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PHOTOCHEMICAL REARRANGEMENT OF MORTONIN C

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Abstract—Irradiation of Mortonin C (**1a**) produced the photoproducts **4a** and **8a** as a result of a photochemically induced ring contraction of the tetrahydro-oxepine nucleus. The structure and stereochemistry of **4a** and **8a** were proved by chemical degradation and spectroscopic analysis.

Mortonin C (**1a**) is a natural product isolated from several species of *Mortonia* genus (Celastraceae family). The structure and stereochemistry proposed[1] for it has been recently confirmed by X-ray crystallographic analysis.[2]

Mortonin C (**1a**), as mortonins A **2a**[3] and B **2b**[1], contains a tetrahydro-oxepine nucleus in its structure. The photochemical behavior of mortonin A was recently studied.[4] It led to the isolation of the tetrahydrofurane derivative **3**. Formation of **3** could be envisaged as a photochemically induced ring contraction produced by a concerted 1,3-sigmatropic shift, or by the formation of a biradical species as a result of a vinylogous β cleavage.[5] This photoreaction was proved to proceed through sensitation produced by the benzoate ester group present in the starting material.

We decided to study the photochemical behaviour of mortonin C, **1a**, in order to see if the ring contraction of the tetrahydro-oxepine nucleus observed in the photolysis of mortonin A, **2a**, is a general reaction.

Irradiation of a methanolic solution of mortonin C, **1a**, at 300 nm for 8 hr, gave a mixture of two major photoproducts and recovered starting material. The photoproducts were purified by chromatography of their methyl esters.

Photomortonin C methyl ester was obtained in 42% yield (of transformed product). Structure **4b** was assigned to it on the following considerations. Its IR spectrum showed the presence of an OH group (3520 cm^{-1}) and a CO band at 1725 cm^{-1} ascribed to the methyl ester group at C-5 and the C-1 and C-9 benzoate esters. The proton NMR spectrum (Table 1) showed the aromatic protons as multiplets between 7.5 and 8.0 ppm (10 H); a doublet of doublets at 6.12 (J = 6 and 10 Hz, 1H) could be assigned to H-1 by comparison with the proton NMR spectrum of mortonin C methyl ester **1b**. A doublet (J = 3.5 Hz, 1H) observed at 5.37 was attributed to H-9, and a complex signal centered at 5.10 (2H) was assigned to H-8 and H-7. The methyl ester is responsible for a singlet (3H) which appeared at 3.78, and a broad signal at 3.15 (1H) which disappeared on D_2O addition was assigned to the C-4 OH group. Two singlets at 1.75 and 1.65 (3H each) were attributed to the isopropylidene Me groups; the C-4 Me group and the C-10 angular Me group are responsible for two singlets (3H each) which appeared at 1.45 and 1.25 respectively.

Catalytic reduction of **4b** gave a dihydro derivative **5** whose proton NMR spectrum showed H-9 as a doublet (J = 3.5 Hz) at 5.36, and H-8 as a multiplet centered at 4.41. The isopropyl Me groups are shown as two doublets (J = 6 Hz) at 0.93 and 0.90 ppm.

Ozonolysis of **4b** gave the lactol **6**. Its proton NMR spectrum showed H-9 as a doublet (J = 7.5 Hz, 1H) at 5.38; a singlet (1H) observed at 4.96 was attributed to H-7, and a doublet (J = 7.5 Hz, 1H) at 4.58 to H-8. In the Me region there are observed two singlets at 1.48 and 1.28 (3H each) which could be assigned to C-4 and C-10 Me groups.

Oxidation of the lactol **6** with Jones' reagent, gave the δ-lactone ester **7**. Its IR spectrum showed the absence of OH absorption, a CO band at 1765 which could be attributed to a strained δ-lactone, and the benzoate absorption at 1730, 1605 and 1595 cm^{-1}. In the proton NMR spectrum **7** showed a doublet (J = 7.5 Hz) at 5.45 attributed to H-9 superimposed on the H-1 signal (2H); a doublet at 5.00 (J = 7.5 Hz, 1H) was assigned to H-8.

