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Sulfonium Ylides

Demonstration of 11–21-Membered Intramolecular Sulfonium Ylides: Regio- and Diastereoselective Synthesis of Spiro-Oxindole-Incorporated Macrocycles

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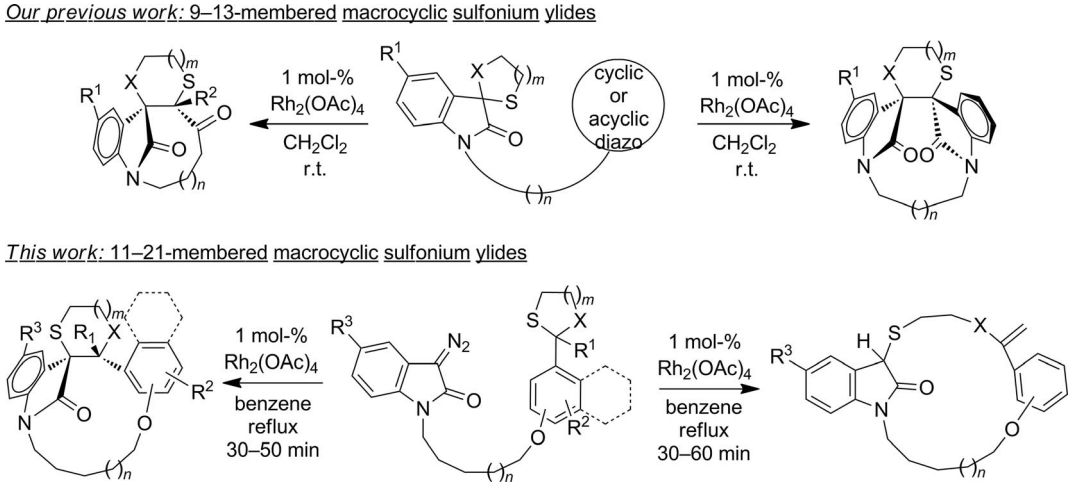
Abstract: An expeditious and convenient method for the generation of 11–21-membered intramolecular macrocyclic sulfonium ylides using catalytic $Rh_2(OAc)_4$ is presented. Using this approach, a wide variety of sulfur-macrocycles incorporating the oxindole unit were produced in good yields and with high diastereoselectivity. Interestingly, tetracyclic macrocycles were also attained in good yields and with good regioselectivity using the disclosed sulfonium ylides. Ring-opening reactions of tetracyclic macrocycles were also demonstrated.

Introduction

Reactions of diazocarbonyl compounds with metal catalysts constitute a widely illustrated approach in producing metallo-carbenoids, which enable an assortment of reactions, such as cyclopropanations, C–H or heteroatom–H insertions, and ylide formations.[1] Rhodium- or copper-carbenoids can efficiently react with sulfides to generate sulfonium ylides; subsequent [1,2]-Stevens rearrangement has been applied as a key C–C bond forming strategy in the synthesis of several natural products.[2] Inter- and intramolecular sulfonium ylide reactions[3] employing metallo-carbenoids have been investigated for several cyclic as well as acyclic compounds. However, only a few reports have discussed the synthesis of macrocycles via metallo-carbenoid-mediated sulfonium ylides. Davies[4] and co-workers have reported the formation of four–ten-membered intramolecular sulfonium ylides in the presence of $Rh_2(OAc)_4$ catalyst as a way to synthesize a wide variety of stable sulfonium ylides. More recently, Kido[5] and co-workers reported the synthesis of vinyl-substituted lactones via the application of nine-membered intramolecular cyclic sulfonium ylides. Recently, we reported[6] the rhodium(II) acetate-catalyzed generation of nine- to thirteen-membered intramolecular macrocyclic sulfonium ylides and their reactions (Scheme 1). However, we failed to demonstrate the production of greater than thirteen-membered intra-



Scheme 1. Reactions of intramolecular macrocyclic sulfonium ylides.

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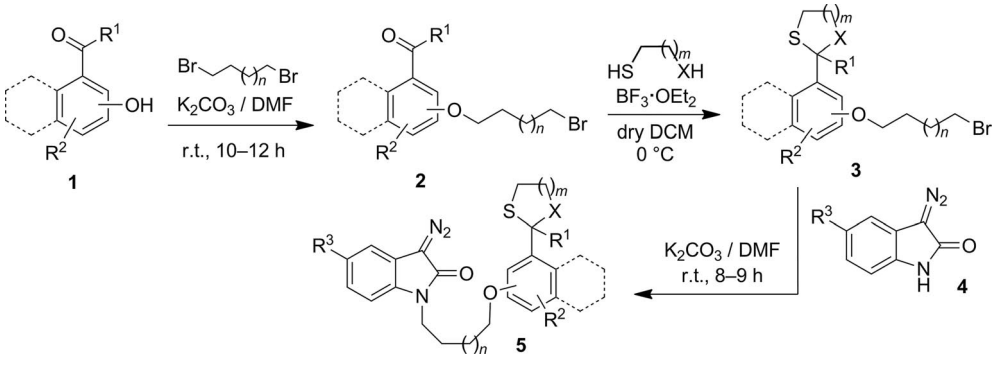
molecular macrocyclic sulfonium ylides. Generally, macrocycles have been synthesized using high dilution techniques[7]/templates[8] and have received a great deal of attention due to their large number of applications.[9] From a synthetic point of view, there are many methods available for the synthesis of oxindoles bearing quaternary carbon centers; coupling reactions and cyclization methods are among the most prominent. In particular, reactions of compounds bearing a thio group at the oxindole 3-position have been widely investigated.[10,11] We sought to develop new methods for the construction of oxindoles bearing quaternary carbon centers with a thio group at the 3-position using transition metal-catalyzed reactions of intramolecular macrocyclic sulfonium ylides. Based on the above limitations and our desire to generate greater than thirteen-membered sulfonium ylides, we herein demonstrate a mild and convenient method for making a wide variety of sulfur macrocycles incorporating an oxindole unit. $Rh_2(OAc)_4$ serves as a catalyst enabling reactions with high regio- and diastereoselectivity that proceed through 11–21-membered macrocyclic sulfonium ylide intermediates.

Results and Discussion

To demonstrate the utility of macrocyclic sulfonium ylides, required diazoamides **5a**–**p** were assembled by *O*-alkylation of hydroxybenzaldehydes, 2-hydroxynaphthaldehyde or hydroxyacetophenone **1** using dibromoalkanes in the presence of K_2CO_3/DMF to afford[12] corresponding bromo compounds **2** (Scheme 2). The carbonyl group was then protected using a literature precedented procedure to afford the thiol-protected bromo compounds **3**. Subsequent *N*-alkylation of 3-diazooxindoles **4** with **3** in the presence of K_2CO_3/DMF furnished the appropriate diazoamides **5a**–**p** in 80–91 % yield (Scheme 2 and Table 1).

To further our ongoing efforts to construct[6,13] functionalized sulfur macrocycles, we investigated the metal-catalyzed decomposition of diazoamides **5** involved in generating macrocyclic sulfonium ylides. In this reaction, solvents and temperature play an important role in dictating product distribution. Thus, reactions of diazoamide **5a** were examined in various organic solvents. In line with our previous report,[6,13] the reaction of diazoamide **5a** with rhodium(II) acetate dimer catalyst in dichloromethane was performed at room temperature but did not yield desired product **6a**. In general, the decomposition of the diazo group bearing a sulfide unit requires high temperature and long reaction times because the catalyst activity of $Rh_2(OAc)_4$ is diminished by sulfur atoms.[14] Based on this observation, solvents and reaction temperature were changed. In the next attempt, diazoamide **5a** in 1,2-dichloroethane at 40 °C gave only a 40 % yield of macrocycle **6a**. The reaction was re-



Scheme 2. Synthesis of diazoamides **5a**–**p**.

Table 1. Summary of syntheses for diazoamides **5a**–**p**.

Entry	Product	*n*	*m*	Aldehydes/ketones	R^1	R^2	R^3	X	Yield [%][a]
1	**5a**	6	2	2-hydroxybenzaldehyde	H	4-OCH_3	H	S	90
2	**5b**	5	1	3-hydroxybenzaldehyde	H	4-OCH_3	H	S	87
3	**5c**	9	1	3-hydroxybenzaldehyde	H	4-OCH_3	H	O	82
4	**5d**	5	2	2-hydroxynaphthaldehyde	H	H	H	S	88
5	**5e**	6	1	2-hydroxynaphthaldehyde	H	H	H	O	85
6	**5f**	2	1	2-hydroxynaphthaldehyde	H	H	H	O	80
7	**5g**	2	1	3-hydroxybenzaldehyde	H	H	H	S	67
8	**5h**	3	2	2-hydroxybenzaldehyde	H	H	H	S	88
9	**5i**	2	2	2-hydroxyacetophenone	CH_3	H	H	S	84
10	**5j**	2	1	2-hydroxyacetophenone	CH_3	H	H	O	90
11	**5k**	2	1	2-hydroxyacetophenone	CH_3	H	Cl	O	85
12	**5l**	3	1	2-hydroxyacetophenone	CH_3	H	H	O	84
13	**5m**	6	1	2-hydroxyacetophenone	CH_3	H	H	O	86
14	**5n**	7	1	2-hydroxyacetophenone	CH_3	H	H	O	80
15	**5o**	0	1	2-hydroxyacetophenone	CH_3	H	H	O	80
16	**5p**	0	1	2-hydroxyacetophenone	CH_3	H	Br	O	78

[a] Yield of the isolated product.

peated with 1 mol-% of rhodium(II) acetate dimer as a catalyst in refluxing benzene to furnish 16-membered macrocycle **6a** having the spiro-1,4-dithiepane unit. Compound **6a** was obtained as a single diastereomer (Scheme 3) in 95 % yield via intramolecular macrocyclic sulfonium ylide formation followed by a Stevens rearrangement.[6] In the present reaction, the decomposition proceeded quickly at reflux and the reaction was completed within 30 min. However, a low yield of the product was observed when the reaction was carried out using $Cu(acac)_2$. The results show that $Rh_2(OAc)_4$ is superior to $Cu(acac)_2$ for promoting formation of macrocycle **6a**. The structure of **6a** was confirmed by ^1H and ^{13}C NMR spectroscopy and mass spectrometry analyses. In addition, the structure and stereochemistry of compound **6a** were determined by X-ray crystal structure analysis (Figure 1). No other isomers were detected by either ^1H NMR or HPLC analyses of the crude reaction mixture.

