Synthesis of 1-Hydroxybicyclo[3.2.1]oct-3-en-2-ones by Acyloin Rearrangement of 1-Methoxy- or 1-*tert*-Butyldimethylsilyloxy-bicyclo[2.2.2]oct-5-en-2-ones

Sadamu KATAYAMA,*[,a] Hajime HIRAMATSU,[b] Keiichi AOE,[b] and Masashige YAMAUCHI*[,a]

Faculty of Pharmaceutical Sciences, Josai University,[a] Keyakidai, Sakado, Saitama 350-02 and Analytical Research Laboratory, Tanabe Seiyaku Co., Ltd.,[b] Kashima, Yodogawaku, Osaka 532, Japan.
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1-Hydroxy- or 1,8-dihydroxy-bicyclo[3.2.1]oct-3-en-2-ones were obtained from 1-methoxy- or 1-*tert*-butyldimethylsilyloxy-bicyclo[2.2.2]oct-5-en-2-ones *via* successive processes involving demethylation or desilylation and acyloin rearrangement by reaction with acids or tetra-*n*-butylammonium fluoride (TBAF).

Key words acyloin rearrangement; bicyclo[3.2.1]oct-3-en-2-one; bicyclo[2.2.2]oct-5-en-2-one; demethylation; regioselective monodesilylation

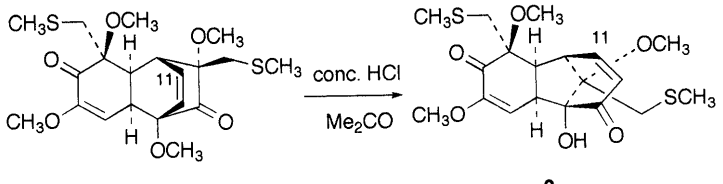
Acyloin rearrangement is a 1,2-migration of an α-alkyl or α-aryl group on α-hydroxyketones or α-hydroxyaldehydes to form isomeric α-hydroxyketones with the oxygen functions interchanged, induced by acid or base.[1] This rearrangement has been studied mostly in steroids[2] or other ring systems with conformational rigidity.[3] However, two examples of the conversion of a bicyclic[2.2.2]-octenone ring system into a bicyclo[3.2.1]octenone by treatment with formic acid or BF_3 have been reported.[4,5] The bicyclo[3.2.1]octane moiety forms the core of various natural products, such as quadrone[4] or the gibberellins,[6] and so could be a synthon for these natural products. Here, we describe the synthesis of 1-hydroxybicyclo[3.2.1]oct-3-en-2-ones (**2**, **5**, **6**, or **7**) from bicyclo-[2.2.2]oct-5-en-2-ones (**1**, **3**, or **4**), having a methoxy or *tert*-butyldimethylsilyl (TBS)oxy group at the bridgehead C-1 position, by treatment with acids or tetra-*n*-butylammonium fluoride (TBAF) (Charts 1, 2).

Results and Discussion

In order to deprotect the enol ether, compound **1** was treated with concentrated HCl in Me_2CO. The product was not the expected one, but was supposed to be a ring rearrangement product **2** having a bicyclo[3.2.1]oct-3-en-2-one ring system, which might be formed by a process including acyloin rearrangement. The structure of **2** was determined on the basis of the spectral data. The infrared (IR) spectrum displayed a ν(O–H) absorption at 3450 cm^{-1}, and the ^{1}H-NMR spectrum showed the characteristic signal of the olefinic β-proton (11-H) of the conjugated enone at δ 7.3, at lower field (*ca.* 1 ppm) than the olefinic 11-proton of the starting material **1**, as well as the signal at δ 4.4 based on the alcoholic proton. The relative stereochemistry of **2** was confirmed by the X-ray crystallographic method (Fig. 1).

Then, we applied the rearrangement reaction to various 1,3-dimethoxy-bicyclo[2.2.2]oct-5-en-2-ones (**3**).[7] The reaction of **3** with an excess of acid (concentrated HCl or 46% HF) was carried out in Me_2CO at 50 °C to afford, after the usual work-up, 1-hydroxybicyclo[3.2.1]octenones (**5**). The results are summarized in Table 1. The alcohols (**5**) were obtained in moderate yields in the case of the compounds (**3a—f**) having an alkyl or acyl substituent at C-7, although the reaction of **3g** having a formyl group was accompanied with epimerization at C-7 to give a 3 : 2 epimeric mixture, as determined from the ^{1}H-NMR spectrum (Table 6). The reaction of the compounds (**3h—k**) having a cyano or an alkoxycarbonyl group at C-7 did not give the desired products, but resulted in the formation of unidentified products. As to acid, HF was much more effective than HCl. The structure of **5** was supported by the absorption due to ν(O–H) at 3400—3550 cm^{-1} in the IR spectrum, and the characteristic low field signal at δ 7.3—7.5 due to the olefinic β-proton (4-H) of the conjugated enone, as well as the signal at δ 4.1—4.6 due to the alcoholic proton in the ^{1}H-NMR spectra (Table 6).

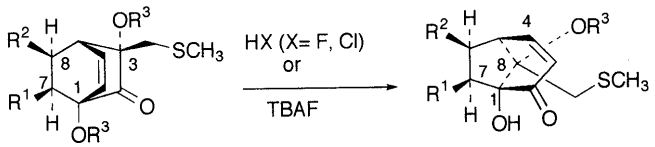
Next we examined the acyloin rearrangement reaction of the 1,3-bis-*tert*-butyldimethylsilyloxybicyclo[2.2.2]octenones (**4**). These compounds were prepared by Diels–Alder reaction of an appropriate dienophile (**8**) with the dimer (**11**) of 2,6-*tert*-butyl-dimethylsilyloxycyclohexa-2,4-dienone (**9**), which was obtained by the regio-selective 1,3-bis-silylation of pyrogallol followed by treatment with the Corey–Kim reagent (**12**),[8] by heating in a sealed tube at 120 °C (Chart 3). The reaction proceeded regio- and stereo-selectively to give the corresponding endo adduct **4** as a single product in the same manner as in the prep-



1 2

Chart 1

* To whom correspondence should be addressed.



3 R^3= CH_3
4 R^3= $SiMe_2{}^tBu$

5 R^3= CH_3
6 R^3= H
7 R^3= $SiMe_2{}^tBu$

Chart 2

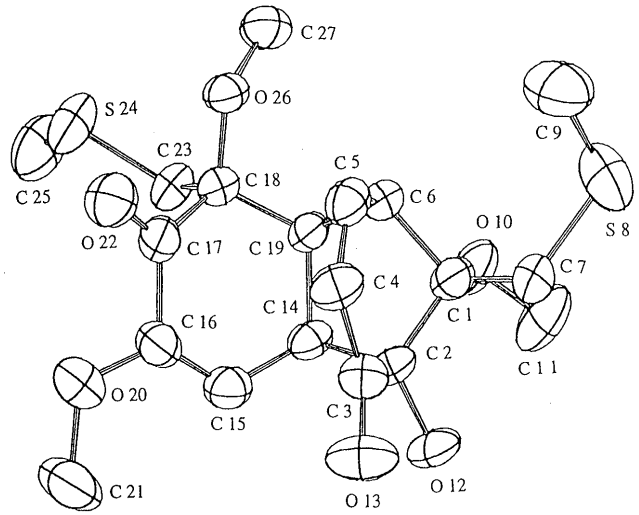


Fig. 1. ORTEP II Diagram[12] of Compound **2**

Displacement ellipsoids are drawn at the 50% probability level.

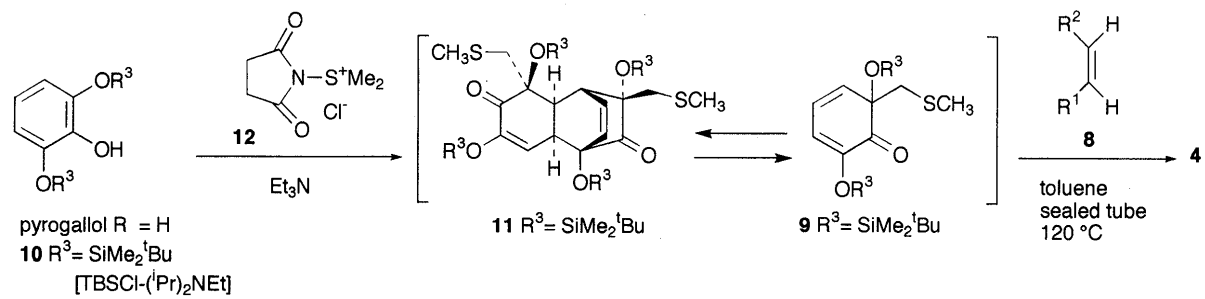
aration of **3**[7] (Table 2). The ^{1}H-NMR spectrum of compound **4** showed the following characteristic signals; four and two singlets at δ −0.26—0.34 and 0.87—0.99 due to two pairs of dimethylsilyl and *tert*-butylsilyl protons on the TBS-group, a singlet and an AB quartet at δ 2.0—2.1 and 2.7—2.8 due to a pair of methylthio and thiomethylene protons, and two signals ($J_{5,6}$ 8.2—8.6 Hz) at δ 5.7—6.1 and 6.1—6.5 due to vicinal vinyl protons (Table 5). The stereochemistry was confirmed by the ^{1}H–^{1}H vicinal couping constants ($J_{7,8\text{-endo}}$ 4.6—6.3 Hz, $J_{7,8\text{-exo}}$ 9.6—10.2 Hz) between 7-H and 8-H (9-H and 9a-H in the case of **4a**) in the ^{1}H-NMR, as in the case of **3**.[7,9]

Then, **4** was treated with TBAF at room temperature (method A) to remove the silyl group. The desilylation at the C-1 and the C-3 oxy groups followed by the acyloin rearrangement proceeded to afford 1,8-dihydroxy-bicyclo[3.2.1]octenone (**6**) as an unstable oil (Table 3). The reaction of moderately rigid compounds such as **4a—c** gave the rearrangement products **6a—c** in good yields. However, the others afforded little or none of the desired products. This may be due to the lability of the products; for example, most of the diols (**6**), on standing at room temperature for a long time, were transformed to unidentified products. The reaction of the aldehyde (**4g**) at −30 °C gave not the dihydoxy compound (**6g**), but the monohydroxy compound **7g** in 43% yield, whereas, at room temperature, an unidentified product was formed.

