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HIGH-PRESSURE MEDIATED ASYMMETRIC DIELS-ALDER REACTION OF CHIRAL SULFINYLACRYLATE DERIVATIVES AND ITS APPLICATION TO CHIRAL SYNTHESIS OF (–)-COTC AND (–)-GABOSINE C[†]

Tamiko Takahashi,* Yoko Yamakoshi,[‡] Kazuya Okayama, Junko Yamada, Wei-Ying Ge, and Toru Koizumi[§]
Faculty of Pharmaceutical Sciences, Toyama Medical & Pharmaceutical University, 2630 Sugitani, Toyama 930-0194, Japan

Abstract – The asymmetric Diels-Alder reactions of chiral sulfinylacrylate derivatives **(1** and **2)** with dienes **(3**–**12)** were examined under high-pressure (1.2 GPa) conditions. The *endo* cycloadduct **(13e)** obtained from sulfinyl acrylate **(1)** and 2-methoxyfuran **(5)** was converted to (–)-COTC **(25)** and (–)-gabosine C **(26)**.

The asymmetric Diels-Alder (D-A) reaction is one of the most efficient tools for constructing optically active cyclic compounds bearing up to four stereogenic centers in a single operation.[1] In a large number of highly asymmetric D-A reactions, there are numerous examples of cycloadditions of chiral dienophiles with active dienes such as cyclopentadiene.[2] Although considerable effort has been devoted to designing powerful chiral dienophiles which react with less active dienes such as furans, there are few successful examples of such cycloadditions.[3] Having negative volume of activation, D-A reaction is amenable to high-pressure conditions.[4] Moreover, high-pressure techniques have been known to be an efficient method not only for the synthesis of molecules sensitive to Lewis acid catalysis but also for enhancement of asymmetric induction.[5] Applying this technique, asymmetric D-A reactions would proceed without a Lewis acid between unactivated dienophiles and less active dienes,[6] and this strategy could have wide application. In a previous report,[7] we demonstrated high-pressure mediated asymmetric D-A reaction of chiral sulfinylacrylate derivatives **(1**[8] and **2)** with furan **(4)** or 2-methoxyfuran **(5)**. We wish to report here the scope and limitations of this method and the application of the cycloadduct **(13e)** to the chiral synthesis of a glyoxalase I inhibitor, (–)-COTC **(25)**[3c,9] and (–)-gabosine C (antibiotic KD16-U1) **(26)**[10] in detail.

(+)-*Z*-3-(2-*exo*-Hydroxy-10-bornyl)propenamide **(2)** was prepared in two steps from 10-mercapto-2-*exo*-borneol[8] by successive Michael addition to propiolamide[11] and selective *m*CPBA oxidation in 43% overall yield. In order to establish the scope and limitations of high-pressure mediated asymmetric D-A reaction of the dienophiles **(1** and **2)**, we investigated this reaction with various non-activated dienes **(4**–**7**, **9**–**12)** and with Danishefsky's diene **(8)** (Figure 1).

In our preliminary experiments, the steric course of the cycloaddition of **1** and **2** with cyclopentadiene **(3)** under high-pressure conditions was compared with that under atmospheric pressure conditions (Figures 1

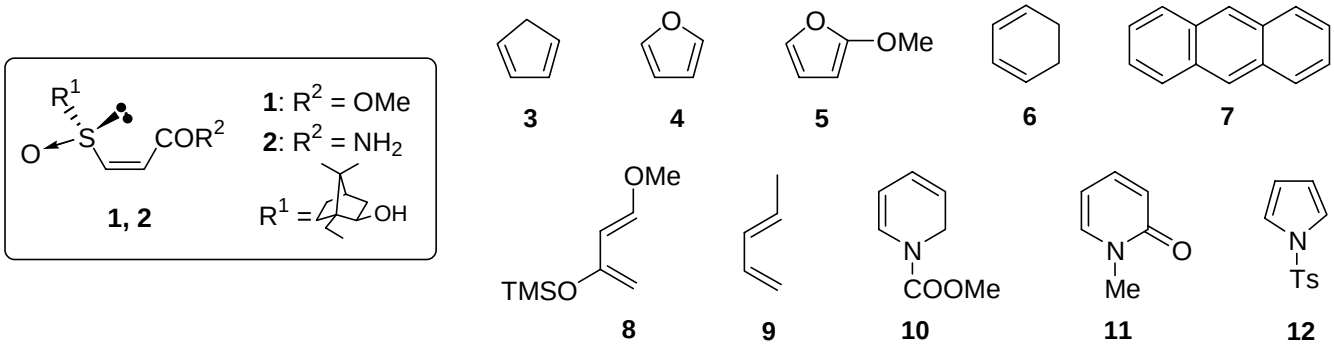


Figure 1

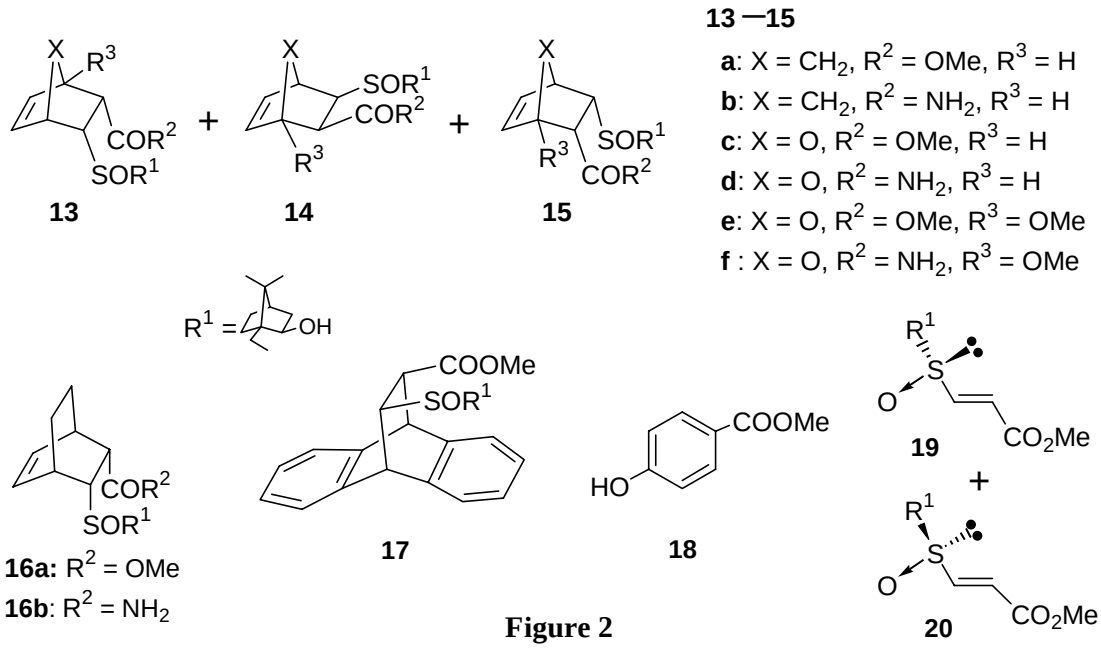


Figure 2

and 2). Reactions of **1** with **3** in CH_2Cl_2 proceeded readily at rt under both atmospheric and high-pressure (1.2 GPa) conditions to give the same *endo* cycloadduct **(13a)** as a single diastereomer in 92 and 88% yields, respectively. Similar reactions of **2** with **3** in CH_2Cl_2/MeOH (1:1) under atmospheric or high-pressure conditions gave *endo* cycloadduct **(13b)** and *exo* cycloadduct **(14b)** in 87 and 5% yields or 81 and 9% yields, respectively. All of these reactions proceeded with high diastereoselectivity and regioselectivity. The structure of **13a** was confirmed by comparison of its spectral data with those in the literature[8] and the absolute configuration of product **(13b)** was determined by X-Ray diffraction analysis. From these results, the same steric course was suggested for the reaction of **1** or **2** with **3** under both atmospheric and high-pressure conditions.[3b–e] The conformation for C=C–S=O of **1** and **2** should be oriented *s-trans* due to strong dipole-dipole repulsion between sulfinyl and carbonyl groups. An attack of **3** from the less hindered face (lone pair-side) is favored to give adducts **(13a,b)** (Figure 3).

