

TRIPHENYLPHOSPHINE CATALYZED AROMATIC ELECTROPHILIC SUBSTITUTION OF 2-HYDROXYACETOPHENONE MEDIATED BY VINYLTRIPHENYLPHOSPHONIUM CATION

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Abstract

Protonation of the highly reactive 1:1 intermediate produced in the reaction between triphenylphosphine and dimethyl acetylenedicarboxylate by 2-hydroxyacetophenone leads to vinyltriphenylphosphonium salt, which undergoes aromatic electrophilic substitution reaction with the conjugate base to produce compounds **4**, **5**, and **6** in 1:1.2:0.5 ratios.

Introduction

We have recently described [1] the synthesis of dialkyl 2*H*-chromene derivatives (**1**) from the reaction of triphenylphosphine, 2-hydroxybenzaldehyde and dialkyl acetylenedicarboxylates using intramolecular Wittig reaction [2-5]. With the purpose of preparation of 2*H*-chromenes having a methyl group at C-4, such as **2**, we performed the reaction of 2-hydroxyacetophenone with triphenylphosphine and dimethyl acetylenedicarboxylate. This reaction did not afford the corresponding 2*H*-chromene (**2**), but yielded compounds **4-6** in fairly good yields.

Organophosphorus compounds have been extensively

used in organic synthesis as useful reagents as well as ligands of a number of transition metal catalysts [6-8]. However, there are few reactions in which organophosphorus (III) species work as catalysts [9-11].

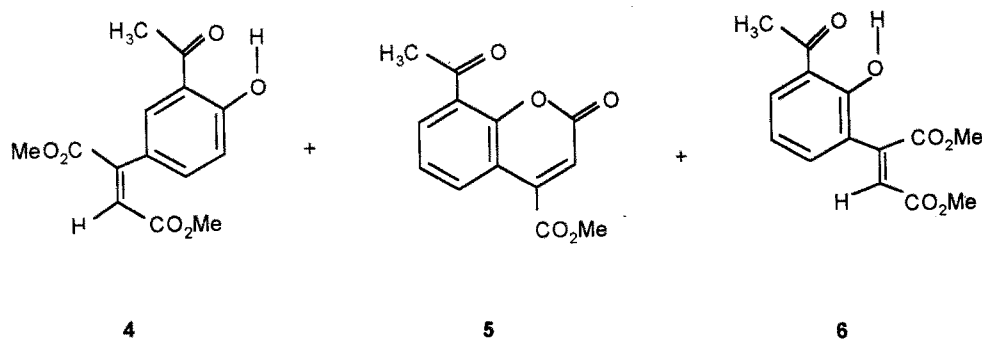
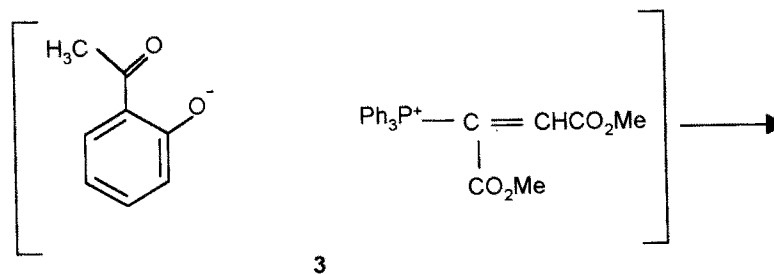
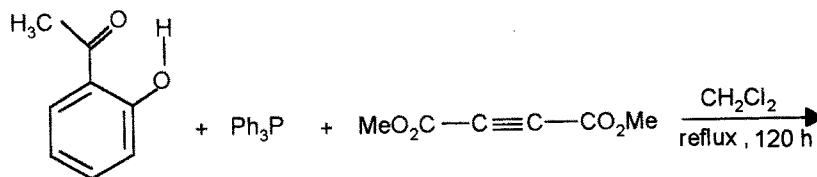
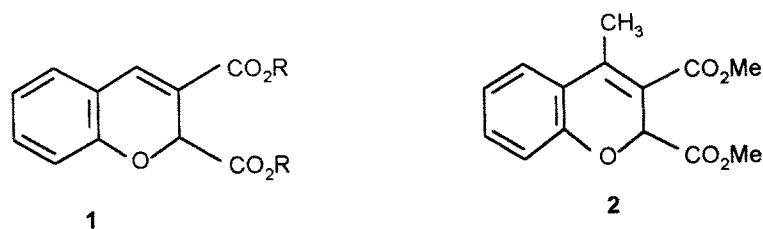
Results and Discussion

Compounds **4-6** apparently result from initial addition of triphenylphosphine to the acetylenic ester concomitant protonation of the reactive 1:1 adduct, followed by electrophilic attack of the vinyltriphenylphosphonium cation to the aromatic ring at *ortho* and *para* positions relative to the strong activating group [12]. The coumarin derivative **5** is probably produced by intramolecular transesterification of the *E* diastereoisomer **7**.