Our principal aim is to synthesize interesting macrocyclic systems via the use of sulfonium ylides. With the optimized reaction conditions in hand, we subsequently tested the compatibility of this reaction with various substrates; the results are presented in Scheme 3. The use of macrocycles **6b** and **6c**, bearing

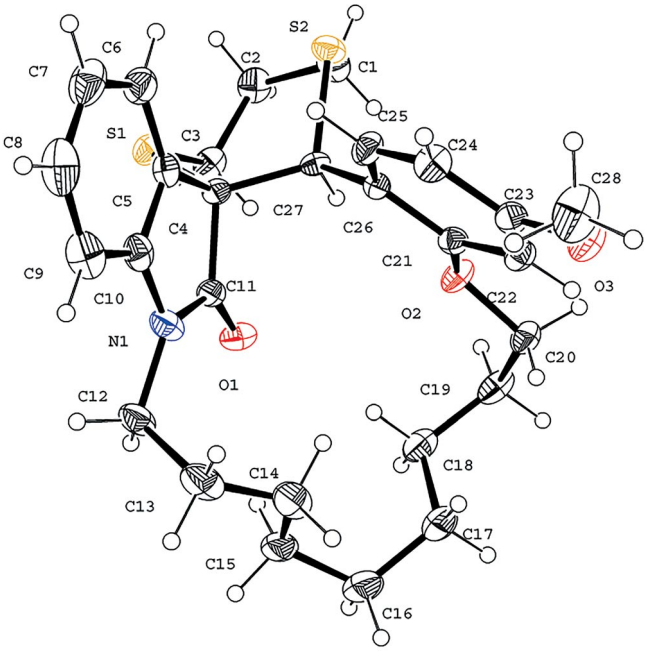
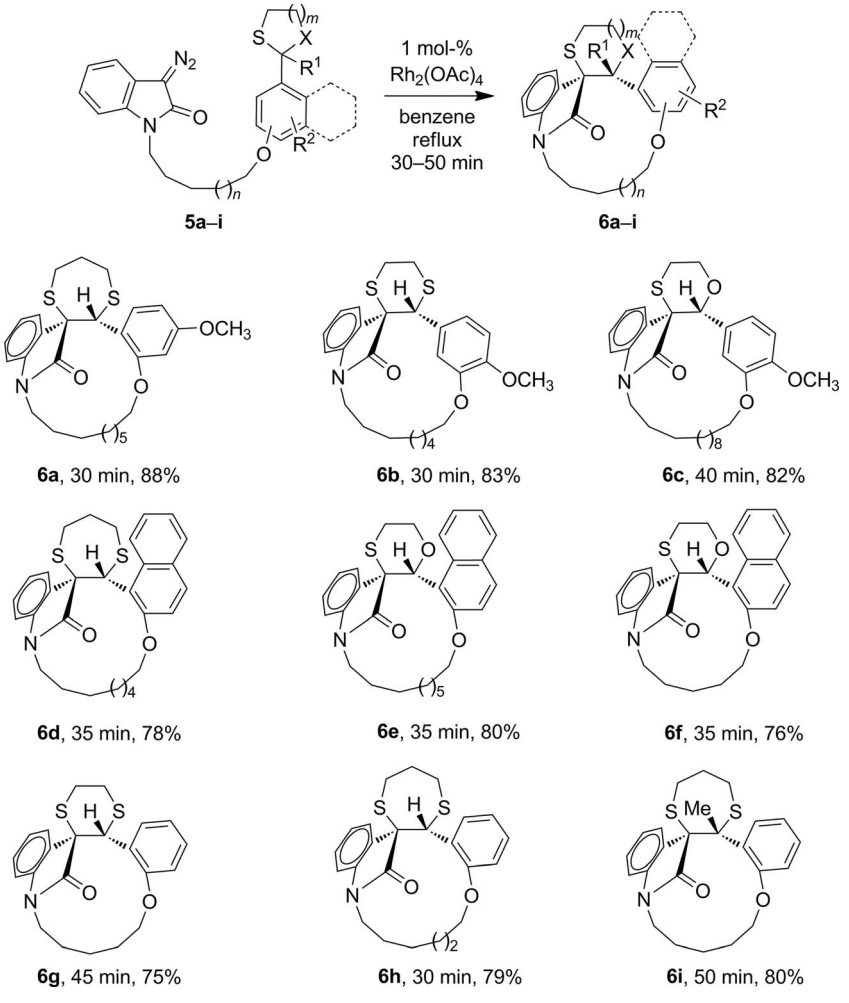


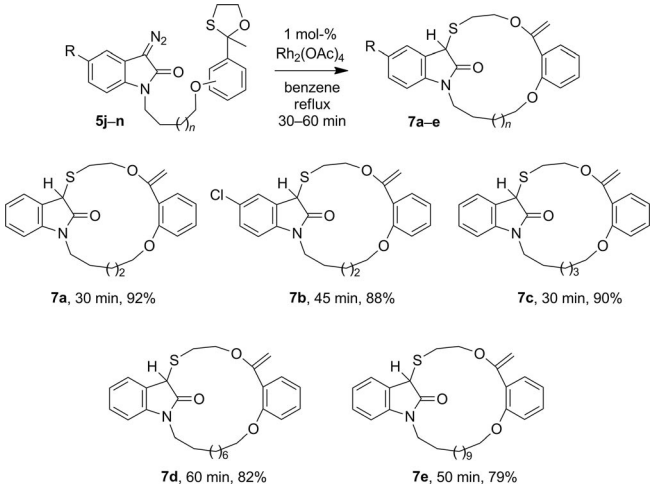
Figure 1. ORTEP view of macrocycle **6a** with 50 % probability of ellipsoids.



Scheme 3. Diastereoselective synthesis of macrocycles **6a**–**i**. [a] Reaction conditions: **5a** (1 mmol), 1 mol-% of $Rh_2(OAc)_4$, solvent (15 mL). [b] Yield of the isolated product.

a methoxy group *para* to the aldehyde, led to higher yields than did substrates lacking the methoxy group and did so in a completely diastereoselective manner. Naphthyl ring annulated spiro-1,4-oxathiane, -dithiepane macrocycles **6d**, **6e** and **6f** also were generated in good yields (Scheme 3). Similar methodology was applied to generate macrocycles **6g** and **6h** in good yields and reaction of diazoamide **5i** tethered to hydroxyacetophenone furnished corresponding methyl-substituted product **6i**, also in good yield. The stereochemistry for compounds **6b**–**i** was tentatively assigned on the basis of the crystal structure obtained for **6a**. However, reactions with the benzophenone derivative did not furnish product.

Next, diazoamides **5j**–**n** were prepared from mercaptoethanol-protected acetophenone derivatives instead of the appropriate dithiol-protected substrates. Initially, diazoamide **5j** was subjected to the optimized reaction conditions (see above); however, this reaction did not yield the expected [1,2]-rearranged macrocycle with a spiro-oxindole unit. Instead, we observed the regioselective formation of interesting tetracyclic macrocycle **7a** in high yield (Scheme 4). The ^{1}H NMR spectrum of **7a** shows the newly formed exocyclic double bond by way of two doublets at δ = 3.92 and 4.03 ppm, respectively, and a singlet for the CH proton at δ = 4.26 ppm. The ^{13}C NMR spectrum of **7a** shows a CH-carbon at δ = 46.1 ppm corresponding to the indole-3-carbon and the newly formed quaternary carbon at δ = 86.1 ppm. In addition, the structure of compound **7a** was unambiguously determined by X-ray crystallographic analysis (Figure 2). Encouraged by these results, we evaluated the substrate scope for this synthetic approach using various sizes of tetracyclic macrocycles; the results are shown in Scheme 4.



Scheme 4. Regioselective synthesis of tetracyclic macrocycles **7a**–**e**. [a] Reaction conditions: **5** (1 mmol), 1 mol-% of $Rh_2(OAc)_4$, solvent (15 mL). [b] Yield of the isolated product.

Reaction of the chloro-substituted diazoamide gave corresponding tetracyclic macrocycle **7b** in high yield (Scheme 4). We then generalized this reaction by regioselectively synthesizing several tetracyclic macrocycles **7b**–**e** up to the 23-membered ring using various spacer lengths.

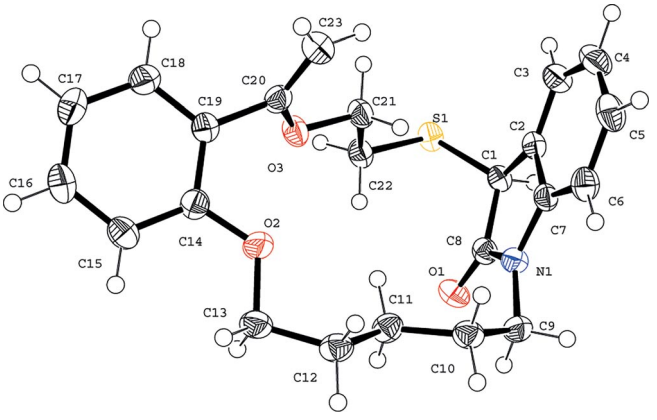
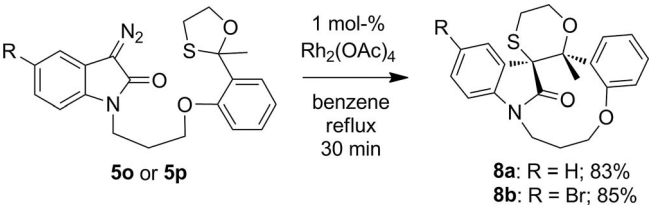


Figure 2. ORTEP view of tetracyclic macrocycle **7a** with 50 % probability of ellipsoids.

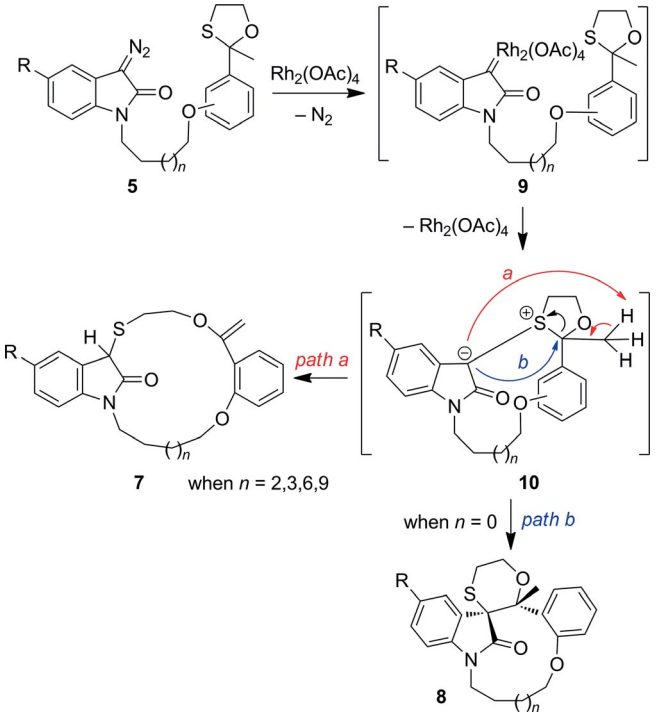
In all the above reactions, we did not observe the formation of any [1,2]-rearrangement products. The length of the spacer plays an important role in this transformation. However, the reaction of diazoamides **5o** and **5p**, with shorter spacers, under similar conditions furnished products **8a** and **8b** in 83 % and 85 % yields, respectively, via Stevens rearrangement with complete regio- and diastereoselectivity (Scheme 5). No tetracyclic products of type **7** were observed when using **5o** and **5p** as starting materials.



Scheme 5. Regio- and diastereoselective synthesis of spiro-1,4-oxathianes **8a** and **8b**.

Spiro-macrocycles **6** are produced in line with our earlier report.[6] The mechanism for regioselective formation of tetracyclic macrocycles **7** and macrocycles **8** having the spiro-oxindole is depicted in Scheme 6. Reaction of diazo compounds **5** with rhodium(II) acetate dimer as a catalyst might produce corresponding rhodium carbenoids **9**. The initially formed transient rhodium(II) carbenoids **9** may then undergo reaction with the thioether sulfur to form sulfonium ylides **10**. Further, the abstraction of a proton from a neighbouring methyl group producing the exocyclic double bond followed by C–S bond cleavage would yield tetracyclic macrocycles **7** (Scheme 6, path a). However, sulfonium ylides **10** with relatively short spacers may undergo Stevens rearrangement affording spiro-macrocycles **8** (Scheme 6, path b).