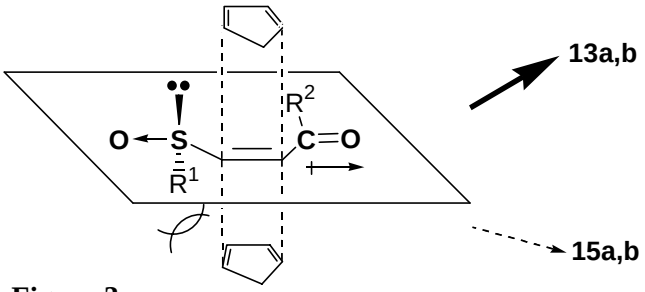


Figure 3

Most of the attempts to achieve the D-A reactions of dienophiles **(1** and **2)** with dienes **(4**–**12)** under thermal conditions (50–100 °C) were unsuccessful and the starting dienophiles were recovered. Reactions

of **1** with **6** and **8** in CH_2Cl_2 at 50 °C for 3 days in a sealed tube gave cycloadduct **(16a)** (9% yield) and methyl 4-hydroxybenzoate **(18)**[12] (8% yield), respectively. The adduct of **1** with **8** was not stable under the reaction conditions, and decomposed by spontaneous elimination of sulfenic acid and methanol as well as desilylation to afford **18**. In the presence of $ZnCl_2$, a sluggish reaction was observed between **1** and **6** to give **16a** (33% yield) at 70 °C after 4 days, whereas no reaction proceeded at all in the cases of **1** with **7** and **9**–**12**. In contrast, D-A reaction took place under high-pressure (1.2 GPa) conditions. The most significant results are summarized in Table 1. The high-pressure reaction conditions proved to be very effective for asymmetric D-A reactions of **1** and **2** with dienes **(4**–**7)** in respect of diastereoselectivity (from 95:5 to 100:0) and regioselectivity (from 71:29 to 100:0) giving the cycloadducts **(13**–**17)** (entries 1–7). Due to lower reactivity of the amide **2**, the diastereoselectivity of the reactions of **2** may be higher than that of the ester **1**. The configuration of *endo* and *exo* cycloadducts **(13**–**16)** was deduced by ^{1}H-NMR spectra and mechanistic consideration.[3b–e] Reaction of **1** with **8** gave **18** in low yield (entry 8). In the reaction of **1** with **9**, only isomerized dienophiles **19**[13] and **20**[13] were obtained (entry 9). All reactions of **2** with **7**–**12** as well as of **1** with **10**–**12** did not occur at all. From these results, high-pressure mediated conditions are proved to be especially suited for the asymmetric D-A reaction of the dienophiles **(1** and **2)** with furans **(4** and **5)**.

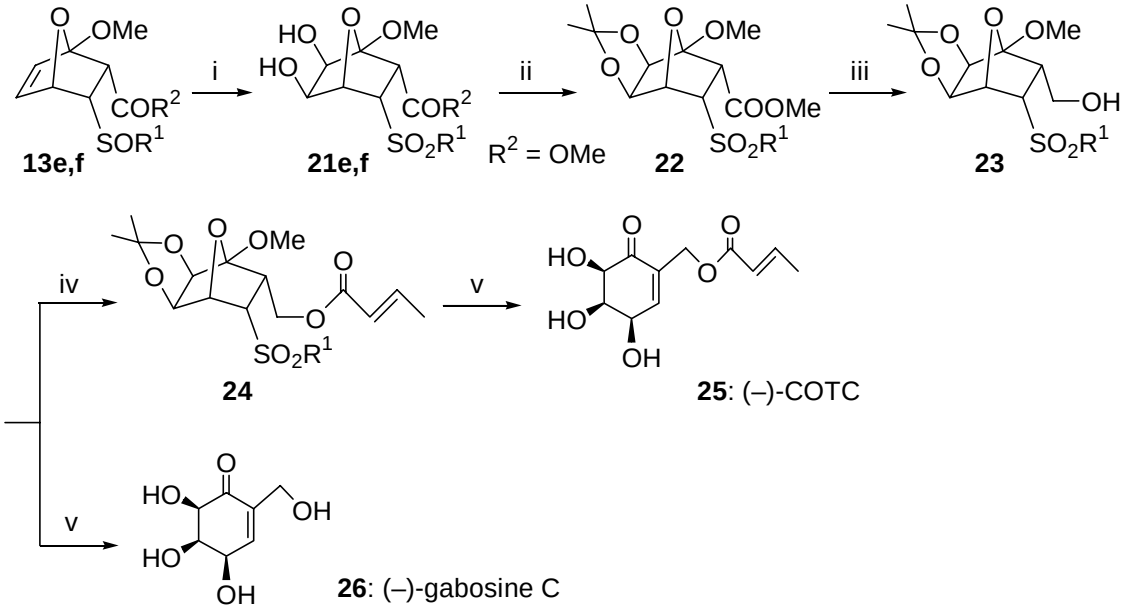
Table 1. High-Pressure (1.2 GPa) Mediated Asymmetric D-A Reactions of Chiral Sulfinylacrylate Derivatives **(1** and **2)** with Dienes **(4**–**9)**

			reaction conditions				
entry	dienophile	diene	temp.	solv.[a]	time (days)	products (ratio)[b]	yield (%)
1	**1**	**4**	rt[c]	A	3	**13c**/**14c**/**15c** (82:14:4)	94
2	**2**	**4**	rt[c]	B	3	**13d** (100)	81
3	**1**	**5**	rt[c]	A	3	**13e**/**14e** (71:29)	d
4	**2**	**5**	rt[c]	B	3	**13f**/**14f** (92:8)	e
5	**1**	**6**	50 °C	A	3	**16a**	32
6	**2**	**6**	50 °C	B	7	**16b**	28
7	**1**	**7**	80 °C	A	7	**17**	13
8	**1**	**8**	80 °C	A	3	**18**	18
9	**1**	**9**	50 °C	A	7	**19**/**20** (85:15)	26

a) A: CH_2Cl_2; B: CH_2Cl_2/MeOH (1:1). b) Ratios were determined by ^{1}H-NMR spectroscopy. c) Rt. d) Because of its instability, **13e** was isolated as diol **(21e)** after dihydroxylation (53% yield from **1**). e) Because of its instability, **13f** was isolated as diol **(21f)** after dihydroxylation (63% yield from **2**).

