 1H), 6.79 (dd, J = 7.7, 0.8 Hz, 1H), 6.74 (t, J = 2.1 Hz, 1H), 6.43 (s, 1H), 3.78 (s, 3H), 2.92 (t, J = 7.5 Hz, 2H), 2.56 (t, J = 8.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.2, 143.3, 140.7, 137.0, 132.8, 132.3, 131.5, 129.9, 128.6, 128.5, 127.9, 127.3, 126.3, 122.6, 120.7, 114.5, 114.3, 112.3, 55.6, 36.2, 34.2; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.3, 129.9, 128.6, 128.5, 127.9, 127.3, 126.3, 122.6, 120.7, 114.5, 114.3, 112.3, 55.6, 36.2, 34.2. Anal. Calcd for $C_{23}H_{21}NO_3S$: C, 70.56; H, 5.41; N, 3.58. Found: 70.79; H, 5.52; N, 3.39.

*Preparation of 3-Cyclopropyl-2-(3-methoxyphenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ch**).* 94% yield (63 mg), white solid: mp 173−175 °C; IR (KBr) 1602, 1332, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.77 (d, J = 7.8 Hz, 1H), 7.53 (td, J = 7.6, 0.8 Hz, 1H), 7.38 (t, J = 7.5 Hz, 1H), 7.34 (d, J = 7.9 Hz, 1H), 7.22 (t, J = 4.7 Hz, 1H), 6.88−6.78 (m, 3H), 6.27 (s, 1H), 3.76 (s, 3H), 1.44 (p, J = 6.7 Hz, 1H), 0.71 (d, J = 6.8 Hz, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.1, 146.1, 137.3, 133.2, 132.3, 131.4, 129.7, 127.4, 127.0, 122.5, 121.2, 114.7, 114.6, 107.7, 55.6, 15.3, 8.3; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.3, 129.7, 127.4, 127.0, 122.5, 121.2, 114.7, 114.6, 107.7, 55.6, 15.3, 8.3. Anal. Calcd for $C_{18}H_{17}NO_3S$: C, 66.03; H, 5.23; N, 4.28. Found: C, 66.28; H, 5.31; N, 4.15.

*Preparation of 3-Hexyl-2-(3-methoxyphenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14ci**).* 91% yield (69 mg), red gummy liquid: IR (KBr) 1596, 1348, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, J = 7.8 Hz, 1H), 7.58 (td, J = 7.5, 1.0 Hz, 1H), 7.45−7.39 (m, 2H), 7.25 (t, J = 8.0 Hz, 1H), 6.88 (dd, J = 7.9, 2.4 Hz, 1H), 6.76 (dd, J = 7.6, 1.0 Hz, 1H), 6.72 (t, J = 2.2 Hz, 1H), 6.47 (s, 1H), 3.78 (s, 3H), 2.25 (t, J = 7.4 Hz, 2H), 1.62−1.53 (m, 4H), 1.32−1.20 (m, 4H), 0.85 (t, J = 6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.1, 144.5, 137.1, 133.0, 132.3, 131.5, 129.8, 127.7, 127.1, 122.6, 120.7, 114.4, 114.3, 111.8, 55.6, 34.1, 31.6, 28.5, 27.6, 22.6, 14.2; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.3, 129.8, 127.7, 127.1, 122.6, 120.7, 114.4, 114.3, 111.8, 55.6, 34.1, 31.6, 28.5, 27.6, 22.6, 14.2. Anal. Calcd for

DOI: 10.1021/acs.joc.5b00274
J. Org. Chem. 2015, 80, 3940−3948

$C_{21}H_{25}NO_3S$: C, 67.89; H, 6.78; N, 3.77. Found: 67.73; H, 6.68; N, 3.94.

