Regioselective Functionalization of the Methylene Group Adjacent to Cyclopropyl Sulfide *via* Mercury(II)-Mediated Regioselective Ring-Opening Reaction

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A regioselective bond-cleavage of the cyclopropyl sulfide (2) was performed with mercury(II) salt to supply the homoallyl anion synthon (3) bearing two reactive sites at the α and δ positions. The reaction of 3 with *n*-Bu_3SnH and I_2 gave α-functionalized products (8 and 9, respectively). On the other hand, recyclization of 3 into δ-functionalized cyclopropyl sulfides (2, 12, 13) was accomplished by treatment with several electrophiles (H^+, D^+, allyl iodide). Moreover, the synthesis of δ-oxygenated cyclopropyl sulfide (15) was achieved by the additive Pummerer reaction of the γ,δ-unsaturated γ-sulfinyl alkylmercury chloride (14) which was obtained by *m*-chloroperbenzoic acid oxidation of 3.

Key words cyclopropyl sulfide; ring-cleavage; electrophile-mediated cyclopropanation; cyclopropylcarbinyl functionalization; alkylmercury chloride; homoallyl anion synthon

For several decades, cyclopropyl compounds have received much attention because of their biological activity and synthetic utility as key intermediates for various kinds of natural products.[1] In particular, recently developed convenient methods for chiral cyclopropanes[2] enhance their versatility as not only chiral building blocks for asymmetric synthesis, but also chiral components of peptide mimics.[3] However, in spite of the synthetic diversity of the chiral cyclopropanes, few methods have been reported for functionalizing a methylene group adjacent to a cyclopropane ring, except for non-regioselective oxidation[4] and halogenation.[5]

In the course of our studies on the asymmetric synthesis of (+)-grandisol and (−)-solavetivone starting from a known compound (**1**)[6] *via* sulfur-atom-directed cyclopropylcarbinol rearrangement[7] and tandem cyclopropylcarbinyl radical rearrangement-cyclization reaction,[8] we encountered the serious problem of introducing an oxygen atom at the C5′-position of the cyclopropyl sulfide (**2**) (Chart 1). In order to achieve this, we planned a two-step sequence, that is temporary transformation of **2** into a reactive intermediate (**3**) *via* a regioselective 'a'-bond cleavage, followed by electrophilic ring-closure reaction, giving rise to the desired C5′-functionalized cyclopropanes (**4**). If the initial ring-opening reaction of **2** is performed with metal oxidants (MY_n), metal homoenolates (**3**: $X=MY_{n-1}$) bearing two reactive sites (α- and γ-position or α- and δ-position) would be produced depending on the substituent (Z) and reaction conditions (Chart 2).[9] Such an electrophilic ring-opening reaction of the cyclopropyl sulfides has been little developed in comparison with that of the cyclopropanol derivatives.[10] Herein we describe in detail a novel regioselective 'a'-bond cleavage of the cyclopropyl sulfide (**2**) with mercury(II) trifluoroacetate [$Hg(TFA)_2$][6] and a regioselective C5′-functionalization along with cyclopropanation of the resultant ring-opened product, which possesses two reactive sites at the α- and δ-position (**3**: X=HgCl).[11]

Results

Synthesis Initially, in order to examine the electrophilic ring-opening reaction, we synthesized **2** from the sulfoxide (**1**)[6] in a three-step sequence as described in Chart 3. Reduction of the sulfoxide (**2**) was accomplished by reaction with trifluoroacetic anhydride in the presence of sodium iodide in acetone to afford **5** in quantitative yield. Hydroboration-oxidation of **5** gave the primary alcohol (**6**), which was protected with acetic anhydride in pyridine to provide the desired acetate (**3**) in 77% overall yield from **1**.

Ring-Opening Reaction Electrophilic ring-cleavage of **2** with various types of Lewis acid and metal oxidant such

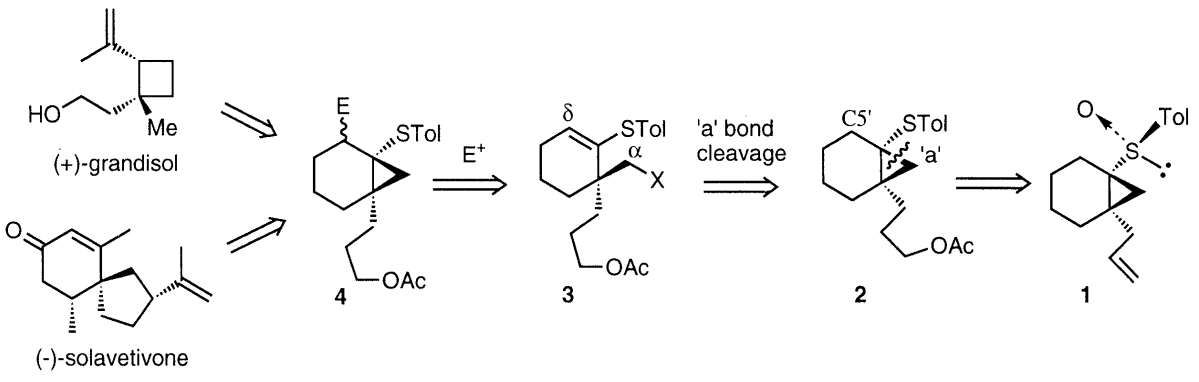

Chart 1

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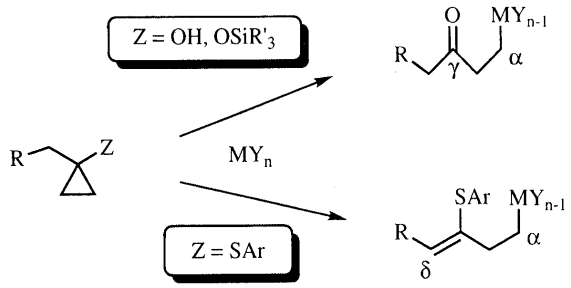


Chart 2

Table 1. $Hg(TFA)_2$-Mediated Ring-Opening of the Cyclopropyl Sulfide (**2**)

Entry	Reaction conditions[a]	Yield (%)	
		3	**7**
1	$Hg(TFA)_2$; sat. aq. NaCl	67	25
2	$Hg(TFA)_2$, NaOAc; sat. aq. NaCl	84	6
3	$Hg(TFA)_2$, $CaCO_3$; sat. aq. NaCl	66	34

a) All reactions were carried out in CH_2Cl_2 at room temperature.

