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Design and synthesis of carbohydrate based medium sized sulfur containing benzannulated macrocycles: applications of Sonogashira and Heck coupling

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ABSTRACT

Palladium catalyzed intramolecular Sonogashira and Heck coupling reactions have been applied for diversity-oriented synthesis of sulfur containing carbohydrate based medium sized ring macrocycles. The process involves design and synthesis of building blocks with predisposed functional units prerequisite for C–C coupling. Both *cis*- and *trans*-fused benzannulated medium sized macrocyles with different ring sizes (8–13-membered) fused at different positions of furannose and pyranose moiety have been achieved.

1. Introduction

Discovery and progress in cross coupling reactions have opened a new paradigm in synthetic chemistry.[1] Especially palladium catalyzed C–C bond forming coupling reactions have enabled considerably the prowess of synthetic chemist to take new challenges for the generation of new structural frameworks.[2] Sonogashira and Heck coupling are among the most important and widely used sp^2–sp and sp^2–sp^2 C–C bond forming reactions, respectively. These are frequently employed in the synthesis of natural products, biologically active molecules, heterocycles, molecular electronics, dendrimers and conjugated polymers or nanostructures.[3,4]

Carbohydrate fused bi-cyclic systems containing medium to large sized heterocyclic rings are encountered in innumerable number of biologically active natural products.[5] The possible role of these medium sized ring macrocycles in antibiotics has always drawn the attention of synthetic chemists to synthesize oxygen and nitrogen containing benzannulated medium sized rings fused with carbohydrates,[6,7] which are difficult to prepare owing to the ring strain and transannular interactions. Very recently, Daniel Werz et al., reported Pd-catalyzed ring annulations using monosaccharides for the construction of small sized oxygen and nitrogen containing bi-cyclic and tri-cyclic benzannulated molecular systems.[8] Despite these applications, there is no report of palladium catalyzed C–C bond forming intramolecular coupling reactions in the construction of rigid medium sized sulfur containing carbohydrate based macrocycles with defined stereochemistry. The sulfur containing products are attaining a legal superiority in the gamete of modern world bioactives.[9] For example, the versatility of sulfur has been exploited significantly in drug discovery efforts, as evidenced by the fact that several of the 200 top-selling pharmaceutical agents in 2010[10] contain sulfur and, in many cases, the sulfur atom is contained in a ring. With our interest in the synthesis of benzannulated medium sized macrocycles from carbohydrates,[11] herein we want to report the design and synthesis of medium sized sulfur containing benzannulated macrocycles using carbohydrate as chiral pool. The facile variation of the carbohydrate part leads to a high degree of structural diversity.

2. Results and discussions

Our approach was designed to mirror our route to the formation of oxygen-containing macrocycles.[9] Thus, we designed two types of

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scaffolds (**A**) and (**B**) (Fig. 1) keeping in view the basic requirements for Sonogashira and Heck coupling under the concept of build/couple/pair strategy.[12] In order to synthesize medium sized sulfur macrocycles with particular ring size, we designed different scaffolds (Fig. 2), which could be synthesized from carbohydrates either involving 1,2-OH or 3,5,6-OH so that remaining hydroxyl groups after deprotection can be utilized. All the newly designed furan based scaffolds were prepared from 1,2,5,6-di-*O*-acetonide-α-D-glucofuranose (**1**) by the strategic installation of functional groups as discussed in Scheme 1. In general the synthesis involves acetonide deprotection, alkylation/arylation, epoxidation, epoxide opening, sugar aldehyde generation and glycosylation reactions. It is noteworthy that using glycosylation reactions we managed to create both cis- and trans-stereochemistry (relative to 2-OH), which enable us to generate *cis*/*trans*-fused benzannulated macrocycles present in natural products. The allose derivative **II** was prepared by 3-OH oxidation of **1** with PDC followed by $NaBH_4$ reduction to get the inversion product.

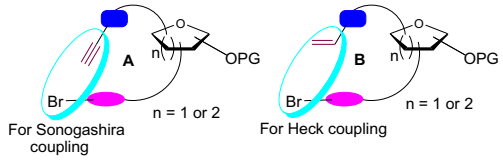


Fig. 1. General structure of chiral scaffolds for Sonogashira and Heck coupling reactions.

With all building blocks for Sonogashira and Heck coupling reactions in hand, **I** was selected as model substrate for coupling reaction. Thus, the scaffold **I** was allowed to undergo intramolecular Sonogashira reaction using the heterogeneous catalyst developed in our lab (Scheme 4).[6] It was found that the reaction proceeds smoothly leading to the generation of sulfur containing medium sized benzannulated ring **Ia** in 86% yield. The structure of **Ia** was confirmed through various spectroscopic techniques. The disappearance of acetylene peak (δ=2.5 ppm) in the ^{1}H NMR and appearance of a new quaternary carbon (δ=75 ppm) in ^{13}C NMR of **Ia** was in full agreement with the assigned structure. Encouraged by the results, all the furan based building blocks (**II**, **IV**, **VI**, **VII** and **X**) with terminal alkyne group and aryl halide group were subjected to intramolecular C–C bond formation under standardized reaction conditions to yield the corresponding medium sized macrocycles in good to excellent yields (Table 1, entries 1–6). The scope of the reagent system was explored by extending the study to pyran based scaffolds (**XI**, **XIII**, **XV**, **XVI**, **XVII** and **XVIII**). In all the cases the macrocycle formed smoothly in good to excellent yield (Table 1, entries 7–12).

After obtaining the satisfactory results in Sonogashira reaction, next we attempted Heck coupling with substrate **III**. Thus, in our initial experiment **III** was allowed to undergo intramolecular Heck coupling (Scheme 5) using different Pd catalysts (Table 2, entries 1–10). We observed that $Pd(OAC)_2$ in presence of Cs_2CO_3 is the appropriate catalyst for this purpose (59%, Table 2, entry 7). Having optimized the reaction conditions for Heck coupling, all the furan based building units were subjected to same reaction conditions