Table 1. Preparation of **5** by Acidic Acyloin Rearrangement of **3** and Physicochemical Data

Compd. No.	R^1	R^2	Yield (%) [HF (HCl)-treatment]	mp (°C) (Recryst. solv.)[a]	Formula	Analysis (%) Calcd (Found)		
						C	H	N
5a			59 (0)	Oil	$C_{18}H_{20}O_3S$		316.1136[b] (316.1138)	
5b	–CH=CH–CH_2–		83 (21)	65—67 (B–H)	$C_{14}H_{18}O_3S$	63.13 (63.09	6.81 6.81	0.00 0.00)
5c	–CH=CH–$C(CH_3)_2$–		38 (0)	142—144 (E)	$C_{17}H_{22}O_3S$	66.64 (66.40	7.24 7.21	0.00 0.00)
5d	–CH=$C(CH_3)$–	H	58 (0)	62—62.5 (H)	$C_{14}H_{20}O_3S$	62.66 (62.58	7.51 7.43	0.00 0.00)
5e	CH_3CO	H	81 (60)	Oil	$C_{13}H_{18}O_4S$		270.0926[b] (270.0927)	
5f	EtCO	H	(63)	Oil	$C_{14}H_{20}O_4S$		284.1083[b] (284.1075)	
5g	CHO	H	(77)[c]	Oil	$C_{12}H_{16}O_4S$		256.0770[b] (256.0797)	
5h	CO_2CH_3	H	0					
5k	CN	H	0					

a) Abbreviations: E, ethanol; B, benzene; H, hexane. *b*) HR-MS data. *c*) The product was obtained as a 3 : 2 epimeric mixture of C-7 (whose ratio was determined from the ^{1}H-NMR spectrum.



pyrogallol R = H
10 R^3= $SiMe_2{}^tBu$
[TBSCl-(^{i}Pr)$_2$NEt]

11 R^3= $SiMe_2{}^tBu$

9 R^3= $SiMe_2{}^tBu$

8

4

Chart 3

Table 2. Preparation of **4** by Diels–Alder Reaction and Physicochemical Data

Compd. No.	R^1	R^2	Yield (%)	mp (°C) (Recryst. solv.)[a]	Formula	Analysis (%) Calcd (Found)		
						C	H	N
4a			93	144—146.5 (E–B)	$C_{29}H_{46}O_3SSi_2$	65.61 (65.35	8.73 8.69	0.00 0.00)
4b	–CH=CH–CH_2–		77	109—111 (E–EE)	$C_{25}H_{44}O_3SSi_2$	62.45 (62.27	9.22 9.15	0.00 0.00)
4c	–CH=CH–$C(CH_3)_2$–		91	Oil	$C_{28}H_{48}O_3SSi_2$		520.2863[b] (520.2862)	
4e	CH_3CO	H	70	Oil	$C_{24}H_{44}O_4SSi_2$		484.2499[b] (484.2494)	
4g	CHO	H	69	91.5—92.5 (B–H)	$C_{23}H_{42}O_4SSi_2$	58.68 (58.54	8.99 8.89	0.00 0.00)
4h	CO_2CH_3	H	83	Oil	$C_{24}H_{45}O_5SSi_2$		501.2527[c] (501.2525)	
4i	CO_2Et	H	66	Oil	$C_{25}H_{46}O_5SSi_2$		514.2605[b] (514.2589)	
4j	$CO_2{}^tBu$	H	83	Oil	$C_{27}H_{50}O_5SSi_2$		542.2917[b] (542.2910)	
4k	CN	H	58	117—119 (B–H)	$C_{23}H_{41}NO_3SSi_2$	59.05 (59.03	8.83 8.78	2.99 2.74)
4l	(*E*)-CH=$CHCO_2Et$	H	91	Oil	$C_{27}H_{48}O_5SSi_2$		540.2761[b] (540.2761)	
4m	CONHCO	H	83	215—217.5 (B–H)	$C_{24}H_{41}NO_5SSi_2$	56.32 (56.58	8.07 8.03	2.74 2.50)
4n	CONMeCO	H	89	153—155.5 (B–H)	$C_{25}H_{43}NO_5SSi_2$	57.10 (57.24	8.24 8.15	2.66 2.41)

a) Abbreviations: E, ethanol; B, benzene; EE, ethyl ether; H, hexane. *b*) HR-MS data. *c*) HR-FAB-MS (positive ion mode) data.

Table 3. Preparation of **6** by Acyloin Rearrangement of **4** Using TBAF and Physicochemical Data

Compd. No.	R^1	R^2	Yield (%)	mp (°C) (Recryst. solv.)	Formula	Analysis (%) Calcd			Found		
						C	H	N	C	H	N
6a			93	Oil	$C_{17}H_{18}O_3S$		302.0977[a]			302.1003	
6b	–CH=CH–CH_2–		42	Oil	$C_{13}H_{16}O_3S$		252.0821[a]			252.0826	
6c	–CH=CH–$C(CH_3)_2$–		90	Oil	$C_{16}H_{20}O_3S$		292.1133[a]			292.1148	
6e	CH_3CO	H	40	Oil	$C_{12}H_{16}O_4S$		256.0770[a]			256.0778	
6g	CHO	H	0[b]								
6h	CO_2CH_3	H	43	Oil	$C_{12}H_{16}O_5S$		272.0719[a]			272.0731	
6j	$CO_2{}^tBu$	H	36	Oil	$C_{15}H_{22}O_5S$		314.1188[a]			314.1182	
6k	CN	H	45	Oil	$C_{11}H_{13}NO_3S$		239.0616[a]			239.0591	

a) HR-MS data. *b*) The reaction of **4g** at −30 °C gave the monohydroxy compound **7g** as an oil in 43% yield. High-resolution MS Found: M^+, 356.1481. $C_{17}H_{28}O_4SSi$ requires M, 356.1478.

The structures of **6** were confirmed by the ^{1}H-NMR spectra, which displayed signals at δ 3.2—3.7 and 4.0—4.6 due to two alcoholic protons and at δ 7.0—7.5 due to the olefinic β-proton of the conjugated enones, and by the IR spectra, which showed a strong ν(O–H) absorption at 3400—3550 cm^{-1} (Table 7).

On the other hand, in the treatment of **4** with acid (HF)–acetonitrile (MeCN) (method B) the regioselective monodesilylation of the C-1 oxy group, followed by the acyloin rearrangement, took place to give the 8-*tert*-butyldimethylsilyloxy-1-hydroxybicyclo[3.2.1]oct-3-en-2-ones (**7**) in satisfactory yields (Table 4). In contrast to the reaction using TBAF, the rearrangement products **7** were obtained in good yields in the case of the compounds (**4h—n**) having a cyano, alkoxycarbonyl, or amide group at C-7, whereas the relatively rigid compounds **4a—c** gave poorer yields. In the reaction of the aldehyde **4g**, an unidentified product was also formed. The structures of **7** were determined on the basis of spectral data. The IR spectra showed a ν(O-H) absorption at 3400—3500 cm^{-1}. The ^{1}H-NMR spectra displayed two singlets and a singlet at δ 0.2—0.3 and 0.9—1.0 due to a pair of the dimethylsilyl and *tert*-butylsilyl protons on the TBS-group, and signals at δ 4.0—5.3 and 7.0—7.5 due to the alcoholic proton and the olefinic β-proton of the conjugated enone, respectively (Table 8).

The formation of the 1-hydroxybicyclo[3.2.1]octenones from the bicyclo[2.2.2]octenones can be reasonably explained in terms of protonation or the participation of the tetrabutylammonium cation at the 2-carbonyl func-

Table 4. Preparation of **7** by Acidic Acyloin Rearrangement of **4** and Physicochemical Data

Compd. No.	R^1	R^2	Yield (%)	mp (°C) (Recryst. solv.)[a]	Formula	Analysis (%) Calcd (Found)		
						C	H	N
7a			43	147.5—148.5 (B–H)	$C_{23}H_{32}O_3SSi$	66.30 (66.09	7.74 7.73	0.00 0.00)
7b	$-CH=CH-CH_2-$		57	Oil	$C_{19}H_{30}O_3SSi$		366.1685[b] (366.1682)	
7c	$-CH=CH-C(CH_3)_2-$		54	Oil	$C_{22}H_{34}O_3SSi$		406.1998[b] (406.2003)	
7e	CH_3CO	H	41	84—86.5 (B–H)	$C_{18}H_{30}O_4SSi$	58.34 (58.05	8.16 8.11	0.00 0.00)
7g	CHO	H	0					
7h	CO_2CH_3	H	88	Oil	$C_{18}H_{30}O_5SSi$		386.1584[b] (386.1604)	
7i	CO_2Et	H	69	Oil	$C_{19}H_{32}O_5SSi$		400.1740[b] (400.1724)	
7j	$CO_2{}^tBu$	H	90	Oil	$C_{21}H_{36}O_5SSi$		—[c]	
7k	CN	H	79	98—100.5 (E)	$C_{17}H_{27}NO_3SSi$	57.74 (57.56	7.71 7.59	3.96 3.66)
7l	$CH=CHCO_2Et$	H	85	61—63 (B–H)	$C_{21}H_{34}O_5SSi$	59.12 (58.84	8.03 7.95	0.00 0.00)
7m	$-CONHCO-$		92	211—213 (B)	$C_{18}H_{27}NO_5SSi$	54.38 (54.17	6.85 6.68	3.52 3.26)
7n	$-CON(CH_3)CO-$		76	152.5—154 (E)	$C_{19}H_{29}NO_5SSi$	55.45 (55.43	7.10 6.97	3.40 3.13)

a) Abbreviations: E, ethanol; B, benzene; H, hexane. *b*) HR-MS data. *c*) Not determined.