The second photoproduct isolated was proved to be the C-8 epimer of photomortonin C, **8a**. Its methyl ester was obtained as a crystalline product with m.p. 137–138° in 35% yield (of transformed material) after chromatography. The IR spectrum was very similar to that of **4b** differing only in the fingerprint region. The proton NMR spectrum showed H-1 as a typical doublet of doublets (J = 5 and 10 Hz, 1H) at 5.87, a complex signal observed at 5.25 (3H) was assigned to H-9, H-8 and H-7; two pairs of doublets (J = 1 Hz) at 1.70 and 1.65 (3H each) were ascribed to the isopropylidene Me groups; the C-4 and C-10 Me groups were observed as singlets (3H each) at 1.50 and 1.35 ppm respectively.

Catalytic hydrogenation of **8b** gave the dihydro-derivative **9** whose proton NMR spectrum showed distinctly H-9 as a doublet (J = 7 Hz) at 5.22; a multiplet (1H) observed at 4.40 was ascribed to H-8. The C-11 *gem* dimethyl group was responsible for a pair of doublets (J = 6 Hz, 3H each) at 0.92 and 0.95 ppm.

Ozonolysis of **8b** gave the aldehyde **10** which showed in the proton NMR spectrum the aldehyde proton at 9.95 (s, 1H); H-9 and H-8 were observed as doublets (J = 6 Hz) at 5.55 and 4.35 respectively. In the methyl region there were observed only two singlets (3H each) at 1.42 and 1.40 ascribed to C-4 and C-10 Me groups.

Oxydation of **10** with Jones' reagent gave the acid **11a** which was immediately esterified with ethereal diazomethane solution to give the diester **11b**. Its IR spectrum showed OH band at 3500 and a strong CO absorption at 1725 cm^{-1}. In the proton NMR spectrum H-9 and H-8 were observed as doublets (J = 6 Hz, 1H each) at 5.82 and 4.80; the two methyl esters are responsible for two singlets (3H each) at 3.80 and 3.75, and the C-4 and C-10

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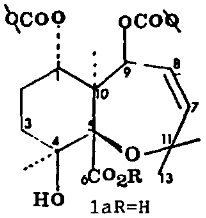
Table 1. ^{1}H NMR chemical shifts of photoproducts and their derivatives

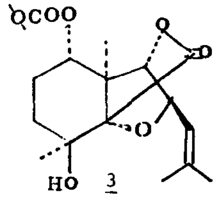
	H_1	H_9	H_8	H_7	C_{11} (Me)$_2$	C_4 (Me) C_{10} (Me)	C_5-CO_2Me	Others *
3	5.12 dd (6,8)	4.52 d (1)	5.58 dd (1,8.5)	5.25 m	1.76 d (1.5) 1.85 d (1)	1.5 s 1.2 s		
4b	6.12 dd (6,10)	5.37 d (3.5)	5.10 m	5.10 m	1.75 s 1.65 s	1.45 s 1.25 s	3.78 s	3.15 (OH)
8b	5.87 dd (5,10)	5.25 m	5.25 m	5.25 m	1.70 d (1) 1.65 d (1)	1.50 s 1.35 s	3.80 s	2.60 (OH)
5	6.16 dd (6,10)	5.36 d (3.5)	4.40 m		0.94 d (6) 0.92 d (6)	1.42 s 1.22 s	3.78 s	2.90 (OH)
9	5.75 dd (5,10)	5.22 d (7)	4.40 m		0.92 d (6) 0.95 d (6)	1.50 s 1.35 s	3.80 s	2.65 (OH)
6	5.56 m	5.38 d (7.5)	4.58 d (7.5)	4.96 brs	- - - -	1.48 s 1.28 s	3.86 s	2.80 (2OH)
7	5.46 m	5.45 d (7.5)	5.00 d (7.5)	- - - -	- - - -	1.54 s 1.32 s	3.88 s	- - - -
10	5.60 m	5.55 d (6)	4.60 d (6)	9.95 s	- - - -	1.42 s 1.40 s	3.80 s	
11b	5.60 dd (5,10)	5.82 d (6)	4.80 d (6)	- - - -	- - - -	1.55 d 1.45 s	3.80 s	2.65 (OH) 3.75 s (3H, C_8-CO_2

The coupling constants in Hz are in parentheses.

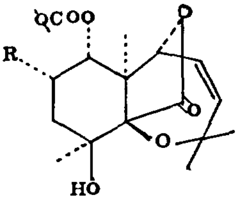
* All the compounds, except 3, showed ten aromatic protons as multiplets between 7.5 and 8.0 ppm. Compound 3 showed five aromatic protons.



