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A New and Simple Synthesis of 3*H*-Benzo[*f*]chromen-3-one and 2*H*-Benzo[*h*]chromen-2-one Derivatives

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Summary. Protonation of the highly reactive 1:1-intermediate produced in the reaction between triphenylphosphine and dimethyl acetylenedicarboxylate by naphthols lead to vinyl triphenylphosphonium salts which undergo an aromatic electrophilic substitution reaction with the conjugated base to produce the title compounds.

Keywords. Triphenylphosphine; Dimethyl acetylenedicarboxylate; Naphthol.

Introduction

Coumarins are an important class of naturally occurring organic compounds exhibiting useful pharmacological activities. In addition, they are used as food and cosmetic additives [1], optical brightening agents [2], and dispersed fluorescent and laser dyes [3]. The derivatives of coumarin usually occur as secondary metabolites present in seeds, roots, and leaves of many plant species.

Several polycyclic coumarin derivatives have been shown to be potent inhibitors of tumor induction by carcinogenic polycyclic aromatic hydrocarbons [4–7]. However, investigations of anti-carcinogenic activity have been primarily confined to coumarin derivatives available from plant sources, the majority of which are highly oxygenated. Coumarins can be mainly synthesized by the *Claisen* rearrangement, the *Perkin* reaction, the *Pechmann* reaction, and the *Knoevenagel* condensation [8]. The present report deals with a new and simple synthesis of benzo-annelated coumarins.

Results and Discussion

In continuation of our ongoing research to develop syntheses of coumarins [9] with the aim to prepare of polycyclic coumarins, we reacted naphthols with triphenyl phosphine (**2**) and dimethyl acetylenedicarboxylate (**1**) based on the well-established chemistry of trivalent phosphorus nucleophiles [10, 11]. It is reasonable to assume

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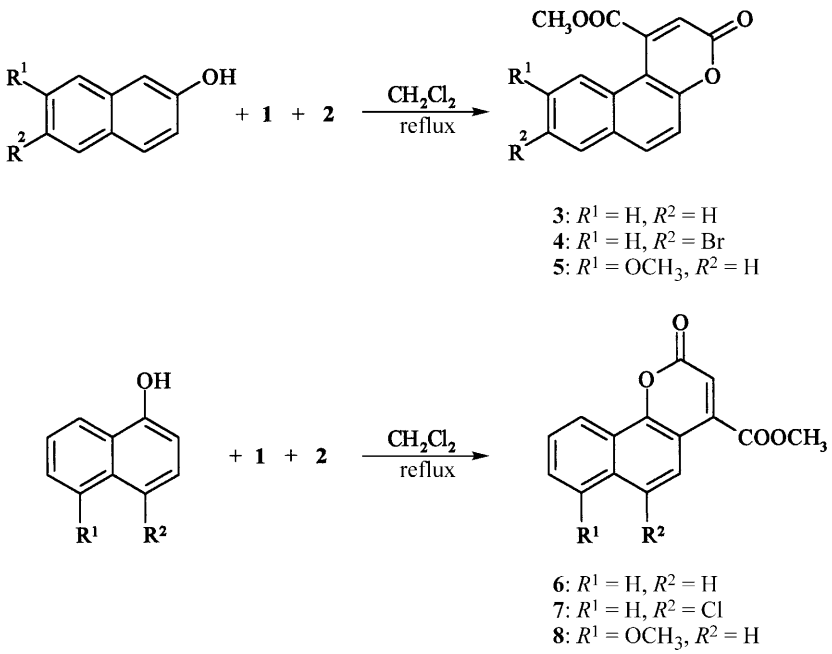

Scheme 1

that the coumarins **3**–**7** result from the initial addition of **2** to **1** and a concomitant protonation of the reactive 1:1-adducts, an electrophilic attack of the vinyltriphenyl phosphonium cation to the aromatic ring in the *ortho* position relative to the strongly activating group. The benzocoumarin derivatives **3**–**8** were then presumably produced by intramolecular lactonization. The structures of **3**–**8** were deduced from their elemental analyses and their IR, ^{1}H, and ^{13}C NMR data. In addition, the mass spectra of the compounds displayed molecular ion peaks at appropriate m/z-values.