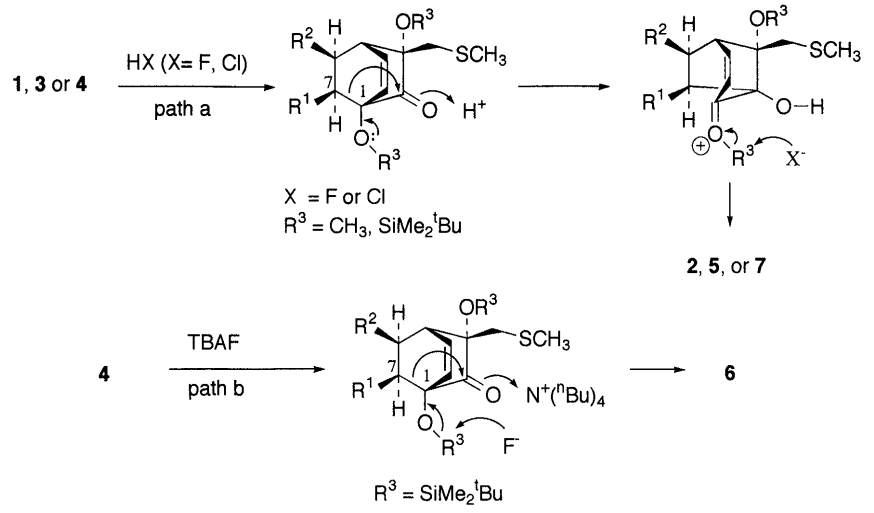


Chart 4

tion, followed by the acyloin rearrangement *via* path a or path b as shown in Chart 4.

In conclusion, it was demonstrated that the acid treatment of 1-methoxy or 1-*tert*-butyldimethylsilyloxybicyclo[2.2.2]oct-5-en-2-ones (**1**, **3**, or **4**) gave the 1-hydroxybicyclo[3.2.1]oct-3-en-2-ones (**2**, **5**, or **7**, respectively), *via* regioselective demethylation or regioselective desilylation at the C-1 oxy group followed by the acyloin rearrangement. Moreover, rearrangement of **4** was found to proceed in TBAF–tetrahydrofuran (THF) to afford the 1,8-dihydroxy compounds **6**.

Experimental

Spectral data were obtained using the following apparatus: IR spectra on a JASCO IR-810 spectrophotometer; mass spectra (MS) on a JEOL JMS-700 mass spectrometer by direct insertion at 70 ev; ^{1}H-NMR spectra (270 MHz) and ^{13}C-NMR spectra (67.8 MHz) on a JEOL EX-270 instrument in chloroform-*d* ($CDCl_3$) with chemical shifts being reported in δ units from tetramethylsilane as an internal standard and coupling constants in hertz. Column chromatography was carried out on silica gel (100—200 mesh, Micro Bead 4B, Fuji-Davison Chemical Ltd.).

(1α,2α,3*R,7α,8α,12*S**)-8-Hydroxy-3,5,12-trimethoxy-3,12-bismethylthiomethyltricyclo[6.3.1.0^{2,7}]dodeca-5,10-diene-4,9-dione (2)** A solution of the dimer **1** (1.05 g, 2.45 mmol) of 2,6-dimethoxy-6-methylthiomethylcyclohexa-2,4-dienone[7] in concentrated HCl–acetone (2.0—100 ml) was stirred at 50 °C for 3 d. Excess of $NaHCO_3$ powder (5 g) was added and the solvent was evaporated. The residue was extracted with methylene dichloride (100 ml), and the organic layer was filtered with the aid of Celite. The filtrate was dried over $MgSO_4$, and the solvent was evaporated. The purification of the residue by column chromatography on silica gel (eluent: 30% ethyl acetate in hexane) afforded **2** (0.94 g, 93% yield) as a crystalline product, mp 151.5—153.5 °C (benzene–hexane). IR ν_{max} (KBr)/cm^{-1}: 3450, 1715, 1660, 1635 cm^{-1}. ^{1}H-NMR δ: 2.05 (3H, s, CH_3S), 2.10 (3H, s, CH_3S), 2.66 (2H, ABq, J=13.9, CH_2S), 2.94 (2H, ABq, J=13.9, CH_2S), 3.24—3.31 (1H, m,

