Tetrahedron Vol. 41, No. 6, pp. 995 to 1005, 1985
Printed in Great Britain.

0040–4020/85 $3.00 + .00
Pergamon Press Ltd.

NEW PROSTANOIDS FROM SOFT CORAL[1]

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(*Received in USA* 29 *August* 1983)

Abstract—Four new anti-tumor active prostanoids, named claviridenone-a (3), claviridenone-b (4), claviridenone-c (5), and claviridenone-d (6), as well as 20-acetoxy-claviridenone-b (7) and 20-acetoxy-claviridenone-c (8), have been isolated from the Okinawan soft coral (stolonifer) *Clavularia viridis* QUOY and GAIMARD (Stolonifera, Clavulariidae). The absolute stereostructures of these six prostanoids have been elucidated on the basis of chemical and physicochemical evidence which includes the application of the CD exciton chirality method to their various benzoyl derivatives having benzoate and conjugated diene chromophores. Claviridenones possess a characteristic cross-conjugated dienone–enone chromophore.

Marine prostanoids

Prostaglandins (PG's) exhibit a variety of significant physiological activities. They have been known as autacoids occurring in various terrestrial animal organs and in recent years shown to be distributed also in marine life such as fish.[2] In 1969, Weinheimer and Spraggins reported the first high-yield isolation of nonmammalian-type (15*R*)-PGA_2 (1) and the methyl ester acetate (2) from the Caribbean gorgonean *Plexaura homomalla*.[3a] This finding stimulated a worldwide survey of PG's in marine life. It was demonstrated that some forms of *P. homomalla* contained various mammalian-type (15*S*)-PG's such as PGA_2,[3b,c] 5,6-*trans*-PGA_2,[3d] PGE_2,[3b] 13,14-*cis*-PGA_2 15-acetate,[3e] 13,14-dihydro-PGA_2 acetate methyl ester,[3e] and 13,14-dihydro-PGA_2.[3e] Later on, by monitoring the activity towards isolated guinea-pig ileum, $PGF_{2\alpha}$ was isolated from the Japanese coastal gorgonean *Euplexaura erecta*.[3f] The occurrence of PG's in marine life other than gorgoneans has been also reported. The isolation of PGE_2 and $PGF_{2\alpha}$ from the Australian red alga *Gracilaria lichenoides* was the first reported occurrence of PG's in a plant.[3g] The Red Sea soft coral *Lobophyton depressum* was shown to contain $PGF_{2\alpha}$ 11-acetate methyl ester and its 18-acetoxyl derivative as well as their two corresponding free carboxylic acids.[3h] Recently, Scheuer *et al.* demonstrated the occurrence of a series of highly functionalized halogenated prostanoids (named punaglandins) together with small amounts of pregnanes in the Hawaiian octocoral *Telesto riisei*.[3i] Although the structures of these prostanoids are still under investigation, the authors have pointed out that *T. riisei* lacks symbiotic photosynthetic algae and it is thus likely that this octocoral biosynthesizes the prostanoids.[3i]

In a continuing search for bioactive marine natural products, we have investigated the chemical constituents of the Okinawan soft coral *Clavularia viridis* QUOY and GAIMARD (subclass: Octocorallia; order: Stolonifera; family: Clavulariidae) and isolated six new prostanoids which comprise anti-tumor active claviridenone-a (3), claviridenone-b (4), claviridenone-c (5), and claviridenone-d (6), all having a characteristic cross-conjugated dienone–enone chromophore,[4a,b] and 20-acetoxy-claviridenone-b (7) and 20-acetoxy-claviridenone-c (8). This paper deals with details of the absolute stereostructure elucidation of these highly unsaturated prostanoids on the basis of chemical and physicochemical evidence, including the application of the CD exciton chirality method.[5]

Planar structures of claviridenones. Repeated chromatographic separation (SiO_2 column and HPLC) of the AcOEt soluble portion of the soft coral, which was collected in July 1981 at Kohamajima coral reefs, Okinawa Prefecture, Japan, furnished six prostanoids named claviridenone-a (3), claviridenone-b (4), claviridenone-c (5), claviridenone-d (6), 20-acetoxy-claviridenone-b (7), and 20-acetoxy-claviridenone-c (8) in 0.3, 3, 5, 3, 0.4, 0.6% yields respectively from the AcOEt soluble portion. Very recently, claviridenones have been found to exhibit the growth inhibitory activity against L 1210 leukemia cultured cells: IC_{50} 0.2–0.4 μg/ml.[6]

Claviridenones are unstable oils. The IR spectrum of claviridenone-b (4) showed presence of an ester function and a conjugated enone chromophore, while the UV spectrum suggested presence of the cross-conjugated dienone moiety in 4. The detailed ^{1}H NMR (200 and 500 MHz) and ^{13}C NMR (22.5 and 50 MHz) analyses demonstrated that claviridenone-b (4) is a monocyclic fatty acid analog comprising partial structures **i**, **ii**, **iii**, **iv** and **v** (Tables 1 and 2; Chart 1).

In the ^{1}H NMR examination of the tetrahydro derivative 9, which was prepared by $NaBH_4$ reduction of claviridenone-b (4), a 20% NOE was observed on the H-6 signal (δ 6.65, dd, J = 15.6 and 11.2 Hz) upon irradiation of H-9 (δ 4.74, br dd, J = *ca* 4.5 and 9 Hz) while 13% NOE observed when H-6 was irradiated. Furthermore, comparison of the ^{13}C NMR data for claviridenone-b (4, Table 2) with those for *cis*-2-octene[7a] and linoleic acid[7b] and the MS analysis led to the formulation of a prostanoid structure (4, except stereochemistry) for claviridenone-b.

Table 1. ^{1}H NMR data[a]

	3	4	5
2-H_2	2.37(t,J=7.3)	2.39(t,J=7.8)	2.38(t,J=7.6)
3-H_2	ca.2.02(m)	2.03(m)	ca.2.03(m)
4-H	5.83(dt,J=8.5,7.5)	5.44(dt,J=6.1,5.5)	5.42(dt,J=7.0,7.0)
5-H	5.76(dd,J=10.8,8.5)	6.02(dd,J=15.4,6.1)	6.02(dd,J=14.2,7.0)
6-H	7.62(dd,J=10.8,12.2)	7.74(dd,J=15.4,11.2)	6.74(dd,J=14.2,11.7)
7-H	7.02(d,J=12.2)	6.51(d,J=11.2)	6.87(d,J=11.7)
10-H	6.36(d,J=6.2)	6.36(d,J=6.4)	6.41(d,J=6.3)
11-H	7.50(d,J=6.2)	7.51(d,J=6.4)	7.47(d,J=6.3)
13-H_2	2.64,2.84(AB in ABX, J_{AB}=14.4,J_{AX}=7.4, J_{BX}=7.3)	2.68,2.82(AB in ABX, J_{AB}=14.4,J_{AX}=7.0, J_{BX}=7.5)	2.66,2.89(AB in ABX, J_{AB}=14.4,J_{AX}=8.3, J_{BX}=6.8)
14-H	5.27(X in ABX,dt-like)	5.21(X in ABX,dt-like,J=11.0,ca.7.3)	5.20(X in ABX,dt-like)
15-H	5.54(m)	5.52(dt,J=11.0,7.5)	5.52(m)
16-H_2	ca.1.95(m)	1.96(dt,J=7.5,7.5)	1.96(m)
17~19	1.23~1.32(6H,m)	1.23~1.32(6H,m)	1.23~1.32(6H,m)
20-H_3	0.88(t,J=6.8)	0.88(t,J=6.8)	0.88(t,J=6.8)
$COOCH_3$	3.68(s)	3.68(s)	3.68(s)
OAc	2.03(s),2.07(s)	2.02(s),2.10(s)	2.06(s),2.07(s)

	6		7	8
2-H_2	2.38(t,J=7.4)	2-H_2	2.39(t,J=7.6)	2.38(t,J=7.3)
3-H_2	ca.1.95(m)	3-H_2	2.05(m)	2.02(m)
4-H	5.85(m)	4-H	5.44(dt,J=6.1,6.4)	5.41(dt,J=7.3,5.8)
5-H	5.85(m)	5-H	6.03(dd,J=15.3,6.1)	6.04(dd,J=14.6,7.3)
6-H	6.59(dd,J=10.0,12.7)	6-H	7.74(dd,J=15.3,11.6)	6.75(dd,J=14.6,12.2)
7-H	7.27(d,J=12.7)	7-H	6.52(d,J=11.6)	6.87(d,J=12.2)
10-H	6.43(d,J=6.4)	10-H	6.36(d,J=6.1)	6.41(d,J=6.1)
11-H	7.48(d,J=6.4)	11-H	7.50(d,J=6.1)	7.48(d,J=6.1)
13-H_2	2.66,2.96(AB in ABX, J_{AB}=14.4,J_{AX}=7.8, J_{BX}=7.0)	13-H_2	2.62,2.87(AB in ABX, J_{AB}=14.3,J_{AX}=7.6, J_{BX}=7.7)	2.69,2.88(AB in ABX, J_{AB}=14.3,J_{AX}=8.2, J_{BX}=7.0)
14-H	5.20(X in ABX,dt-like)	14-H	5.23(X in ABX,dt-like,J=11.0,ca.7.5)	5.21(X in ABX,dt-like,J=11.0,ca.7.6)
15-H	5.52(m)	15-H	5.51(dt,J=11.0,7.3)	5.51(dt,J=11.0,6.7)
16-H_2	1.95(m)	16-H_2	1.99(m)	1.96(m)
17~19	1.23~1.32(6H,m)	17~18	1.34(4H,m)	1.33(4H,m)
20-H_3	0.88(t,J=6.8)	19-H_2	1.61(tt,J=6.7,6.7)	1.61(tt,J=6.7,6.7)
$COOCH_3$	3.70(s)	20-H_2	4.04(t,J=6.7)	4.04(t,J=6.7)
OAc	2.03(s),2.05(s)	$COOCH_3$	3.67(s)	3.68(s)
		OAc	2.02,2.05,2.10(s)	2.05,2.07,2.08(s)

a) 4, 7 and 8 were measured at 500 MHz in $CDCl_3$ and 3, 5 and 6 were at 200 MHz in $CDCl_3$.

