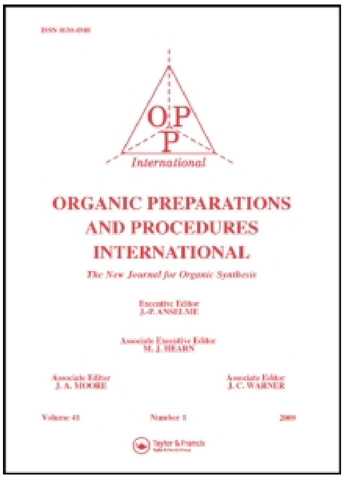

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LOW TEMPERATURE OZONOLYSIS OF METHYL O-METHYL PODOCARPATE

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LOW TEMPERATURE OZONOLYSIS OF METHYL O-METHYL PODOCARPATE

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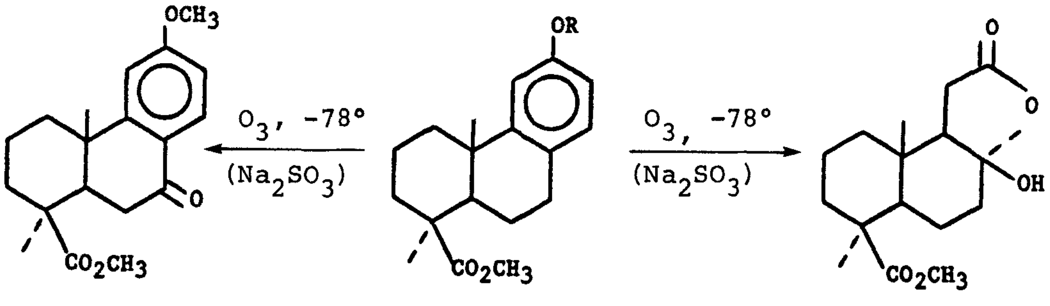
The low temperature ozonolysis of methyl podocarpate (Ia) results in oxidation of its phenolic C-ring with concomitant formation of the hydroxy lactone (II).[1] This reaction has been successfully utilized in the preparation of compounds of pharmaceutical interest and in the synthesis of natural products.[2-4] The related derivative methyl O-methylpodocarpate (Ib) is commonly encountered during synthesis in the podocarpate series,[5-9] but no account of its ozonolysis has appeared in the literature. We now report that the ozonolysis of II results in the formation of ketone III as the major product. The observed benzylic oxidation is envisaged to result from the initial and subsequent insertion of ozone into the carbon-hydrogen bonds at the activated methylene position.[10] Other examples of benzylic oxidation during ozonolysis have been reported.[11-13]



III I II

a) R = H b) R = CH_3

EXPERIMENTAL SECTION

Mps were determined with an Electrothermal capillary apparatus and are uncorrected. Infrared spectra (KBr pellet) were recorded using a Perkin-Elmer Model 580 spectrometer. Proton NMR specra ($CDCl_3$ solvent) were obtained with a Varian EM-390 spectrometer using Me_4Si as an internal standard. Mass spectral analyses were conducted using a DuPont 491 mass spectrometer. Gas-liquid chromatographic (GLC) analyses were performed on a Varian 3700 gas chromatograph equipped with dual flame ionization detectors using 3% OV-1 and 3% OV-17 columns (270°). Silanized glass columns (6 ft x 2 mm i.d.) were employed using nitrogen as a carrier gas (25 ml/min). Thin layer chromatography (TLC) was carried out on plates of silica gel G (Analtech, Newark, DE) using visualization of the components after spraying with molybdic acid.[14] Solvent systems for TLC analyses were: 10% ether in toluene; 10% ethyl acetate in toluene; 35% ethyl acetate in chloroform. Elemental analyses were performed by Galbraith Laboratories, Knoxville, Tennessee. Authentic samples of Ib and III were prepared by known by methods.[6,7,9]

Ozonolysis of Methyl O-Methylpodocarpate (Ib).- Methyl O-methylpodocarpate (5.0 g, 16.6 mmol) was dissolved by warming in 150 ml of anhydrous methanol in a 250 ml gas absorption vessel fitted with a fritted-glass bubbler, 50 ml of anhydrous CH_2Cl_2 was then added and the vessel cooled to -78° (Dry Ice-acetone) and a slow stream of ozone ws passed through the solution for 6 hrs. The solution was then poured into a 1 l. beaker and allowed to stand until the excess ozone (blue color) disappeared. A solution of 10 g of Na_2SO_3 in 200 ml of water was then added and the solution mechanically stirred for 24 hrs. while passing a stream of nitrogen over the liquid surface. Water (200 ml) was then added and the solution extracted with CH_2Cl_2. The combined extracts were evaporated under reduced pressure to yield 4.75 g of a colorless syrup. GLC analysis of the material showed two major components which were identified as Ib (49%) and III (48%) using authentic standards. TLC analysis (10% ether-toluene) also indicated two major components (Rf 0.77, Ib; Rf 0.41, III) with mobility identical with those of authentic compounds.

The reaction product was subjected to column chromatography using a solvent gradient of ether in toluene. The fractions containing the less polar product were pooled, evaporated under reduced pressure, and recrystallized from methanol-water to yield 1.9 g (38%) of the starting material Ib (identical mp. GLC, TLC IR, NMR and MS). The fractions containing the more polar product were pooled, evaporated under reduced pressure, and recrystallized from methanol-water to yield 2.2 g (42%) of III, mp. 121-123°; lit.[6,7,9] 122-124°, 121-123°, 121-123°.

IR(cm^{-1}): 2900, 1725, 1675, 1600; NMR($CDCl_3$): δ 0.99 (s, 3H, $C-CH_3$), 1.20 (s, 3H, $C-CH_3$), 3.52 (s, 3H, $O-CH_3$), 3.70 (s, 3H, $O-CH_3$), 6.53 (s, 2H, aromatic), 7.83 (1H, d, J = 8 Hz, aromatic); mass spectrum, m/e (rel. intensity): 316 (96%), 257 (13%), 241 (100%), 215 (17%), 201 (45%), 190 (62%), and 175 (65%). The IR, NMR, and MS of III were identical with those of an authentic sample. GLC and TLC analysis indicated this material to be identical with the authentic sample.

Anal. Calcd. for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65

Found: C, 72.02; H, 7.74

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SYNTHESIS AND ELECTROPHILIC SUBSTITUTION REACTIONS OF FLUORINE CONTAINING ARYLGLYOXAL 2-ARYLHYDRAZONES

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Recently, hydrazidoyl bromides (α-ketohydrazonyl halides) have aroused interest as versatile reaction intermediates for the synthesis of a variety of heterocyclic systems such as 1,4-dihydro-1,2,4,5-tetrazines, 4,5-dihydro-1H-pyrazoles, pyrazoles, 1,3,4-oxadiazolines and Δ^2-triazolines in already through 1,3-dipolar cycloaddition or nucleophilic substitution reactions.[1-4] A comprehensive survey of the available literature suggested further areas of investigation.[1,5]

We now report the bromination, chlorination and nitration reactions of arylglyoxal 2-arylhydrazones (III) under controlled conditions.

EXPERIMENTAL SECTION

Melting points are uncorrected. IR spectra were recorded on a Perkin-Elmer 157G spectrophotometer as KBr pellets. ^{1}H NMR specra were obtained on Bruker HX-90 using CDCl$_3$ as solvent and TMS as internal standard. Mass spectra were recorded on Kratos 30 and/or 50.