In order to confirm the absolute configuration of major *endo* adduct **(13)**, **13e** was converted to (–)-COTC **(25)** and gabosine C **(26)** (Scheme 1). Dihydroxylation of **13e** afforded diol **(21e)** (53% yield from **1**). Acetonide formation of **21e** gave **22** (64% yield). Reaction of **22** with $LiAlH_4$ afforded alcohol **(23)** which was esterified with crotonic anhydride to give **24** (43% yield from **22**). Treatment of **24** with trifluoroacetic acid (TFA) afforded (–)-COTC **(25)** (29% yield). Likewise, treatment of **23** with TFA gave

(–)-gabosine C **(26)** (51% yield from **22**). ^{1}H-NMR and IR spectra of **25** and **26** were identical with those reported.[3c,9,10] From these results, the absolute configuration of **13e** was determined as shown in Figure 2



i) cat. OsO_4, Me_3NO, acetone, 0 °C then rt, **21e**: 53% from **1**, **21f**: 63% from **2**; ii) 2,2-dimethoxypropane, cat. *p*-TsOH, acetone, reflux, 64%; iii) $LiAlH_4$, THF, rt; iv) crotonic anhydride, pyridine, DMAP, benzene, rt, 43% from **22**; v) 80% aqueous TFA, –20 °C, **25**: 29%, **26**: 51% from **22.**

Scheme 1

and Scheme 1. Accordingly, the steric course of the reaction was confirmed to be the same in these asymmetric cycloadditions under both atmospheric and high-pressure conditions.

In conclusion, we have successfully developed high-pressure mediated asymmetric D-A reaction of unactivated dienophiles, sulfinylacrylate derivatives **(1** and **2)**, with less active dienes. This technique proved to be very effective for combination of **1** and **2** with the dienes **(4**–**7)** in respect of diastereoselectivity and regioselectivity. However, the dienes **(8**–**12)** were not suited for this reaction. Transformation of the major *endo* adduct **(13e)** to (–)-COTC **(25)** and (–)-gabosine C **(26)** provided not only determination of the absolute configuration of **13e** but also a new strategy for a chiral synthesis of natural polyoxygenated cyclohexane derivatives.

EXPERIMENTAL

Melting points were measured with a Yanaco micro melting point apparatus and are uncorrected. Microanalyses were performed by Microanalysis Center of Toyama Medical & Pharmaceutical University. Spectroscopic measurements were carried out with the following instruments: optical rotations, JASCO DIP-1000 digital polarimeter; IR, Perkin-Elmer 1600 Series FTIR; ^{1}H-NMR, Varian Gemini 300 (300 MHz) and Varian Unity 500 (500 MHz) for solutions in $CDCl_3$, $CDCl_3$/CD_3OD or CD_3OD with Me_4Si as internal standard; ^{13}C-NMR, Varian Gemini 300 (75 MHz) for solutions in CD_3OD with Me_4Si as internal standard; MS and HRMS spectra, JEOL JMS D-200 and JEOL JMS AX-505H. High-pressure reactions were carried out by using an ordinary high-pressure apparatus. Column chromatography, flash column chromatography, and preparative TLC (PLC) were performed on Kieselgel 60 (Merck, Art. 7734, Art. 9385 and Art. 7748, respectively) and cellulose (Merck, Art. 15275).

***Z*-3-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylthio)propenamide** A solution of 10-mercapto-2-*exo*-borneol[8] (8.0 g, 43 mmol) in MeOH/H_2O (9:1, 50 mL) was added dropwise to a solution of propiolamide[11] (3.0 g, 43 mmol) in MeOH/H_2O (9:1, 150 mL) with stirring at –20 °C. After being stirred at –20 °C for 15 min, Et_3N (15 drops) was added to the reaction mixture. The mixture was stirred at rt for 8 h and MeOH was evaporated. The aqueous layer was extracted with AcOEt (200 mL x 3). Combined extracts were washed with brine, dried over $MgSO_4$ and concentrated. The residue [10.8 g, a mixture of *Z* and *E* isomers (7:3) by ^{1}H-NMR] was recrystallized from AcOEt/hexane to give *Z*-3-({(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylthio)propenamide (6.1 g, 56%) as colorless needles. mp 155–156 °C. $[\alpha]_D^{26}$ –25.1° (*c* 1.00, MeOH). IR (KBr) 3432, 3305, 3214, 2952, 2916, 1643, 1564, 1564, 1305 cm^{-1}. ^{1}H-NMR ($CDCl_3/CD_3OD$, 1:1) δ 0.89 and 1.06 (each 3H, s, Me x 2), 1.0–1.1 (1H, m, bornyl H), 1.2–1.3 (1H, m, bornyl H), 1.55–1.65 (1H, m, bornyl H), 1.7–1.8 (4H, m, bornyl H), 2.67 (1H, d, *J* = 12.6 Hz, 10-H^a), 3.17 (1H, d, *J* = 12.6 Hz, 10-H^b), 3.85 (1H, dd, *J* = 7.8 and 3.7 Hz, 2-H), 5.87 (1H, d, *J* = 10.0 Hz, CH=), 7.14 (1H, d, *J* = 10.0 Hz, CH=). MS *m/z* 255 (M^+). *Anal.* Calcd for $C_{13}H_{21}NO_2S$: C, 61.14; H, 8.29; N, 5.49. Found: C, 60.90; H, 8.32; N, 5.27.

***Z*-3-({(1*S*,2*R*,4*R*,R_S)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)propenamide (2)** A solution of *m*-CPBA (80%, 1.264 g, 5.86 mmol) in dry CH_2Cl_2 (20 mL) was added dropwise to a solution of *Z*-3-({(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylthio)propenamide (1.271 g, 4.99 mmol) in dry CH_2Cl_2 (50 mL) with stirring at –20 °C under argon. After being stirred at –20 °C for 3 h, the reaction mixture was diluted with $CHCl_3$ (50 mL) and the organic layer was washed with 5% $NaHCO_3$ (50 mL) followed by brine (40 mL), dried over $MgSO_4$ and concentrated. The residue was recrystallized from AcOEt/MeOH/hexane to give **2** (1.02 g, 76%) as colorless prisms. mp 210–212 °C. $[\alpha]_D^{26}$ +330.1° (*c* 1.01, MeOH). IR (KBr) 3315, 3306, 3292, 3276, 3204, 2938, 2913, 1688, 1660, 1611, 1399, 1081, 1033 cm^{-1}. ^{1}H-NMR ($CDCl_3/CD_3OD$, 1:1) δ 0.87 and 1.08 (each 3H, s, Me x 2), 1.15–1.25 (1H, m, bornyl H), 1.5–1.6 (1H, m, bornyl H), 1.75–2.0 (5H, m, bornyl H), 3.02 (1H, d, *J* = 12.8 Hz, 10-H^a), 3.44 (1H, d, *J* = 12.8 Hz, 10-H^b), 4.04 (1H, dd, *J* = 7.9 and 4.2 Hz, 2-H), 6.51 (1H, d, *J* = 9.8 Hz, CH=), 6.79 (1H, d, *J* = 9.8 Hz, CH=). MS *m/z* 272 (M^+ + 1), 255 (M^+ – O). *Anal.* Calcd for $C_{13}H_{21}NO_3S$: C, 57.53; H, 7.80; N, 5.16. Found: C, 57.73; H, 7.77; N, 5.14.

Typical Procedure for Asymmetric Diels-Alder Reaction of a Dienophile (1 or 2) with a Diene (3–12) under Atmospheric Pressure Conditions A solution of a dienophile **(1**[7] or **2)** (0.20–0.83 mmol) and **3** (4.1–17 mmol) in dry CH_2Cl_2 (3–40 mL) or in dry CH_2Cl_2/MeOH (1:1) (3–40 mL) was stirred in a sealed tube under the conditions as shown in Table 1. After evaporation of the solvent, the residue was purified by column chromatography on silica gel with hexane followed by hexane/AcOEt (1:1) or AcOEt (for the reaction of **1** with **3**) or with hexane followed by $CHCl_3$/MeOH (10:1) (for the reaction of **2** with **3**). The ratio of products were determined by ^{1}H-NMR spectroscopy of the crude mixture.

