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IRIDOIDS—XXIII

ISOLATION OF AUCUBIGENIN AND ITS ACID-CATALYZED REARRANGEMENT†

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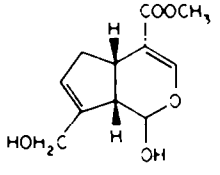
Abstract—Aucubigenin 3, the unstable aglycone of aucubin 2, has been successfully isolated. In acidic medium 3 is converted into the acetal 6 whose structure resulted to be 1,10-anhydro-6-desoxy-7,8-dihydro-7,8-dihydroxyaucubigenin.

Iridoid glucosides have been always described as substances characterized by the high instability of their aglycones, particularly in acidic medium,[1] in which they give coloured compounds,[1,2] rapidly converted in black degradation products. This behaviour has till now thwarted, in most cases, the obtaining of iridoid aglycones from parent glucosides.

The only natural iridoid aglycone so far isolated is genipine 1[3] whose carbomethoxy group at C-4, conjugated with the enol-ether double bond, has probably a stabilizing effect on the hemiacetalic ring.

In fact only from 4-carbomethoxy iridoids it has been possible to obtain, by enzymatic hydrolysis, the corresponding free aglycones,[4] while those of other iridoids have been isolated only as acetylderivatives[5] or hydrogenated products.[3,6]

In this paper we report on the behaviour of aucubin 2, the most naturally diffused iridoid, whose aglycone (aucubigenin) had been always described as particularly unstable.[7]



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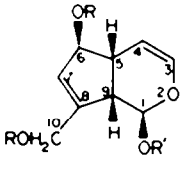

2: R = H, R' = β-Gluc
3: R = R' = H
4: R = R' = Ac

The enzymatic hydrolysis of 2 with β-glucosidase afforded, besides degradation products, a less polar iridoid compound that, extracted with EtOAc, proved to be very stable at low temperatures (−20°), even for a long time, and sufficiently stable at room temperature to allow its chromatographic purification on silica gel and the registration of its PMR spectrum (Table 1) that resulted in good agreement with the structure of aucubigenin 3.

By acetylation under mild conditions, 3 gave the more stable tri-O-acetylderivative 4 (molecular formula $C_{15}H_{18}O_7$ and negative $[\alpha]_D$ value) showing no more hydroxyl bands in IR spectrum.

Complete evidence for aucubigenin structure was given by the detailed analysis of the PMR Spectrum of 4 (Table 1), confirmed by spin decoupling experiments.

The irradiation of the double doublet at δ 6.23 (H-3) reduced the other double doublet at δ 4.96 into a doublet, clearly assignable to the olefinic H-4 ($J_{3,4}$ = 3.3 Hz); the reverse irradiation simplified, as expected, the double doublet at δ 6.23 into a doublet ($J_{3,4}$ = 2.0 Hz). As both H-3 and H-4 signals collapsed into equally spaced doublets ($J_{3,4}$ = 6.3 Hz) by irradiation of the broad signal at δ 2.95, this latter we attributed to the H-5; the same irradiation sharpened also the broad signal at δ 5.33, consequently assigned to H-6. The irradiation of the doublet at δ 6.04 (J = 4.5 Hz) of the hemiacetalic H-1 transformed the broad signal at δ 3.17 (H-9) into a doublet ($J_{1,9}$ = 7.5 Hz) while the reverse irradiation (besides simplifying the doublet at δ 6.04 into a singlet) sharpened the broad signal at δ 5.90 which we assign to the olefinic H-7.

As regards the absolute configuration of 4, we attribute a β-configuration (identical to that of 2) to the hemiacetal hydroxyl because the comparison of the $[M]_D$ value of 4 (−351°) with those of 2 (−595°) and of its hexa-O-acetylderivative 5 (−930°) clearly indicates that the configuration of the C-1 centre of 2 has not changed in the mild hydrolytic conditions.[4] The absolute configurations of the other asymmetric centres (C-5, C-6 and C-9) of 4 are obviously identical with those of the corresponding centres of 2.