Claviridenone-a (3), claviridenone-c (5), and claviridenone-d (6) possess the same molecular composition as claviridenone-b (4). As shown in Tables 1 and 2, these compounds gave analogous ^{1}H and ^{13}C NMR signals attributable to their ω-chains and unsaturated 5-membered rings. Thus, it has become clear that all four claviridenones are prostanoids having a *cis*-14-ene ω-chain and are geometrical isomers of each other in regard to their conjugated 5,7-diene chromophores. Since the four claviridenones (3, 4, 5, 6) were noticed to isomerize while allowing to stand in the laboratory for a while, the benzene solution of each claviridenone was irradiated in a Pyrex tube with fluorescent lamps (15 W × 2) for 40 hr. It was found that each claviridenone (3, 4, 5 or 6) was photo-isomerized under these irradiation conditions, to an identical mixture of four claviridenones (3, 4, 5 and 6) in 1:6:12:2 ratio. Therefore, it has become clear that the four claviridenones possess the common absolute stereostructures at C-4 and C-12, but differ at their dienone geometries.

In regard to the 5,7-diene geometry in each claviridenone, the ^{1}H NMR examinations were informative. Thus, *Z* geometry of Δ^5 in claviridenone-a (3) and -d (6) was determined from the $J_{5,6}$-values (10.8 and 10.0 Hz for 3 and 6), while claviridenone-b (4) and -c (5) were shown to possess the 5*E* geometry ($J_{5,6}$ = 15.4 and 14.2 Hz for 4 and 5). On the other hand, the geometry of Δ^7 was elucidated from the chemical shift of the H-6 signal. In the 7*Z* compounds (3, 4), the H-6 signals were observed at δ 7.62 and 7.74, whereas in the 7*E* isomers (5, 6), these signals were observed at lower positions (δ 6.74 and 6.59) due to the anisotropic effect of the C-9 carbonyl moiety.

The ^{1}H and ^{13}C NMR spectra of 20-acetoxy-claviridenone-b (7) and 20-acetoxy-claviridenone-c (8) showed signals assignable to the α-chains and the 5-membered ring enone moieties that were virtually superimposable to those of claviridenone-b (4) and claviridenone-c (5). However, these spectra clearly indicated absence of the terminal methyl group but presence of C-19 CH_2OCOCH_3 group (δ 4.04, 2H, t, J = 6.7 Hz; δ 2.05, 3H, s; δ c 64.4, t) in 7 and 8 as compared with 4 and 5. Finally, the detailed ^{1}H NMR decoupling experiments (500 MHz) have led to the structures 7

Table 2. ^{13}C NMR data[a]

carbon	3	4	5	6	7	8	10	12	19	20
1	172.9	173.4	173.2	173.2	173.0	172.8	173.1	173.2	63.2	62.8
2	29.1[b]	29.1[b]	29.1[b]	29.1[b]	28.9[b]	28.9[b]	29.2[b]	29.5[b]	28.0[b]	28.6
3	29.6[b]	29.4[b]	29.3[b]	30.0[b]	29.2[b]	29.1[b]	29.8[b]	29.8[b]	34.7	31.1
4	68.2	72.7	73.0	69.6	72.5	72.7	73.4	73.3	72.2	74.9
5	136.6[c]	141.3	141.5	139.0	141.1	141.2	133.1	133.2	139.4	132.4
6	127.9	133.8	129.6	124.8[c]	133.4	129.3	126.6	125.8	124.1	124.0[b]
7	136.5[c]	137.0	135.3	135.4[d]	136.7	135.0	128.3	128.4	128.3	128.0
8	137.1	136.0	137.3	137.9	135.6	136.9	148.9	144.2	144.5	151.6
9	194.2	194.3	193.6	193.5	193.9	193.1	75.5	76.2	75.1	75.5
10	126.1	126.8	127.2	124.6[c]	126.5	126.7	32.0	29.8[b]	32.3	32.6
11	156.7	156.3	158.3	158.1	156.0	157.9	37.1	37.8	37.5	39.1
12	85.0	85.5	85.4	85.4	85.2	85.0	88.0	87.6	89.4	79.3
13	36.1	35.7	36.1	36.0	35.6	35.9	32.6	33.7	32.9	36.0
14	121.5	121.7	121.4	121.4	121.8	121.5	123.1	123.0	123.6	124.2[b]
15	134.7	135.1	135.3	135.3[d]	134.2	134.4	134.2	134.5	134.4	133.5
16	27.4	27.5	27.5	27.5	27.3	27.2	27.5	27.6	27.7[b]	27.5
17	29.8[b]	29.9[b]	29.7[b]	30.0[b]	29.8[b]	29.5[b]	29.4[b]	29.3[b]	29.3	29.3
18	31.5	31.6	31.5	31.5	25.6	25.5	31.5	31.6	31.6	31.6
19	22.5	22.6	22.6	22.5	28.5[b]	28.5[b]	22.5	22.6	22.6	22.6
20	14.0	14.0	14.0	14.0	64.4	64.3	14.0	14.1	14.1	14.1
$COO\underline{C}H_3$	51.6	51.8	51.8	51.8	51.6	51.6	51.7	51.7		
$CH_3\underline{C}-$	170.1	170.3	170.2	170.1	171.0	171.0	170.8	170.0		
	169.8	169.9	169.7	169.4	170.0	169.7	170.0	169.5		
	21.5	21.7	21.2	21.2	169.6	169.3	21.6	21.7		
	21.0	21.0	21.0	20.9	21.6	21.1	21.1	21.2		
					20.9	20.9				
					20.9	20.9				

a) 3, 4, 5, 6 and 10 were measured at 50 MHz in $CDCl_3$ and 7, 8, 12, 19 and 20 were at 22.5 MHz in $CDCl_3$.

b~d) The assignments for these signals within the same vertical column may be interchanged.

and **8** for 20-acetoxy-claviridenone-b and 20-acetoxy-claviridenone-c.[8]

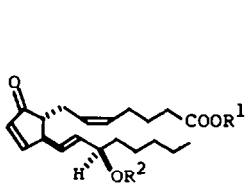
Absolute stereostructures of claviridenones. Two tetrahydro derivatives, **10** and its 9-epimer (**11**), which were obtained by $NaBH_4$ reduction of claviridenone-c (**5**), possess OH functions at C-4, C-9, and C-12, which are allylic to the 5,7-diene chromophores. In order to determine the absolute stereostructures at C-4 and C-12 of the claviridenones, we synthesized various benzoate derivatives as shown in Scheme 1 and examined them by the application of the CD exciton chirality method.[5]

Since two 9-benzoates **12** and **14**, which were synthesized from **10** and **11**, can be predicted to have opposite chiralities between the respective benzoate and dienone chromophores (Fig. 1), we first synthesized various 9-benzoates (**12–14, 21–25**) and examined their CD spectra.

As shown in Table 3, **12** exhibited a negative first Cotton effect at longer wavelength, while **14** showed a positive first Cotton effect in their CD spectra, thus the 9*R* and the 9*S* configurations in **12** and **14** have been determined as predicted. In the cases of 9-*p*-methoxybenzoate (**13**), 9-*p*-bromobenzoate (**22**), and 9-*p*-cyanobenzoate (**23**), which have the benzoate $\pi \rightarrow \pi^*$ transitions at wavelengths closer to the diene $\pi \rightarrow \pi^*$ transition wavelength (*ca* 240–250 nm), intense excition-split CD curves were observed. It has become clear that the CD exciton chirality method[5] may be extended to the benzoate/conjugated diene system irrespective of the diene geometry. In addition, in the CD spectra of the respective 9-benzoate derivatives, it was found that the CD amplitudes of the first and the second Cotton effects were not identical and these amplitude differences coincided approximately with the CD amplitudes of the parent 9-hydroxyl compounds (**9–11, 26, 27**). In other words, in the CD spectra of these benzoate/conjugated diene systems, the observed CD curves have arisen from the addition of the Cotton effect due to the coupling of two excitons and the Cotton effect due to the diene helicity.

