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# Syntheses of 6-8-5 tricyclic ring systems by carbonylative [2+2+1] cycloaddition of bis(allene)s

M.T. Soraya Shafawati, Fuyuhiko Inagaki, Takamasa Kawamura, Chisato Mukai *

*Division of Pharmaceutical Sciences, Graduate School of Medical Sciences, Kanazawa University, Kakuma-machi, Kanazawa 920-1192, Japan*

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ABSTRACT

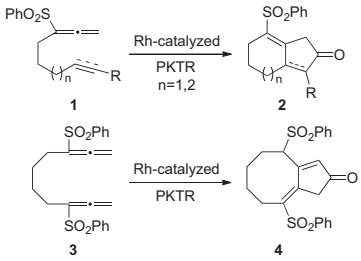
The synthetic route for the construction of the 6-8-5 tricyclic carbon frameworks has been developed. The [RhCl(CO)dppp]$_2$-catalyzed intramolecular Pauson–Khand-type reaction of the bis(allene)s, derived from dimedone, provided the corresponding bicyclo[6.3.0] skeleton in one operation.



## 1. Introduction

We have recently been involved in the investigation of the Rh(I)-catalyzed intramolecular Pauson–Khand-type reaction (PKTR) between allene and the π-component aiming at the development of an efficient procedure for the construction of bicyclo[m.3.0] compounds ($m$=4–6). Thus, the efficient construction of both the bicyclo[4.3.0] and bicyclo[5.3.0] frameworks **2** from the allene–alkyne and allene–alkene species **1** could be achieved (Scheme 1).[1,2] Furthermore, it is noteworthy that the PKTR of the bis(allene)s **3** emerged as a powerful tool for constructing the larger-sized bicyclo[6.3.0] undecadienone skeletons **4**.[1g,h] It was, however, not the case for the allene–alkyne and allene–alkene species **1** in which the corresponding bicyclo[6.3.0] skeletons were hardly formed in satisfactory yields.

Both the ophiobolin and fusicoccin families have the common 5-8-5 tricyclic core skeletons as exemplified by fusicoauritone and ophiobolin A (Fig. 1).[3] These natural products show a wide variety of potentially useful physiological activities, such as an anti-tumor activity and anti-parasitic activity.[4] Because of their unique and challenging structures, several total syntheses as well as synthetic studies on the formation of the core tricyclic systems have been reported.[5–7] In spite of many efforts to construct the medium-sized ring system including the eight-membered ring, it is still a challenging task.[8] We envisioned that the newly developed Rh(I)-catalyzed PKTR of bis(allene)s[1g,h]




**Scheme 1.** Rh(I)-catalyzed intramolecular PKTR of allene and π-component.

leading to the bicyclo[6.3.0] derivative would provide an alternative route for the preparation of the core tricyclic carbon framework (5-8-5 ring system) of the ophiobolin and fusicoccin families.

The simple retrosynthetic analysis for the construction of the 5-8-5 tricyclic ring systems **8** is shown in Scheme 2. Bis(propargyl alcohol) derivatives **6** would be derived from the cycloalkane-1,3-

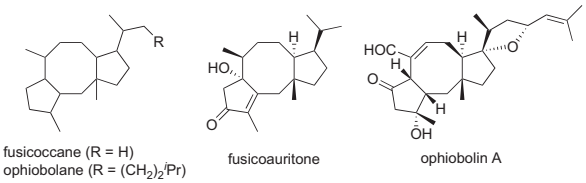



**Fig. 1.** Natural products possessing dicyclopenta[$a$,$d$]cyclooctane ring systems.

* Corresponding author. E-mail address: mukai@p.kanazawa-u.ac.jp (C. Mukai).

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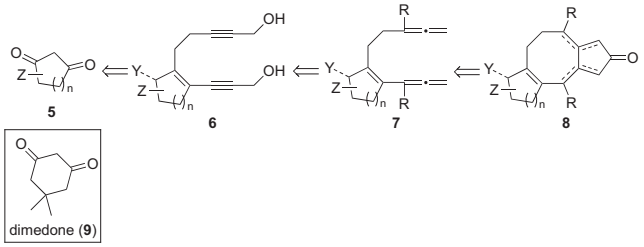
dione **5** by the conventional carbon–carbon forming reactions. Various types of bis(allene)s **7** (R=H, $CO_2Me$, $SO_2Ph$, $P(O)(OEt)_2$ etc.) should be obtained from **6** by the transformation reaction of the propargyl alcohols into allenes. Based on the previous results, the Rh(I)-catalyzed PKTR of bis(allene)s **7** would be expected to produce the corresponding bicyclo[6.3.0] derivatives **8**. In this study as a preliminary examination, we focused on the preparation of the 6-8-5 ring system **8** ($n$=2) instead of the 5-8-5 ring system **8** ($n$=1) from the commercially available and inexpensive dimedone (**9**) to confirm the feasibility of our plan.