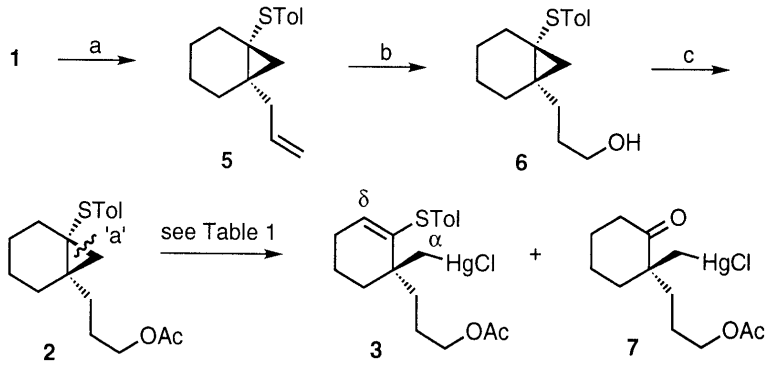


Chart 3: a) $(CF_3CO)_2O$, NaI, acetone, r.t. (100%); b) $BH_3 \cdot Me_2S$, THF, 0 °C; 3 M NaOH, 30% H_2O_2, r.t. (84%); c) Ac_2O, pyridine, r.t. (92%)

Chart 3

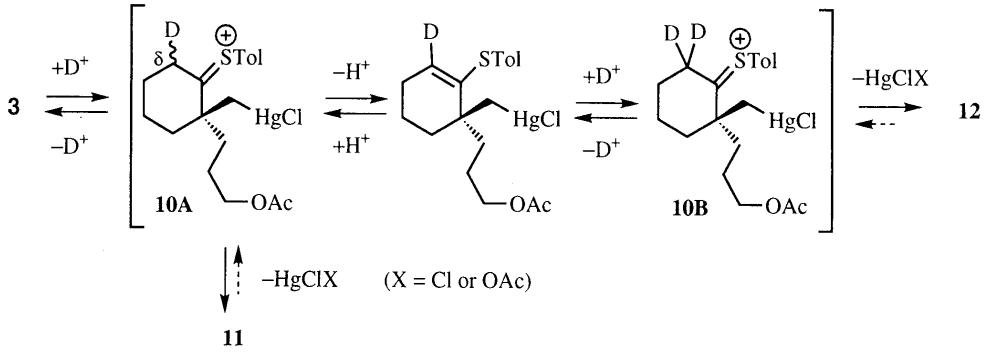
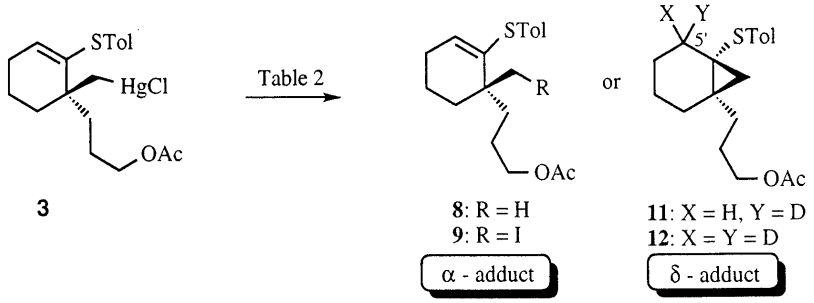


Chart 4

as $Zn(OTf)_2$, $Pd(OAc)_2$, BBr_3, and $SbCl_5$ were carried out, but only poor results were obtained. Finally, we found that mercury salts such as $Hg(OAc)_2$ and $Hg(TFA)_2$ gave the desired 'a'-bond cleaved product (**3**) effectively.[12] Although the reaction with the former salt required several days to consume the starting material, the reaction with the latter was completed within 12 h, giving rise to **3** in 67% yield together with the ketone (**7**) in 25% yield. Furthermore, addition of sodium acetate (NaOAc) to the reaction mixture suppressed the hydration of **3**, resulting in an improved yield of **3** (84%). Calcium carbonate ($CaCO_3$) was less effective than NaOAc (Table 1).

Electrophile-Mediated Cyclopropanation As we had succeeded in the stereoselective synthesis of **3**, we next examined its potential as a homoallyl anion synthon for developing electrophile-mediated recyclization of **3** (Table 2).[13] In a preliminary experiment with tri-*n*-butyltin hydride (*n*-Bu_3SnH)[14] or iodide (I_2), it was revealed that sole activation of the alkylmercury moiety of **3** led to formation of the α-substituted products (**8**,**9**) (entries 1—2). Therefore, we considered double activation methodology for the cyclopropanation, that is employing (i) electrophiles strong enough to react with the vinylic sulfide moiety of **3** and (ii) soft nucleophiles which can activate the C–Hg bond for the cyclization of the resulting δ-substituted thionium intermediate (**10A** and B) as shown in Chart 4. Some useful information emerged from experiments with several protic acids (entries 3—5). The cyclopropanation into **2** immediately occurred in 82% yield on treatment of **3** with concentrated HCl in CH_3CN at room temperature. Similarly, treatment of **3** with titanium tetrachloride ($TiCl_4$) in AcOH[15] afforded **2** in quantitative yield. On the other hand, treatment of **3** with *p*-toluenesulfonic acid monohydrate (*p*-TsOH·H_2O) in CH_2Cl_2 gave the hydrated product (**7**). To investigate the reaction mechanism in more detail, we undertook the following experiment on **2** and **3**. Treatment of **3** and **2** with a 1 M solution of $TiCl_4$ in deuterated acetic acid (AcOD) and with a mixture of mercuric chloride ($HgCl_2$) and $TiCl_4$ in AcOD furnished the dideuterated product

Table 2. α- and δ-Regioselective Functionalization of **2** and **3** in the Presence of Various Additives



Entry	Substrate	Reaction condition	Product (Yield (%))	Deuterated ratio[a)]
1	**3**	Bu_3SnH, CH_2Cl_2, −40 °C→0 °C	**8** (43)	
2		I_2, Bu_4NI, CH_2Cl_2, 0 °C	**9** (100)	
3		*c*.HCl, CH_3CN, r.t.	**2** (82)	
4		$TiCl_4$, HOAc, r.t.	**2** (99)	
5		*p*-TsOH·H_2O, CH_2Cl_2, r.t.	**7** (44)	
6		$TiCl_4$, DOAc, r.t.	**11** and **12** (98)	192%
7	**2**	$TiCl_4$, $HgCl_2$, DOAc, r.t., 36 h	**11** and **12** (97)	122%
8		$TiCl_4$, DOAc, r.t., 36 h	**2** (95)	Not detected
9		$HgCl_2$, DOAc, r.t., 36 h	**2** (100)	Not detected

a) The ratios were determined from the 500 MHz ^{1}H-NMR spectra. r.t. = room temperature.

