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A FACILE SYNTHESIS OF YLIDENEBUTENOLIDES

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In connection with a projected total synthesis of the biosynthetically unusual diterpene isoeremolactone,[1] we required a simple, mild method for the preparation of a 4-alkylidene-2-methylbut-2-enolide (1, R = alkyl). Although synthetic routes to compounds of this type are known, they generally require the use of quite severe reaction conditions and frequently proceed only in poor yield. In view of the considerable versatility of the Wittig olefin synthesis, it appeared likely that an ylid of structure (2) might be employed to effect the required conversion. Such an ylid would be essentially a vinylogous form of the stable α-(γ-butyrolactonylidene)triphenylphosphorane which was used several years ago in some highly effective syntheses of α-benzylidene-γ-butyrolactones.[2]

The ylid (2) was readily prepared by way of compounds (3), (4) and (5). Dye-sensitised photo-oxygenation[3] of 3-methyl-2-furoic acid in methanol gave the pseudoester (6), which was hydrolysed by dilute aqueous acid to the hydroxylactone[4] (7), purified by vacuum sublimation, m.p. 73-74.5°; λ_{max}^{EtOH} 205 nm, ε 5700; $\nu_{max}^{CHCl_3}$ 3570, 1765, 1670, 1093, 1015 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 6.91 (C3-H, multiplet, $J_{3,4}$ 0.5 Hz, $J_{allylic}$ 1.1 Hz); 6.11 (C4-H, broadened singlet which sharpened slightly on exchange with D_2O, $J_{homoallylic}$ 1.2 Hz); 5.59 (OH, broadened singlet); 1.92 (CH_3, distorted triplet).

The hydroxylactone was readily reduced by alkaline methanolic sodium borohydride[5] to the lactone[6] (3), which was converted to the unstable bromolactone (4) by N-bromosuccinimide[7] in refluxing carbon tetrachloride. Immediate treatment of the bromolactone with 1.1 molar equivalent of triphenylphosphine in refluxing benzene deposited the phosphonium salt (5) as a gum, which when dissolved in cold water and treated with dilute sodium hydroxide solution formed a bright yellow precipitate of the ylid (2), m.p. 186-189° (dec.). After washing with water to remove excess alkali, the ylid could be dried under vacuum at 25° and then stored for several days at -15^{o}, after which time it slowly decomposed.

Reaction of excess (2) with *p*-nitrobenzaldehyde in refluxing dichloromethane gave, after isolation by preparative t.l.c., 2-methyl-4-(*p*-nitrobenzylidene)but-2-enolide (1, R = $-C_6H_4NO_2$; 24%), yellow needles from methanol, m.p. 186-188^{o}; λ_{max}^{EtOH} 229, 341 nm, ε 6200, 20,400; $\nu_{max}^{CHCl_3}$ 1767, 1643, 1597, 1350 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 8.26 (*meta*-Ar$\underline{H}_2$, doublet 9.2 Hz); 7.46 (C3-$\underline{H}$, broadened singlet) superimposed on 7.50 (*ortho*-Ar$\underline{H}_2$, doublet); 6.65 (=C$\underline{H}$Ar, broadened singlet); 2.12 (C$\underline{H}_3$, broadened singlet). Similarly, *p*-anisaldehyde gave 4-(*p*-methoxybenzylidene)-2-methylbut-2-enolide (1, R = $-C_6H_4OCH_3$; 30%), pale yellow microcrystals after vacuum sublimation, m.p. 55-57^{o}; λ_{max}^{EtOH} 247, 351 nm, ε 8800, 19,160; $\nu_{max}^{CHCl_3}$ 1750, 1601, 1305, 1067, 1000 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 7.48 (C3-$\underline{H}$, multiplet $J_{3,5}$ 1.0 Hz, $J_{allylic}$ 1.5 Hz); 7.29 (*meta*-Ar$\underline{H}_2$, doublet of triplets, $J_{\underline{ortho}}$ 9.2 Hz, $J_{\underline{meta}}$ 2.5 Hz); 6.90 (*ortho*-Ar$\underline{H}_2$, doublet of triplets); 6.56 (=C$\underline{H}$Ar, broadened singlet); 3.83 (-OC$\underline{H}_3$, singlet); 2.06 (allylic -C$\underline{H}_3$, distorted triplet).

As a trial of an aliphatic case, primary terpineol[8] (8) was oxidised by a modified Collins procedure[9] to the aldehyde (9), which reacted with the ylid as before to afford the alkylidenebutenolide (1, R = 2-(4'-methylcyclohex-3'-enyl)propylidene; 31%), b.p. 120^{o} (bath)/0.5 mm; λ_{max}^{EtOH} 279 nm, ε 17,600; $\nu_{max}^{CCl_4}$ 1780, 1664, 1064 cm^{-1}; $\delta_{TMS}^{CDCl_3}$ 7.24 (C3-$\underline{H}$, broadened singlet); 5.47 (C1'-$\underline{H}$, doublet, 11.4 Hz) superimposed on 5.31 (C3"-$\underline{H}$, envelope); 2.02 (C2-C$\underline{H}_3$, broadened singlet); 1.64 (C4"-C$\underline{H}_3$, broadened singlet); 1.11 (>CH-C$\underline{H}_3$, doublet 6.6 Hz); 0.8-2.5 (8 x aliphatic protons, multiplet).

Because of the dearth of suitable model systems of known stereochemistry, it is not possible at this stage to specify the configurations of the three ylidenebutenolides, beyond the observation that each appears to be a single isomer. Hopefully the eventual application of the procedure to the synthesis of isoeremolactone will provide further information on this point.

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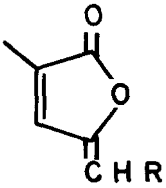
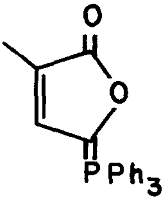


(1)



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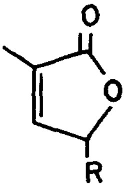


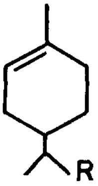
(3) R = H

(4) R = Br

(5) R = $\overset{\oplus}{P}Ph_3$ $Br^{\ominus}$

(6) R = OMe

(7) R = OH



(8) R = CH_2OH

(9) R = CHO

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