Typical Procedure for Asymmetric Diels-Alder Reaction of a Dienophile (1 or 2) with a Diene (3–12) under High-Pressure Conditions A solution of a dienophile **(1** or **2)** (0.21–2.21 mmol) and **3** (4.1–22.8 mmol) in dry CH_2Cl_2 (10 mL) or in dry CH_2Cl_2/MeOH (1:1) (10 mL) was placed in a Teflon tube plugged with a Teflon stopper. The tube was placed in a high-pressure reactor and pressurized to 1.2 Gpa under the conditions as shown in Table 1. The pressure was released and the reaction mixture was

concentrated. The ratio of products was determined by ^{1}H-NMR spectroscopy of the crude mixture. The mixture from the reaction of **1** or **2** with **3** was purified by the procedure described as above. The products, yield and diastereomer excess are listed in Table 1.

(1*R*,*R*$_S$)-Methyl 3-*endo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylate (13a): Colorless plates. mp 136–139 °C (lit.,[6] mp 130 °C). $[\alpha]_D^{26}$ –1.9° (*c* 0.33, $CHCl_3$) (lit.,[6] $[\alpha]_D^{20}$ +4.44° (*c* 1, $CHCl_3$)). IR ($CHCl_3$) 3392, 2955, 1730 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.82 and 1.11 (each 3H, s, Me x 2), 1.1–1.9 (7H, m, bornyl H), 1.42 (1H, d, *J* = 9.3 Hz, 7-H^a), 1.68 (1H, d, *J* = 9.3 Hz, 7-H^b), 2.94 (1H, d, *J* = 12.6 Hz, 10'-H^a), 3.05 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.35–3.4 (2H, m, 1-H and 2-H), 3.53 (1H, br s, 4-H), 3.63 (1H, dd, *J* = 8.8 and 3.3 Hz, 3-H), 3.64 (3H, s, OMe), 4.03 (1H, dd, *J* = 8.0 and 4.1 Hz, 2'-H), 4.2-4.25 (1H, br, OH), 6.33 (1H, dd, *J* = 5.5 and 2.8 Hz, CH=), 6.49 (1H, dd, *J* = 5.5 and 2.8 Hz, CH=).

(1*R*,*R*$_S$)-3-*endo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxamide (13b): Colorless needles. mp 277–278 °C. $[\alpha]_D^{26}$ +28.3° (*c* 0.73, MeOH). IR (KBr) 3374, 3206, 2967, 1660, 1391, 1074, 1031 cm^{-1}. ^{1}H-NMR ($CDCl_3$/CD_3OD, 1:1) δ 0.82 and 1.08 (each 3H, s, Me x 2), 1.1–1.2 (1H, m, bornyl H), 1.4–1.45 (1H, m, bornyl H), 1.51 (1H, d, *J* = 11.0 Hz, 7-H^a), 1.6–1.85 (5H, m, bornyl H), 1.71 (1H, d, *J* = 10.9 Hz, 7-H^b), 2.95 (1H, d, *J* = 12.8 Hz, 10'-H^a), 3.01 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.36 (1H, br s, 1-H), 3.43 (1H, dd, *J* = 8.8 and 3.4 Hz, 2-H), 3.47 (1H, br s, 4-H), 3.56 (1H, dd, *J* = 8.8 and 3.4 Hz, 3-H), 4.02 (1H, dd, *J* = 8.2 and 4.0 Hz, 2'-H), 6.31 (1H, dd, *J* = 5.7 and 2.9 Hz, CH=), 6.49 (1H, dd, *J* = 5.8 and 2.8 Hz, CH=). MS *m/z* 338 (M^+ + 1), 337 (M^+). *Anal.* Calcd for $C_{18}H_{27}NO_3S$: C, 64.06; H, 8.06, N, 4.15. Found: C, 64.04; H, 8.04; N, 4.19.

(1*S*,*R*$_S$)-3-*exo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)bicyclo[2.2.1]hept-5-ene-2-*exo*-carboxamide (14b): Crystalline mass (a mixture of **13b**/**14b**, 95:5). For **14b**: ^{1}H-NMR ($CDCl_3$/CD_3OD, 1:1) δ (a mixture of **13b**/**14b**, 95:5): 0.83 and 1.07 (each 3H, s, Me x 2), 2.82 (1H, d, *J* = 12.8 Hz, 10'-H^a), 3.01 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.10 (1H, br s, 1-H), 3.41 (1H, d, *J* = 8.8 Hz, 2-H), 6.29 (1H, dd, *J* = 5.7 and 2.9 Hz, CH=), 6.36 (1H, dd, *J* = 5.7 and 2.9 Hz, CH=).

(1*R*,*R*$_S$)-Methyl 3-*endo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)-7-oxabicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylate (13c): Colorless oil (a mixture of **13c**/**14c**/**15c**/**1**, 80:13:2:5) . For **13c**: ^{1}H-NMR ($CDCl_3$) (a mixture of **13c**/**14c**/**15c**/**1**, 80:13:2:5) δ 0.85 and 1.13 (each 3H, s, Me x 2), 1.1–1.9 (7H, m, bornyl H), 3.08 (1H, d, *J* = 12.6 Hz, 10'-H^a), 3.20 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.53 (1H, dd, *J* = 9.2 and 4.5 Hz, 2-H), 3.67 (3H, s, OMe), 3.85 (1H, dd, *J* = 9.2 and 4.5 Hz, 3-H), 3.99 (1H, dd, *J* = 8.6 and 4.1 Hz, 2'-H), 5.31 (1H, ddd, *J* = 4.5, 1.3 and 1.3 Hz, 1-H), 5.35 (1H, ddd, *J* = 4.5, 1.2 and 1.2 Hz, 4-H), 6.64 (1H, dd, *J* = 5.8 and 1.7 Hz, CH=), 6.83 (1H, dd, *J* = 5.8 and 1.5 Hz, CH=).

(1*S*,*R*$_S$)-Methyl 3-*exo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)-7-oxabicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylate (14c): Colorless oil (a mixture of **13c**/**14c**/**15c**/**1**, 80:13:2:5) . For **14c**: ^{1}H-NMR ($CDCl_3$) (a mixture of **13c**/**14c**/**15c**/**1**, 80:13:2:5) δ 2.85 (1H, d, *J* = 8.1 Hz, 2-H), 2.90 (1H, d, *J* = 12.8 Hz, 10'-H^a), 3.09 (1H, d, *J* = 8.1 Hz, 3-H), 3.11 (1H, d, *J* = 13.0 Hz, 10'-H^b), 3.75 (3H, s, OMe), 4.05 (1H, dd, *J* = 8.4 and 4.2 Hz, 2'-H), 5.43 (1H, br s, 1-H), 5.64 (1H, br s, 4-H), 6.52 (1H, dd, *J* = 5.8 and 1.7 Hz, CH=), 6.54 (1H, dd, *J* = 5.8 and 1.7 Hz, CH=).

(1*S*,R_S)-Methyl 3-*endo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)-7-oxabicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylate (15c): Colorless oil (a mixture of **13c**/**14c**/**15c**/**1**, 80:13:2:5) . For **15c**: ^{1}H-NMR ($CDCl_3$) (a mixture of **13c**/**14c**/**15c**/**1**, 80:13:2:5) δ 3.74 (3H, s, OMe), 5.07 (1H, m, 1-H), 5.23 (1H, m, 4-H), 6.42 (1H, dd, *J* = 5.8 and 1.7 Hz, CH=), 6.72 (1H, dd, *J* = 5.8 and 1.7 Hz, CH=).