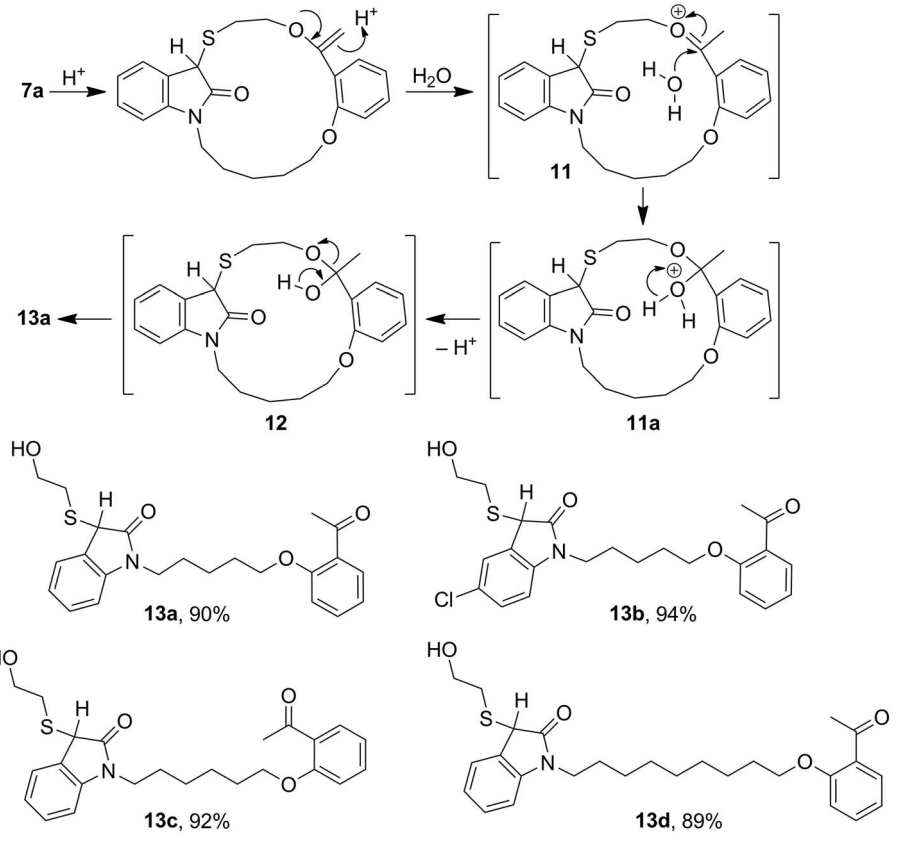
To explore the reactivity of tetracyclic macrocycles **7**, we examined their hydration reactions using acids/H_2O. It is well known that exocyclic olefins react with water in the presence of acid catalyst to afford the corresponding secondary or tertiary alcohols. Based on this reasoning, the reaction of macrocycle **7a** was performed with *p*TsOH·H_2O in DCM as a solvent. The reaction was completed within a few minutes to yield the Mark-



Scheme 6. Proposed mechanism for regioselective formation of tetracyclic macrocycles **7** and macrocycles **8** having spiro-oxindole unit.

ovnikov addition product hemiacetal **12** as an intermediate via protonation on enol ether **7a** followed by nucleophilic attack of water upon oxonium species **11**. It was found that compound **12** is very labile and was converted to acyclic compound **13a** in 90 % yield through hemiacetal decomposition of intermediate **12** (Scheme 7). The hydration reaction of compound **7a** was also accomplished in the presence of moist DCM solvent. In this case, the complete conversion of product **13a** was achieved without adding any acid to **7a**. To understand the role of water during the reaction a controlled experiment was performed using NMR techniques. Towards this end, macrocyclic compound **7a** was dissolved in $CDCl_3$, placed in the NMR tube and the ^{1}H-NMR spectrum was recorded. Next, a drop of water was added to **7a** using a capillary tube in the NMR tube and NMR spectra recorded at specific time intervals. Review of the NMR data revealed that **7a** was slowly converted into **13a** over the course of 1 h (Figure 3). This experiment indicates that the hydration reaction likely requires only traces of some acidic impurity available in $CDCl_3$. Acyclic product **13a** was obtained without using any purification techniques. Subsequent ring-opening reactions of **7b**–**d** were also carried out; corresponding acyclic products **13b**–**d** were obtained in good yields (Scheme 7).

In order to study the effect of diastereoselectivity in an intermolecular reaction, a reaction of 1 equiv. thioacetal **15** and



Scheme 7. Ring-opening reactions of tetracyclic macrocycles **7a**–**d**. [a] Reaction conditions: Compound **7** (1 mmol), a drop of H_2O in 5 mL of DCM solvent. [b] Yield of the product **13**.

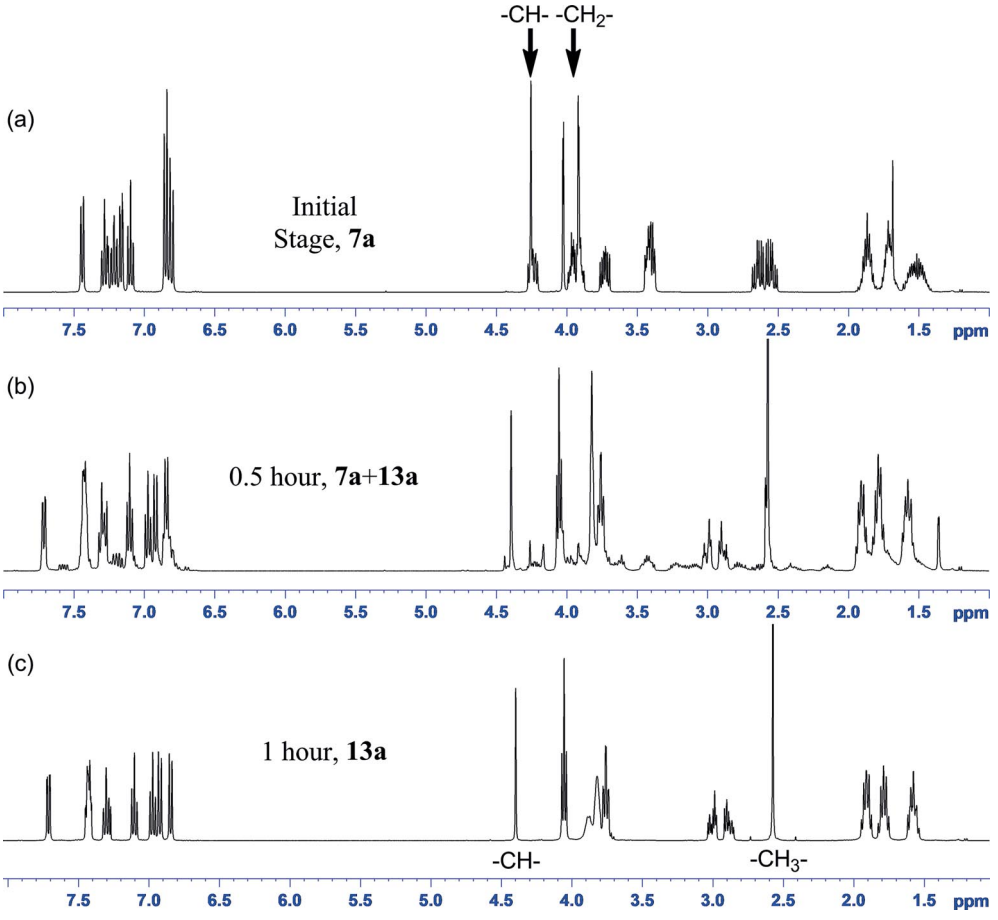
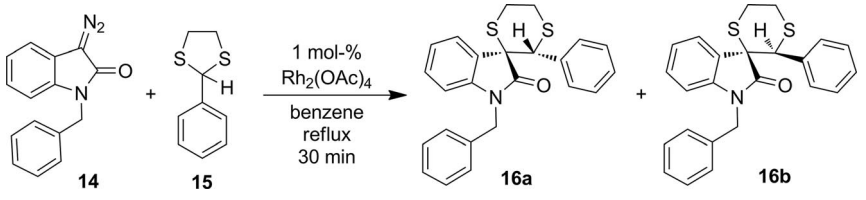


Figure 3. ^{1}H-NMR analyses conversion spectrum of compound **7a** to **13a** in NMR tube. [a] ^{1}H-NMR spectrum of **7a** in $CDCl_3$. [b] ^{1}H-NMR spectrum of **7a** 0.5 h after addition of H_2O. [c] ^{1}H-NMR spectrum after 1 h indicating complete conversion to **13a**.



Scheme 8. Synthesis of spiro-1,4-dithianes **16a**,**b** in an intermolecular manner.

1.2 equiv. 3-diazooxindole **14** in the presence of 1 mol-% rhodium(II) acetate dimer under optimized conditions (see above) was performed. This reaction furnished ring enlarged spiro-1,4-dithianes **16a**,**b** in 90 % yield as a diastereomeric mixture (86:14, in favor of **16a**) (Scheme 8).

Conclusions

In conclusion, we have demonstrated a facile method by which to generate 11–21-membered macrocyclic sulfonium ylides in the presence of catalytic $Rh_2(OAc)_4$. Subsequent Stevens rearrangement afforded 11–21-membered sulfur macrocycles incorporating an oxindole unit without using high dilution/template techniques. Interestingly, synthesis of tetracyclic macrocycles from mercaptoethanol-protected diazo compounds was also delineated in a regioselective manner.

Experimental Section

General Methods: The melting points are uncorrected. Infrared spectra were recorded using ATR technique with a Bruker Alpha FT-IR spectrophotometer. ^{1}H and ^{13}C NMR spectra were recorded with a Bruker 400 MHz FT-NMR spectrometer (model: Avance DPX 400) at room temperature (25 °C). The chemical shift (δ) and coupling constant (J) values are given in parts per million and Hertz, respectively. Tetramethylsilane (TMS) was used as an internal standard for all ^{1}H NMR studies. Carbon types were determined from DEPT-135 and ^{13}C NMR experiments. High resolution mass analyses were performed using electrospray ionization (ESI) technique with Orbitrap LC-MS and microTOF-Q II spectrometers. X-ray analyses were performed with a Bruker Smart Apex II diffractometer. Solvents were purified by distillation prior to use according to usual methods. DCM was dried using P_2O_5. DMF was purified through vacuum distillation using CaH_2 and stored over molecular sieves (4 Å). Thin-layer chromatography was performed using silica/alumina plates

and components were visualized by observation under iodine/UV light at 254 nm. Column chromatography was performed over silica gel (100–200 mesh)/neutral alumina, for column elution process hexane/EtOAc mixture was used as the eluent unless otherwise stated. All air sensitive reactions were conducted in oven-dried glassware under a positive pressure of an argon or nitrogen with magnetic stirring.

General Procedure for Diazoamides 5a–p: To an oven-dried flask, a solution containing appropriate diazo compound **4** (250 mg, 1 mmol) and potassium carbonate (543 mg, 2.5 mmol) in dry DMF was made under argon atmosphere. To this reaction mixture, a solution of appropriate bromo thioacetals (1.2 mmol) in dry DMF was slowly added over a period of 10 min and then a catalytic amount of tetrabutylammonium iodide was added. The progress of the reaction was monitored using TLC. After completion of the reaction, DMF was removed under reduced pressure. The reaction mixture was then extracted with dichloromethane (3 × 25 mL) and the combined organic layers washed with water (3 × 25 mL), brine (2 × 25 mL) and dried (anhydrous Na_2SO_4). The solvent was removed under reduced pressure and the resulting residue purified using silica gel column chromatography (hexanes/ethyl acetate, 80:20) to afford respective diazoamides **5a**–**p**.