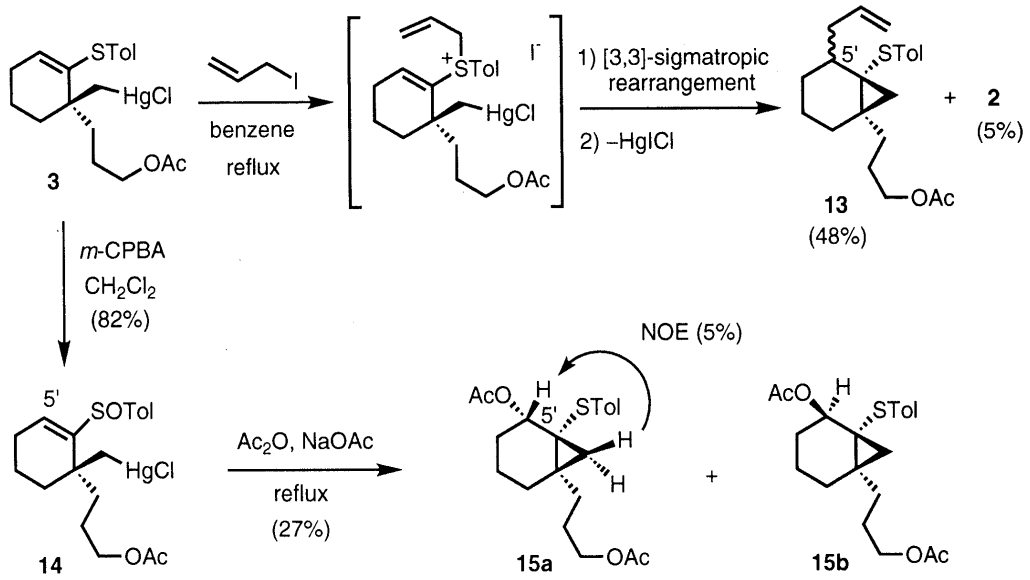


Chart 5

(**12**) along with a small amount of monodeuterated product (**11**) (entries 6 and 7), whereas neither **11** nor **12** was obtained on treatment of **2** with $HgCl_2$ in AcOD and $TiCl_4$ in AcOD (entries 8 and 9). These results suggest that not only the formation of the thionium intermediate, but also the presence of the chloride anion would be essential for the cyclization of **3** into **2** (Chart 4).

The structures of **11** and **12** were deduced from the mass and 500 MHz ^{1}H-NMR spectra. In the mass spectrum, the parent peak of the product in entry 6 shifted from M^+ to $M^+ + 2$ in comparison with **2**. The signals of the two 5′-protons, observed at δ 1.96—2.16 ppm in the ^{1}H-NMR spectrum of **2**, could not be seen in that of the product in entry 6. The isolation of **11** and **12** possessing deuterium at C5′ strongly suggests the involvement of a reactive species such as **10A** and **10B**.

Based on these findings, we attempted a tandem allylation-[3,3]sigmatropic rearrangement[16] reaction of **3** and an additive Pummerer reaction[17] of the sulfoxide **14** for introducing other functionalities such as allyl and acetoxyl groups at the δ-position (Chart 5). In the former reaction, treatment of **3** with allyl iodide in refluxing benzene for 4 h gave the C5′-allylated cyclopropane (**13**) in 48% yield as an inseparable epimeric mixture with 5% contamination of **2**. The ratio of C5′-diastereoisomers of **13** was estimated to be 10 : 1 from the 500 MHz ^{1}H-NMR spectrum, though the stereochemistry could not be determined.

For the latter reaction, the vinylic sulfoxides (**14**) were prepared by *m*-chloroperbenzoic acid (*m*-CPBA) oxidation of **3** as a 9 : 11 diastereoisomeric mixture in 82% yield. Unfortunately, several attempts at the Pummerer

