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Chemical Transformation of Terpenoids. I. Syntheses of (3*S*)-1-Vinyl-, (3*S*)-1-Hydroxypropenyl-, and (3*S*)-1-Epoxyethyl-1,2,2-trimethylcyclopentane Derivatives from *d*-Camphor *via* *d*-Camphoric Acid

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As part of a series of studies on the transformation of terpenoids, four 1,2,2-trimethylcyclopentane derivatives, *i.e.*, (+)-(1*S*,3*S*)-3-acetoxymethyl-1,2,2-trimethyl-1-vinylcyclopentane (**5**), (+)-(1*S*,3*S*)-3-acetoxymethyl-1-(3′-hydroxypropenyl)-1,2,2-trimethylcyclopentane (**7**), (+)-(1*R*,3*S*,1′*S*)-3-acetoxymethyl-1-(1′,2′-epoxyethyl)-1,2,2-trimethylcyclopentane (**8**), and (+)-(1*R*,3*S*,1′*R*)-3-acetoxymethyl-1-(1′,2′-epoxyethyl)-1,2,2-trimethylcyclopentane (**9**), were synthesized from *d*-camphor (**1**) *via* *d*-camphoric acid (**2**). All four compounds (**5**, **7**, **8**, **9**) retain the C-4 configuration of *d*-camphor at their C-3 positions.

Keywords——*d*-camphor; *d*-camphoric acid; 1-vinyl-1,2,2-trimethylcyclopentane; 1-hydroxypropenyl-1,2,2-trimethylcyclopentane; 1-epoxyethyl-1,2,2-trimethylcyclopentane; Horeau's method

Conversions of naturally abundant terpenoids to more valuable substances are important and interesting subjects of investigation in natural products chemistry. As a continuation of our investigations on the chemical transformations of triterpenoids[1] and sesquiterpenoids,[2] we have been working on the chemical transformation of *d*-camphor (**1**), which is one of most readily available optically active terpenoids, to higher terpenoids of interest from the viewpoint of their chemical structures and biological activities.[3] Transformations from *d*-camphor are also of interest in that they may be of use for providing optically active building-blocks for syntheses of various natural products. In this and the following papers, we present the results of studies in which *d*-camphor has been utilized as a starting material.

Our investigation began with the examination of optically active 1,2,2-trimethylcyclopentane derivatives (A) which were prepared from *d*-camphor (**1**) *via* several reaction steps. These cyclopentanes (A) contain an R^1 residue at C-1 which is presumably a precursor function for effecting the generation of a carbonium cation intermediate during the process of transformation from the cyclopentanes (A). It is presumed that i) when the transformation proceeds through a cation (B) *via* path a or b (a 1,2-migration of a C-C bond in the ring), a ring-enlarged product (C), *i.e.* a cyclohexane derivative, may be formed, whereas ii) when it occurs *via* path c (a 1,2-shift of a methyl group at C-1), a cyclopentane derivative may be produced *via* another carbonium cation intermediate (D). It is noteworthy in these proposed paths that the C-3 configuration in (A) (asterisked) is retained throughout the conversion. In addition, the cyclohexane derivatives (C) seem to be versatile compounds for the preparation of optically active 1,3,3-trimethylcyclohexanes (E) which in turn are promising building-blocks for syntheses of terpenoidal derivatives: *e.g.* taxane,[4] cyperane,[5] and pallescensin C[6] (the plane structures of these compounds are shown).

This paper describes syntheses of four 1,2,2-trimethylcyclopentane derivatives of type A from *d*-camphor (**1**) *via* *d*-camphoric acid (**2**). They are (+)-(1*S*,3*S*)-3-acetoxymethyl-1,2,2-trimethyl-1-vinylcyclopentane (**5**), (+)-(1*S*,3*S*)-3-acetoxymethyl-1-(3′-hydroxypropenyl)-1,2,2-trimethylcyclopentane (**7**), (+)-(1*R*,3*S*,1′*S*)-3-acetoxymethyl-1-(1′,2′-epoxyethyl)-1,2,2-trimethylcyclopentane (**8**), and (+)-(1*R*,3*S*,1′*R*)-3-acetoxymehtyl-1-(1′,2′-epoxyethyl)-1,2,2-

trimethylcyclopentane (**9**) [referred to hereafter as (+)-(3*S*)-vinylcyclopentane (**5**), (+)-(3*S*)-hydroxypropenylcyclopentane (**7**), (+)-(3*S*)-(1′*S*,2′)-epoxyethylcyclopentane (**8**), and (+)-(3*S*)-(1′*R*,2′)-epoxyethylcyclopentane (**9**), respectively]. All four cyclopentanes (**5**, **7**, **8**, **9**) possess a 3*S* configuration and have a vinyl, a hydroxypropenyl, or an epoxyethyl function at C-1 from which various types of transformation reactions (*via* path a, b, or c) may be initiated under acidic conditions through an intermediary carbonium cation at C-1′ (*cf.* B).

Nitric acid oxidation of *d*-camphor (**1**) gave *d*-camphoric acid (**2**)[7] which possesses a desired (3*S*)-1,2,2-trimethylcyclopentane skeleton. Methylation of **2** with diazomethane followed by reduction with lithium aluminum hydride afforded a diol (**3**) in 94% yield. For the preparation of this diol (**3**) on a larger scale (*e.g.* more than 50 g), reduction with di-