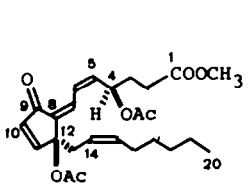
Next, the CD exciton chirality method was applied to determine the C-12 absolute configuration of claviridenones. $LiAlH_4$ reduction of **10** gave the tetraol (**15**) which was subjected to t-butyldimethylsilylation (TBDMS) to furnish the tri-TBDMS and di-TBDMS derivatives (**16, 17**). Benzoylation or *p*-nitrobenzoylation of **16** in the presence of AgCN[9] provided the 12-benzoate (**18**) or the 12-*p*-nitrobenzoate (**19**) (Scheme 1). As shown in Fig. 2, **18** gave a complicated CD spectrum which was presumably due to the overlap of the benzoate/diene exciton-split CD curve and the 5,7-diene helicity CD curve. However, the CD spectrum of **19** exhibited a positive first Cotton effect at 265 nm due to the coupling of the *p*-nitrobenzoate/diene excitons. Thus, the 12*R* configuration has been substantiated.[10]

Recently, Nakanishi *et al.* reported that the CD exciton chirality method can be applied to the determination of the absolute configurations of acyclic allylic alcohols.[11] In order to determine the C-4 absolute configurations of the claviridenones, we next

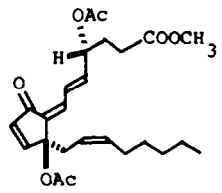


1 : $R^1 = R^2 = H$

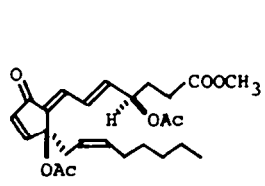
2 : $R^1 = CH_3$, $R^2 = Ac$



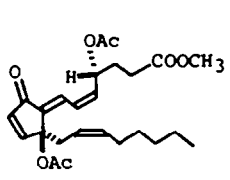
3 claviridenone-a



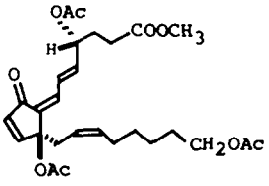
4 claviridenone-b



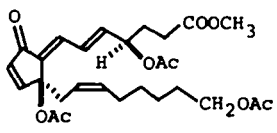
5 claviridenone-c



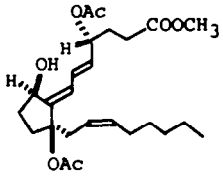
6 claviridenone-d



7 20-acetoxy-claviridenone-b



8 20-acetoxy-claviridenone-c



9

i $\rangle C{=}CH{-}CH{=}CH{-}CH(OAc){-}CH_2{-}CH_2{-}COOCH_3$, ii $-CO{-}CH{=}CH{-}$▨

iii ▨$-CH_2{-}CH{=}CH{-}CH_2{-}(CH_2)_n{-}$, iv $-(CH_2)_m{-}CH_3$, v $-\overset{|}{\underset{|}{C}}{-}OAc$

(▨ denotes a quaternary carbon, n + m = 3)

Chart 1.

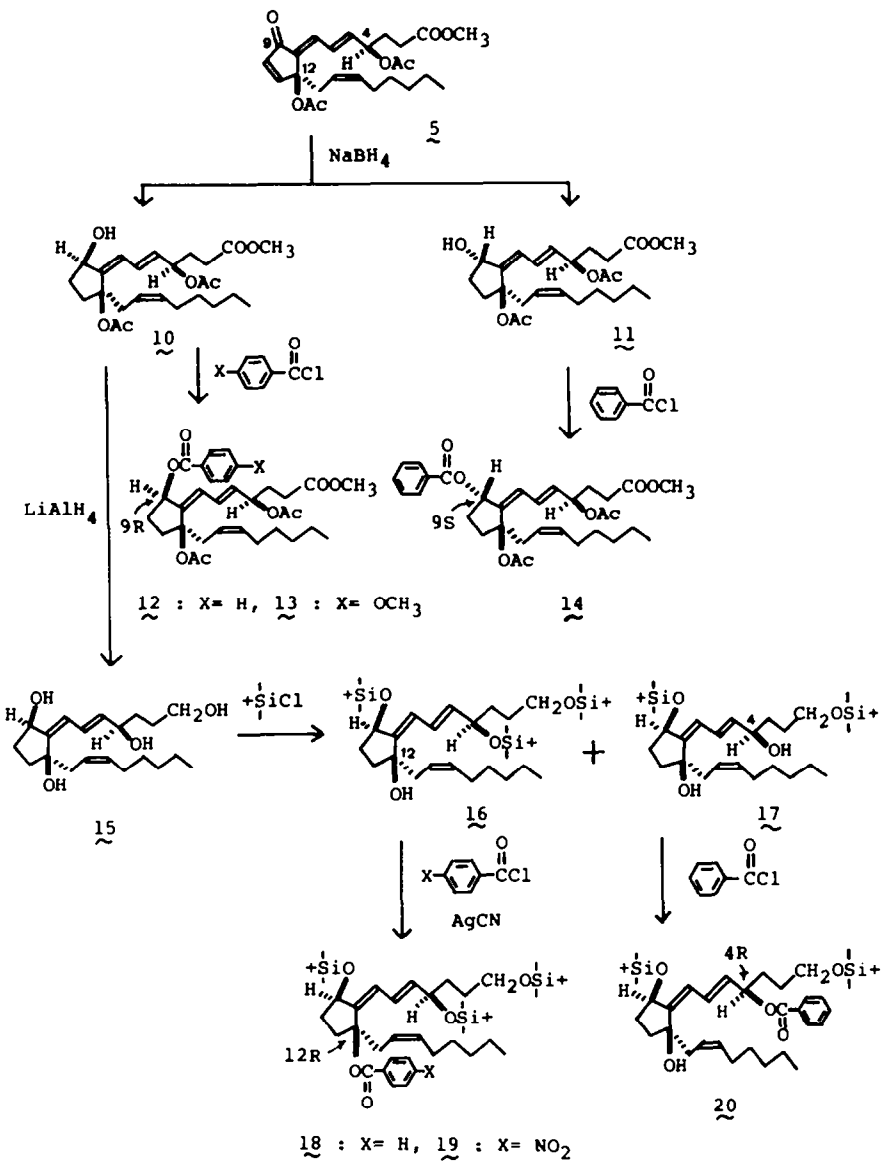
examined the applicability of the chirality method to the acyclic conjugated diene/allylic benzoate system. The above-mentioned di-TBDMS derivative (**17**) was benzoylated under ordinary conditions to afford the 4-benzoate (**20**). In the ^1H NMR spectrum of **20** (in CD_3OD), the $J_{4,5}$ value was 7.0 Hz,[11] and the CD spectrum of **20** (in CH_3OH) showed a negative first Cotton effect at 246 nm (Table 4). Consequently, the configuration around the 4-benzoate/5,7-diene moiety in **20** was presumed as shown in Fig. 3, thus the 4*R* configuration in **20** has been determined. The CD spectrum of di-TBDMS 4-benzoate (**29**), which was derivable from claviridenone-d (**6**) via **28**, also exhibited a negative first Cotton effect at 247 nm (Table 4). It has now been demonstrated that the CD exciton chirality method can be applicable to the acyclic conjugated diene/allylic benzoate-system.

In order to confirm the 4*R* configuration in claviridenones chemically, we finally applied Horeau's method[12] to **32**, which was obtained by splitting the 5,6-double bond of claviridenones via ozonolysis followed by the reaction procedure as shown in Scheme 2. The recovered α-phenylbutyric acid showed $[\alpha]_D + 4.6°$ ($c = 0.7$, benzene), so that the 4*R* configuration in the claviridenones has been again confirmed.

Based on the above mentioned evidence, the absolute stereostructures of claviridenone-a (**3**), claviridenone-b (**4**), claviridenone-c (**5**), claviridenone-d (**6**), 20-acetoxy-claviridenone-b (**7**), and 20-acetoxy-claviridenone-c (**8**) have been elucidated. After completion of our work we became aware of independent work by Kikuchi, Yamada *et al.* They elucidated the structures of three prostanoids named clavulone I, clavulone II, and clavulone III which were isolated from the same kind of soft coral.[13] The structures proposed for clavulone I, II and III are identical with those of our claviridenone-d (**6**), -c (**5**), and -b (**4**), respectively. Very recently, we have been able to identify these three prostanoids by comparison of their physicochemical data.[14]

EXPERIMENTAL

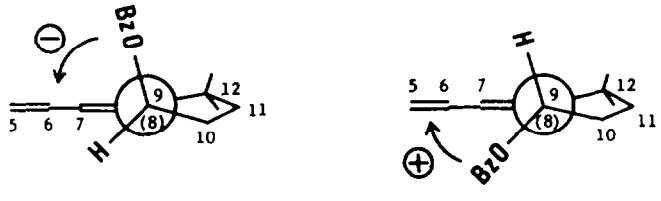
Instrumentation. IR spectra were obtained using a Hitachi 260-30 grating spectrometer. Optical rotations were measured with a JASCO DIP-181 digital polarimeter. ^1H NMR spectra were measured with JEOL JNM FX-500S (500 MHz), JEOL JNM FX-200 (200 MHz), and JEOL FX-90Q (90 MHz) spectrometers with Me_4Si as the internal standard. ^{13}C NMR spectra were determined on JEOL JNM FX-200 (50 MHz) and JOEL FX-90Q (22.5 MHz) spec-



Scheme 1.

trometers with Me_4Si (0 ppm) or $CDCl_3$ (77.1 ppm) as the internal standard. UV spectra were obtained using a Hitachi 330 spectrometer. CD spectra were taken on a JASCO J-500A spectropolarimeter and a JASCO DP-501 data processor. Low resolution and high resolution mass spectra (MS, High MS) were measured with a JEOL D-300 mass spectrometer and a JEOL 01SG mass spectrometer.

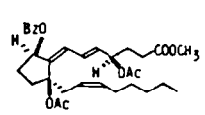
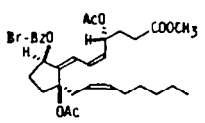
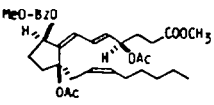
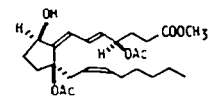
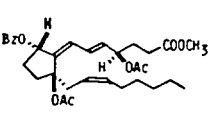
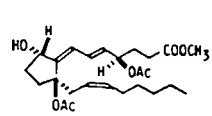
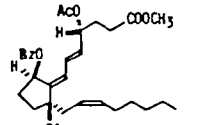
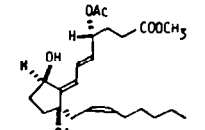
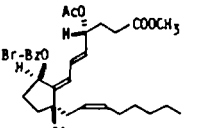
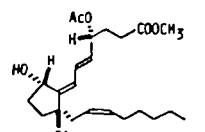
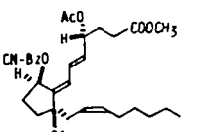
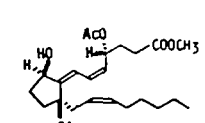
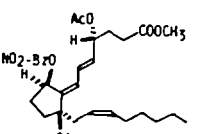
Isolation of claviridenones. The fresh soft coral (Japanese name: tsutsu-umizuta, finely cut, 3 kg) was extracted with acetone at 20° and the syrup, obtained by evaporation of acetone under reduced pressure below 35°, was partitioned by an AcOEt–water solvent system. Removal of the solvent under reduced pressure from the AcOEt phase afforded the residue (30 g) which was subjected to column chro-



12 (9R) 14 (9S)

Fig. 1.