The surprising ease of isolation of aucubigenin prompted us to investigate its behaviour in acidic medium. Experiments carried out on 3 in aqueous HCl, in different conditions of temperature, time and acid concentration, showed its constant transformation into 6, as well as into variable amounts of black degradation products. 6, which is a stable, crystalline product with the same molecular formula ($C_9H_{12}O_4$) of aucubigenin, still contains the enol-ether system of aucubin (identity of UV spectra) but differs from this latter in its highly positive $[M]_D$ value (+289°) and in its chemical and spectroscopic characteristics. In fact 6, by acetylation under mild conditions, was transformed into the mono-O-acetylderivative 7 whose IR spectrum, besides OH bands, showed in the acetal region (1200–1040 cm^{-1}) a higher number of peaks than in 4, so indicating the probable formation in 6 of a new acetal linkage. The comparison of the PMR spectra of 6 and 7 (Table 1) showed a paramagnetic shift of ~1 ppm (δ 5.11 → 6.08) for the double doublet at δ 5.11 (1 H), clearly indicating the existence in 6 of a very

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‡In alphabetical order

Table 1. PMR assignments*

Compound (solvent)	H-1	H-3	H-4	H-5	H-6 or 2H-6	H-7	CH_2-8	H-9
2 (D_2O)†	5.28(d) $J_{1,9}$ 5.0	6.35(dd) $J_{3,4}$ = 6.0 $J_{3,1}$ = 1.5	5.16(dd) $J_{3,4}$ = 6.0 $J_{4,5}$ = 3.7	2.84(bsgf)	4.60(bsg)‡	5.89(bs)	4.34(bs)	3.16(pt)
3 (D_2O)†	4.82(d)§ $J_{1,9}$ = nm¶	5.84(bsgf)	4.92(dd) $J_{3,4}$ = 6.0 $J_{4,5}$ = 3.5	2.50(bsgf)	4.70§	5.84(bsgf)	4.20(bs)	2.80(bsgf)
4 ($CDCl_3$)	6.04(d) $J_{1,9}$ = 4.5	6.23(dd) $J_{3,4}$ = 6.3 $J_{3,1}$ = 2.0	4.96(dd) $J_{3,4}$ = 6.3 $J_{4,5}$ = 3.3	2.95(bsg)	5.33(bsg)	5.90(bsg)	4.74(bs)	3.17(bsg)
6 (D_2O)†	5.70(d) $J_{1,9}$ = 6.3	6.00(dd) $J_{3,4}$ = 5.7 $J_{3,1}$ = 1.9	5.81(dd) $J_{3,4}$ = 5.7 $J_{4,5}$ 2.7	3.45(bsgf)	2.2–1.5(cm)	5.11(dd) $J_{6,7}$ = 8.7 $J_{6,5}$ = 3.5	δ_A = 4.00, δ_B = 3.80 } AB system J_{AB} = 10.0	2.66(dd) $J_{1,9}$ = 8.3 $J_{5,9}$ = 6.3
7 ($CDCl_3$)	5.58(d) $J_{1,9}$ 5.7	5.83(s)‖	5.83(s)‖	3.28(cm)	2.2–1.7(cm)‖	6.08(dd) $J_{6,7}$ = 8.0 $J_{6,5}$ = 5.0	δ_A = 4.04, δ_B = 3.86 } AB system J_{AB} = 10.0	2.68(dd) $J_{5,9}$ = 9.0 $J_{1,9}$ = 5.7
7 (C_5D_5N)	5.49(d) $J_{1,9}$ 5.3	5.29(dd) $J_{3,4}$ = 5.7 $J_{3,1}$ = 1.7	5.41(dd) $J_{3,4}$ = 5.7 $J_{4,5}$ = 2.4	2.76(bsgf)	2.1–1.3(cm)‖	6.19(dd) $J_{6,7}$ 8.0 $J_{6,5}$ = 5.0	δ_A 3.89, δ_B = 3.71 } AB system J_{AB} = 10.0	2.27(dd) $J_{5,9}$ = 8.3 $J_{1,9}$ 5.3
8 ($CDCl_3$)	5.54(d) $J_{1,9}$ = 5.0	5.89(dd) $J_{3,4}$ = 5.0 $J_{3,1}$ = 1.7	6.13(dd) $J_{3,4}$ = 5.0 $J_{4,5}$ = nm¶	3.32(bsgf)	2.1–1.7(cm)‖	6.09(dd) $J_{6,7}$ = 8.0 $J_{6,5}$ = 5.0	δ_A = 4.20, δ_B = 4.07 } AB system J_{AB} = 10.0	3.01(dd) $J_{5,9}$ = 8.0 $J_{1,9}$ 5.0
8 (C_5D_5N)	5.45(d) $J_{1,9}$ = 4.7	5.35(dd) $J_{3,4}$ = 5.7 $J_{3,1}$ = 1.7	6.05(dd) $J_{3,4}$ = 5.7 $J_{4,5}$ = 2.4	2.73(bsg)	1.9–1.4(cm)‖	6.19(dd) $J_{6,7}$ = 8.0 $J_{6,5}$ = 5.0	δ_A = 4.38, δ_B = 4.08 } AB system J_{AB} = 10.0	2.73(dd)**
9 (D_2O)†	5.70(d) $J_{1,9}$ = 6.3	6.00(dd) $J_{3,4}$ = 5.7 $J_{3,1}$ = 1.9	5.81(dd) $J_{3,4}$ = 5.7 $J_{4,5}$ = 2.7	3.44(bsgf)	2.04(bsf)	5.10(bsf)	δ_A = 4.00, δ_B = 3.80 } AB system J_{AB} = 10.0	2.66(dd) $J_{5,9}$ = 8.3 $J_{1,9}$ 6.3