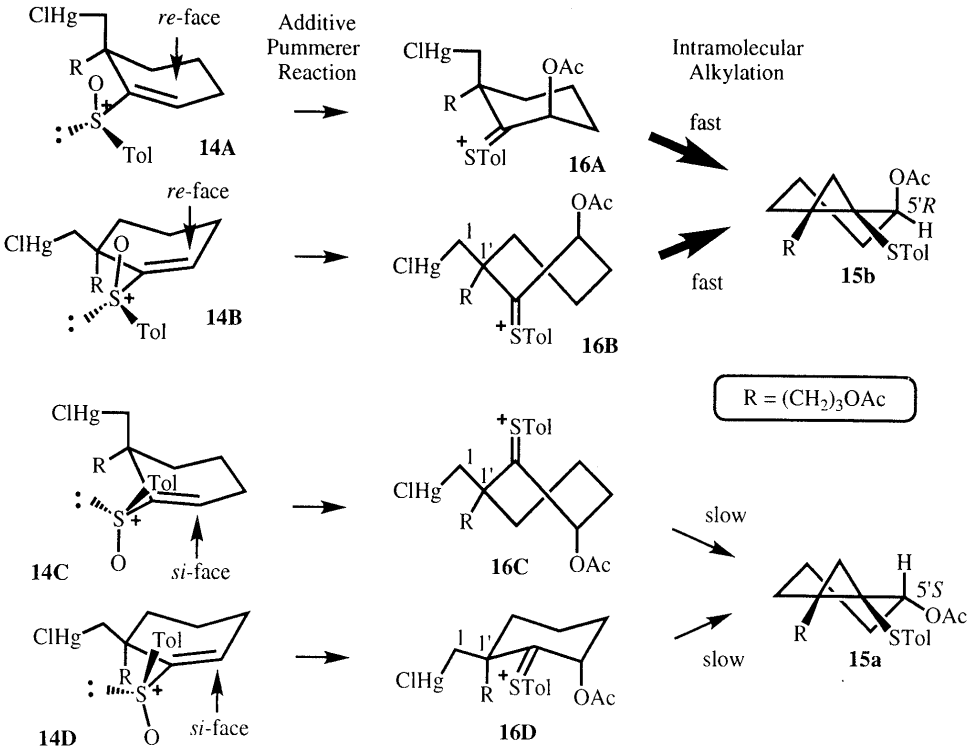


Chart 6

reaction mostly resulted in deoxygenation of the sulfoxide, yielding the sulfide (**2**). We finally found that the desired C5′-acetoxy cyclopropyl compound (**15**) could be obtained under restricted conditions in the absence of halide and strong acid. Exposure of **14** to acetic anhydride in the presence of 1.2 eq of NaOAc at 80 °C gave rise to a mixture of **15a** and **15b** in 41% yield based on the consumed starting material (Chart 4).[18] The ratio of **15a** and **15b** was revealed to be 13 : 87 by means of HPLC analysis and the configurations of these compounds were determined from the observation of a distinct nuclear Overhauser effect (NOE) enhancement (4%) between the C5′-H and the C7′-pro*R*-H of **15a**.

The stereoselective formation of **15b** can be explained as follows (Chart 6). The predominant conformations of the two diastereomeric vinylic sulfoxides (**14**) are considered to be **14A**/**14B** and **14C**/**14D**, respectively, wherein the S–O bonds are oriented parallel to the *p*-orbitals of the C=C double bonds and the lone pairs of the sulfur atoms occupy less-hindered sites. Therefore, taking into consideration the molecular orbital theory that *S*N2′ reactions proceed *via syn* attack to the leaving groups,[19] *re*-face attack should prevail in **14A** and **14B**, giving rise to the chair intermediate (**16A**) and the twist-boat intermediate (**16B**), respectively. Both intermediates would afford the *β*-acetoxy cyclopropane (**15b**) *via* intramolecular nucleophilic addition of the alkylmercury chloride moiety. On the other hand, in **16C** and **16D**, which are obtained from *si*-face attacks of the acetoxy anion in **14C** and **14D**, orbital interaction of the C–Hg bond with the C=S$^+$ double bond would be very unfavorable for the cyclization and, before cyclization into **15a**, conformational flipping should occur, placing the mercuriomethyl group in a quasi-axial orientation. Therefore **15a** would not be obtained mainly due to the intervention of side-reactions.

As mentioned above, we succeeded in the regioselective functionalization of the methylene group adjacent to the cyclopropyl sulfide (**2**) *via* the cyclopropyl ring-opening product, *γ*,*δ*-unsaturated *γ*-sulfenyl alkylmercury chloride (**3**). In every case, formation of the sulfonium intermediates and promotion of the C–Hg bond by chloride, iodide, and acetoxyl groups hold the key to efficient cyclopropanation. We are now elaborating **15a** into (+)-grandisol and (−)-solavetivone.

Experimental

Melting points are uncorrected. Optical rotations were measured using a JASCO DIP-360 digital polarimeter. IR spectra were measured with a Hitachi 260-10 IR spectrometer as a $CHCl_3$ solution of the sample, or with a Horiba FT-210 IR spectrometer as a neat sample on KBr powder by the diffuse reflection measurement method. ^{1}H-NMR spectra were measured with a Varian VXR-200 spectrometer (200 MHz), a Hitachi 250RT spectrometer (250 MHz), a JNM-EX270 spectrometer (270 MHz) or a JEOL JNM-GX500 spectrometer (500 MHz). ^{13}C-NMR spectra were measured with a JEOL JNM-EX270 spectrometer (67.8 MHz). All signals are expressed as ppm downfied from tetramethylsilane used as an internal standard (δ value). The following abbreviations are used: singlet (s), doublet (d), triplet (t), multiplet (m), broad (br). Mass spectra were taken with a Shimadzu QP-1000 mass spectrometer and a JEOL JMS-D300 mass spectrometer. HPLC analyses were performed using a Waters 6000A pump, a Waters *μ*-Porasil (3.9 mm × 30 cm) column, and a Soma S-310 UV detector (at 254 nm). Unless otherwise noted, all reactions were performed in anhydrous solvents. Merck Kieselgel 60 was used as an adsorbent for column chromatography. All extracts were dried over anhydrous $MgSO_4$.

3-[(1*S*,6*R*)-6-(*p*-Tolylthio)bicyclo[4.1.0]hept-1-yl]prop-1-ene (5) Trifluoroacetic anhydride (1.42 ml, 10.0 mmol) was added to a mixture of the sulfoxide (**1**) (1.00 g, 3.65 mmol), NaI (1.65 g, 11.0 mmol), and acetone (10 ml) at 0 °C under a nitrogen atmosphere. The mixture was stirred for 5 min at the same temperature, then the reaction was quenched with sodium thiosulfate solution. After removal of acetone, the resulting mixture was extracted with ether. The ethereal layer was washed with water and brine, dried, then concentrated *in vacuo*. The residue was purified by column chromatography (hexane) to give the sulfide (**5**)

(940 mg, 100%) as a colorless oil. $[\alpha]_D^{25}$ +65.6° (c=1.11, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.76 (1H, d, J=5.4 Hz, C7′-H_a), 0.86 (1H, d, J=5.4 Hz, C7′-H_b), 1.14—2.25 (8H, m), 2.31 (3H, s, Ar-CH_3), 2.40 (1H, dd, J=14.6, 6.4 Hz, C3-H_a), 2.55 (1H, dd, J=14.6, 6.4 Hz, C3-H_b), 4.98—5.14 (2H, m, C1-H), 5.73—5.96 (1H, m, C2-H), 7.09 (2H, d, J=8.2 Hz, Ar-H), 7.19 (2H, d, J=8.2 Hz, Ar-H). IR ($CHCl_3$): 2935, 2860, 1642 (C=C), 1498 (aromatic), 1458, 1096, 918, 804 cm^{-1}. MS m/z (%): 258 (M^+, 9), 217 (100), 93 (32). *Anal.* Calcd for $C_{17}H_{22}S$: C, 79.01; H, 8.58; S, 12.41. Found: C, 79.08; H, 8.49; S, 12.33.