Table 3. UV (MeOH) and CD (MeOH) data

Compound	UV and CD Maxima	Compound	UV and CD Maxima
12 	245(ε 20000) 229(ε 25000) $[\theta]_{246}$ −95000 $[\theta]_{225}$ +37000	25 	243(ε 42000) $[\theta]_{255}$ −272000 $[\theta]_{235}$ +85000
13 	249(ε 36000) $[\theta]_{262}$ −159000 $[\theta]_{241}$ +69000	10 	250(ε 23000) $[\theta]_{248}$ −35000
14 	242(ε 25000) $[\theta]_{245}$ +64000 $[\theta]_{228}$ −79000	11 	250(ε 25000) $[\theta]_{253}$ +7000 $[\theta]_{230}$ −7000
21 	232(ε 28000) $[\theta]_{246}$ −111000 $[\theta]_{226}$ +79000	9 	247(ε 23000) $[\theta]_{250}$ −27000
22 	243(ε 35000) $[\theta]_{253}$ −240000 $[\theta]_{234}$ +133000	26 	245(ε 18000) $[\theta]_{245}$ +6500
23 	240(ε 44000) $[\theta]_{252}$ −264000 $[\theta]_{232}$ +150000	27 	250(ε 22000) $[\theta]_{247}$ −43000
24 	248(ε 35000) $[\theta]_{262}$ −131000 $[\theta]_{239}$ +66000		

matography (SiO_2, Merck, 60–230 mesh, 1.5 kg). The eluate with n-hexane–AcOEt (3:1) gave a claviridenone-a fraction (825 mg), claviridenone-b (4) (830 mg), a mixture of claviridenone-b and claviridenone-c (890 mg), and claviridenone-c (5) (1.16 g). Successive elution with n-hexane–AcOEt (2:1) gave claviridenone-d (6) (930 mg), a fraction containing 20-acetoxy-claviridenone-b and 20-acetoxy-claviridenone-c (900 mg), and a fraction containing minor amounts of more polar claviridenones. The claviridenone-a fraction (825 mg) was further purified by HPLC [Waters Assoc. ALC/GPC 201 or Shimadzu LC-5A with Semi Prep μPORASIL (Waters Assoc.)] eluting with n-hexane–AcOEt (3:1) and again purified by eluting with $CHCl_3$–AcOEt (10:1) to furnish claviridenone-a (3) (80 mg). The mixture of claviridenone-b and -c (890 mg) was purified with a Lobar column [LiChroprep Si 60 (40–63 μm)] eluting with n-hexane–AcOEt (3:1) to furnish 4 (230 mg) and 5 (445 mg). The fraction containing 20-acetoxy-claviridenone-b and 20-acetoxy-claviridenone-c (900 mg) was purified successively by a Lobar column chromatography (elution with $CHCl_3$–AcOEt 10:1) and by HPLC [Semi Prep Cosmosil ($5C_{18}$), elution with MeOH–H_2O (6:1)] to furnish 7 (110 mg) and 8 (170 mg). Compound 3, colorless oil, $[\alpha]_D^{31}$ − 82.2° (*c* = 0.5, $CHCl_3$); HR MS: M^+ = 446.230 (Calc for $C_{25}H_{34}O_7$ = 446.230); IR ($CHCl_3$) 1732, 1690, 1632, 1220 cm^{-1}; UV (MeOH) 230 nm (ε 12,000), 294 nm (ε 14,000); ^1H NMR: Table 1; ^{13}C NMR: Table 2; MS *m/z* (%): 446 (M^+, 2), 404 (M^+ − 42, 2), 386 (M^+ − AcOH, 16), 344 (M^+ − 42–AcOH, 50), 287 (M^+ − 42-C_4H_9–AcOH, 43), 233 (M^+ − 42-C_8H_{15}–AcOH, 31), 201 (100). Compound 4, colorless oil, $[\alpha]_D^{31}$ + 22.4° (*c* = 0.6, $CHCl_3$); HR MS: M^+ = 446.229 (Calc for $C_{25}H_{34}O_7$ = 446.230); IR ($CHCl_3$) 1730, 1693, 1634, 1235 cm^{-1}; UV (MeOH) 230 nm (ε 13,300), 296 (ε 13,100); ^1H NMR: Table 1; ^{13}C NMR: Table 2; MS *m/z* (%): 446 (M^+, 2), 404 (M^+ − 42, 2), 386 (M^+ − AcOH, 15), 344 (M^+-42–AcOH, 50), 287 (M^+-42-C_4H_9–AcOH, 46), 233 (M^+-42-C_8H_{15}–AcOH, 34), 201 (100). Compound 5, colorless oil; $[\alpha]_D^{31}$ + 8.4° (*c* = 3.0, $CHCl_3$); HR MS: M^+ = 446.232 (Calc for $C_{25}H_{34}O_7$ = 446.230); IR ($CHCl_3$)

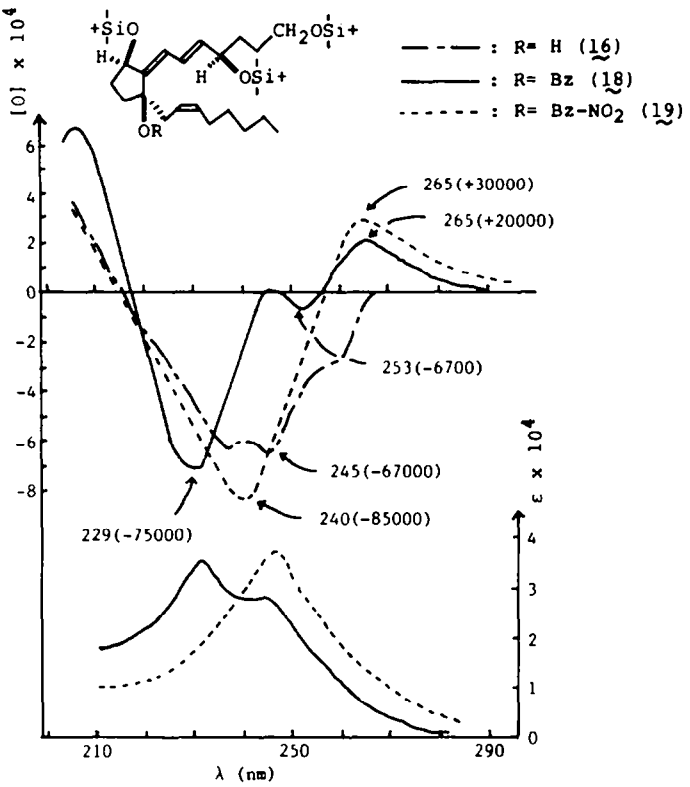
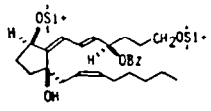
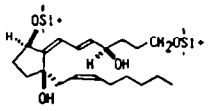
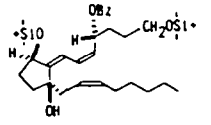
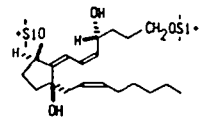


Fig. 2. UV (MeOH) and CD (MeOH) data.

Table 4. UV (MeOH) and CD (MeOH) data

Compound	UV and CD Maxima	Compound	UV and CD Maxima
20 	244(ε 29000) 238(ε 28500) $[\Theta]_{246}$ -149000 $[\Theta]_{223}$ +45000	17 	245(ε 29000) 240(ε 26000) $[\Theta]_{245}$ -55000 $[\Theta]_{238}$ -53000
29 	247(ε 27500) 239(ε 28000) $[\Theta]_{247}$ -114000 $[\Theta]_{224}$ +51000	28 	245(ε 26000) $[\Theta]_{243}$ -25000

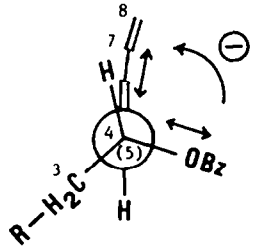
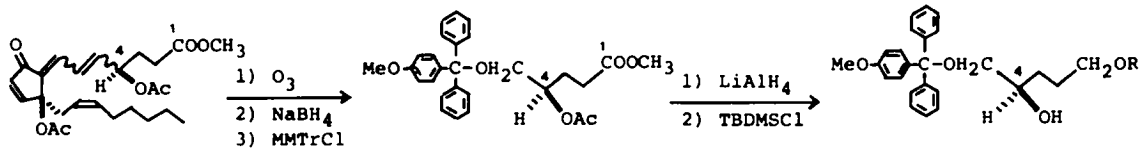


Fig. 3.



claviridenones 30 31 : R= H 32 : R= $\overset{t}{Si}+$

Scheme 2.

