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# Diterpenoids. XXXV.[1] A-Ring Substitution of Hydrofluorene Compound derived from *l*-Abietic Acid[2,3]

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A-ring substitution of hydrofluorene compound derived from *l*-abietic acid (I) was accomplished and several hydrofluorenes with A-ring substituent were synthesized.

In our previous studies,[5] many hydrofluorene derivatives have been synthesized from *l*-abietic acid (I) *via* a benzilic acid rearrangement of a diketo ester (V). It is interesting that a strong sweetener[6] (II) and a compound[5a] (III) with the gibberellin skeleton (*cf.* gibberellin $A_{12}$ (IV)) were found among these hydrofluorene derivatives. However, the hydrofluorene derivatives do not have any A-ring substituents, and it was expected that the A-ring modification will open a wider possibility for their utilization.

The rearranged compound (VI) is regarded as a potential intermediate in the conversion of *l*-abietic acid (I) to hydrofluorene derivatives. In our previous paper,[1] we concluded that the rearranged compound (VI) has a nonsteroidal form (VI-A), in which 6$\beta$-hydroxyl group is located near the C-3 site in the A-ring. Therefore, the 6$\beta$-hydroxyl group may be considered to attack the C-3 position by intramolecular radical reaction. On the basis of this idea, synthesis of the A-ring substituted hydrofluorenes was attempted by the use of 6$\beta$-hydroxy diester (VI) as the starting material.

The 6$\beta$-hydroxy diester (VI) was oxidized ($Pb(OAc)_4$, $I_2$, benzene, reflux) to give three compounds. The resulting products were chromatographed on alumina and separated into the known keto ester[7] (VII) (15.8% yield) and two kinds of unknown diesters; (VIII), $C_{19}H_{21}O_5I$, bp 155—160° (bath temp.)/0.07 mmHg, (7.8% yield), NMR $\tau$: 6.60 (d, 1H, $J$=1 Hz; 5$\alpha$-H), 5.30 (d, 1H, $J$=1 Hz; 3$\alpha$-H), 8.20 (dd, 1H, $J$=12.4, 14.8 Hz; 1$\alpha$-H), 7.92 (dd, 1H, $J$=7, 14.8 Hz; 1$\beta$-H), 6.31 (dd, 1H, $J$=7, 12.4 Hz; 2$\beta$-H), and (IX), $C_{19}H_{22}O_5$, mp 102—104° (59.8% yield), NMR $\tau$: 6.66 (d, 1H, $J$=1 Hz; 5$\alpha$-H), 5.67 (dd, 1H, $J$=1, 6.5 Hz; 3$\alpha$-H).

The stereochemistry of the two diesters (VIII and IX) was determined reliably as follows:

First, the skeleton of VIII and IX was certified by chemical evidence. Catalytic hydrogenation of the iodo-epoxy diester (VIII) afforded an epoxy diester (IX). This diester (VIII) was cleaved by zinc reduction to give an unsaturated diester (X). Subsequently, hydrogenation of the diester (X) afforded the starting material (VI). Considering the above chemical

1) Part XXXIV: T. Nakata, Y. Ohtsuka, A. Tahara (the late), and S. Takada, *Chem. Pharm. Bull.* (Tokyo), **23**, 2318 (1975).
2) A part of the work was published as a preliminary communication: A. Tahara and T. Nakata, *Tetrahedron Letters*, **1972**, 4507. Dr. Akira Tahara passed away suddenly on January 2, 1975.
3) The hydrofluorene compounds were obtained from *l*-abietic acid in this work and the usual numbering for diterpenes was used for the hydrofluorene derivatives.
4) Location: *Wako-shi, Saitama.*
5) *a*) A. Tahara and Y. Ohtsuka, *Chem. Pharm. Bull.* (Tokyo), **18**, 859 (1970); *idem*, *J. Chem. Soc.* (Perkin I), **1972**, 320; *b*) *Idem*, *Chem. Pharm. Bull.* (Tokyo), **20**, 1637 (1972); *idem*, *ibid.*, **20**, 1648 (1972).
6) A. Tahara, T. Nakata, and Y. Ohtsuka, *Nature*, **233**, 619 (1971); A. Tahara, T. Nakata, H. Nakaya, and K. Kagiwada, *Yakugaku Zasshi*, **93**, 951 (1973); A. Tahara, T. Nakata, Y. Ohtsuka, S. Takada, and T. Tanabe, *ibid.*, **93**, 957 (1973).
7) M. Ohta, *Chem. Pharm. Bull.* (Tokyo), **5**, 256 (1957); A. Tahara, O. Hoshino, and T. Ohsawa, *ibid.*, **17**, 68 (1969).