*Preparation of 2-(4-Methylphenyl)-3-phenyl-2H-1,2-benzothiazine 1,1-dioxide (**14da**).* 95% yield (71 mg), white solid: mp 192−194 °C; IR (KBr) 1616, 1346, 1176 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.83 (d, J = 7.8 Hz, 1H), 7.69−7.63 (m, 3H), 7.59 (d, J = 7.4 Hz, 1H), 7.50 (td, J = 7.7, 0.8 Hz, 1H), 7.33−7.28 (m, 3H), 7.05 (s, 1H), 7.02−6.97 (m, 4H), 2.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.4, 137.9, 135.1, 134.8, 133.1, 132.5, 132.0, 129.6, 129.5, 128.7, 128.6, 128.0, 127.9, 127.3, 123.3, 114.1, 21.1; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.5, 129.6, 129.5, 128.7, 128.6, 128.0, 127.9, 127.3, 123.3, 114.1, 21.1; HRMS (ES^+) MH^+, found 348.1055. $C_{21}H_{18}NO_2S$ requires 348.1058.

*Preparation of 3-(4-Ethoxyphenyl)-2-(4-methylphenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14db**).* 93% yield (78 mg), white solid: mp 179−181 °C; IR (KBr) 1604, 1348, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, J = 7.8 Hz, 1H), 7.63 (td, J = 7.9, 1.1 Hz, 1H), 7.60−7.54 (m, 3H), 7.46(td, J = 7.7, 1.0 Hz, 1H), 7.00−6.96 (m, 4H), 6.95 (s, 1H), 6.80 (d, J = 8.8 Hz, 2H), 3.97 (q, J = 7.0 Hz, 2H), 2.20 (s, 3H), 1.37 (t, J = 7.0 Hz, 3H) ; ^{13}C NMR ($CDCl_3$, 100 MHz) δ 160.1, 143.3, 137.8, 134.9, 133.4, 132.5, 131.7, 129.6, 129.4, 128.1, 127.8, 127.4, 127.2, 123.3, 114.6, 112.5, 63.6, 21.1, 14.8; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.5, 129.6, 129.4, 128.1, 127.8, 127.2, 123.3, 114.6, 112.5, 63.6, 21.1, 14.8. Anal. Calcd for $C_{23}H_{21}NO_3S$: C, 70.56; H, 5.41; N, 3.58. Found: C, 70.75; H, 5.23; N, 3.50.

*Preparation of 2,3-Bis(4-methylphenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14dd**).* 90% yield (70 mg), white solid: mp 187−189 °C; IR (KBr) 1608, 1346, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.81 (d, J = 7.6 Hz, 1H), 7.64 (t, J = 7.5 Hz, 1H), 7.56 (t, J = 7.7 Hz, 3H), 7.48 (t, J = 7.5 Hz, 1H), 7.12 (d, J = 7.8 Hz, 2H), 7.05−6.88 (m, 5H), 2.29 (s, 3H), 2.20 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.5, 139.8, 137.9, 134.9, 133.3, 132.5, 132.3, 131.9, 129.6, 129.5, 128.4, 127.9, 127.9, 127.2, 123.3, 113.4, 21.4, 21.2; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.5, 129.6, 129.5, 128.4, 127.9, 127.9, 127.2, 123.3, 113.4, 21.4, 21.2. Anal. Calcd for $C_{22}H_{19}NO_2S$: C, 73.10; H, 5.30; N, 3.88. Found: 73.31; H, 5.49; N, 3.70.

*Preparation of 2-(4-Methylphenyl)-3-(2-phenylethyl)-2H-1,2-benzothiazine 1,1-dioxide (**14dg**).* 92% yield (74 mg), red gummy liquid: IR (KBr) 1616, 1346, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, J = 7.7 Hz, 1H), 7.57 (td, J = 7.6, 0.8 Hz, 1H), 7.43 (td, J = 7.6, 0.6 Hz, 1H), 7.37 (d, J = 7.8 Hz, 1H), 7.23 (d, J = 6.8 Hz, 2H), 7.18−7.16 (m, 3H), 7.10−7.07 (m, 4H), 6.41 (s, 1H), 2.90 (t, J = 7.5 Hz, 2H), 2.53 (t, J = 7.5 Hz, 2H), 2.35 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.4, 140.7, 138.9, 133.3, 132.9, 132.2, 131.4, 130.0, 128.6, 128.5, 128.3, 127.8, 127.2, 126.3, 122.5, 111.8, 36.2, 34.0, 21.3; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.3, 130.0, 128.6, 128.5, 128.3, 127.8, 127.2, 126.3, 122.5, 111.8, 36.2, 34.0, 21.3. Anal. Calcd for $C_{23}H_{21}NO_2S$: C, 73.57; H, 5.64; N, 3.73. Found: C, 73.79; H, 5.48; N, 3.92.