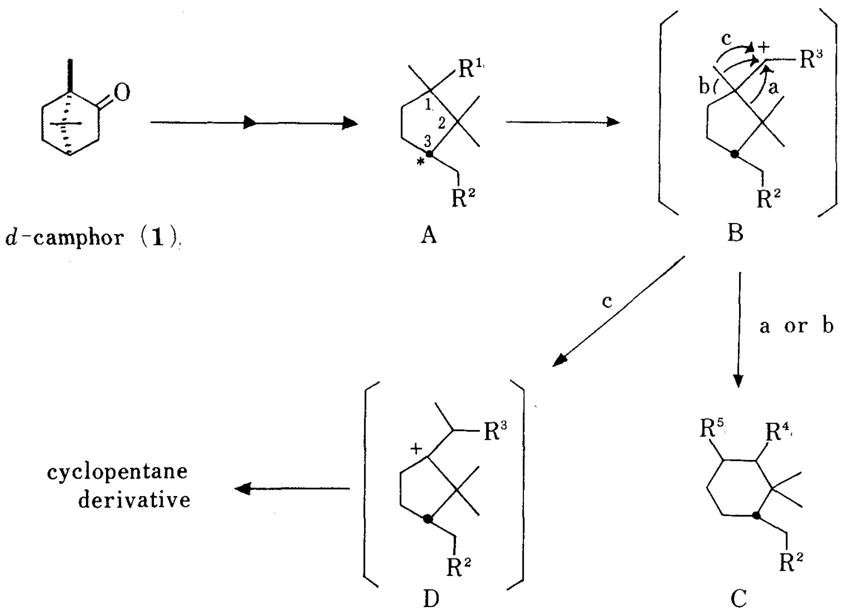

Chart 1

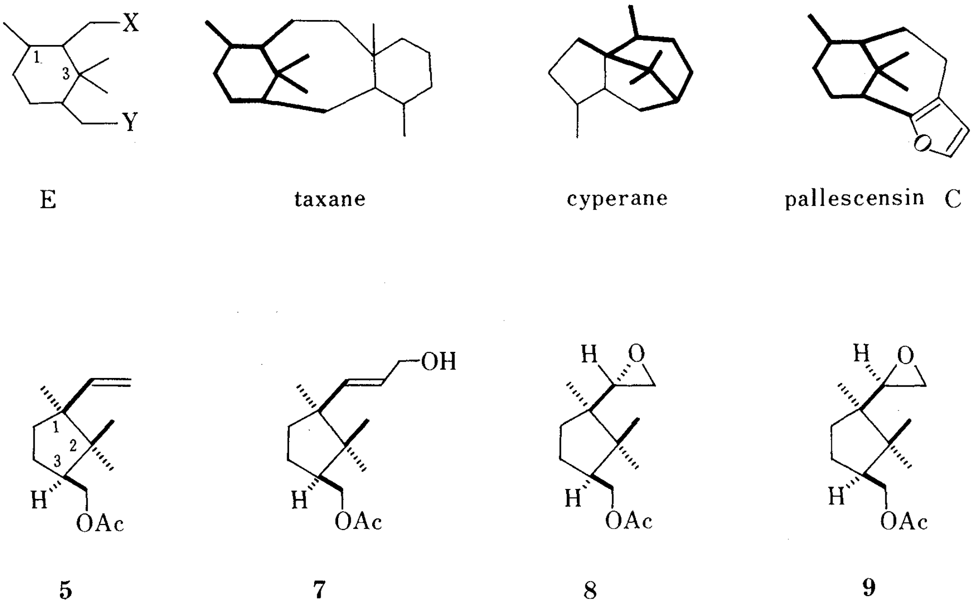

Chart 2

borane generated in the reaction vessel was advantageous although it gave a somewhat smaller yield (88%, see "Experimental"). In order to modify the 1-hydroxymethyl group of **3** to an aldehydic function, partial acetylation of **3** under various conditions was examined.

Acetylation of the diol (**3**) with acetic anhydride and sodium acetate in dichloromethane at room temperature furnished two monoacetates (**3a**, 40%; **3b**, 12%) and a diacetate (**3c**, 18%) together with unchanged **3** (27%). The infrared (IR) and proton nuclear magnetic resonance (^{1}H NMR) spectra of the major monoacetate are consistent with the desired structure **3a** having a hydroxymethyl group at C-1 [3440(br) cm^{-1}; δ 3.37, 3.50 (1H each, ABq, $J=9$ Hz)] and an acetoxymethyl group at C-3 [1737 cm^{-1}; δ 2.00 (3H, s), 3.8—4.1 (2H, AB in ABX)]. The structure of the other monoacetate (**3b**) was clarified on a similar basis. **3b** contains an acetoxymethyl group at C-1 [1747 cm^{-1}; δ 2.01 (3H, s), 3.91 (2H, s)] and a hydroxymethyl group at C-3 [3400 (br) cm^{-1}; δ 3.3—3.7 (2H, AB in ABX)]. The IR and ^{1}H NMR spectra of the diacetate are consistent with the structure **3c**. Hydrolysis of **3b** and **3c** with 10% methanolic potassium hydroxide readily yielded the parent diol (**3**) almost quantitatively.

Oxidation of the monoacetate (**3a**) with pyridinium chlorochromate (PCC)[8] quantitatively yielded an aldehyde (**4**) (2715, 1728 cm^{-1}; δ 9.67, 1H, s), which, on methylenation with methyltriphenylphosphonium bromide and dimsyl sodium, was converted to a vinylcyclopentane derivative: (+)-(3*S*)-vinylcyclopentane (**5**) in 83% yield. The formation of a vinyl group at C-1 was shown by IR absorption bands at 3080, 1645, 910 cm^{-1} and by the presence of ABC-type signals of three-proton intensity at δ 4.8—5.9 in the ^{1}H NMR spectrum. The retention of an acetoxymethyl group at C-3 was confirmed by the IR absorption band at 1745 cm^{-1} and ^{1}H NMR signals at δ 1.91 (3H, s) and δ 3.98 (2H, d, $J=6$ Hz). Three tertiary methyl groups in **4** were also retained in **5** as shown by three-proton singlets at δ 0.71, 0.91, and 0.97.

When the aldehyde (**4**) was subjected to formylolefination by initial treatment with diethyl 2-(cyclohexylimino)ethylphosphonate[9] and sodium hydride followed by hydrolysis with aqueous oxalic acid, an α,β-unsaturated aldehyde (**6**) was obtained. The presence of an *E*-α,β-unsaturated aldehyde group in **6** was substantiated by the ultraviolet (UV) absorption maximum at 222 nm (ε 17200), the IR absorption bands at 2720, 1690, and 1630 cm^{-1}, and the ^{1}H NMR signals: one-proton doublet at δ 9.50 ($J_{AX}=8$ Hz, $J_{BX}=0$ Hz) and two AB-type signals of one-proton each in an ABX system at δ 5.95 and 6.80 ($J_{AB}=16$ Hz). Reduction of **6** with sodium borohydride in an ice-cooled mixture of ether and methanol yielded (+)-(3*S*)-hydroxypropenylcyclopentane (**7**) in 94% yield. The IR spectrum shows hydroxyl and acetoxyl absorption bands (3420, 1745 cm^{-1}), while the ^{1}H NMR spectrum exhibits a four-proton multiplet at δ 3.8—4.1, ascribable to methylene protons on a carbon bearing an acetoxyl group and to other methylene protons on a carbon adjacent to an olefinic carbon and having a hydroxyl group. It also shows olefinic two-proton signals at δ 5.2—5.9 (m).