1735, 1700, 1637, 1230 cm^{-1}; UV (MeOH) 230 nm (ϵ 11,700), 293 nm (ϵ 15,000); ^1H NMR: Table 1; ^{13}C NMR: Table 2; MS *m/z* (%): 446 (M^+, 4), 404 (M^+–42, 2), 386 (M^+ – AcOH, 21), 344 (M^+ – 42–AcOH, 59), 287 (M^+ – 42–C_4H_9–AcOH, 49), 233 (M^+ – 42–C_8H_{15}–AcOH, 36), 201 (100). Compound **6**, colorless oil; $[\alpha]_D^{11}$ – 24.9° (*c* = 2.6, $CHCl_3$); HR MS: M^+ = 446.231 (Calc for $C_{25}H_{34}O_7$ = 446.230); IR ($CHCl_3$) 1733, 1700, 1635, 1220 cm^{-1}; UV (MeOH) 231 nm (ϵ 10,300), 294 nm (ϵ 12,700); ^1H NMR: Table 1; (200 MHz, d_6-benzene) δ: 2.03 (2H, t, *J* = 7.3, 2-H_2), 1.73 (2H, m, 3-H_2), 5.77 (1H, dt-like, *J* = 10.2, *ca* 7, 4-H), 5.61 (1H, dd, *J* = 10.2, 10.2, 5-H), 6.59 (1H, dd, *J* = 12.7, 10.2, 6-H), 7.69 (1H, d, *J* = 12.7, 7-H), 6.22 (1H, d, *J* = 6.4, 10-H), 7.12 (1H, d, *J* = 6.4, 11-H), 2.60, 2.88 (AB in ABX, J_{AB} = 14.2, J_{AX} = 7.8, J_{BX} = 7.3, 13-H_2), 5.19 (X in ABX, dt-like, *J* = 10.2, *ca* 7.5, 14-H), 5.40 (1H, m, 15-H), *ca* 1.86 (2H, m, 16-H_2), 1.21 (6H, br s, 17, 18, 19-H_2), 0.88 (3H, t, *J* = 6.8, 20-H_3), 1.65, 1.66 (3H each, s, OAc × 2); ^{13}C NMR: Table 2; MS *m/z* (%): 446 (M^+, 2), 404 (M^+ – 42, 2), 386 (M^+ – AcOH, 14), 344 (M^+ – 42–AcOH, 47), 287 (M^+ – 42–C_4H_9–AcOH, 43), 233 (M^+ – 42–C_8H_{15}–AcOH, 31). Compound **7**, colorless oil; $[\alpha]_D^{20}$ + 32° (*c* = 2.3, $CHCl_3$); HR MS: M^+ = 504.238 (Calc for $C_{27}H_{36}O_9$ = 504.236); IR ($CHCl_3$) 1728, 1696, 1638, 1226 cm^{-1}; UV (MeOH) 230 nm (ϵ 13,000), 296 (ϵ 13,000); ^1H NMR: Table 1; ^{13}C NMR: Table 2; MS *m/z* (%): 504 (M^+, 1), 462 (M^+ – 42, 5), 444 (M^+ – AcOH, 15), 402 (M^+ – 42–AcOH, 56), 233 (M^+ – 42–$C_{10}H_{17}O_2$–AcOH, 34), 201 (100). Compound **8**, colorless oil; $[\alpha]_D^{20}$ + 3° (*c* = 1.1, $CHCl_3$); HR MS: M^+ = 504.235 (Calc for $C_{27}H_{36}O_9$ = 504.236); IR ($CHCl_3$) 1717, 1640, 1215 cm^{-1}; UV (MeOH) 230 nm (ϵ 12,500), 292 (ϵ 17,000); ^1H NMR: Table 1; ^{13}C NMR: Table 2; MS *m/z* (%): 504 (M^+, 0.7), 462 (M^+ – 42, 3), 444 (M^+ – AcOH, 8), 402 (M^+ – AcOH – 42, 34), 233 (M^+ – 42–$C_{10}H_{17}O_2$–AcOH, 33), 201 (100). Purification of the more polar fractions furnished the 4-deacetyl derivative of claviridenone-b (5 mg) and the 4-deacetyl derivative of claviridenone-d (24 mg). 4-Deacetyl-claviridenone-b, colorless oil; $[\alpha]_D^{20}$ – 1° (*c* = 0.3, $CHCl_3$); HR MS: M^+ = 404.219 (Calc for $C_{23}H_{32}O_6$ = 404.220); IR ($CHCl_3$) 3400, 1724, 1695, 1636, 1237 cm^{-1}; UV (MeOH) 231 nm (ϵ 11,000), 299 (ϵ 11,000); ^1H NMR (500 MHz, $CDCl_3$) δ: 2.49 (2H, t, *J* = 7.3, 2-H_2), 1.94 (2H, m, 3-H_2), 4.37 (1H, m, 4-H), 6.09 (1H, dd, *J* = 15.3, 6.1, 5-H), 7.72 (1H, dd, *J* = 15.3, 11.6, 6-H), 6.55 (1H, d, *J* = 11.6, 7-H), 6.37 (1H, d, *J* = 6.1, 10-H), 7.51 (1H, d, *J* = 6.1, 11-H), 2.64, 2.87 (AB in ABX, J_{AB} = 14.3, J_{AX} = 7.3, J_{BX} = 7.3, 13-H_2), 5.22 (X in ABX, dt-like, *J* = 11.0, 7.3, 14-H), 5.53 (1H, dt, *J* = 11.0, 7.3, 15-H), 1.97 (2H, m, 16-H_2), 1.26 (6H, m, 17, 18, 19-H_2), 0.89 (3H, t, *J* = 7.1, 20-H_3), 3.69 (3H, s, $COOCH_3$), 2.04 (3H, s, OAc). 4-Deacetyl-claviridenone-d, colorless oil; $[\alpha]_D^{20}$ + 10° (*c* = 0.8, $CHCl_3$); HR MS: M^+ = 404.217 (Calc for $C_{23}H_{32}O_6$ = 404.220); IR ($CHCl_3$) 3440, 1727, 1700, 1635, 1235 cm^{-1}; UV (MeOH) 232 nm (ϵ 11,000), 297 (ϵ 14,000); ^1H NMR (500 MHz, $CDCl_3$) δ: 2.47 (2H, t, *J* = 7.3, 2-H_2), 1.87 (2H, m, 3-H_2), 4.84 (1H, dt, *J* = 9.1, 4.9, 4-H), 5.97 (1H, dd, *J* = 10.4, 9.1, 5-H), 6.55 (1H, dd, *J* = 12.8, 10.4, 6-H), 7.20 (1H, d, *J* = 12.8, 7-H), 6.42 (1H, d, *J* = 6.1, 10-H), 7.49 (1H, d, *J* = 6.1, 11-H), 2.67, 2.97 (AB in ABX, J_{AB} = 14.6, J_{AX} = 7.3, J_{BX} = 7.4, 13-H_2), 5.18 (X in ABX, dt-like, *J* = 11.0, *ca* 7.6, 14-H), 5.52 (1H, dt, *J* = 11.0, 7.3, 15-H), 1.96 (2H, m, 16-H_2), 1.29 (6H, m, 17, 18, 19-H_2), 0.88 (3H, t, *J* = 7.0, 20-H_3), 3.70 (3H, s, $COOCH_3$), 2.04 (3H, s, OAc).

$NaBH_4$ *Reduction of claviridenone-b* (**4**) *giving* **9** *and* **26**. A soln of **4** (430 mg) in 20 mL THF–MeOH (2:1) was treated with $NaBH_4$ (55 mg) and stirred for 15 min. The mixture was poured into ice water and the whole mixture was extracted with AcOEt. The AcOEt phase was washed with satd aqNaCl, dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the residue (430 mg). Column chromatography (SiO_2, elution with n-hexane–AcOEt 2:1) of the product gave **9** (345 mg) and **26** (38 mg). **9**, colorless oil; $[\alpha]_D^{28}$ – 48° (*c* = 0.4, $CHCl_3$); HR MS: M^+ = 450.262 (Calc for $C_{25}H_{38}O_7$ = 450.262); IR ($CHCl_3$) 3470 (br), 1725, 1225 (br) cm^{-1}; UV and CD: Table 3; ^1H NMR (200 MHz, $CDCl_3$) δ: 2.37 (2H, t, *J* = 7.6, 2-H_2), 5.33 (1H, m, 4-H), 5.65 (1H, dd, *J* = 15.5, 7.3, 5-H), 6.65 (1H, dd, *J* = 15.5, 11.0, 6-H), 6.08 (1H, d, *J* = 11.0, 7-H), 4.74 (1H, br dd, *J* = *ca* 4.5, 9, 9-H), *ca* 2.3–2.5 (2H, m, 13-H_2), *ca* 5.39 (1H, m, 14-H), *ca* 5.35 (1H, m, 15-H), 0.85 (3H, t, *J* = 6.8, 20-H_3), 4.12 (1H, br d, *J* = 9, 9-OH), 3.67 (3H, s, $COOCH_3$), 2.05, 2.01 (3H each, s, OAc × 2); ^{13}C NMR (50 MHz, $CDCl_3$) δ_C: 173.7 (s, 1-C), 29.1 (t, 2-C), 29.8 (t, 3-C), 73.2 (d, 4-C), 132.2 (d, 5-C), 125.5 (d, 6-C), 129.1 (d, 7-C), 149.5 (s, 8-C), 70.9 (d, 9-C), 31.3 (t, 10-C), 37.8 (t, 11-C), 88.0 (s, 12-C), 32.8 (t, 13-C), 122.8 (d, 14-C), 133.6 (d, 15-C), 27.4 (t, 16-C), 29.4 (t, 17-C), 31.4 (t, 18-C), 22.5 (t, 19-C), 14.0 (q, 20-C), 51.5 (q, $COOCH_3$), 170.1 (s), 170.3 (s), 22.2 (q), 21.1 (q) [OAc × 2]; MS *m/z* (%): 450 (M^+, 1), 390 (M^+ – AcOH, 4), 372 (M^+ – H_2O–AcOH, 2), 348 (M^+ – 42–AcOH, 5), 330 (M^+ – 2AcOH, 26). **26**, colorless oil; $[\alpha]_D^{22}$ + 36° (*c* = 2.0, $CHCl_3$); HR MS: M^+ = 450.263 (Calc for $C_{25}H_{38}O_7$ = 450.262); IR ($CHCl_3$) 3465 (br), 1727, 1225 cm^{-1}; UV and CD: Table 3; ^1H NMR (200 MHz, $CDCl_3$) δ: 2.37 (2H, t, *J* = 7.7, 2-H_2), 5.34 (1H, m, 4-H), 5.67 (1H, dd, *J* = 15.1, 7.1, 5-H), 6.68 (1H, dd, *J* = 15.1, 11.2, 6-H), 6.22 (1H, d, *J* = 11.2, 7-H), 4.99 (1H, br dt, *J* = 2.0, *ca* 6, 9-H), 2.59, 2.81 (AB in ABX, J_{AB} = 14.9, J_{AX} = 7.0, J_{BX} = 6.4), *ca* 5.40 (1H, m, 14-H), *ca* 5.51 (1H, m, 15-H), 0.88 (3H, t, *J* = 6.8, 20-H_3), 3.69 (3H, s, $COOCH_3$), 2.05, 1.96 (3H each, s, OAc × 2); ^{13}C NMR (50 MHz, $CDCl_3$) δ_C: 173.1 (s, 1-C), 29.5 (t, 2-C), 29.8 (t, 3-C), 73.3 (d, 4-C), 132.6 (d, 5-C), 126.5 (d, 6-C), 128.9 (d, 7-C), 149.3 (s, 8-C), 71.5 (d, 9-C), 32.9 (t, 10-C), 36.8 (t, 11-C), 88.5 (s, 12-C), 33.9 (t, 13-C), 123.4 (d, 14-C), 136.6 (d, 15-C), 27.5 (t, 16-C), 29.3 (t, 17-C), 31.5 (t, 18-C), 22.6 (t, 19-C), 14.0 (q, 20-C), 51.7 (q, $COOCH_3$), 170.1 (s), 169.7 (s), 21.1 (q), 22.1 (q) [OAc × 2].