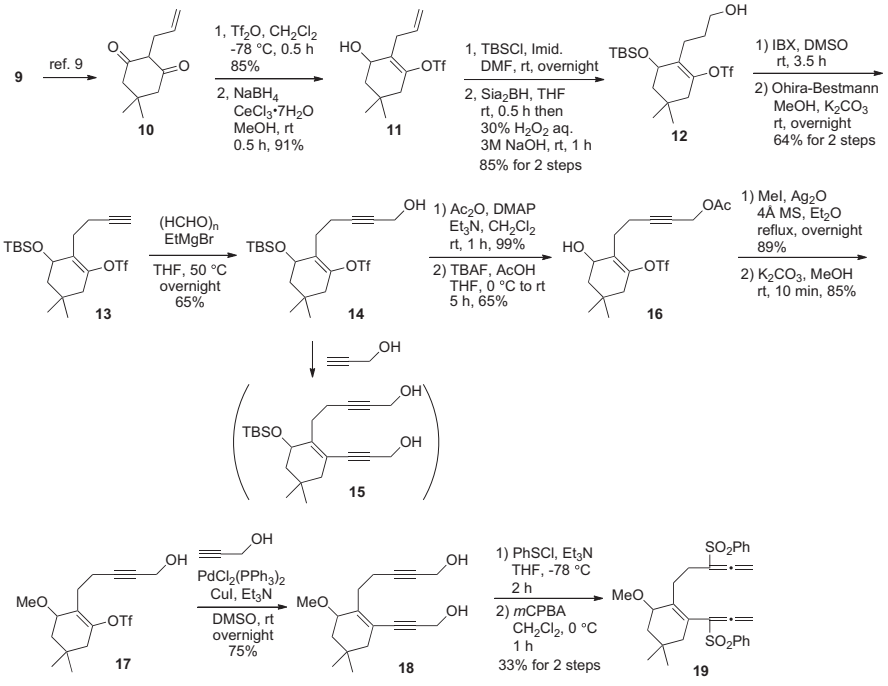



**Scheme 2.** Synthetic plan for tricyclic systems.

## 2. Results and discussion

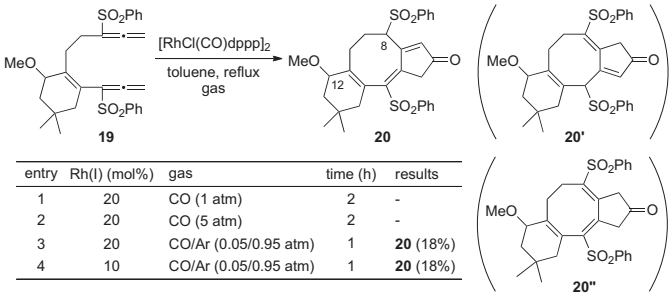
The known allylated dimedone **10**,[9] easily derived from dimedone (**9**), was treated with triflic anhydride to form the vinyl triflate in 85% yield, which was reduced with $NaBH_4$ to give the corresponding alcohol **11** in 91% yield (Scheme 3). The allylic alcohol moiety of **11** was protected with the TBS group, and the terminal alkene was exposed to a hydroboration–oxidation protocol with disiamylborane and hydrogen peroxide to afford the primary alcohol **12** in 85% overall yield. The one-carbon homologation of the primary alcohol **12** was achieved by consecutive oxidation with IBX and treatment with Ohira–Bestmann reagent to produce **13** in a 64% overall yield. Hydroxymethylation of the alkyne **13** using EtMgBr and $(HCHO)_n$ afforded **14** in 65% yield, however, the Sonogashira coupling reaction of which with the propargyl alcohol under several conditions did not furnish the diyne derivative **15** at all. We tentatively assumed that the bulky silyloxy functionality of **14** might cause the trouble encountered for introduction of the alkyne moiety. Thus, the less bulkier methoxy group was chosen as an alternative functional group. Acetylation of the primary alcohol of **14** (99% yield) was followed by desilylation with TBAF to afford the allyl alcohol derivative **16** in 65% yield. Exposure of **16** to MeI and $Ag_2O$ effected methylation to produce the corresponding methoxy derivative, deacetylation of which was carried out by methoxide to provide **17** in 85% yield. The vinyl triflate **17** was treated with propargyl alcohol under the typical Sonogashira conditions to afford the desired bis(propargyl alcohol) derivative **18** in 75%. The diol derivative **18** was then converted into the bis(phenylsulfonylallene) **19** in 33% overall yield via the successive phenylsulfenyl ester formation, [2,3]-sigmatropic rearrangement and oxidation.[1g]

With the required bis(phenylsulfonylallene) **19** in hand, several reaction conditions of the PKTR were examined. The treatment of **19** with 20 mol % $[RhCl(CO)dppp]_2$ in toluene at 120 °C under an atmosphere of CO gave an intractable complex mixture (Table 1, entry 1). Increasing the CO pressure to 5 atm did not affect the reaction and the complex mixture was again observed (entry 2). On the contrary, decreasing the CO pressure (under an atmosphere consisting of 0.05 atm of CO and 0.95 atm of Ar)[1j,10] produced an 18% yield of the desired tricyclic compound **20** (entry 3). A similar result (18%) was obtained when the loading amount of the catalyst was reduced to 10 mol % (entry 4). The formation of **20** could be rationalized by the initial formation of **20″**, followed by the formal 1,3-hydrogen shift. An alternative 1,3-hydrogen shift from **20″** would lead to the **20′**. The exclusive formation of **20** might reflect the fact that its structure is more stable than that of **20′** presumably due to the fully conjugated triene functionality of the former. The distance between the $C_{12}$-stereogenic center and the newly created $C_8$-one is too far to control each other's




**Scheme 3.** Preparation of bis(phenylsulfonylallene)s **19**.

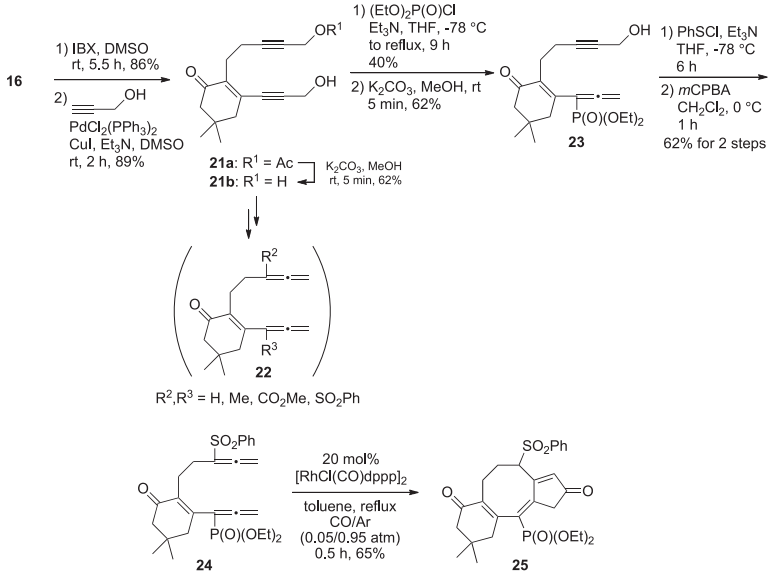
**Table 1**
Rh(I)-catalyzed PKTR of **19**




| entry | Rh(I) (mol%) | gas | time (h) | results |
|---|---|---|---|---|
| 1 | 20 | CO (1 atm) | 2 | - |
| 2 | 20 | CO (5 atm) | 2 | - |
| 3 | 20 | CO/Ar (0.05/0.95 atm) | 1 | **20** (18%) |
| 4 | 10 | CO/Ar (0.05/0.95 atm) | 1 | **20** (18%) |

stereochemistry. Thus, it is thought that the tricyclic product **20** consisted of two stereoisomers because of the two stereogenic centers ($C_8$- and $C_{12}$-positions), although the TLC behavior as well as their spectral data indicate that this product seems to be a single stereoisomer.