Diazoamide 5a: Red thick oil (747 mg), yield 90 %. IR (neat): $\tilde{\nu}_{max}$ = 2988, 2945, 2132, 1754, 1664, 1323, 1165, 1080, 777, 760 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.82–0.95 (m, 1 H), 1.23–1.48 (m, 9 H), 1.66–1.73 (m, 2 H), 1.77–1.87 (m, 2 H), 1.90–1.95 (m, 1 H), 2.10–2.16 (m, 1 H), 2.86 (dt, J_1 = 14.0, J_2 = 4.0 Hz, 2 H), 3.06 (td, J_1 = 14.4, J_2 = 2.0 Hz, 2 H), 3.37 (s, 3 H), 3.81 (t, J = 7.2 Hz, 2 H), 3.95 (t, J = 6.4 Hz, 2 H), 5.59 (s, 1 H), 6.40 (d, J = 2.4 Hz, 1 H), 6.47 (dd, J_1 = 8.4, J_2 = 2.4 Hz, 1 H), 6.92 (d, J = 7.6 Hz, 1 H), 7.06 (t, J = 7.6 Hz, 1 H), 7.15–7.18 (m, 2 H), 7.47 (d, J = 8.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.4, 26.0, 26.9, 28.1, 29.1, 29.2, 29.5, 32.6, 40.8, 43.5, 55.3, 60.6, 68.6, 99.6, 104.8, 108.9, 116.9, 118.3, 120.3, 121.9, 125.4, 129.7, 133.9, 156.1, 160.6, 166.7 ppm. $C_{28}H_{35}N_3O_2S_2$ (525.72): calcd. C 63.97, H 6.71, N 7.99; found C 63.80, H 6.60, N 7.88.

Diazoamide 5b: Red thick oil (684 mg), yield 87 %. IR (neat): $\tilde{\nu}_{max}$ = 2983, 2933, 2137, 1717, 1626, 1292, 1261, 1110, 938, 743 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.36–1.46 (m, 8 H), 1.68–1.71 (m, 2 H), 1.78–1.87 (m, 2 H), 3.29–3.36 (m, 2 H), 3.44–3.52 (m, 2 H), 3.80 (t, J = 7.2 Hz, 2 H), 3.83 (s, 3 H), 4.02 (t, J = 6.8 Hz, 2 H), 5.61 (s, 1 H), 6.76 (d, J = 8.0 Hz, 1 H), 6.92 (d, J = 8.0 Hz, 1 H), 7.01–7.09 (m, 3 H), 7.16–7.20 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.9, 26.8, 28.1, 29.1, 29.2, 29.23, 40.2, 40.7, 56.1, 56.6, 60.7, 68.9, 108.9, 111.2, 112.6, 116.9, 118.3, 120.2, 121.9, 125.4, 132.0, 133.9, 148.5, 149.3, 166.7 ppm. $C_{26}H_{31}N_3O_3S_2$ (497.67): calcd. C 62.75, H 6.28, N 8.44; found C 62.90, H 6.18, N 8.32.

Diazoamide 5c: Red thick oil (697 mg), yield 82 %. IR (neat): $\tilde{\nu}_{max}$ = 2936, 2861, 2131, 1753, 1691, 1322, 1165, 1081, 760, 567 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.26–1.33 (m, 14 H), 1.41–1.46 (m, 2 H), 1.65–1.73 (m, 2 H), 1.78–1.87 (m, 2 H), 3.17–3.20 (m, 1 H), 3.24–3.30 (m, 1 H), 3.80 (t, J = 7.6 Hz, 2 H), 3.84 (s, 3 H), 3.88–3.94 (m, 1 H), 4.02 (t, J = 6.8 Hz, 2 H), 4.49–4.53 (m, 1 H), 5.98 (s, 1 H), 6.81 (d, J = 8.0 Hz, 1 H), 6.92 (d, J = 7.6 Hz, 1 H), 6.98 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1 H), 7.04 (d, J = 2.0 Hz, 1 H, Ar H), 7.07 (d, J = 7.6 Hz, 1 H), 7.16–7.19 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.9, 26.8, 28.1, 28.5, 28.9, 29.1, 29.2, 29.2, 32.6, 33.1, 40.1, 40.7, 56.1, 56.5, 60.7, 68.9, 108.9, 111.2, 112.6, 116.9, 118.3, 120.2, 121.9, 125.4, 132.0, 133.9, 148.5, 149.3, 166.7 ppm. $C_{30}H_{39}N_3O_4S$ (537.71): calcd. C 67.01, H 7.31, N 7.81; found C 67.19, H 7.40, N 7.94.

Diazoamide 5d: Red thick oil (739 mg), yield 88 %. IR (neat): $\tilde{\nu}_{max}$ = 3054, 2985, 2108, 1714, 1609, 1468, 1349, 1264, 728, 700 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.38–1.42 (m, 6 H), 1.50–1.54 (m, 2 H), 1.68–1.72 (m, 2 H), 1.81–1.88 (m, 2 H), 1.99–2.10 (m, 1 H), 2.20–2.25 (m, 1 H), 2.95 (dt, J_1 = 13.6, J_2 = 3.6 Hz, 2 H), 3.14 (td, J_1 = 14.4, J_2 = 1.6 Hz, 2 H), 3.80 (t, J = 7.2 Hz, 2 H), 4.13 (t, J = 6.4 Hz, 2 H), 6.45 (s, 1 H), 6.91 (d, J = 7.6 Hz, 1 H), 7.05 (td, J_1 = 7.6, J_2 = 0.8 Hz, 1 H), 7.13–7.21 (m, 3 H), 7.33 (td, J_1 = 8.0, J_2 = 0.8 Hz, 1 H), 7.51 (td, J_1 = 7.2, J_2 = 1.2 Hz, 1 H), 7.71–7.75 (m, 2 H), 9.07 (d, J = 8.4 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.9, 26.1, 26.8, 28.1, 29.2, 29.3, 29.5, 33.3, 40.7, 44.8, 60.7, 70.2, 108.9, 114.8, 116.9, 118.3, 120.6, 121.9, 123.8, 125.4, 125.7, 126.6, 128.2, 129.8, 130.3, 132.9, 133.9, 152.5, 166.7 ppm. $C_{30}H_{33}N_3O_2S_2$ (531.73): calcd. C 67.76, H 6.26, N 7.90; found C 67.93, H 6.35, N 7.75.

Diazoamide 5e: Red thick oil (690 mg), yield 85 %. IR (neat): $\tilde{\nu}_{max}$ = 2970, 2885, 2101, 1732, 1620, 1455, 1339, 1146, 1040, 726 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.26–1.48 (m, 10 H), 1.66–1.71 (m, 2 H), 1.77–1.86 (m, 2 H), 3.34–3.37 (m, 1 H), 3.45–3.52 (m, 1 H), 3.80 (t, J = 7.6 Hz, 2 H), 3.89–3.95 (m, 1 H), 4.04–4.22 (m, 2 H), 4.73–4.77 (m, 1 H), 6.92 (d, J = 8.0 Hz, 1 H), 7.04–7.08 (m, 2 H), 7.15–7.20 (m, 3 H), 7.33 (t, J = 7.2 Hz, 1 H), 7.45–7.46 (m, 1 H), 7.74 (d, J = 8.0 Hz, 1 H), 7.78 (d, J = 9.2 Hz, 1 H), 7.51 (d, J = 8.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.9, 26.1, 26.8, 28.0, 29.2, 29.3, 29.4, 33.3, 40.6, 44.9, 60.5, 70.1, 108.8, 114.8, 116.8, 118.3, 120.5, 121.9, 123.8, 125.4, 125.6, 126.6, 128.2, 129.8, 130.3, 132.9, 134.0, 152.5, 166.7 ppm. $C_{30}H_{33}N_3O_3S$ (515.66): calcd. C 69.87, H 6.45, N 8.15; found C 69.68, H 6.33, N 8.30.

Diazoamide 5f: Red thick oil (580 mg), yield 80 %. IR (neat): $\tilde{\nu}_{max}$ = 2980, 2934, 2131, 1715, 1616, 1290, 1265, 1109, 935, 745 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.42–1.50 (m, 2 H), 1.54–1.63 (m, 2 H), 1.69–1.76 (m, 2 H), 2.88 (dt, J_1 = 14.0, J_2 = 3.6 Hz, 2 H), 3.08 (td, J_1 = 14.4, J_2 = 2.0 Hz, 2 H), 3.73 (t, J = 7.2 Hz, 2 H), 4.01 (t, J = 6.4 Hz, 2 H), 5.67 (s, 1 H), 6.84 (dd, J_1 = 8.4, J_2 = 2.8 Hz, 2 H), 6.95 (t, J = 7.6 Hz, 1 H), 7.14–7.21 (m, 3 H), 7.22 (td, J_1 = 8.4, J_2 = 1.2 Hz, 1 H), 7.50 (dd, J_1 = 8.4, J_2 = 2.0 Hz, 1 H), 7.55–7.57 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.4, 25.7, 27.2, 28.9, 40.2, 43.9, 43.9, 60.4, 68.1, 109.8, 111.8, 116.9, 118.3, 120.5, 121.8, 123.8, 125.4, 125.6, 126.6, 128.2, 129.8, 130.3, 132.9, 133.9, 152.5, 166.7 ppm. $C_{26}H_{25}N_3O_3S$ (459.56): calcd. C 67.95, H 5.48, N 9.14; found C 67.72, H 5.42, N 9.10.

Diazoamide 5g: Red thick oil (450 mg), yield 67 %. IR (neat): $\tilde{\nu}_{max}$ = 2965, 2880, 2112, 1730, 1619, 1454, 1340, 1142, 1043, 728 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.42–1.50 (m, 2 H), 1.66–1.77 (m, 4 H), 3.21–3.29 (m, 2 H), 3.36–3.44 (m, 2 H), 3.77 (t, J = 7.2 Hz, 2 H), 3.86 (t, J = 6.0 Hz, 2 H), 5.51 (s, 1 H), 6.68 (dd, J_1 = 8.4, J_2 = 1.6 Hz, 1 H), 6.86 (d, J = 7.6 Hz, 1 H), 6.97–7.01 (m, 3 H), 7.08–7.18 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.5, 27.9, 28.9, 40.2, 40.6, 56.2, 60.7, 67.6, 108.9, 114.0, 114.1, 116.9, 118.4, 120.2, 121.9, 125.4, 129.4, 133.8, 141.9, 159.1, 166.8 ppm. $C_{22}H_{23}N_3O_2S_2$ (425.56): calcd. C 63.97, H 6.71, N 7.99; found C 63.80, H 6.62, N 7.88.

Diazoamide 5h: Red thick oil (630 mg), yield 88 %. IR (neat): $\tilde{\nu}_{max}$ = 2978, 2886, 2113, 1730, 1615, 1449, 1336, 1142, 1039, 728 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.42–1.59 (m, 4 H), 1.71–1.96 (m, 5 H), 2.11–2.15 (m, 1 H), 2.86 (dt, J_1 = 14.4, J_2 = 3.2 Hz, 2 H), 3.06 (td, J_1 = 14.4, J_2 = 2.0 Hz, 2 H), 3.83 (t, J = 7.2 Hz, 2 H), 3.99 (t, J = 6.4 Hz, 2 H), 5.67 (s, 1 H), 6.82 (d, J = 8.4 Hz, 1 H), 6.93 (t, J = 6.4 Hz, 2 H), 7.06 (t, J = 7.6 Hz, 1 H), 7.15–7.26 (m, 3 H), 7.56 (dd, J_1 = 7.6, J_2 = 1.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.4, 25.8, 26.6, 28.1, 29.1, 32.4, 40.6, 43.9, 60.7, 68.3, 108.9, 111.9, 116.9, 118.4, 120.9, 121.9, 125.4, 127.6, 129.1, 129.3, 133.8, 154.9, 166.7 ppm. $C_{24}H_{27}N_3O_2S_2$ (453.62): calcd. C 63.55, H 6.00, N 9.26; found C 63.33, H 6.15, N 9.18.