3-[(1*S*,6*R*)-6-(*p*-Tolylthio)bicyclo[4.1.0]hept-1-yl]propanol (6) Borane–dimethylsulfide complex (2.24 ml, 10 M solution) was added to a solution of the olefin (**5**) (2.89 g, 2.87 mmol) in THF (10 ml) at 0 °C under a nitrogen atmosphere. After being stirred at the same temperature for 1 h, the mixture was treated successively with water, 3 N NaOH solution (5.39 ml), and 30% H_2O_2 solution (5.88 ml), and then stirring was continued for an additional 1.5 h at room temperature. The reaction mixture was diluted with water and extracted with AcOEt. The extract was washed with saturated sodium thiosulfate solution, water, brine, dried, and concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 4 : 1) to give the alcohol (**6**) (2.59 g, 84%) as colorless crystals. mp 47—48 °C (not recrystallized). $[\alpha]_D^{24}$ +45.7° (c=1.11, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.68 (1H, d, J=5.1 Hz, C7′-H_a), 0.83 (1H, d, J=5.1 Hz, C7′-H_b), 1.18—1.56 (4H, m, C3′-H, C4′-H), 1.51 (1H, br s, OH), 1.57—1.94 (6H, m, C2-H, C3-H, C2′-H), 2.03 (1H, ddd, J=13.7, 7.7, 6.0 Hz, C5′-H_a), 2.11 (1H, ddd, J=13.7, 6.8, 6.8 Hz, C5′-H_b), 2.30 (3H, s, Ar-CH_3), 3.57—3.67 (2H, m, C1-H), 7.08 (2H, d, J=8.6 Hz, Ar-H), 7.17 (2H, d, J=8.6 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 20.90 (Ar-CH_3), 21.28 (C3′), 23.18 (C4′), 23.31 (C7′), 28.59 (C1′ or C6′), 29.54 (C2′), 29.96 (C2), 31.50 (C1′ or C6′), 32.89 (C5′), 33.48 (C3), 63.11 (C1), 127.67 (Ar-CH), 129.49 (Ar-CH), 133.41 (Ar-quaternary carbon), 134.75 (Ar-quaternary carbon). IR (KBr): 3340 (OH), 2941, 2856, 1493 (aromatic), 1452, 1059, 802, 492 cm^{-1}. MS m/z (%): 276 (M^+, 35), 217 (80), 124 (100). *Anal.* Calcd for $C_{17}H_{24}OS$: C, 73.86; H, 8.75; S, 11.60. Found: C, 73.77; H, 8.75; S, 11.53.

3-[(1*S*,6*R*)-6-(*p*-Tolylthio)bicyclo[4.1.0]hept-1-yl]propyl Acetate (2) Acetic anhydride (1.76 ml, 18.7 mmol) was added to a solution of the alcohol (**6**) (2.58 g, 9.35 mmol) in pyridine (10 ml) at 0 °C under a nitrogen atmosphere, and the mixture was stirred at room temperature for 6 h. After removal of pyridine, water was added to the residue and the resulting mixture was extracted with ether. The extract was washed with saturated $CuSO_4$ solution, water, and brine, then the organic phase was dried and concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 10 : 1) to give the acetate (**2**) (2.74 g, 92%) as colorless crystals. mp 65—66 °C (not recrystallized). $[\alpha]_D^{27}$ +49.6° (c=1.01, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.68 (1H, d, J=5.1 Hz, C7′-H_a), 0.84 (1H, d, J=5.1 Hz, C7′-H_b), 1.21—1.48 (4H, m, C3′-H, C4′-H), 1.64—1.92 (6H, m, C2-H, C3-H, C2′-H), 2.02 (3H, s, CH_3CO), 2.05 (1H, ddd, J=13.7, 7.7, 6.0 Hz, C5′-H_a), 2.11 (1H, ddd, J=13.7, 6.8, 6.8 Hz, C5′-H_b), 2.31 (3H, s, Ar-CH_3), 3.99—4.09 (2H, m, C1-H), 7.09 (2H, d, J=8.6 Hz, Ar-H), 7.18 (2H, d, J=8.6 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 20.90 (Ar-CH_3), 20.97 (CH_3CO), 21.26 (C3′), 23.11 (C4′), 23.34 (C7′), 25.91 (C2), 28.38 (C1′ or C6′), 29.47 (C2′), 31.47 (C1′ or C6′), 32.89 (C5′), 33.59 (C3), 64.62 (C1), 127.78 (Ar-CH), 129.49 (Ar-CH), 133.33 (Ar-quaternary carbon), 134.84 (Ar-quaternary carbon), 171.10 (CO). IR (KBr): 2931, 2856, 1740 (CO), 1599 (aromatic), 1493 (aromatic), 1452, 1363, 1242, 1038, 804 cm^{-1}. MS m/z (%): 318 (M^+, 46), 217 (100), 135 (75). *Anal.* Calcd for $C_{19}H_{26}O_2S$: C, 71.66; H, 8.23; S, 10.07. Found: C, 71.39; H, 8.09; S, 10.02.