(1*R*,R_S)-3-*endo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)-7-oxabicyclo[2.2.1]hept-5-ene-2-*endo*-carboxamide (13d): Colorless plates. mp 182–185 °C (CH_2Cl_2/hexane). $[\alpha]_D^{26}$ +33.6° (*c* 0.75, MeOH). IR (KBr) 3376, 3192, 2945, 1696, 1659, 1392, 1323, 1075, 1028 cm^{-1}. ^{1}H-NMR ($CDCl_3$/CD_3OD) δ 0.81 and 1.09 (each 3H, s, Me x 2), 1.1–1.2 (1H, m, bornyl H), 1.35–1.45 (1H, m, bornyl H), 1.6–1.9 (5H, m, bornyl H), 2.97 (1H, d, *J* = 12.6 Hz, 10'-H^a), 3.07 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.50 (1H, dd, *J* = 8.8 and 4.7 Hz, 2-H), 3.72 (1H, dd, *J* = 8.8 and 4.3 Hz, 3-H), 3.99 (1H, dd, *J* = 8.3 and 4.1 Hz, 2'-H), 5.30 (1H, dd, *J* = 4.6 and 1.0 Hz, 1-H), 5.33 (1H, br d, *J* = 4.3 Hz, 4-H), 6.59 (1H, dd, *J* = 5.9 and 1.6 Hz, CH=), 6.86 (1H, dd, *J* = 5.9 and 1.6 Hz, CH=). MS *m/z* 272 ($M^+ - C_4H_4O + 1$), 68 (C_4H_4O). *Anal.* Calcd for $C_{17}H_{25}NO_4S$: C, 60.15; H, 7.42, N, 4.13. Found: C, 60.15; H, 7.12; N, 3.99.

(1*R*,R_S)-Methyl 3-*endo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)-1-methoxy-7-oxabicyclo[2.2.1]hept-5-ene-2-*endo*-carboxylate (13e): Colorless oil (a mixture of **13e**/**14e**/unidentified compound/**1**, 49:13:29:9) . For **13e**: ^{1}H-NMR ($CDCl_3$) (a mixture of **13e**/**14e**/unidentified compound/**1**, 49:13:29:9) δ 0.84 and 1.12 (each 3H, s, Me x 2), 1.0–1.9 (7H, m, bornyl H), 2.83 (1H, d, *J* = 12.8 Hz, 10'-H^a), 3.20 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.34 (1H, d, *J* = 9.6 Hz, 2-H), 3.5–3.6 (1H, m, 3-H), 3.60 and 3.68 (each 3H, s, OMe x 2), 4.06 (1H, dd, *J* = 9.6 and 4.7 Hz, 2'-H), 5.17 (1H, dd, *J* = 4.5 and 1.9 Hz, 4-H), 6.68 (1H, d, *J* = 5.8 Hz, 6-H), 6.88 (1H, dd, *J* = 5.6 and 1.9 Hz, 5-H).

(1*S*,R_S)-Methyl 3-*exo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)-1-methoxy-7-oxabicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylate (14e): Colorless oil (a mixture of **13e**/**14e**/unidentified compound/**1**, 49:13:29:9) . For **14e**: ^{1}H-NMR ($CDCl_3$) (a mixture of **13e**/**14e**/unidentified compound/**1**, 49:13:29:9) δ 0.85 and 1.11 (each 3H, s, Me x 2), 2.35 (1H, d, *J* = 12.6 Hz, 10'-H^a), 2.93 (1H, d, *J* = 7.7 Hz, 2-H), 2.99 (1H, d, *J* = 12.8 Hz, 10'-H^b), 3.10 (1H, d, *J* = 7.9 Hz, 3-H), 3.76 and 3.84 (each 3H, s, OMe x 2), 5.44 (1H, d, *J* = 1.9 Hz, 4-H), 6.50 (1H, d, *J* = 5.8 Hz, 6-H), 6.65 (1H, dd, *J* = 5.7 and 2.0 Hz, 5-H).

(1*R*,R_S)-3-*endo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)-1-methoxy-7-oxabicyclo[2.2.1]hept-5-ene-2-*endo*-carboxamide (13f): Colorless needles. mp 182–184 °C. $[\alpha]_D^{26}$ –35.1° (*c* 0.77, MeOH). IR (KBr) 3380, 3204, 2954, 1697, 1662, 1341, 1075, 1033 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.82 and 1.11 (each 3H, s, Me x 2), 1.0–1.9 (7H, m, bornyl H), 3.09 (1H, d, *J* = 12.4 Hz, 10'-H^a), 3.24 (1H, d, *J* = 12.2 Hz, 10'-H^b), 3.33 (1H, d, *J* = 9.0 Hz, 2-H), 3.65 (3H, s, OMe), 4.0–4.05 (1H, m, 2'-H), 4.02 (1H, dd, *J* = 9.1 and 4.6 Hz, 3-H), 5.23 (1H, dd, *J* = 4.5 and 1.9 Hz, 4-H), 5.32 (1H, br s, NH), 6.33 (1H, br s, NH), 6.56 (1H, d, *J* = 5.8 Hz, 6-H), 7.00 (1H, dd, *J* = 5.3 and 1.9 Hz, 5-H). MS *m/z* 369 (M^+). *Anal.* Calcd for $C_{18}H_{27}NO_5S$: C, 58.51; H, 7.37; N, 3.79. Found: C, 58.16; H, 7.30; N, 3.91.

(1*R*,R_S)-Methyl 3-*endo*-({(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)bicyclo[2.2.2]oct-5-ene-2-*endo*-carboxylate (16a) Colorless needles. mp 149–151 °C. $[\alpha]_D^{26}$ –

18.9° (*c* 0.33, $CHCl_3$). IR (KBr) 3423, 2926 1735, 1719, 1647, 1429, 1162, 1078 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.82 and 1.10 (each 3H, s, Me x 2), 1.1–1.2 (1H, m, bornyl H), 1.25–1.9 (6H, m, bornyl H), 2.73 (1H, d, *J* = 13.2 Hz, 10'-H^a), 3.0–3.05 (1H, m, 1- or 4-H), 3.00 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.14 (1H, dd, *J* = 9.9 and 2.2 Hz, 3-H), 3.25 (1H, dd, *J* = 9.9 and 2.2 Hz, 2-H), 3.3–3.4 (1H, m, 4- or 1-H), 3.64 (3H, s, OMe), 4.02 (1H, ddd, *J* = 8.2, 4.4, and 3.3 Hz, 2'-H), 4.13 (1H, d, *J* = 2.7 Hz, OH), 6.39 (1H, ddd, *J* = 10.7, 6.3, and 1.9 Hz, 5- or 6-H), 6.43 (1H, ddd, *J* = 9.3, 6.3, and 1.9 Hz, 6- or 5-H). MS *m/z* 349 (M^+ – OH), 335 (M^+ – CH_3O). *Anal.* Calcd for $C_{20}H_{30}O_4S$: C, 65.57; H, 8.11. Found: C, 65.54; H, 8.25.