Experimental

Melting points were measured on an electrothermal 9100 apparatus and are uncorrected. Elemental analyses were performed using a Heraeus CHN–O-Rapid analyzer; the results were in good agreement with the calculated values. IR spectra were recorded on a Philips PU 9800 FTIR spectrometer. ^{1}H and ^{13}C NMR spectra were measured with a JEOL EX-90A spectrometer at 90 and 22.6 MHz. Mass spectra were obtained with a Finnigan-MaH8430 mass spectrometer operating at an ionization potential of 70 eV. **1**, **2**, and the naphthols were obtained from Fluka (Buchs, Switzerland) and were used without further purification.

General procedure

To a magnetically stirred solution of 0.524 g **2** (2 mmol) and 2 mmol of the appropriate naphthol in 10 cm^3 CH_2Cl_2, a solution of 0.284 g **1** (2 mmol) in 10 cm^3 CH_2Cl_2 was added at $-5°C$ over 10 min. The reaction mixture was then refluxed for 120 h. Silica gel (0.5 g) was added, and the solution was evaporated. The silica gel was placed on top of a column of 10 g silica gel and first eluted with hexane, gradually increasing the polarity of the eluent using 80:20 and 60:40 mixtures of hexane and diethyl ether. The solvent was removed under reduced pressure, and the product was obtained.

3-Oxo-3H-benzo[f]chromene-1-carboxylic acid methyl ester (**3**; $C_{15}H_{10}O_4$)

Yield: 85%; m.p.: 138°C; ^{1}H NMR (90 MHz, δ, $CDCl_3$): 7.2–8.0 (m, $4H_{ar}$), 8.04 (d, $J = 9.0$ Hz, $1H_{ar}$), 7.50 (d, $J = 9.0$ Hz, $1H_{ar}$), 6.59 (s, H-2), 4.06 (s, OCH_3) ppm; ^{13}C NMR (22.6 MHz, δ, $CDCl_3$): 167.6 (CO_{ester}), 159.3 ($CO_{lactone}$), 154.7 (C–O), 145.7 (C), 134.4 (CH), 130.7 (C), 129.3 (CH), 128.1 (CH), 127.8 (C), 126.03 (CH), 123.1 (CH), 117.1 (CH), 115.4 (CH), 109.9 (C), 53.47 (OCH_3) ppm; MS (70 eV): $m/z = 254.20$.

8-Bromo-3-oxo-3H-benzo[f]chromene-1-carboxylic acid methyl ester (**4**; $C_{15}H_9O_4Br$)

Yield: 92%; m.p.: 186°C; ^{1}H NMR (90 MHz, δ, $CDCl_3$): 8.65 (1H, d, CH), 8.57 (1H, d, CH), 8.25 (1H, d, CH), 7.82 (1H, d, CH), 7.40 (1H, d, CH), 6.92 (1H, s, CH), 3.96 (s, OCH_3) ppm; ^{13}C NMR (22.6 MHz, δ, $CDCl_3$): 161.2 (CO_{ester}), 159.2 ($CO_{lactone}$), 153.3 (C–O), 148.3 (C), 138.3 (C), 131.03 (CH), 130.23 (CH), 129.6 (CH), 128.6 (CH), 127.1 (CH), 120.2 (CH), 118.8 (C), 111.34 (C), 109.23 (C), 53.04 (OCH_3) ppm; MS (70 eV): $m/z = 333.01$.