*bs = broad singlet, bsf = broad singlet with fine structure, bsg = broad signal, bsgf = broad signal with fine structure, d = doublet, dd = double doublet, cm = complex multiplet, nm = no measurable, pt = pseudotriplet, s = singlet; †internal reference HDO (δ 4.70); ‡this signal, partly covered by HDO signal, has been displayed shifting with NaI the HDO signal; §the high field line is superimposed to HDO signal; ¶covered by HDO signal; ‖the signal is overlapped to the acetyl signals; **obscured by other signals; ††overlapped to H-5 signal; ‡‡H-3 and H-4 are equivalent also in acetone-d_6.

deshielded methine proton geminal with an OH group (e.g. the H-6 of **2** appears at δ 4.60).

By further acetylation **7** gave the bis-*O*-acetylderivative **8**, a completely acetylated compound (IR spectrum). The difficult acetylation of **7** is consistent with the presence of a tertiary OH, further on confirmed by the comparison of the PMR spectra of **7** and **8** (Table 1).

†An iridoid derivative rather similar to **6** is 1,10-anhydro-7,8-dihydrogenipin, obtained in small amounts by Djerassi *et al.*[10] during the catalytic hydrogenation of genipin.

‡In the spectrum registered for spin decoupling experiments (coaxial tube, TMS ext. ref.) all signals were shifted to lower field of exactly 0.40 ppm with respect to the mentioned values (ref. HDO).

§The H-4 signal appears in **6** very near that of H-3 being anomalously deshielded in comparison with the corresponding signal of aucubin **2** (Table 1) and of other similar iridoids.[9]

¶This proton is further on coupled with H-9, H-4 and H-3.

‖The multiplet exhibits only 13 lines because of the overlapping of three lines

The analysis of the PMR spectra of **6**, **7** and **8**, greatly simplified by using the double resonance technique, enables us to propose for **6** the structure of 1,10 - anhydro - 6 - deoxy - 7,8 - dihydro - 7,8 - dihydroxyaucubigenin.† In the PMR spectrum of **6**‡ (Table 1) the assignment of the two double doublets at δ 6.00 and 5.81 to the olefinic H-3 and H-4 respectively,§ was further confirmed by their collapsing in two equally spaced doublets ($J_{3,4}$ = 5.7 Hz) owing to irradiation of the broad signal at δ 3.45 therefore attributable to the H-5. By irradiation of the doublet at δ 5.70 of the hemiacetalic H-1, the double doublet at δ 2.66 became a doublet which consequently was attributed to the H-9, still coupled to the H-5 ($J_{5,9}$ = 8.3 Hz); and the reverse irradiation simplified, as expected, the doublet at δ 5.70 ($J_{1,9}$ = 6.3 Hz) into a singlet.

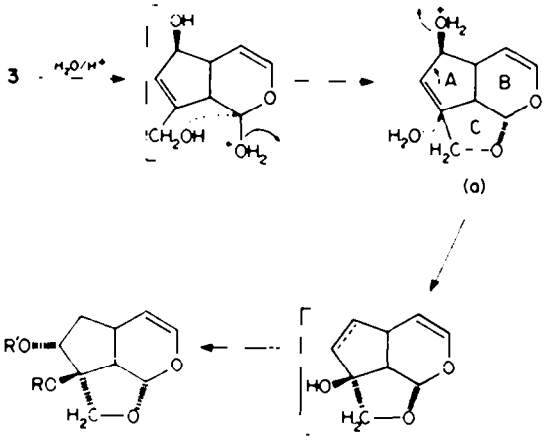
The complex multiplet between δ 2.2 and 1.5 is the AB part (2H-6 geminal protons) of an unsymmetrical four-spin ABXY system[9] where X = H-5 (very broad signal at δ 3.45¶), Y = H-7 (double doublet at δ 5.11) and J_{XY} = 0. The analysis of the AB part (16 lines‖) was simplified by