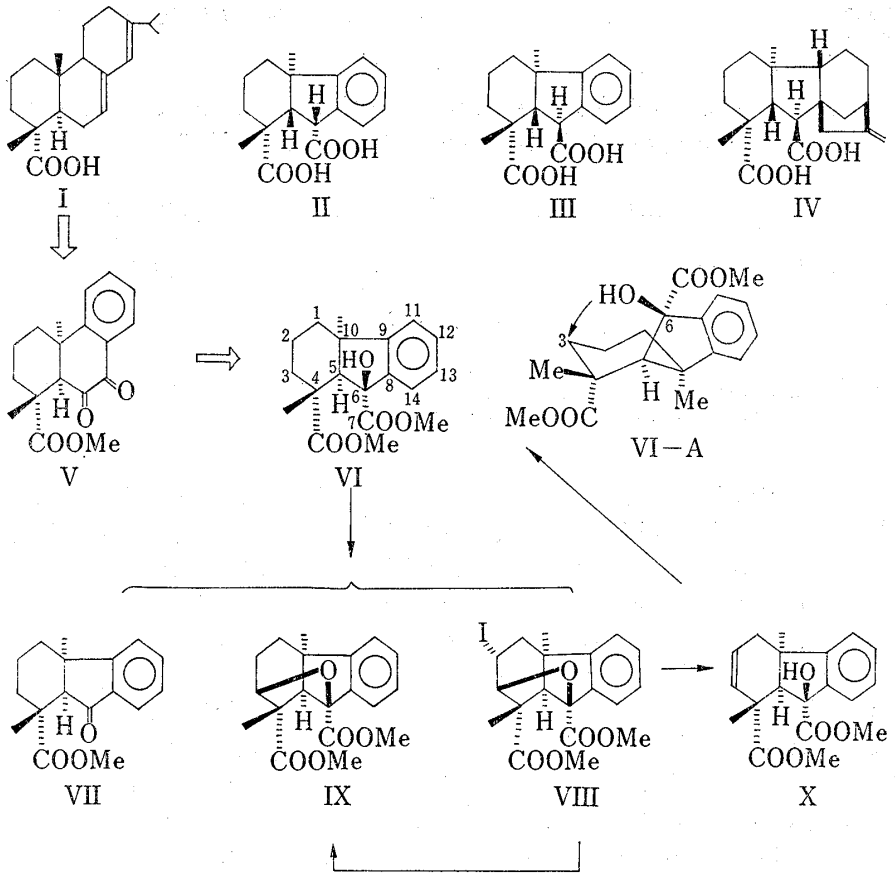


Chart 1

relation, both products (VIII and IX) can be assumed to have the same hydrofluorene skeleton as the starting material (VI).

Next, the structure of the two epoxy diesters (VIII and IX) was further examined by the detailed analysis of their NMR patterns and coupling constants. In the epoxy diester (IX), the doublet splitting ($J$=1 Hz) at $\tau$ 6.66 due to 5$\alpha$-H was observed, which was certified by the decoupling technique to be a long-range coupling with 3$\alpha$-H by the W-rule.[8] 3$\alpha$-H appeared at $\tau$ 5.67 with a doublet-doublet splitting ($J$=1, 6.5 Hz). One ($J$=1 Hz) is also a long-range coupling with 5$\alpha$-H, and the another ($J$=6.5 Hz) should be a coupling with 2$\alpha$-H in the boat A-ring (the flagpoles are at C-1 and C-4). The coupling constant is almost consistent with the calculated $J$ value[9] ($\phi_{2\alpha,3\alpha}$=20°, $J_{\text{calc.}}$=8.8 Hz; $\phi_{2\beta,3\alpha}$=100°, $J_{\text{calc.}}$=0.5 Hz) in the boat A-ring. In the iodo-epoxy diester (VIII), 5$\alpha$-H also has a long-range coupling ($J$=1 Hz) with 3$\alpha$-H by the W-rule.[8] Furthermore, 3$\alpha$-H had only a long-range coupling ($J$=1 Hz) with 5$\alpha$-H, and no coupling with 2-$H_2$. Accordingly, the iodine atom has 2$\alpha$-configuration in the boat A-ring ($\phi_{2\beta,3\alpha}$=100°, $J_{\text{calc.}}$=0.5 Hz). This elucidation was also ascertained by the ABX type coupling ($J_{1\alpha,2\beta}$=12.4 Hz, $J_{1\beta,2\beta}$=7 Hz, $J_{1\alpha,1\beta}$=14.8 Hz) between 2$\beta$-H and 1-$H_2$. These coupling constants are almost consistent with the calculated $J$ value[9] ($\phi_{1\alpha,2\beta}$=170°, $J_{\text{calc.}}$=15.5 Hz; $\phi_{1\beta,2\beta}$=50°, $J_{\text{calc.}}$=4.1 Hz) in the boat A-ring. From these results, structures of the two diesters (VIII and IX) were unequivocally determined to be the boat A-ring and having 3,6-epoxide bridge (with 2$\alpha$-I in VIII).