Table 5. Spectral Data for **4**

Compd. No.	IR (KBr or neat) cm^{-1}	MS *m/z* M^+	^{1}H-NMR δ (ppm)	^{13}C-NMR δ (ppm)
4a	1740, 1625	530	−0.08, 0.01, 0.27, and 0.34 (3H × 4, s), 0.91 (9H, s), 0.99 (9H, s), 2.10 (3H, s), 2.68 (1H, dd, *J*=16.8, 4.6), 2.74 (2H, ABq, *J*=13.0), 3.21 (1H, dd, *J*=16.8, 10.2), 3.32—3.36 (1H, m), 3.42—3.50 (1H, m), 3.52 (1H, dm, *J*=9.2), 5.73 (1H, dm, *J*=8.6), 6.14 (1H, dd, *J*=8.6, 6.6), 7.08—7.20 (3H, m), 7.58 (1H, dm, *J*=7.3)	−4.4, −3.9, −3.2, and −2.9 (CH_3 × 4), 18.7, (CH_3), 18.8 (C × 2), 26.1 (CH_3 × 3), 26.2 (CH_3 × 3), 35.8 (CH), 38.3 (CH_2), 43.6 (CH_2), 46.7 (CH), 54.5 (CH), 76.3 (C), 84.7 (C), 123.8 (CH), 125.7 (CH), 127.3 (CH), 127.4 (CH), 131.0 (CH), 134.1 (CH), 141.5 (C), 144.7 (C), 208.2 (C)
4b	1740, 1623	480	−0.02, 0.00, 0.26, and 0.31 (3H × 4, s), 0.89 (9H, s), 0.92 (9H, s), 1.97 (1H, dm, *J*=17.2), 2.09 (3H, s), 2.60 (1H, dddm, *J*=17.2, 9.9, 2.0), 2.73 (2H, ABq, *J*=13.2), 3.04—3.23 (3H, m), 5.65—5.78 (2H, m), 5.85 (1H, d, *J*=8.6), 6.13 (1H, dd, *J*=8.6, 6.6)	−3.8, −3.6, −3.3, and −2.7 (CH_3 × 4), 17.2 (CH_3), 18.6 (C), 18.8 (C), 26.0 (CH_3 × 3), 26.1 (CH_3 × 3), 34.5 (CH), 39.4 (CH_2), 43.6 (CH_2), 46.5 (CH), 56.5 (CH), 76.6 (C), 84.3 (C), 129.1 (CH), 130.4 (CH), 134.2 (CH × 2), 208.1 (C)
4c	1737, 1615	520	−0.03, −0.01, 0.27, and 0.33 (3H × 4, s), 0.91 (9H, s), 0.93 (9H, s), 1.74 (3H, s), 1.82 (3H, s), 2.09 (3H, s), 2.72 (2H, ABq, *J*=12.9), 3.21 (1H, dm, *J*=7.6), 3.48 (1H, dm, *J*=6.6), 3.60 (1H, dm, *J*=7.6), 5.72 (1H, dm, *J*=8.2), 5.82 (1H, dm, *J*=5.6), 6.06 (1H, dd, *J*=8.2, 6.6), 6.47 (1H, dd, *J*=5.6, 1.7)	−3.8, −3.6, −3.3, and −2.7 (CH_3 × 4), 17.2 (CH_3), 18.6 (C), 18.8 (C), 21.2 (CH_3), 22.9 (CH_3), 26.0 (CH_3 × 3), 26.1 (CH_3 × 3), 39.3 (CH), 43.6 (CH_2), 45.2 (CH), 55.0 (CH), 76.7 (C), 84.5 (C), 122.5 (C), 130.3 (CH), 132.0 (CH), 132.9 (CH), 135.9 (CH), 141.9 (C), 208.6 (C)
4e	1742, 1720, 1640	484	−0.02, 0.02, 0.25, and 0.31 (3H × 4, s), 0.87 (9H, s), 0.89 (9H, s), 1.61 (1H, ddd, *J*=12.5, 6.3, 2.6), 2.07 (3H, s), 2.22 (3H, s), 2.34 (1H, ddd, *J*=12.5, 9.6, 2.9), 2.72 (2H, ABq, *J*=13.5), 3.09 (1H, dd, *J*=9.6, 6.3), 3.20—3.25 (1H, m), 5.91 (1H, dm, *J*=8.6), 6.38 (1H, dd, *J*=8.6, 6.9)	−3.9, −3.5, −3.3, and −2.9 (CH_3 × 4), 17.3 (CH_3), 18.5 (C), 18.7 (C), 26.0 (CH_3 × 6), 26.1 (CH_2), 32.5 (CH_3), 41.8 (CH), 43.0 (CH_2), 51.2 (CH), 75.8 (C), 83.3 (C), 130.5 (CH), 133.3 (CH), 205.0 (C), 208.1 (C)
4g	1725, 1608	470	0.01, 0.02, 0.30, and 0.32 (3H × 4, s), 0.88 (9H, s), 0.91 (9H, s), 1.84 (1H, ddd, *J*=13.2, 5.3, 3.0), 2.07 (3H, s), 2.34 (1H, ddd, *J*=13.2, 9.9, 2.6), 2.73 (2H, ABq, *J*=13.2), 2.84 (1H, ddd, *J*=9.9, 5.3, 1.8), 3.22—3.25 (1H, m), 5.95 (1H, dm, *J*=8.3), 6.40 (1H, dd, *J*=8.3, 6.9), 9.76 (1H, d, *J*=1.8)	−2.7, −3.3, −3.6, and −3.8 (CH_3 × 4), 17.2 (CH_3), 18.7 (C), 18.8 (C), 22.4 (CH_2), 25.9 (CH_3 × 3), 26.0 (CH_3 × 3), 41.7 (CH), 43.1 (CH_2), 53.0 (CH), 76.1 (C), 82.7 (C), 131.1 (CH), 134.9 (CH), 201.2 (CH), 205.2 (C)
4h	1750, 1645, 1617	500	0.00 (6H, s), 0.22 and 0.25 (3H × 2, s), 0.88 (18H, s), 1.61 (1H, ddd, *J*=12.5, 6.3, 2.6), 2.07 (3H, s), 2.50 (1H, ddd, *J*=12.5, 9.9, 3.0), 2.75 (2H, ABq, *J*=13.2), 2.93 (1H, ddd, *J*=9.9, 6.3, 1.0), 3.19—3.24 (1H, m), 3.65 (3H, s), 5.97 (1H, dm, *J*=8.6), 6.38 (1H, dd, *J*=8.6, 6.9)	−3.9, −3.7, −3.3, and −2.9 (CH_3 × 4), 17.2 (CH_3), 18.4 (C), 18.7 (C), 25.6 (CH_3 × 3), 25.9 (CH_3 × 3), 27.3 (CH_2), 41.6 (C-4), 43.0 (CH_2), 45.9 (CH), 51.8 (CH_3), 75.7 (C), 82.4 (C), 131.2 (CH), 132.9 (CH), 173.4 (C), 204.7 (C)
4i	1740, 1610	514	−0.01 (6H, s), 0.23 and 0.29 (3H × 2, s), 0.87 (9H, s), 0.88 (9H, s), 1.24 (3H, t, *J*=6.9), 1.59 (1H, ddd, *J*=12.5, 6.3, 2.6), 2.07 (3H, s), 2.50 (1H, ddd, *J*=12.5, 9.9, 3.0), 2.74 (2H, ABq, *J*=13.2), 2.89 (1H, ddd, *J*=9.9, 6.3, 1.0), 3.19—3.22 (1H, m), 3.99—4.19 (2H, m), 5.98 (1H, d, *J*=8.6), 6.35 (1H, dd, *J*=8.6, 6.9)	−3.9, −3.6, −3.3, and −2.9 (CH_3 × 4), 14.1 (CH_3), 17.2 (CH_3), 18.4 (C), 18.7 (C), 25.7 (CH_3 × 3), 25.9 (CH_3 × 3), 27.4 (CH_2), 41.6 (CH), 43.1 (CH_2), 46.1 (CH), 60.8 (CH_3), 75.7 (C), 82.5 (C), 131.4 (CH), 132.6 (CH), 173.0 (C), 204.9 (C)
4j	1740, 1635	542	−0.02, 0.00, 0.19, and 0.29 (3H × 4, s), 0.88 (9H, s), 0.91 (9H, s), 1.42 (9H, s), 1.51 (1H, ddd, *J*=12.5, 5.9, 2.6), 2.07 (3H, s), 2.51 (1H, ddd, *J*=12.5, 10.1, 3.0), 2.73 (2H, ABq, *J*=13.2), 2.75 (1H, ddd, *J*=9.9, 5.9, 1.0), 3.16—3.19 (1H, m), 6.04 (1H, dm, *J*=8.6), 6.29 (1H, dd, *J*=8.6, 6.9)	−4.0, −3.3, −3.3, and −3.0 (CH_3 × 4), 17.2 (CH_3), 18.5 (C), 18.7 (C), 25.9 (CH_3 × 6), 27.7 (CH_2), 28.1 (CH_3), 41.6 (CH), 43.1 (CH_2), 47.1 (CH), 75.7 (C), 80.7 (C), 82.6 (C), 131.7 (CH), 132.0 (CH), 171.9 (C), 205.3 (C)
4k	2250, 1750, 1612	467	−0.03, 0.06, 0.26, and 0.29 (3H × 4, s), 0.87 (9H, s), 0.97 (9H, s), 1.73 (1H, ddd, *J*=13.2, 5.3, 3.3), 2.06 (3H, s), 2.68 (1H, ddd, *J*=13.2, 10.2, 2.6), 2.74 (2H, ABq, *J*=13.5), 2.97—3.02 (1H, m), 3.20—3.23 (1H, m), 6.08 (1H, dm, *J*=8.6), 6.53 (1H, dd, *J*=8.6, 6.9)	−3.8, −3.7, −3.3, and −2.9 (CH_3 × 4), 15.5 (C), 17.2 (CH_3), 18.6 (C), 25.7 (CH_3 × 3), 25.9 (CH_3 × 3), 27.0 (CH_2), 34.5 (CH), 41.0 (CH), 42.7 (CH_2), 75.8 (C), 81.0 (C), 120.1 (C), 131.4 (CH), 135.2 (CH), 204.0 (C)
4l	1772, 1722, 1655, 1610	542	−0.02, −0.01, 0.22, and 0.29 (3H × 4, s), 0.86 (9H, s), 0.87 (9H, s), 1.26 (3H, t, *J*=6.9), 1.31 (1H, ddd, *J*=12.9, 5.8, 3.0), 2.06 (3H, s), 2.51 (1H, ddm, *J*=12.9, 3.0), 2.73 (2H, ABq, *J*=13.2), 2.71—2.80 (1H, m), 3.12—3.15 (1H, m), 4.17 (2H, q, *J*=6.9), 5.78 (1H, dd, *J*=15.5, 0.7), 5.88 (1H, dm, *J*=8.6), 6.38 (1H, dd, *J*=8.6, 6.8), 6.78 (1H, dd, *J*=15.5, 8.6)	−3.9, −3.6, −3.3, and −2.8 (CH_3 × 4), 14.3 (CH_3), 17.2 (CH_3), 18.7 (C), 22.6 (C), 25.8 (CH_3 × 3), 25.9 (CH_3 × 3), 27.5 (CH_2), 41.3 (CH), 43.1 (CH_2), 44.4 (CH), 60.1 (CH_2), 76.0 (C), 83.2 (C), 123.0 (CH), 131.6 (CH), 133.9 (CH), 148.7 (CH), 166.2 (C), 206.1 (C)
4m	3400, 1778, 1710, 1685	511	0.27, 0.28, 0.30, and 0.31 (3H × 4, s), 0.86 (9H, s), 0.95 (9H, s), 2.07 (3H, s), 2.74 (2H, ABq, *J*=13.5), 3.02 (1H, dd, *J*=8.3, 0.7), 3.60 (1H, ddm, *J*=8.3, 3.3), 3.65 (1H, ddd, *J*=6.3, 3.3, 1.7), 6.03 (1H, d, *J*=8.6), 6.29 (1H, dd, *J*=8.6, 6.3)	−3.9, −3.7, −3.4, and −2.8 (CH_3 × 4), 17.3 (CH_3), 18.5 (C), 18.7 (C), 25.6 (CH_3 × 3), 25.9 (CH_3 × 3), 42.4 (CH), 42.6 (CH_2), 43.0 (CH), 47.4 (CH), 74.8 (C), 81.7 (C), 131.4 (CH), 132.7 (CH), 173.3 (C), 178.0 (C), 204.0 (C)
4n	1778, 1740, 1703	525	−0.26, −0.29, 0.28, and 0.31 (3H × 4, s), 0.86 (9H, s), 0.97 (9H, s), 2.06 (3H, s), 2.74 (2H, ABq, *J*=13.5), 2.94 (3H, s), 2.99 (1H, d, *J*=8.6), 3.55 (1H, dd, *J*=8.6, 3.3), 3.77 (1H, ddd, *J*=6.6, 3.3, 1.7), 5.95 (1H, dm, *J*=8.3), 6.21 (1H, dd, *J*=8.3, 6.6)	−3.9, −3.7, −3.4, and −2.8 (CH_3 × 4), 17.3 (CH_3), 18.6 (C), 18.7 (C), 25.1 (CH_3), 25.7 (CH_3 × 3), 25.9 (CH_3 × 3), 41.1 (CH), 42.6 (CH_2), 43.0 (CH), 46.3 (CH), 74.8 (C), 81.6 (C), 131.3 (CH), 132.7 (CH), 173.4 (C), 177.7 (C), 204.4 (C)

1-H), 3.43—3.48 (1H, m, 7-H), 3.49 (3H, s, CH_3O), 3.59 (3H, s, CH_3O), 3.60 (3H, s, CH_3O), 3.80 (1H, dd, J=5.9, 9.5, 2-H), 4.37 (1H, s, OH), 5.38 (1H, d, J=4.8, 6-H), 6.09 (1H, d, J=9.5, 10-H), 7.37 (1H, dd, J=7.3, 9.5, 11-H). ^{13}C-NMR δ: 16.9 (CH_3S), 17.1 (CH_3S), 32.0 (CH_2S), 41.3 (CH_2S), 42.1 (C-7), 44.0 (C-2), 48.0 (C-1), 52.5 (CH_3O), 52.6 (CH_3O), 55.5 (CH_3O), 81.5, 87.9, 94.6 (C-3, -8, -12), 109.0 (C-6), 129.4 (C-10), 150.9 (C-5), 155.4 (C-11), 193.5, 200.7 (C-4, -9). MS m/z(%): 414 (0.5, M^+), 61 (base). *Anal.* Calcd for $C_{19}H_{26}O_6S_2$: C, 55.05; H, 6.32. Found: C, 55.22; H, 6.24.