(1*R*)-[1-(3-Acetoxypropyl)-2-(*p*-tolylthio)cyclohex-2-en-1-yl]methylmercury Chloride (3) and (1*R*)-[1-(3-Acetoxypropyl)-2-oxocyclohex-1-yl]methylmercury Chloride (7) A mixture of the cyclopropyl sulfide (**2**) (28.0 mg, 0.0881 mmol), NaOAc (7.7 mg, 0.094 mmol), $Hg(OCOCF_3)_2$ (60.0 mg, 0.141 mmol), and CH_2Cl_2 (1.0 ml) was stirred at room temperature for 12 h under a nitrogen atmosphere. The reaction was quenched with water, and the resulting mixture was extracted with CH_2Cl_2. The extract was shaken with brine for 15 min, then the organic phase was dried and concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 1 : 2) to give the vinylic sulfide (**3**) (41 mg, 84%) and the ketone (**7**) (2.5 mg, 6%). **3**: colorless oil. $[\alpha]_D^{27}$ −0.3° (c=0.970, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.44—1.76 (7H, m, C5′-H, C6′-H_a, C1″-H, C2″-H), 1.80—1.90 (1H, m, C6′-H_b), 1.99 (1H, d, J=12.0 Hz, C1-H_a), 2.04—2.16 (2H, m, C4′-H), 2.06 (3H, s, CH_3CO), 2.07 (1H, d, J=12.0 Hz, C1-H_b), 2.33 (3H, s, Ar-CH_3), 3.98 (2H, t, J=6.0 Hz, C3″-H), 5.72 (1H, t, J=3.8 Hz, C3′-H), 7.14 (2H, d, J=8.1 Hz, Ar-H), 7.31 (2H, d, J=8.1 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 18.84 (C5′), 20.92 (CH_3CO), 21.01 (Ar-CH_3), 23.45 (C2″), 27.12 (C4′), 36.81 (C6′), 38.84 (C1″), 43.36 (C1), 43.60 (C1′), 64.41 (C3″), 130.08 (Ar-CH), 130.38 (quaternary carbon), 131.63 (Ar-CH), 133.71 (C3′), 137.62 (quaternary carbon), 139.82 (quaternary carbon), 170.97 (CO). IR ($CHCl_3$): 2940, 1734 (CO), 1496 (aromatic), 1250, 1038 cm^{-1}. MS m/z (%): 555 (M^+, 7), 317 (63), 133 (100). *Anal.* Calcd for $C_{19}H_{25}ClHgO_2S$: C, 41.23; H, 4.55. Found: C, 41.51; H, 4.59. **7**: colorless oil. $[\alpha]_D^{28}$ +29.5° (c=0.950, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.12—2.16 (11H, m), 1.93 (1H, d, J=10.0 Hz, CH_a-Hg), 2.06 (3H, s, CH_3CO), 2.20—2.63 (2H, m, $-CH_2CO$), 4.05 (2H, t, J=5.3 Hz, CH_2OAc). IR ($CHCl_3$): 2940, 1734 (CO), 1688 (CO), 1368, 1240, 1044 cm^{-1}. MS m/z (%): 446 (M^+, 0.4), 211 ($M^+ - HgCl$, 17), 151 (100).

3-[(1*S*)-1-Methyl-2-(*p*-tolylthio)cyclohex-2-en-1-yl]propyl Acetate (8) (Table 2, Entry 1) A solution of n-Bu_3SnH (59.1 mg, 0.203 mmol) in CH_2Cl_2 (3.4 ml) was added to a solution of **3** (93.8 mg, 0.169 mmol) in CH_2Cl_2 (3.4 ml) at −40 °C, and then the reaction mixture was allowed to warm to room temperature over 5 min. The reaction was quenched with water and the mixture was extracted with ether. The extract was washed with brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : ether = 15 : 1) to give the hydrogenated product (**8**) (23.2 mg, 43%) as a colorless oil. $[\alpha]_D^{24}$ +6.83° (c=1.21, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.0—2.4 (10H, m), 1.14 (3H, s, CH_3), 2.05 (3H, s, CH_3CO), 2.36 (3H, s, Ar-CH_3), 3.95—4.12 (2H, m, C_1-H), 5.54 (1H, t, J=4.0 Hz, C3′-H), 7.10 (2H, d, J=8.2 Hz, Ar-H), 7.29 (2H, d, J=8.2, Ar-H). IR ($CHCl_3$): 2940, 1736 (CO), 1504 (aromatic), 1466, 1376, 1260, 1046 cm^{-1}. MS m/z (%): 318 (M^+, 64), 218 (47), 135 (100). High MS Calcd for $C_{19}H_{26}O_2S$: 318.1653. Found: 318.1658.

3-[(1*S*)-1-Iodomethyl-2-(*p*-tolylthio)cyclohex-2-en-1-yl]propyl Acetate (9) (Table 2, Entry 2) n-Bu_4NI (13.3 mg, 0.0360 mmol) was added to a solution of **3** (20.0 mg, 0.0360 mmol) in CH_2Cl_2 (1 ml) at room temperature. The mixture was stirred for 5 min, then I_2 (9.1 mg, 0.0359 mmol) was added at the same temperature and stirring was continued for 20 min. The reaction was quenched with sodium thiosulfate solution and the resulting mixture was extracted with ether. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 10 : 1) to give the iodide (**9**) (16.0 mg, 100%) as a colorless oil. $[\alpha]_D^{31}$ +26.6° (c=0.725, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 1.2—2.2 (10H, m), 2.06 (3H, s, CH_3CO), 2.34 (3H, s, Ar-CH_3), 3.52 (2H, s, CH_2I), 3.88—4.20 (2H, m, C1-H), 5.66 (1H, t, J=4.0 Hz, C3′-H), 7.12 (2H, d, J=8.0 Hz, Ar-H), 7.31 (2H, d, J=8.0 Hz, Ar-H). IR ($CHCl_3$): 2945, 1732 (CO), 1496 (aromatic), 1452, 1370, 1254, 1044 cm^{-1}. MS m/z (%): 444 (M^+, 100), 443 (60), 133 (59), 91 (44). High MS Calcd for $C_{19}H_{25}IO_2S$: 444.0619. Found: 444.0629.

Reaction of 3 with 35% HCl (Table 2, Entry 3) A mixture of **3** (50.0 mg, 0.0901 mmol), 35% HCl (0.1 ml), and CH_3CN (0.9 ml) was stirred for 24 h at room temperature. The reaction was quenched with saturated $NaHCO_3$ solution and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 10 : 1→4 : 1) to give the cyclopropyl sulfide (**2**) (23.5 mg, 82%).

Reaction of 3 with $TiCl_4$ in AcOH (Table 2, Entry 4) $TiCl_4$ (2.4 μl, 22 μmol) was added to a solution of **3** (3.0 mg, 5.4 mmol) in AcOH (0.04 ml) at room temperature. The mixture was stirred for 5 min, then the reaction was quenched with saturated $NaHCO_3$ solution and the whole was extracted with ether. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 10 : 1→4 : 1) to give the cyclopropylsulfide (**2**) (1.7 mg, 99%).