the two distinct irradiations at δ 5.11 and 3.45 that simplified, as expected, the multiplet structure in two octets with different sets of coupling constants. The octet (AB part of the simpler three-spin ABX system) obtained by irradiating the Y part (H-7) showed the residual coupling constants $J_{AB} = J_{6'6'} = -13.7$ Hz, $J_{AX} = J_{5,6'} = 6.0$ Hz and $J_{BX} = J_{5,6'} = 3.3$ Hz. The irradiation of the X part (H-5) gave rise to the other octet (AB part of the three-spin ABY system) with the coupling constants: $J_{AB} - J_{6'6'} = -13.7$ Hz, $J_{AY} = J_{6,7} = 8.7$ Hz and $J_{BY} - J_{6',7} = 3.5$ Hz. The existence of this ABXY system enabled us to exclude for **6** the alternative structure with the reverse sequence 2H-7 and H-6. In this case the methylene protons should appear as a multiplet of only 8 lines (now AB part of a simple ABX system) while the X part would be more complex, owing to additional coupling with H-5 and its irradiation should simplify the 8 lines multiplet into a double doublet (simple AB system).

The single and decoupled PMR spectra (Table 1)† of the mono and bis-*O*-acetylderivatives (**7** and **8** respectively), besides confirming the previous analysis, allowed the tertiary OH function at C-8 to be located, according to the deshielding that the adjacent 2H-10 (AB system) and H-9 undergo in **8**.

Owing to the fast intramolecular reaction **3**→**6** and to the lack of observable intermediates, the whole reaction may be considered as a concerted mechanism (Scheme 1).

The closure of the acetalic ring C in (a) is possible only from the α-side although it occurs with a certain strain. The stabilization of the new ring occurs through the β-hydration of the allylic carbocation at C-8 and the regioselective and stereospecific hydration of the double bond of the hypothetical intermediate (b). The regioselectivity may be related to the higher nucleophilicity of the C-6 which is due to the prevalence of the inductive effect of the enol-ether system while the high stereospecificity (the epimeric alcohol at C-7 is absent) may be explained by taking into account the fact that the β orientation of the neighbouring C-8 induces preferentially the α-solvation of the incipient carbocation at C-7. Chemical support for the regioselectivity of the final hydration was obtained by repeating the transformation **3**→**6** with 2N DCl in D_2O which afforded the monodeuteroderivative **9**, showing the same chromatographic behaviour of **6**. The comparison of the PMR spectrum of **9** with that of **6** (Table 1) confirmed that the deuterium atom (nearly 95% isotopic purity was obtained) was linked to C-6. In fact the complex multiplet of **6** between δ 2.2 and 1.5 (2H-6, AB part of the ABXY system) is reduced in **9** to a broad singlet with fine structure (~1 H integral value in the mentioned region) centred at δ 2.04. The disappearance of the high-field part of the multiplet identified the residual proton as the H-6' (B proton); and the double doublet at δ 5.11 of the H-7 proton of **6** (Y part of the ABXY system) became in **9** a broad singlet with fine structure.



Scheme 1.

Concerning the absolute configuration of the five asymmetric centres (C-1, C-5, C-7, C-8 and C-9) of **6**, that of C-5 and C-9 must be identical with that of the corresponding centres of **3** (and therefore of **2**) as these centres are not involved in the transformation **3**→**6**.

The inversion of configuration of the C-1 centre is supported by the comparison of the highly negative $[M]_D$ value (-351°) of **4** with that highly positive (+289°) of **6**, in good agreement with the $[M]_D$ variations observed in the comparison of α and β forms of glucose[10] and of iridoid C-1 derivatives.[11]

The α-configuration at C-1 involves necessarily, as previously discussed, the α-orientation of the CH_2-8.

The absolute configuration of C-7 has been established by selective esterification of the secondary OH of **6** with racemic α-phenylbutyric anhydride (Horeau's method). The dextrorotatory *S*-α-phenylbutyric acid obtained (optical yield 30%) indicates a *R*-configuration for the C-7 centre and consequently an α-orientation for the OH-7.