(1*R*,*R*$_S$)-3-*endo*-(1*S*,2*R*,4*R*)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)bicyclo[2.2.2]oct-5-ene-2-*endo*-carboxamide (16b) Colorless plates. mp 268 °C (decomp). $[\alpha]_D^{27}$ –12.8° (*c* 0.35, $CHCl_3$). IR (KBr) 3380, 2940, 1661, 1408, 1075, 966 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.81 and 1.09 (each 3H, s, Me x 2), 1.05–1.1 (1H, m, bornyl H), 1.35–1.85 (6H, m, bornyl H), 2.82 (1H, d, *J* = 13.2 Hz, 10'-H^a), 2.95–3.0 (1H, m, 1- or 4-H), 2.99 (1H, d, *J* = 13.2 Hz, 10'-H^b), 3.03 (1H, brd, *J* = 10.4 Hz, 3-H), 3.21 (1H, dd, *J* = 9.9 and 2.7 Hz, 2-H), 3.35–3.5 (1H, m, 4- or 1-H), 4.01 (1H, ddd, *J* = 7.7, 3.8, and 3.8 Hz, 2'-H), 4.08 (1H, d, *J* = 2.7 Hz, OH), 5.38 (1H, br, NH), 5.77 (1H, br, NH), 6.49 (1H, dd, *J* = 7.1 and 7.1 Hz, 5- or 6-H), 6.59 (1H, ddd, *J* = 7.7, 6.3, and 1.1 Hz, 6- or 5-H). MS *m/z* 351 (M^+). *Anal.* Calcd for $C_{19}H_{29}NO_3S$: C, 64.92; H, 8.32, N, 3.99. Found: C, 64.97; H, 8.27; N, 3.92.

(1*R*,*R*$_S$)-Methyl 9,10-Dihydro-12-*endo*-{(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl-9,10-ethanoanthracene-11-*endo*-carboxylate (17) Yellow plates. mp 236–238 °C. $[\alpha]_D^{27}$ +9.06° (*c* 0.20, $CHCl_3$). IR (KBr) 3396, 2938 1732, 1458, 1232, 1076, 1053, 1000 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.74 and 1.04 (each 3H, s, Me x 2), 0.8–1.9 (7H, m, bornyl H), 2.69 (1H, d, *J* = 12.6 Hz, 10'-H^a), 3.01 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.33 (1H, dd, *J* = 9.9 and 2.2 Hz, 11- or 12-H),), 3.38 (1H, dd, *J* = 9.9 and 1.6 Hz, 11- or 12-H), 3.61 (3H, s, OMe), 4.01 (1H, ddd, *J* = 7.1, 4.4 and 2.7 Hz, 2'-H), 4.15 (1H, d, *J* = 2.7 Hz, OH), 4.70 (1H, d, *J* = 2.2 Hz, 9- or 10-H), 5.09 (1H, d, *J* = 2.2 Hz, 4- or 1-H), 7.1–7.25 (4H, m, ArH x 4), 7.3–7.35 (2H, m, ArH x 2), 7.4–7.45 (1H, m, ArH), 7.45–7.5 (1H, m, ArH). MS *m/z* 463 (M^+ – 1). *Anal.* Calcd for $C_{28}H_{32}O_4S$: C, 72.38; H, 6.94. Found: C, 72.15; H, 6.87.

Methyl 4-Hydroxybenzoate (18) Colorless plates. mp 125–128 °C (lit.,[12] mp 127 °C). IR (KBr) 3312, 1681, 1607, 1589, 1514, 1435, 1279, 850 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 3.81 (3H, s, OMe), 5.97 (1H, s, OH), 6.97 (2H, d, *J* = 8.8 Hz, ArH x 2), 7.87 (2H, d, *J* = 8.8 Hz, ArH x 2). MS *m/z* 152 (M^+). HRMS calcd for $C_8H_8O_2$: 152.0473. Found: 152.0484.

Methyl *E*-3-({(1*S*,2*R*,4*R*,*R*$_S$)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)propenoate (19) Colorless oil. $[\alpha]_D^{29}$ –98.6° (*c* 0.37, $CHCl_3$). IR (neat) 3436, 2953, 1728, 1296, 1078, 1037 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.85 and 1.08 (each 3H, s, Me x 2), 0.8–1.9 (7H, m, bornyl H), 2.58 (1H, d, *J* = 13.2 Hz, 10'-H^a), 3.27 (1H, d, *J* = 13.2 Hz, 10'-H^b), 3.62 (1H, d, *J* = 3.3 Hz, OH), 3.83 (3H, s, OMe), 4.12 (1H, ddd, *J* = 8.2, 3.7, and 3.7 Hz, 2'-H), 6.71 (1H, d, *J* = 14.8 Hz, CH=), 7.63 (1H, d, *J* = 15.3 Hz, CH=). ^{13}C-NMR ($CDCl_3$) δ 20.0 (CH_3), 20.6 (CH_3), 27.3 (CH_2), 30.8 (CH_2), 38.7 (CH_2), 45.2 (CH), 48.6 (C), 51.7 (C), 52.6 (OCH_3), 55.1 (CH_2), 77.1 (CH), 126.0 (CH), 149.8 (CH), 164.3 (CO). MS *m/z* 287 (M^+ + 1), 270 (M^+ – O). HRMS calcd for $C_{14}H_{22}O_4S$: 286.1239. Found: 286.1257.

Methyl *E*-3-({(1*S*,2*R*,4*R*,*S*$_S$)-2-Hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfinyl)propenoate (20) Colorless oil. $[\alpha]_D^{27}$ +77.5° (*c* 0.34, $CHCl_3$). IR (neat) 3408, 2953, 1728, 1296, 1076, 1037

cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.84 and 1.12 (each 3H, s, Me x 2), 0.8–1.9 (7H, m, bornyl H), 2.59 (1H, d, *J* = 14.3 Hz, 10'-H^a), 3.08 (1H, d, *J* = 3.8 Hz, OH), 3.51 (1H, d, *J* = 13.7 Hz, 10'-H^b), 3.83 (3H, s, OMe), 4.08 (1H, ddd, *J* = 7.1, 3.7, and 3.7 Hz, 2'-H), 6.69 (1H, d, *J* = 14.8 Hz, CH=), 7.71 (1H, d, *J* = 14.8 Hz, CH=). ^{13}C-NMR ($CDCl_3$) δ 20.8 (CH_3), 21.1 (CH_3), 28.1 (CH_2), 32.4 (CH_2), 40.8 (CH_2), 45.4 (CH), 49.9 (C), 53.0 (C), 53.3 (OCH_3), 53.6 (CH_2), 76.7 (CH), 126.0 (CH), 151.5 (CH), 164.5 (CO). MS *m/z* 287 (M^+ + 1), 270 (M^+ – O). HRMS calcd for $C_{14}H_{22}O_4S$: 286.1239. Found: 286.1261.

