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PHOTOLYSIS OF MORTONIN†‡

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Abstract—Irradiation of mortonin (**2a**), gave an isomeric photoproduct called photomortonin, whose structure was proved to be **3a**.

Mortonin ($C_{22}H_{26}O_6$) is a natural product isolated from *Mortonia Gregii* (Gray). In a previous study[1] structure **1** was proposed for it mainly based on spectroscopic data of mortonin and some of its derivatives. Recently[2] structure **1** was revised to **2a** taking into account chemical and spectroscopic evidence and biogenetic considerations.

When a methanolic solution of mortonin (1 mg/ml) was irradiated at 300 nm, an isomer, photomortonin ($C_{22}H_{26}O_6$) was obtained in 50% yield. Structure **3a** was assigned to it on the following considerations. Its IR spectrum showed the presence of the secondary benzoate ester (1715, 1600, 1590 cm^{-1}), which was confirmed by the NMR spectrum [aromatic protons as multiplets at 7.45 (3H) and 8.2 ppm (2H) and a doublet centred at 5.12 ppm (1H, J = 6 and 8 Hz) due to the proton attached to C_1 which also supports the benzoate ester]. The IR spectrum of photomortonin showed also bands due to a tertiary hydroxyl group (3570 cm^{-1}) and a saturated γ-lactone function (1790 cm^{-1}). The NMR spectrum of photomortonin, suggested the presence of an isopropylidene moiety: two vinylic methyl groups as doublets at 1.76 (J = 1.5 Hz) and 1.85 ppm (J = 1 Hz), coupled to a vinylic proton, which appeared at 5.25 ppm (m, 1H). The vinylic proton was shown to be also coupled to a signal centred at 5.58 ppm (d, d J = 8.5 and 1 Hz) which was attributed to a proton on a C atom which supports an ethereal oxygen. The proton at the closure of the γ-lactone function appeared as a doublet (J = 1 Hz) centred at 4.52 ppm and was shown, by double resonance experiments, to be coupled to the proton at the ethereal oxygen attachment. A singlet at 1.2 ppm (3H) was attributed to a Me group on a fully substituted C atom; and a singlet at 1.5 ppm (3H) was assigned to the Me group attached to the C atom bearing the tertiary OH function.

The presence of the secondary benzoate group in photomortonin, was demonstrated when the ketone (**4**) was obtained on saponification followed by oxidation with Jones reagent. It showed a band at 1720 cm^{-1} in the IR spectrum, which suggested the formation of a cyclohexanone; the angular Me group in the NMR spectrum was shifted to 1.40 ppm.

The existence of an isopropylidene moiety in photomortonin, was demonstrated in the following manner: Catalytic hydrogenation of photomortonin gave a dihydroproduct (**5**), whose NMR spectrum showed the presence of an isopropyl group (two doublets centred at 1 ppm, J = 6 Hz, 6 H). The proton at the ethereal oxygen attachment is shown as a doublet of triplets centred at 4.9 ppm (J = 0.5 and 7.00 Hz).

Ozonolysis of photomortonin, followed by oxidation with Jones reagent and esterification of the acid so obtained with ethereal diazomethane, gave the ester (**6**), whose NMR spectrum showed the presence of an angular Me group at 1.2 ppm (s, 3H), and the C_4 Me group at 1.5 ppm (s, 3H). The proton at the closure of the saturated γ-lactone function, was responsible for a doublet (J = 1 Hz) at 4.91 ppm, which was shown to be coupled to the signal at 5.32 ppm (d, J = 1 Hz, 1H) due to the H_8 at the ethereal oxygen attachment. The Me of the ester group gave a singlet at 3.79 ppm.

Dehydration of the ester (**6**) gave the anhydroester (**7**) whose NMR spectrum showed the presence of only one Me group, the angular one, at 1.14 ppm. The exocyclic methylene formed in this reaction, was represented by two broad signals at 5.5 and 6.2 ppm (1H each).

The above described data prove the presence of an isopropylidene moiety in photomortonin. They also prove that one of the attachments of the ethereal oxygen is in α position to the closure of the γ-lactone and to the vinylic proton of the isopropylidene chain. We can then establish partial structure **a** for photomortonin.