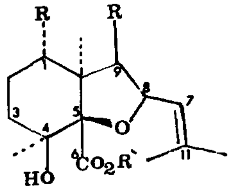
1aR=H
bR=Me



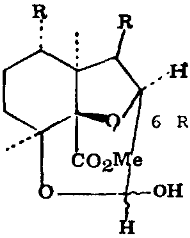
3



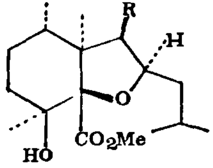
2aR=H
bR=OAc



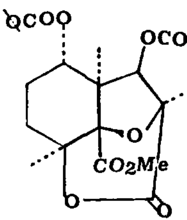
4aR=OCOØ, R'=H
bR=OCOØ, R'=Me



6 R=OCOØ



5 R=OCOØ



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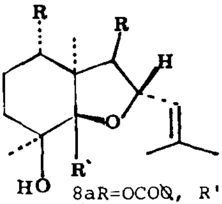
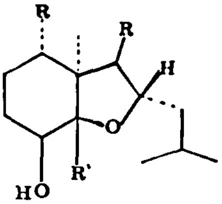
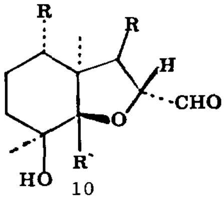


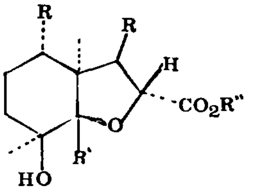
8aR=OCOΦ, R'=CO$_2$H
bR=OCOΦ, R'=CO$_2$Me



9
R=OCOΦ
R'=CO$_2$Me



10
R=OCOΦ
R'=CO$_2$Me



11 aR=OCOΦ, R'=CO$_2$Me, R''H
bR=OCOΦ, R'=CO$_2$Me, R''=Me

quaternary Me groups were observed as singlets (3H each) at 1.55 and 1.45 ppm.

The series of reactions described for the methyl esters of photomortonin C and *epi*-photomortonin C proved the structures **4b** and **8b** proposed for them.

The different coupling constants found for H-9 in both photoproducts suggested an α or β orientation of the isopropylidene chain attached at C-8, however it is not possible[6] to ascribe the right stereochemistry to C-8 based on the J values found for H-9. The β orientation assigned to the isopropylidene group in photomortonin C, **4a**, was based mainly on the formation of the lactol **6** and the δ-lactone-**7** on exhaustive oxidation, this intramolecular cyclization is only possible when the aldehyde formed by ozonolysis has the same orientation as the OH group at C-4 which has been found to be β in mortonin C.[1,2]

Epi-photomortonin C, **8a**, was also obtained when a chloroform solution of mortonin C was treated with silica gel at 40° for five days.

EXPERIMENTAL

Mps are uncorrected. IR spectra were recorded in CHCl$_3$ unless otherwise stated. ^{1}H NMR spectra were recorded in CDCl$_3$ using TMS as int. standard, chemical shifts are given in δ.

Isolation of mortonin C. Mortonin C, **1a**, was isolated from the leaves of *M. hidalgensis* as previously described.[7]

Photolysis of Mortonin C. A soln of **1a** (500 mg) in dry MeOH (300 ml) was irradiated at 300 nm in an Argon atm at 20–30°. The reaction was followed by TLC. After 9 hr the solvent was removed under vacuum. The product obtained from six irradiations (3 g) was chromatographed over silica gel (300 g). Elution with acetone-CHCl$_3$ (10%) gave unchanged mortonin C (1.837 g) and a mixture of photoproducts (900 mg). The mixture of photoproducts in ethyl ether was treated with ethereal diazomethane soln. The mixture of methyl esters of the photoproducts was chromatographed on SiO$_2$. Elution with AcOEt-hexane (1 : 3) gave **46** (380 mg) as an oilly product $[\alpha]_D^{20} = +40.27$ (*c*, 0.221 CHCl$_3$); ν_{max} 3540(OH), 1735 and 1710 (esters CO's), 1605 and 1585 (aromatic double bonds). MS, *m/z*: 463.3(0.4)(M$^+$-59), 421(1); 400(M$^+$-122, 0.4); 300(1); 278(0.3); 202(9.5); 195(8); 105(100); $C_{30}H_{34}O_8$ requires [M$^+$] at *m/z* 522.