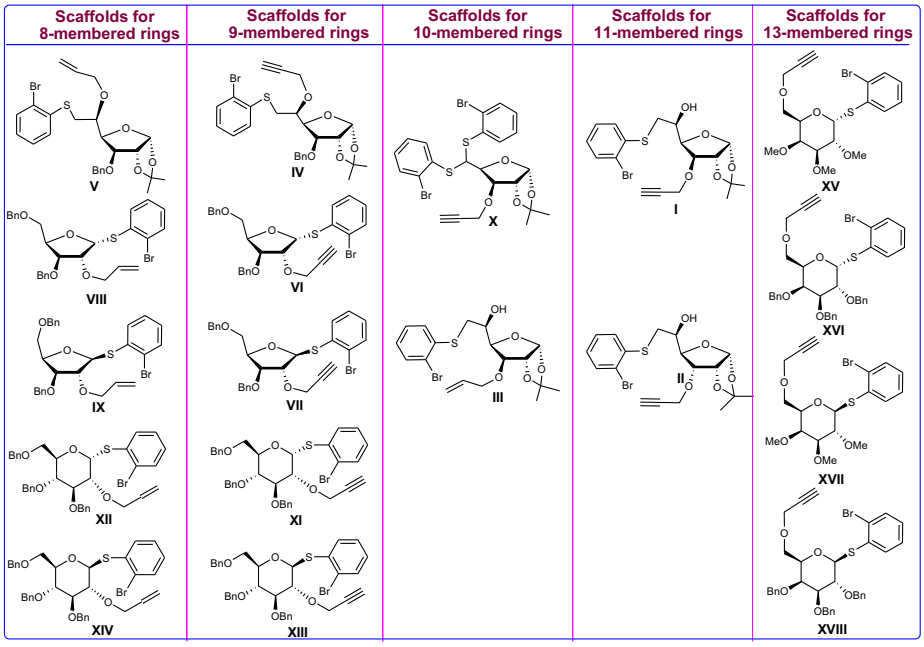


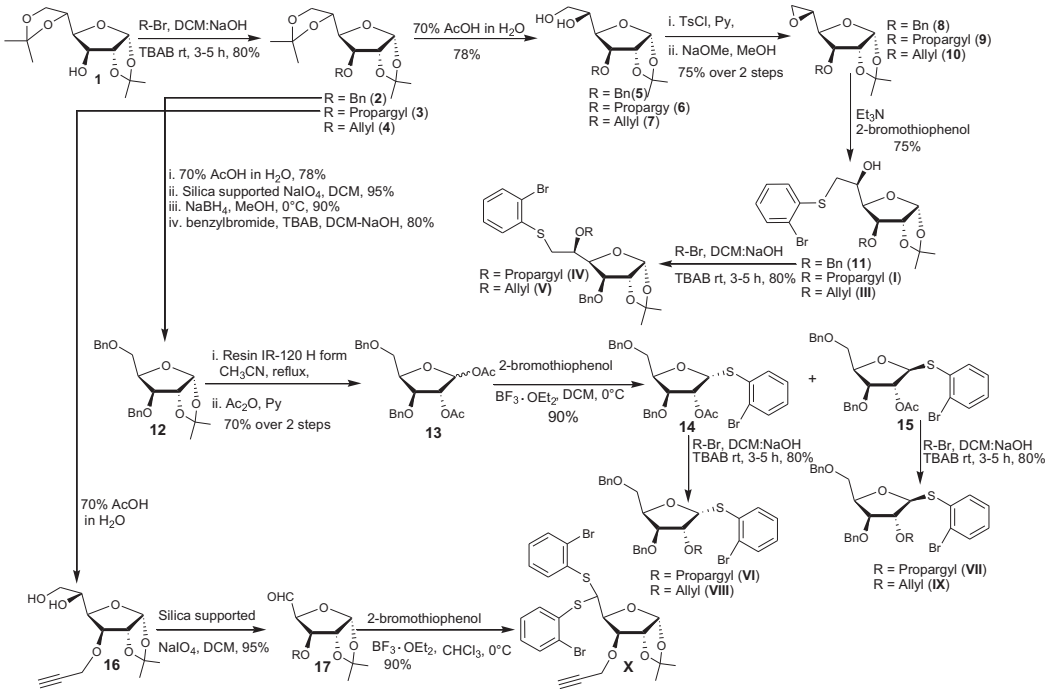
Fig. 2. Designed furan and pyran building blocks for the synthesis of 8–13-membered rings by Sonogashira and Heck coupling.

Further, in order to synthesize pyran based building blocks **XI** and **XIII**, D-glucal (**18**) was subjected to benzylation, oxidation using *m*-CPBA followed by glycosylation using suitably substituted bromothiophenol and finally alkylation (Scheme 2).

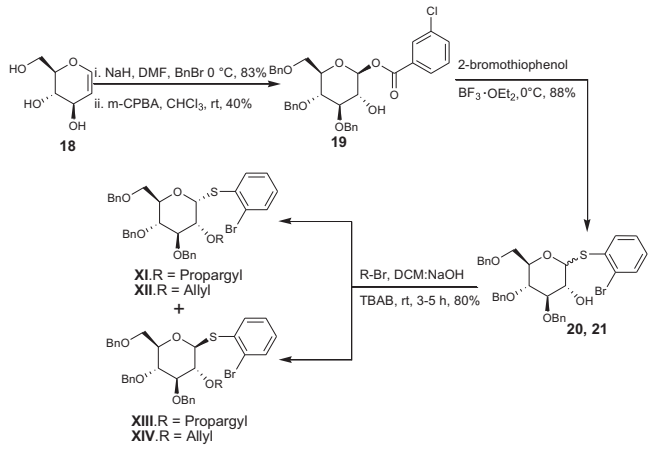
To investigate the possibility of macrocyclization between 6-*O*-propargyl and aryl bromide derived from anomeric position 1,2,3,4-di-*O*-acetonide-α-D-galactopyranoside (**22**) was utilized to obtain bridgehead building blocks **XV**–**XVIII** as depicted in Scheme 3.

(Table 3, entries 1–4) to derive the corresponding cyclized products. Similarly, pyran based building blocks **34** and **36** also yielded the desired medium sized macrocycle in moderate yield (Table 3, entries 5 and 6).

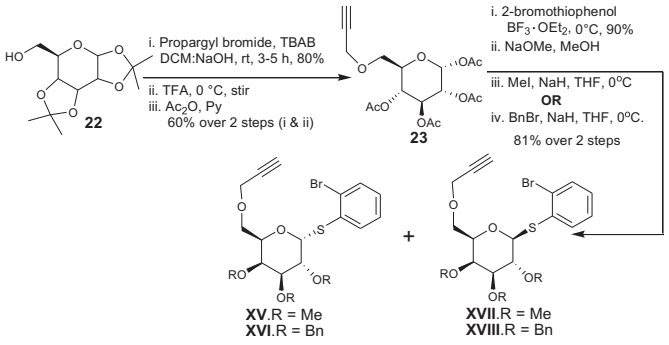
Some of the products synthesized above can be utilized for the synthesis of conformationally locked nucleosides, e.g., the isopropylidene unit of the product **Xa** has been de-protected followed by acetylation gives anomeric mixture (αβ) of diacetate **Xab**, which



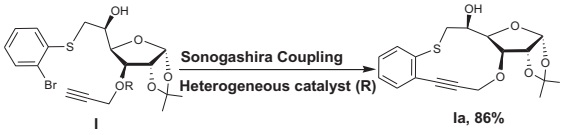
Scheme 1. Synthetic strategies applied for the synthesis of furan based building blocks.



Scheme 2. Synthesis of pyran based building blocks using 1,2-position of sugar moiety.



Scheme 3. Synthesis of pyran based building blocks using 1,6-position of sugar moiety.



Scheme 4. Cyclization of substrate **I** by Sonogashira coupling.

can be converted to nucleoside using literature procedure.[13] Since the C–C triple bond is not common in biologically active macrocycles, **Xa** has also been subjected to Pd–C/H_2 hydrogenation giving the product **Xac** (Scheme 6).

3. Conclusion

Design and synthesis of diversity oriented medium sized sulfur containing carbohydrate fused benzannulated macrocycles (8–13-membered) have been achieved using Pd-catalyzed C–C bond coupling. Both *cis*- and *trans*-fused medium sized rings have been generated taking advantage of glycosylation reaction. The downstream products originated will be used to generate targeted natural product analogues.

4. Experimental section

4.1. General information

Proton NMR spectra and carbon-13 NMR spectra were recorded on Bruker 200, 400 and 500 MHz spectrometers (Model No. D 205/52-2382, Avance 500) with TMS as the internal standard. Chemical shifts are expressed in parts per million (ppm). MS were recorded on Waters LC Mass spectrometer (Model No. Symapt MS). Silica gel coated aluminium plates were used for TLC. Elemental analyses were performed on Vario Elementar, Model No. EL-III (installed at CSIR-IIIM, Jammu, India). Reagents and solvents used were mostly of LR grade.

