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Total synthesis of (±)-methyl-kinamycin C

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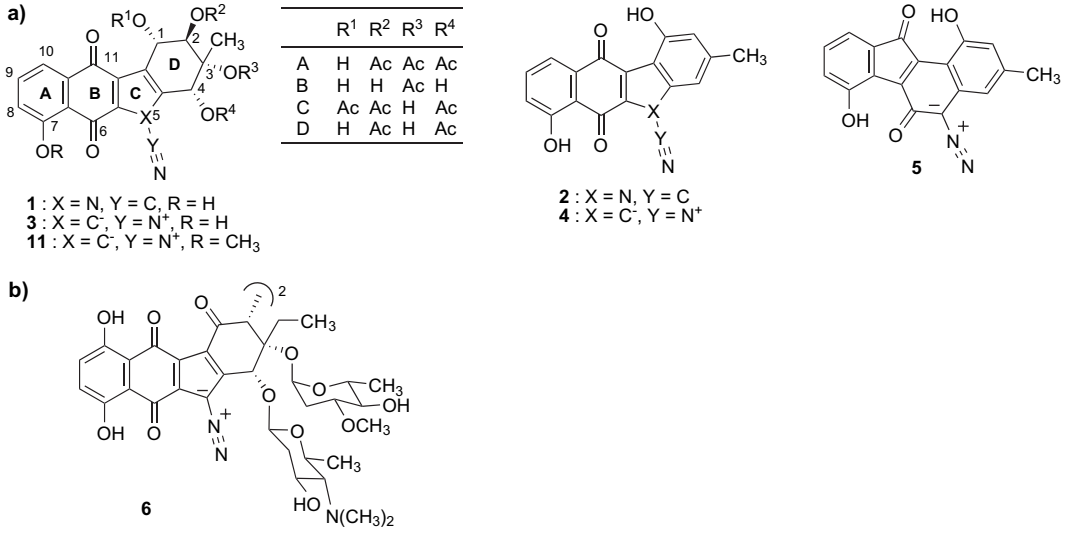
Abstract—The first total synthesis of the proposed structure for methyl-kinamycin C (methyl-KC), derived from KC, was achieved via two key steps: Diels–Alder reaction of benzindenone and Danishefsky-type diene, and the stereoselective construction of highly oxygenated D ring. Good accordance of the spectral data of synthesized title compound with those of natural KC and its derivative was observed.

1. Introduction

Kinamycins A–D were first isolated from a culture broth of *Streptomyces murayamaensis* sp. nov. Hata and Ohtani by Ōmura et al. in 1970.[1,2] These kinamycins exhibit strong activity against Gram-positive bacteria, and kinamycin C (KC) shows antitumor activity.[2b,3] Their structures were originally determined to be linearly-fused tetracyclic 6-6-5-6 ring systems containing a fully oxygenated D ring with four sequential chiral centers from spectral data[4] and X-ray crystallography of the *p*-bromobenzoate of KC.[5] The arrangement of the three atoms (one carbon and two nitrogens) in the substituent on the C ring, which could not be determined by X-ray crystallographic analysis, has been determined as a cyanamide structure (**1** as a whole structure) by chemical correlation.[4] In 1989, Gould and Seaton[6] reported the isolation of prekinamycin with an aromatized D ring from the same *S. murayamaensis* and proposed that it had the cyanamide structure **2** based on the characteristic IR absorption (2162 cm^{-1}).[7] However, the synthesized **2** was not identical to natural prekinamycin,[8] and, in 1994, Gould et al.[9] and Dmitrienko et al.[10] independently revised



	R^1	R^2	R^3	R^4
A	H	Ac	Ac	Ac
B	H	H	Ac	H
C	Ac	Ac	H	Ac
D	H	Ac	H	Ac

Figure 1. (a) The originally proposed (**1** and **2**) and revised (**3** and **4**) structures of kinamycins and prekinamycins, and the re-revised structure of isoprekinamycin (**5**); (b) structure of lomaiviticin A (**6**).

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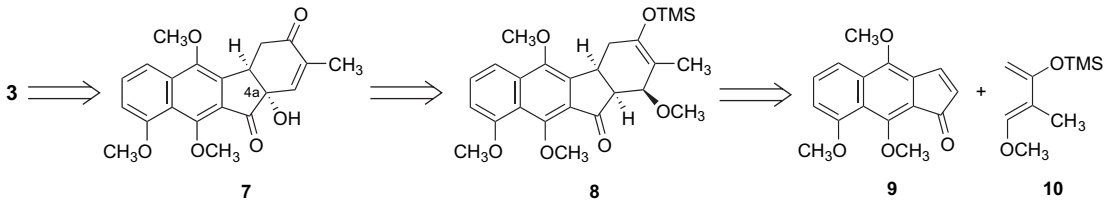


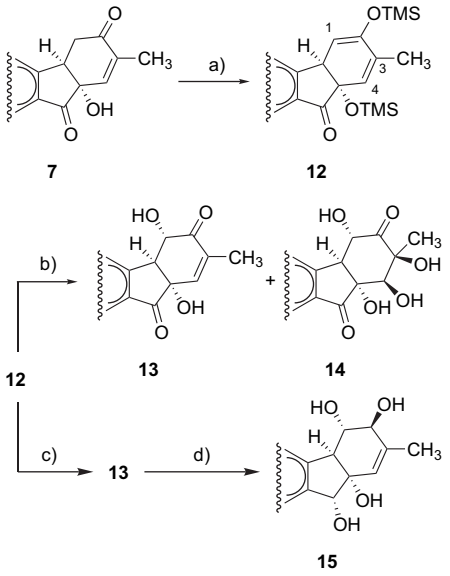
Scheme 1. Retrosynthesis of kinamycins (**3**) via Diels–Alder reaction of **8** and **9**.

the C ring structures of kinamycins and prekinamycins from cyanamides **1** and **2** to diazoalkanes **3** and **4** on the basis of a re-evaluation of the X-ray crystallographic and spectral data. Unfortunately, the linear 6-6-5-6 ring system of the synthesized prekinamycin **4** was not identical to the natural product,[11] and in 2000 the structure of natural prekinamycin was re-revised to the angular 6-5-6-6 ring system **5**[12,13] (Fig. 1a). On the other hand, He et al.[14] recently reported the isolation of lomaiviticin A (**6**) from *Micromonospora lomaivitiensis* and proposed a dimerized kinamycin-type diazoalkane structure (Fig. 1b) based on the presence of a signal at 78.8 ppm in the ^{13}C NMR spectrum.[15] Quite recently, Lei and Porco[16] reported the enantioselective total synthesis of the compound with structure **3** (for KC) to elucidate that kinamycins are not cyanamides **1** but diazoalkanes **3**.

We have continued the synthetic studies toward kinamycins.[1c] Our basic strategy for the synthesis of diazoalkane **3** is as follows: (1) construct the tetracyclic ring structure **7** via Diels–Alder reaction of the benz[*f*]indenone **9** and Danishefsky-type diene **10** followed by hydrolysis and oxygenation of the adduct **8**; and (2) stereoselectively introduce oxygen functionalities on the D ring (Scheme 1). This strategy has previously been used to synthesize a tricyclic model compound, which lacks the A ring.[17] We have already reported the synthesis of tetracyclic core **7** with hydroxy group at position 4a,[18] which plays an important role for further diastereoselective introduction of oxygen functions. We herein report the first total synthesis of (±)-methyl-KC (**11**) (Fig. 1a), derived from natural KC on methylation by Ōmura et al.[4]

2. Results and discussions

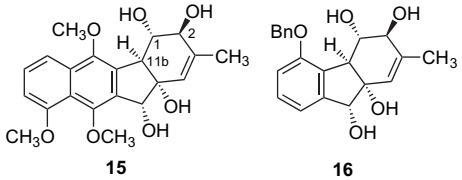
At first, according to model system,[17] oxidation of silyl enol ether **12** derived from racemic enone **7**[18] by a combination of catalytic amount of OsO_4 and 1.5 equiv of *N*-methylmorpholine-*N*-oxide (NMO) was attempted. A desired α-hydroxyketone **13** was obtained after hydrolysis of trimethylsilyl (TMS) groups with aqueous HCl; however, the yield of **13** was very low (16–30%) and generation of tetraol **14**,[19] which has wrong relative configuration at positions 3 and 4, was observed in 26–35% yield. On the other hand, Rubottom oxidation with *m*-chloroperoxybenzoic acid (*m*CPBA)[20] gave only **13** albeit in 40% yield. Reduction of ketone functions on **13** with diisobutylaluminum hydride (DIBAL-H) afforded tetraol **15** in 40% yield (Scheme 2), the desired relative configuration at positions 1 and 2 of which was determined by the similarity in spectral data of model compound **16** (Table 1) and NOE enhancements (Fig. 2). However, we decided to explore new synthetic route because of low yield in both steps.



Scheme 2. Trials for hydroxylation of silyl enol ether **12**. Conditions and reagents: (a) TMSOTf, Et_3N, CH_2Cl_2, −15 °C, 25 min (63%); (b) 1, OsO_4, NMO, THF–H_2O (20:1), 5 °C–rt, 20 h; 2, 10% HCl, CH_3OH, rt, 20 min (16–30% for **13**, 26–35% for **14**); (c) 1, *m*CPBA, $NaHCO_3$, CH_2Cl_2, rt, 14 h; 2, 10% HCl, CH_3OH, rt, 10 min (40%) and (d) DIBAL-H, THF, −78 °C, 1 h (40%).

Donohoe et al.[21] reported *syn*-selective dihydroxylation of cyclic allylic alcohols in stoichiometric amount of OsO_4 and *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA). Thus, **7** was subjected to diastereoselective dihydroxylation controlled by the hydroxyl group at position 4a using the OsO_4–TMEDA system to give the *cis*,*cis*-triol **17** exclusively. The relative configuration of **17** was determined by NOE enhancement of the corresponding acetate **18** (Fig. 3a).[22] Rubottom oxidation of the corresponding silyl enol ether **19** with *m*CPBA preferentially afforded the undesired 1β-silyloxyketone **20**; however, complete isomerization of **20** to the desired 1α-silyloxyketone **21** was achieved by leaving

Table 1. Selected ^1H NMR data of tetraols **15** and **16** in $CDCl_3$[a]



Tetraol	H-1[b]	H-2[b]	H-11b[b]
15	3.58 (dd, 11.3, 7.1)	4.39 (d, 7.1)	3.63 (d, 11.3)
16[c]	3.52 (dd, 11.3, 7.3)	4.26 (d, 7.3)	3.47 (d, 11.3)

[a] Coupling pattern and *J* values are shown in parenthesis.
[b] The numbering is based on that of **15**.
[c] A small portion of CD_3OD was added.