2,6-Di-*tert*-butyldimethylsilyloxyphenol (10). (Method A) *tert*-Butyldimethylsilyl chloride (24.84 g, 0.165 mol) in methylene dichloride (50 ml) was added to a solution of pyrogallol (9.15 g, 0.073 mol) and diisopropylamine (35 ml, 0.207 mol) in methylene dichloride (200 ml) at -10 °C under an argon atmosphere, and the mixture was stirred at room temperature for 15 h. The reaction mixture was dissolved in hexane (400 ml), then washed with cooled water (3 × 50 ml) and brine (1 × 50 ml), and dried over anhydrous $MgSO_4$. Removal of the solvent gave a pale yellow oil, which was chromatographed on silica gel (eluent: 2% ethyl acetate in hexane) to afford **10** (20.018 g, 78%) as an oil. IR ν_{max} (neat)/cm^{-1}: 3550, 1610. ^{1}H-NMR δ: 0.03 (12H, s, CH_3Si × 4), 0.81 [18H, s, $(CH_3)_3C$ × 2], 5.06 (1H, br s, OH), 6.23—6.42 (3H, m, H_{arom}). ^{13}C-NMR δ: -4.4 (CH_3Si × 4), 18.3 ($\underline{C}Me_3$ × 2), 25.7 [$(\underline{C}H_3)_3C$ × 2], 113.1 (C-3, -5), 118.4 (C-4), 139.1 (C-1), 143.4 (C-2, -6). MS m/z (%): 354 (2, M^+), 281 (65), 239 (36), 73 (base) (Found: M^+, 354.2049. $C_{18}H_{34}O_3Si_2$ requires M, 354.2047).

(Method B) TBS chloride (25.00 g, 0.167 mol) was added to a mixture of pyrogallol (9.15 g, 0.073 mol), imidazole (24 g, 36.3 mol), and dry dimethylformamide (25 ml) at -30 °C under an argon atmosphere, and the whole was stirred at the same temperature for 2 d. It was dissolved in hexane–ethyl ether (160—40 ml), and the solution was washed with cooled water (3 × 10 ml) and brine (1 × 20 ml), and dried over anhydrous $MgSO_4$. Removal of the solvent gave a pale yellow oil, which was chromatographed on silica gel (eluent: 1% ethyl acetate in hexane) to afford 1,2,3-tri-*tert*-butyldimethylsilyloxybenzene (8.296 g, 24%) as an oil. ^{1}H-NMR δ: 0.15 (6H, S, CH_3Si × 2), 0.23 (12H, S, CH_3Si × 4), 0.96 [18H, s, $(CH_3)_3C$ × 2], 1.03 [9H, s, $(CH_3)_3C$], 6.50—6.68 (3H, m, H_{arom}). ^{13}C-NMR δ: -3.9 (CH_3Si × 2), -3.6 (CH_3Si × 4), 18.5 ($\underline{C}Me_3$), 18.8 ($\underline{C}Me_3$ × 2), 26.2 [$(\underline{C}H_3)_3C$ × 2], 26.3 [$(\underline{C}H_3)_3C$], 114.3 (CH_{arom} × 2), 120.1 (CH_{arom}), 138.5 (C_{arom}), 148.9 (C_{arom} × 2). MS m/z (%): 469 (1, M^+ + 1), 468 (3, M^+), 281 (86), 239 (22), 73 (base) (Found: M^+, 468.2912. $C_{24}H_{48}O_3Si_3$ requires M, 468.2912). Further elution with 1% ethyl acetate in hexane gave **10** (14.149 g, 43%) as an oil.

(1α,2α,3*R,7α,8α,10*S**)-3,5,8,10-Tetra-*tert*-butyldimethylsilyloxy-3,10-bis-methylthiomethyltricyclo[6.2.2.0^{2,7}]dodeca-5,11-diene-4,9-dione (11)** Dimethyl sulfide (20 ml, 0.272 mol) was added dropwise to a suspension of *N*-chlorosuccinimide (NCS, 23.60 g, 0.177 mol) in anhydrous methylene dichloride (600 ml) at -30 °C under an argon atmosphere, and stirring was continued for 1 h at the same temperature. Then, a solution of a phenol **10** (20.85 g, 0.064 mol) in anhydrous methylene dichloride (50 ml) was added. After 1 h, triethylamine (39 ml,

Table 6. Spectral Data for **5**

Compd. No.	IR (KBr or neat) cm^{-1}	MS m/z M^+	^{1}H-NMR δ (ppm)	^{13}C-NMR δ (ppm)
5a	3430, 1678, 1605	316	2.06 (3H, s), 2.65 (1H, dd, J=17.5, 3.6), 2.67 (2H, ABq, J=13.5), 3.07 (1H, dd, J=17.5, 10.6), 3.36 (1H, dd, J=7.3, 7.3), 3.63 (3H, s), 3.67—3.78 (1H, m), 4.24 (1H, dm, J=9.9), 4.47 (1H, br s), 5.86 (1H, d, J=9.6), 7.00—7.12 (4H, m), 7.25 (1H, dd, J=9.6, 7.3)	16.8 (CH_3), 32.4 (CH_2), 33.3 (CH_2), 40.7 (CH), 48.1 (CH), 52.6 (CH_3), 57.4 (CH), 91.9 (C), 94.5 (C), 124.2 (CH × 2), 126.4 (CH), 127.2 (CH), 128.2 (CH), 141.2 (C), 143.5 (C), 153.2 (CH), 201.3 (C)
5b	3488, 1680, 1610	266	2.00 (1H, dm, J=17.8), 2.06 (3H, s), 2.44 (1H, ddm, J=17.8, 10.2), 2.67 (2H, ABq, J=13.5), 3.27 (1H, dd, J=7.6, 7.3), 3.45 (1H, dddd, J=10.9, 10.2, 6.9, 3.3), 3.56 (3H, s), 3.62 (1H, dm, J=10.9), 4.19 (1H, br s), 5.50—5.59 (2H, m), 6.19 (1H, d, J=9.6), 7.25 (1H, dd, J=9.6, 7.6)	16.8 (CH_3), 32.7 (CH_2), 34.0 (CH_2), 39.9 (CH), 47.7 (CH), 52.5 (CH_3), 59.1 (CH), 91.7 (C), 93.8 (C), 128.3 (CH), 129.8 (CH), 132.8 (CH), 153.1 (CH), 202.0 (C)
5c	3548, 1666	306	1.71 (3H, s), 1.85 (3H, s), 2.07 (3H, s), 2.67 (2H, ABq, J=13.5), 3.49 (1H, dd, J=7.6, 7.3), 3.59 (3H, s), 3.69 (1H, dm, J=8.3), 3.87 (1H, ddm, J=8.3, 7.3), 4.26 (1H, br s), 5.75—5.78 (1H, m), 6.07 (1H, d, J=9.6), 6.19 (1H, dd, J=5.9, 2.0), 7.03 (1H, dd, J=9.6, 7.6)	16.8 (CH_3), 20.8 (CH_3), 21.6 (CH_3), 32.5 (CH_2), 44.9 (CH), 47.7 (CH), 57.0 (CH), 52.7 (CH_3), 91.3 (C), 93.1 (C), 124.8 (C), 127.1 (CH), 132.7 (CH), 134.4 (CH), 138.5 (C), 153.7 (CH), 201.7 (C)
5d	3450, 1680, 1610	268	1.68 (3H, s), 1.68 (1H, ddm, J=17.2, 5.0), 2.07 (3H, s), 2.56 (1H, ddd, J=17.2, 10.4, 6.9), 2.67 (2H, ABq, J=13.9), 3.06 (1H, dd, J=7.6, 6.9), 3.32 (1H, dd, J=10.4, 5.0), 3.39 (3H, s), 4.16 (1H, br s), 4.64 (1H, br s), 4.78 (1H, br s), 6.22 (1H, d, J=9.6), 7.45 (1H, dd, J=9.6, 7.6)	16.8 (CH_3), 23.7 (CH_3), 29.7 (CH_2), 31.9 (CH_2), 44.0 (CH), 48.4 (CH), 52.5 (CH_3), 90.3 (C), 94.8 (C), 112.1 (CH_2), 127.3 (CH), 143.7 (C), 156.0 (CH), 201.1 (C)
5e	3436, 1712, 1672, 1604	270	1.97 (1H, ddm, J=12.5, 4.6), 2.07 (3H, s), 2.11 (3H, s), 2.44 (1H, ddd, J=12.5, 10.2, 6.9), 2.65 (2H, ABq, J=13.9), 3.04—3.10 (1H, m), 3.60 (3H, s), 3.75 (1H, dd, J=10.2, 4.6), 4.41 (1H, br s), 6.23 (1H, d, J=9.6), 7.41 (1H, dd, J=9.6, 7.6)	17.2 (CH_3), 27.7 (CH_2), 30.9 (CH_3), 31.7 (CH_2), 44.2 (CH), 53.0 (CH_3), 56.6 (CH), 91.4 (C), 93.5 (C), 127.3 (CH), 156.2 (CH), 200.8 (C), 207.7 (C)
5f	3444, 1712, 1680, 1612	284	0.96 (3H, t, J=7.3), 1.90 (1H, ddm, J=12.2, 4.9), 2.07 (3H, s), 2.39—2.53 (1H, m), 2.45 (2H, q, J=7.3), 2.65 (2H, ABq, J=13.9), 3.04—3.10 (1H, m), 3.59 (3H, s), 3.77 (1H, dd, J=10.4, 4.9), 4.38 (1H, br s), 6.26 (1H, d, J=9.6), 7.39 (1H, dd, J=9.6, 7.6)	7.6 (CH_3), 17.0 (CH_3), 28.3 (CH_2), 31.6 (CH_2), 37.0 (CH_2), 44.2 (CH), 52.9 (CH_3), 55.6 (CH), 91.3 (C), 93.4 (C), 127.4 (CH), 155.5 (CH), 200.9 (C), 210.4 (C)
5g	3430, 1718, 1680	256	(major component) 1.74 (1H, ddm, J=13.2, 9.2), 2.09 (3H, s), 2.32—2.38 (1H, m), 2.68 (2H, ABq, J=13.9), 2.68—2.77 (1H, m), 3.09—3.19 (1H, m), 3.53 (3H, s), 4.27 (1H, br s), 6.26 (1H, d, J=9.6), 7.50 (1H, dd, J=9.6, 7.3), 9.91 (1H, d, J=2.3); (minor component) 1.95 (1H, ddm, J=12.9, 4.3), 2.08 (3H, s), 2.42 (2H, ABq, J=13.9), 2.42—2.50 (1H, m), 2.68—2.77 (1H, m), 3.09—3.19 (1H, m), 3.61 (3H, s), 4.46 (1H, br s), 6.22 (1H, d, J=9.6), 7.47 (1H, dd, J=9.6, 6.9), 9.59 (1H, d, J=1.0)	

