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ABSOLUTE STEREOCHEMISTRY OF NEW PROSTANOIDS CLAVULONE I, II AND III, FROM CLAVULARIA VIRIDIS QUOY AND GAIMARD[1]

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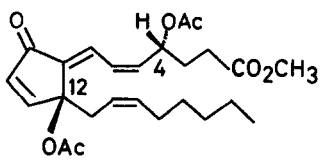
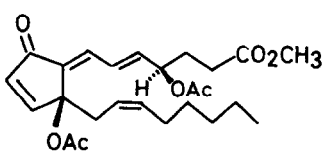
Summary: Absolute configurations at the C-4 and -12 positions of a new type of prostanoids clavulone I (1), II (2) and III (3), isolated from Clavularia viridis Quoy and Gaimard, have been elucidated on the basis of chemical and spectral evidence.

In a previous paper,[2] the isolation and structures of a new type of prostanoids clavulone I, II and III from the Japanese Stolonifer Clavularia viridis Quoy and Gaimard have been reported. Here we wish to describe evidence for the stereochemistry of the chiral centers at the C-4 and -12 positions of clavulone I, II and III as depicted in 1, 2 and 3, respectively.

Clavulone I (1), II (2) and III (3) each have the same absolute stereochemistry at both the C-4 and -12 positions as shown by the following isomerization



1



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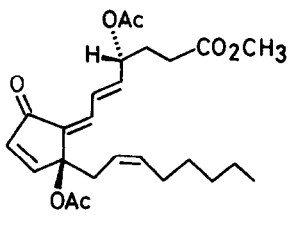
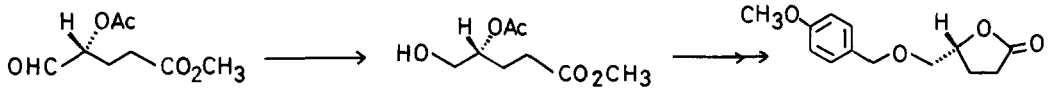


3

experiment. Treatment of clavulone I (1) with oxalic acid in methanol at room temperature for 20 days afforded clavulone II (2)(18% isolated yield) and III(3) (9% isolated yield) with recovery of 1 (26%), showing that each compound differs only in the geometry of the double bond at the C-5 or -7 position.

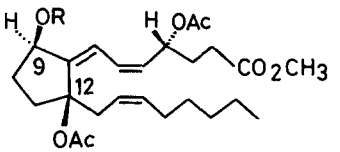
The absolute configuration at the C-4 position in clavulones was established by converting the aldehyde (4) obtained by ozonolysis[2] of 1 to the lactone (6), whose enantiomer[3] has been synthesized from D-glyceraldehyde acetonide. Reduc-



4 5 6

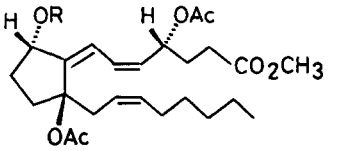
tion of 4 with sodium borohydride in methanol at room temperature for 1 h gave the alcohol (5). Treatment of 5 with p-methoxybenzyl bromide in tetrahydrofuran and N,N-dimethylformamide in the presence of sodium hydride at room temperature for 4 h, followed by the usual work-up, gave the lactone (6)[4,5]; $[\alpha]_D$ -13°(c 0.03, $CHCl_3$). The spectral data of 6 were identical with those of the enantiomer of 6, which has the S configuration,except for the sign of the optical rotation. This finding proved the stereochemistry at the C-4 position in 1 to be the R configuration, and also disclosed the same configuration at C-4 for 2 and 3.

The absolute configuration at the C-12 position in clavulones was determined by examination of the CD spectra of the p-bromobenzoates (8) and (10) which were prepared from clavulone I (1). Reduction of 1 with sodium borohydride in methanol at room temperature for 30 min gave two epimeric alcohols (7)[2,6], and