On the other hand, oxidation of (+)-(3*S*)-vinylcyclopentane (**5**) with *m*-chloroperbenzoic acid at 35°C in dichloromethane furnished two epoxides, (+)-(3*S*)-(1′*S*,2′)-epoxyethylcyclopentane (**8**) and (+)-(3*S*)-(1′*R*,2′)-epoxyethylcyclopentane (**9**), in 70 and 19% yields, respectively. However, when the aldehyde (**4**) was treated with trimethyloxosulfonium iodide[10] and sodium hydride, the above-mentioned minor epoxide (**9**) was predominantly formed: **8** in 6% yield and **9** in 66% yield.

The IR spectrum of the epoxide **8** shows absorption bands attributable to an epoxidic function (3040, 870, 814 cm^{-1}) and an acetoxyl group (1744 cm^{-1}) while the ^{1}H NMR spectrum lacks signals due to a vinyl group but shows signals at δ 2.1—2.8 (3H, ABC type) which are ascribable to an epoxyethyl moiety. The epoxide (**9**) also exhibits similar IR absorption bands and ^{1}H NMR signals (see "Experimental").

In regard to the C-1′ configuration of both epoxides (**8**, **9**), the 1′*S* and 1′*R* configurations were determined by the application of Horeau's method[11] to the two diol-monoacetates (**10b** and **12b**) which were derivable from **8** and **9**, respectively. Thus, reduction of **8** and **9** with

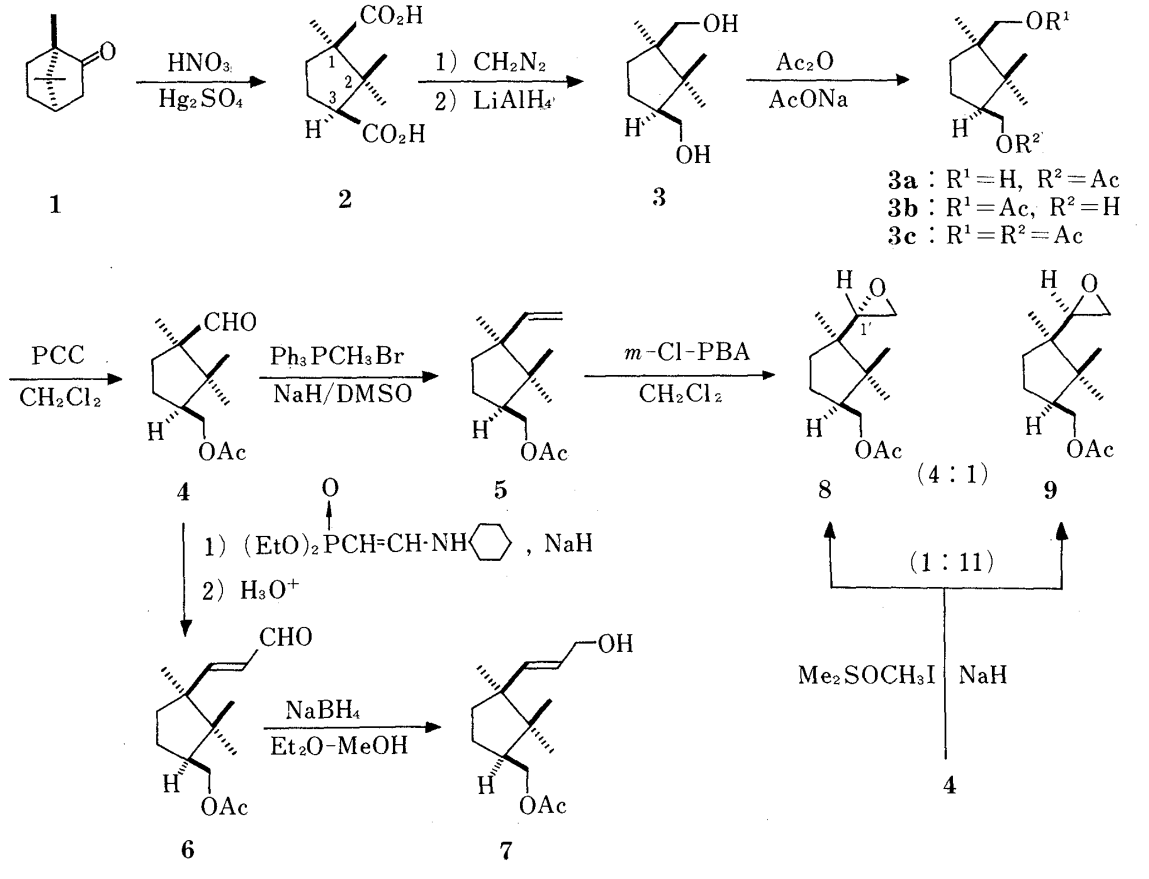

Chart 3

lithium aluminum hydride quantitatively yielded the corresponding diols (**10a**, **12a**). The IR spectra of both diols lack absorption bands due to epoxidic and acetoxyl functions but show hydroxyl absorption bands (**10a**, 3320(br) cm^{-1}; **12a**, 3300(br) cm^{-1}). The ^{1}H NMR spectra of both diols show signals attributable to one newly formed secondary methyl group which is attached to a carbon (C-1′) bearing a hydroxyl group (**10a**, δ 1.11, 3H, d, J=6 Hz; **12a**, δ 1.03, 3H, d, J=6 Hz) and signals due to three protons attached to two carbons each bearing a hydroxyl group (**10a**, δ 3.2—3.9, 3H, m; **12a**, δ 3.2—4.0, 3H, m).

Acetylation of **10a** with acetic anhydride and pyridine under ice-cooling yielded a monoacetate (**10b**, 53%) and a diacetate (**10c**, 14%) with a 30% recovery of **10a**. The introduction of one acetoxyl group at the primary carbinol of **10a** was corroborated by the IR spectrum (3470, 1746 cm^{-1}) and the ^{1}H NMR spectrum (δ 2.00, 3H, s, and δ 3.8—4.2, 2H, AB in ABX). On the other hand, acetylation of **12a** with acetic anhydride and sodium acetate in dichloromethane at room temperature yielded only a monoacetate (**12b**, 60%) while **12a** was recovered in 33% yield. The structure **12b** having a free secondary hydroxyl group, a secondary methyl group, and a primary acetoxymethyl group was ascertained by analysis of the IR and the ^{1}H NMR spectra as described for **10b**.