Photo-isomerization of claviridenones. A soln of **3**, **4**, **5** or **6** (25 mg each) in 3 mL benzene in a Pyrex tube was irradiated with fluorescent lamps (15 W × 2) at 20° for 40 hr. Each product was examined by TLC [Kieselgel 60 F_{254} (Merck, DC-Fertig-Platten), developing twice with n-hexane–AcOEt (3:1)] and HPLC [Semi Prep μPORASIL, elution with n-hexane–AcOEt (3:1)] to identify with **3** (R_f = 0.55, t_R = 12'00"), **4** (0.39, 14'30"), **5** (0.37, 16'00"), and

6 (0.33, 18'30"). The composition of each photo-isomerization product was found to be almost identical (3:4:5:6 = 1:6:12:2) as judged from the area of each peak on HPLC. The major products **4** and **5** obtained by respective photo-isomerization of **3** and **6** were separated by HPLC and identified with authentic compounds by ^{1}H NMR (200 MHz, $CDCl_3$) and $[\alpha]_D$. **4** obtained from **3**: $[\alpha]_D^{20}$ + 21° (*c* = 0.4, $CHCl_3$); **4** from **6**: $[\alpha]_D^{20}$ + 22° (*c* = 0.5, $CHCl_3$); **5** from **3**: $[\alpha]_D^{20}$ + 9° (*c* = 0.5, $CHCl_3$); **5** from **6**: $[\alpha]_D^{20}$ + 8° (*c* = 1.0, $CHCl_3$).

$NaBH_4$ *Reduction of claviridenone-c* (**5**) *giving* **10** *and* **11**. An ice-cooled soln of **5** (1.12 g) in 60 mL THF–MeOH (2:1) was treated with $NaBH_4$ (200 mg) and stirred for 10 min. The mixture was poured into ice water and the whole was extracted with AcOEt. Work-up of the AcOEt extract as described for **4** gave two tetrahydro derivatives **10** (850 mg) and **11** (95 mg). **10**, colorless oil; $[\alpha]_D^{21}$ − 24° (*c* = 1.0, $CHCl_3$); HR MS: M^+ = 450.259 (Calc for $C_{25}H_{38}O_7$ = 450.261); IR ($CHCl_3$) 3490 (br), 1725, 1230 (br) cm^{-1}; UV and CD: Table 3; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.35 (2H, t, *J* = 7.6, 2-H_2), 5.30 (1H, dt, *J* = 7.1, 6.7, 4-H), 5.56 (1H, dd, *J* = 14.9, 7.1, 5-H), 6.66 (1H, dd, *J* = 14.9, 11.7, 6-H), 6.28 (1H, d, *J* = 11.7, 7-H), 4.37 (1H, br s, 9-H), 2.60, 2.42 (AB in ABX, J_{AB} = 14.9, J_{AX} = 6.1, J_{BX} = 7.7, 13-H_2), 5.5–5.6 (2H, m, 14, 15-H), 0.89 (3H, t, *J* = 7.0, 20-H_3), 3.67 (3H, s, $COOCH_3$), 2.08, 2.03 (3H each, s, OAc × 2), 3.94 (1H, br s, 9-OH), 6% NOE was observed on the 7-H signal upon the irradiation of 9-H; ^{13}C NMR: Table 2; MS *m/z* (%): 450 (M^+, 5), 390 (M^+ − AcOH, 10), 348 (M^+ − 42–AcOH, 10), 330 (M^+ − 2AcOH, 35). **11**, colorless oil; $[\alpha]_D^{23}$ − 13° (*c* = 1.0, $CHCl_3$); HR MS: M^+ = 450.262 (Calc for $C_{25}H_{38}O_7$ = 450.262); IR (CCl_4) 3600, 3500 (br), 1736, 1234 cm^{-1}; UV and CD: Table 3; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.35 (2H, t, *J* = 7.4, 2-H_2), 5.31 (1H, dt, *J* = 7.1, 6.5, 4-H), *ca* 5.5 (1H, m, 5-H), 6.72 (1H, dd, *J* = 15.0, 11.5, 6-H), 6.15 (1H, d, *J* = 11.5, 7-H), 4.75 (1H, br s, 9-H), *ca* 5.5 (2H, m, 14, 15-H), 0.89 (3H, t, *J* = 6.8, 20-H_3), 3.76 (3H, s, $COOCH_3$), 2.05, 2.03 (3H each, s, OAc × 2); ^{13}C NMR (50 MHz, $CDCl_3$) δ$_C$: 172.3 (s, 1-C), 29.5 (t, 2-C), 29.9 (t, 3-C), 73.5 (d, 4-C), 132.2 (d, 5-C), 124.1 (d, 6-C), 128.5 (d, 7-C), 149.4 (s, 8-C), 74.9 (d, 9-C), 32.2 (t, 10-C), 38.1 (t, 11-C), 87.1 (s, 12-C), 32.8 (t, 13-C), 123.5 (d, 14-C), 134.1 (d, 15-C), 27.6 (t, 16-C), 29.3 (t, 17-C), 31.6 (t, 18-C), 22.6 (t, 19-C), 14.1 (q, 20-C), 51.7 (q, $COOCH_3$), 170.0 (s), 169.8 (s), 21.6 (q), 21.2 (q) [OAc × 2].

$NaBH_4$ *Reduction of claviridenone-d* (**6**) *giving* **27**. Claviridenone-d (**6**) was subjected to $NaBH_4$ reduction in the same way as described above to furnish the tetrahydro derivative **27**. **27**, colorless oil; $[\alpha]_D^{23}$ − 81° (*c* = 0.5, $CHCl_3$); HR MS: M^+ = 450.261 (Calc for $C_{25}H_{38}O_7$ = 450.260); ^{1}H NMR (200 MHz, $CDCl_3$) δ: 6.69 (1H, d, *J* = 12.2, 7-H), 4.41 (1H, br dd, *J* = 9.5, *ca* 4.9, 9-H), 3.97 (1H, br d, *J* = 9.5, 9-OH).

Benzoylation of **10** *giving* **12**. A soln of **10** (15 mg) in 0.5 mL pyridine was treated with benzoyl chloride (0.1 mL) and the whole soln was stirred under an N_2 atmosphere at 22° (r.t.) for 10 min. The mixture was poured into ice water and the whole was extracted with AcOEt. The AcOEt phase was washed with satd aq $NaHCO_3$ and satd aq NaCl and dried over $MgSO_4$. The product, obtained by removing the solvent under reduced pressure, was purified by SiO_2 column chromatography (elution with n-hexane–AcOEt 10:1) to furnish the benzoate **12** (19 mg). **12**, colorless oil; $[\alpha]_D^{20}$ − 61.5° (*c* = 0.9, $CHCl_3$); HR MS: M^+ = 554.288 (Calc for $C_{32}H_{42}O_8$ = 554.288); IR (CCl_4) 1736, 1721, 1696, 1600, 1268 cm^{-1}; UV and CD: Table 3; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.35 (2H, t, *J* = 7.5, 2-H_2), *ca* 5.3 (1H, m, 4-H), 5.55 (1H, dd, *J* = 15.0, 7.3, 5-H), 6.77 (1H, dd, *J* = 15.0, 11.5, 6-H), 6.19 (1H, d, *J* = 11.5, 7-H), 5.73 (1H, br t, *J* = 6, 9-H), 2.75, 2.59 (AB in ABX, J_{AB} = 14.2, J_{AX} = 7.1, J_{BX} = 7.7, 13-H_2), *ca* 5.5 (2H, m, 14, 15-H), 0.89 (3H, t, *J* = 7.0, 20-H_3), 8.12 (2H, d, *J* = 7.0), 7.45(2H, t, *J* = 7.0), 7.56 (1H, t, *J* = 7.0); ^{13}C NMR: Table 2; MS *m/z* (%): 554 (M^+, 0.05), 494 (M^+ − AcOH, 0.3), 435 (M^+ − AcOH–$COOCH_3$, 0.5), 434 (M^+ − 2AcOH, 0.5), 432 (M^+ − C_6H_5COOH, 0.4), 105 (C_7H_5O, 100).

p-*Methoxybenzoylation of* **10** *giving* **13**. A soln of **10** (35 mg) in 0.5 mL pyridine was treated with *p*-methoxybenzoyl chloride (40 mg) and the whole solution was stirred under an N_2 atmosphere at 35° for 2 hr. Work-up of the reaction mixture as described above furnished the *p*-methoxybenzoate **13** (40 mg). **13**, colorless oil; HR MS: M^+ = 584.299 (Calc for $C_{33}H_{44}O_9$ = 584.299); UV and CD: Table 3.