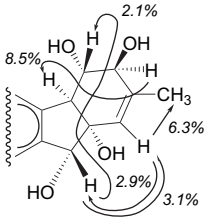


Figure 2. Selected NOE enhancements of **15**.

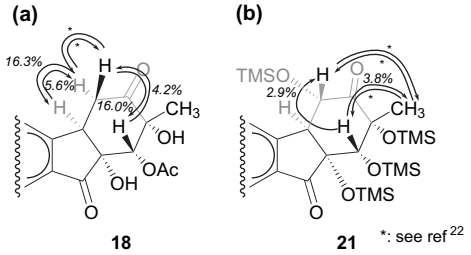
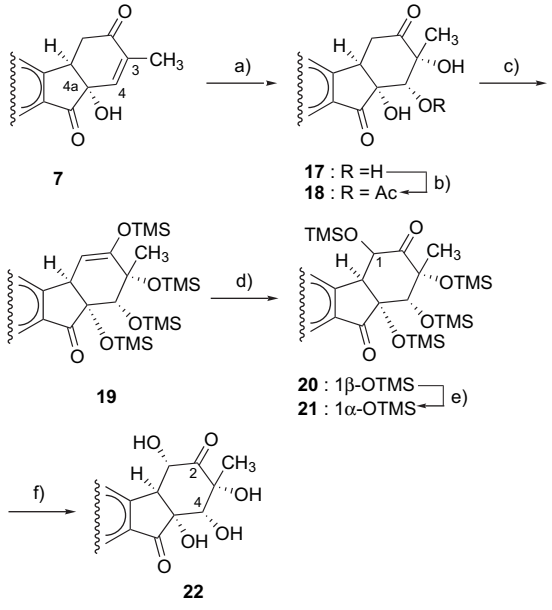


Figure 3. Selected NOE enhancements of **18** (a) and **21** (b).

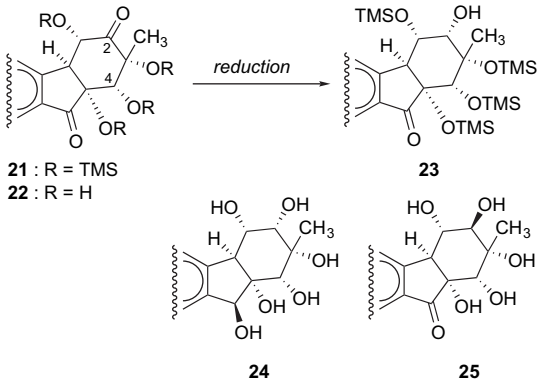
either the purified **20** at 4 °C for 1 month or the crude oxidation product at room temperature (rt) for 3–4 days. Relative configuration of 1α-silyloxyketone **21** was determined by the NOE enhancements (Fig. 3b).[22] Complete deprotection of TMS groups on **21** by methanol–H_2O systems[23] afforded **22** (Scheme 3).



Scheme 3. Preparation of tetraol **22** via triol **17**. Conditions and reagents: (a) 1, OsO_4, TMEDA, CH_2Cl_2, −78 °C, 1 h; 2, $NaHSO_3$, H_2O, pyridine, rt, 24 h (66%); (b) Ac_2O, pyridine, CH_2Cl_2, rt, 6 h (71%); (c) (from **17**) TMSOTf, Et_3N, CH_2Cl_2, 0 °C, 1 h (78%); (d) *m*CPBA, $NaHCO_3$, CH_2Cl_2, −45 °C, 4.5 h; (e) on pure **20**: 4 °C, 1 month; on crude **20**: rt, 3–4 days (67–71%) and (f) CH_3OH–H_2O (3:1), rt, 24 h (91%).

Reduction of the silyloxyketone **21** with zinc borohydride [$Zn(BH_4)_2$][24] gave the corresponding alcohol **23** in 82% yield as a single diastereoisomer (run 1, Table 2). However, X-ray crystallographic analysis of **23**[25] revealed to be an undesired 2α-alcohol as a result of reduction at vacant β-site avoiding steric repulsion of bulky TMS groups

Table 2. Diastereoselective reductions of ketones **21** and **22**[a]



Run	Substrate	Conditions	Product (%)
1	**21**	A	**23** (82)
2	**22**	A	**24** (73)
3	**22**	B	**25** (83)

[a] Conditions: A: $Zn(BH_4)_2$, Et_2O (+THF), −18∼−10 °C, 4 h; B: $(CH_3)_4NBH(OAc)_3$, CH_3CN, AcOH, −40 °C, 2 h.

(Fig. 4a). Treatment of hydroxyketone **22** using this reaction system afforded the corresponding hexaol **24** (run 2), which shows similar signal pattern in ^1H NMR spectrum [δ: 3.30 ppm (d, *J*=3.5 Hz) for H-2] to that of silyloxyalcohol **23** [δ: 3.45 ppm (d, *J*=2.4 Hz) for H-2]. The stereochemical induction could be reasonably explained by reduction at vacant β-site of **22**, even possible chelation between ketone and α-hydroxy groups. Therefore, we turned to utilize tetramethylammnonium triacetoxyborohydride [$(CH_3)_4NBH(OAc)_3$][26] as a reducing reagent for diastereoselective reduction via a six-membered ring transition state containing B–O bond formation between the reagent and the hydroxy oxygen at β-position of ketone function. Thus, tetraol **22** was treated with $(CH_3)_4NBH(OAc)_3$ in acetonitrile (CH_3CN)–acetic acid (AcOH) at −40 °C to give desired pentaol **25**, which possesses different ^1H NMR spectral properties [δ: 3.63 ppm (d, *J*=6.9 Hz) for H-2] from that of hexaol **24** (run 3). To elucidate the relative configuration of **25**, the structure of the corresponding triacetate **26** (see, Scheme 4) was analyzed by X-ray crystallography (Fig. 4b),[27] which showed that **25** has the correct stereochemistry for kinamycins and the reduction had occurred at α-site as expected.

However, attempts to convert triacetate **26** to enone **34** (vide infra) by dehydration gave erratic results. Conversion of diol **26** to xanthate **27** was in very low yield (13%) and the following Chugaev reaction of xanthate **27** gave fluorenone **28** with displacement of xanthate to methythio group at position 3.[28] On the other hand, **26** was treated with Burgess reagent [$(C_2H_5)_3N^+SO_2N^-CO_2CH_3$][29] to give fluorenone **29** with sulfonamide moiety at position 3 in 37% yield, and further chemical manipulations resulted in low reproducibility (Scheme 4). These troubles may be due to the existence of free hydroxyl group at the position 3 in **26**. This situation caused us to modify the strategy, starting once again from the tetraol **22**.

Diacetate **30**, which was prepared by selective acetylation of secondary alcohols in tetraol **22**, was subjected to

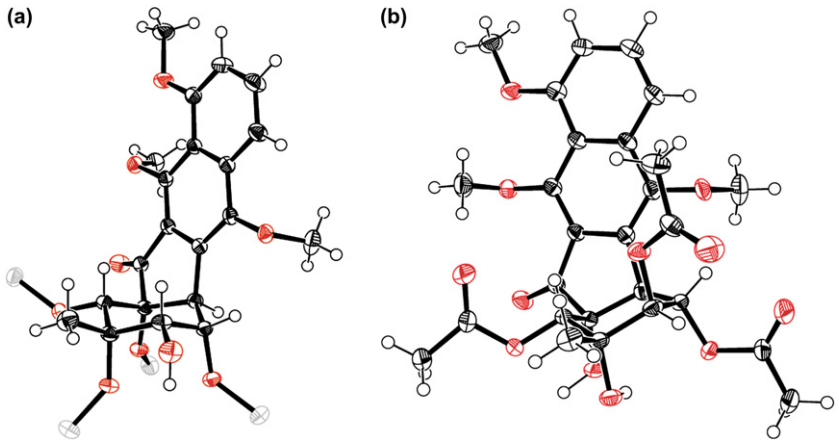
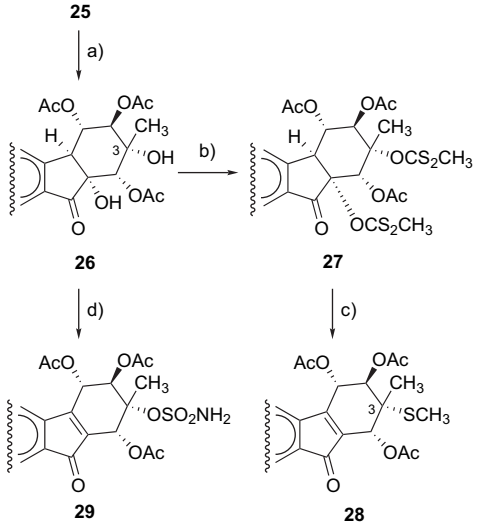
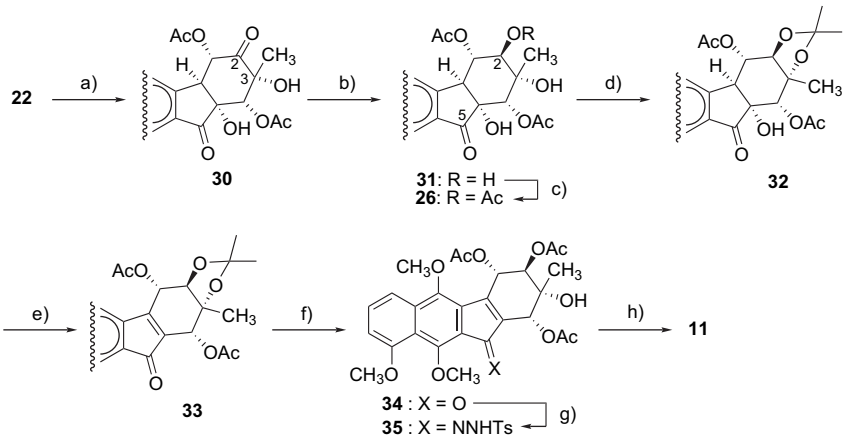


Figure 4. ORTEP views of X-ray crystallography of alcohol **23** (a) and triacetate **26** (b). Methyl groups on TMS in **23** were omitted for clarity.