*Preparation of 3-Hexyl-2-(4-methylphenyl)-2H-1,2-benzothiazine 1,1-dioxide (**14di**).* 90% yield (69 mg), red gummy liquid: IR (KBr) 1622, 1348, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.78 (d, J = 7.9 Hz, 1H), 7.57 (td, J = 7.6, 1.0 Hz, 1H), 7.44−7.39 (m, 2H), 7.16 (d, J = 8.1 Hz, 2H), 7.06 (dt, J = 8.3, 1.7 Hz, 2H), 6.46 (s, 1H), 2.34 (s, 3H), 2.24 (t, J = 7.4 Hz, 2H), 1.56 (p, J = 7.3 Hz, 2H), 1.32−1.20 (m, 6H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.6, 138.7, 133.4, 133.1, 132.2, 131.3, 129.9, 128.3, 127.6, 127.0, 122.5, 111.4, 34.0, 31.6, 28.5, 27.5, 22.6, 21.3, 14.1; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.2, 129.9, 128.3, 127.6, 127.0, 122.5, 111.4, 34.0, 31.6, 28.5, 27.5, 22.6, 21.3, 14.1; HRMS (ES^+) MNa^+, found 378.1503. $C_{21}H_{25}NNaO_2S$ requires 378.1504.

*Preparation of 2,3-Diphenyl-2H-1,2-benzothiazine 1,1-dioxide (**14ea**).* 95% yield (71 mg) as a white solid: mp 226−228 °C; IR (KBr) 1606, 1348, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.83 (d, J = 7.8 Hz, 1H), 7.68−7.64 (m, 3H), 7.60 (d, J = 7.4 Hz, 1H), 7.51 (t, J = 7.4 Hz, 1H), 7.33−7.27 (m, 3H), 7.21−7.10 (m, 5H), 7.06 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.3, 137.4, 135.0, 133.1, 132.6, 132.1, 129.6, 128.9, 128.8, 128.7, 128.1, 128.0, 127.8, 127.5, 123.2, 114.3; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.6, 129.6, 128.9, 128.8, 128.7, 128.1, 128.0, 127.8, 127.5, 123.2, 114.3; HRMS (ES^+) MH^+, found 334.0902. $C_{20}H_{16}NO_2S$ requires 334.0902.

*Preparation of 3-(4-Methylphenyl)-2-phenyl-2H-1,2-benzothiazine 1,1-dioxide (**14ed**).* 92% yield (72 mg), white solid: mp 179−181 °C; IR (KBr) 1610, 1346, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J = 7.7 Hz, 1H), 7.65 (t, J = 7.8 Hz, 1H), 7.59−7.53 (m, 3H), 7.49 (t, J = 7.6 Hz, 1H), 7.22−7.17 (m, 2H), 7.15−7.09 (m, 5H), 7.02 (s, 1H), 2.29 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.4, 139.8, 137.5, 133.2, 132.5, 132.2, 132.0, 129.5, 128.9, 128.5, 127.9, 127.9, 127.8, 127.5, 123.2, 113.6, 21.4; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.5, 129.5, 128.9, 128.5, 127.9, 127.9, 127.8, 127.5, 123.3, 113.6, 21.4. Anal. Calcd for $C_{21}H_{17}NO_2S$: C, 72.60; H, 4.93; N, 4.03. Found: C, 72.76; H, 4.76; N, 4.15.