0.280 mol) was added, and stirring was continued for 1 h at the same temperature. Then, cooled 10% aqueous NaOH (89 ml) was added, and the whole was extracted with hexane (600 ml). The organic layer was washed with saturated aqueous NH_4Cl (2 × 100 ml) and brine (1 × 100 ml), and dried over anhydrous $MgSO_4$. The solvent was evaporated off, and the resulting residue was chromatographed on silica gel (eluent: 2% ethyl acetate in hexane) to afford **11** (19.42 g, 79%) as a colorless solid, mp 122—124 °C (benzene–hexane). IR ν_{max} (KBr)/cm^{-1}: 1740, 1710, 1638. ^{1}H-NMR δ: −0.06, 0.00, 0.01, 0.19, 0.22, 0.28, 0.31, 0.32 (3H × 8, s, CH_3Si × 8), 0.91 [27H, s, $(CH_3)_3C$ × 3], 0.94 [9H, s, $(CH_3)_3C$], 2.00 (3H, s, CH_3S), 2.07 (3H, s, CH_3S), 2.65 (2H, ABq, J = 13.5, CH_2S), 2.80 (2H, ABq, J = 13.2, CH_2S), 3.08 (1H, dd, J = 8.6, 4.1, 7-H), 3.36 (1H, dm, J = 8.6, 2-H), 3.53 (1H, dm, J = 6.9, 1-H), 5.69 (1H, dm, J = 8.6, 12-H), 5.81 (1H, d, J = 4.1, 6-H), 6.12 (1H, dd, J = 8.6, 6.9, 11-H). ^{13}C-NMR δ: −4.6, −4.2, −3.8, −3.7, −3.2, −2.8, −2.2, −2.0 (CH_3Si × 8), 17.3, 17.8, 18.6, 19.4 ($\underline{C}Me_3$ × 4), 18.3, 18.9 ($\underline{C}H_3S$ × 2) 25.7, 26.0, 26.1, 26.5 [$(\underline{C}H_3)_3C$ × 4], 41.7, 42.6, 45.0 (C-1, -2, -7), 43.4, 49.9 (CH_2S × 2), 77.3, 81.5, 86.1 (C-3, -8, -10), 120.7 (C-6), 131.4 (C-11), 135.3 (C-12), 148.7 (C-5), 195.5, 209.3 (C-4, -9). MS m/z (%): 828 (0.3, M^+), 771 (1), 309 (base), 239 (24), 73 (41), 61 (39). *Anal.* Calcd for $C_{40}H_{76}O_6S_2Si_4$: C, 57.92; H, 9.23. Found: C, 57.83; H, 9.14.

General Procedure for Preparation of 1,3-Di-*tert*-butyldimethylsilyloxy-3-methylthiomethylbicyclo[2.2.2]oct-5-en-2-ones (4) A solution of the dimer (**11**) (1.42 g, 1.7 mmol) and the dienophiles (**8a**) (1.99 g, 17.1 mmol) in dry toluene solution (50 ml) was heated in a sealed tube at 120 °C for 2 d. Removal of the solvent under reduced pressure and chromatography of the residue over silica gel (eluent: 10% ethyl acetate in hexane) furnished the adduct **4a** (1.69 g, 93%).

The bicyclo[2.2.2]octenones (**4b—n**) were prepared similarly from the corresponding dienophiles (**8b—n**) and **11**. Physicochemical data for **4a—n** are summarized in Tables 2 and 5.

General Procedure for Preparation of 1-Hydroxy-8-methoxy-8-methylthiomethylbicyclo[3.2.1]oct-3-en-2-ones (5) from 3 A solution of **3a**[7] (1.65 g, 5.0 mmol) in 46% aqueous HF (or concentrated HCl)–acetone (2.0—100 ml) was stirred at 50 °C for 2 d. Excess of $NaHCO_3$ powder (5 g) was added and the solvent was evaporated. The residue was extracted with methylene dichloride (100 ml), and the organic layer was filtered with the aid of Celite. The filtrate was dried over $MgSO_4$, and the solvent was evaporated. The purification of the residue by column chromatography on silica gel (eluent: 10% ethyl acetate in hexane) afforded the 1-hydroxy-8-methoxybicyclo[3.2.1]octenone (**5a**) (0.93 g, 59%).

The 1-hydroxy-8-methoxybicyclo[3.2.1]octenones (**5b—g**) were prepared similarly from the corresponding bicyclo[2.2.2]octenones (**3b—g**).[7] Physico-chemical data for **5a—g** are summarized in Tables 1 and 6.

General Procedure for Preparation of 1,8-Dihydroxy-8-methylthiomethylbicyclo[3.2.1]oct-3-en-2-ones (6) from 4 by Treatment with TBAF (Method A) A 1 M solution of TBAF–THF (14 ml) was added to a solution of **4a** (2.65 g, 5.0 mmol) in THF (80 ml) at −30 °C. The reaction mixture was stirred for 24 h at room temperature, then quenched by adding brine. Usual work-up and purification by column chromatography on silica gel (eluent: 30% ethyl acetate in hexane) afforded the 1,8-dihydroxybicyclo[3.2.1]octenones (**6a**) (1.40 g, 93%).

The 1,5-dihydroxybicyclo[3.2.1]octenones (**6b—k**) were prepared similarly from the corresponding bicyclo[2.2.2]octenones (**4b—k**). Physicochemical data for **6a—k** are summarized in Tables 3 and 7.

(1α,5α,6*S,8*S**)-8-*tert*-Butyldimethylsilyloxy-5-hydroxy-8-methylthiomethyl-4-oxobicyclo[3.2.1]oct-2-ene-6-carboxyaldehyde (7g)** A 1 M solution of TBAF–THF (14 ml) was added to a solution of **4g** (2.35 g, 5.0 mmol) in THF (80 ml) at −30 °C. The reaction mixture was stirred for 24 h at the same temperature, then quenched by adding brine. Usual work-up and purification by column chromatography on silica gel (eluent: 20% ethyl acetate in hexane) afforded **7g** (0.77 g, 43%) as a colorless