We could synthesize the desired 6-8-5 tricyclic compound **20**, but the chemical yield was far from being satisfactory. In addition, we encountered the puzzling stereochemical problem during the conversion of **19** into **20**. It is obvious that the methoxy group on the cyclohexene ring of the substrate **19** caused the issue. Therefore, we changed methoxy functionality to a ketone functionality. The secondary alcohol of **16** was oxidized with IBX to furnish the ketone in 86% yield, which was then exposed to the Sonogashira coupling conditions with propargyl alcohol to afford the diyne derivative **21a** in 89% yield (Scheme 4). The resulting diyne compound was deacylated under basic conditions to produce the corresponding bis(propargyl alcohol) **21b** in 62% yield. In order to improve the chemical yield in the PKTR of the bis(allene) compound, we tried to introduce several types of functionalities, such as the H,[11] Me,[1j] $CO_2Me$,[1j] and $SO_2Ph$ groups, on the bis(allene) moiety ($R^2$ and $R^3$ positions) of **22** from the common bis(propargyl alcohol) derivative **21b**, but the bis(allene)s having different functional groups could not be obtained. Upon exposure to diethyl chlorophosphite, the propargyl alcohol moiety of **21a** was converted to the allenyl diethyl phosphonate in 40% yield.[12] The resulting allene derivative was converted into the alcohol **23** in 62% yield, which was successively treated with benzenesulfenyl chloride and *m*CPBA to produce the bis(allene) derivative **24** possessing phosphonate and sulfonyl groups on the bis(allene) moiety in 62% yield. The PKTR of **24** with 20 mol % $[RhCl(CO)dppp]_2$ under the previously used CO/Ar atmosphere (0.05/0.95 atm) proceeded well to afford the corresponding 6-8-5 membered compound **25** in 65% yield.




**Scheme 4.** Preparation of tricyclic derivative **25**.

## 3. Conclusions

In summary, we have successfully developed a synthetic method for the construction of the 6-8-5 tricyclic ring systems by the Rh(I)-catalyzed intramolecular PKTR of bis(allene) species that were derived from the commercially available dimedone. Application of the procedure described here to the synthesis of the 5-8-5 tricyclic ring system, a core carbon framework of the ophiobolin and fusicoccin families, is currently in progress.

## 4. Experimental

### 4.1. General

Melting point is uncorrected. IR spectra were measured in $CHCl_3$. $^1H$ NMR spectra were measured in $CDCl_3$. $CHCl_3$ (7.26 ppm) for silyl compounds and tetramethylsilane (0.00 ppm) for compounds without a silyl group were used as internal standards. $^{13}C$ NMR spectra were measured in $CDCl_3$ (77.0 ppm) as an internal standard. All reactions were carried out under a nitrogen atmosphere unless otherwise stated. Silica gel (silica gel 60, 230–400 mesh) was used for chromatography. Organic extracts were dried over anhydrous $Na_2SO_4$. 2-Allyl-5,5-dimethylcyclohexane-1,3-dione (**2**) is a known compound.[9]

### 4.2. 2-Allyl-3-hydroxy-5,5-dimethylcyclohex-1-enyl trifluoromethanesulfonate (11)

To a solution of **10** (2.4 g, 13 mmol) and Hunig's base (4.6 mL, 27 mmol) in $CH_2Cl_2$ (65 mL) was slowly added $Tf_2O$ (2.7 mL, 16 mmol) at −78 °C. After stirring for 0.5 h, the reaction was quenched with water, extracted with $CH_2Cl_2$. The extract was washed with water, brine, dried, and concentrated to dryness. The

residue was passed through a short pad of silica gel with hexane/AcOEt (2:1) to afford a vinyl triflate derivative (3.4 g, 85%) as a yellow oil. IR 3028, 1686, 1663, 1420, 1246, 1229, 1207, 1138 $cm^{-1}$; $^1H$ NMR $\delta$ 5.73 (ddt, 1H, $J$=16.8, 10.0, 6.2 Hz), 5.07 (d, 1H, $J$=16.8 Hz), 5.03 (d, 1H, $J$=10.0 Hz), 3.11 (d, 2H, $J$=6.2 Hz), 2.63 (s, 2H), 2.35 (s, 2H), 1.11 (s, 6H); $^{13}C$ NMR $\delta$ 196.8, 160.8, 132.9, 128.8, 118.2 (q, $J_{CF}$=320 Hz), 116.9, 50.7, 42.3, 32.8, 27.9, 27.4; DARTMS $m/z$ 313 ($M^+$+1, 64); DARTHRMS calcd for $C_{12}H_{16}F_3O_4S$ 313.0721, found 313.0715. To a solution of the vinyl triflate (2.4 g, 7.7 mmol) and $CeCl_3\cdot 7H_2O$ (3.4 g, 9.2 mmol) in MeOH (19 mL) was added $NaBH_4$ (580 mg, 15 mmol) at room temperature. After stirring for 1 h, the reaction mixture was quenched with aqueous $NH_4Cl$, extracted with AcOEt. The extract was washed with water, brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (6:1) to afford **11** (3.7 g, 91%) as a colorless oil. IR 3589, 3421, 1691, 1637, 1412, 1248, 1225, 1207, 1138 $cm^{-1}$; $^1H$ NMR $\delta$ 5.86–5.76 (m, 1H), 5.19 (dd, 1H, $J$=17.0, 1.4 Hz), 5.12 (dd, 1H, $J$=10.1, 1.4 Hz) 4.37–4.34 (m, 1H), 3.16 (dd, 1H, $J$=14.6, 6.0 Hz), 3.07 (dd, 1H, $J$=14.6, 7.8 Hz), 2.33 (d, 1H, $J$=16.5 Hz), 2.07 (d, 1H, $J$=16.5 Hz), 1.83 (ddd, 2H, $J$=13.3, 6.0, 1.4 Hz), 1.44 (dd, 1H, $J$=13.3, 8.7 Hz), 1.08 (s, 3H), 0.97 (s, 3H). $^{13}C$ NMR $\delta$ 144.6, 134.0, 129.2, 118.3 (q, $J$=320 Hz), 117.6, 67.1, 44.4, 41.4, 31.5, 30.6, 30.1, 26.4; EIMS $m/z$ 314 ($M^+$, 2.8); EIHRMS calcd for $C_{12}H_{17}F_3O_4S$ 314.0800; found 314.0795.