Table 1
Synthesis of carbohydrate based medium sized oxo-sulfur benzannulated macrocycles using Sonogashira reaction

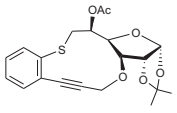
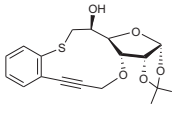
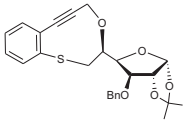
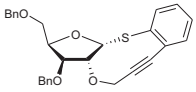
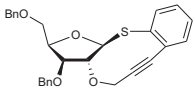
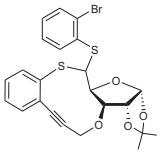
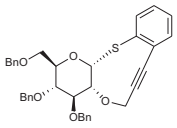
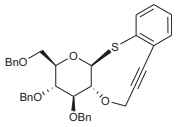
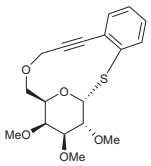
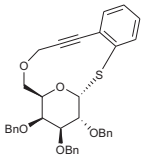
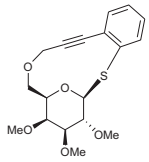
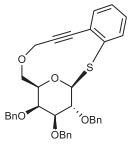
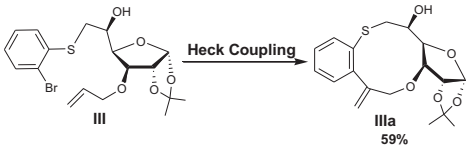
S no.	Substrate[a]	Product[b]	Time (h)	Yield[c] (%)
1	**I**	 **Ia**	20	86
2	**II**	 **IIa**	20	86
3	**IV**	 **IVa**	20	85
4	**VI**	 **VIa**	19	88
5	**VII**	 **VIIa**	24	88
6	**X**	 **Xa**	24	90
7	**XI**	 **XIa**	23	81
8	**XIII**	 **XIIIa**	21	82
9	**XV**	 **XVa**	22	81
10	**XVI**	 **XVIa**	20	83

Table 1 (*continued*)

S no.	Substrate[a]	Product[b]	Time (h)	Yield[c] (%)
11	**XVII**	 **XVIIa**	19	82
12	**XVIII**	 **XVIIIa**	20	83

[a] Reaction conditions: substrate (100 mg, 0.25 mmol), CuI (0.0125 mg, 5 mol %), 4.7 wt % heterogeneous catalyst R (100 mg), THF (2 mL), rt.
[b] Characterized through spectroscopic analysis.
[c] Isolated yield after column chromatography.



Scheme 5. Cyclization of substrate **III** by Heck coupling.

Table 2
Comparative study of different commercially available catalysts for Heck reaction

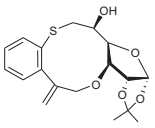
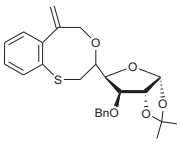
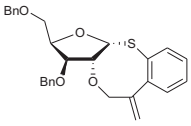
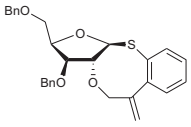
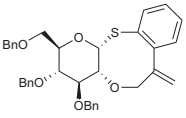
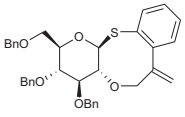
Entry	Catalyst[a,b]	Base	Solvent	Temp (°C)	Yield (%)
1	R	No ext. base	DMF	rt	02
2	R	No ext. base	THF	rt	02
3	R	No ext. base	DMF	100	02
4	R	No ext. base	THF	100	02
5	$Pd(PPh_3)_2Cl_2$	Et_2NH	DMF	100	50
6	$Pd(PPh_3)Cl_2$	Et_3N	DMF	100	50
7	$Pd(OAc)_2$	Cs_2CO_3	DMF	100	59
8	$Pd(OAc)_2$	KCO_3	DMF	100	57
9	$Pd(PPh_3)_4$	$(i\text{-}Pr)_2NH$	DMF	100	58
10	$Pd(PPh_3)_4$	$(i\text{-}Pr)_2NH$	THF	100	58

R (heterogeneous catalyst)=bis(μ-chloro) bis[2-(di-*tert*-butylphosphino)-2-methylpropyl]dipalladium ($C_{24}H_{52}Cl_2P_2Pd_2$).
[a] Reaction conditions: for entries 1–4: substrate (**III**) (200 mg, 0.28 mmol), 4.7 wt % heterogeneous catalyst (R) (200 mg),[6] solvent (2 mL), under N_2 environment.
[b] Reaction conditions: for entries 5–10: substrate (**III**) (100 mg, 0.25 mmol), homogeneous Pd catalyst (10 mol %), base (2.75 equiv), TBAB (1 equiv), solvent (3 mL), 100 °C under N_2 environment.

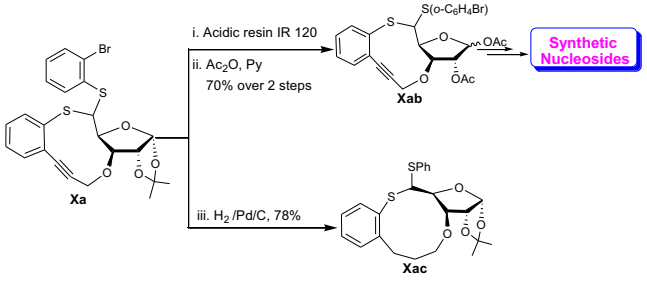
4.2. Typical procedure (1) for cyclization via intramolecular Sonogashira reaction

To a solution of **I** (100 mg, 0.25 mmol) in dry THF (2.0 mL) was added 4.7 wt % heterogeneous palladium catalyst (100 mg) developed by our own lab[9] and co-catalyst CuI (0.0125 mg, 5 mol %). The reaction mixture was allowed to stir at room temperature for 20 h under nitrogen atmosphere. After ascertaining completion of the reaction by TLC, the mixture was filtered and the solvent was evaporated under vacuum. The product was extracted with ethyl acetate, dried over anhydrous Na_2SO_4 and purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to yield **Ia** (83.85 mg, 86%). R_f (35% EtOAc/hexane) 0.45; IR ($CHCl_3$) 2850, 2210, 1734 cm^{-1}; H NMR (500 MHz, $CDCl_3$):

Table 3
Synthesis of carbohydrate based medium sized oxo-sulfur benzannulated macrocycles using Heck reaction

S no.	Substrate[a]	Product[b]	Time (h)	Yield[c] (%)
1	**III**	 **IIIa**	12	59
2	**V**	 **Va**	8	57
3	**VIII**	 **VIIIa**	10	58
4	**IX**	 **XIa**	12	59
5	**XII**	 **XIIa**	8	58
6	**XIV**	 **XIVa**	12	58

[a] Reaction conditions: substrate (100 mg, 0.28 mmol), $Pd(OAc)_2$ (0.028 mg, 10 mol %), Cs_2CO_3 (251 mg, 2.75 equiv), TBAB (92 mg, 1 equiv), DMF (3 mL), 100 °C under N_2 environment.
[b] Identified through ^1H NMR and ^{13}C NMR.
[c] Isolated yield after column chromatography.



Scheme 6. Probable application of benzannulated macrocycles in the synthesis of conformationally locked synthetic nucleosides.

δ 1.33 (s, 3H), 1.50 (s, 3H), 1.93 (s, 3H), 3.19 (dd, J=6.3, 4.5 Hz, 1H), 3.58 (dd, J=2.9, 5.4 Hz, 1H), 3.92–4.13 (m, 1H), 4.23–4.29 (m, 2H), 4.51(dd, J=3.2, 3.0 Hz, 1H), 4.57 (d, J=3.6 Hz, 1H), 5.90 (d, J=3.7 Hz, 1H), 5.95 (d, J=3.6 Hz, 1H), 7.03–7.10 (m, 1H, Ar), 7.26–7.27 (m, 1H, Ar), 7.34–7.55 (m, 1H, Ar), 7.66 (d, J=11.9 Hz, 1H, Ar), 7.64 (dd, J=1.2, 7.6 Hz, 1H, Ar), 8.05 (dd, J=1.2, 7.6 Hz, 1H, Ar); C NMR (500 MHz, $CDCl_3$): δ 20.8, 26.4, 26.8, 35.0, 57.5, 68.8, 70.8, 74.8, 79.3, 80.8, 81.4, 105.2, 112.3, 124.5, 127.0, 127.8, 128.6, 129.6, 137.5, 169.7; ESI MS (m/z): 390 $[M+Na]^+$. Anal. Calcd for $C_{20}H_{22}O_6S$: C, 61.52; H, 5.68. Found: C, 61.40; H, 5.59.