Table 7. Spectral Data for **6**

Compd. No.	IR (KBr or neat) cm^{-1}	MS m/z M^+	^{1}H-NMR δ (ppm)	^{13}C-NMR δ (ppm)
6a	3496, 1685, 1610	302	2.11 (3H, s), 2.58 (2H, s), 2.68 (1H, dd, J = 17.5, 3.3), 3.10 (1H, ddm, J = 17.5, 10.6), 3.22 (1H, br s), 3.30 (1H, dd, J = 7.3, 6.9), 3.77—3.85 (1H, m), 4.28 (1H, d, J = 9.9), 4.33 (1H, br s), 5.85 (1H, d, J = 9.9), 7.01—7.14 (4H, m), 7.19 (1H, dd, J = 9.9, 7.6)	17.4 (CH_3), 33.3 (CH_2), 37.6 (CH_2), 41.6 (CH), 49.5 (CH), 57.5 (CH), 88.2 (C), 92.7 (C), 124.3 (CH × 2), 126.6 (CH), 127.3 (CH), 129.1 (CH), 141.1 (C), 143.6 (C), 152.8 (CH), 200.8 (C)
6b	3548, 1666	252	2.01 (1H, dm, J = 18.2), 2.11 (3H, s), 2.40—2.53 (1H, m), 2.59 (2H, ABq, J = 13.9), 3.20 (1H, br s), 3.18—3.23 (1H, m), 3.50—3.62 (1H, m), 3.66 (1H, dm, J = 9.6), 4.12 (1H, br s), 5.53—5.61 (2H, m), 6.19 (1H, d, J = 9.6), 7.20 (1H, dd, J = 9.6, 7.6)	17.4 (CH_3), 34.0 (CH_2), 37.8 (CH_2), 40.6 (CH), 49.2 (CH), 59.2 (CH), 87.9 (C), 91.7 (C), 129.1 (CH), 129.6 (CH), 133.2 (CH), 152.8 (CH), 201.4 (C)
6c	3540, 1700, 1660	292	1.72 (3H, s), 1.87 (3H, s), 2.12 (3H, s), 3.32 (2H, ABq, J = 13.9), 3.46 (1H, dd, J = 7.6, 7.3), 3.50 (1H, br s), 3.73 (1H, dm, J = 8.2), 3.92—3.97 (1H, m), 3.95 (1H, br s), 5.78 (1H, dd, J = 5.6, 2.3), 6.67 (1H, d, J = 9.6), 6.21 (1H, dd, J = 5.6, 2.0), 7.00 (1H, dd, J = 9.6, 7.6)	17.4 (CH_3), 20.8 (CH_3), 21.7 (CH_3), 37.8 (CH_2), 45.4 (CH), 48.7 (CH), 57.1 (CH), 87.7 (C), 91.4 (C), 125.2 (C), 127.7 (CH), 132.4 (CH), 134.7 (CH), 138.3 (C), 153.5 (CH), 201.3 (C)
6e	3440, 1708, 1665, 1603	256	2.03 (1H, ddm, J = 12.5, 4.3), 2.11 (3H, s), 2.13 (3H, s), 2.56 (1H, ddd, J = 12.5, 10.6, 6.6), 2.57 (2H, ABq, J = 13.9), 3.01 (1H, ddm, J = 7.3, 6.6), 3.47 (1H, br s), 3.78 (1H, dd, J = 10.6, 4.6), 4.33 (1H, br s), 6.23 (1H, d, J = 9.6), 7.35 (1H, dd, J = 9.6, 7.3)	17.4 (CH_3), 27.5 (CH_2), 30.3 (CH_3), 36.5 (CH_2), 45.2 (CH), 56.3 (CH), 87.1 (C), 91.2 (C), 127.5 (CH), 155.3 (CH), 199.9 (C), 207.0 (C)
6h	3480, 1728, 1686, 1615	272	1.97 (1H, ddm, J = 12.5, 4.3), 2.11 (3H, s), 2.59 (2H, ABq, J = 14.2), 2.75 (1H, ddd, J = 12.5, 10.5, 6.6), 3.04 (1H, dd, J = 9.6, 6.6), 3.28 (1H, br s), 3.62 (3H, s), 3.63 (1H, dd, J = 10.9, 4.3), 4.30 (1H, br s), 6.27 (1H, d, J = 9.6), 7.38 (1H, dd, J = 9.6, 7.6)	17.3 (CH_3), 29.5 (CH_2), 36.5 (CH_2), 45.2 (CH), 48.4 (CH), 52.1 (CH_3), 86.5 (C), 91.0 (C), 127.6 (CH), 155.0 (CH), 173.0 (C), 199.4 (C)
6j	3430, 1722, 1670, 1660	314	1.38 (9H, s), 1.95 (1H, ddm, J = 12.5, 4.3), 2.11 (3H, s), 2.59 (2H, ABq, J = 14.2), 2.69 (1H, ddd, J = 12.5, 10.9, 6.6), 3.01 (1H, ddm, J = 7.3, 6.6), 3.22 (1H, br s), 3.51 (1H, dd, J = 10.9, 4.3), 4.23 (1H, br s), 6.24 (1H, d, J = 9.6), 7.36 (1H, dd, J = 9.6, 7.3)	17.4 (CH_3), 27.9 (CH_3 × 3), 29.2 (CH_2), 36.6 (CH_2), 45.2 (CH), 49.1 (CH), 81.6 (C), 86.8 (C), 91.0 (C), 127.5 (CH), 155.0 (CH), 171.6 (C), 199.5 (C)
6k	3425, 2245, 1680	239	1.85 (1H, ddm, J = 12.9, 4.1), 2.12 (3H, s), 2.61 (2H, ABq, J = 14.2), 2.87—3.06 (1H, m), 3.14 (1H, dd, J = 6.9, 6.6), 3.63 (1H, dd, J = 10.9, 4.1), 3.67 (1H, br s), 4.60 (1H, br s), 6.41 (1H, dm, J = 9.6), 7.54 (1H, dd, J = 9.6, 6.9)	17.2 (CH_3), 31.4 (CH_2), 33.0 (CH), 36.0 (CH_2), 45.3 (CH), 85.2 (C), 91.1 (C), 119.6 (C), 127.0 (CH), 156.2 (CH), 197.6 (C)