8) S. Sternhell, *Rev. Pure Appl. Chem.*, **14**, 15 (1964).
9) The coupling constants ($J_{\text{calc.}}$) were calculated from the dihedral angle ($\phi$) of the Dreiding model by using the equation of Williamson and Johnson [K.L. Williamson and W.S. Johnson, *J. Am. Chem. Soc.*, **83**, 4623 (1961)].

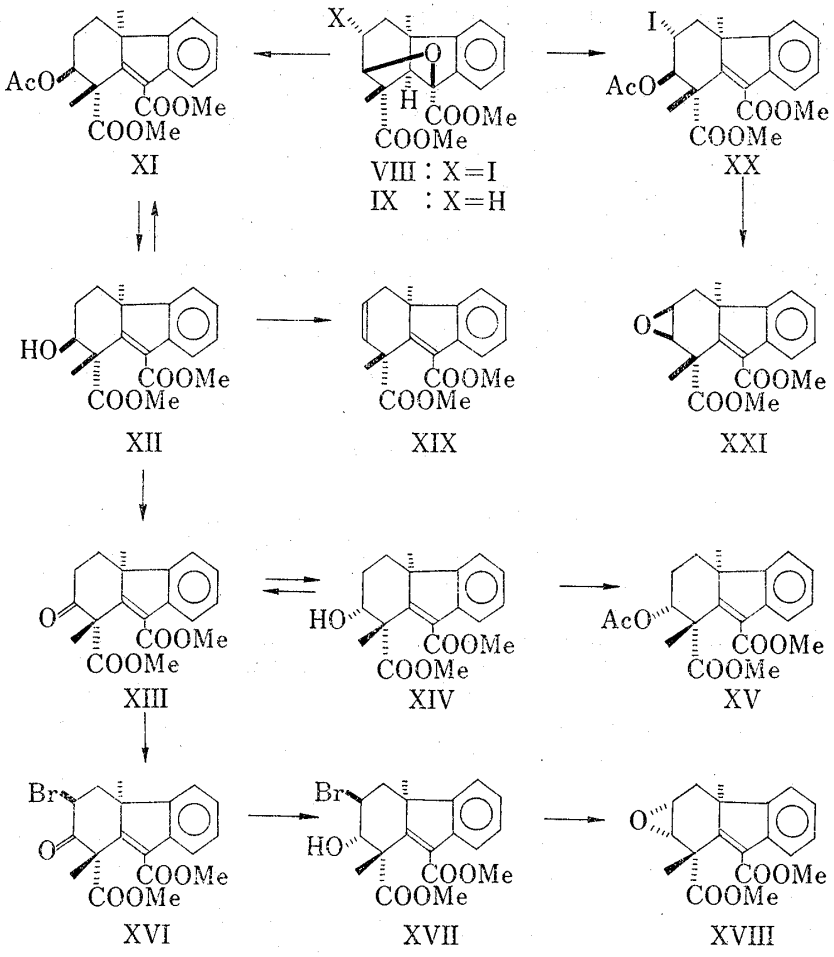


Chart 2

Several hydrofluorenes with A-ring substituent were synthesized from the two epoxy diesters (VIII and IX).