4.3. Typical procedure (2) for cyclization via intramolecular Heck reaction

To a solution of **III** (0.28 mmol, 100 mg) in dry DMF (3 mL) were added $Pd(OAc)_2$ (0.028 mg, 10 mol %), Cs_2CO_3 (251 mg, 2.75 equiv) and tetrabutylammonium bromide (74.00 mg, 1 equiv). The reaction mixture was stirred at 100 °C for 12 h. After completion of the reaction as monitored through TLC, the reaction was quenched by addition of solution of ammonium chloride. The product was extracted with ethyl acetate, dried over anhydrous Na_2SO_4 and purified by column chromatography on silica gel using petroleum ether/ethyl acetate as the eluent to yield **IIIa** (57.82 mg, 59%). R_f (50% EtOAc/hexane 0.50); IR ($CHCl_3$) 3500–3300 (br), 2985, 2931, 1645 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.48 (s, 3H), 2.75 (d, J=5.2 Hz, 1H), 3.06 (dd, J=8.4, 14.0 Hz, 1H), 3.45 (dd, J=2.8, 13.6 Hz, 1H), 4.10–4.20 (m, 4H), 4.56 (d, J=3.6 Hz, 1H), 5.21 (dd, J=1.6, 10.4 Hz, 1H), 5.28 (dd, J=1.6, 14.0 Hz, 1H), 5.91 (d, J=7.2 Hz, 1H), 7.05 (dd, J=1.2, 7.6 Hz, 1H, Ar), 7.27 (m, 1H, Ar), 7.40 (m, 1H, Ar), 7.54 (dd, J=1.2, 8.0 Hz, 1H, Ar); ^{13}C NMR (500 MHz, $CDCl_3$): δ 26.2, 26.8, 38.5, 67.3, 71.2, 81.6, 82.3, 105.1, 111.8, 118.2, 123.89, 126.9, 127.9, 133.0, 133.6, 136.9, 148.5; ESI MS (m/z): 350 $[M+Na]^+$. Anal. Calcd for $C_{18}H_{22}O_5S$: C, 61.69; H, 6.33. Found: C, 61.60; H, 5.99.

4.4. Preparation and spectral analysis of IIa

Prepared by following the typical procedure for Sonogashira reaction (1) by using **II** (100 mg, 0.23 mmol) to yield the desired product **IIa** as a semi-solid (68.80 mg, 86%). R_f (50% EtOAc/hexane 0.5); IR ($CHCl_3$) 3600–3200 (br), 2920, 2850, 2214 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.36 (s, 3H), 1.57 (s, 3H), 3.09 (dd, J=9.6, 14.0 Hz, 1H), 3.23 (dd, J=3.6, 14.0 Hz, 1H), 4.01 (m, 1H), 4.10 (dd, J=3.6, 7.6 Hz, 1H), 4.24 (dd, J=4.4, 8.8 Hz, 1H), 4.31 (d, J=16.4 Hz, 1H), 4.47 (d, J=16.8 Hz, 1H), 4.68 (t, J=4, 1H), 5.79 (d, J=3.6 Hz, 1H), 7.07 (m, 1H, Ar), 7.26 (m, 1H, Ar), 7.36 (d, J=7.6 Hz, 1H, Ar), 7.55 (m, 1H, Ar); ^{13}C NMR (500 MHz, $CDCl_3$): δ 26.6, 26.8, 36.2, 57.7, 68.9, 71.5, 75.2, 76.4, 77.3, 79.9, 104.2, 113.4, 124.3, 127.2, 128.1, 132.1, 133.1, 136.8; ESI MS (m/z): 348 $[M+Na]^+$. Anal. Calcd for $C_{18}H_{20}O_5S$: C, 62.05; H, 5.79. Found: C, 62.00; H, 5.68.

4.5. Preparation and spectral analysis of IVa

Prepared by following the typical procedure for Sonogashira reaction (1) by using **IV** (100 mg, 0.19 mmol) to yield the desired product **IVa** as a semi-solid (70.74 mg, 85%). R_f (35% EtOAc/hexane 0.48); IR ($CHCl_3$) 2919, 2850, 2210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.48 (s, 3H), 3.14 (dd, J=4.6, 12.8 Hz, 1H), 3.51 (dd, J=2.8, 12.8 Hz, 1H), 4.08–4.14 (m, 2H), 4.17 (d, J=16.0 Hz, 1H), 4.30 (dd, J=2.8, 9.2 Hz, 1H), 4.37 (d, J=16.0 Hz, 1H), 4.58 (d, J=11.6 Hz, 1H), 4.60 (d, J=4.0 Hz, 1H), 4.65 (d, J=11.6 Hz, 1H), 5.89 (d, J=3.6 Hz, 1H), 6.99 (d, J=1.2 Hz, 1H, Ar), 7.23–7.45 (m, 6H, Ar), 7.51 (d, J=1.2 Hz, 1H, Ar); ^{13}C NMR (500 MHz, $CDCl_3$): δ 26.4, 26.9, 35.7, 58.7, 70.6, 72.0, 74.8, 75.4, 80.5, 81.5, 81.9, 105.1, 112.1, 123.5, 126.5, 127.7, 127.7, 127.8, 128.4, 128.5, 128.5, 132.9, 134.6, 137.3, 137.9; ESI MS (m/z): 438 $[M+Na]^+$. Anal. Calcd for $C_{25}H_{26}O_5S$: C, 68.47; H, 5.98. Found: C, 68.42; H, 5.97.

4.6. Preparation and spectral analysis of VIa

Prepared by the typical procedure (1) for Sonogashira reaction by using **VI** (100 mg, 0.18 mmol) to yield the desired product **IVa** as

a semi-solid (72.55 mg, 88%). R_f (35% EtOAc/hexane) 0.48; IR ($CHCl_3$) 2919, 2210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.69 (dd, J=5.2, 10.0 Hz, 1H), 3.79 (dd, J=5.6, 10.0 Hz, 1H), 4.18 (dd, J=2.4, 4.4 Hz, 1H), 4.40 (d, J=4.0 Hz, 1H), 4.46 (dd, J=2.4, 5.2 Hz, 1H), 4.51 (d, J=12.0 Hz, 1H), 4.53–4.63 (m, 4H), 4.68 (d, J=12 Hz, 1H), 5.82 (d, J=5.2 Hz, 1H), 7.15–7.35(m, 14H, Ar); ^{13}C NMR (400 MHz, $CDCl_3$): δ 58.9, 67.8, 71.3, 72.4, 73.4, 75.2, 78.4, 81.7, 83.9, 88.4, 125.3, 127.6, 127.6, 127.7, 127.8, 127.8, 128.1, 128.4, 128.5, 128.5, 131.9, 132.1, 132.2, 132.9, 136.5, 137.5, 138.2; ESI MS (m/z): 458 $[M+Na]^+$. Anal. Calcd for $C_{28}H_{26}O_4S$: C, 73.34; H, 5.71. Found: C, 73.29; H, 5.60.