Diazoamide 5i: Red thick oil (600 mg), yield 84 %. IR (neat): $\tilde{\nu}_{max}$ = 2937, 2859, 2132, 1750, 1693, 1320, 1161, 1087, 764, 564 cm^{-1}. ^1H

NMR ($CDCl_3$, 400 MHz): δ = 1.59–1.66 (m, 2 H), 1.76–1.83 (m, 2 H), 1.86–1.20 (m, 4 H), 1.96 (s, 3 H), 2.71–2.81 (m, 4 H), 3.85 (t, J = 6.8 Hz, 2 H), 3.99 (t, J = 6.0 Hz, 2 H), 6.87–6.94 (m, 3 H), 7.06 (t, J = 7.6 Hz, 1 H), 7.15–7.26 (m, 3 H), 7.90 (dd, J_1 = 7.6, J_2 = 1.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.7, 24.8, 27.8, 28.5, 29.0, 29.1, 40.6, 52.0, 60.7, 68.0, 108.9, 113.4, 116.8, 118.4, 119.7, 121.9, 125.4, 128.7, 130.6, 131.1, 133.9, 157.2, 166.7 ppm. $C_{24}H_{27}N_3O_2S_2$ (453.62): calcd. C 63.55, H 6.00, N 9.26; found C 63.36, H 5.90, N 9.12.

Diazoamide 5j: Red thick oil (600 mg), yield 90 %. IR (neat): $\tilde{\nu}_{max}$ = 2934, 2090, 1688, 1608, 1465, 1357, 1236, 1045, 755 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.62–1.72 (m, 2 H), 1.78–1.87 (m, 2 H), 1.88 (s, 3 H), 1.91–1.96 (m, 2 H), 2.88–2.92 (m, 1 H), 3.03–3.10 (m, 1 H), 3.87 (t, J = 6.8 Hz, 2 H), 3.97–4.08 (m, 3 H), 4.36–4.41 (m, 1 H), 6.84 (d, J = 8.0 Hz, 1 H), 6.89 (td, J_1 = 7.6, J_2 = 0.8 Hz, 1 H), 6.95 (d, J = 7.6 Hz, 1 H), 7.05 (td, J_1 = 8.4, J_2 = 0.8 Hz, 1 H), 7.14–7.20 (m, 3 H), 7.42 (dd, J_1 = 7.6, J_2 = 1.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.8, 27.8, 29.0, 30.8, 33.4, 40.6, 60.7, 67.6, 70.8, 92.5, 109.0, 111.8, 116.9, 118.4, 120.2, 121.9, 123.0, 125.4, 128.2, 133.9, 134.9, 155.1, 166.7 ppm. $C_{23}H_{25}N_3O_3S$ (423.52): calcd. C 65.23, H 5.95, N 9.92; found C 65.41, H 5.84, N 9.85.

Diazoamide 5k: Red thick oil (504 mg), yield 85 %. IR (neat): $\tilde{\nu}_{max}$ = 2928, 2089, 1682, 1607, 1462, 1350, 1239, 1047, 752 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.61–1.69 (m, 2 H), 1.77–1.85 (m, 2 H), 1.88 (s, 3 H), 1.90–1.96 (m, 2 H), 2.88–2.92 (m, 1 H), 3.05–3.11 (m, 1 H), 3.86 (t, J = 6.8 Hz, 2 H), 3.96–4.08 (m, 3 H), 4.38–4.43 (m, 1 H), 6.84 (dd, J_1 = 8.4, J_2 = 0.8 Hz, 1 H), 6.86 (d, J = 8.4 Hz, 1 H), 6.90 (td, J_1 = 7.6, J_2 = 0.8 Hz, 1 H), 7.13 (dd, J_1 = 8.4, J_2 = 2.0 Hz, 1 H), 7.17 (d, J = 1.6 Hz, 1 H), 7.19–7.21 (m, 1 H), 7.42 (dd, J_1 = 8.0, J_2 = 2.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.6, 27.8, 29.0, 30.8, 34.0, 40.8, 60.9, 67.5, 70.8, 92.5, 109.7, 111.7, 118.2, 118.4, 120.2, 122.9, 125.4, 127.3, 128.2, 132.4, 134.8, 155.1, 166.2 ppm. $C_{23}H_{24}ClN_3O_3S$ (457.97): calcd. C 60.32, H 5.28, N 9.18; found C 60.48, H 5.42, N 9.29.

Diazoamide 5l: Red thick oil (581 mg), yield 84 %. IR (neat): $\tilde{\nu}_{max}$ = 2924, 2099, 1682, 1604, 1458, 1358, 1235, 1043, 744 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.44–1.52 (m, 2 H), 1.57–1.67 (m, 2 H), 1.73–1.89 (m, 4 H), 1.91 (s, 3 H), 2.88–2.93 (m, 1 H), 3.05–3.11 (m, 1 H), 3.84 (t, J = 7.2 Hz, 2 H), 3.96–4.08 (m, 3 H), 4.37–4.41 (m, 1 H), 6.84–6.95 (m, 3 H), 7.04–7.08 (m, 1 H), 7.15–7.25 (m, 3 H), 7.42 (dd, J_1 = 7.6, J_2 = 0.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.0, 26.6, 28.1, 29.8, 30.8, 33.4, 40.7, 60.7, 67.8, 70.8, 92.6, 108.9, 111.8, 116.9, 118.4, 120.2, 121.9, 122.9, 125.4, 128.2, 133.9, 134.9, 155.2, 166.7 ppm. $C_{24}H_{27}N_3O_3S$ (437.55): calcd. C 63.55, H 6.00, N 9.26; found C 63.72, H 6.15, N 9.34.

Diazoamide 5m: Red thick oil (650 mg), yield 86 %. IR (neat): $\tilde{\nu}_{max}$ = 2928, 2094, 1682, 1606, 1465, 1358, 1236, 1044, 747 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.35 (s, 8 H), 1.51–1.56 (m, 2 H), 1.68–1.73 (m, 2 H), 1.82–1.91 (m, 2 H), 1.92 (s, 3 H), 2.90–2.92 (m, 1 H), 3.06–3.12 (m, 1 H), 3.81 (t, J = 7.2 Hz, 2 H), 3.96–4.09 (m, 3 H), 4.39–4.41 (m, 1 H), 6.85–6.93 (m, 3 H), 7.04–7.08 (m, 1 H), 7.15–7.25 (m, 3 H), 7.42 (d, J = 8.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.2, 26.9, 28.1, 29.2, 29.3, 29.4, 30.8, 33.4, 40.8, 60.6, 68.1, 70.8, 92.6, 108.9, 111.8, 116.9, 118.3, 120.1, 121.8, 122.9, 125.4, 128.2, 134.0, 134.9, 155.3, 166.7 ppm. $C_{27}H_{33}N_3O_3S$ (479.63): calcd. C 67.61, H 6.93, N 8.76; found C 67.78, H 6.88, N 8.72.

Diazoamide 5n: Red thick oil (624 mg), yield 80 %. IR (neat): $\tilde{\nu}_{max}$ = 2929, 2092, 1685, 1607, 1462, 1358, 1231, 1048, 746 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.25–1.42 (m, 10 H), 1.50–1.58 (m, 2 H), 1.66–1.73 (m, 2 H), 1.81–1.91 (m, 2 H), 1.93 (s, 3 H), 2.90–2.93 (m, 1 H), 3.06–3.12 (m, 1 H), 3.80 (t, J = 7.2 Hz, 2 H), 3.96–4.08 (m, 3 H), 4.37–4.42 (m, 1 H), 6.85–6.93 (m, 3 H), 7.06 (td, J_1 = 7.2, J_2 = 0.8 Hz, 1 H), 7.15–7.21 (m, 3 H), 7.42 (dd, J_1 = 7.6, J_2 = 1.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.3, 26.9, 28.1, 29.3, 29.3, 29.4, 29.5, 30.8, 33.4, 40.8, 60.7, 68.1, 70.8, 92.6, 108.9, 111.8, 116.9, 118.4, 120.1, 121.9, 122.9, 125.4, 128.2, 134.0, 134.9, 155.3, 166.7 ppm. $C_{28}H_{35}N_3O_3S$ (493.66): calcd. C 68.12, H 7.15, N 8.51; found C 68.28, H 7.08, N 8.46.

Diazoamide 5o: Red thick oil (624 mg), yield 80 %. IR (neat): $\tilde{\nu}_{max}$ = 2936, 2092, 1685, 1606, 1468, 1351, 1230, 1040, 756 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.20 (s, 3 H), 2.91–2.38 (m, 2 H), 2.95–2.99 (m, 1 H), 3.13–3.19 (m, 1 H), 4.05–4.18 (m, 4 H), 4.20–4.27 (m, 1 H), 4.42–4.47 (m, 1 H), 6.84 (d, J = 8.0 Hz, 1 H), 6.94 (t, J = 7.2 Hz, 1 H), 7.07 (t, J = 7.2 Hz, 1 H), 7.15–7.25 (m, 4 H), 7.47 (dd, J_1 = 7.6, J_2 = 1.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.3, 31.1, 33.5, 38.4, 60.8, 65.4, 70.9, 92.5, 109.3, 111.9, 116.7, 118.3, 120.6, 122.0, 123.1, 125.6, 128.3, 134.0, 134.8, 154.8, 166.8 ppm. $C_{21}H_{21}N_3O_3S$ (395.47): calcd. C 63.78, H 5.35, N 10.63; found C 63.60, H 5.24, N 10.49.

Diazoamide 5p: Red thick oil (620 mg), yield 78 %. IR (neat): $\tilde{\nu}_{max}$ = 2938, 2090, 1688, 1607, 1465, 1350, 1233, 1039, 759 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.19 (s, 3 H), 2.90–2.39 (m, 2 H), 2.93–3.02 (m, 1 H), 3.16–3.20 (m, 1 H), 4.04–4.19 (m, 4 H), 4.20–4.26 (m, 1 H), 4.40–4.46 (m, 1 H), 6.83 (d, J = 8.0 Hz, 1 H), 6.90 (t, J = 7.2 Hz, 1 H), 7.05 (t, J = 7.2 Hz, 1 H), 7.16–7.27 (m, 3 H), 7.49 (dd, J_1 = 7.6, J_2 = 1.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 28.3, 31.1, 33.5, 38.3, 60.8, 65.3, 70.9, 92.5, 109.2, 111.8, 116.7, 118.4, 120.6, 122.0, 123.1, 125.7, 128.3, 133.9, 134.8, 154.8, 166.8 ppm. $C_{21}H_{20}BrN_3O_3S$ (474.37): calcd. C 53.17, H 4.25, N 8.86; found C 53.01, H 4.14, N 8.74.

General Procedure for Macrocycles 6a–i Having Spiro-oxindole Unit: A solution of diazoamide **5a–i** (100 mg, 1.0 mmol) and rhodium(II) acetate dimer (1 mol-%) in dry benzene (10 mL) was stirred at reflux conditions for 30–50 min. The progress of the reaction was monitored using TLC. After completion of the reaction, the reaction mixture was concentrated under reduced pressure and purified by column chromatography (SiO_2, hexane/ethyl acetate 75: 25) to afford respective macrocycles **6a–i**.