Scheme 4. Trials for dehydration of alcohol **26**. Conditions and reagents: (a) Ac_2O, pyridine, DMAP, CH_2Cl_2, rt, 24 h (51%); (b) 1, NaH, THF, 0 °C, 30 min; 2, CS_2, 0 °C, 30 min; 3, CH_3I, 0 °C, 2.5 h (13%); (c) neat, 300 °C, 20 mmHg, 10 min (87%) and (d) $(C_2H_5)_3N^+SO_2N^-CO_2CH_3$, toluene, 80 °C, 5 h (37%).

diastereoselective reduction with $(CH_3)_4NBH(OAc)_3$ controlled via five-membered ring chelation[30] from the hydroxy group at the position 3 to give triol **31** with the desired stereochemistry in a ratio of ca. 5:1. Partial over-reduction of the ketone at the position 5 was encountered, but convergence to **31** was achieved by MnO_2 oxidation of the crude product. The relative configuration of **31** was determined by conversion to triacetate **26**, which was previously obtained in Scheme 4. Ketalization of the triol **31**[31] and purification by column chromatography gave ketal **32** as a single diastereoisomer. Dehydration of **32** with Burgess reagent afforded the benzofluorenone system **33**. Deketalization and partial acetylation gave the triacetyl enone **34**, which was converted to the tosylhydrazone **35** by treatment with tosylhydrazine in the presence of $BF_3 \cdot OEt_2$.[32] When **35** was subjected to ammonium cerium nitrate (CAN) oxidation, not only the expected oxidation to naphthoquinone but also spontaneous desulfination leading to diazoalkane formation occurred to yield compound **11** with the structure corresponding to methyl-KC. Our synthesized compound shows a characteristic signal due to a diazocarbon at 77.8 ppm in the ^{13}C NMR spectrum[15] and absorption attributable to a diazo group at 2146 cm^{-1} in the IR spectrum,[4] which has good accordance with reported data for natural KC and the derived methyl-KC (Scheme 5).



Scheme 5. Total synthesis of methyl-KC (**11**). Conditions and reagents: (a) Ac_2O, pyridine, 0 °C, 12 h (70%); (b) 1, $(CH_3)_4NBH(OAc)_3$, CH_3CN, AcOH, −25 °C, 12 h; 2, MnO_2, AcOEt, rt, 24 h (69% as a diastereomeric mixture at position 2); (c) Ac_2O, pyridine, rt, 24 h (62%); (d) (from **31**) 2-methoxypropene, $TsOH \cdot H_2O$, DMF, rt, 23 h then separation (67%); (e) $(C_2H_5)_3N^+SO_2N^-CO_2CH_3$, toluene, 80 °C, 24 h (52%); (f) 1, $TsOH \cdot H_2O$, CH_2Cl_2, CH_3OH, rt, 28 h; 2, Ac_2O, pyridine, rt, 9 h (85%); (g) $TsNHNH_2$, $BF_3 \cdot OEt_2$, toluene, rt, 4 h (59%) and (h) CAN, CH_3CN, H_2O, 0 °C, 10 min (55%).

3. Conclusion

We have achieved the first total synthesis of the proposed structure for methyl-KC (**11**) via two key steps: Diels–Alder reaction of benzindenone and Danishefsky-type diene, followed by the stereoselective construction of a highly oxygenated D ring. The spectral data of synthesized methyl-KC (**11**) showed good accordance with reported data for natural KC and methyl-KC derived by Ōmura et al. Currently, we are endeavoring to develop synthetic routes for the enantioselective synthesis of the kinamycins themselves as well as the synthesis of non-natural diastereomers that could potentially be used either as antibiotics or antitumor compound.

4. Experimental section

4.1. General

All melting points were measured on a micro-melting point hot stage (Yanaco) and are uncorrected. IR spectra were recorded on a JASCO FT/IR-300E spectrophotometer; ATR=attenuated total reflectance system. ^{1}H NMR spectra were recorded on JEOL JNM-GSX400A (400 MHz), -ECP400 (400 MHz), -GSX500A (500 MHz) or -ECP600 (600 MHz), using tetramethysilane (0.00 ppm) or residual chloroform ($CHCl_3$) (7.26 ppm) as an internal standard. ^{13}C NMR spectra were recorded on JEOL JNM-ECP400 (100 MHz), -GSX500A (125 MHz), -LA500 (125 MHz), -ECA600 (150 MHz) or -ECP600 (150 MHz), using the middle resonance of $CDCl_3$ (77.0 ppm) as an internal standard; δ in parts per million, J in hertz, dif.=diffused. EIMS were recorded on a JEOL GC-Mate with direct inlet. FABMS were recorded on a JMS-HX110 with *m*-nitrobenzyl alcohol as a matrix. For TLC was used TLC plates, Silica gel 60 F_{254} (Merck No. 5715) and for column chromatography Silica gel 60, spherical particle size 63–210 μm (Kanto Chemical No. 37564-85 for normal, No. 37565-84 for neutral). Anhydrous dichloromethane (CH_2Cl_2) and diethyl ether (Et_2O) were purchased from Kanto Chemicals. Anhydrous tetrahydrofuran (THF) was purchased from Wako Pure Chemical. Anhydrous CH_3CN was distilled from CaH_2. Burgess reagent [$(C_2H_5)_3N^+SO_2N^-CO_2CH_3$] was used as purchased from Aldrich.

4.1.1. (±)-(4a*RS*,11b*SR*)-6,7,11-Trimethoxy-3-methyl-1,4a-bis(trimethylsilanyloxy)-4a,11b-dihydrobenzo[*b*]-fluoren-5-one (12). To a solution of **7** (599 mg, 1.63 mmol) in CH_2Cl_2 (6 mL), Et_3N (0.49 mL, 3.52 mmol) and TMSOTf (0.64 mL, 3.39 mmol) were added successively at −15 °C and the whole was stirred at −15 °C for 25 min. Saturated aqueous $NaHCO_3$ was added and the whole was extracted with $CHCl_3$. The organic layer was washed with H_2O and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by column chromatography (CC) (neutral SiO_2, benzene–AcOEt=3:1) to give **12** as a yellow oil (523 mg, 63%).

IR ($CHCl_3$, cm^{-1}) 1719. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 0.19, 0.24 (each 9H, s, TMS), 1.73 (3H, d, J=1.3 Hz, CH_3), 3.95, 3.99, 4.00 (each 3H, s, 3×OCH_3), 4.06 (1H, d, J=6.2 Hz, H-11b), 5.49 (1H, br s, H-4), 5.74 (1H, d, J=6.2 Hz, H-1), 6.86 (1H, d, J=7.9 Hz, H-8), 7.50 (1H, dd, J=7.9, 7.9 Hz, H-9), 7.72 (1H, d, J=7.9 Hz, H-10). EIMS *m*/*z* 512 (M^+, 14.5%), 73 (100%).

4.1.2. (±)-(1*RS*,4a*RS*,11b*RS*)-1,4a-Dihydroxy-6,7,11-trimethoxy-3-methyl-4a,11b-dihydro-1*H*-benzo[*b*]fluorene-2,5-dione (13), (±)-(1*RS*,3*RS*,4*RS*,4a*SR*,11b*RS*)-1,3,4,4a-tetrahydroxy-6,7,11-trimethoxy-3-methyl-3,4,4a,11b-tetrahydro-1*H*-benzo[*b*]fluorene-2,5-dione (14). (a) With OsO_4 and NMO: To a solution of **12** (81 mg, 0.16 mmol) in THF–H_2O (20:1, 0.5 mL), OsO_4 (2.2 mg, 8.7 μmol) and NMO (23 mg, 0.19 mmol) were added and the whole was stirred at 5 °C for 20 h. Na_2SO_3 10% (5 mL) was added and the whole was stirred at room temperature (rt) for 15 min. The whole was extracted with AcOEt and the organic layer was washed with 10% Na_2SO_3, H_2O, and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was dissolved in CH_3OH (1 mL). HCl 10% (0.5 mL) was added and the whole was stirred at rt for 20 min. Saturated aqueous $NaHCO_3$ (5 mL) was added and the whole was extracted with AcOEt. The organic layer was washed with H_2O and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by CC (benzene–CH_3OH=10:1) to give **13** as yellow prisms (18 mg, 30%) and **14** as a yellow oil (23 mg, 35%).

Compound **13**: mp 190–192 °C. IR ($CHCl_3$, cm^{-1}) 3552, 3471, 1715. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.92 (3H, s, CH_3), 3.21, 4.00 (1H, s, OH, exchangeable with D_2O), 4.02, 4.04, 4.05 (each 3H, s, 3×OCH_3), 4.30 [1H, dd (d with D_2O), J=9.0, 2.0 Hz (J=9.0 Hz with D_2O), H-1], 6.70 (1H, d, J=1.3 Hz, H-4), 6.94 (1H, d, J=8.1 Hz, H-8), 7.60 (1H, dd, J=8.1, 8.1 Hz, H-9), 7.76 (1H, d, J=8.1 Hz, H-10) (increment of the integration of 1H for H-11b was observed around the peaks of OCH_3). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 16.0, 51.6, 56.4, 62.1, 63.4, 75.3, 77.6, 107.2, 114.9, 121.1, 121.7, 130.7, 133.5, 136.3, 136.6, 139.9, 149.1, 156.6, 159.5, 197.4, 198.1. HREIMS *m*/*z* calcd for $C_{21}H_{20}O_4$: 384.1209; found: 384.1208.