*Preparation of 3-Cyclopropyl-2-phenyl-2H-1,2-benzothiazine 1,1-dioxide (**14eh**).* 94% yield (63 mg), white solid: mp 90−101 °C; IR (KBr) 1612, 1338, 1170 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.80 (d, J = 7.8 Hz, 1H), 7.57 (t, J = 7.2 Hz, 1H), 7.44−7.35 (m, 5H), 7.28−7.25 (m, 2H), 6.31 (s, 1H), 1.44 (p, J = 7.0 Hz, 1H), 0.73 (t, J = 5.0 Hz, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 146.1, 136.3, 133.2, 132.3, 131.4, 129.2, 129.0, 128.7, 127.4, 127.0, 122.5, 107.7, 15.3, 8.3; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.3, 129.2, 129.0, 128.7, 127.4, 127.0, 122.5, 107.7, 15.3, 8.3. Anal. Calcd for $C_{17}H_{15}NO_2S$: C, 68.66; H, 5.08; N, 4.71. Found: C, 68.86; H, 4.93; N, 4.81.

*Preparation of 3-Hexyl-2-phenyl-2H-1,2-benzothiazine 1,1-dioxide (**14ei**).* 91% yield (70 mg), red gummy liquid: IR (KBr) 1608, 1350, 1172 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.79 (d, J = 7.9 Hz, 1H), 7.58 (td, J = 7.8, 1.2 Hz, 1H), 7.45−7.35 (m, 5H), 7.20−7.17 (m, 2H), 6.49 (s, 1H), 2.24 (t, J = 7.4 Hz, 2H), 1.56 (p, J = 7.6 Hz, 2H), 1.29−1.23 (m, 6H), 0.86 (t, J = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 144.5, 136.0, 133.0, 132.3, 131.5, 129.2, 128.6, 128.4, 127.7, 127.1, 122.5, 111.9, 34.1, 31.5, 28.5, 27.5, 22.6, 14.1; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.3, 129.2, 128.6, 128.4, 127.7, 127.1, 122.5, 111.9, 34.1, 31.5, 28.5, 27.5, 22.6, 14.1. Anal. Calcd for $C_{20}H_{23}NO_2S$: C, 70.35; H, 6.79; N, 4.10. Found: C, 70.09; H, 6.92; N, 4.27.

*Preparation of 2-(2-Chlorophenyl)-3-phenyl-2H-1,2-benzothiazine 1,1-dioxide (**14fa**).* 90% yield (67 mg), white solid: mp 199−201 °C; IR (KBr) 1608, 1342, 1174 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.86 (d, J = 7.7 Hz, 1H), 7.70−7.65 (m, 3H), 7.58 (d, J = 7.5 Hz, 1H), 7.52 (td, J = 7.6, 0.9 Hz, 1H), 7.33−7.29 (m, 4H), 7.12−7.02 (m, 3H), 6.91 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 143.7, 135.0, 134.9, 134.5, 133.0, 132.6, 132.1, 130.8, 130.4, 129.8, 128.6, 128.5, 128.1, 127.8, 127.3, 122.7, 113.3; ^{13}C DEPT-135 ($CDCl_3$, 100 MHz) 132.6, 130.8, 130.4, 129.8, 128.6, 128.5, 128.1, 127.8, 127.3, 122.7, 113.3. Anal. Calcd for $C_{20}H_{14}ClNO_2S$: C, 65.30; H, 3.84; N, 3.81. Found: C, 65.50; H, 3.97; N, 3.63.

*Preparation of 2-(4-Methoxyphenyl)-3-phenyl-2H-1,2-benzothiazine 1,1-dioxide (**14ga**).* 97% yield (72 mg), white solid: mp 165−167 °C; IR (KBr) 1598, 1332, 1186 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.82 (d, J = 6.8 Hz, 1H), 7.73−7.54 (m, 4H), 7.54−7.42 (m, 1H), 7.37−7.24 (m, 3H), 7.10−6.90 (m, 3H), 6.67 (d, J = 7.2 Hz, 2H), 3.67 (s, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 158.9, 143.4, 134.9, 133.0, 132.4, 131.7, 130.6, 129.9, 129.4, 128.6, 128.4, 127.8, 123.1, 114.1, 113.6, 55.3. Anal. Calcd for $C_{21}H_{17}NO_3S$: C, 69.40; H, 4.71; N, 3.85. Found: C, 69.56; H, 4.62; N, 3.77.