4.7. Preparation and spectral analysis of VIIa

Prepared by the typical procedure for Sonogashira reaction (1) by using **VII** (100 mg, 0.18 mmol) to yield the desired product **VIIa** as a semi-solid (70.07 mg, 85%). R_f (35% EtOAc/hexane) 0.48; ($CHCl_3$) 2919, 2210 cm^{-1}; H NMR (400 MHz, $CDCl_3$): δ 3.80 (m, 2H), 4.06 (dd, J=1.6, 5.2 Hz, 1H), 4.16 (s, 2H), 4.31 (t, J=2.4 Hz, 1H), 4.35 (dd, J=5.2, 11.2 Hz, 1H), 4.60–4.52 (m, 3H), 4.69 (dd, J=5.2, 12.0 Hz, 1H), 5.37 (d, J=2.8 Hz, 1H), 7.03–7.04 (m, 1H, Ar), 7.06–7.33 (m, 11H, Ar), 7.64 (dd, J=1.2, 7.6 Hz, 1H, Ar), 7.66 (dd, J=1.6, 8.0 Hz, 1H, Ar); ^{13}C NMR (400 MHz, $CDCl_3$): δ 58.1, 68.6, 71.0, 72.2, 73.5, 75.0, 80.9, 81.5, 86.8, 88.6, 124.3, 127.6, 127.7, 127.7, 127.8, 127.8, 127.8, 127.9, 128.0, 128.3, 128.3, 128.5, 128.5, 130.9, 132.8, 137.1, 137.5, 138.2; ESI MS (m/z): 458 $[M+Na]^+$. Anal. Calcd for $C_{28}H_{26}O_4S$: C, 73.34; H, 5.71. Found: C, 73.25; H, 5.61.

4.8. Preparation and spectral analysis of Xa

Prepared by the typical procedure for Sonogashira reaction (1) by using **X** (100 mg, 0.17 mmol) to yield the desired product **Xa** as a semi-solid (77.27 mg, 90%). R_f (20% EtOAc/hexane) 0.6; IR ($CHCl_3$) 2920, 2850, 2210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 1.31 (s, 3H), 1.45 (s, 3H), 4.15 (d, J=12.4 Hz, 1H), 4.21 (s, 1H), 4.24 (d, J=12.4 Hz, 1H), 4.45 (dd, J=2.8, 9.6 Hz, 1H), 4.67 (d, J=3.6 Hz, 1H), 5.06 (d, J=9.6 Hz, 1H), 5.95 (d, J=3.6 Hz, 1H), 7.07 (m, 1H, Ar), 7.24 (m, 2H, Ar), 7.44 (m, 1H, Ar), 7.54 (m, 2H, Ar), 7.64 (dd, J=1.2, 7.6 Hz, 1H, Ar), 8.05 (dd, J=1.2, 7.6 Hz, 1H, Ar); ^{13}C NMR (500 MHz, $CDCl_3$): δ 26.3, 26.8, 54.6, 58.6, 70.9, 74.9 81.5, 81.9, 82.6, 105.1, 112.1, 118.2, 124.8, 126.4, 127.9, 128.6, 128.9, 129.5, 130.1, 132.9, 133.1, 133.4, 134.7, 135.1, 138.1; ESI MS (m/z): 505 $[M+Na]^+$. Anal. Calcd for $C_{23}H_{21}BrO_4S_2$: C, 54.65; H, 4.19. Found: C, 54.60; H, 4.11.

4.9. Preparation and spectral analysis of XIa

Prepared by the typical procedure for Sonogashira reaction (1) by using **XI** (100 mg, 0.15 mmol) to yield the desired product **XIa** as a semi-solid (70.23 mg, 81%). R_f (35% EtOAc/hexane) 0.45; IR ($CHCl_3$) 2919, 2210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.53–3.56 (m, 2H), 3.59–3.69 (m, 3H), 3.75 (dd, J=1.6, 10.8 Hz, 1H), 4.48–4.61 (m, 4H), 4.67 (d, J=10.0 Hz, 1H), 4.74 (d, J=9.6 Hz, 1H), 4.82 (dd, J=3.6, 10.8 Hz, 2H), 4.95 (d, J=10.8 Hz, 1H), 7.18–7.69 (m, 19H, Ar); ^{13}C NMR (400 MHz, $CDCl_3$): δ 60.7, 69.0, 73.5, 75.1, 75.9, 77.6, 79.2, 80.5, 86.0, 86.3, 124.5, 127.6, 127.7, 127.8, 127.8, 127.9, 128.0, 128.2, 128.2, 128.3, 128.4, 128.5, 128.6, 130.9, 131.9, 132.0, 132.1, 132.2, 132.9, 133.1, 136.0, 138.0, 138.2; ESI MS (m/z): 578 $[M+Na]^+$. Anal. Calcd for $C_{36}H_{34}O_5S$: C, 74.71; H, 5.92. Found: C, 74.67; H, 5.83.

4.10. Preparation and spectral analysis of XIIIa

Prepared by the typical procedure for Sonogashira reaction (1) by using **XIII** (100 mg, 0.15 mmol) to yield the desired product **XIIIa** as a semi-solid (71.09 mg, 82%). R_f (35% EtOAc/hexane) 0.43; IR ($CHCl_3$) 2919, 2210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.58 (dd, J=1.6, 10.8 Hz, 1H), 3.75 (m, 2H), 3.90 (t, 9.2 Hz, 1H), 4.07 (dd, J=5.6, 9.6 Hz, 1H), 4.28 (dd, J=1.6, 10.0 Hz, 1H), 4.40 (d, J=12.0 Hz, 1H), 4.47–4.51 (m, 3H), 4.58 (d, J=12.0 Hz, 1H), 4.81 (dd, J=10.8, 14.8 Hz, 2H), 4.95 (d, J=10.8 Hz, 1H), 5.91 (d, J=5.5 Hz, 1H), 7.04 (dt J=1.6, 7.6, 9.2 Hz, 1H, Ar), 7.13–7.16(m, 2H, Ar), 7.19 (dd J=1.2, 14.8 Hz, 1H, Ar), 7.25–7.38 (m, 13H, Ar), 7.53 (dd J=1.2, 8.0 Hz, 1H, Ar), 7.60 (dd J=1.6, 8.0 Hz, 1H, Ar); ^{13}C NMR (400 MHz, $CDCl_3$): δ 58.5, 68.4, 71.1, 71.6, 73.4, 75.1, 75.2, 75.7, 77.4, 79.2, 82.4, 85.3, 126.1, 127.7, 127.8, 127.9, 127.9, 127.9, 127.9, 127.9, 128.2, 128.3, 128.3, 128.3, 128.3, 128.4, 128.5, 128.5, 128.5, 128.5, 132.6, 133.1, 135.0, 138.0, 138.5, 139; ESI MS (m/z): 578 $[M+Na]^+$. Anal. Calcd for $C_{36}H_{34}O_5S$: C, 74.71; H, 5.92. Found: C, 74.65; H, 5.85.