The ether bridge of the epoxy diester (IX) was cleaved by treatment with boron trifluoride-etherate in acetic anhydride to give an unsaturated 3-acetoxy diester (XI) quantitatively. Acid hydrolysis of 3-acetoxy diester (XI) afforded 3-hydroxy diester (XII), mp 157—160°, NMR $\tau$: 5.66 (broad s, $Wh/2$=8 Hz; 3$\alpha$-H), which returned to the original acetoxy diester (XI) by acetylation. The 3-hydroxy diester (XII) was oxidized by Jones reagent to the 3-keto diester (XIII), NMR $\tau$: 7.10—7.28 (m, 2H; 2-$H_2$). The nuclear magnetic resonance (NMR) spectrum of this compound (XIII), in which there are two protons adjacent to the keto group, supports the presence of the keto group at C-3 position. Sodium borohydride reduction of the 3-keto diester (XIII) yielded another 3-hydroxy diester (XIV), mp 180—184°, NMR $\tau$: 6.57—6.93 (m, $Wh/2$=30 Hz; 3$\beta$-H), which returned to the original keto diester (XIII) by the Jones oxidation. Accordingly, the two hydroxy diesters (XII and XIV) are stereoisomers with respect to the 3-hydroxyl group. The configurational assignments of 3-hydroxyl group in XII and XIV were determined by comparison of NMR patterns due to 3$\alpha$- and 3$\beta$-H. Since 3-H in XIV was observed at a higher magnetic field and had wider half-height band width than that in XII, 3-H in XIV must be axial and that in XII equatorial. Namely, XIV is an equatorial 3$\alpha$-hydroxy isomer, while XII is an axial 3$\beta$-hydroxy one. 3$\alpha$-Hydroxy diester (XIV) was acetylated to 3$\alpha$-acetoxy diester (XV). Bromination of the 3-keto diester (XIII) yielded a 2$\beta$-bromo diester (XVI), NMR $\tau$: 5.24 (dd, $J$=8, 11.5 Hz; 2$\alpha$-H), which was reduced by sodium borohydride to give 2$\beta$-bromo-3$\alpha$-hydroxy diester (XVII), NMR $\tau$: 6.67 (broad d, $J$=10.6 Hz; 3$\beta$-H). The configurations of 2-bromo atom and 3-hydroxyl group in XVI and XVII were determined as equatorial 2$\beta$-Br and equatorial 3$\alpha$-OH, respectively,

from their NMR spectra. 2$\beta$-Bromo-3$\alpha$-hydroxy diester (XVII) was treated with sodium methoxide to give an $\alpha$-epoxy diester (XVIII), mp 208—214°. 3$\beta$-Hydroxy diester (XII) was dehydrated ($SOCl_2$, pyridine, 80°) to $\Delta^2$-diester (XIX), NMR $\tau$: 4.20 (m, 2H, 2- and 3-olefinic protons). The iodo-epoxy diester (VIII) was also cleaved by boron trifluoride-etherate to iodo acetate (XX), NMR $\tau$: 7.86 (s, 3H; OAc), which was hydrolyzed (1N KOH) to give the $\beta$-epoxy diester (XXI), mp 105—109°.

Thus, the first attempt on the substitution of hydrofluorene A-ring was accomplished and some A-ring substituted hydrofluorenes were synthesized. The epoxy diesters (VIII and IX) are regarded as an important intermediate for the synthesis of 1-, 2-, and 3-substituted hydrofluorenes. The reaction opens the possibility for synthesized more interesting compounds such as a sweetener and gibberellin skeleton. This study is in progress.

## Experimental

All melting points were measured on a micro hot-stage and uncorrected. Nuclear magnetic resonance (NMR) spectra were measured at 100 MHz in $CDCl_3$ *vs.* $Me_4Si$ as internal reference. The coupling constants ($J$) and half-height band width ($Wh/2$) are given in Hz. Mass spectra were measured on JEOL's JMS-01S mass spectrometer with the direct sample inlet system (ionizing potential at 75 eV).