Further elution with the same mixture of solvents gave **8b** (310 mg), m.p. 137–138°; $[\alpha]_D^{25} = +35.90$ (*c*0.153, CHCl$_3$); ν_{max} 3520(OH), 1735, 1725 and 1700 (esters CO's), 1605 and 1585 (aromatic double bonds). MS, *m/z*: 463.5(0.3), 421(0.1), 400(M$^+$-122, 2), 278(0.1), 202(10.1), 195(12.5), 105(100); $C_{30}H_{34}O_8$ requires [M$^+$] at *m/z* 522.

Catalytic hydrogenation of photomortonin C methyl ester **4b** *and epiphotomortonin C methyl ester* **8b**. The photoproduct **4b** (80 mg) in AcOEt (10 ml) was catalytically hydrogenated using 10%Pd/C as catalyst. The oilly product obtained **5** showed ν_{max} 3540(OH), 1725 (esters CO's), 1605 and 1585 (aromatic double bonds). MS, *m/z*: 524.4 (M$^+$, 0.3), 402 (M$^+$-122, 0.5), 280 (M$^+$-244, 0.4), 223.3 (30.4), 197 (0.5), 105 (100), $C_{30}H_{36}O_8$ requires [M$^+$] at *m/z* 524.

Catalytic hydrogenation of **8b** gave the dihydro-derivative **9** m.p. 95–97°. ν_{max} 3450 (OH), 1725 (CO's), 1605 and 1585 (aromatic double bonds). MS, *m/z*: 524 (M$^+$, 0.2), 465.5 (M$^+$-59, 1.4), 446 (1.2), 402 (M$^+$-122, 2.5), 280 (0.3, 223.3 (44.4), 105 (100); $C_{30}H_{36}O_8$ requires [M$^+$] at *m/z* 524.

Oxidation of photomortononin C methyl ester. **4b** (80 mg) in AcOEt (50 ml) was ozonized at −70°. The ozonide was catalytically hydrogenated. Lactol **6** was obtained as an oilly product. ν_{max} 3500 (OH), 1725 (CO's), 1605 and 1585 (aromatic double bonds).

The lactol **6** without purification, in acetone (5 ml) was treated with Jones' reagent at 5°. The lactone **7** obtained (46 mg) showed m.p. 126–128°. ν_{max} 1765 (strained δ lactone CO), 1735 (esters CO's), 1605 and 1585 (aromatic double bonds). MS, *m/z*: 466 (M$^+$-28, 0.2), 419 (0.2), 345 (466-121, 0.2), 328 (466-122-16, 1.5), 223 (345-122, 0.5), 165 (15), 105 (100); $C_{27}H_{26}O_9$ requires [M$^+$] at *m/z* 494.

Oxidation of epiphotomortonin C methyl ester **8b**. Ozonolysis of **8b** (50 mg) in AcOEt (50 ml) at −70°, followed by catalytic hydrogenation of the ozonide, gave the aldehyde **10**, m.p. 91–93°. ν_{max} 3450 (OH), 1725 (CO's), 1605 and 1585 (aromatic double bonds), MS, *m/z*: 374 (M$^+$-122, 0.9), 274 (2.0), 252 (M$^+$ − 244, 1.4), 242 (5.7), 195 (4.0), 170 (8.6), 169 (28.7), 137 (17.3), 105 (100); $C_{27}H_{28}O_9$ requires [M$^+$] at *m/z* 496.

Oxidation of **10** in acetone with Jones' reagent at 5°, gave the acid **11a** which was treated with ethereal diazo-methane soln to yield the diester **11b**, m.p. 177–178°; ν_{max} 3500 (OH), 1730 and 1720 (esters

CO's), 1605 and 1585 (aromatic double bonds). MS, *m/z*: 467 (M^+-59, 1.6), 449 (0.1), 404 (M^+-122, 2), 345 (1.8), 285 (0.5), 282 (M^+-244, 0.1), 223 (24.1), 105 (100); $C_{28}H_{30}O_{10}$ requires [M^+] at *m/z* 526.

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