4.11. Preparation and spectral analysis of XVa

Prepared by the typical procedure for Sonogashira reaction (1) by using **XV** (100 mg, 0.23 mmol) to yield the desired product **XVa** as a semi-solid (65.21 mg, 81%). R_f (35% EtOAc/hexane) 0.45; IR ($CHCl_3$) 2920, 2810, 2210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.45 (s, 3H), 3.46 (s, 3H), 3.52 (s, 3H), 3.55–3.65 (m, 1H), 3.83 (dd, J=3.2, 7.2 Hz, 2H), 3.88 (t, J=2.8 Hz, 2H), 4.10 (dd, J=2.0, 4.4 Hz, 2H), 4.24 (dd, J=3.2, 7.2 Hz, 1H), 5.63 (d, J=2.4 Hz, 1H), 7.10 (dd, J=1.2, 7.6 Hz, 1H, Ar), 7.24–7.26 (m, 2H), 7.22–7.38 (m, 1H, Ar), 7.55 (dd, J=1.2, 8.0 Hz, 1H, Ar), 7.64 (dd, J=1.2, 8.0 Hz, 1H, Ar); ^{13}C NMR (400 MHz, $CDCl_3$): δ 58.3, 59.3, 61.3, 61.4, 67.8, 72.1, 74.8, 74.9, 77.1, 79.0, 85.8, 86.2, 124.0, 127.5, 127.9, 130.6, 132.8, 136.4; ESI MS (m/z): 350 $[M+Na]^+$. Anal. Calcd for $C_{18}H_{22}O_5S$: C, 61.69; H, 6.33. Found: C, 61.63; H, 6.28.

4.12. Preparation and spectral analysis of XVIa

Prepared by the typical procedure for Sonogashira reaction (1) by using **XVI** (100 mg, 0.15 mmol) to yield the desired product **XVIa** as a semi-solid (71.96 mg, 83%). R_f (35% EtOAc/hexane) 0.48; IR ($CHCl_3$) 2919, 2210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.57–3.67 (m, 4H), 3.96 (d, J=2.6 Hz, 1H), 4.05 (t, J=9.3 Hz, 1H), 4.12 (d, J=7.8 Hz, 2H), 4.66 (d, J=11.4 Hz, 1H), 4.71 (dd, J=9.8, 4.4 Hz, 2H), 4.76 (s, 2H), 4.82 (d, J=10.0 Hz, 1H), 4.99 (d, J=11.4 Hz, 1H), 7.01 (ddt, J=22.8, 7.5, 1.5 Hz, 2H), 7.22–7.38 (m, 14H), 7.40 (dd, J=7.8, 1.6 Hz, 2H), 7.50 (dd, J=7.8, 1.5 Hz, 1H), 7.69 (dd, J=7.8, 1.6 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 59.1, 68.7, 72.1, 73.2, 73.3, 74.5, 75.7, 75.8, 76.8, 77.2, 83.9, 86.3, 127.3, 127.4, 127.5, 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 128.1, 128.1, 128.2, 128.3, 128.3, 128.3, 128.4, 128.4, 128.5, 128.5, 128.6, 128.7, 130.7, 132.8, 138.1; ESI MS (m/z): 578 $[M+Na]^+$. Anal. Calcd for $C_{36}H_{34}O_5S$: C, 74.71; H, 5.92. Found: C, 74.63; H, 5.85.

4.13. Preparation and spectral analysis of XVIIa

Prepared by the typical procedure for Sonogashira reaction (1) by using **XVII** (100 mg, 0.23 mmol) to yield the desired product **XVIIa** as a semi-solid (66.01 mg, 82%). R_f (35% EtOAc/hexane) 0.43; IR ($CHCl_3$) 2919, 2810, 2210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.24 (dd, J=2.8, 9.2 Hz, 1H), 3.35–3.40 (m, 1H), 3.54–3.56 (m, 1H), 3.56 (s, 3H), 3.60 (s, 3H), 3.61 (s, 3H), 3.73–3.81 (m, 3H), 4.12 (dd, J=2.4, 10.0 Hz, 2H), 4.59 (d, J=9.6 Hz, 1H), 7.04–7.06 (m, 1H, Ar), 7.25 (dd, J=1.2, 8.0 Hz, 1H, Ar), 7.52 (dd, J=1.2, 8.0 Hz, 1H, Ar), 7.59 (dd, J=1.2, 8.0 Hz, 1H, Ar); ^{13}C NMR (400 MHz, $CDCl_3$): δ 58.3, 59.3, 61.3, 61.4, 67.8, 72.1, 74.8, 74.9, 77.1, 79.0, 85.8, 86.04, 124.0, 127.5, 127.9, 130.6, 132.8, 136.4; ESI MS (m/z): 350 $[M+Na]^+$. Anal. Calcd for $C_{18}H_{22}O_5S$: C, 61.69; H, 6.33. Found: C, 61.64; H, 6.29.

4.14. Preparation and spectral analysis of XVIIIa

Prepared by the typical procedure for Sonogashira reaction (1) by using **XVIII** (100 mg, 0.15 mmol) to yield the desired product **XVIIIa** as a semi-solid (71.09 mg, 82%). R_f (35% EtOAc/hexane) 0.45; IR ($CHCl_3$) 2920, 2210 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.62–3.71 (m, 2H), 3.76 (dd, J=8.8, 5.5 Hz, 1H), 4.06–4.11 (m, 1H), 4.14 (dd,

J=8.9, 3.1 Hz, 3H), 4.28–4.33 (m, 1H), 4.35 (d, J=3.2 Hz, 1H), 4.47 (dd, J=13.9, 2.1 Hz, 3H), 4.52 (d, J=3.3 Hz, 1H), 4.63–4.71 (m, 2H), 7.06 (dt, J=7.7, 1.5 Hz, 1H), 7.20–7.40 (m, 16H), 7.54 (dd, J=7.9, 1.2 Hz, 1H), 7.61 (dd, J=7.9, 1.4 Hz, 1H); ^{13}C NMR (400 MHz, $CDCl_3$): δ 59.1, 68.7, 72.1, 73.2, 73.3, 74.5, 75.7, 75.8, 76.8, 77.2, 83.9, 86.9, 127.3, 127.4, 127.5, 127.6, 127.6, 127.7, 127.8, 127.8, 127.9, 128.1, 128.1, 128.2, 128.3, 128.3, 128.3, 128.4, 128.4, 128.5, 128.5, 128.6, 128.7, 130.7, 132.8, 138.1; ESI MS (m/z): 578 $[M+Na]^+$. Anal. Calcd for $C_{36}H_{34}O_5S$: C, 74.71; H, 5.92. Found: C, 74.61; H, 5.81.

4.15. Preparation and spectral analysis of Va

Prepared by the typical procedure for Heck reaction (2) by using the substrate **V** (100 mg, 0.19 mmol) to yield the desired product **Va** as a semi-solid (47.65 mg, 57%). R_f (35% EtOAc/hexane) 0.5; IR ($CHCl_3$) 2985, 2931, 1645 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.32 (s, 3H), 1.49 (s, 3H), 2.15 (dd, J=6.8, 13.6 Hz, 1H), 3.54 (dd, J=2.8, 13.6 Hz, 1H), 3.94 (dd, J=5.6, 12.4 Hz, 1H), 4.03–4.06 (m, 1H), 4.07 (dd, J=2.8, 9.2 Hz, 1H), 4.21 (dd, J=5.612.4 Hz, 1H), 4.31 (dd, J=3.2, 8.8 Hz, 1H), 4.54 (d, J=11.6 Hz, 1H), 4.61 (d, J=3.6 Hz, 1H), 4.67 (d, J=11.6 Hz, 1H), 5.06 (dd, J=1.6, 10.4 Hz, 1H), 5.18 (dd, J=1.6, 17.2 Hz, 1H), 5.91 (d, J=4.0 Hz, 1H), 6.96–6.98 (m, 1H, Ar), 6.99–7.35 (m, 6H, Ar), 7.39 (dd, J=1.2, 8.0 Hz, 1H), 7.52 (dd, J=1.2, 8.0 Hz, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 26.4, 26.8, 36.1, 71.9, 71.9, 74.8, 80.9, 81.7, 81.9, 105.1, 111.9, 116.8, 123.4, 126.3, 127.6, 127.7, 127.9, 128.4, 128.5, 128.5, 132.8, 134.6, 137.4, 138.5, 148.2; ESI MS (m/z): 440 $[M+Na]^+$. Anal. Calcd for $C_{25}H_{28}O_5S$: C, 68.16; H, 6.41. Found: C, 68.11; H, 6.39.