### 4.3. 3-(*tert*-Butyldimethylsilyloxy)-2-(3-hydroxypropyl)-5,5-dimethylcyclohex-1-enyl trifluoromethanesulfonate (12)

To a solution of **11** (2.0 g, 6.4 mmol) and imidazole (2.2 g, 32 mmol) in DMF (21 mL) was added TBSCl (2.9 g, 19 mmol) at 0 °C. After warming to room temperature, the mixture was stirred overnight. Then the mixture was quenched with aqueous $NH_4Cl$, extracted with AcOEt. The extract was washed with brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane/AcOEt (20:1) to afford the crude vinyl triflate. To a solution of the crude vinyl triflate in THF (62 mL) was added $(Sia)_2BH$ (0.50 M in THF, 24 mL, 12 mmol) at 0 °C. After stirring for 30 min at room temperature, the reaction mixture were added $H_2O_2$ (18 mL) and 3 M NaOH (18 mL) at 0 °C. The mixture was further stirred for 1 h at room temperature, then extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (4:1) to afford **12** (2.4 g, 85% from **11**) as a colorless oil. IR 3626, 3441, 1693, 1463, 1248, 1225, 1207, 1140 $cm^{-1}$; $^1H$ NMR $\delta$ 4.39–4.36 (m, 1H), 3.64 (t, 2H, $J$=6.4 Hz), 2.40–2.25 (m, 3H), 2.04 (d, 1H, $J$=16.9 Hz), 1.78–1.65 (m, 3H), 1.46 (dd, 1H, $J$=13.3, 7.8 Hz), 1.05 (s, 3H), 0.97 (s, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.10 (s, 3H). $^{13}C$ NMR $\delta$ 144.5, 131.5, 117.2 (q, $J$=320 Hz), 67.9, 62.6, 44.8, 41.2, 31.3, 30.6, 30.0, 26.8, 25.8, 22.8, 18.0, −4.0, −4.9; DARTMS $m/z$ 447 ($M^+$+1, 7.0); DARTHRMS calcd for $C_{18}H_{34}F_3O_5SSi$ 447.1848, found 447.1855.

### 4.4. 3-(*tert*-Butyldimethylsilyloxy)-2-(but-3-ynyl)-5,5-dimethylcyclohex-1-enyl trifluoromethanesulfonate (13)

To a solution of **12** (2.0 g, 6.0 mmol) in DMSO (60 mL) was added IBX (3.4 g, 12 mmol) at room temperature. After stirring for 3.5 h at the same temperature, the reaction was quenched by addition of saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$. Then the mixture was extracted with $Et_2O$, washed with water and brine, dried, and concentrated to dryness to afford the crude aldehyde. To a solution of the crude aldehyde and Ohira–Bestmann reagent (960 mg, 5.0 mmol) in MeOH (70 mL) was added $K_2CO_3$ (1.2 g, 8.3 mmol) at room temperature. After stirring overnight, the mixture was quenched with saturated aqueous $NaHCO_3$, extracted with $Et_2O$. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (10:1) to afford **13** (1.7 g, 64% from **12**) as a yellow oil. IR 3308, 1248, 1225, 1207, 1140 $cm^{-1}$; $^1H$ NMR $\delta$ 4.45–4.41 (m, 1H), 2.57–2.47 (m, 2H), 2.38–2.29 (m, 3H), 2.06 (d, 1H, $J$=16.9 Hz), 1.94 (t, 2H, $J$=2.7 Hz), 1.71–1.67 (m, 1H), 1.44 (dd, 1H, $J$=13.1, 8.2 Hz), 1.05 (s, 3H), 0.98 (s, 3H), 0.90 (s, 9H), 0.14 (s, 3H), 0.11 (s, 3H). $^{13}C$ NMR $\delta$ 145.2, 130.0, 118.3 (q, $J$=320 Hz), 83.0, 68.9, 68.1, 44.8, 41.3, 31.4, 30.2, 26.5, 25.8, 25.3, 18.0, 16.9, −3.9, −4.9; FABMS $m/z$ 441 ($M^+$+1, 32.2); FABHRMS $m/z$ calcd for $C_{14}H_{32}F_3O_4SSi$ 441.1743, found 441.1727.

### 4.5. 3-(*tert*-Butyldimethylsilyloxy)-2-(5-hydroxypent-3-ynyl)-5,5-dimethylcyclohex-1-enyl trifluoromethanesulfonate (14)

To a solution of **13** (758 mg, 1.65 mmol) in THF (9 mL) was added EtMgBr (1.5 M, 5.0 mL, 6.6 mmol) at 0 °C. After stirring for 2 h at 50 °C, paraformaldehyde (149 mg) was added to the reaction mixture, and the mixture was further stirred overnight at the room temperature. Then the reaction was quenched with aqueous $NH_4Cl$, extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (4:1) to afford **14** (473 mg, 65%) as a yellow oil. IR 3608, 3421, 1409, 1248, 1225, 1207, 1140 $cm^{-1}$; $^1H$ NMR $\delta$ 4.42–4.40 (m, 1H), 4.19 (t, 2H, $J$=2.1 Hz), 2.54–2.46 (m, 2H), 2.40–2.38 (m, 2H), 2.30 (d, 1H, $J$=16.8 Hz), 2.08 (d, 1H, $J$=16.8 Hz), 1.71 (s, 1H), 1.68 (ddd, 1H, $J$=13.1, 5.8, 1.0 Hz), 1.44 (dd, 1H, $J$=13.1, 8.2 Hz), 1.05 (s, 3H), 0.99 (s, 3H), 0.89 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H). $^{13}C$ NMR $\delta$ 145.2, 130.0, 118.2 (q, $J$=320 Hz), 84.7, 79.3, 67.8, 51.3, 44.8, 41.2, 31.4, 30.2, 26.3, 25.7, 25.2, 18.0, 16.9, −3.9, −4.9. DARTMS $m/z$ 471 ($M^+$+1, 4.0); DARTHRMS calcd for $C_{20}H_{34}F_3O_5SSi$ 471.1848, found 471.1836.