When **10b** was treated with (±)-α-phenylbutyric anhydride in pyridine at 32°C for 42 h, an α-phenylbutyrate (**11**) was formed together with α-phenylbutyric acid which exhibited a positive specific rotation, $[\alpha]_D$ +4.8° (benzene), thus indicating the 1′*R* configuration of the diol-monoacetate **10b**. When a similar reaction was carried out on the other diol-monoacetate (**12b**), another α-phenylbutyrate (**13**) was produced together with α-phenylbutyric acid of $[\alpha]_D$ −0.9° (benzene). This result defined the 1′*S* configuration of **12b**. In consequence, 1′*S* and 1′*R* configurations in the two epoxides **8** and **9**, respectively, have been established.

Formation of the 1′*S* epoxide (**8**), as a major product in peracid oxidation of **5** but as a

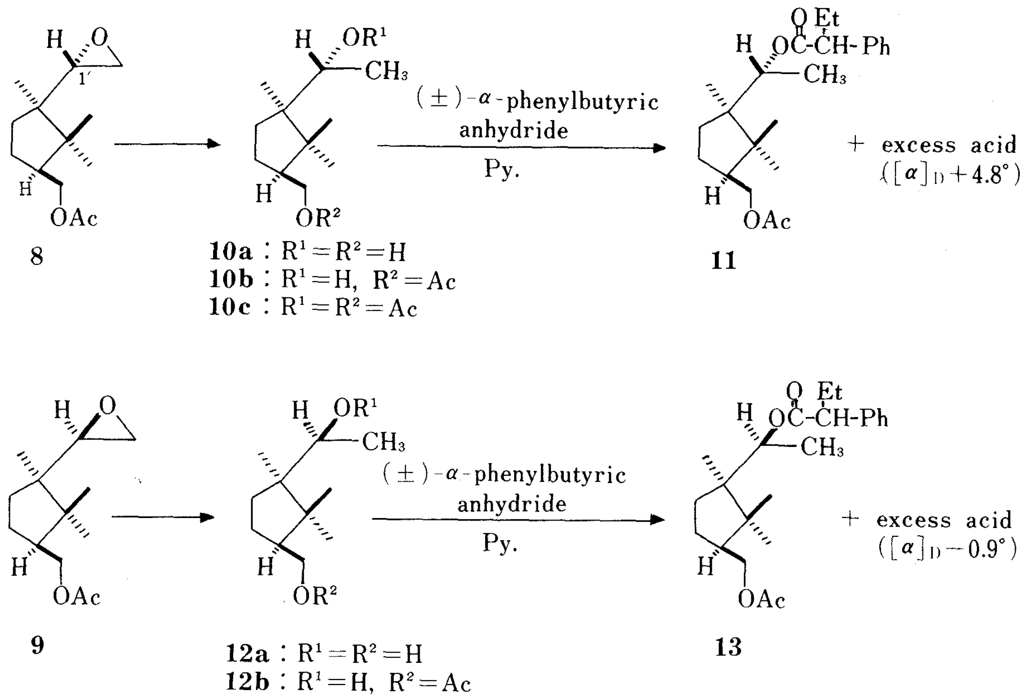

Chart 4

minor one in the reaction of **4** with trimethyloxosulfonium iodide–sodium hydride, is considered to indicate favored intermediary conformations of the vinyl group in **5** and the aldehydic group in **4** during the progress of each reaction.

Thus, four optically active cyclopentane derivatives, (+)-(3*S*)-vinylcyclopentane (**5**), (+)-(3*S*)-hydroxypropenylcyclopentane (**7**), (+)-(3*S*)-(1′*S*,2′)-epoxyethylcyclopentane (**8**), and (+)-(3*S*)-(1′*R*,2′)-epoxyethylcyclopentane (**9**), have been synthesized from *d*-camphor (**1**) *via* *d*-camphoric acid (**2**). Each compound retains the 3*S* configuration which comes from the C-4 configuration of *d*-camphor (**1**). Transformation studies using these derivatives (**5**, **7**, **8**, **9**) as starting compounds will be reported in the following paper.

Experimental

The following instruments were used to obtain physical data: melting points, Yanagimoto micro-melting apparatus (recorded uncorrected); specific rotations, JASCO DIP-181 digital polarimeter; IR spectra, Hitachi 260-30 or EPI-G3 infrared spectrometer; UV spectra, Hitachi 330 spectrophotometer; ^{1}H NMR spectra, Hitachi R-22 (90 MHz) NMR spectrometer (with TMS as an internal standard); high resoluiton mass spectra, JEOL D-300 mass spectrometer; mass spectra, Hitachi RMU-6E mass spectrometer or JEOL D-300 mass spectrometer. For high performance liquid chromatography (HPLC), a Waters ALC-100 machine (column: μ–Porasil) with an RI detector was used. Silica gel (Merck 70—230 mesh) and pre-coated TLC plates (Merck, silica gel 60 F_{254}) were used for column and thin–layer chromatography. All reactions were carried out under a nitrogen atmosphere.$^{7)}$

Nitric Acid Oxidation of *d*-Camphor (1)——A mixture of **1** (100 g) in 50% HNO_3 (1.0 l) and Hg_2SO_4 (20 g) was heated under reflux for 24 h. After cooling, a precipitate was collected by filtration, suspended in water (1.0 l) and treated with $Ca(OH)_2$ (*ca.* 50 g). The whole mixture was filtered and the filtrate was acidified with conc. HCl. The resulting white solid was collected by filtration and crystallized from EtOH–H_2O (2: 7) to afford *d*-camphoric acid (**2**) (101 g, 77%). Mp and $[\alpha]_D$ of **2** obtained here were identical with reported values.$^{7)}$

Reduction of *d*-Camphoric Acid (2) **giving the Diol** (3)——a) Diazomethane Methylation followed by $LiAlH_4$ Reduction: An ice-cooled solution of **2** (20 g) in ether (130 ml) was treated with excess ethereal diazomethane and the whole solution was left to stand at 5°C overnight. After treatment with AcOH to decompose excess diazomethane, the solvent was removed under reduced pressure to furnish dimethyl ester (22.6 g). The dimethyl ester was dissolved in THF (60 ml) and the solution was added dropwise over a period of 30 min into a suspension of $LiAlH_4$ (4.1 g) in THF (120 ml) and the whole was stirred at room temperature for 10 min. The reaction was quenched with EtOAc and aq. 10% H_2SO_4, then the mixture was extracted with EtOAc. Work-up of the EtOAc in the usual manner and removal of the solvent under reduced pressure furnished a diol (**3**, 16.2 g, 94% from **2**).