Structures **4-6** were assigned to the isolated products on the basis of their elemental analyses and IR, ¹H and ¹³C NMR spectra. The mass spectra of isomeric products **4** and **6** are similar, as expected, and confirm their molecular weights. Compound **5** exhibited different fragmentation patterns. IR spectroscopy was applied to distinguish the

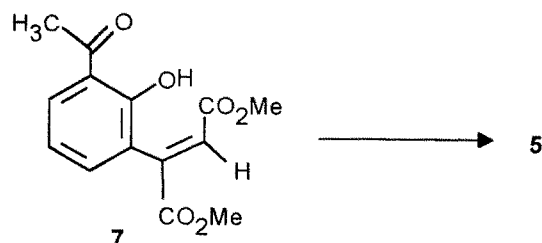
Keywords: Triphenylphosphine; Acetylenic ester; 2-Hydroxyacetophenone; Aromatic substitution; Coumarin derivatives; Vinylation

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benzopyran structure **5** from the phenol derivatives **4** and **6**. Thus, IR spectra of the latter compounds showed strong OH stretching bands at about 3450 cm⁻¹.

The resonance peaks in the ¹H and ¹³C NMR spectra



of the three products **4**, **5** and **6** are listed in Table 1. ¹H NMR spectroscopy was applied to distinguish structure **4** from **6**. Thus, the NMR spectrum of **4** displayed an ABM pattern for the aromatic protons, while compound **6** exhibited an ABC pattern. The assignment of the *E* and *Z* configurations of **4** and **6** are based on the chemical shifts of the vinylic protons. The vinylic proton of the *E* isomer appears at lower field as a result of anisotropic deshielding of the ester carbonyl groups [13]. Partial assignments of the ¹³C resonances in compounds **4-6** are given in Table 1.

We anticipate that the reactions described herein represent a simple entry into the synthesis of

polyfunctional benzene systems. We are currently using this methodology in the preparation of novel, functionalized aromatic compounds.

Experimental Section

General

Melting points were measured on an Electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN-O-Rapid analyzer. IR spectra were recorded on a Philips PU9800 FT-IR spectrometer. ^1H and ^{13}C NMR spectra were measured with a JEOL EX-90A spectrometer at 90 and 22.6 MHz, respectively. Mass spectra were recorded on a Finnigan-Matt 8430 mass spectrometer operating at an ionization potential of 70 eV. Dimethyl acetylenedicarboxylate, 2-hydroxyacetophenone, and triphenylphosphine were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

Preparation of 4, 5 and 6

To a magnetically stirred solution of triphenylphosphine (0.524 g, 2 mmol), and 2-hydroxyacetophenone (0.272 g, 2 mmol) in CH_2Cl_2 (4 ml) was added dropwise a mixture of dimethyl acetylenedicarboxylate (0.284 g, 2 mmol) in CH_2Cl_2 (2 ml) at -7°C over 15 min. The reaction mixture was then refluxed for 120 h. Silica gel (0.5 g) was added and the solvent was evaporated. Dry silica gel and the residue were placed over a column of silica gel (10 g) and elution first made with hexane and was continued gradually increasing the polarity of the eluent by using 80:20 and 60:40 compositions of hexane and diethyl ether. With this solvent, a mixture of a colorless oil was obtained which was solidified after a few hours (0.152 g, m.p. $99-101^\circ\text{C}$, 38%) and was identified as dimethyl (*E*)-2(3-acetyl-4-hydroxyphenyl)but-2-enedioate (**4**); $\nu_{\text{max}}/\text{cm}^{-1}$ (KBr) 3440 (O-H), 1730 and 1709 (C=O), 1647 (C=C); m/z (%) 278 (M^+ , 12), 262 (M^+-CH_3 , 100), 219