The anomalous deshielding of H-7 could be ascribed to the stereospecific effect of the "axial" OH-8, eclipsing the cis "axial" H-7 owing to the higher rigidity given to the cyclopentane ring of **6** (Dreiding models) by the closure of the tetrahydrofuran system. An analogous effect is observed on methyl protons of rigid cyclohexane derivatives, which are deshielded by an adjacent eclipsing hydroxyl group.[12]

The β-orientation of the H-7 and the well known relation ($J_{cis} > J_{trans}$) existing between the coupling constants of cyclopentane derivatives,[13] enabled us to assign a β-configuration to the H-6 ($J_{6,7} = 8.7$ Hz) and an α-configuration to the H-6' ($J_{6',7} = 3.5$ Hz). It is interesting to note that the mentioned relation is verified in **6** also for the couplings of H-5 with H-6 and H-6',‡ being $J_{5,6'} = J_{5,6} = 6.0$ Hz and $J_{5,6'} = J_{trans} = 3.3$ Hz.

The disappearance in the PMR spectrum of the monodeuteroderivative **9** of the lines of resonance relative to the proton at higher field (H-6) is in accordance with an high stereospecificity of attack of deuterium atom from the convex side of **3**.

The rather easy isolation of aucubigenin from **2**, besides the satisfactory yields (33%) of the transformation **3**→**6**, indicate that the aglycone of aucubin is not so unstable as it was supposed.

†In $CDCl_3$ (Table 1) the H-3 and H-4 of **7** are accidentally equivalent (one singlet) while in **8** the same protons give rise to two different double doublets, being however the H-4 more deshielded ($\Delta\delta = 0.24$) than H-3. In C_6D_6 on the contrary the H-3 and H-4 are always not equivalent and the H-4 appears to lower field than H-3 either in **7** or, particularly, in **8**. Different solvent effects are showed by the comparison of the spectra of **7** and **8** in both $CDCl_3$ and C_6D_6.

‡As pointed out in a previous paper,[9a] the value of the coupling constant $J_{5,6}$ in iridoid compounds having at C-6 only one proton geminal with an OH group was found to be practically identical for either cis or trans relation, probably owing to the preferential "equatorial" orientation assumed for the 6-OH group.

EXPERIMENTAL

Silica gel (Merck, 140–230 mesh) used for column chromatography was washed several times with hot water then dried and activated at 120° for 12 h. Silica gel F_{254} (Merck) and cellulose F (Merck) plates were used in TLC. Cellulose plates were eluted with BuOH–MeOH–H_2O (7:1:3) while R_f values were determined on paper chromatograms (Schleicher and Schüll Nr 2043b Mgl) eluted with BuOH–AcOH–H_2O (63:10:27). Visualization of spots was achieved by spraying either with 2N H_2SO_4 and heating for 2–3 min at 100° (silica gel plates) or with a 0.7% soln of vanillin in 2% methanolic HCl and heating for 2–3 min at 100° (cellulose plates and paper chromatograms). M.ps were determined on a Kofler block and are uncorrected. IR spectra were recorded on a Perkin Elmer 257 and UV spectra on a Perkin Elmer 137 spectrophotometers. Optical rotations were measured on a Galileo instrument. PMR spectra were registered with a Perkin Elmer R-32 (90 MHz) instrument, using TMS as internal reference for the spectra run in $CDCl_3$ while for those in D_2O the HDO signal (δ 4.70 from TMS) was taken as internal reference and the TMS signal as external reference. Spin decoupling experiments were performed with the spin decoupler accessory of the Perkin Elmer R-32 instrument using frequency sweep mode. Chemical shifts are expressed in δ (ppm downfield from TMS) and J are quoted in Hz. Mass spectra were determined at 70 eV and 135° on a AEI MS-12 instrument using a direct inlet system.

Aucubigenin **3**. **2** (100 mg), treated with β-glucosidase (Fluka AG) (50 mg) in H_2O (3 ml) for 2.5 h at 25°, was transformed into the less-polar compound **3** (R_f: 2 0.31; 3 0.69). When **2** had reacted completely, the mixture was extracted with EtOAc (10 ml × 8). The collected extracts, evaporated *in vacuo* at room temp., gave a residue (35 mg) which chromatographed on silica gel (7 g) eluting with EtOAc–MeOH (9:1) afforded pure **3** (28 mg) as colourless oil.

