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A Novel Synthesis of 4-Propyl-2*H*-1-benzopyran-2-ones

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Reaction of 2-hydroxybutyrophenones **1–5** with ethoxycarbonylmethylenetriphenylphosphorane furnishes the 4-propyl-2*H*-1-benzopyran-2-ones **6–10**.

(Keywords: Ethoxycarbonylmethylenetriphenylphosphorane; 2-Hydroxybutyrophenones; Insecticidal properties; 4-Propyl-2H-1-benzopyran-2-ones; Wittig reaction)

Eine neue Synthese von 4-Propyl-2H-1-benzopyran-2-onen

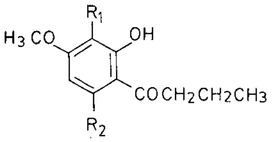
Die Reaktion von 2-Hydroxybutyrophenonen **1—5** ergab mit Ethoxycarbonylmethylentriphenylphosphoran die 4-Propyl-2*H*-1-benzopyran-2-one **6—10**.

Introduction

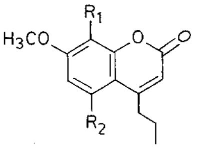
A number of 4-propylcoumarins (4-propyl-2*H*-1-benzopyran-2-ones) have been isolated[1] from plants of various *Mammea species*. These coumarins are found to possess insecticidal properties[2–4]. The structures of the natural 4-propylcoumarins have been established by spectroscopic methods and degradative studies. No considerable efforts have been made so far to synthesise them. The methods available for the synthesis of 4-propylcoumarins are (i) *Pechmann* condensation[5–7] of phenols with ethyl butyryl acetate and (ii) reaction[8] of β-diketones with $HBr-Ac_2O$. In general the yields reported by these procedures are not satisfactory. We report herein a general and efficient method for the synthesis of 4-propyl-2*H*-1-benzopyran-2-ones. It involves the *Wittig* reaction[9] of 2-hydroxybutyrophenones **1–5** with ethoxycarbonylmethylenetriphenylphosphorane $[(C_6H_5)_3P=CH\cdot COOC_2H_5]$.

Results and Discussion

Initially the reaction of 2-hydroxy-4-methoxybutyrophenone[10] (**1**) with ethoxycarbonylmethylenetriphenylphosphorane in anhyd. benzene gave only one product in excellent yield (80%). It was assigned the structure 7-methoxy-4-propyl-2*H*-1-benzopyran-2-one (**6**) on the basis of its elemental analysis, IR and ¹H-NMR spectral data. Using the same procedure different 4-propyl-2*H*-1-benzopyran-2-ones **6**–**10** have been synthesised starting from the appropriate 2-hydroxybutyrophenones **2**–**5**. The ketones 2-hydroxy-4-methoxy-3-methylbutyrophenone (**3**) and 2-hydroxy-4-methoxy-6-methylbutyrophenone (**5**) were obtained by *Friedel-Crafts* reaction of *n*-butyryl chloride with 1,3-dimethoxy-2-methylbenzene and 1,3-dimethoxy-5-methylbenzene, respectively, while **2** and **4** are known earlier[10]. The compounds 7-methoxy-8-methyl-4-propyl-2*H*-1-benzopyran-2-one (**8**) and 7-methoxy-5-methyl-4-propyl-2*H*-1-benzoopyran-2-one (**10**) have been synthesised for the first time.



1-5



6-10

	R_1	R_2
1, 6	H	H
2, 7	OCH_3	H
3, 8	CH_3	H
4, 9	H	OCH_3
5, 10	H	CH_3

All these coumarins exhibited a C=O band in their IR spectra between 1 710 and 1 700 cm^{-1}. The ¹H-NMR spectral data confirmed the proposed structures.

Neutral conditions, superior yields and ready availability of the stable phosphorane render the present method attractive and enhance its utility.

Acknowledgement

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Experimental

All melting points are uncorrected. ^{1}H-NMR spectra ($CDCl_3$; *TMS*; δ/ppm) were recorded on a Perkin-Elmer R-32 (90 MHz) spectrometer. IR spectra (KBr; cm^{-1}) were measured on a Perkin-Elmer Grating Infrared spectrophotometer, model 621. The experimental C, H values for compounds **3**, **5** and **6**–**10** were in full agreement with the given structures.

Preparation of 2-Hydroxy-4-methoxy-3-methylbutyrophenone (**3**)

General Procedure

To a cooled and stirred solution of 1,3-dimethoxy-3-methylbenzene (5 g, 0.0142 mol) in absolute diethyl ether (15 ml) and anhydrous aluminium chloride (11.2 g, 0.084 mol) was added butyryl chloride (4.5 g, 0.042 mol) over 1 h and stirring continued for a further 4 h. Working up of the reaction mixture gave **3** (4.8 g) which crystallised from benzene—petroleum ether as colourless needles, m.p. 65–66°.

Preparation of 7-methoxy-4-propyl-2H-1-benzopyran-2-one (**6**)

General Procedure

A mixture of **1**[10] (1.95 g, 0.01 mol) and ethoxycarbonylmethylenetriphenylphosphorane (5.2 g, 0.015 mol) was refluxed in dry benzene (25 ml), according to the time given below. After evaporation of the solvent the residue was chromatographed over silica gel. Elution of the column with benzene—petroleum ether (3 : 1) gave **6** (1.7 g). It crystallised from benzene—petroleum ether as colourless prisma, m.p. 76–78°.