4.16. Preparation and spectral analysis of VIIIa

Prepared by the typical procedure for Heck reaction (2) by using the substrate **VIII** (100 mg, 0.18 mmol) to yield the desired product **VIIIa** as a semi-solid (48.02 mg, 58%). R_f (35% EtOAc/hexane) 0.48; IR ($CHCl_3$) 2985, 2931, 1645 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.71 (dd, J=5.6, 10.0 Hz, 1H), 3.81 (dd, J=6.0, 10.0 Hz, 1H), 4.06–4.14 (m, 3H), 4.24 (dd, J=2.4, 6.8 Hz, 1H), 4.51–4.65 (m, 4H), 4.74 (d, J=14.0 Hz, 1H), 5.29 (dd, J=1.6, 10.5 Hz, 1H), 5.32 (dd, J=1.6, 17.2 Hz, 1H), 5.83 (d, J=4.8 Hz, 1H), 7.03–7.05(m, 1H, Ar), 7.24–7.33 (m, 11H, Ar), 7.54 (dd, J=1.2, 8.0 Hz, 1H), 7.60 (dd, J=1.2, 7.6 Hz, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 67.6, 72.3, 72.4, 73.4, 78.4, 81.6, 83.8, 88.5, 118.1, 124.9, 127.5, 127.6, 127.7, 127.8, 127.9, 127.9, 128.3, 128.5, 131.6, 132.6, 132.7, 132.8, 133.9, 137.7, 138.2, 148.1; ESI MS (m/z): 460 $[M+Na]^+$. Anal. Calcd for $C_{28}H_{28}O_4S$: C, 73.02; H, 6.13. Found: C, 72.98; H, 6.10.

4.17. Preparation and spectral analysis of IXa

Prepared by the typical procedure for Heck reaction (2) by using the substrate **IX** (100 mg, 0.18 mmol) to yield the desired product **IXa** as a semi-solid (48.85 mg, 59%). R_f (35% EtOAc/hexane) 0.44; IR ($CHCl_3$) 2985, 2931, 1642 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.80 (dd, J=6.4, 10.8 Hz, 1H), 3.85 (dd, J=5.6, 10.0 Hz, 1H), 4.01–4.06 (m, 3H), 4.17–4.18 (m, 1H), 4.14 (dd, J=10.4, 11.2 Hz, 1H), 4.52 (d, J=3.6 Hz, 1H), 4.55 (d, J=3.6 Hz, 1H), 4.59 (d, J=12.0 Hz, 1H), 4.68 (d, J=12.0 Hz, 1H), 5.20 (d, J=12.0 Hz, 1H), 5.26 (d, J=16 Hz, 1H), 5.40 (d, J=2.8 Hz, 1H), 7.04–7.05(m, 1H, Ar), 7.26–7.35 (m, 10H, Ar), 7.53 (dd, J=1.2, 11.6 Hz, 2H), 7.68 (dd, J=1.2, 12.0 Hz, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 67.6, 72.3, 72.4, 73.4, 78.4, 81.6, 83.8, 88.5, 118.1, 124.9, 127.5, 127.6, 127.7, 127.8, 127.9, 127.9, 128.3, 128.5, 131.6, 132.6, 132.7, 132.8, 133.9, 137.7, 138.2, 148.1; ESI MS (m/z): 460 $[M+Na]^+$. Anal. Calcd for $C_{28}H_{28}O_4S$: C, 73.02; H, 6.13. Found: C, 72.95; H, 6.07.

4.18. Preparation and spectral analysis of XIIa

Prepared by the typical procedure for Heck reaction (2) by using the substrate **XII** (100 mg, 0.15 mmol) to yield the desired product **XIIa** as a semi-solid (50.46 mg, 58%). R_f (30% EtOAc/hexane) 0.45; IR ($CHCl_3$) 2985, 2931, 1645 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.57 (d, J=10.7 Hz, 1H), 3.67–3.81 (m, 2H), 3.91–3.94 (m, 2H), 4.14 (d, J=5.5 Hz, 1H), 4.20 (d, J=5.8 Hz, 1H), 4.27–4.61 (m, 4H), 4.83 (t, J=11.0 Hz, 2H), 5.02 (d, J=10.7 Hz, 1H), 5.22 (d, J=11.2 Hz, 1H), 5.33 (d, J=11.2 Hz, 1H), 5.86 (d, 3.6 Hz, 1H), 7.08–7.36 (m, 17H, Ar), 7.05–7.09 (m, 2H, Ar); ^{13}C NMR (400 MHz, $CDCl_3$): δ 68.4, 71.5, 71.6, 73.4, 75.1, 75.8, 77.2, 79.5, 82.5, 85.3, 118.0, 126.1, 127.6, 127.6, 127.7, 127.7, 127.7, 127.7, 127.8, 127.8, 127.9, 127.9, 128.0, 128.0, 128.0, 128.1, 128.3, 128.4, 128.4, 132.7, 133.1, 134.4, 135.5, 138.0, 138.5, 139.0, 148.8; ESI MS (m/z): 580 $[M+Na]^+$. Anal. Calcd for $C_{36}H_{36}O_5S$: C, 74.46; H, 6.25. Found: C, 74.34; H, 6.12.

4.19. Preparation and spectral analysis of XIVa

Prepared by the typical procedure for Heck reaction (2) by using the substrate **XIV** (100 mg, 0.15 mmol) to yield the desired product **XIVa** as a semi-solid (50.46 mg, 58). R_f (30% EtOAc/hexane) 0.41; IR ($CHCl_3$) 2985, 2931, 1645 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.44–3.78 (m, 6H), 4.21–4.30 (m, 1H), 4.39 (d J=5.8 Hz, 1H), 4.45 (d, J=5.7 Hz, 1H), 4.53–4.60 (m, 2H), 4.7 (d, J=9.7 Hz, 1H), 4.82–4.96 (m, 3H), 5.18 (d, J=10.0 Hz, 1H), 5.27 (d, J=10.0 Hz, 1H), 7.02–7.33 (m, 17H), 7.53 (d, J=7.7 Hz, 1H), 7.63 (d J=7.8 Hz, 1H, Ar); ^{13}C NMR (400 MHz, $CDCl_3$): δ 69.0, 73.4, 74.4, 75.1, 75.9, 77.6, 79.2, 80.5, 86.3, 86.7, 117.8, 124.1, 127.5, 127.5, 127.6, 127.6, 127.7, 127.7, 127.8, 127.8, 127.8, 127.9, 127.9, 127.9, 127.9, 128.3, 128.4, 128.4, 128.5, 132.8, 134.5, 137.0, 138.5, 138.7, 138.9, 147.1; ESI MS (m/z): 580 $[M+Na]^+$. Anal. Calcd for $C_{36}H_{36}O_5S$: C, 74.46; H, 6.25. Found: C, 74.37; H, 6.10.