### 4.6. 5-[6-Hydroxy-4,4-dimethyl-2-(trifluoromethylsulfonyloxy) cyclohex-1-enyl]pent-2-ynyl acetate (16)

To a solution of **14** (344 mg, 0.732 mmol) in $CH_2Cl_2$ (7 mL) were added $Ac_2O$ (0.20 mL, 3.2 mmol), DMAP (26 mg, 0.22 mmol), and $Et_3N$ (0.20 mL, 1.4 mmol) at 0 °C. After stirring for 1 h at room temperature, the reaction was quenched with water, extracted with $CH_2Cl_2$. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (8:1) to afford the acetate derivative (369 mg, 99%) as a yellow oil. IR 2237, 1738, 1410, 1248, 1227, 1207, 1140 $cm^{-1}$; $^1H$ NMR $\delta$ 4.62 (s, 2H), 4.42–4.39 (m, 1H), 2.49 (t, 2H, $J$=7.3 Hz), 2.40 (t, 2H, $J$=7.3 Hz), 2.30 (d, 1H, $J$=16.8 Hz), 2.07–2.04 (m, 4H), 1.68 (dd, 1H, $J$=12.7, 5.8 Hz), 1.44 (dd, 1H, $J$=12.7, 8.2 Hz), 1.05 (s, 3H), 0.98 (s, 3H), 0.89 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H). $^{13}C$ NMR $\delta$ 170.3, 145.3, 129.9, 118.2 (q, $J$=326 Hz), 85.9, 74.8, 68.0, 52.7, 44.8, 41.2, 31.4, 30.3, 26.3, 25.7, 25.0, 20.7, 18.0, 17.1, −3.9, −4.9. DARTMS $m/z$ 513 ($M^+$+1, 1.3); DARTHRMS calcd for $C_{22}H_{36}F_3O_6SSi$ 513.1954, found 513.1964. To a solution of the acetate derivative (343 mg, 0.669 mmol) in THF (7 mL) was added TBAF (1.0 M in THF, 0.80 mL, 0.80 mmol, neutralized with AcOH) at 0 °C. After stirring for 5 h at room temperature, the reaction was quenched with aqueous $NH_4Cl$, extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (3:1) to afford **16** (175 mg, 65%) as a yellow oil. IR 3587, 3529, 1732, 1375, 1411, 1248, 1225, 1140 $cm^{-1}$. $^1H$ NMR 4.62 (t, 2H, $J$=2.1 Hz), 4.45–4.43 (m, 1H), 2.65–2.61 (m, 1H), 2.56–2.50 (m, 2H), 2.47–2.41 (m, 1H), 2.35–2.31 (m, 1H), 2.07–2.05 (m, 4H), 1.87 (ddd, 1H, $J$=13.1, 5.8, 1.7 Hz), 1.41 (dd, 1H, $J$=13.1, 8.9 Hz), 1.08 (s, 3H), 1.00 (s, 3H). $^{13}C$ NMR $\delta$ 170.5, 145.2, 123.0, 118.1 (q, $J$=320 Hz), 86.2, 75.1, 66.7, 52.6, 44.7, 41.3, 31.4, 30.4, 25.7, 24.6, 20.7, 16.8. FABMS $m/z$ 421 ($M^+$+1, 79.1); FABHRMS $m/z$ calcd for $C_{16}H_{21}F_3O_6SNa$ 421.0909, found 421.0907.

### 4.7. 2-(5-Hydroxypent-3-ynyl)-3-methoxy-5,5-dimethylcyclohex-1-enyl trifluoromethanesulfonate (17)

MeI (0.50 mL, 4.5 mmol) was added to a mixture of $Ag_2O$ (1.6 g, 6.7 mmol), 4 Å molecular sieve (400 mg) and **16** (256 mg, 0.643 mmol) in $Et_2O$ (7 mL). After stirring overnight at 50 °C, the precipitates were filtered through a pad of Celite. The solvent of filtrate was removed in vacuo and the residue was chromatographed with hexane/AcOEt (4:1) to afford the methoxy compound (227 mg, 89%) as a yellow oil. IR 1740, 1412, 1246, 1227, 1207, 1142 $cm^{-1}$; $^1H$ NMR $\delta$ 4.63 (t, 2H, $J$=2.1 Hz), 4.03–4.00 (m, 1H), 3.34 (s, 3H), 2.60–2.56 (m, 1H), 2.48–2.41 (m, 3H), 2.33–2.29 (m, 1H), 2.08–2.05 (m, 4H), 1.79 (ddd, 1H, $J$=13.0, 5.8, 1.7 Hz), 1.43 (dd, 1H, $J$=13.0, 8.6 Hz), 1.07 (s, 3H), 0.99 (s, 3H). $^{13}C$ NMR $\delta$ 170.3, 145.9, 128.5, 118.3 (q, $J$=320 Hz), 86.1, 75.2, 74.9, 56.1, 52.7, 41.4, 39.1, 31.4, 30.2, 26.2, 25.0, 20.7, 16.9. FABMS $m/z$ 413 ($M^+$+1, 12); FABHRMS $m/z$ calcd for $C_{17}H_{24}F_3O_6S$ 413.1246, found 413.1241. To a solution of the methoxy compound (11 mg, $2.9\times10^{-2}$ mmol) in MeOH (0.5 mL) was added $K_2CO_3$ (4 mg, 0.03 mmol). After stirring for 10 min, the mixture was quenched with water and extracted with AcOEt. The extract was washed with brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (1:2) to afford **17** (9.5 mg, 85%) as a yellow oil. IR 3607, 3445, 1693, 1410, 1246, 1227, 1205, 1140 $cm^{-1}$; $^1H$ NMR $\delta$ 4.20–4.19 (m, 2H), 4.04–4.00 (m, 1H), 3.35 (s, 3H), 2.60 (dt, 1H, $J$=13.1, 7.2 Hz), 2.49–2.41 (m, 3H), 2.30 (dt, 1H, $J$=16.9, 2.3 Hz), 2.07 (d, 1H, $J$=16.9 Hz), 1.83–1.78 (m, 1H), 1.44 (dd, 1H, $J$=13.3, 8.7 Hz), 1.07 (s, 3H), 1.01 (s, 3H); $^{13}C$ NMR $\delta$ 145.8, 128.6, 118.2 (q, $J$=320 Hz), 84.8, 79.4, 75.0, 56.1, 51.2, 41.3, 39.1, 31.3, 30.2, 26.1, 25.2, 16.7; DARTMS $m/z$ 371 ($M^+$+1, 29); DARTHRMS calcd for $C_{15}H_{22}F_3O_5S$ 371.1140, found 371.1137.