Compound **14**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 1.59 (3H, s, CH_3), 3.00, 3.32 (each 1H, br s, 2×OH, exchangeable with D_2O), 3.73 (1H, d, J=8.8 Hz, H-1; s with addition of D_2O), 4.01, 4.02, 4.04 (each 3H, s, 3×OCH_3), 4.19 (1H, br s, H-4), 4.55 (1H, br s, OH, exchangeable with D_2O), 4.78 (1H, br d, J=8.8 Hz, OH, exchangeable with D_2O), 6.94 (1H, d, J=8.0 Hz, H-8), 7.61 (1H, dd, J=8.0, 8.0 Hz, H-9), 7.71 (1H, d, J=8.0 Hz, H-10).

(b) With *m*CPBA: To a mixture of **12** (94 mg, 0.18 mmol) and $NaHCO_3$ (32 mg, 0.38 mmol) in CH_2Cl_2 (2 mL), a solution of *m*CPBA (70%, 50 mg, 0.20 mmol) was added at −30 °C and the whole was stirred at same temperature for 4 h and at −15 °C for 2.5 h. After addition of *m*CPBA (70%, 50 mg, 0.20 mmol) and $NaHCO_3$ (30 mg, 0.36 mmol), the whole was stirred at rt for 14 h. Aqueous $NaHSO_3$ 10% (2.5 mL) was added and the whole was extracted with $CHCl_3$. The organic layers were combined and washed with H_2O and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo. The residue was dissolved in CH_3OH (1 mL) and treated with 10% HCl (three drops) at rt. After 10 min, saturated aqueous $NaHCO_3$

(2 mL) was added and the whole was extracted with $CHCl_3$. The organic layers were combined and washed with H_2O and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by CC (neutral SiO_2, benzene–CH_3OH=10:1) to give yellow prisms (28 mg, 40%). The spectral data was identical with that of **13**.

4.1.3. (±)-(1*RS*,2*RS*,4a*RS*,5*SR*,11b*RS*)-6,7,11-Trimethoxy-3-methyl-1,2,5,11b-tetrahydrobenzo[*b*]fluorene-1,2,4a,5-tetraol (15). To a solution of **13** (27 mg, 70 μmol) in THF (1 mL), DIBAL-H (1 M solution in toluene, 0.28 mL, 0.28 mmol) was added at −78 °C and the whole was stirred at −78 °C for 1 h. HCl 10% was added and the whole was extracted with AcOEt. The organic layer was washed with H_2O and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by preparative TLC (benzene–AcOEt=10:1) to give **15** as an orange oil (11 mg, 40%).

IR ($CHCl_3$, cm^{-1}): 3502. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.90 (3H, s, CH_3), 2.66 (1H, s, OH, exchangeable with D_2O), 3.58 (1H, dd, J=11.3, 7.1 Hz, H-1), 3.63 (1H, d, J=11.3 Hz, H-11b), 3.75 (1H, s, OH, exchangeable with D_2O), 3.91, 3.99, 4.03 (each 3H, s, 3×OCH_3), 4.07, 4.22 (each 1H, s, 2×OH, exchangeable with D_2O), 4.39 (1H, d, J=7.1 Hz, H-2), 5.35 (1H, s, H-5), 5.65 (1H, br s, H-4), 6.92 (1H, d, J=7.8 Hz, H-8), 7.45 (1H, dd, J=7.8, 7.8 Hz, H-9), 7.69 (1H, d, J=7.8 Hz, H-10). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 18.4, 29.7, 53.6, 56.1, 61.8, 62.4, 75.0, 79.3, 80.1, 106.5, 114.7, 120.9, 124.9, 126.9, 130.7, 131.3, 132.0, 136.8, 148.6, 150.7, 156.2. HREIMS *m*/*z* calcd for $C_{21}H_{24}O_7$: 388.1522; found: 388.1535.

4.1.4. (±)-(3*RS*,4*SR*,4a*RS*,11b*RS*)-3,4,4a-Trihydroxy-6,7,11-trimethoxy-3-methyl-3,4,4a,11b-tetrahydro-1*H*-benzo[*b*]fluorene-2,5-dione (17). To a solution of **7** (255 mg, 0.69 mmol) and TMEDA (0.12 mL, 0.78 mmol) in CH_2Cl_2 (70 mL), a solution of OsO_4 (193 mg, 0.76 mmol) in CH_2Cl_2 (5 mL) was added at −78 °C and the whole was stirred at −78 °C for 1 h. The solvent was evaporated in vacuo and the residue was treated with a solution of $NaHSO_3$ (400 mg, 3.84 mmol) in H_2O–pyridine (1:1, 4 mL) at rt for 24 h. The whole was extracted with AcOEt and the organic layer was washed with H_2O and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by CC (benzene–CH_3OH=10:1) to give **17** as a yellow needles (185 mg, 66%).

Mp 171–175 °C (dec). IR ($CHCl_3$, cm^{-1}) 3490, 1720. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.30 (3H, s, CH_3), 2.89 (1H, dd, J=14.6, 8.9 Hz, H-1β), 3.44 (1H, dd, J=14.6, 8.9 Hz, H-1α), 3.58, 3.64 (each 1H, br s, OH, exchangeable with D_2O), 3.80 (1H, dd, J=8.9, 8.9 Hz, H-11b), 3.92, 3.94, 4.01 (each 3H, s, 3×OCH_3), 6.92 (1H, d, J=8.1 Hz, H-8), 7.58 (1H, dd, J=8.1, 8.1 Hz, H-9), 7.70 (1H, d, J=8.1 Hz, H-10). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 22.9, 37.6, 42.3, 56.4, 61.3, 63.4, 74.6, 76.1, 80.7, 107.1, 114.3, 121.1, 121.5, 130.6, 135.2, 136.5, 148.5, 155.6, 159.5, 199.3, 210.0. EIMS *m*/*z* 403 (100%), 288 (22%), 257 (50%), 140 (14%), 116 (30%). Anal. Calcd for $C_{21}H_{22}O_8$: C: 62.68, H: 5.51; found: C: 62.72, H: 5.51.

4.1.5. (±)-(3*RS*,4*SR*,4a*RS*,11b*RS*)-3,4a-Dihydroxy-6,7,11-trimethoxy-3-methyl-2,5-dioxo-3,4,4a,11b-tetrahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (18). A mixture of **17** (19 mg, 48 μmol), Ac_2O (5 μL, 48 μmol), and pyridine (4 μL, 48 μmol) in CH_2Cl_2 (0.2 mL) was stirred at rt for 6 h. The whole was diluted with $CHCl_3$ and washed with H_2O and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by preparative TLC (*n*-hexane–AcOEt=1:1×3) to give **18** as a yellow oil (15 mg, 71%).

IR ($CHCl_3$, cm^{-1}) 3507, 1724. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.22 (3H, s, CH_3), 2.23 (3H, s, Ac), 3.09 (1H, dd, J=14.7, 8.4 Hz, H-1β), 3.58 (1H, dd, J=14.7, 8.4 Hz, H-1α), 3.82 (1H, dd, J=8.4, 8.4 Hz, H-11b), 3.91, 3.98, 4.01 (each 3H, s, 3×OCH_3), 5.25 (1H, s, H-1), 6.93 (1H, d, J=8.1 Hz, H-8), 7.59 (1H, dd, J=8.1, 8.1 Hz, H-9), 7.71 (1H, d, J=8.1 Hz, H-10). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 20.6, 21.7, 37.0, 41.9, 56.4, 61.3, 63.0, 73.2, 76.2, 80.5, 107.1, 114.4, 120.7, 121.7, 130.7, 133.5, 136.6, 148.8, 155.9, 159.5, 170.2, 198.1, 208.6. HRFABMS *m*/*z* calcd for $C_{23}H_{24}O_9$: 444.1420; found: 444.1438.

4.1.6. (±)-(3*RS*,4*SR*,4a*RS*,11b*SR*)-6,7,11-Trimethoxy-3-methyl-2,3,4,4a-tetrakis(trimethylsilanyloxy)-3,4,4a,11b-tetrahydrobenzo[*b*]fluoren-5-one (19). To a solution of **18** (100 mg, 0.25 mmol) in CH_2Cl_2 (1 mL), Et_3N (0.35 mL, 2.51 mmol) and TMSOTf (0.27 mL, 1.48 mmol) were added and the whole was stirred at 0 °C for 1 h. Saturated aqueous $NaHCO_3$ was added and the whole was extracted with $CHCl_3$. The organic layer was washed with H_2O and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by CC (neutral SiO_2, benzene–AcOEt=5:1) to give **19** as a yellow oil (134 mg, 78%).

IR ($CHCl_3$, cm^{-1}) 1722. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.06, 0.13, 0.15, 0.25 (each 9H, s, 4×TMS), 1.15 (3H, s, CH_3), 3.77 (1H, br s, H-4), 3.94, 4.01, 4.02 (each 3H, s, 3×OCH_3), 5.33 (1H, d, J=4.9 Hz, H-1), 6.87 (1H, d, J=8.0 Hz, H-8), 7.53 (1H, dd, J=8.0, 8.0 Hz, H-9), 7.70 (1H, d, J=8.0 Hz, H-10) (increment of the integration of 1H for H-11b was observed around the peaks of OCH_3). LRFABMS *m*/*z* 691 [$(M+H)^+$].

4.1.7. (±)-(1*RS*,3*RS*,4*RS*,4a*SR*,11b*RS*)- and (±)-(1*RS*,3*SR*,4*SR*,4a*SR*,11b*RS*)-6,7,11-Trimethoxy-3-methyl-1,3,4,4a-tetrakis(trimethylsilanyloxy)-3,4,4a,11b-tetrahydro-1*H*-benzo[*b*]fluorene-2,5-dione (20 and 21). To a mixture of **19** (908 mg, 1.31 mmol) and $NaHCO_3$ (234 mg, 2.78 mmol) in CH_2Cl_2 (8 mL), a solution of *m*CPBA (70%, 648 mg, 2.73 mmol) in CH_2Cl_2 (4.5 mL) was added at −45 °C and the whole was stirred at −45 °C for 4.5 h. Aqueous Na_2SO_3 10% was added and the whole was extracted with $CHCl_3$. The organic layer was washed with saturated aqueous $NaHCO_3$, H_2O, and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was purified by CC (neutral SiO_2, benzene–AcOEt=20:1) to give **20** as a pale green oil (702 mg). Isomerization at 4 °C for 1 month under an argon atmosphere followed by CC gave **21** as a yellow oil (663 mg, 71%).

