

III. R=p-HO.C₆H₄ IV. R=p-CH₃OCOC₆H₄

V. R=o-HO.C₆H₄ VI. R=C₆H₅CH₂.

Work is in progress to screen the esters III-VI for antisickling action.

EXPERIMENTAL

Unless otherwise stated the following generalisations apply. The melting points (m.p.) were determined using Electrothermal m.p. apparatus and are uncorrected. Ultra-violet (U.V.) spectra were recorded for solutions in dichloromethane with the aid of either Unicam SP 8000 or Unicam SP 8-100 ultraviolet recording spectrophotometers. Molecular weights (M.W) were measured by mass spectrometry (M.S.9 instrument). Infra-red spectra (I.R.) were obtained using Unicam SP 1100 infrared spectrophotometer. Nuclear magnetic resonance spectra (N.M.R.) were determined on either Perkin-Elmer 60 MHz R-12A or EM-360 60 MHz spectrometer using tetramethylsilane as internal standard.

ACETONYL P-HYDROXYBENZOATE (III)

p-Hydroxybenzoic acid (6.9 g, 0.05 mole) was dissolved in 80 ml of ethyl acetate contained in a 250 ml round-bottomed flask. To the resultant solution were added 10.5 ml (0.08 mole) of anhydrous triethylamine (dried over KOH pellets) and 8.0 ml (0.1 mole) of chloroacetone, and the mixture was refluxed for 5 hours. The flask was then cooled and the contents filtered under reduced pressure from the precipitated triethylamine hydrochloride. The latter was washed with ethyl acetate and the washings combined with the filtrate. The filtrate, a dark brown liquid, was freed of ethyl acetate by evaporation under reduced pressure. The dark brown, viscous residue was left to stand at 30° in a fume cupboard.

The crude product (5.38 g) was recrystallised to constant m.p. from aqueous ethanol (25%). The pure ester III was a light yellow crystalline solid. It was soluble in ethanol, methanol, ether, slightly soluble in chloroform and apparently insoluble in water. M.p. 118.5 - 120°.

U.V. spectrum showed λ_{\max} at 249 nm. I.R. spectrum; max (cm⁻¹): 3420 (phenolic OH, sharp and intense), 1730 (aliphatic ketone), 1700 (aryl ester), 1610 and 1600 (indicative of a C=C conjugated double bond in an aromatic ring), 1280 (C-O-C of an ester) and 855 (typical C-H out-of-plane bending vibration, showing a 1,4-disubstituted benzene ring). N.M.R. (δ): 2.20 (CH₃, 3H, s), 4.82 (CH₂, 2H, s), 6.80 (2H, d, J=7.8 Hz) and 7.90 (2H, d, J=7.8 Hz) - aromatic protons. Total number of protons: 10, phenolic proton indistinguishable but confirmed by acetylation. M⁺ = 194.

ACETYLTION OF ESTER III (IV)

Ester III (0.5 g) was dissolved in pyridine (0.5 ml) and redistilled acetyl chloride (0.5 ml) was added dropwise, shaking after each addition. The resultant mixture was heated on a water-bath at 50-60° for 5 minutes. The mixture was cooled and poured into cold water (15 ml), stirring vigorously until crystallization occurred. A white, crystalline product with the characteristic sweet smell of esters was obtained on recrystallization from aqueous ethanol (50%). M.p. 100-102° I.R. spectrum showed no peak at around 3420 cm⁻¹.

ACETONYL SALICYLATE (V)

The same procedure as for ester III was employed using twice the quantities of reagents. The crude yield was 20.6 g. Recrystallization from aqueous ethanol (50%) gave the pure ester V as a white, crystalline solid, m.p. 71-73°, soluble in ethanol, methanol, ether, chloroform, and apparently insoluble in water.

U.V.: λ_{\max} 239 nm and 310 nm. I.R. max (cm⁻¹) 3220 (phenolic OH lowered by strong intramolecular hydrogen bonding, fairly broad), 1730 (aliphatic ketone), 1680 (aryl ester carbonyl stretching, lowered by strong intramolecular hydrogen bonding), 1620 and 1590 (C=C conjugated double bond in an aromatic ring), 1255 (C-O-C of an ester), 760 (C-H out-of-plane deformation indicative of a 1,2-disubstituted benzene nucleus). N.M.R. (δ): 2.25 (CH₃, 3H, s) 4.90 (CH₂ + H, s) 7.90 (1H, m), 7.45 (1H, m) and 6.95 (2H, m) - aromatic protons; 10.40 (phenolic H, s). M⁺ = 194.

Ester V could not be acetylated under the conditions used for ester III.

ACETONYL PHENYLACETATE (VI)

The following reagents were used: 13.6 g (0.1 mole) of phenylacetic acid, 21 ml (0.16 mole) of triethylamine and 16 ml of chloroacetone (0.2 mole).

The same reaction conditions as for ester III were applied. The residue obtained by evaporation of ethyl acetate under reduced pressure was extracted 5 times with ether. The ethereal extracts were evaporated to dryness and the residue was redissolved in ether. The solution was shaken subsequently with a saturated aqueous solution of NaHCO₃, (to remove unreacted acid), and water. The ethereal layer was separated and dried over anhydrous MgSO₄. The ether was distilled off and the residue fractionated to give the ester (VI) as a dark-brown liquid boiling over the range 120.5-122° soluble in methanol, dichloromethane, ethanol, and very slightly soluble in water.

U.V.: λ_{\max} 236.5 nm and 261.5 nm I.R. max (cm⁻¹): 1760-1730 (strong, fairly broad and likely to incorporate both the aliphatic ester and ketone groups), 1260 (C-O-C of an ester), 1380 (C-H vibra-

tion of acetyl group), 730 and 710 (monosubstituted benzene nucleus). N.M.R. (δ): 7.20 (aromatic protons, 5H, s), 3.65 ($-\text{CH}_2\text{CO}_2$, 2H, s), 4.50 ($\text{O}-\text{CH}_2-\text{CO}$, 2H, s) and 1.90 (COCH_3 , 3H, s).

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