### 4.8. 5-[2-(3-Hydroxyprop-1-ynyl)-6-methoxy-4,4-dimethylcyclohex-1-enyl]pent-2-yn-1-ol (18)

To a solution of $PdCl_2(PPh_3)_2$ (63 mg, $9.0\times10^{-2}$ mmol), CuI (37 mg, 0.20 mmol) and **17** (480 mg, 1.3 mmol) in dry DMSO (8 mL) were added propargyl alcohol (0.20 mL, 3.9 mmol) and triethylamine (0.60 mL, 3.9 mmol). After stirring overnight at room temperature, the mixture was quenched with aqueous $NH_4Cl$ and extracted with $Et_2O$. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane–AcOEt (1:1) to afford **18** (269 mg, 75%) as a yellow oil. IR 3605, 3448 $cm^{-1}$; $^1H$ NMR $\delta$ 4.42 (s, 2H), 4.22 (t, 2H, $J$=1.8 Hz), 3.88–3.85 (m, 1H), 3.33 (s, 3H), 2.71–2.57 (m, 2H), 2.49–2.33 (m, 2H), 2.09 (d, 1H, $J$=16.9 Hz), 1.90 (d, 1H, $J$=16.9 Hz), 1.76 (ddd, 1H, $J$=12.8, 6.4, 1.8 Hz), 1.40 (dd, 1H, $J$=12.8, 8.7 Hz), 0.98 (s, 3H), 0.91 (s, 3H); $^{13}C$ NMR $\delta$ 142.5, 118.3, 90.9, 86.4, 85.5, 78.8, 75.7, 56.1, 51.6, 51.4, 44.0, 39.6, 30.5, 30.2, 30.1, 26.1, 17.8; DARTMS $m/z$ 277 ($M^+$+1, 9); DARTHRMS calcd for $C_{17}H_{25}O_3$ 277.1804, found 277.1793.

### 4.9. 3-Methoxy-5,5,-dimethyl-2-(3-phenylsulfonylpenta-3,4-dienyl)-1-(1-phenylsulfonylpropa-1,2-dienyl)cyclohex-1-ene (19)

To a solution of **18** (300 mg, 1.09 mmol) in THF (16 mL) were added $Et_3N$ (1.4 mL, 9.8 mmol) and PhSCl (0.97 mL, 8.7 mmol) in THF (4 mL) at −78 °C. After stirring for 2 h at the same temperature, the reaction was quenched with water, extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane/AcOEt (10:1) to afford the crude sulfoxide. To a solution of the crude sulfoxide in $CH_2Cl_2$ (1 mL) was added a *m*CPBA (400 mg, 2.34 mmol) at 0 °C. After stirring for 1 h at the same temperature, the reaction was quenched with aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$, and extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with $CH_2Cl_2$/hexane/AcOEt (4:1:1) to afford **19** (189 mg, 33%) as a yellow oil. IR 1967, 1936, 1373, 1150 $cm^{-1}$; $^1H$ NMR $\delta$ 7.88–7.82 (m, 4H), 7.64–7.58 (m, 2H), 7.55–7.53 (m, 2H), 7.51–7.48 (m, 2H) 5.31 (t, 2H, $J$=3.4 Hz), 5.19 (s, 2H), 3.68–3.66 (m, 1H), 3.18 (s, 3H), 2.22–2.15 (m, 2H), 2.13–2.04 (m, 2H), 1.96 (d, 1H, $J$=17.2 Hz), 1.87 (td, 1H, $J$=12.7, 5.2 Hz), 1.71 (ddd, 1H, $J$=12.7, 5.8, 1.7 Hz), 1.35 (1H, dd, $J$=12.7, 8.6 Hz), 0.94 (s, 3H), 0.86 (s, 3H); $^{13}C$ NMR $\delta$ 207.5, 207.4, 140.2, 140.1, 139.4, 133.6, 133.4, 129.0, 128.9, 128.3, 128.0, 125.1, 113.7, 113.4, 84.5, 82.1, 75.9, 56.1, 44.2, 39.5, 30.3, 30.1, 28.6, 26.3, 24.9; DARTMS $m/z$ 525 ($M^+$+1, 26); DARTHRMS calcd for $C_{29}H_{33}O_5S_2$ 525.1769, found 525.1766.

### 4.10. General procedure for rhodium(I)-catalyzed carbonylative [2+2+1] cycloaddition

To a solution of the bis(allene) (0.1 mmol) in toluene (1 mL) was added 10 or 20 mol % of $[RhCl(CO)dppp]_2$. The reaction mixture was heated at reflux under an atmosphere consisting of 0.05 atm of CO and 0.95 atm of Ar until the complete disappearance of the starting material (monitored by TLC). Toluene was evaporated off, and the residual oil was chromatographed with hexane/AcOEt or $CH_2Cl_2$/AcOEt to afford the cyclized product. The chemical yields are summarized in Table 1 and Scheme 4.