Compound **20**: IR (neat, cm^{-1}) 1718. ^1H NMR (400 MHz, $CDCl_3$) δ: −0.07, 0.08, 0.21, 0.24 (each 9H, s, 4×TMS), 1.12 (3H, s, CH_3), 3.53 (1H, d, J=1.3 Hz, H-1 or H-11b), 3.93 (1H, d, J=1.3 Hz, H-11b or H-1), 4.01, 4.021, 4.025 (each 3H, s, 3×OCH_3), 4.20 (1H, s, H-4), 6.93 (1H, d, J=7.9 Hz, H-8), 7.59 (1H, dif. t, J=8.2 Hz, H-9), 7.74 (1H, d, J=8.4 Hz, H-10). EIMS m/z 706 (M^+, 64%), 460 (59%), 309 (60%), 73 (100%).

Compound **21**: IR ($CHCl_3$, cm^{-1}) 1750, 1715. ^1H NMR (400 MHz, $CDCl_3$) δ: −0.08, 0.01 (each 9H, s, 2×TMS), 0.17 (total 18H, s, 2×TMS), 1.21 (3H, s, CH_3), 3.92 (1H, d, J=7.7 Hz, H-11b), 4.017, 4.024, 4.07 (each 3H, s, 3×OCH_3), 4.09 (1H, d, J=7.7 Hz, H-1), 4.25 (1H, s, H-4), 6.92 (1H, d, J=8.1 Hz, H-8), 7.56 (1H, dd, J=8.1, 8.1 Hz, H-9), 7.82 (1H, d, J=8.1 Hz, H-10). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 0.2, 1.2, 1.9, 3.0, 24.9, 56.1, 56.3, 61.2, 63.1, 80.4, 81.0, 82.9, 83.7, 106.8, 115.1, 121.0, 123.3, 130.0, 135.4, 136.3, 149.4, 155.5, 159.3, 199.8, 206.1. HRFABMS m/z calcd for $C_{33}H_{54}O_9Si_4Na$: 729.2743; found: 729.2722.

4.1.8. (±)-(1*RS*,3*SR*,4*SR*,4a*SR*,11b*RS*)-1,3,4,4a-Tetrahydroxy-6,7,11-trimethoxy-3-methyl-3,4,4a,11b-tetrahydro-1*H*-benzo[*b*]fluorene-2,5-dione (22). To a solution of **21** (432 mg, 0.61 mmol) in CH_3OH (20 mL), H_2O (6 mL) was added and the whole was stirred at rt for 24 h. The whole was concentrated to ca. 5 mL and extracted with $CHCl_3$. The organic layer was washed with brine then dried over $MgSO_4$. The solvent was evaporated in vacuo and the residue was washed with Et_2O and AcOEt to give **22** as pale yellow needles (233 mg, 91%).

Mp 175–179 °C. IR ($CHCl_3$, cm^{-1}) 3516, 1723. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.37 (3H, s, CH_3), 3.40 (1H, d, J=7.6 Hz, OH, exchangeable with D_2O), 3.57 (1H, d, J=7.6 Hz, H-11b), 3.81 (1H, s, OH, exchangeable with D_2O), 3.93 (1H, d, J=7.6 Hz, H-4, changed into s by addition of D_2O), 3.99, 4.03, 4.06 (each 3H, s, 3×OCH_3), 4.44 (1H, d, J=7.2 Hz, H-8), 7.63 (1H, dif. t, J=8.3 Hz, H-9), 7.75 (1H, d, J=8.3 Hz, H-10). ^{13}C NMR (100 MHz, $CDCl_3$+CD_3OD) δ: 23.6, 52.4, 56.3, 62.0, 63.3, 73.0, 74.2, 75.7, 82.2, 107.1, 114.5, 121.4, 121.5, 130.4, 133.6, 136.2, 148.6, 155.2, 159.3, 198.8, 210.1. HREIMS m/z calcd for $C_{21}H_{22}O_9$: 418.1264; found: 418.1251.

4.1.9. (±)-(1*RS*,2*RS*,3*RS*,4*RS*,4a*SR*,11b*RS*)-2-Hydroxy-3-methyl-1,3,4,4a-tetrakis(trimethylsilanyloxy)-6,7,11-trimethoxy-1,2,3,4,4a,11b-hexahydrobenzo[*b*]fluoren-11-one (23). A mixture of $ZnCl_2$ (200 mg, 1.47 mmol), which was dried by heat gun under reduced pressure, and Et_2O (2 mL) was refluxed for 2 h. After cooling to rt, the supernatant was transferred to a suspension of $NaBH_4$ (135 mg, 3.57 mmol) in Et_2O (7.5 mL) and the mixture was stirred at rt for overnight. The supernatant was used as a 0.15 M solution of $Zn(BH_4)_2$ in Et_2O. To a solution of **21** (46 mg, 65 μmol) in Et_2O (1 mL), the $Zn(BH_4)_2$ solution (5.0 mL, 0.75 mmol) was added at −10 °C and the whole was stirred at −10 °C for 4 h. H_2O was added and the whole was extracted with AcOEt. The organic layer was washed with H_2O and brine then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by CC (neutral SiO_2, n-hexane–AcOEt=5:1) to give **23** as pale green needles (38 mg, 82%).

Mp 190–210 °C (dec). IR (KBr, cm^{-1}) 3446, 3220, 1727. ^1H NMR (600 MHz) δ: −0.06, 0.05, 0.209, 0.212 (each 9H, s, 4×TMS), 1.11 (3H, s, CH_3), 3.45 (1H, dd, J=9.6, 2.4 Hz, H-2, changed into d, J=2.4 Hz by addition of D_2O), 3.80–3.90 (3H, m, H-1, H-4, and H-11b), 4.01, 4.039, 4.044 (each 3H, s, 3×OCH_3), 4.10 (1H, br s, OH, exchangeable with D_2O), 6.90 (1H, d, J=7.8 Hz, H-8), 7.54 (1H, dif. t, J=7.8 Hz, H-9), 7.80 (1H, d, J=8.4 Hz, H-10). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 0.0, 1.0, 2.1, 3.0, 25.9, 49.9, 56.3, 61.3, 63.4, 74.4, 76.1, 77.4, 77.5, 84.4, 106.6, 115.0, 120.8, 123.1, 130.0, 134.0, 136.0, 149.4, 154.9, 159.2, 200.3. HREIMS calcd for $C_{33}H_{56}O_9Si_4$: 708.3001; found: 708.3015.

4.1.10. (±)-(1*RS*,2*RS*,3*RS*,4*SR*,4a*RS*,5*RS*,11b*RS*)-3-Methyl-6,7,11-trimethoxy-1,2,3,4,4a,5,11b-hexahydrobenzo[*b*]fluorene-1,2,3,4,4a,11b-hexaol (24). To a solution of **22** (31 mg, 74 μmol) in THF (1.6 mL), a $Zn(BH_4)_2$ solution (vide supra, 1 mL, 0.15 mmol) was added at −18 °C and the whole was stirred at −18 °C for 4 h. HCl 2% was added and the whole was extracted with $CHCl_3$. The organic layer was washed with H_2O and brine then dried over $MgSO_4$. The solvent was evaporated in vacuo to give **24** as pale yellow prisms (23 mg, 73%).

Mp 158–164 °C (dec). IR (KBr, cm^{-1}) 3433. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.33 (3H, s, CH_3), 3.30 (1H, d, J=3.5 Hz, H-2), 3.55 (1H, s, H-4), 3.86, 3.90 (each 3H, s, 2×OCH_3), 3.95 (1H, d, J=3.3 Hz, H-11b), 4.02 (3H, s, OCH_3), 4.70 (1H, s, OH, exchangeable with D_2O), 4.99 (1H, br s, H-1, changed into dif. t, J=3.3 Hz by addition of D_2O), 5.46 (1H, s, H-5), 6.92 (1H, d, J=7.7 Hz, H-8), 7.44 (1H, dif. t, J=8.3 Hz, H-9), 7.69 (1H, d, J=8.6 Hz, H-10). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 23.3, 49.9, 56.1, 61.3, 62.6, 69.8, 71.0, 71.5, 76.5, 83.2, 84.2, 106.5, 114.9, 120.4, 125.7, 126.9, 129.6, 132.4, 148.5, 149.5, 156.0. HREIMS m/z calcd for $C_{21}H_{26}O_9$: 422.1576; found: 422.1584.

4.1.11. (±)-(1*RS*,2*RS*,3*RS*,4*RS*,4a*SR*,11b*RS*)-1,2,3,4,4a-Pentahydroxy-6,7,11-trimethoxy-3-methyl-1,2,3,4,4a,11b-hexahydrobenzo[*b*]fluorene-5-one (25). To a solution of $(CH_3)_4NBH(OAc)_3$ (73 mg, 0.28 mmol) in CH_3CN (0.2 mL) and AcOH (0.2 mL), tetraol **22** (12 mg, 29 μmol) in CH_3CN (1.5 mL) was added at −40 °C and the whole was stirred at −40 °C for 2 h. After addition of 0.5 M aqueous Rochelle salt (1.5 mL), the whole was gradually warmed to rt within 1.5 h and evaporated. HCl 10% (1 mL) was added to the residue and the whole was extracted with $CHCl_3$. The organic layer was washed with brine and evaporated in vacuo. The residue was purified by CC ($CHCl_3$–CH_3OH=10:1) to give **25** as a yellow amorphous product (10 mg, 83%).

IR (neat, cm^{-1}) 3422, 1719. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.20 (3H, s, CH_3), 3.61 (1H, s, H-4), 3.63 (1H, d, J=6.9 Hz, H-2), 3.87 (1H, dif. t, J=8.1 Hz, H-1), 3.91 (1H, d, J=5.5 Hz, OH, exchangeable with D_2O), 3.99, 4.02, 4.04 (each 3H, s, 3×OCH_3), 4.17 (1H, d, J=9.3 Hz, H-11b), 6.93 (1H, d, J=8.0 Hz, H-8), 7.60 (1H, dif. t, J=9.3 Hz, H-9), 7.67 (1H, d, J=8.6 Hz, H-10). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 20.6, 50.5, 56.3, 62.0, 63.3, 72.1, 72.9, 75.6, 81.1, 106.8, 114.3, 121.2, 121.5, 128.8, 130.3, 130.9, 135.8, 147.9, 155.9, 159.4, 200.0. HRFABMS m/z calcd for $C_{21}H_{25}O_9$: 421.1499; found: 421.1475.