7 R = H

8 R = -C(=O)-C6H4-Br



9 R = H

10 R = -C(=O)-C6H4-Br

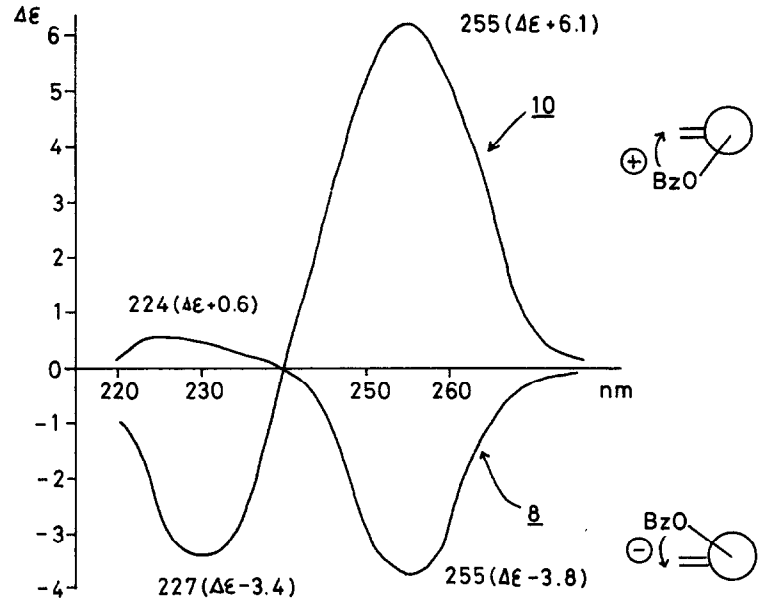


Fig.1. CD Spectra of p-bromobenzoates (8) and (10) in EtOH

(9)[7] in 57% and 13% yield, respectively. The relative stereochemistry at the C-9 and -12 positions in 7 and 9 was elucidated by comparison of their ^{1}H-NMR spectra. In 7, the C-9 proton appeared at δ 4.42 ppm (brdd,J=5.5,9.6 Hz, changed to a doublet (J=5.5 Hz) upon addition of D_2O), while in 9 the corresponding proton shifted downfield to δ 4.76 ppm (brt,J=7.3 Hz). This showed that the C-9 proton in 9 is located in the proximity of the acetoxyl group at the C-12 position and deshielded by the C-O bond at C-12, indicating the trans relationship between the hydroxyl group at C-9 and the acetoxyl group at C-12 in 9, and thus the cis relationship between the two groups in 7. The cis stereochemistry in 7 was further supported by the observation of intramolecular hydrogen bonding between the hydroxyl proton at C-9 and the carbonyl oxygen of the acetoxyl group at C-12 in the ^{1}H-NMR spectrum. The hydroxyl proton at C-9 appeared as a doublet at a relatively downfield position; δ 3.99 ppm (1H,d,J=9.6 Hz, disappeared upon addition of D_2O).

Application of the exciton chirality method[8] for the p-bromobenzoates of 7 and 9 provided evidence for the absolute configurations at the C-9 position, thus

indicating the absolute configuration at the C-12 position. The CD spectra of the p-bromobenzoates (8)[9] and (10)[10] obtained by treatment of 7 and 9 with p-bromobenzoyl chloride in carbon tetrachloride in the presence of triethylamine and N,N-dimethylaminopyridine, respectively, are shown in Fig.1. In 8 the negative Cotton effect at 255 nm ($\Delta\varepsilon$ -3.8) caused by the interaction between the two chromophores (the diene and p-bromobenzoyloxy groups) is observed, while the positive Cotton effect at 255 nm ($\Delta\varepsilon$ +6.1) is observed in 10. The negative Cotton effect in 8 indicates the negative chirality of the two chromophores and thus the R configuration at the C-9 position. These results lead to the assignment of the stereochemistry at the C-12 position as R for clavulone I (1), and the same R configuration at C-12 for clavulone II (2) and III (3).

References and Notes

1. This paper constitutes Part IX of "Studies on Marine Natural Products".
2. H.Kikuchi,Y.Tsukitani,K.Iguchi and Y.Yamada,Tetrahedron Lett.,23,5171(1982).
3. Unpublished data from this laboratory.
4. Hydrolysis and lactonization took place during the work-up procedure.
5. 6: pale yellow oil. IR($CHCl_3$) 1770, 1610, 1510, 1245, 1210 cm^{-1}. ^{1}H-NMR(270 MHz,$CDCl_3$) δ 3.56(1H,dd,J=10.5,4.0 Hz), 3.64(1H,dd,J=10.5,3.3 Hz), 3.81(3H,s) 4.50(2H,s), 4.67(1H,m), 6.88(2H,d,J=8.2 Hz), 7.23(1H,d,J=8.2 Hz).
6. 7: IR($CHCl_3$) 3400, 1735, 1720, 1240 cm^{-1}. ^{1}H-NMR(270 MHz,$CDCl_3$) δ 0.86(3H,t, J=6.9 Hz), 2.03(3H,s), 2.04(3H.s), 3.69(3H,s), 3.99(1H,d,J=9.6 Hz,disappeared upon addition of D_2O), 4.42(1H,brdd,J=5.5,9.6 Hz), 5.40(1H,t,J=10.6 Hz), 5.45 (1H,m), 5.56(1H,m), 5.71(1H,m), 6.49(1H,t,J=12.2 Hz), 6.69(1H,d,J=12.2 Hz).
7. 9: colorless oil. $[\alpha]_D$ +41.7(c 0.12,$CHCl_3$). UV(EtOH) 248nm(ε 19,800). IR ($CHCl_3$) 3350, 1725 cm^{-1}. ^{1}H-NMR(270 MHz,$CDCl_3$) δ 0.88(3H,t,J=6.3 Hz), 1.98(3H, s), 2.03(3H,s), 3.68(3H,s), 4.76(1H,brt,J=7.3 Hz), 5.34-5.63(3H,m), 5.74(1H,m) 6.54-6.57(2H,m).
8. N.Harada,J.Iwabuchi,Y.Yokota,H.Uda and K.Nakanishi, J.Amer.Chem.Soc., 103, 5590(1981).
9. 8: pale yellow oil. $[\alpha]_D$ -184°(c 0.49,$CHCl_3$). UV(EtOH) 242nm (ε 25,400). IR(film) 1735, 1720, 1595, 1270, 1240 cm^{-1}. ^{1}H-NMR(270 MHz,$CDCl_3$) δ 0.89(3H,t, J=6.6 Hz), 2.00(3H,s), 2.03(3H,s), 3.62(3H,s), 5.35-5.47(2H,m), 5.53-5.72 (3H,m), 6.55-6.67(2H,m), 7.59(2H,d,J=8.2 Hz), 7.98(2H,d,J=8.2 Hz).
10. 10: pale yellow oil. $[\alpha]_D$ +125°(c 0.04,$CHCl_3$). UV(EtOH) 243nm (ε 34,600),248 nm(sh,ε 33,600). IR($CHCl_3$) 1730, 1720, 1590, 1265 cm^{-1}. ^{1}H-NMR(90 MHz,$CDCl_3$) δ 0.88(3H,t,J=6 Hz), 2.02(6H,s), 3.66(3H,s), 5.25-5.95(5H,m), 6.60-6.70(2H, m), 7.67(2H,d,J=9 Hz), 8.02(2H,d,J=9 Hz).

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