Benzoylation of **11** *giving* **14**. A soln of **11** (50 mg) in 0.5 mL pyridine was treated with benzoyl chloride (0.1 mL) and the whole soln was stirred under an N_2 atmosphere at 20° (r.t.) for 10 min. Work-up of the mixture as described above furnished the benzoate **14** (31 mg). **14**, colorless oil; HR MS: M^+ = 554.290 (Calc for $C_{32}H_{42}O_8$ = 554.288); UV and CD: Table 3; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 5.30 (1H, dt, *J* = 6.8, 6.6, 4-H), 6.72 (1H, dd, *J* = 15.0, 11.6, 6-H), 6.31 (1H, d, *J* = 11.6, 7-H), 5.92 (1H, t, *J* = 5.3, 9-H), 0.86 (3H, t, *J* = 7.0, 20-H_3); ^{13}C NMR (50 MHz, $CDCl_3$) δ$_C$: 172.9 (s, 1-C), 29.3 (t, 2-C), 29.7 (t, 3-C), 73.2 (d, 4-C), 133.5 (d, 5-C), 127.4 (d, 6-C), 128.1 (d, 7-C), 144.5 (s, 8-C), 78.7 (d, 9-C), 30.0 (t, 10-C), 38.6 (t, 11-C), 87.3 (s, 12-C), 34.5 (t, 13-C), 123.3 (d, 14-C), 133.8 (d, 15-C), 27.6 (t, 16-C), 29.3 (t, 17-C), 31.5 (t, 18-C), 22.5 (t, 19-C), 14.0 (q, 20-C).

Syntheses of **21**, **22**, **23**, **24** *and* **25**. Various benzoates (**21**–**25**) (Table 3) were synthesized in the same manner as described above. **21**, colorless oil; HR MS: M^+ = 554.288 (Calc for $C_{32}H_{42}O_8$ = 554.288). **22**, colorless oil; HR MS: M^+ = 632.201, 634.195 (Calc for $C_{32}H_{41}O_8$ ^{79}Br = 632.199, $C_{32}H_{41}O_8$ ^{81}Br = 634.196). **23**, colorless oil; HR MS: M^+ = 579.283 (Calc for $C_{33}H_{41}NO_8$ = 579.283). **24**, colorless oil; HR MS: M^+ = 599.273 (Calc for $C_{32}H_{41}NO_{10}$ = 599.273). **25**, colorless oil; HR MS: M^+ = 632.201, 634.198 (Calc for $C_{32}H_{41}O_8$ ^{79}Br = 632.199, $C_{32}H_{41}O_8$ ^{81}Br = 634.197).

$LiAlH_4$ *Reduction of* **10** *giving the tetraol* **15**. An ice-cooled soln of **10** (500 mg) in 30 mL dry THF was treated with $LiAlH_4$ (63 mg) and stirred for 10 min. The reaction was quenched by successive treatment with AcOEt, MeOH, and water and the whole was extracted with AcOEt. The AcOEt phase was washed successively with dil aq HCl, satd aq $NaHCO_3$, satd aq NaCl, and dried over $MgSO_4$. The product, obtained after removal of the solvent under reduced pressure, was purified by column chromatography [SiO_2, elution with $CHCl_3$–MeOH (10:1)] to furnish **15** (230 mg). **15**, colorless oil; $[\alpha]_D^{20}$ − 99° (*c* = 1.4, $CHCl_3$); IR ($CHCl_3$) 3460 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.69 (2H, t, *J* = 5.6, 1-H_2), 4.27 (1H, m, 4-H), 5.71 (1H, dd, *J* = 15.0, 6.8, 5-H), 6.92 (1H, dd, *J* = 15.0, 11.5, 6-H), 6.24 (1H, d, *J* = 11.5, 7-H), 4.38 (1H, br s, 9-H), 2.61, 2.41 (AB in ABX, J_{AB} = 14.3, J_{AX} = 7.7, J_{BX} = 7.0, 13-H_2), *ca* 5.5 (2H, m, 14, 15-H), 0.88 (3H, t, *J* = 6.8, 20-H_3).

t-*Butyldimethylsilylation of* **15** *giving* **16** *and* **17**. A soln of **15** (230 mg) in 3 mL dry DMF was treated with t-butyldimethylsilyl chloride (307 mg) and imidazole (400 mg) and the whole mixture was stirred under an N_2 atmosphere at 20° (r.t.) for 20 min. The mixture was poured into ice water and the whole was extracted with AcOEt. The AcOEt phase was washed with satd aq NaCl and dried over $MgSO_4$. The product, obtained after removal of the solvent under reduced pressure, was purified by SiO_2 column chromatography (elution with n-hexane–AcOEt 5:1) to furnish **16** (339 mg) and **17** (57 mg). **16**, colorless oil; HR MS: M^+ = 680.502 (Calc for $C_{38}H_{76}O_4Si_3$ = 680.505); IR (CCl_4) 3600, 1457, 1249 cm^{-1}; UV (MeOH) 240 nm (ε 26,000), 245 (ε 28,000); CD: Fig. 2; ^{1}H NMR (200 MHz, $CDCl_3$) δ: 3.61 (2H, br s, 1-H_2), 4.20 (1H, m, 4-H), 5.65 (1H, dd, *J* = 15.0, 6.4, 5-H), 6.83 (1H, dd, *J* = 15.0, 11.8, 6-H), 6.10 (1H, d, *J* = 11.8, 7-H), 4.30 (1H, br t, *J* = 7.2, 9-H), 0.94, 0.90, 0.89 (each 9H, s), 0.13, 0.10, 0.05, 0.03 (each 3H, s), 0.04 (6H, s); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ$_C$: 63.3 (t, 1-C), 28.7 (t, 2-C), 34.8 (t, 3-C), 73.2 (d, 4-C), 138.7 (d, 5-C), 124.7 (d, 6-C), 124.8 (d, 7-C), 149.8 (s, 8-C), 75.7 (d, 9-C), 32.7 (t, 10-C),

38.8 (t, 11-C), 79.4 (s, 12-C), 36.0 (t, 13-C), 125.4 (d, 14-C), 133.2 (d, 15-C), 27.6 (t, 16-C), 29.4 (t, 17-C), 31.6 (t, 18-C), 22.7 (t, 19-C), 14.1 (q, 20-C). **17**, colorless oil; HR MS: M^+ = 566.417 (Calc for $C_{32}H_{62}O_4Si_2$ = 566.418); IR ($CHCl_3$) 3600, 3380 (br), 1093 cm^{-1}; UV and CD: Table 4; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.64 (2H, br s, 1-H_2), 4.19 (1H, m, 4-H), 5.68 (1H, dd, J = 15.1, 6.8, 5-H), 6.89 (1H, dd, J = 15.1, 11.7, 6-H), 6.10 (1H, d, J = 11.7, 7-H), 4.28 (1H, br t, J = 7.1, 9-H), 0.93, 0.89 (both 9H, s), 0.11, 0.09 (both 3H, s), 0.06 (6H, s); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ_c: 63.4 (t, 1-C), 28.9 (t, 2-C), 34.5 (t, 3-C), 72.4 (d, 4-C), 137.8 (d, 5-C), 124.6 (d, 6-C), 125.9 (d, 7-C), 150.5 (s, 8-C), 75.6 (d, 9-C), 37.7 (t, 10-C), 38.9 (t, 11-C), 79.4 (s, 12-C), 36.1 (t, 13-C), 124.3 (d, 14-C), 133.5 (d, 15-C), 27.6 (t, 16-C), 29.4 (t, 17-C), 31.6 (t, 18-C), 22.6 (t, 19-C), 14.1 (q, 20-C).