Macrocycle 6a: White solid (84 mg), yield 88 %; m.p. 151–152 °C. IR (neat): $\tilde{\nu}_{max}$ = 2923, 2855, 1709, 1606, 1352, 1200, 1165, 1044, 736 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 0.82–0.90 (m, 4 H), 1.09–1.14 (m, 1 H), 1.21–1.56 (m, 8 H), 1.71–1.74 (m, 1 H), 1.98–1.08 (m, 1 H), 2.43–2.87 (m, 1 H), 2.30–3.13 (m, 4 H), 3.59–3.66 (m, 1 H), 3.63 (s, 3 H), 3.91–3.96 (m, 1 H), 4.03–4.10 (m, 1 H), 4.18–4.23 (m, 1 H), 5.27 (s, 1 H), 5.99 (dd, J_1 = 8.8, J_2 = 2.4 Hz, 1 H), 6.33 (d, J = 2.8 Hz, 1 H), 6.53 (d, J = 8.4 Hz, 1 H), 6.66 (d, J = 8.0 Hz, 1 H), 7.08 (td, J_1 = 7.6, J_2 = 0.8 Hz, 1 H), 7.25 (td, J_1 = 7.6, J_2 = 1.2 Hz, 1 H), 7.90 (dd, J_1 = 7.2, J_2 = 0.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.8, 23.1, 25.0, 25.3, 26.9, 27.4, 28.0, 28.6, 33.6, 36.9, 38.3, 50.6, 55.2, 57.9, 66.1, 98.5, 103.6, 108.3, 119.8, 121.9, 126.3, 128.8, 129.2, 130.7, 142.8, 155.6, 159.5, 177.6 ppm. HRMS (ESI): calcd. for $C_{28}H_{35}NO_3S_2$ [M + Na]$^+$ 520.1956, found 520.1949.

Crystal Data for Macrocycle 6a: $C_{28}H_{35}NO_3S_2$, M = 497.69, 0.28 × 0.09 × 0.06 mm, orthorhombic, space group *Pcba* with a = 16.404(2) Å, b = 9.8784(12) Å, c = 31.474(4) Å, α = 90.00, β = 90.00, (2), γ = 90.00, V = 5100.1(11) Å^3, T = 150(2) K, R_1 = 0.0756, wR_2 = 0.1703 on observed data, z = 8, $D_{calcd.}$ = 1.296 mg cm^{-3}, F(000) = 2128, Absorption coefficient: 0.239 mm^{-1}, λ = 0.71073 Å, 5289 reflections were collected on a smart apex CCD single crystal diffractometer 4330 observed reflections [$I \geq 2\sigma(I)$]. The largest difference peak and hole: 0.843 and –0.341 e Å^{-3}, respectively. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using SHELXL-97 software.

Macrocycle 6b: White solid (78 mg), yield 83 %; m.p. 142–143 °C. IR (neat): $\tilde{\nu}_{max}$ = 2927, 2858, 1705, 1605, 1511, 1462, 1358, 1137,

736 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.61–0.70 (m, 1 H), 0.75–0.87 (m, 1 H), 1.02–1.11 (m, 1 H), 1.20–1.45 (m, 8 H), 1.89–1.97 (m, 1 H), 2.84–2.93 (m, 1 H), 3.10–3.18 (m, 2 H), 3.55–3.64 (m, 2 H), 3.70 (s, 3 H), 3.98–4.12 (m, 2 H), 4.36–4.41 (m, 1 H), 4.95 (s, 1 H), 6.14 (dd, J_1 = 8.4, J_2 = 2.0 Hz, 1 H), 6.43 (d, J = 8.4 Hz, 1 H), 6.76 (d, J = 7.6 Hz, 1 H), 6.83 (d, J = 2.0 Hz, 1 H), 7.16 (t, J = 7.6 Hz, 1 H), 7.32 (td, J_1 = 7.6, J_2 = 0.8 Hz, 1 H), 8.58 (dd, J_1 = 7.2, J_2 = 0.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22.3, 22.4, 24.9, 25.6, 25.7, 26.0, 33.0, 38.7, 52.0, 52.0, 55.9, 67.3, 108.9, 111.2, 115.6, 119.3, 121.9, 125.8, 128.5, 129.5, 131.1, 141.9, 146.1, 149.2, 173.4 ppm. HRMS (ESI): calcd. for $C_{26}H_{31}NO_3S_2$ [M + Na]$^+$ 492.1643, found 492.1640.

Macrocycle 6c: White solid (78 mg), yield 82 %; m.p. 175–176 °C. IR (neat): $\tilde{\nu}_{max}$ = 2926, 2854, 1706, 1605, 1513, 1462, 1262, 1140, 735 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.80–0.88 (m, 2 H), 1.06–1.28 (m, 15 H), 1.43–1.58 (m, 2 H), 1.68–1.73 (m, 1 H), 2.61 (d, J = 14.0 Hz, 1 H), 3.10–3.17 (m, 1 H), 3.33–3.38 (m, 1 H), 3.65–3.68 (m, 1 H), 3.70 (s, 3 H), 3.79–3.85 (m, 2 H), 4.30 (td, J_1 = 12.4, J_2 = 2.0 Hz, 1 H), 4.66 (d, J = 13.2 Hz, 1 H), 5.22 (s, 1 H), 6.38 (d, J = 1.2 Hz, 1 H), 6.55 (d, J = 8.4 Hz, 1 H), 6.66–6.69 (m, 2 H), 7.09–7.13 (m, 1 H), 7.22–7.26 (m, 1 H), 8.00 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 24.3, 24.7, 25.0, 25.7, 26.3, 26.5, 26.8, 27.2, 27.2, 27.8, 39.8, 51.9, 56.0, 67.8, 70.4, 84.9, 108.7, 110.1, 112.0, 120.6, 122.1, 125.1, 128.4, 129.2, 131.3, 142.5, 147.6, 149.4, 172.8 ppm. HRMS (ESI): calcd. for $C_{30}H_{39}NO_4S$ [M + H]$^+$ 510.2678, found 510.2676.

Macrocycle 6d: White solid (74 mg), yield 78 %; m.p. 238–239 °C. IR (neat): $\tilde{\nu}_{max}$ = 2925, 2859, 1698, 1603, 1463, 1352, 1240, 1070, 740 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.32–1.49 (m, 7 H), 1.63–1.77 (m, 4 H), 1.87–1.96 (m, 1 H), 2.07–2.18 (m, 1 H), 2.42–2.47 (m, 1 H), 2.61–2. 65 (m, 1 H), 2.97–3.01 (m, 1 H), 3.32–3.38 (m, 1 H), 3.63–3.71 (m, 2 H), 3.94–4.00 (m, 2 H), 4.15–4.22 (m, 1 H), 6.11 (s, 1 H), 6.40 (td, J_1 = 7.6, J_2 = 0.4 Hz, 1 H), 6.64 (d, J = 8.0 Hz, 1 H), 7.23 (d, J = 7.6 Hz, 1 H), 6.95 (td, J_1 = 8.0, J_2 = 1.2 Hz, 1 H), 7.04 (d, J = 8.8 Hz, 1 H), 7.33 (td, J_1 = 8.0, J_2 = 0.8 Hz, 1 H), 7.55–7.61 (m, 2 H), 7.67 (d, J = 8.4 Hz, 1 H), 9.25 (d, J = 8.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.3, 23.8, 25.1, 25.2, 26.0, 26.3, 28.0, 30.7, 34.4, 34.7, 40.3, 50.0, 62.6, 69.4, 108.0, 114.1, 119.6, 121.7, 121.8, 123.5, 123.7, 125.2, 126.4, 128.2, 128.3, 128.8, 129.5, 129.5, 129.8, 133.9, 141.7, 153.1, 175.8 ppm. HRMS (ESI): calcd. for $C_{30}H_{33}NO_2S_2$ [M + H]$^+$ 504.2031, found 504.2050.

Macrocycle 6e: White solid (76 mg), yield 80 %; m.p. 239–240 °C. IR (neat): $\tilde{\nu}_{max}$ = 2923, 2855, 1705, 1462, 1352, 1239, 1096, 1042, 743 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.26–1.45 (m, 7 H), 1.62–1.84 (m, 6 H), 3.21–3.29 (m, 2 H), 3.43–3.48 (m, 1 H), 3.42–3.48 (m, 1 H), 3.89–3.94 (m, 1 H), 4.03–4.08 (m, 1 H), 4.15–4.22 (m, 1 H), 4.33–4.00 (m, 1 H), 4.00–4.49 (m, 1 H), 6.14 (s, 1 H), 6.42 (t, J = 7.6 Hz, 1 H), 6.61 (d, J = 7.6 Hz, 1 H), 6.72 (d, J = 7.6 Hz, 1 H), 6.96 (td, J_1 = 7.6, J_2 = 0.8 Hz, 1 H), 7.01 (d, J = 8.8 Hz, 1 H), 7.33 (t, J = 6.8 Hz, 1 H), 7.49–7.53 (m, 1 H), 7.61 (d, J = 8.8 Hz, 1 H), 7.17 (d, J = 8.0 Hz, 1 H), 9.30 (d, J = 8.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.3, 24.8, 25.0, 25.9, 26.0, 26.4, 27.6, 29.3, 40.3, 52.7, 64.0, 70.9, 76.9, 108.0, 115.9, 121.7, 123.7, 125.9, 126.5, 128.1, 128.5, 129.0, 129.8, 130.3, 133.2, 142.7, 155.2, 177.5 ppm. HRMS (ESI): calcd. for $C_{30}H_{33}NO_3S$ [M + Na]$^+$ 488.2259, found 488.2260.

Macrocycle 6f: White solid (72 mg), yield 76 %; m.p. 218–219 °C. IR (neat): $\tilde{\nu}_{max}$ = 2925, 2856, 1702, 1605, 1462, 1353, 1237, 1095, 746 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.47–1. 54 (m, 1 H), 1.62–1.87 (m, 4 H), 1.96–2.04 (m, 1 H), 3.13–3.21 (m, 1 H), 3.28–3.42 (m, 2 H), 3.69–3.73 (m, 1 H), 4.07–4.11 (m, 1 H), 4.20–4.34 (m, 2 H), 4.48–4.55 (m, 1 H), 5.98 (s, 1 H), 6.29 (t, J = 7.6 Hz, 1 H), 6.49 (d, J = 7.6 Hz, 1 H), 6.62 (d, J = 7.6 Hz, 1 H), 6.86 (d, J = 9.2 Hz, 1 H), 6.92 (td, J_1 = 7.6, J_2 = 0.8 Hz, 1 H), 7.34 (td, J_1 = 7.6, J_2 = 0.8 Hz, 1 H), 7.54 (d, J = 9.2 Hz, 1 H), 7.55–7.60 (m, 1 H), 7.67 (d, J = 8.0 Hz, 1 H), 9.30 (d, J = 9.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.9, 22.8, 24.0, 27.2, 39.0, 52.8, 53.4, 63.5, 64.3, 79.1, 107.8, 112.0, 120.7, 121.6, 123.4, 125.4, 125.9, 126.2, 128.0, 128.1, 128.3, 129.3, 129.7, 133.2, 141.4, 153.1, 180.5 ppm. HRMS (ESI): calcd. for $C_{26}H_{25}NO_3S$ [M + Na]$^+$ 454.1453, found 454.1454.

Macrocycle 6g: White solid (70 mg), yield 75 %; m.p. 214–215 °C. IR (neat): $\tilde{\nu}_{max}$ = 2925, 2852, 1706, 1609, 1512, 1467, 1260, 1143, 736 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.83–0.93 (m, 1 H), 1.56–1.26 (m, 1 H), 1.35–1.51 (m, 2 H), 1.61–1.69 (m, 1 H), 1.78–1.86 (m, 1 H), 2.94–2.97 (m, 1 H), 3.17–3.24 (m, 2 H), 3.48–3.63 (m, 2 H), 3.91–4.04 (m, 2 H), 4.25–4.30 (m, 1 H), 4.96 (s, 1 H), 6.51 (d, J = 7.6 Hz, 1 H), 6.56 (d, J = 8.0 Hz, 1 H), 6.68 (dd, J_1 = 8.0, J_2 = 1.6 Hz, 1 H), 6.82 (t, J = 7.6 Hz, 1 H), 6.91 (s, 1 H), 7.10 (t, J = 7.6 Hz, 1 H), 7.20 (t, J = 7.6 Hz, 1 H), 8.34 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22.3, 25.5, 26.1, 30.0, 31.8, 40.6, 50.6, 52.8, 68.9, 108.3, 119.0, 120.3, 121.4, 122.0, 125.6, 128.5, 128.6, 130.7, 137.7, 141.9, 158.3, 174.4 ppm. HRMS (ESI): calcd. for $C_{22}H_{23}NO_2S_2$ [M + Na]$^+$ 420.1068, found 420.1070.