(1*S*)-Methyl 5,6-*exo*-Dihydroxy-3-*endo*-({(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}-methylsulfonyl)-1-methoxy-7-oxabicyclo[2.2.1]heptane-2-*endo*-carboxylate (21e) A mixture of the sulfoxide **(1)** (419 mg, 1.46 mmol) and 2-methoxyfuran **(5)** (453 mg, 4.62 mmol) in dry CH_2Cl_2 (10 mL) was placed in a Tefron tube plugged with a Tefron stopper. The tube was placed in a high-pressure reactor and pressurized to 1.2 GPa at rt for 3 days. The pressure was released and the reaction mixture was concentrated to give a colorless oil (784 mg). A part of the resulting residue (327 mg) was subjected to the following reaction promptly because of the instability of the adducts. 0.1 M Solution of OsO_4 in *t*-BuOH (0.43 mL, 0.043 mmol) and triethylamine *N*-oxide dihydrate (377 mg, 3.4 mmol) were added to a solution of the crude adducts (327 mg) in acetone (18 mL) at 0 °C. The mixture was allowed to warm to rt with stirring for 3 h 20 min and concentrated. The residue was purified by flash column chromatography on silica gel with AcOEt and by subsequent recrystallization from CH_2Cl_2 to give **21e** (141 mg) as colorless plates. Calculated yield of **21e** from **1** was 53%. mp 189-191 °C. $[\alpha]_D^{25}$ +5.86° (*c* 4.15, $CHCl_3$). IR (KBr) 3356, 2956, 1732, 1332, 1073 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.80 and 1.09 (each 3H, s, Me x 2), 1.1–1.9 (7H, m, bornyl H), 2.57 (1H, d, *J* = 12.6 Hz, 10'-H^a), 2.8–3.0 (1H, br, OH), 3.13 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.4–3.85 (2H, br, OH x 2), 3.52 (1H, dd, *J* = 11.5, 4.9 Hz, 3-H), 3.58 (1H, dd, *J* = 11.5, 1.1 Hz, 2-H), 3.67 and 3.75 (each 3H, s, OMe x 2), 4.04 (1H, dd, *J* = 8.5, 4.1 Hz, 2'-H), 4.07 (1H, d, *J* = 6.6 Hz, 5-H), 4.58 (1H, dd, *J* = 4.9, 1.1 Hz), 4.76 (1H, d, *J* = 6.0 Hz, 6-H). MS *m/z* 434 (M^+). *Anal.* Calcd for $C_{19}H_{30}O_9S$: C, 52.52; H, 6.96. Found: C, 52.53; H, 6.86.

(1*S*)-5,6-*exo*-Dihydroxy-3-*endo*-({(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}-methylsulfonyl)-1-methoxy-7-oxabicyclo[2.2.1]heptane-2-*endo*-carboxamide (21f) 0.1 M Solution of OsO_4 in *t*-BuOH (0.80 mL, 0.080 mmol) and triethylamine *N*-oxide dihydrate (1.20 g, 10.8 mmol) were added at 0 °C to an acetone/MeOH (10:3, 39 mL) solution of the crude adducts, which were prepared from dienophile **(2)** (600 mg, 2.21 mmol) and 2-methoxyfuran **(5)** (2.1 mL, 22.8 mmol) in CH_2Cl_2/ MeOH (1:1, 10 mL). After being stirred for 21 h at 0 °C, the reaction mixture was concentrated. The residue was purified by flash column chromatography on silica gel with $CHCl_3$/MeOH (20:1) and by subsequent recrystallization from CH_2Cl_2/hexane/MeOH to give **21f** (586 mg, 63%) as colorless needles. mp 200–202 °C. $[\alpha]_D^{26}$ –19.5° (*c* 0.81, MeOH). IR (KBr) 3462, 3184, 2956, 1675, 1651, 1325, 1163 cm^{-1}. ^{1}H-NMR ($CDCl_3$/MeOH) δ 0.84 and 1.09 (each 3H, s, Me x 2), 1.1–1.25 (1H, m, bornyl H), 1.4-1.55 (1H, m, bornyl H), 1.7–1.9 (5H, m, bornyl H), 2.91 (1H, d, *J* = 12.6 Hz, 10'-H^a), 3.09 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.50 (1H, dd, *J* = 11.0, 1.1 Hz, 2-H), 3.56 (1H, dd, *J* = 11.0, 4.9 Hz, 3-H), 3.69 (3H, s, OMe), 4.02 (1H, dd, *J* = 8.2, 3.8 Hz, 2'-H), 4.14 (1H, d, *J* = 6.6 Hz, 6- or 5-H), 4.47 (1H, dd, *J* = 4.9, 1.1 Hz, 4-H), 4.66 (1H, d, *J* = 6.0 Hz, 5- or 6-H). MS *m/z* 404 (M^+ + 1). *Anal.* Calcd for $C_{18}H_{29}NO_8S$: C, 51.53; H, 6.97; N, 3.34. Found: C, 51.29; H, 7.09; N, 3.39.

(1*S*)-Methyl 5,6-*O*,*O*-Isopropylidene-5,6-*exo*-dihydroxy-3-*endo*-({(1*S*,2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfonyl)-1-methoxy-7-oxabicyclo[2.2.1]heptane-2-*endo*-carboxylate (22) 2,2-Dimethoxypropane (450 mg, 4.3 mmol) and catalytic amount of *p*-toluenesulfonic acid were added to a solution of **21e** (187 mg, 0.43 mmol) in acetone (7 mL) and the reaction mixture was refluxed for 5 h. After concentration of the reaction mixture, CH_2Cl_2 (50 mL) was added to the residue. The organic layer was washed with saturated $NaHCO_3$ (50 mL) and brine (50 mL), dried over $MgSO_4$ and concentrated to give a brownish oil (192 mg). The residue was purified by flash column chromatography on silica gel with hexane/AcOEt (1:1) and by subsequent recrystallization from CH_2Cl_2 to give **22** (130 mg, 64%) as colorless needles. mp 164–167 °C. $[\alpha]_D^{26}$ –6.67° (*c* 5.21, $CHCl_3$). IR (KBr) 3364, 2946, 1735, 1626, 1374, 1316, 1155, 1021 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.80 and 1.10 (each 3H, s, Me x 2), 1.1–1.9 (7H, m, bornyl H), 1.32 and 1.53 (each 3H, s, Me x 2), 2.55 (1H, d, *J* = 12.1 Hz, 10'-H^a), 3.11 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.50 (1H, d, *J* = 11.0 Hz, 2-H), 3.56 (1H, dd, *J* = 11.5, 5.0 Hz, 3-H), 3.67 and 3.76 (each 3H, s, OMe x 2), 3.88 (1H, br d, *J* = 2.2 Hz, OH), 4.0–4.1 (1H, m, 2'-H), 4.41 (1H, d, *J* = 6.0 Hz, CH=), 4.63 (1H, dd, *J* = 5.0, 1.1 Hz, 4-H), 5.10 (1H, d, *J* = 5.5 Hz, CH=). MS *m/z* 434 (M^+ – CH_3O). *Anal.* Calcd for $C_{22}H_{34}O_9S$: C, 55.68; H, 7.22. Found: C, 55.87; H, 7.22.

(1*S*)-2-*endo*-Crotonyloxymethyl-5,6-*O*,*O*-isopropylidene-5,6-*exo*-dihydroxy-3-*endo*-({(1*S*, 2*R*,4*R*)-2-hydroxy-7,7-dimethylbicyclo[2.2.1]heptan-1-yl}methylsulfonyl)-1-methoxy-7-oxabicyclo[2.2.1]heptane (24) $LiAlH_4$ (6.4 mg 0.17 mmol) was added portionwise to a solution of **22** (26.7 mg, 0.056 mmol) in THF (5 mL) and the reaction mixture was stirred at –20 °C under nitrogen for 3 h. The reaction was quenched with anhydrous Na_2SO_4 followed by saturated Na_2SO_4 and the whole mixture was stirred at rt for 30 min. The precipitates were filtered off and washed with acetone followed by $CHCl_3$. The combined filtrate was dried over $MgSO_4$ and concentrated to give a colorless oil (25.7 mg). The crude product was subjected to next reaction without purification because of its instability on silica gel. For **23**: ^{1}H-NMR ($CDCl_3$) δ 0.83 and 1.12 (each 3H, s, Me x 2), 1.1–1.9 (7H, m, bornyl H), 1.32 and 1.53 (each 3H, s, Me x 2), 2.6-2.8 (1H, m, 2-H), 3.00 (1H, d, *J* = 13.2 Hz, 10'-H^a), 3.33 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.48 (1H, dd, *J* = 11.5, 5.5 Hz, 3-H), 3.64 (3H, s, OMe), 3.8-3.95 (2H, m, C*H*$_2$OH), 3.95–4.05 (1H, m, 2'-H), 4.40 (1H, d, *J* = 5.5 Hz, CH=), 4.60 (1H, d, *J* = 5.5, Hz, 4-H), 5.14 (1H, d, *J* = 6.1 Hz, CH=). MS *m/z* 415 (M^+ – CH_3O), 399 (M^+ – CH_3O – OH).