Benzoylation of **16** *giving* **18**. A soln of **16** (20 mg) in 0.5 mL pyridine was treated with AgCN (20 mg) and benzoyl chloride (20 mg) and the whole mixture was heated with stirring at 80° under an N_2 atmosphere for 6 hr. After dilution with AcOEt, the mixture was passed through a Celite column. The AcOEt eluate was then washed with satd aq NaCl, satd aq $NaHCO_3$ and dried over $MgSO_4$. The product, which was obtained after removal of the solvent under reduced pressure, was purified by SiO_2 column chromatography (elution with n-hexane–AcOEt 20:1) to furnish **18** (15 mg). **18**, colorless oil; $[\alpha]_D^{20}$ − 4.3° (c = 0.3, $CHCl_3$); IR (CCl_4) 1721 (sh), 1711, 1250 cm^{-1}; UV (MeOH) 232 nm (ϵ 35,000), 247 (ϵ 27,000); CD: Fig. 2; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.53 (2H, br s, 1-H_2), 4.13 (1H, m, 4-H), 5.64 (1H, dd, J = 15.0, 5.6, 5-H), 6.73 (1H, dd, J = 15.0, 11.6, 6-H), 6.15 (1H, dd, J = 11.6, 2.0, 7-H), 4.39 (1H, br t, J = 8, 9-H), 3.10, 2.71 (AB in ABX, J_{AB} = 14.0, J_{AX} = 7.5, J_{BX} = 7.0, 13-H_2), 0.95, 0.89, 0.77 (each 9H, s), 0.14, 0.12, − 0.12, − 0.13 (each 3H, s), 0.03 (6H, s), 7.84 (2H, d, J = 7.0), 7.39 (2H, t, J = 7.0), 7.57 (1H, t, J = 7.0); ^{13}C NMR (22.5 MHz, $CDCl_3$) δ_c: 63.3 (t, 1-C), 28.2 (t, 2-C), 34.7 (t, 3-C), 72.5 (d, 4-C), 138.8 (d, 5-C), 124.3 (d, 6-C), 128.2 (d, 7-C), 145.1 (s, 8-C), 75.2 (d, 9-C), 32.4 (t, 10-C), 37.8 (t, 11-C), 87.9 (s, 12-C), 32.9 (t, 13-C), 123.6 (d, 14-C), 134.0 (d, 15-C), 27.6 (t, 16-C), 29.4 (t, 17-C), 31.6 (t, 18-C), 22.6 (t, 19-C), 14.1 (q, 20-C); MS m/z (%): 784 (M^+, 0.7), 662 ($M^+ - C_6H_5COOH$, 25).

p-*Nitrobenzoylation of* **16** *giving* **19**. A soln of **16** (30 mg) in 1 mL pyridine was treated with AgCN (130 mg) and p-nitrobenzoyl chloride (90 mg) and the whole mixture was stirred at 60° under an N_2 atmosphere for 3 hr. Work-up of the mixture as described above furnished **19** (10 mg). **19**, colorless oil; $[\alpha]_D^{27}$ − 5.9° (c = 0.4, $CHCl_3$); HR MS: M^+ = 829.512 (Calc for $C_{45}H_{79}NO_7Si_3$ = 829.516); IR (CCl_4) 1718, 1605, 1225 cm^{-1}; UV (MeOH) 247 nm (ϵ 37,000); CD: Fig. 2; ^{13}C NMR: Table 2.

Benzoylation of **17** *giving* **20**. A soln of **17** (20 mg) in 1 mL pyridine was treated with benzoyl chloride (0.1 mL) and stirred under an N_2 atmosphere at 20° (r.t.) for 15 min. Work-up of the mixture in the usual manner furnished the benzoate **20** (22 mg). **20**, colorless oil; $[\alpha]_D^{20}$ − 32° (c = 0.5, $CHCl_3$); HR MS: M^+ = 670.445 (Calc for $C_{39}H_{66}O_5Si_2$ = 670.445); IR (CCl_4) 3592, 1712, 1264 cm^{-1}; UV and CD: Table 4; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.65 (2H, t, J = 6.1, 1-H_2), 5.60 (1H, dt, J = 6.7, 6.1, 4-H), 5.74 (1H, dd, J = 15.0, 6.7, 5-H), 7.07 (1H, dd, J = 15.0, 11.5, 6-H), 6.11 (1H, d, J = 11.5, 7-H), 4.29 (1H, br t, J = 7.0, 9-H), 2.58, 2.40 (AB in ABX, J_{AB} = 14.0, J_{AX} = 7.7, J_{BX} = 6.6, 13-H_2), 0.93, 0.89 (both 9H, s), 0.11, 0.09 (both 3H, s), 0.05 (6H, s), 8.06 (2H, d, J = 8.0), 7.43 (2H, t, J = 8.0), 7.55 (1H, t, J = 8.0); ^{13}C NMR: Table 2; MS m/z (%): 670 (M^+, 0.1), 652 ($M^+ - H_2O$, 3), 548 ($M^+ - C_6H_5COOH$, 32).

Synthesis of the benzoate **29** *from claviridenone-d* (**6**). The benzoate **29** was synthesized from **6** via **28** through the same reaction procedure as carried out for the synthesis of **20** from **5** via **17**. **28**, colorless oil; UV and CD: Table 4. **29**, colorless oil; HR MS: M^+ = 670.442 (Calc for $C_{39}H_{66}O_5Si_2$ = 670.445); UV and CD: Table 4; ^1H NMR (200 MHz, $CDCl_3$) δ: 3.63 (2H, t, J = 6.1, 1-H_2), 4.35 (1H, br t, J = *ca* 7.8, 9-H), 5.54 (1H, dt-like, J = 11.0, 7.3, 15-H), 0.97, 0.88 (each 9H, s), 0.19, 0.13 (each 3H, s), 0.04 (6H, s), 8.05 (2H, d, J = 6.8), 7.28–7.55 (3H, m).

Degradation of claviridenones giving **32**. A soln of claviridenones (200 mg, a mixture of **3**, **4**, **5** and **6**) in 10 mL CH_2Cl_2 was bubbled through with a stream of ozonated O_2 at 0° for 75 min. The mixture was treated with $NaBH_4$ (1 g) at 0° and stirred under an N_2 atmosphere for 1.5 hr. After filtration, the solvent was removed under reduced pressure to give the residue. The residue was dissolved in 2 mL pyridine and treated with p-anisylchlorodiphenyl-methane (245 mg) and the whole mixture was stirred under an N_2 atmosphere at 20° (r.t.) for 36 hr. The product, obtained after removal of the solvent under reduced pressure, was purified by SiO_2 column chromatography (elution with $CHCl_3$–MeOH 200:1) to furnish **30** (130 mg). **30**, ^1H NMR (90 MHz, $CDCl_3$) δ: 2.08 (3H, s, OAc), 3.65 (3H, s, $COOCH_3$), 3.79 (3H, s), 7.21–7.40 (m, MMTr). To a suspension of $LiAlH_4$ (22 mg) in 2 mL dry ether was added a soln of **30** (130 mg) in 2 mL dry ether and the whole mixture was stirred under an N_2 atmosphere at 20° for 30 min. After dilution with 10 mL $CHCl_3$, the mixture was filtered. The product, obtained after removal of the solvent under reduced pressure, was purified by SiO_2 column chromatography (elution with $CHCl_3$–MeOH 200:1) to furnish **31** (65 mg). **31**, colorless oil; $[\alpha]_D^{20}$ + 3.5° (c = 1.0, benzene); IR ($CHCl_3$) 3585, 3415, 1605 cm^{-1}; UV (MeOH) 230 nm (ϵ 12,000), 275 (ϵ 1300); ^1H NMR (90 MHz, $CDCl_3$) δ: 3.78 (3H, s), 7.24–7.40 (m); MS m/z (%): 392 (M^+, 0.1), 274 (66), 273 (MMTr, 100). A soln of **31** (35 mg) in 2 mL dry DMF was treated with t-butyldimethylsilyl chloride (20 mg) and imidazole (16 mg) and stirred at 0° under an N_2 atmosphere for 45 min. The reaction mixture was poured into ice water and worked up as described above to furnish **32** (20 mg). **32**, colorless oil; $[\alpha]_D^{20}$ + 4° (c = 1.1, benzene); IR ($CHCl_3$) 3580, 1606 cm^{-1}; UV (MeOH) 230 nm (ϵ 15,000), 275 (ϵ 1500); ^1H NMR (90 MHz, $CDCl_3$) δ: 0.03 (6H, s), 0.87 (9H, s), 3.79 (3H, s), 7.22–7.40 (m); MS m/z (%): 505 ($M^+ - 1$, 0.1), 274 (88), 272 (100).

Application of Horeau's method. A soln of **32** (20 mg) in 1 mL pyridine was treated with (±)-α-phenylbutyric anhydride (18 mg) and stirred at 20° (r.t.) under an N_2 atmosphere for 48 hr. After addition of 1 mL water, the reaction mixture was stirred further for 1 hr and partitioned by an AcOEt–aq $NaHCO_3$ solvent system. Work-up of the AcOEt phase in the usual manner followed by SiO_2 column chromatography (elution with n-hexane–AcOEt 4:1) furnished the ester **33** (9 mg) together with recovered **32** (12 mg). The aq $NaHCO_3$ phase was acidified with 2N aq HCl and the whole was extracted with AcOEt. Purification of the AcOEt extract by SiO_2 column chromatography (elution with n-hexane–AcOEt 3:1) recovered α-phenylbutyric acid (7 mg), $[\alpha]_D^{20}$ + 4.6° (c = 0.7, benzene). **33**, colorless oil; $[\alpha]_D^{20}$ + 1.3° (c = 0.5, benzene); IR ($CHCl_3$) 1720, 1247 cm^{-1}; UV (MeOH) 228 nm (ϵ 11,000), 277 (ϵ 1200); ^1H NMR (90 MHz, $CDCl_3$) δ: 0.00, 0.24 (total 6H, s), 0.87, 0.90 (total 9H, s), 3.82, 3.83 (total 3H, s), 7.20–7.40 (m); MS m/z (%): 652 (M^+, 0.1), 274 (100), 273 (100).

Acknowledgement—One of the authors (M.K.) thanks the Ministry of Education, Science, and Culture of Japan for financial support (Grant No. 58771587).

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[14]We thank Professor Y. Yamada for generously showing us the physical data for clavulone I, II and III.