Macrocycle 6h: White solid (74 mg), yield 79 %; m.p. 186–187 °C. IR (neat): $\tilde{\nu}_{max}$ = 2927, 2865, 1702, 1605, 1487, 1352, 1237, 1167, 730 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 0.82–0.89 (m, 1 H), 1.12–1.19 (m, 1 H), 1.27–1.33 (m, 1 H), 1.56–1.64 (m, 1 H), 1.73–1.91 (m, 4 H), 2.04–2.12 (m, 1 H), 2.38–2.43 (m, 1 H), 2.69–2.73 (m, 1 H), 3.06–3.19 (m, 2 H), 3.25–3.30 (m, 1 H), 3.84–3.91 (m, 1 H), 4.04–4.15 (m, 2 H), 4.28–4.35 (m, 1 H), 5.24 (s, 1 H), 6.59 (d, J = 8.4 Hz, 1 H), 6.63–6.66 (m, 2 H), 6.89 (t, J = 7.6 Hz, 1 H), 6.94 (td, J_1 = 8.4, J_2 = 1.2 Hz, 1 H), 7.08 (t, J = 7.6 Hz, 1 H), 7.16 (dd, J_1 = 7.6, J_2 = 1.2 Hz, 1 H), 7.39 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.1, 25.0, 25.0, 26.5, 28.9, 33.3, 37.5, 38.0, 53.6, 59.2, 67.4, 108.5, 110.7, 119.3, 121.8, 126.5, 127.3, 128.0, 128.2, 128.6, 131.8, 141.65, 153.7, 177.2 ppm. HRMS (ESI): calcd. for $C_{24}H_{27}NO_2S_2$ [M + Na]$^+$ 448.1381, found 448.1362.

Macrocycle 6i: White solid (75 mg), yield 80 %; m.p. 193–194 °C. IR (neat): $\tilde{\nu}_{max}$ = 2922, 2857, 1698, 1603, 1482, 1355, 1234, 1172, 1057, 737 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.33–1.41 (m, 1 H), 1.64–1.84 (m, 3 H), 1.95–2.03 (m, 1 H), 2.12–2.30 (m, 3 H), 2.40 (s, 3 H), 3.00–3.13 (m, 3 H), 3.37–3.43 (m, 1 H), 3.61–3.69 (m, 1 H), 3.82–3.85 (m, 1 H), 3.96–4.01 (m, 1 H), 4.09–4.15 (m, 1 H), 6.53 (d, J = 8.0 Hz, 1 H), 6.63–6.73 (m, 3 H), 6.94 (td, J_1 = 8.4, J_2 = 1.2 Hz, 1 H), 7.03 (t, J = 6.8 Hz, 1 H), 7.52 (s, 1 H), 7.84 (dd, J_1 = 8.0, J_2 = 1.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22.8, 23.7, 23.3, 24.8, 28.7, 29.6, 31.3, 38.6, 60.5, 62.9, 66.2, 108.0, 111.4, 119.3, 121.0, 125.6, 127.8, 128.0, 129.7, 130.0, 132.2, 141.3, 156.2, 174.3 ppm. HRMS (ESI): calcd. for $C_{24}H_{27}NO_2S_2$ [M + H]$^+$ 426.1561, found 426.1567.

General Procedure for Tetracyclic Macrocycles 7a–e: Rhodium(II) acetate dimer (1 mol-%) catalyst was added to a stirred solution of dry benzene (5 mL) under nitrogen atmosphere at reflux conditions. An appropriate solution of diazoamides **5j–n** (100 mg, 1.0 mmol) in dry benzene (5 mL) was added dropwise over 30–60 min. Then, the reaction was monitored using TLC. The solvent was removed under reduced pressure after the reaction was completed. The residue was subjected to silica gel column (100–200 mesh) chromatography using hexanes/EtOAc to furnish respective tetracyclic macrocycles **7a–e**.

Tetracyclic Macrocycle 7a: White solid (86 mg), yield 92 %; m.p. 211–212 °C. IR (neat): $\tilde{\nu}_{max}$ = 3454, 2930, 2858, 1708, 1601, 1464, 1350, 1301, 1235, 1042, 752 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.13–1.61 (m, 2 H), 1.66–1.77 (m, 2 H), 1.80–1.92 (m, 2 H), 2.51–2.68 (m, 2 H), 3.38–3.45 (m, 2 H), 3.70–3.77 (m, 1 H), 3.88–3.99 (m, 2 H), 3.92 (d, J = 2.4 Hz, 1 H), 4.03 (d, J = 2.4 Hz, 1 H), 4.21–4.28 (m, 1 H),

4.26 (s, 1 H), 6.80–6.86 (m, 3 H), 7.10 (t, J = 7.6 Hz, 1 H), 7.16 (dd, J_1 = 7.6, J_2 = 1.6 Hz, 1 H), 7.22 (td, J_1 = 8.4, J_2 = 2.0 Hz, 1 H), 7.28 (t, J = 7.6 Hz, 1 H), 7.44 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 24.2, 27.0, 27.8, 30.2, 40.9, 46.1, 66.3, 68.2, 86.1, 108.7, 112.5, 120.3, 123.0, 125.3, 127.3, 127.7, 129.3, 129.8, 130.4, 143.9, 156.5, 159.4, 174.4 ppm. HRMS (ESI): calcd. for $C_{23}H_{25}NO_3S$ [M + H]$^+$ 396.1633, found 396.1630.

Crystal Data for Tetracyclic Macrocycle 7a: $C_{23}H_{25}NO_3S$, M = 395.50, 0.45 × 0.32 × 0.24 mm, triclinic, space group $P\bar{1}$ with a = 8.6848(7) Å, b = 9.7801(8) Å, c = 12.7044(11) Å, α = 107.8050(10), β = 93.5390(10), γ = 94.2270(10), V = 1020.57(15) Å^3, T = 273(2) K, R_1 = 0.0357, wR_2 = 0.0893 on observed data, z = 2, $D_{calcd.}$ = 1.287 mg cm^{-3}, F(000) = 420, Absorption coefficient: 0.182 mm^{-1}, λ = 0.71073 Å, 4360 reflections were collected on a smart apex CCD single crystal diffractometer 4083 observed reflections [$I \geq 2\sigma(I)$]. The largest difference peak and hole: 0.300 and –0.233 e Å^{-3}, respectively. The structure was solved by direct methods and refined by full-matrix least-squares on F^2 using SHELXL-97 software.

Tetracyclic Macrocycle 7b: White solid (83 mg), yield 88 %; m.p. 208–209 °C. IR (neat): $\tilde{\nu}_{max}$ = 3456, 2931, 2857, 1706, 1602, 1464, 1348, 1306, 1232, 1038, 753 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.39–1.56 (m, 2 H), 1.67–1.89 (m, 4 H), 2.52–2.69 (m, 2 H), 3.35–4.41 (m, 1 H), 3.45–3.50 (m, 1 H), 3.75–3.82 (m, 1 H), 3.89–3.99 (m, 2 H), 4.00 (d, J = 2.4 Hz, 1 H), 4.04 (d, J = 2.4 Hz, 1 H), 4.21–4.28 (m, 1 H), 4.26 (s, 1 H), 6.78 (d, J = 8.4 Hz, 1 H), 6.81 (d, J = 8.4 Hz, 1 H), 6.86 (td, J_1 = 7.2, J_2 = 0.4 Hz, 1 H), 7.17–7.28 (m, 3 H), 7.44 (d, J = 0.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 24.2, 27.0, 27.6, 30.2, 41.1, 45.9, 66.1, 68.1, 86.2, 109.6, 112.5, 120.4, 125.6, 127.6, 128.5, 129.0, 129.3, 129.9, 130.4, 142.41, 156.5, 159.4, 174.0 ppm. HRMS (ESI): calcd. for $C_{23}H_{24}ClNO_3S$ [M + Na]$^+$ 452.1063, found 452.1059.

Tetracyclic Macrocycle 7c: White solid (84 mg), yield 90 %; m.p. 243–244 °C. IR (neat): $\tilde{\nu}_{max}$ = 3456, 2933, 2862, 1706, 1606, 1460, 1348, 1302, 1228, 1040, 754 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.34–1.50 (m, 4 H), 1.64–1.78 (m, 4 H), 2.58–2.71 (m, 2 H), 3.34–3.40 (m, 1 H), 3.54–3.61 (m, 1 H), 3.70–3.77 (m, 1 H), 3.84–3.94 (m, 3 H), 4.09 (s, 1 H) 4.18–4.25 (m, 1 H), 4.27 (s, 1 H), 6.79–6.86 (m, 3 H), 7.11 (t, J = 7.6 Hz, 1 H), 7.19 (t, J = 6.4 Hz, 2 H), 7.29 (t, J = 7.6 Hz, 1 H), 7.45 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.4, 26.7, 27.0, 27.8, 28.8, 40.5, 46.0, 66.5, 68.7, 86.1, 108.8, 113.7, 120.5, 123.0, 125.3, 126.9, 127.9, 129.2, 129.7, 130.3, 143.7, 156.6, 159.1, 174.7 ppm. HRMS (ESI): calcd. for $C_{24}H_{27}NO_3S$ [M + H]$^+$ 410.1790, found 410.1784.

Tetracyclic Macrocycle 7d: White solid (77 mg), yield 82 %; m.p. 231–232 °C. IR (neat): $\tilde{\nu}_{max}$ = 3458, 2931, 2857, 1701, 1608, 1467, 1352, 1307, 1236, 1040, 750 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.26–1.50 (m, 10 H), 1.63–1.75 (m, 4 H), 2.84–2.93 (m, 2 H), 3.34–3.50 (m, 1 H), 3.87–4.00 (m, 4 H), 4.07–4.14 (m, 1 H), 4.23 (d, J = 1.6 Hz, 1 H), 4.29 (s, 1 H), 4.46 (d, J = 1.6 Hz, 1 H), 6.82–6.88 (m, 3 H), 7.07 (t, J = 7.6 Hz, 1 H), 7.21 (t, J = 8.0 Hz, 1 H), 7.26–7.31 (m, 2 H), 7.39 (d, J = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.4, 26.0, 27.1, 27.5, 27.8, 28.2, 28.6, 40.0, 45.0, 67.1, 68.4, 87.2, 108.7, 112.8, 120.1, 122.7, 125.3, 125.7, 126.9, 129.2, 129.4, 129.7, 143.7, 156.6, 158.0, 175.2 ppm. HRMS (ESI): calcd. for $C_{27}H_{33}NO_3S$ [M + Na]$^+$ 474.2079, found 474.2073.

Tetracyclic Macrocycle 7e: White solid (75 mg), yield 79 %; m.p. 204–205 °C. IR (neat): $\tilde{\nu}_{max}$ = 3453, 2932, 2855, 1705, 1604, 1460, 1356, 1307, 1237, 1040, 757 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.20–1.50 (m, 12 H), 1.63–1.76 (m, 4 H), 2.91–2.97 (m, 1 H), 3.07–3.14 (m, 1 H), 3.35–3.41 (m, 1 H), 3.87–4.00 (m, 4 H), 4.09–4.16 (m, 1 H), 4.30 (s, 1 H), 4.33 (d, J = 2.0 Hz, 1 H), 4.61 (d, J = 2.0 Hz, 1 H), 6.82–6.89 (m, 3 H), 7.06 (t, J = 7.2 Hz, 1 H), 7.22 (td, J_1 = 8.0, J_2 = 1.6 Hz, 1 H), 7.29 (t, J = 7.8 Hz, 1 H), 7.36–7.39 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22.67, 25.87, 26.16, 27.08, 28.31, 28.49, 28.72, 29.18, 29.72, 44.64, 67.29, 68.27, 87.58, 108.69, 111.96, 119.89, 122.68, 125.30, 125.44, 126.14, 129.18, 129.44, 143.56, 156.65, 157.60, 175.55 ppm. HRMS (ESI): calcd. for $C_{28}H_{35}NO_3S$ [M + Na]$^+$ 466.2416, found 466.2410.