**Oxidation of Dimethyl 1,2,3,4,5$\alpha$,10-Hexahydro-6$\beta$-hydroxy-4$\beta$,10$\alpha$-dimethylfluorene-4$\alpha$,6$\alpha$-dicarboxylate (VI) with Lead Tetraacetate and Iodide**——Lead tetraacetate (248 mg) and iodide (142 mg) were added to a solution of 6$\beta$-hydroxy diester (VI) (93 mg) in ab. benzene (8 ml) and the mixture was refluxed under nitrogen atmosphere for 3 hr. The precipitate was filtered off and washed with ether. The filtrate was washed with 10% $Na_2S_2O_3$ aq., sat. $NaHCO_3$ aq., sat. NaCl aq., and dried over $Na_2SO_4$. The solvent was evaporated to give oil (109 mg), which was chromatographed on alumina with petr. ether–ether (5:2) as eluent to give oil (VII) (12 mg); the oil was identical (IR spectra) with the authentic 6-keto ester[7] (VII). Next, oil (VIII) (10 mg) was eluted with petr. ether–ether (2:1); bp 155—160° (bath temp.)/$7\times10^{-2}$ mmHg. *Anal.* Calcd. for $C_{19}H_{21}O_5I$: C, 50.02; H, 4.64; I, 27.81. Found: C, 50.31; H, 4.66; I, 27.40. Beilstein test: positive. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1757 (sh), 1742. NMR $\tau$: 8.77 (s, 3H; Me), 8.38 (s, 3H; Me), 6.18 (s, 3H; COOMe), 6.16 (s, 3H; COOMe), 6.60 (d, 1H, $J_{3\alpha,5\alpha}=1$; 5$\alpha$-H), 5.30 (d, 1H, $J_{3\alpha,5\alpha}=1$; 3$\alpha$-H), 8.20 (dd, 1H, $J_{1\alpha,2\beta}=12.4$, $J_{1\alpha,1\beta}=14.8$; 1$\alpha$-H), 7.92 (dd, 1H, $J_{1\beta,2\beta}=7$, $J_{1\alpha,1\beta}=14.8$; 1$\beta$-H), 6.31 (dd, 1H, $J_{1\beta,2\beta}=7$, $J_{1\alpha,2\beta}=12.4$; 2$\beta$-H). Finally, crystals (IX) (55 mg) were eluted with petr. ether–ether (4:3); the crystals were recrystallized from petr. ether–ether to give colorless plates (IX), mp 102—104°. *Anal.* Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 68.96; H, 6.61. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1745, 1735. NMR $\tau$: 8.61 (s, 3H; Me), 8.46 (s, 3H; Me), 6.23 (s, 3H; COOMe), 6.17 (s, 3H; COOMe), 6.66 (d, 1H, $J_{3\alpha,5\alpha}=1$; 5$\alpha$-H), 5.67 (dd, 1H, $J_{3\alpha,5\alpha}=1$, $J_{2\alpha,3\alpha}=6.5$; 3$\alpha$-H).

**Catalytic Hydrogenation of Dimethyl 1,2,3,4,5$\alpha$,10-Hexahydro-3$\beta$,6$\beta$-epoxy-2$\alpha$-iodo-4$\beta$,10$\alpha$-dimethylfluorene-4$\alpha$,6$\alpha$-dicarboxylate (VIII)**——A solution of iodo-epoxy diester (VIII) (34 mg) in ab. EtOH (6 ml) was stirred in the presence of 10% Pd-C (100 mg) and $Et_3N$ (3 drops) under a hydrogen atmosphere at room temperature for 18 hr. The catalyst was filtered off and washed with ether. The filtrate was evaporated and the residue was dissolved in ether. The ether extract was washed with 10% HCl aq., 10% $Na_2CO_3$ aq., sat. NaCl aq., and dried over $Na_2SO_4$. The solvent was evaporated to give crude crystals (27 mg), which were purified by chromatography on alumina with petr. ether–ether (2:1) elution to give crystals (18 mg); the crystals were identical (mp, mixed mp and IR spectrum) with epoxy diester (IX).

**Zinc Reduction of Dimethyl 1,2,3,4,5$\alpha$,10-Hexahydro-3$\beta$,6$\beta$-epoxy-2$\alpha$-iodo-4$\beta$,10$\alpha$-dimethylfluorene-4$\alpha$,6$\alpha$-dicarboxylate (VIII)**——Zinc powder (200 mg) was added to a solution of iodo-epoxy diester (VIII) (21 mg) in AcOH (5 ml) and the mixture was refluxed for 4 hr. Zinc powder was filtered off and washed with ether. The filtrate was washed with $H_2O$, 10% $Na_2CO_3$ aq., sat. NaCl aq., and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (17.5 mg), which were recrystallized from petr. ether–ether to give colorless needles (X), mp 124.5—126°. *Anal.* Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.02; H, 6.70. Beilstein test: negative. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3538, 3514, 1737 (sh), 1726. NMR $\tau$: 8.69 (s, 3H; Me), 8.54 (s, 3H; Me), 6.29 (s, 3H; COOMe), 6.12 (s, 3H; COOMe), 4.20 (s, 2H; olefinic protons).