b) Reduction with Diborane: A mixture of **2** (100 g) and $NaBH_4$ (69 g) in THF (1.0 l) was treated dropwise at room temperature with BF_3-etherate (300 ml) over a period of 1 h. After being stirred for a further 1 h, the reaction mixture was poured into ice-water and extracted with EtOAc. Work-up of the EtOAc extract in the usual manner afforded **3** (76 g, 88%). **3**, mp 137—137.5°C (colorless needles from $CHCl_3$), $[\alpha]_D^{18}$ +65° (c=1.3, EtOH). *Anal.* Calcd for $C_{10}H_{22}O_2$: C, 69.72; H, 11.70. Found: C, 69.54; H, 11.70. IR ν_{max}^{KBr} cm^{-1}: 3300 (br). ^1H NMR (d_6-acetone, δ): 0.80, 1.00, 1.02 (3H each, all s, *tert.* $CH_3 \times 3$), 3.2—3.8 (6H, m, $-C\underline{H}_2-O\underline{H} \times 2$). MS m/z (%): 154 (5, M^+-H_2O), 123 (100).

Acetylation of 3 giving 3a, 3b, and 3c——A solution of **3** (3.37 g) in CH_2Cl_2 (200 ml) was treated with Ac_2O (8 ml) and AcONa (6.6 g) and the whole mixture was stirred at room temperature for 5 h. The reaction mixture was poured into ice-water and the whole was neutralized with $NaHCO_3$ powder and extracted with CH_2Cl_2. Work-up of the CH_2Cl_2 extract in the usual manner and removal of the solvent under reduced pressure gave a product (4.2 g) which was purified by column chromatography (SiO_2 80 g, n-hexane–EtOAc=4: 1) to furnish **3** (0.91 g, 27% recovered), **3a** (1.66 g, 40%), **3b** (0.52 g, 12%), and **3c** (0.90 g, 18%). **3a**: colorless oil, $[\alpha]_D^{29}$ +39° (c=3.6, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{22}O_3$: C, 63.13; H, 8.83. Found: C, 62.86; H, 8.77. IR ν_{max}^{film} cm^{-1}: 3440 (br), 1737. ^1H NMR (CCl_4, δ): 0.81, 0.95, 1.00 (3H each, all s), 2.00 (3H, s, OAc), 3.37, 3.50 (2H, ABq, J=9 Hz, $-C\underline{H}_2OH$), 3.8—4.1 (2H, AB in ABX, $-C\underline{H}_2OAc$). MS m/z (%): 154 (10, $M^+-CH_3CO_2H$), 43 (100). **3b**: colorless oil, $[\alpha]_D^{20}$ +48° (c=1.3, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 3400 (br), 1747. ^1H NMR (CCl_4, δ): 0.80, 0.96, 1.02 (3H each, all s), 2.01 (3H, s), 3.3—3.7 (2H, AB in ABX, $-C\underline{H}_2OH$), 3.91 (2H, s, $-C\underline{H}_2OAc$). High resolution MS (m/z): Calcd for $C_{12}H_{22}O_3$: 214.157. Found: 214.158. MS m/z (%): 214 (1, M^+), 43 (100). **3c**: colorless oil, $[\alpha]_D^{20}$ +36° (c=1.6, $CHCl_3$). *Anal.* Calcd for $C_{14}H_{24}O_4$: C, 65.59; H, 9.44. Found: C, 65.33; H, 9.69. IR ν_{max}^{film} cm^{-1}: 1745. ^1H NMR (CCl_4, δ): 0.80, 0.98, 1.02 (3H each, all s), 1.95, 1.98 (3H each, both s), 3.90 (2H, s, $-\overset{|}{\underset{|}{C}}-C\underline{H}_2OAc$), 3.8—4.1 (2H, AB in ABX, $-CH-C\underline{H}_2OAc$). MS m/z (%): 136 (100, $M^+-CH_3CO_2H \times 2$).

Alkaline Hydrolysis of 3b giving 3——A solution of **3b** (8 g) in 10% KOH–MeOH (100 g) was stirred at room temperature for 3 h. After dilution with water (300 ml), the reaction mixture was concentrated under reduced pressure to yield a residue which was extracted with EtOAc. Work-up of the EtOAc extract in the usual manner gave a diol (**3**, 6.4 g, 99%), which was identical with an authentic sample as judged by ^1H NMR (d_6-acetone), IR (KBr), and $[\alpha]_D$ (EtOH) comparisons.

Alkaline Hydrolysis of 3c giving 3——A solution of **3c** (10 g) in 10% KOH–MeOH (100 g) was stirred at room temperature for 3 h and worked up as described above for **3b** to furnish **3** (6.5 g, 97%).

PCC Oxidation of 3a giving the Aldehyde (4)——A solution of **3a** (38.5 g) in CH_2Cl_2 (500 ml) was treated with PCC (60 g) and the whole was stirred at room temperature for 2 h. After dilution with dry ether (500 ml), the whole mixture was passed through a Florisil column (70—100 mesh, 40 g). Removal of the solvent from the eluate under reduced pressure gave an aldehyde (**4**, 38 g, 99%), colorless oil, $[\alpha]_D^{15}$ +66° (c=1.8, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 2715, 1728 (CHO), 1743 (OAc). ^1H NMR ($CDCl_3$, δ): 0.89, 1.01, 1.11 (3H each, all s), 2.02 (3H, s), 4.02 (2H, d-like, J=*ca.* 6 Hz), 9.67 (1H, s, $-C\underline{H}O$). High resolution MS (m/z): Calcd for $C_{12}H_{20}O_3$: 212.141. Found: 212.142. MS m/z (%): 212 (2, M^+), 109 (100).