Table 1. ^1H and ^{13}C NMR data for compounds 4-6

		δ (ppm, CDCl_3 , TMS)
4	^1H :	2.62 (3 H, CH_3), 3.66 and 3.85 (6 H, 2s, 2 OCH_3), 6.98 (1 H, d, $J=8.2$ Hz, $\text{C}^5\text{-H}$ of Ar), 7.04 (1 H, s, vinylic), 7.36 (1 H, 2d, $J=8.2$ Hz, and $J=1.5$ Hz, $\text{C}^6\text{-H}$ of Ar), 7.72 (1 H, d, $J=1.5$ Hz, $\text{C}^2\text{-H}$ of Ar), 12.4 (1 H, s, $\text{O-H}\cdots\text{O}=\text{C}$)
	^{13}C :	26.59 (CH_3), 51.96 and 53.02 (2 OCH_3), 117.93 (CH), 119.11 and 124.08 (2 C), 128.51, 132.02 and 137.39 (3 CH), 142.85 (C), 162.84 (C^4 of Ar), 165.57 and 166.63 (2 C=O, ester), 204.38 (C=O)
5	^1H :	2.83 (3 H, s, CH_3), 4.03 (3 H, s, OCH_3), 6.99 (1 H, s, vinylic), 7.39 (1 H, t, $J=8.2$ Hz, $\text{C}^6\text{-H}$), 8.01 (1 H, dd, $J=8.2$ Hz and $J=1.5$ Hz, $\text{C}^5\text{-H}$), 8.43 (1 H, dd, $J=8.2$ Hz and $J=1.5$ Hz)
	^{13}C :	32.09 (CH_3), 53.34 (OCH_3), 116.34 (C), 119.39 and 124.56 (2 CH), 128.07 (C), 131.00 and 133.24 (2 CH), 142.48 (C), 152.66 (C^8 of Ar), 158.40 (C=O, lactone), 163.98 (C=O, ester), 197.05 (C=O)
6	^1H :	2.66 (3 H, s, CH_3), 3.79 and 3.89 (6 H, 2s, 2 OCH_3), 6.64 (1 H, s, vinylic), 6.94 (1 H, t, $J=8.1$ Hz, $\text{C}^5\text{-H}$ of Ar), 7.55 (1 H, dd, $J=8.1$ Hz and $J=1.5$ Hz, $\text{C}^6\text{-H}$ of Ar), 7.82 (1 H, dd, $J=8.1$ Hz and $J=1.5$ Hz, $\text{C}^4\text{-H}$ of Ar), 13.17 (1 H, s, $\text{O-H}\cdots\text{O}=\text{C}$)
	^{13}C :	26.84 (CH_3), 52.00 and 52.65 (2 OCH_3), 118.95 (CH), 120.05 (C), 122.33 (CH), 123.75 (C), 131.45 and 136.46 (2 CH), 143.54 (C), 161.09 (C^2 of Ar), 165.69 and 168.01 (2 C=O ester), 204.87 (C=O)

(M^+ -CO₂Me, 40) (Found: C, 61.1; H, 5.0. C₁₄H₁₄O₆ requires C, 60.43; H, 5.07%).

Elution with 50:50 mixture of hexane and diethyl ether yielded a white solid compound (0.178 g, m.p. 116-118°C, 44%), which was identified as 8-acetyl-2H-1-benzopyran-2-one-4-carboxylate (**5**); $\nu_{\max}/\text{cm}^{-1}$ (KBr) 1755, 1730, and 1701 (C=O), 1676 (C=C); m/z (%) 246 (M^+ , 8), 230 (M^+ -CH₄, 80), 187 (M^+ -CO₂Me, 100) (Found: C, 64.0; H, 4.1. C₁₃H₁₀O₅ requires C, 63.41; H, 4.09%).

Elution with 40:60 mixture of hexane and diethyl ether yielded a white solid compound (0.075 g, m.p. 126-127°C, 18%), which was identified as dimethyl (*Z*)-2-(3-acetyl-2-hydroxyphenyl)but-2-enedioate (**6**); $\nu_{\max}/\text{cm}^{-1}$ (KBr) 3435 (O-H), 1732 and 1707 (C=O), 1652 (C=C); m/z (%) 278 (M^+ , 14), 262 (M^+ -CH₄, 100), 219 (M^+ -CO₂Me, 32) (Found: C, 61.0; H, 5.1. C₁₄H₁₄O₆ requires C, 60.43; H, 5.07%).

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