Reaction of 3 with *p*-TsOH · H_2O (Table 2, Entry 5) A mixture of p-TsOH · H_2O (17.1 mg, 0.0901 mmol), **3** (50.0 mg, 0.0901 mmol), and CH_2Cl_2 (2.0 ml) was stirred for 24 h. The reaction was quenched with saturated $NaHCO_3$ solution, and the mixture was extracted with AcOEt. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 4 : 1) to give the ketone (**7**) (17.0 mg, 44%).

3-[(1*S*,6*S*)-6-(*p*-Tolylthio)(5,5-$^2H_2$)bicyclo[4.1.0]hept-1-yl]propyl Acetate (12) (Table 2, Entry 6) A 1 M solution of $TiCl_4$ in AcOD (0.072 ml) was added to **3** (20.0 mg, 0.0901 mmol) at room temperature under a nitrogen atmosphere, and the resulting mixture was stirred for 5 min. The reaction was quenched with saturated $NaHCO_3$ solution, and the

mixture was extracted with ether. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 10 : 1) to give the cyclopropyl sulfide (**12**) (11.3 mg, 98%) as a colorless oil. $[\alpha]_D^{27}$ +43.6° (c = 1.34, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.68 (1H, d, J = 4.9 Hz, C7′-H_a), 0.84 (1H, d, J = 4.9 Hz, C7′-H_b), 1.20—1.50 (4H, m, C3′-H, C4′-H), 1.64—1.92 (6H, m, C2-H, C3-H, C2′-H), 2.03 (3H, s, CH_3CO), 2.31 (3H, s, Ar-CH_3), 3.99—4.11 (2H, m, C1-H), 7.09 (2H, d, J = 8.6 Hz, Ar-H), 7.18 (2H, d, J = 8.6 Hz, Ar-H). IR ($CHCl_3$): 2935, 2865, 1738 (CO), 1496 (aromatic), 1454, 1364, 1242, 1038 cm^{-1}. MS m/z (%): 320 (M^+, 48), 219 (100), 137 (88). High MS Calcd for $C_{19}H_{24}{}^2H_2O_2S$: 320.1777. Found: 320.1772.

Reaction of 2 with $HgCl_2$ and $TiCl_4$ in AcOD (Table 2, Entry 7) A 1 M solution of $TiCl_4$ in AcOD (0.14 ml) was added to a mixture of **2** (22.0 mg, 0.0692 mmol) and $HgCl_2$ (18.7 mg, 0.0689 mmol) at room temperature under a nitrogen atmosphere, and the resulting mixture was stirred at the same temperature for 36 h. The reaction was quenched with saturated $NaHCO_3$ solution, and the resulting mixture was extracted with ether. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 10 : 1) to give a mixture of **2**, **11**, and **12** (21.3 mg, 97%).

Reaction of 2 with $TiCl_4$ in AcOD (Table 2, Entry 8) A 1 M solution of $TiCl_4$ in AcOD (0.16 ml) was added to **2** (10.0 mg, 0.0692 mmol) at room temperature under a nitrogen atmosphere, and the resulting mixture was stirred at the same temperature for 36 h to give the recovered starting material in 95% yield.

Reaction of 2 with $HgCl_2$ in AcOD (Table 2, Entry 9) Reaction of **2** (20.0 mg, 0.0692 mmol) with $HgCl_2$ (25.8 mg, 0.0950 mmol), and AcOD (0.5 ml) at room temperature for 36 h under a nitrogen atmosphere gave only the starting material (**2**) (20.0 mg, 100%).

3-[(1*S*,6*S*)-5-Allyl-6-(*p*-tolylthio)bicyclo[4.1.0]hept-1-yl]propyl Acetate (13) A mixture of allyl iodide (0.400 ml, 4.37 ml), **3** (20.0 mg, 0.432 mmol), and benzene (5.0 ml) was refluxed for 2 h under a nitrogen atmosphere. Additional allyl iodide (0.400 ml, 4.37 ml) was added, and the whole was refluxed for 1 h, then concentrated *in vacuo*. The residue thus obtained was purified by column chromatography (hexane : AcOEt = 10 : 1) to give a mixture of **13** and **2** [81.5 mg (**13**: 48%, the diastereoisomeric ratio = 10 : 1) and (**12**: 5%)]. MS m/z (%): 359 (M^+ + 1, 20), 175 (100), 133 (80). ^{1}H-NMR ($CDCl_3$) δ: 0.46 (10/11 × 1H, d, J = 5.1 Hz), 0.49 (1/11 × 1H, d, J = 6.0 Hz), 0.75 (10/11 × 1H, d, J = 5.1 Hz), 2.01 (3H, s, $COCH_3$), 2.30 (3H, s, Ar-CH_3), 2.69 (10/11 × 1H, m, –C$\underline{H}_a$H$_b$–CH = CH_2), 3.40 (1/11 × 1H, br d, J = 6.0 Hz, –$CH_a\underline{H}_b$–CH = CH_2), 3.96—4.08 (2H, m, –C$\underline{H}_2$OAc), 4.89—5.00 (10/11 × 2H, m, –CH = C$\underline{H}_2$), 5.00—5.08 (1/11 × 2H, m, –CH = C$\underline{H}_2$), 5.62—5.76 (10/11 × 1H, m, –C$\underline{H}$ = CH_2), 5.90—6.04 (1/11 × 1H, m, –C$\underline{H}$ = CH_2), 7.08 (2H, d, J = 8.6 Hz), 7.14 (10/11 × 2H, d, J = 8.6 Hz). δ: 18.65 (C7′), 19.61 (C3'), 20.94 (Ar-CH_3), 21.01 ($COCH_3$), 25.97 (C2), 26.99 (C4′), 29.18 (quaternary carbon), 30.39 (C2′), 33.69 (C3), 37.25 (C5′), 37.36 (quaternary carbon), 38.31 (–$\underline{C}H_2$–CH = CH_2), 64.66 (C1), 115.78 (–CH = $\underline{C}H_2$), 127.39 (Ar-CH), 129.54 (Ar-CH), 133.24 (quaternary carbon), 134.74 (quaternary carbon), 137.70 (–$\underline{C}$H = CH_2), 171.14 (CO).