If we assume that the 1 to 4 relationship between the secondary benzoate group and the C atom which supports the tertiary OH and the Me groups, is maintained in photomortonin as in mortonin, the chemical and spectroscopic evidence presented supports structure **3a** proposed for photomortonin. This means that the irradiation has affected only the tetrahydro oxepin nucleous of mortonin, by excitation of the isolated double bond. We assumed that the benzoate ester acted as an internal or external sensitizer. In order to prove this assumption, the acetate of debenzoyl mortonin (**2b**), was prepared and submitted to the irradiation conditions described for mortonin. Starting material was recovered unchanged. When the irradiation of **2b** was carried out in the presence of methyl benzoate, the expected photoproduct (**3b**) was obtained in 50% yield.§

EXPERIMENTAL

All m.ps were uncorrected. UV spectra were measured in EtOH on a Perkin Elmer 202 Spectrophotometer. IR spectra were recorded with a Perkin Elmer 337 Spectrophotometer. The NMR

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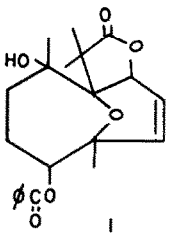
§Photomortonin was also obtained on drastic acid treatment of mortonin. The acetate of photomortonin (**3c**) was obtained when mortonin was treated with tosyl acetate in drastic conditions (Experimental).



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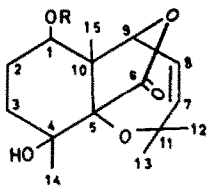

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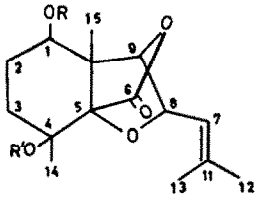
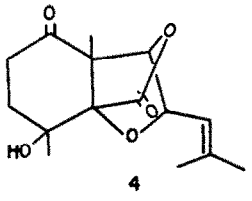
b R = $COCH_3$



3a R = COϕ, R' = H

b R = $COCH_3$, R' = H

c R = COϕ, R' = $COCH_3$



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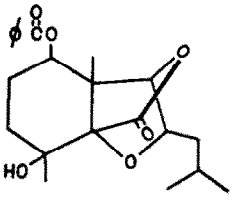

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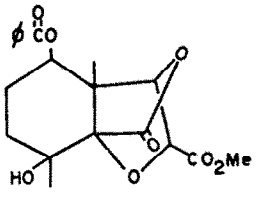

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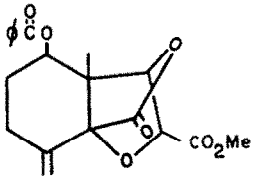

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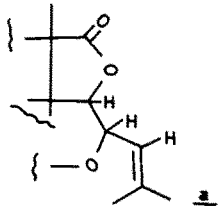

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spectra determined on a Varian A-60A and Varian HA-100 Spectrometers. Chemical Shifts (δ) are given in ppm relative to internal TMS. The experiments of double resonance were taken using a Radio Oscillator Hewlett-Packard 200 AB. The mass spectra were determined on a Hitachi Perkin-Elmer RMU 6D mass spectrometer using direct inlet system.

Isolation of mortonin. Mortonin was isolated from *Mortonia Gregii*, Gray as previously described.[1]

Photolysis of mortonin. A soln of **2a** (1 g) in MeOH (300 ml), was irradiated at 300 nm for 6 hr, under N_2. The solvent was removed under vacuum. The semisolid product obtained from two irradiations (2 g), was chromatographed over silica gel (100 g). Elution with isopropyl ether gave **3a**, (1.2 g), m.p. 130–140°, a mixture of mortonin and photomortonin, and pure **2a** (260 mg). The analytical sample of photomortonin, was prepared by recrystallisation from acetone-isopropyl ether. It showed m.p. 146–148°; ν_{max} 3570, 1790, 1715, 1600, 1590, 900, 865 cm^{-1}; λ_{max} 231 (10000); δ 1.2 (s, 3H, C_{10}–CH_3), 1.5 (s, 3H, C_4–CH_3), 1.76 (d, J = 1.5 Hz, 3H, *trans* C_{11}–CH_3), 1.85 (d, J = 1 Hz, 3H, *cis* C_{11}–CH_3), 4.52 (d, J = 1 Hz, H_9), 5.12 (dd, J = 6 and 8 Hz, 1H), 5.25 (m, 1H, H_7), 5.58 (dd, J = 8.5 and 1 Hz, 1H, H_a), 7.45 and 8.2 (2 m, 5H aromatic). Found: C, 68.65; H, 6.75; O, 24.36. Calc. for $C_{22}H_{26}O_6$: C, 68.38; H, 6.78; O, 24.84%.

