

Reactions of olefinic ester derivatives of aleuritic acid with iodonium nitrate

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Methyl *threo*-16-acetoxy-9(10)-iodo-10(9)-nitratohexadecanoate (VII) and methyl *threo*-16-acetoxy-9(10)-iodo-10(9)-hydroxyhexadecanoate (VIII) have been prepared by reacting methyl 16-acetoxyhexadec-*cis*-9-enoate (VI) which in turn has been prepared from *threo*-aleuritic acid (I) with iodonium nitrate (generated *in situ*).

Organic nitrates¹ are well known for their industrial and pharmaceutical uses. These simple derivatives are prepared by *trans*-stereospecific electrophilic addition of the pseudohalogen, iodonium nitrate (INO₃, generated *in situ*) to olefinic compounds² at room temperature. *threo*-Compounds^{2c} are formed when the addition takes place to *cis*-double bond. These types of compounds have also been prepared from longchain fatty acid systems, like olefinic esters³ and acetylenic esters⁴. We report in this note the preparation of organic nitrates from the olefinic ester derivative of aleuritic acid^{5a,b} which is used as a good starting material for the syntheses of perfumery chemicals⁶ and various bioactive compounds^{5b,7}.

Methyl 16-acetoxyhexadec-*cis*-9-enoate (VI) was treated with INO₃ to get the addition products of methyl *threo*-16-acetoxy-9(10)-iodo-10(9)-nitratohexadecanoate (VII) and methyl *threo*-16-acetoxy-9(10)-iodo-10(9)-hydroxyhexadecanoate (VIII). Compound (VI) was prepared from *threo*-aleuritic acid (I) by simple steps as reported earlier⁸. Pyrolysis of I with ethyl orthoformate (TOF/BzOH) gave 16-hydroxyhexadec-*trans*-9-enoic acid (II)⁹ which was *trans*-hydroxylated with H₂O₂/HCOOH to get (9 *RS*, 10 *SR*)-9, 10, 16-trihydroxyhexadecanoic acid (I-II, *erythro*-aleuritic acid). Compound III on treatment with TOF/BzOH again gave 16-hydroxyhexadec-*cis*-9-enoic acid (IV). It was esterified and acetylated successively with MeOH/H⁺ and Ac₂O-Py (1:1) to get V and VI, respectively. The reaction products VII and VIII obtained from VI were resolved on silica gel column using pet. ether (PE)-ether (E) mixtures. Compound VII exhibited characteristic IR bands at 1250, 875 and 710 for -C-ONO₂ and at 500 cm⁻¹ for (-C-I). Its PMR spectrum showed signals at δ

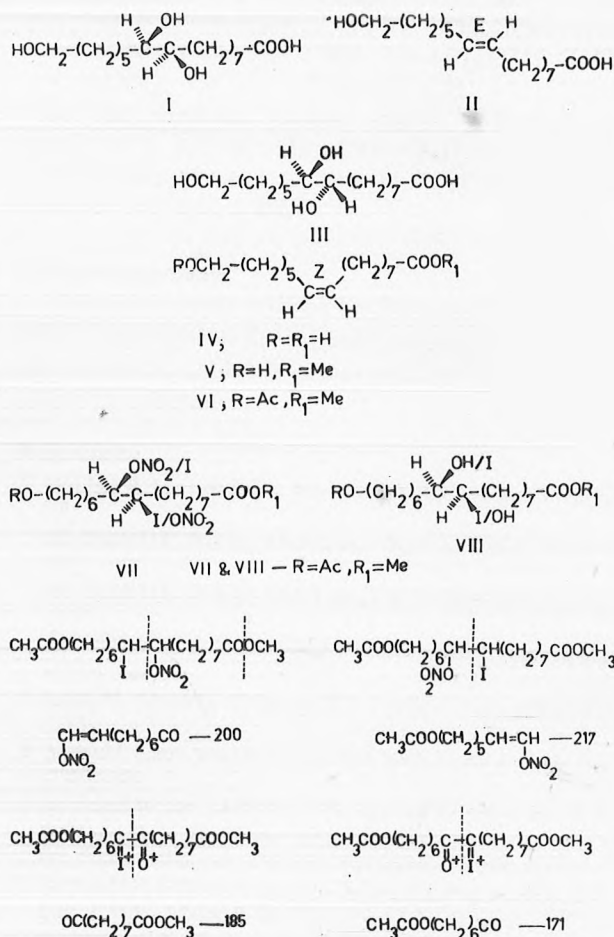


Fig. 1—Mass spectral fragmentations of methyl *threo*-16-acetoxy-9(10)-iodo-10(9)-nitratohexadecanoate (VII)

5.1 and 4.0 as multiplets for the methine protons of -CH-ONO₂ and -CH-I, respectively. The MS fragments at m/z 217, 200, 185 and 171 arising from α-cleavage have been shown with dotted lines in Fig. 1 supporting the structure of VII. The IR spectrum of VIII showed bands at 3400 (-OH), 1110 (CH-OH, 2°OH) and 510 cm⁻¹ (-C-I). The PMR signals at δ 3.8-4.1 [m, 2H, CH(I)-CH(OH)], 3.3 (s, 1H, CH-OH, D₂O exchangeable) and MS fragments also supported the structure of VIII.