9-Methoxy-3-oxo-3H-benzo[f]chromene-1-carboxylic acid methyl ester (**5**; $C_{16}H_{12}O_5$)

Yield: 75%; m.p.: 134–136°C; ^{1}H NMR (90 MHz, δ, $CDCl_3$): 7.4 (1H, d, CH), 7.35 (1H, d, CH), 7.25 (1H, d, CH), 7.2 (1H, dd, CH), 7.1 (1H, d, CH), 6.95 (1H, s, CH), 3.92, 4.0 (s, OCH_3) ppm; ^{13}C NMR (22.6 MHz, δ, $CDCl_3$): 165.01 (CO_{ester}), 158.7 ($CO_{lactone}$), 152.1 (C–O), 151.05 (C), 143.6 (C), 135.1 (C), 129.6 (CH), 128.7 (CH), 126.7 (CH), 119.3 (CH), 116.8 (CH), 115.2 (CH), 112.3 (CH), 107.8 (C), 54.7 (OCH_3), 52.9 (OCH_3) ppm; MS (70 eV): $m/z = 283.92$.

2-Oxo-2H-benzo[h]chromene-4-carboxylic acid methyl ester (**6**; $C_{15}H_{10}O_4$)

Yield: 75%; m.p.: 162°C; ^{1}H NMR (90 MHz, δ, $CDCl_3$): 7.5–8.6 (m, $4H_{ar}$), 8.15 (d, $J = 9.0$ Hz, $1H_{ar}$), 7.65 (d, $J = 9.0$ Hz, $1H_{ar}$), 6.96 (s, CH), 4.03 (s, OCH_3) ppm; ^{13}C NMR (22.6 MHz, δ, $CDCl_3$): 164.4 (CO_{ester}), 159.8 ($CO_{lactone}$), 151.6 (C–O), 143.1 (C), 134.7 (C), 129.1 (CH), 127.5 (CH), 127.1 (CH), 124.4 (CH), 122.85 (C), 122.45 (CH), 121.7 (CH), 118.2 (CH), 111.4 (C), 53.18 (OCH_3) ppm; MS (70 eV): $m/z = 254.02$.

7-Methoxy-2-oxo-2H-benzo[h]chromene-4-carboxylic acid methyl ester (**7**; $C_{16}H_{12}O_5$)

Yield: 70%; m.p.: 177–179°C; ^{1}H NMR (90 MHz, δ, $CDCl_3$): 7.7–8.15 (3H, m), 7.60 (d, $J = 9.0$ Hz, $1H_{ar}$), 7.15 (d, $J = 9.0$ Hz, $1H_{ar}$), 6.97 (1H, s, CH), 3.95, 4.05 (s, OCH_3) ppm; ^{13}C NMR (22.6 MHz, δ, $CDCl_3$): 164.57 (CO_{ester}), 158.7 ($CO_{lactone}$), 151.8 (C–O), 150.7 (C), 143.2 (C), 135.2 (C), 129.2 (CH), 127.6 (CH), 127.4 (C), 119.05 (CH), 117.6 (CH), 115.4 (CH), 111.8 (CH), 107.2 (C), 55.7, 53.18 (OCH_3) ppm; MS (70 eV): $m/z = 283.85$.

6-Chloro-2-oxo-2H-benzo[h]chromene-4-carboxylic acid methyl ester (**8**; $C_{15}H_9O_4Cl$)

Yield: 83%; m.p.: 225–227°C; ^{1}H NMR (90 MHz, δ, $CDCl_3$): 8.8 (1H, s), 7–8.6 (4H), 7.05 (1H, s, CH), 4.15 (s, OCH_3) ppm; ^{13}C NMR (22.6 MHz, δ, $CDCl_3$): 165.04 (CO_{ester}), 160.1 ($CO_{lactone}$), 152.2 (C), 144.8 (C), 135.6 (C), 130.1 (CH), 128.9 (CH), 128.7 (CH), 125.4 (CH), 124.23 (C), 123.9 (C), 123.52 (CH), 119.2 (CH), 112.3 (C), 54.1 (OCH_3) ppm; MS (70 eV): $m/z = 288.50$.

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