The acetate **3b**, was prepared by reaction of photomortonin with Ac_2O in the presence of *p*-toluenesulfonic acid at r.t. The product was crystallised from isopropyl ether-hexane to constant m.p. 135–137°. ν_{max} 1800, 1730, 1725 cm^{-1}; δ: 1.23 (s, 3H, C_{10}–CH_3), 1.80 (br. s, 6H, C_4–CH_3 and *trans* C_{11}–CH_3), 1.88 (d, J = 1 Hz, 3H, *cis* C_{11}–CH_3), 2.02 (s, 3H, $COCH_3$), 4.5 (d, J = 1 Hz, 1H, H_9), 5.25 (m, 2H, H_1 and H_7), 5.65 (dd, J = 8 and 1Hz, 1H, H_a); 7.45 and 8.2 ppm (m, 5H aromatic). Found: C, 67.44; H, 6.43; O, 25.80. Calc. for $C_{24}H_{28}O_7$: C, 67.27; H, 6.59; O, 26.14%.

Dihydrophotomortonin **5**. The photomortonin **3a** (200 mg) in EtOAc (25 ml) was catalytically hydrogenated using 10% Pd/C (30 mg) as catalyst. The analytical sample of **5**, was prepared from acetone-hexane, and showed m.p. 116–116.5°; ν_{max} 3590, 1790, 1720 cm^{-1}; δ: 1.00 (2d, J = 6 Hz, 6H, $C_{11}(CH_3)_2$), 1.2 (s, 3H, C_{10}–CH_3), 1.5 (s, 3H, C_4–CH_3), 4.62 (d, J = 1 Hz, 1H, H_9), 4.9 (dt, J = 0.5 and 7 Hz, 1H, H_a), 5.2 (dd, J = 4 and 9, 1H, H_1), 7.55 and 8.05 (m, 5H aromatic). Found: C, 68.65; H, 6.75; O, 24.36. Calc. for $C_{22}H_{28}O_6$: C, 68.38; H, 6.78; O, 24.84%.

Preparation of ketone **4**. A soln of **3a**, (250 mg) in MeOH (8 ml)

was treated with K_2CO_3 (250 mg) in water (2 ml) at r.t. for 1 hr. The solvent was removed *in vacuo* and water was added. The mixture was extracted with EtOAc, washed with water, dried and evaporated. The amorphous residue obtained (170 mg), which showed the absence of the benzoate group in the IR spectrum, was dissolved in acetone and treated with Jones reagent in an ice bath. The mixture was worked up in the usual manner. **4** was recrystallized from acetone-isopropyl ether to constant m.p. 155–157°; ν_{max} 3580, 1800, 1725; δ 1.4 (s, 3H, C_{10}–CH_3), 1.63 (s, 3H, C_4–CH_3), 1.7 (d, J = 1 Hz, 3H, *cis* C_{11}–CH_3), 1.76 (d, J = 1.5 Hz, 3H, *trans* C_{11}–CH_3), 4.71 (d, J = 1 Hz, 1H, H_9), 4.88 (dd, J = 8 and 1 Hz, 1H, H_8), 5.25 (m, 1H, H_7). Found: C, 64.42; H, 7.15; O, 28.24. Calc. for $C_{15}H_{20}O_5$: C, 68.27; H, 7.19; O, 28.54%.

Ozonolysis of photomortonin. **3a**, (250 mg) in MeOH (30 ml), was ozonised at −70°. The ozonide was catalytically hydrogenated. The oily product obtained, after removal of catalyst and solvent, was dissolved in acetone and treated with Jones' reagent at 5°. The acid product obtained, was treated with ethereal diazomethane. The ester **6**, showed m.p. 186–187° from acetone-isopropyl ether; ν_{max} 3580, 1800, 1760, 1740, 1715, 1600, 1590 cm^{-1}; δ 1.22 (s, 3H, C_{10}–CH_3), 1.52 (s, 3H, C_4–CH_3), 2.7 (m, 1H disappeared with D_2O, OH), 3.75 (s, 3H, CO_2Me), 4.95 (d, J = 1 Hz, 1H, H_9), 5.1 (m, 1H, H_1), 5.35 (d, J = 1 Hz, 1H, H_8), 7.30 and 8.2 ppm (m, 5H, aromatic). Found: C, 61.64; H, 5.59; O, 32.45. Calc. for $C_{20}H_{22}O_8$: C, 61.53; H, 5.68; O, 32.79%.

Anhydro ester **7**. **6**, (80 mg) in anhyd pyridine (5 ml), was treated with $SOCl_2$ (1 ml), at 5°, for 1.5 hr. The mixture was poured onto ice and extracted with EtOAc. The organic soln washed with dil HCl, sat $NaHCO_3$aq and water, dried and evaporated. The residue, in benzene, was passed through alumina, and crystallized to constant m.p. 182–183° from acetone-isopropyl ether; ν_{max} 1805, 1760, 1740, 1710, 1600 cm^{-1}; δ:1.1 (s, 3H, C_{10}–CH_3), 3.8 (s, 3H, CO_2Me), 4.98 (d, J = 1 Hz, 1H, H_9), 5.22 (dd, J = 6 and 10.5 Hz, 1H, H_1), 5.5 (d, J = 1 Hz, 1H, H_8), 5.5 and 6.2 (t, J = 1.5 Hz, 1H each, C_4=CH_2), 7.6 and 8.1 ppm (m, 5H aromatic). Found: C, 64.82; H, 5.44; O, 29.99. Calc. for $C_{20}H_{20}O_7$: C, 64.51; H, 5.41; O, 30.08%.