Experimental

IR spectra (neat, ν_{max} in cm⁻¹) were recorded on a Perkin-Elmer 577 spectrophotometer, PMR spectra (chemical shifts in δ, ppm) in CDCl₃ on a Perkin-Elmer R-32 (60 MHz) instrument using TMS as internal standard, and mass spectra on a JMS-D 30 test

spectrometer. TLC was performed on glass plates coated¹⁰ with silica gel G using PE (40-60°C)-E-AcOH (80:20:1 v/v) as a solvent system and spots were visualised with iodine vapours. INO_3 was prepared¹¹ from silver nitrate (4.53 g, 30.5 mmole) in dry ether (150 ml) and iodine (10.12 g, 79.6 mmole).

Methyl 16-hydroxyhexadec-cis-9-enoate (V)

16-Hydroxyhexadec-cis-9-enoic acid (IV; 9.3 g, 34.3 mmole) was esterified with MeOH (250 ml) and conc. H_2SO_4 (3 ml) to give the crude methyl ester (V) as a light yellow oil (8.4 g, 87.5%). Purification on a silica gel column using PE-E (85:15 v/v) as eluant gave V as a colourless oil; IR: 3400, 1730 and 720 (cis-double bond); PMR: 5.3-5.5 (t, 2H, olefinic protons), 3.5-3.8 (t, 2H, $-\text{CH}_2\text{OH}$), 2.2-2.5 (t, 2H, CH_2COOMe), 3.67 (s, 3H, $-\text{COOCH}_3$), 1.7-2.1 (m, 4H, $-\text{CH}_2-\text{CH}=\text{CH}-\text{CH}_2-$).

Methyl 16-acetoxylhexadec-cis-9-enoate (VI)

Compound V (8.3 g, 29.2 mmole) was acetylated with Ac_2O -Py (1:1, 42 ml) in a well stoppered flask. The contents were shaken occasionally for 1 hr and kept overnight. After usual workup, the crude acetoxy olefinic ester (8.7 g, 92%) was filtered through a silica gel column with PE-E (97:3, v/v) to furnish VI as colourless thin liquid; IR: 3000, 1740, 1360, 1235, 710; PMR: 5.3-5.5 (t, 2H, olefinic protons), 4.0-4.25 (t, 2H, CH_2OAc), 3.7 (s, 3H, COOCH_3), 2.05 (s, 3H, OOCCH_3).

Methyl threo-16-acetoxy-9(10)-iodo-10(9)-nitroatohexadecanoate (VII)

Compound VI (8.7 g, 26.6 mmole) was taken in a dry 250 ml stoppered flask and freshly prepared iodonium nitrate (INO_3) in dry ether (150 ml) was added to it. The contents were stirred for 22 hr at room temperature and extracted with ether. The organic layer was washed successively with water, sodium thiosulphate solution, sodium bicarbonate (10%) and water and dried (Na_2SO_4). Removal of the solvent *in vacuo* gave a brown viscous syrup (8.5 g) showing two spots on TLC. It was column chromatographed over silica gel and elution with PE-E (93:7 v/v) furnished (VII) as a viscous brown liquid (4.6 g, 54%); IR: 2920, 2840, 1725, 1430, 1360, 1230, 1250, 1280, 875, 750, 710, 500; PMR: 5.1 (m, 1H, $>\text{CH}-\text{ONO}_2$), 4.0 (m, 1H, $>\text{CH}-\text{I}$), 3.95 (t like, $-\text{CH}_2\text{OCOCH}_3$, overlapped with the methine proton signal), 3.55 (s, 3H, COOCH_3), 2.1-2.3 (t, 2H, CH_2COOMe), 1.95 (s, 3H, OOCCH_3), 1.25 [br s, chain $-(\text{CH}_2)_n-$]; MS: m/z 217 (3%), 200(45), 185(68), 174(35), 171(1.6),

157(32), 143(2.0), 128(11.6), 126(9.3), 98(11.6) (Found: C, 44.2; H, 6.7; N, 2.8. $\text{C}_{19}\text{H}_{34}\text{O}_7\text{IN}$ requires C, 44.3; H, 6.6; N, 2.7%).

Further, elution with PE-E (84:16, v/v) gave (VIII) as a viscous yellow liquid (0.6 g, 7.0%); IR: 3400, 1725, 1360, 1110 (2OH), 510; PMR: 3.8-4.1 [m, 2H, $\text{CH}(\text{I})-\text{CH}(\text{OH})$], 4.0 (m, $-\text{CH}_2\text{OCOCH}_3$, overlapped with the methine proton signal), 3.6 (s, 3H, COOCH_3), 3.3 (s, 1H, $\text{CH}-\text{OH}$), 2.2 (t, 2H, CHCOOMe) (Found: C, 48.3; H, 7.5. $\text{C}_{19}\text{H}_{33}\text{O}_5\text{I}$ requires C, 44.5; H, 7.4%).

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