4.20. Spectral analysis of Xab

R_f (40% EtOAc/hexane) 0.45; IR ($CHCl_3$) 2214, 1732 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.99 (s, 3H), 2.03 (s, 3H), 4.03 (d, J=7.3 Hz 1H), 4.02 (d, J=8.5 Hz, 1H), 4.11 (d, J=7.1 Hz, 1H), 4.62 (t, J=5.8 Hz, 1H), 4.90 (d, J=5.7 Hz, 1H), 5.23 (s, 1H), 5.99 (d, J=7.1 Hz, 1H), 6.40 (d, J=4.3 Hz, 1H), 6.98–7.05 (m, 3H, Ar), 7.14–7.20 (m, 3H, Ar), 7.43–7.51 (m, 2H, Ar); ^{13}C NMR (500 MHz, $CDCl_3$): δ 20.5, 20.9, 56.6, 58.9, 70.9, 74.9, 75.9, 80.5, 80.8, 93.9, 99.0, 119.9, 126.9, 127.8, 128.0, 128.9, 133.1, 133.1133.2, 133.5, 133.7, 135.2, 169.1, 169.6; ESI MS (m/z): 549 $[M+Na]^+$. Anal. Calcd for $C_{24}H_{21}BrO_6S_2$: C, 52.46; H, 3.85. Found: C, 52.41; H, 3.79.

4.21. Spectral analysis of Xac

R_f (35% EtOAc/hexane) 0.6; IR ($CHCl_3$) 2890, 2850 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.83–0.95 (m, 1H), 1.14–1.19 (m, 1H), 1.31 (s, 3H), 1.40 (d, J=2.7 Hz, 2H), 1.46 (s, 3H), 3.18–3.28 (m, 1H), 3.45–3.59 (m, 1H), 4.04 (d, J=3.3 Hz, 1H), 4.42 (dd, J=9.6, 2.9 Hz, 1H), 4.54 (dd, J=6.1, 2.6 Hz, 1H), 5.03–5.08 (m, 1H), 5.95 (d, J=3.6 Hz, 1H), 7.03–7.11 (m, 1H), 7.22–7.25 (m, 3H), 7.32–7.33 (m, 1H), 7.42–7.45 (m, 1H), 7.49–7.55 (m, 2H), 7.58–7.66 (m, 1H); ^{13}C NMR (500 MHz, $CDCl_3$): δ 25.93, 26.37, 26.82, 29.67, 53.46, 70.48, 81.31, 81.82, 82.44, 105.19, 111.92, 125.93, 127.56, 127.77, 128.63, 128.90, 132.38, 133.08, 134.36, 134.71, 135.23, 135.54, 135.99; ESI MS (m/z): 430 $[M+Na]^+$. Anal. Calcd for $C_{23}H_{26}O_4S_2$: C, 64.16; H, 14.86. Found: C, 63.99; H, 14.81.

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Supplementary material

General procedures, spectral data of starting materials and copies of ^{1}H NMR and ^{13}C NMR spectra of final products.

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.04.090.

References and notes

1. (a) Jana, R.; Pathak, T. P.; Sigman, M. S. *Chem. Rev.* **2011**, *111*, 1417–1492; (b) Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457–2483; (c) Evano, G.; Blanchard, N.; Toumi, M. *Chem. Rev.* **2008**, *108*, 3054–3131; (d) Bates, R. Organic Synthesis Using Transition Metals, WILLEY BLACKWELL: Hoboken, New Jersey, 2000; ISBN: 978-1-84127-107-1; (e) *Metal-catalyzed Cross-coupling Reactions*; de Meijere, A., Diederich, F., Eds.; WILEY-VCH: Weinheim, Germany, 2004; ISBN 3-527-30518-1.
2. (a) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem., Int. Ed.* **2005**, *44*, 4442–4489; (b) Chen, X.; Engle, K. M.; Wang, D. H.; Yu, J. Q. *Angew. Chem., Int. Ed.* **2009**, *48*, 5094–5115.
3. Chinchilla, R.; Nájera, C. *Chem. Rev.* **2007**, *107*, 874–922 and references cited therein.
4. (a) Pastre, J. C.; Correia, C. R. D. *Org. Lett.* **2006**, *8*, 1657–1660; (b) Ouyang, K.; Liang, Y.; Xi, Z. *Org. Lett.* **2012**, *14*, 4572–4575; (c) Deshpande, R.; Jiang, L.; Schmidt, G.; Rakovan, J.; Xiaopin, W.; Wheeler, K.; Wang, H. *Org. Lett.* **2009**, *11*, 4251–4253; (d) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5518–5526; (e) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5526–5531; (f) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5531–5534; (g) Heck, R. F. *J. Am. Chem. Soc.* **1968**, *90*, 5538–5542; (h) Heck, R. F. *J. Am. Chem. Soc.* **1969**, *91*, 6707–6714; (i) Heck, R. F.; Nolley, J. P. *J. Org. Chem.* **1972**, *37*, 2320–2322.
5. (a) Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 551–598; (b) Fenical, P. W.; Hensen, H. R.; Lindel, T. U.S. Patent 5,473,057, 1995; (c) Lindel, P. R.; Jensen, T.; Fenical, W.; Long, B. H.; Casazza, A. M.; Carboni, J.; Fairchild, C. R. *J. Am. Chem. Soc.* **1997**, *119*, 8744–8745; (d) Kurata, K.; Furusaki, A.; Suehiro, K.; Katayama, C.; Suzuki, T. *Chem. Lett.* **1982**, 1031–1034.
6. Allam, A.; Dupont, L.; Behr, J. B.; Royon, R. P. *Eur. J. Org. Chem.* **2012**, 817–823.
7. (a) Ziegler, F. E.; Chakraborty, U. R.; Wiesenfeld, R. B. *Tetrahedron* **1981**, *37*, 4035–4040; (b) Bräse, S.; de Meijere, A. In *Intramolecular Heck Reaction, Synthesis of Carbocycles*; Negishi, N., Ed.; Handbook of Organopalladium Chemistry for Organic Synthesis; Wiley-Interscience: New York, NY, 2002; Vol. I, pp 1223–1254; (c) Balraju, V.; Reddy, D. S.; Periasamy, M.; Iqbal, J. *J. Org. Chem.* **2005**, *70*, 9626–9628.
8. (a) Leibeling, M.; Koester, D. C.; Pawliczek, M.; Schild, S. C.; Werz, D. B. *Nat. Chem. Biol.* **2010**, *6*, 199–201; (b) Leibeling, M.; Milde, B.; Kratzert, D.; Stalke, D.; Werz, D. B. *Chem.—Eur. J.* **2011**, *17*, 9888–9892; (c) Awan, S. I.; Werz, D. B. *Bioorg. Med. Chem.* **2012**, *20*, 1846–1856.
9. Mithen, R. Sulphur-containing Compound. In *Plant Secondary Metabolites. Occurence, Structure and Role in the Human Diet*; Crozier, A., Clifford, M. N., Ashihara, H., Eds.; Blackwell: Oxford, UK, 2006; pp 208–302.
10. (a) Savi, P.; Zachayus, J. L.; Touchard, N. D.; Labouret, C.; Hervé, C.; Uzabiaga, M. F.; Pereillo, J. M.; Culouscou, J. M.; Bono, F.; Ferrara, P.; Herbert, J. M. Proc. Natl. Acad. Sci. U.S.A., **103**, 2006, 11069–11074; (b) Novel Dibenzothiazepine Antipsychotic. US Patent & Trademark Office, Patent Full Text and Image Database; (c) Lim, S. G.; Ng, T. M.; Kung, N. *Arch. Intern. Med.* **2006**, *166*, 49–56.
11. Hussain, A.; Yousuf, S. K.; Kumar, D.; Lambu, M.; Singh, B.; Maity, S.; Mukherjee, D. *Adv. Synth. Catal.* **2012**, *354*, 1933–1940.
12. Uchida, T.; Rodriquez, M.; Schreiber, S. L. *Org. Lett.* **2009**, *11*, 1559–1562.
13. (a) Vorbrüggen, H.; Bennua, B. *Chem. Ber.* **1981**, *114*, 1234–1255; (b) Vorbrüggen, H.; Bennua, B. *Tetrahedron Lett.* **1978**, 1339–1342.