### 4.11. 12-Methoxy-14,14-dimethyl-2,8-bis(phenylsulfonyl)tricyclo[9.4.0.0$^{3,7}$]pentadeca-1(11),2,6-trien-5-one (20)

Compound **20** was a yellow oil. IR 1716, 1308, 1150 $cm^{-1}$; $^1H$ NMR 7.80–7.78 (m, 4H), 7.69 (t, 1H, $J$=7.3 Hz), 7.63–7.49 (m, 5H), 7.14 (s, 1H), 4.24 (dd, 1H, $J$=11.9, 3.7 Hz), 3.56–3.50 (m, 2H), 3.40 (d, 1H, $J$=22.0 Hz), 3.09 (s, 3H), 2.91 (d, 1H, $J$=17.9 Hz), 2.60 (dd, 1H, $J$=12.8, 3.7 Hz), 2.40–2.31 (m, 1H), 2.11–1.98 (m, 2H), 1.84 (d, 1H, $J$=17.9 Hz), 1.66–1.62 (m, 1H), 1.32–1.25 (m, 1H), 1.05 (s, 3H), 0.88 (s, 3H). $^{13}C$ NMR $\delta$ 201.0, 160.9, 144.7, 140.3, 139.8, 138.9, 137.9, 137.4, 134.5, 133.8, 130.7, 129.5, 129.2, 128.8, 127.4, 73.2, 62.8, 55.2, 43.4, 40.0, 38.1, 31.4, 30.2, 27.9, 27.0, 24.3; DARTMS $m/z$ 553 ($M^+$+1, 56); DARTHRMS calcd for $C_{30}H_{33}O_6S_2$ 553.1719, found 553.1716. Regiochemistry of **20** was determined by HMQC and HMBC.

### 4.12. 5-[2-(3-Hydroxyprop-1-ynyl)-4,4-dimethyl-6-oxocyclohex-1-enyl]pent-2-ynyl acetate (21a)

To a solution of **16** (235 mg, 0.590 mmol) in DMSO (6 mL) was added IBX (500 mg, 1.8 mmol) at room temperature. After stirring for 5.5 h, the reaction was quenched with saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$, extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (4:1) to afford the ketone derivative (205 mg, 86%) as a yellow oil. IR 1736, 1686, 1420, 1246, 1227, 1138 $cm^{-1}$; $^1H$ NMR $\delta$ 4.56 (t, 2H, $J$=2.1 Hz), 2.62 (s, 2H), 2.54 (t, 2H, $J$=7.2 Hz), 2.39–2.37 (m, 2H), 2.32 (s, 2H), 2.03 (s, 3H), 1.10 (s, 6H). $^{13}C$ NMR $\delta$ 197.1, 170.1, 161.5, 128.5, 118.2 (q, $J$=320 Hz), 85.3, 75.2, 52.5, 50.6, 42.3, 32.7, 27.7, 22.4, 20.6, 17.3. DARTMS $m/z$ 397 ($M^+$+1, 100); DARTHRMS calcd for $C_{16}H_{20}F_3O_6S$ 397.0933, found 397.0921. To a solution of $PdCl_2(PPh_3)_2$ (18 mg, 0.030 mmol), CuI (11 mg, 0.060 mmol) and the ketone derivative (146 mg, 0.40 mmol) in dry DMSO (3 mL) were added propargyl alcohol (0.10 mL, 1.9 mmol) and $Et_3N$ (0.30 mL, 1.9 mmol). After stirring for 2 h at room temperature, the reaction was quenched with aqueous $NH_4Cl$, extracted with $Et_2O$. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (1:1) to afford **21a** (108 mg, 89%) as a yellow oil. IR 3607, 3447, 1734, 1663 $cm^{-1}$. $^1H$ NMR $\delta$ 4.62 (t, 2H, $J$=2.1 Hz), 4.47 (s, 2H), 2.67 (t, 2H,

$J$=7.1 Hz), 2.59 (br s, 1H), 2.37–2.34 (m, 4H), 2.27 (s, 2H), 2.07 (s, 3H), 1.01 (s, 6H). $^{13}$C NMR $\delta$ 198.1, 170.7, 140.0, 136.7, 101.0, 86.7, 84.0, 74.7, 52.7, 51.42, 51.35, 44.8, 33.3, 27.9, 26.7, 20.8, 17.9. DARTMS $m/z$ 303 ($M^+$+1, 100); DARTHRMS calcd for $C_{18}H_{23}O_4$ 303.1596, found 303.1587.

### 4.13. Diethyl 1-[2-(5-hydroxypent-3-ynyl)-5,5-dimethyl-3-oxocyclohex-1-enyl]propa-1,2-dienylphosphonate (23)

To a solution of **21a** (39 mg, 0.13 mmol) in THF (1.5 mL) were added $Et_3N$ (0.050 mL, 0.26 mmol) and diethyl chlorophosphite (30 mL, 0.20 mmol) at −78 °C. After stirring for 30 min at the same temperature, the reaction mixture was warmed to room temperature and then heated at reflux for 9 h. The reaction mixture was quenched by addition of saturated aqueous $NaHCO_3$, extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with DCM/AcOEt (1:1) to afford the phosphonyl allene (22 mg, 40%) as a yellow oil. IR 1960, 1931, 1738, 1668, 1265, 1024 cm$^{-1}$; $^1$H NMR $\delta$ 5.14 (s, 1H), 5.11 (s, 1H), 4.61 (s, 2H), 4.20–4.07 (m, 4H), 2.56 (t, 2H, $J$=7.8 Hz), 2.47–2.46 (m, 2H), 2.31–2.26 (m, 4H), 2.06 (s, 3H), 1.32 (t, 6H, $J$=7.0 Hz), 1.01 (s, 6H). $^{13}$C NMR $\delta$ 210.2 (d, $J$=3.8 Hz), 198.7, 170.3, 147.2 (d, $J$=3.8 Hz), 135.7 (d, $J$=8.6 Hz), 96.7, 94.8, 87.1, 74.3, 63.0 (d, $J$=6.7 Hz), 52.8, 51.3, 45.0, 33.1, 27.9, 26.3 (d, $J$=1.9 Hz), 20.8, 18.1 (d, $J$=1.9 Hz), 16.2 (d, $J$=6.2 Hz). DARTMS $m/z$ 423 ($M^+$+1, 100); DARTHRMS calcd for $C_{22}H_{32}O_6P$ 423.1937, found 423.1940. To a solution of the phosphonyl allene (16 mg, $4.0\times10^{-2}$ mmol) in MeOH (0.5 mL) was added $K_2CO_3$ (7 mg, 0.04 mmol). After stirring for 5 min, the mixture was quenched with water, extracted with AcOEt. The extract was washed with brine, dried, and concentrated to dryness. The residue was chromatographed with hexane/AcOEt (1:2) to afford **23** (9.5 mg, 62%) as a colorless oil. IR 3597, 3398, 2222, 1960, 1929, 1711, 1666, 1265, 1024 cm$^{-1}$. $^1$H NMR $\delta$ 5.11 (s, 1H), 5.07 (s, 1H), 4.18–4.08 (m, 6H), 2.53 (t, 2H, $J$=7.3 Hz), 2.46–2.45 (m, 2H), 2.35–2.31 (m, 2H), 2.26 (s, 2H), 1.32 (t, 6H, $J$=7.8 Hz), 1.02 (s, 6H). $^{13}$C NMR $\delta$ 210.2 (d, $J$=2.9 Hz), 198.9, 147.4 (d, $J$=3.8 Hz), 135.6 (d, $J$=8.6 Hz), 96.6, 94.7, 84.9, 79.6, 63.0 (d, $J$=6.7 Hz), 51.4, 50.9, 44.9, 33.0, 27.8, 26.0 (d, $J$=1.9 Hz), 17.8 (d, $J$=2.9 Hz), 16.1 (d, $J$=6.7 Hz). DARTMS $m/z$ 381 ($M^+$+1, 100); DARTHRMS calcd for $C_{20}H_{30}O_5P$ 381.1831, found 381.1829.