Crotonic anhydride (34 μL, 0.21 mmol) was added dropwise to a mixture of **23** (25.7 mg), pyridine (18 μL, 0.22 mmol) and catalytic amount of 4-dimethylaminopyridine in benzene (1 mL) and the mixture was stirred at rt for 22 h. CH_2Cl_2 was added to the reaction mixture and washed with 1N HCl. The combined organic layer was washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified by flash column chromatography on silica gel with hexane/AcOEt (9:1 to 3:1), AcOEt gave **24** (8.8 mg, 30%) as colorless needles. mp 162–164 °C. $[\alpha]_D^{28}$ –74.3° (*c* 2.72, $CHCl_3$). IR (KBr) 3416, 2955, 1724, 1656, 1372, 1308, 1176, 1078 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ 0.83, 1.13 and 1.32 (each 3H, s, Me x 3), 1.4–1.9 (7H, m, bornyl H), 1.54 (3H, s, Me), 1.89 (3H, dd, *J* = 7.1, 1.6 Hz, C*H*$_3$CH), 2.71 (1H, d, *J* = 12.6 Hz, 10'-H^a), 2.88 (1H, ddd, *J* = 11.5, 9.1, 5.2 Hz, 2-H), 3.37 (1H, d, *J* = 12.6 Hz, 10'-H^b), 3.51 (1H, dd, *J* = 11.8, 5.8 Hz, 3-H), 3.62 (3H, s, OMe), 3.84 (1H, br d, *J* = 3.3 Hz, OH), 4.00 (1H, ddd, *J* = 8.2, 4.4, 3.3 Hz, 2'-H), 4.28 (1H, dd, *J* = 11.8, 9.1 Hz, C*H*HO), 4.36 (1H, dd, *J* = 11.8, 5.2 Hz, C*H*HO), 4.37 (1H, d, *J*

= 5.5 Hz, CH=), 4.62 (1H, d, *J* = 5.5 Hz, 4-H), 5.16 (1H, d, *J* = 5.5 Hz, CH=), 5.83 (1H, dq, *J* = 15.4, 1.6 Hz, CH_3CH=C*H*), 7.05 (1H, dq, *J* = 15.4, 6.8 Hz, CH_3C*H*=CH). MS *m/z* 483 ($M^+ - CH_3O$). *Anal.* Calcd for $C_{25}H_{38}O_9S$: C, 58.34; H, 7.44. Found: C, 58.38; H, 7.32.

(–)-COTC (25) 80% Aqueous TFA (3 mL) was added to **24** (158 mg, 0.31 mmol) at –20 °C and the whole mixture was stirred at the same temperature for 7 h. The reaction mixture was concentrated. The residue was washed with hexane and crystallized from AcOEt/MeOH/hexane to give **25** (22 mg, 29%) as colorless needles. mp 176–178 °C (lit.,[9] mp 181 °C and lit.,[3c] mp 179–181 °C). $[\alpha]_D^{28}$ –109.7° (*c* 0.23, MeOH) (lit.,[9] $[\alpha]_D^{24}$ –109° (*c* 1.5, MeOH) and lit.,[3c] $[\alpha]_D$ –108° (*c* 0.23, MeOH)). IR (KBr) 3423, 3204, 2944, 1713, 1687, 1654 cm^{-1}. ^{1}H-NMR (CD_3OD) δ 1.89 (3H, dd, *J* = 7.1, 1.6 Hz, Me), 4.28 (1H, d, *J* = 2.2 Hz, 6-H), 4.36 (1H, ddd, *J* = 3.3, 2.7, 2.2 Hz, 5-H), 4.64 (1H, dd, *J* = 3.0, 1.9 Hz, 4-H), 4.75 (1H, ddd, *J* = 13.7, 1.6, 1.6 Hz, C*H*HO), 4.86 (1H, ddd, *J* = 13.7, 2.2, 1.6 Hz, C*H*HO), 5.89 (1H, dq, *J* = 15.9, 1.6 Hz, CH_3CH=C*H*), 6.70 (1H, br s, 3-H), 7.02 (1H, dq, *J* = 15.5, 6.9 Hz, CH_3C*H*=CH). MS *m/z* 213 ($M^+ - C_2H_5$).

(–)-Gabosine C (26) 80% Aqueous TFA (10 mL) was added at –20 °C to **23**, which was prepared from **22** (447 mg, 0.94 mmol) and $LiAlH_4$ (108 mg, 2.83 mmol) in THF (50 mL), and the whole mixture was stirred at the same temperature for 6 h. The reaction mixture was concentrated. The residue was purified by PLC on cellulose with *n*-BuOH/EtOH/H_2O (4:1:2) to give **26** (84 mg, 51% from **22**) as colorless needles. mp 114–115 °C (lit.,[10a,c] mp 113–114 °C and lit.,[10b] mp 112–113 °C). $[\alpha]_D^{28}$ –166° (*c* 0.17, H_2O) (lit.,[10a] $[\alpha]_D^{20}$ –168° (*c* 1.0, H_2O), lit.,[10b] $[\alpha]_D^{20}$ –170° (*c* 1.0, H_2O) and lit.,[10c] $[\alpha]_D^{20}$ –165.7° (*c* 0.2, H_2O)). IR (KBr) 3456, 2924, 1687 cm^{-1}. ^{1}H-NMR (CD_3OD) δ 4.2–4.3 (3H, m, 6-H, C*H*$_2$OH), 4.36 (1H, ddd, *J* = 3.3, 2.8, 2.2 Hz, 5-H), 4.63 (1H, m, 4-H), 6.68 (1H, m, 3-H). ^{13}C-NMR (CD_3OD) δ 59.4 (CH_2), 69.4 (CH), 76.9 (CH), 77.8 (CH), 137.8 (C), 145.1 (CH), 199.3 (CO). MS *m/z* 174 (M^+), 156 ($M^+ - H_2O$), 138 ($M^+ - 2H_2O$).

X-Ray Crystallographic Analysis of 13b A colorless plate crystal of $C_{18}H_{27}NO_3S$ having approximate dimentions of 0.40 x 0.30 x 0.05 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC7R diffractometer with graphite monochromated Mo-Kα radiation and 12 kW rotating anode generator. Crystal data for **13b**: monoclinic, space group, $P2_1$ with *a* = 10.971(3) Å, *b* = 7.338(2) Å, *c* = 12.159(3) Å, β = 116.08(2)°, *V* = 879.1(4) Å^3, and *Z* = 2 (d_{calcd} = 1.275 g cm^{-3}), μ(MoK$_\alpha$) = 2.98 cm^{-1} absorption corrected by ω scans; 2290 unique reflections; 2181 with $I > 3.00\sigma(I)$ were used in refinement; *R* = 4.3%, R_w = 4.4%.

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REFERENCES AND NOTES

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‡ Fellow of the Science and Technology Agency of Japan, on leave from National Institute of Health Sciences.

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