4.1.12. (±)-(1*RS*,2*SR*,3*RS*,4*RS*,4a*SR*,11b*RS*)-2,4-Diacetoxy-3,4a-dihydroxy-6,7,11-trimethoxy-3-methyl-5-oxo-2,3,4,4a,5,11b-hexahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (26). A mixture of **25** (42 mg, 0.10 mmol), Ac_2O (36 mg, 0.36 mmol), pyridine (79 mg, 1.0 mmol), and DMAP (1.2 mg, 10 μmol) in CH_2Cl_2 (0.5 mL) was stirred at rt for 24 h. The whole was evaporated in vacuo. The residue was dissolved in AcOEt and washed with saturated aqueous $CuSO_4$, H_2O, and brine, successively then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by CC ($CHCl_3$–CH_3OH=20:1) to give **26** as a yellow powder (28 mg, 51%).

Mp 253–255 °C. IR ($CHCl_3$, cm^{-1}) 3533, 1745, 1723. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.04 (3H, s, CH_3), 1.77, 2.20, 2.21 (each 3H, s, 3×Ac), 3.76 (1H, br s, OH), 3.93 (1H, br s, H-11b), 3.967, 3.972, 4.01 (each 3H, s, 3×OCH_3), 4.10 (1H, br, OH), 4.98 (1H, s, H-4), 5.13 (1H, dd, J=2.9, 1.5 Hz, H-1), 6.51 (1H, dd, J=2.9, 1.7 Hz, H-2), 6.93 (1H, d, J=7.8 Hz, H-8), 7.58 (1H, dif. t, J=7.8 Hz, H-9), 7.58 (1H, dif. t, J=7.6 Hz, H-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.6, 20.8, 21.3, 21.9, 46.5, 56.3, 62.0, 62.9, 66.2, 70.3, 72.5, 75.0, 81.7, 107.0, 114.0, 120.4, 121.7, 129.9, 130.6, 136.3, 148.3, 155.8, 159.3, 169.5, 169.6, 170.1, 198.2. HRFABMS m/z calcd for $C_{27}H_{31}O_{12}$: 547.1816; found: 547.1798.

4.1.13. (±)-(1*RS*,2*SR*,3*RS*,4*RS*,4a*SR*,11b*RS*)-2,4-Diacetoxy-3,4a-bis(methylsulfanylthiocarboxyoxy)-6,7,11-trimethoxy-3-methyl-5-oxo-2,3,4,4a,5,11b-hexahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (27). To a suspension of NaH (60%, 2.7 mg, 31 μmol) in THF (0.2 mL), a solution of **26** (7.4 mg, 13.6 μmol) in THF (0.3 mL) and DMF (two drops) was added at 0 °C and the whole was stirred at 0 °C for 30 min. A solution of CS_2 (4 μL, 65 μmol) in THF (0.08 mL) was added and the whole was stirred at 0 °C for 30 min. A solution of CH_3I (4 μL, 65 μmol) in THF (0.08 mL) was added and the whole was stirred at 0 °C for 2.5 h. Saturated aqueous NH_4Cl was added and the whole was extracted with AcOEt. The organic layer was washed with H_2O and dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by preparative TLC ($CHCl_3$–CH_3OH=20:1) to give **27** as a brown oil (1.3 mg, 13%).

IR (neat, cm^{-1}) 1714. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.48 (3H, s, CH_3), 1.71, 2.09, 2.25 (each 3H, s, 3×Ac), 2.61, 2.68 (each 3H, s, 2×SCH_3), 3.96 (total 6H, s, 2×OCH_3), 4.01 (3H, s, OCH_3), 5.48 (1H, s, H-11b), 6.26 (1H, s, H-4), 6.27 (1H, d, J=2.1 Hz, H-1 or H-2), 6.56 (1H, d, J=2.1 Hz, H-2 or H-1), 6.92 (1H, d, J=7.5 Hz, 8-H), 7.57 (1H, dif. t, J=7.5 Hz, 9-H), 7.68 (1H, d, J=7.9 Hz, 10-H). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 18.8, 19.2, 19.3, 20.5, 20.9, 22.4, 41.4, 56.3, 62.0, 63.0, 65.4, 69.0, 76.0, 80.0, 89.5, 106.7, 114.0, 121.57, 121.62, 129.2, 130.3, 136.0, 148.2, 155.7, 159.6, 168.9, 169.3, 169.8, 189.4, 212.4, 216.4. HRFABMS m/z calcd for $C_{31}H_{35}O_{12}S_4$: 727.1011; found: 727.1013.

4.1.14. (±)-(1*RS*,2*SR*,3*SR*,4*SR*)-2,4-Diacetoxy-6,7,11-trimethoxy-3-methyl-3-methylsulfanyl-5-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (28). Compound **27** (3 mg, 4.0 μmol) was heated in a glass-tube oven (300 °C/20 mmHg) for 10 min to give a yellow oil, which was purified by CC (benzene–AcOEt=10:1 to 5:1) to give **28** as a yellow oil (2 mg, 87%).

IR (neat, cm^{-1}) 1751, 1740, 1699. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.71 (3H, s, CH_3), 2.71, 2.10, 2.15 (each 3H, s, 3×Ac), 2.31 (3H, s, SCH_3), 3.76, 3.98, 4.04 (each 3H, s, 3×OCH_3), 4.64 (1H, s, H-4), 5.63, 6.07 (each 1H, d, J=7.0 Hz, H-1 and H-2), 6.94 (1H, dd, J=7.6, 2.0 Hz, H-8), 7.47–7.53 (2H, m, H-9 and H-10). ^{13}C NMR (125 MHz, $CDCl_3$) δ: 17.3, 17.7, 20.9, 21.0, 22.1, 45.7, 56.5, 62.6, 63.8, 68.7, 74.8, 82.3, 109.6, 116.1, 119.1, 122.2, 123.9, 125.7, 130.3, 135.7, 140.1, 145.3, 154.8, 160.0, 170.0, 160.2, 170.8, 189.6. LRFABMS m/z 559 [$(M+H)^+$].

4.1.15. (±)-(1*RS*,2*SR*,3*SR*,4*SR*)-2,4-Diacetoxy-6,7,11-trimethoxy-3-methyl-5-oxo-1-sulfamoyloxy-2,3,4,11-tetrahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (29). A mixture of **26** (4.8 mg, 8.8 μmol) and Burgess reagent (6.0 mg, 24.4 μmol) in toluene (0.4 mL) was stirred at 80 °C for 5 h. The solvent was evaporated in vacuo and the residue was purified by preparative TLC ($CHCl_3$–CH_3OH=10:1) to give **29** as a yellow oil (2 mg, 37%).

IR (ATR, cm^{-1}) 1753, 1697. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.84 (3H, s, CH_3), 2.16, 2.18, 2.23 (each 3H, s, 3×Ac), 3.81, 3.99, 4.03 (each 3H, s, 3×OCH_3), 5.03 (2H, br, NH, exchangeable with D_2O), 5.18, 6.04 (each 1H, d, J=5.1 Hz, H-1 or H-2), 6.18 (1H, s, H-4), 6.98 (1H, dd, J=6.8, 2.2 Hz, H-8), 7.52–7.56 (2H, m, H-9 and H-10). HREIMS m/z calcd for $C_{27}H_{29}NO_{13}S$: 607.1359; found: 607.1314.

4.1.16. (±)-(1*RS*,3*SR*,4*SR*,4a*SR*,11b*RS*)-4-Acetoxy-3,4a-dihydroxy-6,7,11-trimethoxy-3-methyl-2,5-dioxo-2,3,4,4a,5,11b-hexahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (31). Compound **22** (200 mg, 0.48 mmol) was added to a mixture of Ac_2O (120 mg, 1.18 mmol) and pyridine (2 mL) and the whole was stirred at 0 °C for 12 h. AcOEt was added and the whole was washed with saturated aqueous $CuSO_4$, H_2O, and brine then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by CC (benzene–AcOEt=1:1) to give **30** as a pale yellow needles (167 mg, 70%).

Mp 223–225 °C. IR (ATR, cm^{-1}) 3374, 1743, 1720. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.35 (3H, s, CH_3), 2.20, 2.38 (each 3H, s, 2×Ac), 3.48, 3.66 (each 1H, s, 2×OH, exchangeable with D_2O), 3.79 (1H, d, J=8.0 Hz, H-11b), 3.83, 3.98, 4.02 (each 3H, s, 3×OCH_3), 5.34 (1H, s, H-4), 5.85 (1H, d, J=8.0 Hz, H-1), 6.96 (1H, d, J=7.7 Hz, H-8), 7.61 (1H, dif. t, J=8.0 Hz, H-9), 7.72 (1H, d, J=8.5 Hz, H-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.55, 20.64, 23.8, 47.1, 56.3, 61.5, 63.0, 73.2, 73.9, 75.4, 81.5, 107.2, 114.7, 120.9, 121.9, 130.7, 131.7, 136.7, 149.1, 155.7, 159.4, 169.5, 170.2, 196.7, 204.0. HREIMS m/z calcd for $C_{25}H_{26}O_{11}$: 502.1474; found: 502.1442.

4.1.17. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,4a*SR*,11b*RS*)-4-Acetoxy-2,3,4a-trihydroxy-6,7,11-trimethoxy-3-methyl-5-oxo-2,3,4,4a,5,11b-hexahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (31). To a solution of $(CH_3)_4NBH(OAc)_3$ (120 mg,

0.46 mmol) in CH_3CN–AcOH (1:1, 1 mL), **30** (43 mg, 86 μmol) was added at −25 °C and the whole was stirred at −25 °C for 21 h. Rochelle salt 0.5 M aqueous (1 mL) was added and the whole was extracted with AcOEt. The organic layer was washed with H_2O then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was treated with MnO_2 (160 mg, 1.84 mmol) in AcOEt (1 mL) at rt for 24 h. The whole was filtered off through Celite pad and the filtrate was evaporated in vacuo. The residue was purified by CC (*n*-hexane–AcOEt=1:3 to 1:5) to give **31** as a pale yellow amorphous product (30 mg, 69% as a ca. 5:1 mixture of diastereoisomers).