Table 8. Spectral Data for **7**

Compd. No.	IR (KBr or neat) cm^{-1}	MS m/z M^+	^{1}H-NMR δ (ppm)	^{13}C-NMR δ (ppm)
7a	3280, 1695, 1610	416	0.29 and 0.31 (3H × 2, s), 0.98 (9H, s), 1.98 (3H, s), 2.69 (2H, ABq, J=12.9), 2.66 (1H, dd, J=17.5, 3.3), 3.08 (1H, dd, J=17.5, 10.3), 3.30 (1H, dd, J=7.3, 6.9), 3.70 (1H, dddd, J=10.3, 9.6, 6.9, 3.3), 4.20 (1H, d, J=9.6), 4.32 (1H, br s), 5.83 (1H, d, J=9.6), 6.99—7.12 (4H, m), 7.23 (1H, dd, J=9.6, 7.3)	−3.0 (CH_3), −2.5 (CH_3), 16.8 (CH_3), 19.0 (C), 26.2 (CH_3 × 3), 33.4 (CH_2), 37.6 (CH_2), 41.5 (CH), 51.0 (CH), 57.3 (CH), 91.5 (C), 93.9 (C), 124.3 (CH), 124.3 (CH), 126.4 (CH), 127.1 (CH), 128.5 (CH), 141.5 (C), 143.6 (C), 153.2 (CH), 201.8 (C)
7b	3390, 1680, 1610	366	0.24 (6H, s), 0.93 (9H, s), 1.91—2.02 (1H, m), 1.97 (3H, s), 2.35—2.48 (1H, m), 2.51 (2H, ABq, J=12.9), 3.18 (1H, ddm, J=7.6, 6.6), 3.41 (1H, dddd, J=13.2, 9.6, 6.6, 3.3), 3.50 (1H, dm, J=9.6), 4.02 (1H, br s), 5.48—5.58 (2H, m), 6.15 (1H, d, J=9.6), 7.21 (1H, dd, J=9.6, 7.6)	−3.1 (CH_3), −2.6 (CH_3), 16.8 (CH_3), 18.9 (C), 26.0 (CH_3 × 3), 34.1 (CH_2), 37.8 (CH_2), 40.5 (CH), 50.7 (CH), 59.0 (CH), 91.1 (C), 92.9 (C), 128.5 (CH), 130.0 (CH), 132.8 (CH), 153.1 (CH), 202.4 (C)
7c	3450, 1675, 1603	406	0.24 and 0.26 (3H × 2, s), 0.94 (9H, s), 1.65 (3H, s), 1.71 (3H, s), 1.97 (3H, s), 2.52 (2H, ABq, J=12.9), 3.40 (1H, dd, J=7.3, 6.9), 3.64 (1H, dm, J=8.2), 3.82 (1H, ddm, J=8.6, 6.9), 4.07 (1H, br s), 5.76 (1H, dd, J=5.6, 2.3), 6.04 (1H, d, J=9.6), 6.17 (1H, dd, J=5.6, 2.0), 7.00 (1H, dd, J=9.6, 7.3)	−3.1 (CH_3), −2.6 (CH_3), 16.8 (CH_3), 18.9 (C), 20.8 (CH_3), 21.7 (CH_3), 26.2 (CH_3 × 3), 37.9 (CH_2), 45.5 (CH), 50.4 (CH), 56.9 (CH), 90.7 (C), 92.4 (C), 124.8 (C), 127.3 (CH), 132.9 (CH), 134.3 (CH), 138.6 (C), 153.5 (CH), 202.2 (C)
7e	3460, 1710, 1665	370	0.27 and 0.29 (3H × 2, s), 0.95 (9H, s), 1.99 (3H, s), 2.03 (1H, ddm, J=12.5, 4.6), 2.09 (3H, s), 2.38 (1H, ddd, J=12.5, 10.2, 6.6), 2.51 (2H, ABq, J=13.2), 3.02 (1H, ddm, J=7.6, 6.6), 3.65 (1H, dd, J=10.2, 4.3), 4.30 (1H, br s), 6.19 (1H, d, J=9.6), 7.40 (1H, dd, J=9.6, 7.6)	−3.1 (CH_3), −2.4 (CH_3), 16.8 (CH_3), 18.9 (C), 26.2 (CH_3 × 3), 27.1 (CH_2), 30.3 (CH_3), 36.4 (CH_2), 46.6 (CH), 56.2 (CH), 90.7 (C), 92.5 (C), 126.8 (CH), 156.2 (CH), 200.7 (C), 207.1 (C)
7g	3450, 1722, 1680, 1602	356	0.26 and 0.27 (3H × 2, s), 0.93 (9H, s), 1.99 (3H, s), 2.00 (1H, dm, J=12.9), 2.43 (1H, ddd, J=12.9, 10.2, 6.6), 2.52 (2H, ABq, J=12.9), 3.05 (1H, ddm, J=7.6, 6.6), 3.48 (1H, ddd, J=10.2, 4.0, 1.3), 4.33 (1H, br s), 6.18 (1H, d, J=9.6), 7.43 (1H, dd, J=9.6, 7.6), 9.90 (1H, d, J=1.3)	−3.1 (CH_3), −2.5 (CH_3), 16.8 (CH_3), 18.9 (C), 25.6 (CH_2), 26.1 (CH_3 × 3), 36.0 (CH_2), 46.9 (CH), 55.8 (CH), 90.2 (C), 92.1 (C), 126.4 (CH), 156.8 (CH), 200.4 (C), 200.8 (CH)
7h	3450, 1740, 1680, 1610	386	0.24 and 0.26 (3H × 2, s), 0.93 (9H, s), 1.91 (1H, ddm, J=12.5, 4.5), 1.98 (3H, s), 2.52 (2H, ABq, J=13.2), 2.60 (1H, ddd, J=12.5, 10.9, 6.6), 3.02 (1H, ddm, J=7.3, 6.6), 3.50 (1H, dd, J=10.9, 4.5), 3.59 (3H, s), 4.22 (1H, br s), 6.23 (1H, d, J=9.4), 7.40 (1H, dd, J=9.4, 7.3)	−3.2 (CH_3), −2.5 (CH_3), 16.8 (CH_3), 18.9 (C), 26.1 (CH_3 × 3), 29.5 (CH_2), 36.4 (CH_2), 46.7 (CH), 48.4 (CH), 52.1 (CH_3), 90.0 (C), 92.2 (C), 127.1 (CH), 155.5 (CH), 173.3 (C), 200.4 (C)
7i	3460, 1740, 1710, 1610	400	0.24 and 0.26 (3H × 2, s), 0.93 (9H, s), 1.19 (3H, t, J=7.3), 1.90 (1H, ddm, J=12.5, 4.3), 1.98 (3H, s), 2.52 (2H, ABq, J=12.9), 2.60 (1H, ddd, J=12.5, 10.8, 6.6), 3.01 (1H, ddm, J=7.3, 6.6), 3.47 (1H, dd, J=10.8, 4.3), 4.05 (2H, q, J=7.3), 4.21 (1H, br s), 6.22 (1H, d, J=9.6), 7.39 (1H, dd, J=9.6, 7.3)	−3.2 (CH_3), −2.5 (CH_3), 14.1 (CH_3), 16.8 (CH_3), 18.9 (C), 26.1 (CH_3 × 3), 29.4 (CH_2), 36.4 (CH_2), 46.7 (CH), 48.3 (CH), 61.0 (CH_2), 90.0 (C), 92.2 (C), 127.1 (CH), 155.4 (CH), 172.8 (C), 200.3 (C)
7j	3410, 1735, 1700, 1610	428	0.23 and 0.24 (3H × 2, s), 0.91 (9H, s), 1.31 (9H, s), 1.88 (1H, ddm, J=12.7, 4.3), 1.90 (3H, s), 2.51 (2H, ABq, J=13.2), 2.60 (1H, ddd, J=12.7, 10.9, 6.6), 3.00 (1H, ddm, J=7.6, 6.6), 3.51 (1H, dd, J=10.9, 4.3), 5.28 (1H, br s), 6.22 (1H, d, J=9.6), 7.37 (1H, dd, J=9.6, 7.6)	−3.1 (CH_3), −2.5 (CH_3), 16.8 (CH_3), 18.9 (C), 26.1 (CH_3 × 3), 28.6 (CH_3 × 3), 29.4 (CH_2), 36.4 (CH_2), 46.7 (CH), 48.3 (CH), 51.4 (C), 90.0 (C), 92.1 (C), 127.1 (CH), 155.3 (CH), 176.9 (C), 200.0 (C)
7k	3440, 2245, 1685, 1605	353	0.23 and 0.24 (3H × 2, s), 0.91 (9H, s), 1.79 (1H, ddm, J=12.9, 4.3), 1.99 (3H, s), 2.52 (2H, ABq, J=13.2), 2.80 (1H, ddd, J=12.9, 10.9, 6.4), 3.10 (1H, ddm, J=7.6, 6.4), 3.45 (1H, dd, J=10.9, 4.3), 4.39 (1H, br s), 6.38 (1H, d, J=9.6), 7.53 (1H, dd, J=9.6, 7.6)	−3.2 (CH_3), −2.6 (CH_3), 16.8 (CH_3), 18.8 (C), 26.0 (CH_3 × 3), 31.6 (CH_2), 33.0 (CH), 36.0 (CH_2), 47.0 (CH), 88.6 (C), 92.1 (C), 119.8 (C), 126.7 (CH), 156.5 (CH), 198.3 (C)
7l	3450, 1720, 1680, 1605	426	0.24 (6H, s), 0.92 (9H, s), 1.24 (3H, t, J=6.9), 1.50 (1H, ddm, J=12.7, 4.3), 1.98 (3H, s), 2.53 (2H, ABq, J=13.2), 2.62 (1H, ddd, J=12.7, 10.2, 6.9), 3.03 (1H, ddm, J=7.6, 6.9), 3.31—3.40 (1H, m), 4.12 (2H, q, J=6.9), 4.12 (1H, br s), 5.77 (1H, dd, J=15.5, 1.3), 6.19 (1H, d, J=9.6), 6.52 (1H, dd, J=15.5, 8.2), 7.49 (1H, dd, J=9.6, 7.6)	−3.1 (CH_3), −2.6 (CH_3), 14.2 (CH_3), 16.8 (CH_3), 18.9 (C), 26.1 (CH_3 × 3), 31.1 (CH_2), 36.7 (CH_2), 45.5 (CH), 47.0 (CH), 60.3 (CH_2), 89.6 (C), 93.8 (C), 123.3 (CH), 126.6 (CH), 146.5 (CH), 157.3 (CH), 165.8 (C), 200.8 (C)
7m	3250, 1780, 1710, 1685, 1600	397	0.26 (6H, s), 0.93 (9H, s), 1.99 (3H, s), 2.51 (2H, ABq, J=13.2), 3.53 (1H, dd, J=7.3, 7.3), 3.65 (1H, d, J=8.9), 3.89 (1H, dd, J=8.9, 7.3), 4.53 (1H, br s), 6.40 (1H, d, J=9.6), 7.31 (1H, dd, J=9.6, 7.3)	−3.2 (CH_3), −2.6 (CH_3), 16.8 (CH_3), 18.8 (C), 26.1 (CH_3 × 3), 36.1 (CH_2), 47.9 (CH), 48.4 (CH), 51.8 (CH), 91.4 (C), 93.4 (C), 129.3 (CH), 151.6 (CH), 175.9 (C), 176.4 (C), 197.5 (C)
7n	3490, 1780, 1705, 1600	411	0.25 and 0.26 (3H × 2, s), 0.92 (9H, s), 1.98 (3H, s), 2.50 (2H, ABq, J=13.2), 2.84 (3H, s), 3.55 (1H, dd, J=7.3, 7.3), 3.62 (1H, d, J=8.6), 3.87 (1H, dd, J=8.6, 7.3), 4.43 (1H, br s), 6.29 (1H, d, J=9.6), 7.25 (1H, dd, J=9.6, 7.3)	−3.3 (CH_3), −2.6 (CH_3), 16.8 (CH_3), 18.8 (C), 24.7 (CH_3), 26.1 (CH_3 × 3), 36.1 (CH_2), 46.6 (CH), 48.3 (CH), 50.6 (CH), 91.1 (C), 93.5 (C), 128.8 (CH), 151.8 (CH), 175.4 (C), 176.2 (C), 197.5 (C)

oil. Physicochemical data for **7g** are summarized in Tables 3 and 8.

General Procedure for Preparation of 8-*tert*-Butyldimethylsilyloxy-1-hydroxy-8-methylthiomethylbicyclo[3.2.1]oct-3-en-2-ones (7) from 4 under an Acidic Condition (Method B) A solution of **4a** (2.65 g, 5.0 mmol) in 46% aqueous HF–MeCN (2.0—100 ml) was stirred at 50 °C for 24 h. The reaction mixture was worked up in the same manner as in method A, and purification by column chromatography on silica gel (eluent: 20% ethyl acetate in hexane) afforded the 1-hydroxybicyclo[3.2.1]octenone (**7a**) (0.89 g, 43%).

Other 1,5-dihydroxybicyclo[3.2.1]octenones (**7b—n**) were prepared similarly from the corresponding bicyclo[2.2.2]octenones (**4b—n**). Physicochemical data for **7a—n** are summarized in Tables 4 and 8.

X-Ray Analysis of Compound 2 A plate-shaped crystal with dimensions of $0.4 \times 0.3 \times 0.2$ mm was used for X-ray crystallography. Formula $C_{19}H_{26}O_6S_2$, $Mr = 414.531$; triclinic, space group $P\text{-}1$; cell parameters: $a = 10.648(1)$, $b = 12.308(1)$, $c = 8.625(1)$ Å, $\alpha = 93.16(1)$, $\beta = 101.25(1)$, $\gamma = 115.56(0)°$, $V = 987.7(1)$ Å^3, $Z = 2$, $D_c = 1.394$ g/cm^3. The intensity data were collected by the $2\theta/w$ scan technique using graphite-monochromated Cu-$K\alpha$ radiation ($\lambda = 1.5418$ Å) on a four-circle diffractometer (Rigaku AFC5R) at 293 K. Of the 3572 reflections up to $\theta_{max} = 130°$, 3049 with $|F_O| > 2(|F_O|)$ were considered to be significant and were used in the refinement. The structure was solved by the direct method using SHELXS-86[10] and refined by a full-matrix least-squares method using SHELXL-93.[11] Residual electron densities in the final difference map were in the range of -1.139 e/Å^3 to 0.903 e/Å^3. The final R-factors converged to $R = 0.054$, $wR = 0.046$. Full crystallographic details have been deposited with the Cambridge Crystallographic Data Center, under the accession code 207/67.

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