Acetate of debenzoyl mortonin. **2a**, (1 g) in MeOH (50 ml), was treated with K_2CO_3 (1 g) in water (2 ml), for 3 hr at r.t. The debenzoyl mortonin obtained, (500 mg), was treated with Ac_2O (2.5 ml) and pyridine (2.5 ml) overnight at r.t., poured onto ice and extracted with EtOAc. The organic soln was washed with dil HCl, $NaHCO_3$ aq and water, dried and evaporated. The solid, **2b**, obtained was crystallized from acetone-hexane. The analytical sample showed m.p. 168–170°; ν_{max} 3600, 1775, 1725 cm^{-1}; δ:1.35 (s, 3H, C_{10}–CH_3), 1.42 (s, 3H, C_{11}–CH_3), 1.48 (s, 6H, C_{11}–CH_3 and C_4–CH_3), 2.02 (s, 3H, –$OCOCH_3$), 2.8 (br. s, 1H, disappeared with D_2O, OH), 4.58 (dd, J = 1 and 7 Hz, 1H, H_9), 5.5 (m, 1H, H_1), 5.67 (dd, J = 7 and 11.5 Hz, 1H, H_8), 6.1 ppm (dd, J = 1 and 11.5 Hz, 1H, H_7). Found: C, 63.15; H, 7.39; O, 29.47. Calc. for $C_{17}H_{24}O_6$, C, 62.95; H, 7.46; O, 29.60%.

Photolysis of the acetate of debenzoyl mortonin. **2b**, (340 mg) in MeOH (300 ml), was irradiated at 300 nm under N_2 for 6 hr. Starting material was recovered unchanged, as shown by spectroscopic data and m.m.p. determination.

The recovered compound (250 mg) in MeOH (300 ml), was irradiated at 300 nm in the presence of methyl benzoate (300 mg). The convertion was followed by TLC. After 6 hr of irradiation, it showed the presence of a photoproduct. The solvent was removed under vacuum. The mixture obtained was chromatographed over silica gel (25 g), using isopropyl ether as eluent. The photoproduct **3b**, could be isolated in this way in 50% yield. The analytical sample was prepared from acetone-hexane and showed m.p. 143–145°; ν_{max} 3580, 1790, 1730, 1665, 900, 870 cm^{-1}; δ:1.12 (s, 3H, C_{10}–CH_3), 1.47 (s, 3H, C_4–CH_3), 1.78 (br. s, 3H, C_{11}–CH_3), 1.81 (br. s, 3H, C_{11}–CH_3), 2.08 (s, 3H, $OCOCH_3$), 4.46 (br. s, 1H, H_9), 4.9 (m, 1H, H_1), 5.1 (m, 1H, H_7), 5.5 ppm (br. d, J = 8 Hz, 1H, H_8). Found: C, 62.83; H, 7.46; O, 30.05. Calc. for $C_{17}H_{24}O_6$: C, 62.95; H, 7.46; O, 29.60%.

Treatment of mortonin with tosyl acetate. Mortonin (200 mg) in acetonitrile (25 ml) was treated with freshly prepared tosyl acetate for 1 hr at r.t., and 2 hr under reflux. The mixture was poured onto ice, extracted with EtOAc, washed with sat $NaHCO_3$ aq and water, dried and the solvent removed under vacuum. The black oily product obtained, was chromatographed on SiO_2. Elution with benzene-EtOAc 5:1, gave an oily material which was purified by TLC. The solid product obtained (50 mg) was identified as photomortonin acetate.

Acid treatment of mortonin. A soln of mortonin (100 mg) in acetonitrile (5 ml), was treated with *p*-toluene sulphonic acid (25 mg), under reflux. Mortonin was totally recovered under these conditions. Mortonin (100 mg) in acetonitrile (5 ml) was treated with *p*-toluene sulphonic acid (200 mg) under reflux for 3 hr. The soln was poured into water, extracted with EtOAc, washed with $NaHCO_3$ aq and water, dried and evaporated. The crude product obtained, showed by TLC, to be a mixture of mortonin and photomortonin. Photomortonin **3a**, (50 mg), m.p. 146–148°, was obtained by fractional crystallization of the mixture from acetone-isopropyl ether.

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