IR (ATR, cm^{-1}) 3508, 1720. ^1H NMR (400 MHz, $CDCl_3$) (for major isomer) δ: 1.16 (3H, s, CH_3), 2.199, 2.202 (each 3H, s, 2×Ac), 3.75 (1H, s, OH), 3.97 (1H, br s, H-2), 3.95, 4.00, 4.02 (each 3H, s, 3×OCH_3), 4.06 (1H, br s, H-11b), 5.13 (1H, s, H-4), 6.51 (1H, dd, *J*=3.1, 2.1 Hz, H-1), 6.92 (1H, d, *J*=7.7 Hz, H-8), 7.58 (1H, dif. t, *J*=8.0 Hz, H-9), 7.69 (1H, d, *J*=7.9 Hz, H-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.6, 21.3, 22.0, 46.7, 56.4, 61.8, 62.9, 69.3, 69.9, 73.8, 75.2, 77.7, 81.8, 107.0, 114.4, 120.3, 121.6, 130.5, 136.3, 147.9, 156.0, 159.5, 167.0, 170.1, 198.3. HREIMS *m*/*z* calcd for $C_{25}H_{28}O_{11}$: 504.1631; found: 504.1661.

4.1.18. Conversion of diacetate 31 to triacetate 26 for identification. A mixture of **31** (3 mg, a 5:1 mixture of diastereoisomers, 6 μmol) and Ac_2O (3 mg, 29 μmol) in pyridine (40 mg, 0.51 mmol) was stirred at rt for 24 h. The solvent was evaporated and the residue was purified by preparative TLC (benzene–AcOEt=1:2) to give a yellow oil (2 mg, 62%). The spectral data were identical with that of **26**.

4.1.18.1. (±)-(1*RS*,2*SR*,3*RS*,4*SR*,4a*SR*,11b*RS*)-4-Acetoxy-2,3-dimethylmethylenedioxy-4a-hydroxy-6,7,11-trimethoxy-3-methyl-5-oxo-2,3,4,4a,5,11b-hexahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (32). A solution of **31** (75 mg, a 5:1 mixture of diastereoisomers, 0.15 mmol) and 2-methoxypropene (2.7 μL, 0.28 mmol) and $TsOH\cdot H_2O$ (1.3 mg, 7 μmol) in DMF (0.3 mL) was stirred at rt for 10 h. A solution of 2-methoxypropene (2.7 μL, 0.28 mmol) and $TsOH\cdot H_2O$ (1.3 mg 7 μmol) in DMF (0.3 mL) was added and the whole was stirred at rt for 11 h. AcOEt (30 mL) was added and the whole was washed with saturated aqueous $NaHCO_3$, H_2O, and brine then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by CC (benzene–AcOEt=1:1 to 1:3) to give **32** as a yellow oil (54 mg, 67%).

IR (ATR, cm^{-1}) 3270, 1745, 1722. ^1H NMR (400 MHz, $CDCl_3$) δ: 0.97, 1.40, 1.46 (each 3H, s, 3×CH_3), 1.96, 2.16, 2.24 (each 3H, s, 3×Ac), 3.91, 4.005, 4.008 (each 3H, s, 3×OCH_3), 4.29 (1H, d, *J*=6.8 Hz, H-11b), 4.51 (1H, d, *J*=9.2 Hz, H-2), 5.25 (1H, dd, *J*=9.2, 6.8 Hz, H-1), 6.24 (1H, s, H-4), 6.91 (1H, d, *J*=8.6 Hz, H-8), 7.55 (1H, dif. t, *J*=8.0 Hz, H-9), 7.69 (1H, d, *J*=8.3 Hz, H-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.1, 21.1, 21.3, 26.2, 28.3, 50.2, 56.4, 61.4, 63.1, 71.9, 76.2, 79.4, 81.7, 107.1, 111.7, 114.9, 120.5, 121.6, 128.3, 130.5, 135.2, 136.6, 149.0, 156.9, 159.43, 169.9, 171.1, 197.1. HREIMS *m*/*z* calcd for $C_{28}H_{32}O_{11}$: 544.1944; found: 544.1948.

4.1.18.2. (±)-(1*RS*,2*SR*,3*RS*,4*SR*)-4-Acetoxy-2,3-(dimethylmethylenedioxy)-6,7,11-trimethoxy-3-methyl-5-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (33). A suspension of **32** (26 mg, 48 μmol) and Burgess reagent (35 mg, 0.14 mmol) in toluene (0.5 mL) was stirred at 80 °C for 24 h. The whole was partitioned with AcOEt (10 mL) and H_2O (1 mL) and the aqueous layer was extracted with AcOEt. The combined organic layers were washed with brine then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by CC (neutral SiO_2, *n*-hexane–AcOEt=1:1 to 1:2) to give **33** as a yellow oil (13 mg, 52%).

IR (ATR, cm^{-1}) 1697. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.31, 1.40, 1.58 (each 3H, s, 3×CH_3), 2.11, 2.19 (each 3H, s, 2×Ac), 3.79, 3.99, 4.04 (each 3H, s, 3×OCH_3), 4.32 (1H, d, *J*=9.1 Hz, H-2), 5.88 (1H, s, H-4), 6.24 (1H, d, *J*=9.1 Hz, H-1), 6.98 (1H, d, *J*=7.7 Hz, H-8), 7.53 (1H, dif. t, *J*=8.0 Hz, H-9), 7.58 (1H, dd, *J*=8.2, 1.3 Hz, H-10). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 18.6, 20.8, 21.2, 26.1, 28.3, 56.5, 62.7, 64.2, 64.8, 67.0, 78.2, 79.6, 109.9, 111.5, 116.2, 119.2, 122.6, 125.4, 130.4, 135.5, 137.3, 147.4, 154.8, 155.1, 160.1, 169.3, 170.3, 188.8. HRIEMS *m*/*z* calcd for $C_{28}H_{30}O_{10}$: 526.1839; found: 526.1788.

4.1.18.3. (±)-(1*RS*,2*SR*,3*SR*,4*SR*)-2,4-Diacetoxy-3-hydroxy-6,7,11-trimethoxy-3-methyl-5-oxo-2,3,4,5-tetrahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (34). A solution of **33** (14 mg, 27 μmol) and $TsOH\cdot H_2O$ (1 mg, 5 μmol) in CH_3OH–CH_2Cl_2 (1:1, 1 mL) was stirred at rt for 20 h. CH_3OH (0.5 mL) was added and the whole was stirred at rt for 8 h. The solvent was evaporated in vacuo. A mixture of Ac_2O (57 mg, 0.56 mmol) in pyridine (100 mg, 1.26 mmol) was added to the residue at rt and the whole was stirred at rt for 9 h. AcOEt was added and the whole was washed with saturated aqueous $CuSO_4$ and H_2O then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by CC (benzene–AcOEt=3:1 to 2:1) to give **34** as a yellow oil (12 mg, 85%, two steps).

IR (ATR, cm^{-1}) 1749, 1698. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.36 (3H, s, CH_3), 2.13, 2.17, 2.19 (each 3H, s, 3×Ac), 2.27 (1H, s, OH), 3.80, 3.99, 4.03 (each 3H, s, 3×OCH_3), 5.49 (1H, d, *J*=6.2 Hz, H-2), 5.90 (1H, s, H-4), 6.05 (1H, d, *J*=6.2 Hz, H-1), 6.97 (1H, d, *J*=6.2 Hz, H-8), 7.52 (1H, dd, *J*=8.0, 6.2 Hz, 7-H), 7.56 (1H, d, *J*=8.0 Hz, 6-H). ^{13}C NMR (100 MHz, $CDCl_3$) δ: 20.2, 20.95, 20.96, 20.98, 56.5, 62.6, 63.9, 67.5, 67.9, 72.4, 75.1, 109.8, 116.2, 118.8, 122.6, 125.2, 130.4, 135.5, 135.6, 147.3, 151.4, 154.9, 169.1, 170.3, 170.4, 170.8, 188.9. HREIMS *m*/*z* calcd for $C_{27}H_{28}O_{11}$: 528.1631; found: 528.1643.

4.1.18.4. (±)-(1*RS*,2*SR*,3*SR*,4*SR*)-2,4-Diacetoxy-3-hydroxy-6,7,11-trimethoxy-3-methyl-5-(*p*-toluenesulfonylhydrazono)-2,3,4,5-tetrahydro-1*H*-benzo[*b*]fluoren-1-yl acetate (31). A mixture of **34** (9 mg, 17 μmol), $TsNHNH_2$ (4 mg, 21 μmol), and $BF_3\cdot OEt_2$ (4.2 μL, 34 μmol) in toluene (0.1 mL) was stirred at rt for 4 h. AcOEt was added and the whole was washed with saturated aqueous $NaHCO_3$, H_2O, and brine then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by CC (hexane–AcOEt 1:1) to give **35** as a reddish brown oil (7 mg, 59%).

IR (ATR, cm^{-1}) 3604, 1747. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.37 (3H, s, CH_3), 2.06 (3H, s, Ac), 2.13 (3H, br, Ac), 2.16 (3H, s, Ac), 2.42 (3H, s, $ArCH_3$), 3.75, 3.83, 4.05 (each 3H, s, 3×OCH_3), 5.49 (1H, d, J=6.3 Hz, H-2), 6.05 (1H, s, H-4), 6.06 (1H, d, J=6.3 Hz, H-1), 6.98 (1H, d, J=7.7 Hz, H-8), 7.34 (1H, d, J=8.3 Hz, Ts-*meta*), 7.51 (1H, dif. t, J=8.1 Hz, H-9), 7.62 (1H, d, J=8.2 Hz, H-10), 7.94 (1H, d, J=8.3 Hz, Ts-*ortho*). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 20.4, 21.1, 21.2, 21.7, 29.8, 56.3, 64.1, 64.5, 68.5, 68.8, 72.9, 75.7, 108.2, 115.8, 119.0, 119.4, 127.4, 128.3, 128.9, 129.7, 133.8, 135.8, 137.8, 144.0, 144.1, 147.2, 147.7, 157.7, 170.6, 170.7, 171.1, 181.9. HREIMS *m/z* calcd for $C_{34}H_{36}N_2O_{12}S$: 696.1988; found: 696.1930.