**Catalytic Hydrogenation of Dimethyl 1,4,5$\alpha$,10-Tetrahydro-6$\beta$-hydroxy-4$\beta$,10$\alpha$-dimethylfluorene-4$\alpha$,6$\alpha$-dicarboxylate (X)**——A solution of $\Delta^2$-6$\beta$-hydroxy diester (X) (17.5 mg) in ab. EtOH (6 ml) was stirred in the presence of platinum oxide (20 mg) under a hydrogen atmosphere at room temperature for 24 hr. The catalyst was filtered off and washed with ether. The filtrate was evaporated to give oil (15 mg), which was identical (IR and NMR spectra) with the starting material (VI).

**Dimethyl 1,2,3,10-Tetrahydro-3$\beta$-acetoxy-4$\beta$,10$\alpha$-dimethyl-4*H*-fluorene-4$\alpha$,6-dicarboxylate (XI)**——Boron trifluoride-etherate (1.7 ml) was added dropwise to a solution of epoxy diester (IX) (525 mg) in acetic anhydride (8 ml) under ice-cooling with stirring, and the mixture was stirred at room temperature for 90 min. The reaction mixture was diluted with $H_2O$ and neutralized with $K_2CO_3$, and then extracted with ether.

The ether extract was washed with sat. $NaHCO_3$ aq., sat. NaCl aq., and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (588 mg), which were recrystallized from petr. ether–ether to give colorless needles (XI), mp 106—107°. *Anal.* Calcd. for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.76; H, 6.47. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1737 (sh), 1730. NMR $\tau$: 8.78 (s, 3H; Me), 8.45 (s, 3H; Me), 8.03 (s, 3H; OAc), 6.31 (s, 3H; COOMe), 6.06 (s, 3H; COOMe), 4.39 (t, 1H, $J=3$; 3α-H).

**Dimethyl 1,2,3,10-Tetrahydro-3β-hydroxy-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate (XII)**——A solution of 3β-acetoxy diester (XI) (417 mg) in EtOH (16 ml)–2N HCl (8 ml) was refluxed for 6 hr. The solvent was removed under reduced pressure and the residue was diluted with $H_2O$ and extracted with ether. The ether extract was washed with 10% KOH aq., sat. NaCl aq., and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (318 mg), which were recrystallized from petr. ether–ether to give colorless prisms (XII), mp 157—160°. *Anal.* Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.14; H, 6.76. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3512, 1735, 1709. NMR $\tau$: 8.80 (s, 3H; Me), 8.36 (s, 3H; Me), 6.33 (s, 3H; COOMe), 6.06 (s, 3H; COOMe), 5.66 (broad s, 1H, $Wh/2=8$; 3α-H).

**Acetylation of Dimethyl 1,2,3,10-Tetrahydro-3β-hydroxy-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate (XII) with Acetic Anhydride**——A solution of 3β-hydroxy diester (XII) (10 mg) in acetic anhydride (2 ml)–pyridine (1 ml) was set aside overnight at room temperature. The reaction mixture was diluted with $H_2O$ and extracted with ether. The ether extract was washed with 10% HCl aq., 10% $Na_2CO_3$ aq., sat. NaCl aq., and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (14 mg), which were recrystallized from petr. ether–ether to give colorless needles; the crystals were identical (mp, mixed mp and IR spectrum) with 3β-acetoxy diester (XI).

**Dimethyl 1,2,3,10-Tetrahydro-4β,10α-dimethyl-3-oxo-4*H*-fluorene-4α,6-dicarboxylate (XIII)**——A mixture of 3β-hydroxy diester (XII) (40 mg) and Jones reagent (0.133 ml) in acetone (4 ml) was stirred under ice-cooling for 1 hr. The reaction mixture was diluted with MeOH, $H_2O$ and extracted with ether. The ether extract was washed with sat. NaCl aq. and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (37 mg), which were recrystallized from petr. ether–ether to give colorless plates (XIII), mp 153—155°. *Anal.* Calcd. for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.65; H, 6.36. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1756, 1712. NMR $\tau$: 8.64 (s, 3H; Me), 8.34 (s, 3H; Me), 6.26 (s, 3H; COOMe), 6.12 (s, 3H; COOMe), 7.10—7.28 (m, 2H; 2-$H_2$).