3: Yield 55.5%; m.p. 65–66 °C; NMR: 0.91 (t, *J* = 7 Hz, 3 H, $CH_2CH_2\mathbf{CH_3}$); 1.60–1.99 (m, 2 H, $CH_2\mathbf{CH_2}CH_3$); 2.10 (s, 3 H, 3-CH_3); 2.88 (t, *J* = 7 Hz, 2 H, $\mathbf{CH_2}CH_2CH_3$); 3.84 (s, 3 H, 4-OCH_3); 6.29 (d, *J* = 9.5 Hz, 1 H, H-5); 7.45 (d, *J* = 9.5 Hz, H-6); 13.02 (s, 1 H, 2-OH, D_2O exchangeable).

5: Yield 50%; m.p. 68–69 °C; NMR: 0.95 (t, 7 Hz, 3 H, $CH_2CH_2\mathbf{CH_3}$); 1.49–1.90 (m, 2 H, $CH_2\mathbf{CH_2}CH_3$); 2.22 (s, 3 H, 6-CH_3); 2.90 (t, *J* = 7 Hz, 2 H, $\mathbf{CH_2}CH_2CH_3$); 3.77 (s, 3 H, 4-OCH_3); 6.10 (d, *J* = 2.5 Hz, 1 H, H-3); 6.20 (d, *J* = 2.5 Hz, 1 H, H-5); 13.55 (s, 1 H, 2-OH, D_2O exchangeable).

6: React. time 35 h; yield 80%; m.p. 76–78 °C (Lit.[5] 145°); IR: 1 710 (C=O), 1 610 (C=C); NMR: 1.02 (t, *J* = 7 Hz, 3 H, $CH_2CH_2\mathbf{CH_3}$); 1.39–1.78 (m, 2 H, $CH_2\mathbf{CH_2}CH_3$); 2.60 (t, *J* = 7 Hz, 2 H, $\mathbf{CH_2}CH_2CH_3$); 3.75 (s, 3 H, 7-OCH_3); 5.95 (s, 1 H, H-3); 6.62 (d, *J* = 2.5 Hz, 1 H, H-8); 6.69 (dd, *J* = 9.5 Hz, 2.5 Hz, 1 H, H-6); 7.34 (d, *J* = 9.5 Hz, 1 H, H-5).

7: React. time 34 h; yield 76%; m.p. 79–80 °C (Lit.[5] 95°); IR: 1 705 (C=O), 1 605 (C=C); NMR: 1.00 (t, *J* = 7 Hz, 3 H, $CH_2CH_2\mathbf{CH_3}$); 1.33–1.77 (m, 2 H, $CH_2\mathbf{CH_2}CH_3$); 2.60 (t, *J* = 7 Hz, 2 H, $\mathbf{CH_2}CH_2CH_3$); 3.83 and 3.88 (each s, each 3 H, 2 × OCH_3); 5.95 (s, 1 H, H-3); 6.72 (d, *J* = 9.5 Hz, 1 H, H-6); 7.14 (d, *J* = 9.5 Hz, 1 H, H-5).

8: React. time 20 h; yield 80%; m.p. 115–116 °C; IR: 1 700 (C=O), 1 595 (C=C); NMR: 1.00 (t, *J* = 7 Hz, 3 H, $CH_2CH_2\mathbf{CH_3}$); 1.47–1.85 (m, 2 H, $CH_2\mathbf{CH_2}CH_3$); 2.20 (s, 3 H, 8-CH_3); 2.61 (t, *J* = 7 Hz, 2 H, $\mathbf{CH_2}CH_2CH_3$); 3.81 (s, 3 H, 7-OCH_3); 5.95 (s, 1 H, H-3); 6.68 (d, *J* = 9.5 Hz, 1 H, H-6); 7.29 (d, *J* = 9.5 Hz, 1 H, H-5).

9: React. time 35 h; yield 75%; m.p. 118–119 °C (Lit.[8] 117–118°); IR: 1 700 (C=O), 1 600 (C=C); NMR: 1.10 (t, *J* = 7 Hz, 3 H, $CH_2CH_2\mathbf{CH_3}$); 1.46–1.83 (m, 2 H, $CH_2\mathbf{CH_2}CH_3$); 2.92 (t, $J = 7$ Hz, 2 H, $\mathbf{CH_2}CH_2CH_3$); 3.88 and 3.92 (each s, each 3 H, 2 × OCH_3); 5.98 (s, 1 H, H-3); 6.31 and 6.46 (each d, $J = 2.5$ Hz, each 1 H, H-6 and H-8).

10: React. time 30 h; yield 65%; m.p. 97–98 °C; IR: 1 710 (C=O), 1 600 (C=C); NMR: 1.00 (t, $J = 7$ Hz, 3 H, $CH_2CH_2\mathbf{CH_3}$); 1.37–1.70 (m, 2 H, $CH_2\mathbf{CH_2}CH_3$); 2.32 (s, 3 H, 5-CH_3); 2.72 (t, $J = 7$ Hz, 2 H, $\mathbf{CH_2}CH_2CH_3$); 3.82 (s, 3 H, 7-OCH_3); 5.95 (s, 1 H, H-3); 6.44 and 6.64 (each d, $J = 2.5$ Hz, each 1 H, H-6 and H-8).

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