■ ASSOCIATED CONTENT

Supporting Information

Scanned copies of ^1H and ^{13}C NMR spectra of all new compounds; CIF files for crystal structures of **14aa**, **14bi**, **14ch** and **14db**; coordinates of optimized structures. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: shovan.mondal@visva-bharati.ac.in, shovanku@gmail.com.

Notes

The authors declare no competing financial interest.

DOI: 10.1021/acs.joc.5b00274
J. Org. Chem. 2015, 80, 3940−3948

■ ACKNOWLEDGMENTS

DST, Government of India, is greatly acknowledged for giving a research grant to S.M. through INSPIRE Faculty Award (No. IFA12/CH/56) and S.D. is thankful to DST for a junior research fellowship under the same project. We again thank the DST (New Delhi) for providing Single Crystal XRD under the DST-FIST program in our department. We are highly grateful to Professor S. K. Chandra, Department of Chemistry, Visva-Bharati, for help in the studies of X-ray data. We also thank Md. Asif Amin (Junior Research Fellow, Indian Association for the Cultivation of Science) for HRMS spectroscopy.

■ REFERENCES

(1) (a) Kaneko, K.; Yoshino, T.; Matsunaga, S.; Kanai, M. *Org. Lett.* **2013**, *15*, 2502. (b) Zhou, A.; Hanson, P. R. *Org. Lett.* **2008**, *10*, 2951. (c) Liu, X. Y.; Li, C. H.; Che, C. M. *Org. Lett.* **2006**, *8*, 2707. (d) Yang, Z.; Xu, J. *Chem. Commun.* **2014**, *50*, 3616. (e) Li, Y.; Ding, Q.; Qiu, G.; Wu, J. *Org. Biomol. Chem.* **2014**, *12*, 149.

(2) (a) Inagaki, M.; Tsuri, T.; Jyoyama, H.; Ono, T.; Yamada, K.; Kobayashi, M.; Hori, Y.; Arimura, A.; Yasui, K.; Ohno, K.; Kakudo, S.; Koizumi, K.; Suzuki, R.; Kato, M.; Kawai, S.; Matsumoto, S. *J. Med. Chem.* **2000**, *43*, 2040. (b) Lebegue, N.; Gallet, S.; Flouquet, N.; Carato, P.; Pfeiffer, B.; Renard, P.; Leonce, S.; Pierre, A.; Chavatteand, P.; Berthelot, P. *J. Med. Chem.* **2005**, *48*, 7363. (c) Wells, G. J.; Tao, M.; Josef, K. A.; Bihovsky, R. *J. Med. Chem.* **2001**, *44*, 3488. (d) Supuran, C. T. *Nat. Rev. Drug Discovery* **2008**, *7*, 168.

(3) Levy, L. *Drugs Future* **1992**, *17*, 451.

(4) (a) Krozowski, Z. *Mol. Cell. Endocrinol.* **1992**, *84*, C25. (b) Kataoka, S.; Kudo, A.; Hirano, H.; Kawakami, H.; Kawano, T.; Higashihara, E.; Tanaka, H.; Delarue, F.; Sraer, J.-D.; Mune, T.; Krozowski, Z. S.; Yan, K. *J. Clin. Endocrinol. Metab.* **2002**, *87*, 877. (c) Wild, S.; Roglic, G.; Green, A.; Sicree, R.; King, H. *Diabetes Care* **2004**, *27*, 1047.

(5) Kim, S. H.; Ramu, R.; Kwon, S. W.; Lee, S. H.; Kim, C. H.; Kang, S. K.; Rhee, S. D.; Bae, M. A.; Ahn, S. H.; Ha, D. C.; Cheon, H. G.; Kim, K. Y.; Ahn, J. H. *Bioorg. Med. Chem. Lett.* **2010**, *20*, 1065.