**Dimethyl 1,2,3,10-Tetrahydro-3α-hydroxy-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate (XIV)**——A mixture of 3-keto-diester (XIII) (20 mg) and $NaBH_4$ (30 mg) in MeOH (4 ml) was stirred at room temperature for 4 hr. The solvent was evaporated and the residue was diluted with $H_2O$ and extracted with ether. The ether extract was washed with sat. NaCl aq. and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (23 mg), which were recrystallized from petr. ether–ether to give colorless prisms (XIV), mp 180—184°. *Anal.* Calcd. for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.05; H, 6.76. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3524, 1727, 1717. NMR $\tau$: 8.77 (s, 3H; Me), 8.23 (s, 3H; Me), 6.31 (s, 3H; COOMe), 6.05 (s, 3H; COOMe), 6.57–6.93 (m, 1H, $Wh/2=30$; 3β-H).

**Jones Oxidation of Dimethyl 1,2,3,10-Tetrahydro-3α-hydroxy-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate (XIV)**——A solution of 3α-hydroxy diester (XIV) (7 mg) in acetone (0.7 ml) was treated with Jones reagent (0.023 ml) as in the case of oxidation of 3β-hydroxy diester (XII) to give crystals (8 mg), which were identical (mp, mixed mp and IR spectrum) with 3-keto diester (XIII).

**Dimethyl 1,2,3,10-Tetrahydro-3α-acetoxy-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate (XV)**——A solution of 3α-hydroxy diester (XIV) (40 mg) in acetic anhydride (4 ml)–pyridine (2 ml) was treated as in the case of acetylation of 3β-hydroxy diester (XII) to give colorless oil (XV) (46 mg), bp 138—142° (bath temp.)/$5\times10^{-3}$ mmHg. *Anal.* Calcd. for $C_{21}H_{24}O_6$: C, 67.73; H, 6.50. Found: C, 67.62; H, 6.29. IR $\nu_{max}^{CCl_4}$ $cm^{-1}$: 1741. NMR $\tau$: 8.72 (s, 3H; Me), 8.38 (s, 3H; Me), 7.88 (s, 3H; OAc), 6.32 (s, 3H; COOMe), 6.06 (s, 3H; COOMe), 5.41 (dd, 1H, $J=4.5$, 10.5; 3β-H).

**Dimethyl 1,2,3,10-Tetrahydro-2β-bromo-4β,10α-dimethyl-3-oxo-4*H*-fluorene-4α,6-dicarboxylate (XVI)**——$Br_2$–AcOH [$Br_2$ (815 mg) in AcOH (5 ml)] (0.12 ml) was added to a solution of 3-keto diester (XIII) (182 mg) in AcOH (14 ml)–47% HBr (several drops) and the mixture was stirred under water-cooling for 1 hr. The reaction mixture was diluted with $H_2O$ and extracted with ether. The ether extract was washed with 10% $Na_2S_2O_3$ aq., sat. $NaHCO_3$ aq., sat. NaCl aq., and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (219 mg), which were recrystallized from ether to give colorless prisms (XVI), mp 178—180°. *Anal.* Calcd. for $C_{19}H_{19}O_5Br$: C, 56.04; H, 4.70. Found: C, 55.92; H, 4.67. Beilstein test; positive. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1859, 1853, 1713. NMR $\tau$: 8.65 (s, 3H; Me), 8.08 (s, 3H; Me), 6.23 (s, 3H; COOMe), 6.09 (s, 3H; COOMe), 7.87 (dd, 1H, $J_{1\beta,2\alpha}=11.5$, $J_{1\alpha,1\beta}=14$; 1β-H), 6.97 (dd, 1H, $J_{1\alpha,2\alpha}=8$, $J_{1\alpha,1\beta}=14$; 1α-H), 5.24 (dd, 1H, $J_{1\alpha,2\alpha}=8$, $J_{1\beta,2\beta}=11.5$; 2α-H).

**Dimethyl 1,2,3,10-Tetrahydro-2β-bromo-3α-hydroxy-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate (XVII)**——A solution of 2β-bromo-3-keto diester (XVI) (30 mg) in MeOH (6 ml) was treated with $NaBH_4$ (45 mg) as in the case of reduction of 3-keto diester (XIII) to give crystals (31 mg), which were recrystallized from ether to give colorless plates (XVII), mp 210—218°. *Anal.* Calcd. for $C_{19}H_{21}O_5Br$: C, 55.76; H, 5.27. Found: C, 56.05; H, 5.27. Beilstein test: positive. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3504, 1725, 1712. NMR $\tau$: 8.73 (s, 3H; Me), 8.16 (s, 3H; Me), 6.28 (s, 3H; COOMe), 6.03 (s, 3H; COOMe), 6.67 (broad d, 1H, $J_{2\alpha,3\beta}=10.6$; 3β-H).