Tri-O-acetylaucubigenin **4**. **3** (50 mg) was treated with anhydrous pyridine (0.5 ml) and Ac_2O (1.0 ml) for 1 h at room temp. After addition of MeOH (3 ml) the soln was left for 20 min, then evaporated *in vacuo* to give crude **4** (60 mg) which chromatographed on silica gel (6 g) in benzene–ether (8:2) gave pure **4** (40 mg) as colourless oil. $[\alpha]_D^{25}$ 191° ($CHCl_3$, *c*, 1.3). IR ($CHCl_3$): 1740, 1670, 1610, 1380, 1240, 1130, 1100, 1020, 980 cm^{-1}. (Found: C, 57.91; H, 5.91. Calc. for $C_{15}H_{18}O_7$: C, 58.06; H, 5.85%).

1,10 - anhydro - 6 - deoxy - 7,8 - dihydro - 7,8 - dihydroxyaucubigenin **6**. An extensive study of the effects of reaction time, temp and acid concentration on the progress of the transformation **3** → **6** was carried out. The following procedure represents the optimal conditions found, different conditions giving major amounts of degradation products. **3** (100 mg) was treated with 2N HCl (3 ml) at 5° for 15 min, checking the reaction on TLC in EtOAc–MeOH (9:1). The soln was then extracted with EtOAc (10 ml × 6); the collected extracts, evaporated *in vacuo* at room temp, gave a residue (40 mg) which chromatographed on silica gel in EtOAc–MeOH (97:3) afforded pure **6** (33 mg) that was crystallized from acetone-hexane (1:9), m.p. 139–141° (dec). $[\alpha]_D^{25}$ + 162° (MeOH, *c*, 0.45). UV (MeOH): λ_{max} 204 nm (3.4). (Found: C, 58.54; H, 6.60. Calc. for $C_9H_{12}O_4$: C, 58.69; H, 6.57%). MS *m/e* (%): 184 (M^+, 0.7), 155 (8.9), 154 (25.9), 153 (15.6), 136 (11.1), 126 (9.6), 111 (10.4), 110 (100.0), 109 (10.4), 108 (11.1), 107 (12.6), 96 (10.4), 95 (29.6), 94 (21.5), 91 (9.6), 83 (11.9), 82 (80.0), 81 (30.4).

Mono-O-acetylderivative **7**. **6** (50 mg) was treated with anhydrous pyridine (0.2 ml) and Ac_2O (0.4 ml) for 1 h at room temp. The mixture, worked up as previously described, afforded an amorphous residue (60 mg) which chromatographed on silica gel in EtOAc afforded pure **7** (45 mg) as colourless oil. IR ($CHCl_3$): 3590, 3410, 1740, 1605, 1360, 1260, 1150, 1125, 1105, 1070, 1030, 1010, 980, 940 cm^{-1}.

Bis-O-acetylderivative **8**. **7** (50 mg), treated with anhydrous pyridine (0.2 ml) and Ac_2O (0.4 ml) for 24 h at 40°, gave after the usual work-up a residue (40 mg) which chromatographed on silica gel in benzene–ether (7:3) afforded pure **8** (35 mg) as colourless oil.

9 (*6-Monodeuteroderivative of* **6**) *by reaction of* DCl *on* **3**. **3** (100 mg) was exchanged with D_2O then treated with 2N DCl in D_2O (3 ml) at 5° for 15 min. The mixture, worked up as described for **6**, gave a residue (45 mg) which chromatographed on silica gel in EtOAc–MeOH (97:3) afforded pure **9** (35 mg) that was crystallized from acetone, m.p. 141–2° (dec) (Found: C, 58.42; H, 7.13. Calc. for $C_9H_{11}DO_4$: C, 58.37; H, 7.07%). MS *m/e* (%): 185 (M^+, 1.1), 156 (2.2), 155 (24.4), 154 (23.3), 137 (12.2), 126 (11.1), 110 (100.0), 109 (12.2), 108 (13.3), 96 (14.4), 95 (22.2), 94 (20.0), 82 (100.0), 81 (25.6).

Determination of the configuration at C-7 of **6** (*Horeau's method*)

6 (18 mg) was treated with racemic α-phenylbutyric anhydride (63 mg) and anhydrous pyridine (104 mg) for 1 h at room temp. After all **6** was reacted (TLC in EtOAc) the soln was diluted with cold ether then, keeping the temp at 0°, it was washed with 2N HCl and extracted twice with cold sat $NaHCO_3$. The collected alkaline extracts were washed with ether, acidified with 2N HCl and extracted twice with ether. This extract, evaporated *in vacuo*, gave α-phenylbutyric acid (18 mg, 100% yield = 17.4 mg). The measured α_D (+0.31°, benzene, *c*, 1.1) corresponds to a 30% optical yield (Calc. for 100% optical purity, α = +1.06°).

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