Compound 8a: White solid, yield 83 %; m.p. 191–192 °C. IR (neat): $\tilde{\nu}_{max}$ = 2928, 2850, 1691, 1605, 1484, 1367, 1234, 1171, 1059, 751 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.76–1.80 (m, 1 H), 2.02–2.10 (m, 1 H), 2.19 (s, 3 H), 2.48 (d, J = 13.2 Hz, 1 H), 3.51–3.58 (m, 2 H), 4.31–4.48 (m, 4 H), 4.62 (t, J = 10.8 Hz, 1 H), 6.52–6.57 (m, 2 H), 6.64 (t, J = 7.6 Hz, 1 H), 6.74 (t, J = 7.6 Hz, 1 H), 6.97 (t, J = 7.6 Hz, 1 H), 6.70 (t, J = 7.6 Hz, 1 H), 7.49 (d, J = 8.0 Hz, 1 H), 7.61 (d, J = 7.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 17.4, 21.3, 23.5, 39.3, 54.7, 60.7, 66.3, 78.1, 108.4, 110.8, 114.1, 120.4, 127.7, 128.1, 129.1, 130.3, 133.2, 135.3, 140.3, 152.2, 174.8 ppm. HRMS (ESI): calcd. for $C_{21}H_{21}NO_3S$ [M + H]$^+$ 368.1320, found 368.1329.

Compound 8b: White solid, yield 85 %; m.p. 183–184 °C. IR (neat): $\tilde{\nu}_{max}$ = 2923, 2855, 1696, 1606, 1480, 1358, 1230, 1170, 1054, 736 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.74–1.78 (m, 1 H), 1.99–2.08 (m, 1 H), 2.17 (s, 3 H), 2.48 (d, J = 13.6 Hz, 1 H), 3.46–3.49 (m, 2 H), 4.31–4.46 (m, 4 H), 4.60 (t, J = 12.4 Hz, 1 H), 6.40 (d, J = 8.0 Hz, 1 H), 6.56 (d, J = 8.0 Hz, 1 H), 6.72 (t, J = 7.6 Hz, 1 H), 6.93 (t, J = 7.2 Hz, 1 H), 7.08 (d, J = 7.6 Hz, 1 H), 7.49 (d, J = 7.6 Hz, 1 H), 7.71 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 17.4, 21.3, 23.5, 39.4, 54.7, 60.7, 66.2, 78.1, 108.4, 110.8, 114.0, 120.4, 127.7, 128.1, 129.1, 130.3, 133.2, 135.3, 140.3, 152.2, 174.8 ppm. HRMS (ESI): calcd. for $C_{21}H_{20}BrNO_3S$ [M + H]$^+$ 446.0426, found 446.0418.

General Procedure for Ring-Opening Reaction of Tetracyclic Macrocycles 7a–d: To a solution of the appropriate tetracyclic macrocycles **7a**–**d** (100 mg, 1.0 mmol) in DCM (5 mL) at room temperature was added a drop of water. This reaction mixture was stirred for 10 min. The reaction was diluted with equal amount of water and ethyl acetate. The aqueous phase was extracted. The combined organic extracts were washed with brine, desiccated with Na_2SO_4 and the solvent removed under reduced pressure. The crude product was purified by column chromatography on silica gel using hexane/EtOAc as an eluent to obtain ring-opening products **13a**–**d**.

Compound 13a: Colourless thick oil (90 mg), yield 90 %. IR (neat): $\tilde{\nu}_{max}$ = 3459, 2932, 2866, 1709, 1604, 1459, 1355, 1300, 1240, 1044, 754 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.54–1.62 (m, 2 H), 1.75–1.83 (m, 2 H), 1.87–1.94 (m, 2 H), 2.57 (s, 3 H), 2.85–2.92 (m, 1 H), 2.97–3.03 (m, 1 H), 3.72–3.89 (m, 5 H), 4.05 (t, J = 6.4 Hz, 2 H), 4.40 (s, 1 H), 6.84 (d, J = 8.0 Hz, 1 H), 6.92 (d, J = 8.4 Hz, 1 H), 6.97 (t, J = 7.2 Hz, 1 H), 7.10 (t, J = 7.6 Hz, 1 H), 7.30 (t, J = 7.6 Hz, 1 H), 7.41–7.45 (m, 2 H), 7.71 (dd, J_1 = 7.6, J_2 = 1.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.6, 27.1, 28.8, 32.0, 35.7, 40.2, 45.4, 62.2, 68.1, 108.6, 112.3, 120.5, 123.1, 125.6, 126.2, 128.3, 129.2, 130.4, 133.7, 142.9, 158.3, 177.0, 199.9 ppm. HRMS (ESI): calcd. for $C_{23}H_{27}NO_4S$ [M + H]$^+$ 414.1739, found 414.1738.

Compound 13b: Colourless thick oil (94 mg), yield 94 %. IR (neat): $\tilde{\nu}_{max}$ = 3419, 2925, 2859, 1703, 1598 1479, 1348, 1292, 1164, 1056, 755 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.52–1.60 (m, 2 H), 1.73–1.80 (m, 2 H), 1.87–1.94 (m, 2 H), 2.58 (s, 3 H), 2.86–2.92 (m, 1 H), 2.98–3.04 (m, 1 H), 3.72–3.83 (m, 5 H), 4.05 (t, J = 6.4 Hz, 2 H), 4.40 (s, 1 H), 6.76 (d, J = 8.4 Hz, 1 H), 6.92 (d, J = 8.4 Hz, 1 H), 6.98 (t, J = 7.6 Hz, 1 H), 7.27 (d, J = 6.8 Hz, 1 H), 7.41–7.45 (m, 2 H), 7.71 (d, J = 6.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.5, 27.0, 28.8, 31.9, 35.7, 40.3, 45.3, 62.2, 68.1, 109.5, 112.3, 120.6, 126.0, 127.9, 128.4, 128.55, 129.2, 130.4, 133.6, 141.4, 158.2, 176.6, 199.9 ppm.

HRMS (ESI): calcd. for $C_{23}H_{26}ClNO_4S$ [M + H]$^+$ 448.1349, found 448.1338.

Compound 13c: Colourless thick oil (92 mg), yield 92 %. IR (neat): $\tilde{\nu}_{max}$ = 3419, 2930, 2861, 1674, 1603, 1457, 1358, 1294, 1238, 1047, 756 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 1.43–1.59 (m, 4 H), 1.69–1.77 (m, 2 H), 1.82–1.89 (m, 3 H), 2.61 (s, 3 H), 2.85–2.91 (m, 1 H), 2.97–3.01 (m, 1 H), 3.67–3.88 (m, 4 H), 4.05 (t, *J* = 6.4 Hz, 2 H), 4.39 (s, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 6.92 (d, *J* = 8.4 Hz, 1 H), 6.97 (t, *J* = 7.6 Hz, 1 H), 7.10 (t, *J* = 7.2 Hz, 1 H), 7.30 (t, *J* = 8.0 Hz, 1 H), 7.41–7.44 (m, 2 H), 7.71 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.9, 26.6, 27.2, 29.1, 32.0, 35.6, 40.3, 45.4, 62.1, 68.3, 108.6, 112.3, 120.5, 123.1, 125.5, 126.2, 128.4, 129.2, 130.4, 133.6, 143.0, 158.4, 176.9, 199.9 ppm. HRMS (ESI): calcd. for $C_{24}H_{29}NO_4S$ [M + Na]$^+$ 450.1715, found 450.1712.

Compound 13d: Colourless thick oil (89 mg), yield 89 %. IR (neat): $\tilde{\nu}_{max}$ = 3424, 2926, 2856, 1674, 1602, 1458, 1357, 1293, 1236, 1018, 752 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = δ = 1.26–1.49 (m, 9 H), 1.67–1.75 (m, 3 H), 1.80–1.87 (m, 2 H), 2.62 (s, 3 H), 2.85–2.91 (m, 1 H), 2.97–3.02 (m, 1 H), 3.70 (t, *J* = 7.6 Hz, 2 H), 3.82 (s, 3 H), 4.05 (t, *J* = 6.4 Hz, 2 H), 4.39 (s, 1 H), 6.84 (d, *J* = 8.0 Hz, 1 H), 6.90–6.99 (m, 2 H), 7.09 (t, *J* = 7.6 Hz, 1 H), 7.26–7.32 (m, 1 H), 7.41–7.45 (m, 2 H), 7.73 (d, *J* = 7.6 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.2, 26.8, 27.3, 29.1, 29.2, 29.3, 32.0, 35.7, 40.5, 45.5, 62.2, 68.5, 108.7, 112.3, 120.4, 123.0, 125.5, 126.3, 128.4, 129.2, 130.4, 133.6, 143.1, 158.5, 176.9, 200.0 ppm. HRMS (ESI): calcd. for $C_{27}H_{35}NO_4S$ [M + Na]$^+$ 492.2184, found 492.2173.

Compound 16a: White solid (72 mg), yield 72 %; m.p. 172–173 °C. IR (neat): $\tilde{\nu}_{max}$ = 3451, 2927, 2854, 1701, 1605, 1470, 1347, 1308, 1231, 1044, 754 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.91–2.98 (m, 1 H), 3.17–3.25 (m, 1 H), 3.61–3.71 (m, 2 H), 4.37 (d, *J* = 16.0 Hz, 1 H), 5.07 (d, *J* = 16.4 Hz, 1 H), 5.10 (s, 1 H), 6.38 (d, *J* = 7.6 Hz, 1 H), 6.42–6.44 (m, 2 H), 6.96–7.26 (m, 10 H), 8.58 (d, *J* = 8.0 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 25.8, 32.7, 43.7, 52.2, 52.2, 109.8, 122.3, 125.8, 126.2, 127.1, 127.2, 128.3, 128.6, 128.7, 128.9, 130.6, 134.6, 137.1, 141.4, 173.4 ppm. HRMS (ESI): calcd. for $C_{24}H_{21}NOS_2$ [M + H]$^+$ 404.1143, found 404.1148.

Compound 16b: White solid (18 mg), yield 18 %; m.p. 174–175 °C. IR (neat): $\tilde{\nu}_{max}$ = 3450, 2928, 2855, 1700, 1606, 1469, 1347, 1308, 1230, 1044, 755 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.71–2.75 (m, 1 H), 3.12–3.14 (m, 1 H), 3.44–3.50 (m, 1 H), 4.18–4.25 (m, 1 H), 4.66 (d, *J* = 16.0 Hz, 1 H), 4.83 (s, 1 H), 4.93 (d, *J* = 15.6 Hz, 1 H), 6.38 (d, *J* = 7.2 Hz, 1 H), 6.97–7.11 (m, 9 H), 7.20–7.22 (m, 3 H), 7.39 (d, *J* = 7.2 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 26.3, 32.2, 43.5, 47.3, 51.9, 109.1, 122.3, 123.8, 127.1, 127.3, 127.9, 128.1, 128.5, 128.6, 128.7, 129.1, 135.4, 137.1, 141.8, 174.6 ppm. HRMS (ESI): calcd. for $C_{24}H_{21}NOS_2$ [M + H]$^+$ 404.1143, found 404.1150.

CCDC 1437706 (for **6a**) and 1437707 (for **7a**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

Supporting Information (see footnote on the first page of this article): Copies of ^{1}H, ^{13}C and DEPT-135 NMR spectra for selected compounds.

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