(6) Brzozowski, F.; Saczewski, F.; Neamati, N. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 5298.

(7) (a) Bihovsky, R.; Tao, M.; Mallamo, J. P.; Wells, G. J. *Bioorg. Med. Chem. Lett.* **2004**, *14*, 1035. (b) Wells, G. J.; Tao, M.; Josef, K. A.; Bihovsky, R. *J. Med. Chem.* **2001**, *44*, 3488.

(8) Rayabarapu, D. K.; Zhou, A.; Jeon, K. O.; Samarakoon, T.; Rolfe, A.; Siddiqui, H.; Hanson, P. R. *Tetrahedron* **2009**, *65*, 3180.

(9) Rolfe, A.; Young, K.; Hanson, P. R. *Eur. J. Org. Chem.* **2008**, *31*, 5254.

(10) Zeng, W.; Chemler, S. R. *J. Am. Chem. Soc.* **2007**, *129*, 12948.

(11) Liu, X. Y.; Li, C. H.; Che, C. M. *Org. Lett.* **2006**, *8*, 2707.

(12) Ishida, N.; Shimamoto, Y.; Yano, T.; Murakami, M. *J. Am. Chem. Soc.* **2013**, *135*, 19103.

(13) (a) Barange, D. K.; Nishad, T. C.; Swamy, N. K.; Bandameedi, V.; Kumar, D.; Sreekanth, B. R.; Vyas, K.; Pal, M. *J. Org. Chem.* **2007**, *72*, 8547. (b) Rambabu, D.; Murthy, P. V. N. S.; Prasad, K. R. S.; Kandale, A.; Deora, G. S.; Rao, M. V. B.; Pal, M. *Tetrahedron Lett.* **2012**, *53*, 6577.

(14) (a) Mondal, S. *Chem. Rev.* **2012**, *112*, 5339. (b) Mondal, S.; Debnath, S. *Tetrahedron Lett.* **2014**, *55*, 1577. (c) Mondal, S.; Debnath, S. *Synthesis* **2014**, *46*, 368. (d) Mondal, S.; Debnath, S.; Das, B. *Tetrahedron* **2015**, *71*, 476. (e) Majumdar, K. C.; Mondal, S. *Chem. Rev.* **2011**, *111*, 7749.

(15) The CCDC reference number for the CIF file of compound **14aa**: CCDC 1052690.

(16) The CCDC reference number for the CIF file of compound **14bi**: CCDC 1042000.

(17) The CCDC reference number for the CIF file of compound **14ch**: CCDC 1041999.

(18) The CCDC reference number for the CIF file of compound **14db**: CCDC 1041998.

(19) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M.; Heyd, J. J.; Brothers, E.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, J.; Gomperts, R.; Stratmann, R. E.; Yazyev, O.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D.; Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. *Gaussian 09*; Gaussian Inc.: Wallingford, CT, 2009.

(20) Becke, A. D. *J. Chem. Phys.* **1996**, *104*, 1040.

(21) Hariharan, P. C.; Pople, J. A. *Theor. Chem. Acc.* **1973**, *28*, 213.

(22) Dunning, T. H., Jr.; Hay, P. J. In *Modern Theoretical Chemistry*; Schaefer, H. F., III, Ed.; Plenum: New York, 1977; Vol. 3, pp 1−28.

(23) (a) Fukui, K. *Acc. Chem. Res.* **1981**, *14*, 363. (b) Hratchian, H. P.; Schlegel, H. B. In *Theory and Applications of Computational Chemistry: The First 40 Years*; Dykstra, C. E., Frenking, G., Kim, K. S., Scuseria, G., Ed.; Elsevier: Amsterdam, 2005; pp 195−249.

(24) Tomasi, J.; Mennucci, B.; Cammi, R. *Chem. Rev.* **2005**, *105*, 2999.

DOI: 10.1021/acs.joc.5b00274
J. Org. Chem. 2015, 80, 3940−3948