(+)-(3*S*)-Vinylcyclopentane (5) from 4——A dimsyl carbanion-DMSO solution [prepared from 9.0 g of NaH (0.19 mol) and 100 ml of DMSO] was mixed with a solution of methyltriphenylphosphonium bromide (100 g, 0.28 mol) in DMSO (100 ml) and the whole was stirred at room temperature for 1 h. After cooling to 0°C, the mixture was treated quickly with a solution of **4** (38 g, 0.18 mol) in DMSO (50 ml) and the whole was stirred at room temperature for 30 min. The mixture was poured into ice-water and extracted with n-hexane. The n-hexane extract was washed successively with aq. 5% HCl, aq. 5% $NaHCO_3$, and sat. saline, then dried over $MgSO_4$. Removal of the solvent under reduced pressure gave a product (38 g) which was purified by distillation to afford **5** ($bp_{1.5}$ 90°C, 33 g, 83%), colorless oil, $[\alpha]_D^{20}$ +57° (c=1.7, $CHCl_3$). *Anal.* Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.09; H, 10.46. IR ν_{max}^{film} cm^{-1}: 3080, 1645, 910 (vinyl), 1745 (OAc). ^1H NMR (CCl_4, δ): 0.71, 0.91, 0.97 (3H each, all s), 1.91 (3H, s), 3.98 (2H, d, J=6 Hz, $-C\underline{H}_2OAc$), 4.8—5.9 (3H, vinyl proton). MS m/z (%): 210 (2, M^+), 43 (100).

Formylmethylenation of 4 giving the Unsaturated Aldehyde (6)——An ice-cooled suspension (0°C) of NaH (1.07 g, 50% in oil, 22 mmol, washed with n-hexane beforehand) in THF (13 ml) was treated dropwise over a period of 15 min with a solution of diethyl 2-(cyclohexylimino)ethylphosphonate (5.8 g, 22 mmol) in THF (15 ml). The mixture was stirred at 0°C for 15 min, and a solution of **4** (4.32 g, 20 mmol) in THF (25 ml) was added. The whole was stirred at room temperature for 3 h then poured into ice-water. The mixture was extracted with ether and the extract was washed with sat. saline and worked up in the usual manner to give a colorless oily product (12 g). A benzene (55 ml) solution of the product was mixed with aq. 0.8% oxalic acid (163 ml) and heated under reflux for 2 h. After cooling, the organic phase was separated. The aqueous phase was extracted with ether and the combined organic phase was washed with sat. saline and dried over Na_2SO_4. Removal of the solvent gave a product (5.2 g) which was purified by column chromatography (SiO_2 500 g, n-hexane–EtOAc=2: 1) to furnish **6** (3.81 g, 80%), colorless oil, $[\alpha]_D^{20}$ +53° (c=0.8, $CHCl_3$). IR ν_{max}^{film} cm^{-1}: 2720, 1690, 1630 (α,β-unsaturated aldehyde), 1743 (OAc). UV λ_{max}^{MeOH} nm (ε): 222

(17200). ^{1}H NMR (CCl_4, δ): 0.78, 1.00, 1.08 (3H each, all s), 1.95 (3H, s), 4.00 (2H, d, $J=7$ Hz, $-\text{C}\underline{\text{H}}_2\text{OAc}$), 5.95 (1H, A in ABX, $J_{AB}=16$ Hz, $J_{AX}=8$ Hz, $-\text{CH}_B{=}\text{C}\underline{\text{H}}_A-\text{CH}_X\text{O}$), 6.80 (1H, B in ABX, $J_{AB}=16$ Hz, $J_{BX}=0$ Hz, $-\text{C}\underline{\text{H}}_B{=}\text{CH}_A-\text{CH}_X\text{O}$), 9.50 (1H, X in ABX, $J_{AX}=8$ Hz, $J_{BX}=0$ Hz, $-\text{CH}_B{=}\text{CH}_A-\text{C}\underline{\text{H}}_X\text{O}$). High resolution MS (*m/z*): Calcd for $\text{C}_{14}\text{H}_{22}\text{O}_3$: 238.157. Found: 238.157. MS *m/z* (%): 238 (3, M^+), 110 (100).

(+)-(3*S*)-Hydroxypropenylcyclopentane (7) **from 6**——A solution of **6** (3.81 g, 16 mmol) in ether–MeOH (10: 1) (90 ml) was treated with NaBH_4 (760 mg, 20 mmol) at 0°C and the mixture was stirred for 10 min. The reaction mixture was poured into ice-water and extracted with EtOAc. Work-up of the EtOAc extract in the usual manner and removal of the solvent under reduced pressure gave a product (3.86 g) which was purified by column chromatography (SiO_2 80 g, benzene–EtOAc=3: 1) to furnish **7** (3.57 g, 94%), colorless oil, $[\alpha]^{28}_{D}$ +40°C ($c=1.1$, CHCl_3). *Anal.* Calcd for $\text{C}_{14}\text{H}_{24}\text{O}_3$: C, 69.96; H, 10.07. Found: C, 69.80; H, 10.05. IR $\nu^{\text{film}}_{\text{max}}$ cm^{-1}: 3420, 1745, 1665. ^{1}H NMR (CCl_4, δ): 0.75, 0.95, 1.00 (3H each, all s), 1.98 (3H, s), 3.8—4.1 (4H, m, $-\text{C}\underline{\text{H}}_2\text{OAc}$, $-\text{CH}{=}\text{CH}-\text{C}\underline{\text{H}}_2\text{OH}$), 5.2—5.9 (2H, m, $-\text{C}\underline{\text{H}}{=}\text{C}\underline{\text{H}}-\text{CH}_2\text{OH}$). MS *m/z* (%): 240 (2, M^+), 108 (100).