### 4.14. Diethyl 1-[5,5-dimethyl-3-oxo-2-(3-phenylsulfonylpenta-3,4-dienyl)cyclohex-1-enyl]propa-1,2-dienylphosphonate (24)

To a solution of **23** (22 mg, $6.0\times10^{-2}$ mmol) in THF (0.5 mL) were added $Et_3N$ (50 mL, 0.36 mmol) and PhSCl (50 mL, 0.36 mmol) in THF at −78 °C. After stirring for 6 h at the same temperature, the reaction was quenched with water, extracted with AcOEt. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was passed through a short pad of silica gel with hexane/AcOEt (1:5) to afford the crude sulfoxide. To a solution of the crude sulfoxide in $CH_2Cl_2$ (1 mL) was added $m$CPBA (21 mg, 0.12 mmol) at 0 °C. After stirring for 1 h at the same temperature, the reaction was quenched with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$, extracted with $CH_2Cl_2$. The extract was washed with water and brine, dried, and concentrated to dryness. The residue was chromatographed with $CH_2Cl_2$/AcOEt (2:1) to afford **24** (19 mg, 62%) as a yellow oil. IR 1963, 1934, 1668, 1620, 1308, 1265, 1145, 1024 cm$^{-1}$. $^1$H NMR $\delta$ 7.85–7.84 (m, 2H), 7.58 (t, 1H, $J$=7.6 Hz), 7.50 (m, 2H), 5.36 (t, 2H, $J$=3.4 Hz), 5.05 (s, 1H), 5.03 (s, 1H), 4.15–4.05 (m, 4H), 2.45–2.41 (m, 4H), 2.25–2.22 (m, 4H), 1.32 (t, 6H, $J$=7.0 Hz), 1.01 (s, 6H). $^{13}$C NMR 209.9, 207.7, 198.6, 147.5 (d, $J$=2.9 Hz), 140.2, 135.7 (d, $J$=10.1 Hz), 133.3, 129.0, 127.9, 113.2, 96.0, 94.7, 84.5, 62.9 (d, $J$=7.2 Hz), 51.3, 44.8, 33.1, 29.5, 27.8, 25.5 (d, $J$=2.9 Hz), 25.4, 16.2 (d, $J$=7.2 Hz). DARTMS $m/z$ 505 ($M^+$+1, 100); DARTHRMS calcd for $C_{26}H_{34}O_6PS$ 505.1814, found 505.1815.

### 4.15. 2-Diethoxyphosphinyl-14,14-dimethyl-8-phenylsulfonyltricyclo[9.4.0.0$^{3,7}$]pentadeca-1(11),2,6-triene-5,12-dione (25)

Compound **25** was brown crystals; mp 169–171 °C ($CH_2Cl_2$); IR 1708, 1670, 1323, 1310, 1263, 1238, 1153, 1024 cm$^{-1}$; $^1$H NMR 7.83–7.81 (m, 2H), 7.70–7.66 (t, 1H, $J$=7.3 Hz), 7.56–7.53 (m, 2H), 7.27 (s, 1H), 4.16–4.02 (m, 5H), 3.86 (dd, 1H, $J$=22.0, 2.7 Hz), 3.25 (dd, 1H, $J$=22.0, 3.2 Hz), 3.22 (dd, 1H, $J$=18.3, 4.1 Hz), 2.96–2.92 (m, 1H), 2.30 (d, 1H, $J$=15.6 Hz), 2.20–2.00 (m, 5H), 1.35 (t, 3H, $J$=6.9 Hz), 1.31 (t, 3H, $J$=6.9 Hz), 1.10 (s, 3H), 0.86 (s, 3H). $^{13}$C NMR $\delta$ 201.5, 196.8, 160.7 (d, $J$=28.9 Hz), 150.7 (d, $J$=7.2 Hz), 150.6 (d, $J$=11.6 Hz), 138.9, 137.3, 134.5, 134.0 (d, $J$=14.5 Hz), 129.4, 128.8, 127.8 (d, $J$=176.3 Hz), 63.3, 62.7 (t, $J$=4.3 Hz), 50.8, 44.0, 41.4 (d, $J$=4.3 Hz), 32.9, 29.8 (d, $J$=8.7 Hz), 27.2, 22.3, 16.4 (d, $J$=5.8 Hz), 16.3 (d, $J$=8.7 Hz), 14.1 (d, $J$=11.6 Hz); DARTMS $m/z$ 533 ($M^+$+1, 27); DARTHRMS calcd for $C_{27}H_{34}O_7PS$ 533.1763, found 533.1755. Regiochemistry of **25** was determined by HMQC and HMBC.

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