**Dimethyl 1,2,3,10-Tetrahydro-2α,3α-epoxy-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate (XVIII)**——A solution of 2β-bromo-3α-hydroxy diester (XVII) (249 mg) in ab. THF (8 ml) and MeONa–MeOH [Na metal (1.55 g) in MeOH (100 ml)] (3.1 ml) was refluxed for 90 min. The reaction mixture was removed under reduced pressure and the residue was diluted with $H_2O$ and extracted with ether. The ether extract was washed with sat. NaCl aq. and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (226 mg), which were recrystallized from petr. ether–ether to give colorless pedestals (XVIII), mp 208—214°. *Anal.* Calcd. for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.46; H, 6.09. Beilstein test: negative. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1731, 1712. NMR τ: 8.47 (s, 3H; Me), 8.38 (s, 3H; Me), 6.22 (s, 3H; COOMe), 6.11 (s, 3H; COOMe).

**Dimethyl 1,10-Dihydro-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate (XIX)**——Thionyl chloride (3.85 ml) was added dropwise to a solution of 3β-hydroxy diester (XII) (1 g) in pyridine (38.5 ml) and the mixture was stirred at 80° for 17 hr. The solvent was evaporated and the residue was dissolved with ether. The ether layer was washed with 5% HCl aq., sat. NaCl., and dried over $Na_2SO_4$. The solvent was evaporated to give oil (950 mg), which was crystallized from petr. ether–ether to give colorless prisms (XIX), mp 112—113°. *Anal.* by high resolution mass spectrometry Calcd. for $C_{19}H_{20}O_4$ ($M^+$; *m/e*): 312.1361. Found: 312.1367. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1737, 1731. NMR τ: 8.68 (s, 3H; Me), 8.50 (s, 3H; Me), 6.35 (s, 3H; COOMe), 6.13 (s, 3H; COOMe), 8.00 (broad d, 1H, $J$=16; 1β-H), 7.45 (dd, 1H, $J$=6, 16; 1α-H), 4.20 (m, 2H; olefinic protons).

**Dimethyl 1,2,3,10-Tetrahydro-3β-acetoxy-2α-iodo-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate ((XX)**——A solution of iodo-epoxy diester (VIII) (224 mg) in acetic anhydride (14 ml) was treated with boron trifluoride–etherate (2 ml) as in the case of epoxy diester (IX) to give crystals (237 mg), which were recrystallized from petr. ether–ether to give colorless prisms (XX), mp 132—135°. *Anal.* Calcd. for $C_{21}H_{23}O_6I$: C, 50.61; H, 4.65. Found: C, 50.93; H, 4.66. Beilstein test: positive. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1745, 1715. NMR (60 MHz) τ: 8.62 (s, 3H; Me), 8.16 (s, 3H; Me), 7.86 (s, 3H; OAc), 6.34 (s, 3H; COOMe), 6.17 (s, 3H; COOMe), 3.64 (d, 1H, $J_{2\beta,3\alpha}$=10.5; 3α-H).

**Dimethyl 1,2,3,10-Tetrahydro-2β,3β-epoxy-4β,10α-dimethyl-4*H*-fluorene-4α,6-dicarboxylate (XXI)**——A solution of iodo-acetoxy diester (XX) (223 mg) in MeOH (13 ml)–1N KOH (5 ml) was stirred at room temperature for 20 hr. The solvent was removed under reduced pressure and the residue was diluted with $H_2O$, and then extracted with ether. The ether extract was washed with sat. NaCl aq. and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (99 mg), which were recrystallized from petr. ether–ether to give colorless prisms (XXI), mp 105—109°. *Anal.* Calcd. for $C_{19}H_{20}O_5$: C, 69.50; H, 6.14. Found: C, 69.63; H, 6.07. IR $\nu_{max}^{KBr}$ $cm^{-1}$: 1727, 1717. NMR τ: 8.72 (s, 3H; Me), 8.22 (s, 3H; Me), 6.27 (s, 3H; COOMe), 6.06 (s, 3H; COOMe). The aqueous solution was acidified with conc. HCl and extracted with ether. The ether extract was washed with sat. NaCl aq. and dried over $Na_2SO_4$. The solvent was evaporated to give crystals (55 mg), which was methylated with $CH_2N_2$–ether; the methylated crystals were identical (mp, mixed mp and IR spectrum) with β-epoxy diester (XXI).

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