(+)-(3*S*)-(1′*S*,2′)-Epoxyethylcyclopentane (8) **and** **(+)-(3*S*)-(1′*R*,2′)-Epoxyethylcyclopentane** (9)——a) *m*-Chloroperbenzoic Acid Oxidation of **5**: A solution of **5** (1.5 g, 7.1 mmol) in CH_2Cl_2 (30 ml) was treated with *m*-chloroperbenzoic acid (2.0 g, 12.2 mmol) and the mixture was stirred at 35°C for 1.5 h. After addition of aq. 5% $\text{Na}_2\text{S}_2\text{O}_3$, the whole was extracted with CH_2Cl_2. The CH_2Cl_2 extract was then washed successively with aq. 5% NaHCO_3 and sat. saline and dried over MgSO_4. Removal of the solvent under reduced pressure gave a product (1.6 g) which was chromatographed on a silica gel column (SiO_2 150 g) with *n*-hexane–EtOAc (5: 1) to furnish **8** (1.1 g, 70%) and **9** (0.3 g, 19%). **8**: colorless oil, $[\alpha]^{14}_{D}$ +44° ($c=1.5$, CHCl_3). *Anal.* Calcd for $\text{C}_{13}\text{H}_{22}\text{O}_3$: C, 68.99; H, 9.80. Found: C, 69.03; H, 9.84. IR $\nu^{\text{film}}_{\text{max}}$ cm^{-1}: 3040, 870, 814 (epoxide), 1744 (OAc). ^{1}H NMR (CCl_4, δ): 0.87, 0.90, 1.00 (3H each, all s), 1.94 (3H, s), 2.1—2.8 (3H, ABC, $-\overset{\diagup\text{O}\diagdown}{\text{C}\underline{\text{H}}-\text{C}\underline{\text{H}}_2}$), 3.7—4.2 (2H, AB in ABX, $-\text{C}\underline{\text{H}}_2\text{OAc}$). MS *m/z* (%): 183 (2, M^+-43), 43 (100). **9**: colorless oil, $[\alpha]^{14}_{D}$ +43° ($c=1.6$, CHCl_3). *Anal.* Calcd for $\text{C}_{13}\text{H}_{22}\text{O}_3$: C, 68.99; H, 9.80. Found: C, 68.75; H, 9.86. IR $\nu^{\text{film}}_{\text{max}}$ cm^{-1}: 3040, 850, 805 (epoxide), 1741 (OAc). ^{1}H NMR (CCl_4, δ): 0.86, 0.92, 1.02 (3H each, all s), 1.96 (3H, s), 2.4—2.9 (3H, ABC, $-\overset{\diagup\text{O}\diagdown}{\text{C}\underline{\text{H}}-\text{C}\underline{\text{H}}_2}$), 3.8—4.3 (2H, AB in ABX, $-\text{C}\underline{\text{H}}_2\text{OAc}$). MS *m/z* (%): 183 (1, M^+-43), 43 (100).

b) Trimethyloxosulfonium Iodide-Sodium Hydride Treatment of **4**: A solution of NaH (31 mg, 60% in oil, 0.78 mmol) in DMSO (1.0 ml) was mixed with a solution of trimethyloxosulfonium iodide (163 mg, 0.78 mmol) in DMSO (1.0 ml) and the whole was stirred at room temperature for 30 min. Next, a solution of **4** (150 mg, 0.71 mmol) in DMSO (1.0 ml) was added, and the whole was stirred at room temperature for 45 min. After addition of ice-water, the reaction mixture was extracted with EtOAc. The extract was washed with sat. saline and dried over MgSO_4. Removal of the solvent under reduced pressure gave a product (130 mg) which was purified by HPLC with *n*-hexane–EtOAc (10: 1, flow rate 3.0 ml/min) to furnish **8** (10 mg, 6%) and **9** (106 mg, 66%).

LiAlH_4 Reduction of 8 giving 10a——A solution of **8** (50 mg, 0.22 mmol) in THF (4 ml) was added dropwise to a suspension of LiAlH_4 (15 mg, 0.40 mmol) in THF (2 ml), and the whole was heated under reflux for 3 h. After decomposition of the excess reagent with ether saturated with water, the reaction mixture was acidified with aq. 5% HCl and extracted with EtOAc. Work-up of the EtOAc extract in the usual manner gave **10a** (40 mg, 98%), mp 107—108°C (colorless needles from acetone), $[\alpha]^{23}_{D}$ +64° ($c=0.16$, MeOH). *Anal.* Calcd for $\text{C}_{11}\text{H}_{22}\text{O}_2$: C, 70.92; H, 11.90. Found: C, 70.70; H, 11.97. IR $\nu^{\text{KBr}}_{\text{max}}$ cm^{-1}: 3320 (br). ^{1}H NMR (d_6-acetone, δ): 0.74, 0.88, 0.98 (3H each, all s), 1.11 (3H, d, $J=6$ Hz), 3.2—3.9 (3H, m, $-\text{C}\underline{\text{H}}_2\text{OH}$, $-\text{C}\underline{\text{H}}(\text{OH})\text{CH}_3$). MS *m/z* (%): 186 (3, M^+), 123 (100).

LiAlH_4 Reduction of 9 giving 12a——A solution of **9** (275 mg, 1.2 mmol) in THF (20 ml) was added dropwise to a suspension of LiAlH_4 (50 mg, 1.3 mmol) in THF (5 ml), and the whole was heated under reflux for 3 h. Work-up in the usual manner gave **12a** (267 mg, 97%), mp 112—113°C (colorless needles from acetone), $[\alpha]^{22}_{D}$ +63° ($c=1.2$, MeOH). *Anal.* Calcd for $\text{C}_{11}\text{H}_{22}\text{O}_2$: C, 70.92; H, 11.90. Found: C, 70.69; H, 11.94. IR $\nu^{\text{KBr}}_{\text{max}}$ cm^{-1}: 3300 (br). ^{1}H NMR (d_6-acetone, δ): 0.84, 0.92, 1.09 (3H each, all s), 1.03 (3H, d, $J=6$ Hz), 3.2—4.0 (3H, m, $-\text{C}\underline{\text{H}}_2\text{OH}$, $-\text{C}\underline{\text{H}}(\text{OH})\text{CH}_3$). MS *m/z* (%): 186 (7, M^+), 123 (100).