(1*R*)-1-(3-Acetoxypropyl)-2-(*p*-tolylsulfinyl)cyclohex-2-en-1-ylmethylmercury Chloride (14) *m*-CPBA (205 mg, 1.19 mmol) was added to a solution of the vinylic sulfide (**3**) (434 mg, 0.782 mmol) in CH_2Cl_2 (5.0 ml) at 0 °C. The mixture was stirred for 10 min at the same temperature, then the reaction was quenched with saturated $NaHCO_3$ solution, and the resulting mixture was extracted with CH_2Cl_2. The extract was washed with water and brine, dried, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 2 : 1) to give the sulfoxide (**14**) (366 mg, 82%, diastereoisomer ratio concerning sulfur atom = 11 : 9) as a colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.3—2.6 (12H, m), 2.05 (9/20 × 3H, s, CH_3CO), 2.07 (11/20 × 3H, s, CH_3CO), 2.43 (3H, s, Ar-CH_3), 3.82—3.93 (9/20 × 2H, m, CH_2OAc), 3.99 (11/20 × 2H, t, J = 6.2 Hz, CH_2OAc), 6.28 (11/20 × 1H, t, J = 3.8 Hz, C3′-H), 6.84 (9/20 × 1H, t, J = 3.4 Hz, C3′-H), 7.31 (9/20 × 2H, d, J = 8.2 Hz, Ar-H), 7.33 (11/20 × 2H, d, J = 8.2 Hz, Ar-H), 7.51 (11/20 × 2H, d, J = 8.2 Hz, Ar-H), 7.54 (11/20 × 2H, d, J = 8.2 Hz, Ar-H). IR ($CHCl_3$): 2990, 2940, 1728 (CO), 1492 (aromatic), 1428, 1362, 1240, 1034 (sulfoxide), 906 cm^{-1}. MS m/z (%): 569 (M^+, 0.9), 333 (100), 133 (78). High MS Calcd for $C_{19}H_{25}{}^{35}Cl^{202}HgO_3S$: 570.0917. Found: 570.0917.

3-[(1*S*,5*S*,6*R*)-5-Acetoxy-6-(*p*-tolylthio)bicyclo[4.1.0]hept-1-yl]propyl Acetate (15a) and 3-[(1*S*,5*S*,6*R*)-5-Acetoxy-6-(*p*-tolylthio)bicyclo[4.1.0]-hept-1-yl]propyl Acetate (15b) A mixture of the sulfoxide (**14**) (50.6 mg, 0.0886 mmol), NaOAc (8.8 mg, 0.107 mmol), and acetic anhydride (2.0 ml) was refluxed for 24 h under a nitrogen atmosphere, then concentrated *in vacuo*. The residue was diluted with AcOEt, washed with saturated $NaHCO_3$ solution, water, and brine, and then concentrated *in vacuo*. The residue was purified by column chromatography (hexane : AcOEt = 10 : 1) to give a mixture of sulfoxides (**15a** and **15b**) (9.1 mg, 27%) and starting material (**14**) (17.2 mg). The mixture of the sulfoxides (**15a** and **15b**) was purified by HPLC (mobile phase; hexane : AcOEt = 10 : 1, flow rate; 1.5 ml/min, t_R; 11.2 min (**15a**) and 12.0 min (**15b**), ratio; **15a** : **15b** = 13 : 87). **15a**: colorless oil. $[\alpha]_D^{32}$ −31° (c = 0.21, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.80 (1H, d, J = 6.0 Hz, C7′-Ha), 0.97 (1H, d, J = 6.0 Hz, C7′-H_b), 1.20—2.00 (12H, m), 1.97 (3H, s, CH_3CO), 2.05 (3H, s, CH_3CO), 2.31 (3H, s, Ar-CH_3), 5.43 (1H, t, J = 3.4 Hz, C5′-H), 7.08 (2H, d, J = 7.7 Hz, Ar-H), 7.25 (2H, d, J = 7.7 Hz, Ar-H). IR (KBr): 2942, 1738 (CO), 1492, 1450, 1369, 1242, 1039, 808 cm^{-1}. MS m/z (%): 377 (M^+ + 1, 4), 316 (92), 133 (100). **15b**: colorless oil. $[\alpha]_D^{28}$ −40° (c = 0.21, $CHCl_3$). ^{1}H-NMR ($CDCl_3$) δ: 0.70 (1H, d, J = 6.0 Hz, C7′-H_a), 1.24 (1H, d, J = 6.0 Hz, C7′-H_b), 1.28—1.45 (3H, m, C3′-H, C4′-H_a), 1.64—1.95 (7H, m, C2-H, C3-H, C2′-H, C4′-H_b), 1.99 (3H, s, CH_3CO), 2.03 (3H, s, CH_3CO), 2.31 (3H, s, Ar-CH_3), 4.00—4.12 (2H, m, C1-H), 5.39 (1H, t, J = 6.0 Hz, C5′-H), 7.08 (2H, d, J = 8.6 Hz, Ar-H), 7.18 (2H, d, J = 8.6 Hz, Ar-H). ^{13}C-NMR ($CDCl_3$) δ: 18.24 (C3′), 20.52 (C7′), 20.90 (Ar-CH_3 and CH_3CO), 21.22 (CH_3CO), 25.97 (C2), 28.97 (C4′), 29.04 (C2′), 31.43 (C1′ or C6′), 33.35 (C3), 35.96 (C1′ or C6′), 64.39 (C1), 74.34 (C5′), 128.90 (Ar-CH), 129.56 (Ar-CH), 132.17 (Ar-quaternary carbon), 135.69 (Ar-quaternary carbon), 170.30 (CO), 171.00 (CO). IR ($CHCl_3$): 2940, 1728 (CO), 1604 (aromatic), 1494 (aromatic), 1394, 1246, 804 cm^{-1}. MS m/z (%): 376 (M^+, 12), 316 (100), 133 (56). High MS Calcd for $C_{21}H_{28}O_4S$: 376.1706. Found: 376.1706.

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