4.1.18.5. (±)-Methyl-kinamycin C (11). To a solution of **35** (6 mg, 8.6 μmol) in CH_3CN (0.1 mL) and CAN (12 mg, 22 μmol) in H_2O (0.18 mL) was added at 0 °C and the whole was stirred at 0 °C for 10 min. The whole was extracted with $CHCl_3$ and the organic layer was washed with H_2O and brine then dried over Na_2SO_4. The solvent was evaporated in vacuo and the residue was purified by CC (*n*-hexane–AcOEt=1:1 to 1:2) to give **11** as a red oil (2.4 mg, 55%).

IR (ATR, cm^{-1}) 3479, 2146, 1741, 1652, 1641. ^1H NMR (400 MHz, $CDCl_3$) δ: 1.28 (3H, s, CH_3), 2.12, 2.19, 2.20 (each 3H, s, 3×Ac), 2.70 (1H, br, OH), 4.03 (3H, s, OCH_3), 5.50 (1H, s, H-4), 5.60 (1H, d, J=7.3 Hz, H-2), 6.23 (1H, d, J=7.3 Hz, H-1), 7.28 (1H, m, H-8), 7.64 (1H, dif. t, J=8.0 Hz, H-9), 7.82 (1H, d, J=6.7 Hz, H-10). ^{13}C NMR (150 MHz, $CDCl_3$) δ: 18.6, 21.1, 21.2, 21.3, 56.6, 68.2, 71.2, 73.8, 75.6, 77.8, 117.4, 120.3, 120.5, 125.4, 127.1, 128.7, 135.2, 136.0, 136.7, 160.3, 170.5, 171.1, 172.2, 178.5, 179.3. HRFABMS *m/z* calcd for $C_{25}H_{23}N_2O_{10}$: 511.1353; found: 511.1359.

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References and notes

1. For reviews, see: (a) Gould, S. J. *Chem. Rev.* **1997**, *97*, 2499–2509; (b) Marco-Contelles, J.; Molina, M. T. *Curr. Org. Chem.* **2003**, *7*, 1433–1442; (c) Kumamoto, T.; Ishikawa, T.; Ōmura, S. *J. Synth. Org. Chem. Jpn.* **2004**, *62*, 49–58.
2. (a) Itō, S.; Matsuya, T.; Ōmura, S.; Otani, M.; Nakagawa, A.; Takeshima, H.; Iwai, Y.; Ohtani, M.; Hata, T. *J. Antibiot.* **1970**, *23*, 315–317; (b) Hata, T.; Ōmura, S.; Iwai, Y.; Nakagawa, A.; Otani, M.; Itō, S.; Matsuya, T. *J. Antibiot.* **1971**, *24*, 353–359.
3. (a) Feldman, K. S.; Eastman, K. J. *J. Am. Chem. Soc.* **2006**, *128*, 12562–12573; (b) Hasinoff, B. B.; Wu, X.; Yalowich, J. C.; Goodfellow, V.; Laufer, R. S.; Adedayo, O.; Dmitrienko, G. I. *Anticancer Drugs* **2006**, *17*, 825–837.
4. (a) Ōmura, S.; Nakagawa, A.; Yamada, H.; Hata, T.; Furusaki, A.; Watanabe, T. *Chem. Pharm. Bull.* **1971**, *19*, 2428–2430; (b) Ōmura, S.; Nakagawa, A.; Yamada, H.; Hata, T.; Furusaki, A.; Watanabe, T. *Chem. Pharm. Bull.* **1973**, *21*, 931–940.
5. Furusaki, A.; Matsui, M.; Watanabé, T.; Ōmura, S.; Nakagawa, A.; Hata, T. *Isr. J. Chem.* **1972**, *10*, 173–187.
6. Seaton, P. J.; Gould, S. J. *J. Antibiot.* **1989**, *42*, 189–197.
7. KC shows characteristic IR absorption at 2150 cm^{-1}. See: Ref. 4.
8. Echavarren, A. M.; Tamayo, N.; Parades, M. C. *Tetrahedron Lett.* **1993**, *34*, 4713–4716.
9. Gould, S. J.; Tamayo, N.; Melville, C. R.; Cone, M. C. *J. Am. Chem. Soc.* **1994**, *116*, 2207–2208.
10. Mithani, S.; Weeratunga, G.; Taylor, N.; Dmitrienko, G. I. *J. Am. Chem. Soc.* **1994**, *116*, 2209–2210.
11. Hauser, F. M.; Zhou, M. *J. Org. Chem.* **1996**, *61*, 5722.
12. Proteau, P. J.; Li, Y.; Chen, J.; Williamson, R. T.; Gould, S. J.; Laufer, R. S.; Dmitrienko, G. I. *J. Am. Chem. Soc.* **2000**, *122*, 8325–8326.
13. The terms prekinamycin and isoprekinamycin are now applied to the structures **4** and **5**, respectively, because Gould reported the isolation of **4** as another metabolite produced by *S. murayamaensis* (Gould, S. J.; Chen, J.; Cone, M. C.; Gore, M. P.; Melville, C. R.; Tamayo, N. *J. Org. Chem.* **1996**, *61*, 5720–5721).
14. He, H.; Ding, W.-D.; Bernan, V. S.; Richardson, A. D.; Ireland, C. M.; Greenstein, M.; Ellestad, G. A.; Carter, G. T. *J. Am. Chem. Soc.* **2001**, *123*, 5362–5363.
15. Diazocarbon of KC was observed at 78.5 ppm in ^{13}C NMR. Seaton, P. J.; Gould, S. J. *J. Am. Chem. Soc.* **1988**, *110*, 5912–5914.
16. Lei, X.; Porco, J. A., Jr. *J. Am. Chem. Soc.* **2006**, *128*, 14790–14791.
17. (a) Kumamoto, T.; Tabe, N.; Yamaguchi, K.; Ishikawa, T. *Tetrahedron Lett.* **2000**, *41*, 5693–5697; (b) Kumamoto, T.; Tabe, N.; Yamaguchi, K.; Yagishita, H.; Iwasa, H.; Ishikawa, T. *Tetrahedron* **2001**, *57*, 2717–2728.
18. Kitani, Y.; Morita, A.; Kumamoto, T.; Ishikawa, T. *Helv. Chim. Acta* **2002**, *85*, 1186–1195.
19. The structure of **14** was deduced by comparison of spectral data with that of by-product obtained in model system (Kumamoto, T.; Ishikawa, T. Unpublished result). The detail will be reported elsewhere.
20. Rubottom, G. M.; Gruber, J. M. *J. Org. Chem.* **1978**, *43*, 1599–1602.
21. Donohoe, T. J.; Blades, K.; Moore, P. R.; Waring, M. J.; Winter, J. J. G.; Helliwell, M.; Newcomb, N. J.; Stemp, G. *J. Org. Chem.* **2002**, *67*, 7946–7956.
22. The NOE enhancements shown as * in Figure 3 were observed, but the intensities were observed over 50% for several times.
23. Modified procedure of Hurst et al. Hurst, D. T.; McInnes, A. G. *Can. J. Chem.* **1965**, *43*, 2004–2011.
24. Nakata, T.; Tanaka, T.; Oishi, T. *Tetrahedron Lett.* **1983**, *24*, 2653–2656.
25. Crystal data of **23**: $C_{33}H_{56}O_9Si_4$, M=709.14, monoclinic, a=11.137(2), b=26.848(6), c=13.373(3) Å, β=102.754(3)°, V=3900.0(14) $Å^3$, T=173 K, space group $P2_1/n$ (No. 14), Z=4, μ(Mo Kα)=0.200 mm^{-1}, 22,803 reflections measured, 8938 unique (R_{int}=0.0569), $R1$ ($F^2>2\sigma$ (F^2))=0.0416, wR (F^2)=0.0999. CCDC 638781.
26. Evans, D. A.; Chapman, K. T.; Carreira, E. M. *J. Am. Chem. Soc.* **1988**, *110*, 3560–3578.
27. Crystal data of **26**: $C_{27}H_{30}O_{12}$, M=546.51, monoclinic, a=8.3565(11), b=20.821(3), c=14.843(2) Å, β=96.861(2)°, V=2564.0(6) $Å^3$, T=173 K, space group $P2_1/n$ (No. 14), Z=4, μ(Mo Kα)=0.112 mm^{-1}, 15,379 reflections measured, 6080 unique (R_{int}=0.0948), 367 parameters refined, $R1$ ($F^2>2\sigma$ (F^2))=0.0538, wR (F^2)=0.1362. CCDC 618952.

28. Displacement of benzylic xanthate to methylthio group in thermal condition was reported: (a) Eto, M.; Nishimoto, M.; Ueshima, T.; Hisano, T.; Harano, K. *J. Chem. Soc., Perkin Trans. 2* **1995**, 1155–1162; (b) Kryczka, B.; Descotes, G. *Bull. Pol. Acad. Sci. Chem.* **1985**, *33*, 475–482.
29. Burgess, E. M.; Penton, H. R., Jr.; Taylor, E. A. *J. Am. Chem. Soc.* **1970**, *92*, 5224–5226.
30. Examples of stereoselective reduction by $(CH_3)_4NBH(OAc)_3$ via five-membered ring transition state for the synthesis of rocaglaols: (a) Diedrichs, N.; Ragot, J. P.; Thede, K. *Eur. J. Org. Chem.* **2005**, 1731–1735; (b) Dobler, M. R.; Bruce, I.; Cederbaum, F.; Cooke, N. G.; Diorazio, L. J.; Hall, R. G.; Irving, E. *Tetrahedron Lett.* **2001**, *42*, 8281–8284.
31. Ketal formation in 4-cyclohexene-*trans*-1,2-diol system has already been reported in the derivatization of kinamycins: see, Ref. 4b.
32. Abad, A.; Arnó, A. M.; Domingo, L. R.; Zaragozá, R. J. *J. Org. Chem.* **1988**, *53*, 3761–3772.