Acetylation of 10a giving 10b and 10c——A solution of **10a** (187 mg, 1.0 mmol) in pyridine (1.9 ml) and Ac_2O (0.2 ml, 2.1 mmol) was left to stand at 0°C for 4 h. The whole was poured into ice-water and extracted with EtOAc. Work-up of the EtOAc in the usual manner gave a product (220 mg), which was purified by column chromatography (SiO_2 10 g, *n*-hexane–EtOAc=3: 1) to furnish **10b** (102 mg, 53%), **10c** (37 mg, 14%), and **10a** (56 mg, 30% recovered). **10b**: colorless oil, $[\alpha]^{22}_{D}$ +41° ($c=0.85$, CHCl_3). IR $\nu^{\text{film}}_{\text{max}}$ cm^{-1}: 3470, 1746. ^{1}H NMR (CDCl_3, δ): 0.77, 0.89, 0.99 (3H each, all s), 1.14 (3H, d, $J=6$ Hz), 2.00 (3H, s), 3.76 (1H, q, $J=6$ Hz, $-\text{C}\underline{\text{H}}(\text{OH})\text{CH}_3$), 3.8—4.2 (2H, AB in ABX, $-\text{C}\underline{\text{H}}_2\text{OAc}$). High resolution MS (*m/z*): Calcd for $\text{C}_{13}\text{H}_{24}\text{O}_3$: 228.172. Found: 228.172. MS *m/z* (%): 168 (14, $\text{M}^+-\text{CH}_3\text{CO}_2\text{H}$), 123 (100). **10c**: colorless oil, $[\alpha]^{22}_{D}$ +42° ($c=3.1$, CHCl_3). IR $\nu^{\text{film}}_{\text{max}}$ cm^{-1}: 1744. ^{1}H NMR (CCl_4, δ): 0.87, 0.97, 1.02 (3H each, all s), 1.15 (3H, d, $J=6$ Hz), 1.91, 1.93 (3H each, both s), 3.7—4.2 (2H, AB in ABX, $-\text{C}\underline{\text{H}}_2\text{OAc}$), 4.97 (1H, q, $J=6$ Hz, $-\text{C}\underline{\text{H}}(\text{OH})\text{CH}_3$). High resolution MS (*m/z*): Calcd for $\text{C}_{15}\text{H}_{26}\text{O}_4$: 270.183. Found: 270.185. MS *m/z* (%): 270 (0.4, M^+), 123 (100).

Acetylation of 12a giving 12b——A solution of **12a** (150 mg, 0.8 mmol) in CH_2Cl_2 (10 ml) was treated with AcONa (330 mg, 3.2 mmol) and Ac_2O (0.4 ml, 4.2 mmol) and stirred at room temperature for 4 h. The mixture was poured into ice-water and extracted with EtOAc. Work-up of the EtOAc extract in the usual manner gave a product (170 mg). Purification of the product by column chromatography (SiO_2 5 g, *n*-hexane–EtOAc=3: 1) furnished **12b** (110 mg, 60%) and **13** (50 mg, 33% recovered). **12b**: colorless oil, $[\alpha]^{17}_{D}$ +59° (c=1.2, $CHCl_3$). IR ν^{film}_{max} cm^{-1}: 3500, 1749. ^1H NMR ($CDCl_3$, δ): 0.88, 0.93, 1.10 (3H each, all s), 1.08 (3H, d, J=6 Hz), 2.01 (3H, s), 3.7—4.2 (3H, m, $-C\underline{H}_2OAc$, $-C\underline{H}(OH)CH_3$). High resolution MS (m/z): Calcd for $C_{13}H_{24}O_3$: 228.172. Found: 228.173. MS m/z (%): 228 (1, M^+), 123 (100).

α-Phenylbutylation of 10b——A solution of **10b** (40 mg, 0.18 mmol) in pyridine (4 ml) was treated with (±)-α-phenylbutyric anhydride (163 mg, 0.53 mmol), and the whole was left to stand at 32°C for 42 h. After addition of water (30 ml), the whole was left to stand for 30 min and extracted with EtOAc. The organic phase was separated and washed with aq. sat. $NaHCO_3$. The combined aqueous phase and washing was washed with EtOAc, and acidified with aq. 5% HCl. Work-up in the usual manner afforded α-phenylbutyric acid (133 mg), $[\alpha]^{17}_{D}$ +4.8° (c=1.6, benzene). The organic phase was washed successively with aq. 5% HCl, aq. sat. $NaHCO_3$, and sat. saline, and worked up in the usual manner to give a product (64 mg). Purification of the product by column chromatography (SiO_2 4 g, *n*-hexane–EtOAc=5: 1) furnished α-phenylbutyrate (**11**, 36 mg, 55%) and **10b** (17 mg, 43% recovered). **11**, colorless oil, $[\alpha]^{17}_{D}$ +0.4° (c=1.0, $CHCl_3$). IR ν^{film}_{max} cm^{-1}: 3065, 3035, 1745, 1734, 1602. ^1H NMR (CCl_4, δ): 0.67, 0.84, 0.96 (3H each, all s), 0.89 (3H, t, J=8 Hz, $-CH_2C\underline{H}_3$), 1.10 (3H, d, J=6 Hz), 1.89 (3H, s), 3.0—3.5 (1H, m, $-O\overset{\overset{O}{\|}}{C}-\overset{\overset{Et}{|}}{C}\underline{H}-Ph$), 3.5—4.1 (2H, AB in ABX, $-C\underline{H}_2OAc$), 4.90 (1H, q, J=6 Hz, $-\overset{\overset{OCO-}{|}}{C}\underline{H}-CH_3$), 7.16 (5H, br.s). High resolution MS (m/z): Calcd for $C_{23}H_{34}O_4$: 374.245. Found: 374.246. MS m/z (%): 374 (3, M^+), 119 (100).

α-Phenylbutylation of 12b——A solution of **12b** (30 mg, 0.13 mmol) in pyridine (2 ml) was treated with (±)-α-phenylbutyric anhydride (114 mg, 0.37 mmol) and the mixture was left to stand at 60°C for 72 h. Work-up of the reaction mixture as described above for **10b** furnished α-phenylbutyric acid (105 mg), $[\alpha]^{17}_{D}$ −0.9° (c=2.2, benzene), α-phenylbutyrate (**13**, 10 mg, 20%), and **12b** (24 mg, 80% recovered). **13**: colorless oil, $[\alpha]^{17}_{D}$ +31° (c=1.0, $CHCl_3$). IR ν^{film}_{max} cm^{-1}: 3065, 3035, 1744, 1732, 1603. ^1H NMR (CCl_4, δ): 0.47, 0.51, 0.96 (3H each, all s), 0.87 (3H, t, J=8 Hz, $-CH_2C\underline{H}_3$), 1.09 (3H, d, J=6 Hz), 1.89 (3H, s), 3.1—3.5 (1H, m, $-O\overset{\overset{O}{\|}}{C}-\overset{\overset{Et}{|}}{C}\underline{H}-Ph$), 3.6—4.0 (2H, AB in ABX, $-C\underline{H}_2OAc$), 4.83 (1H, q, J=6 Hz, $-\overset{\overset{OCO-}{|}}{C}\underline{H}-CH_3$), 7.17 (5H, br.s). High resolution MS (m/z): Calcd for $C_{23}H_{34}O_4$: 374.245. Found: 374.245. MS m/z (%): 374 (1, M^+), 119 (100).

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