SHORT PAPER

J. Chem. Research (S), 2000, 138–139

An unusual product in the condensation of 3-*t*-butyl-2-hydroxy-5-methoxybenzaldehyde with acetylacetone†

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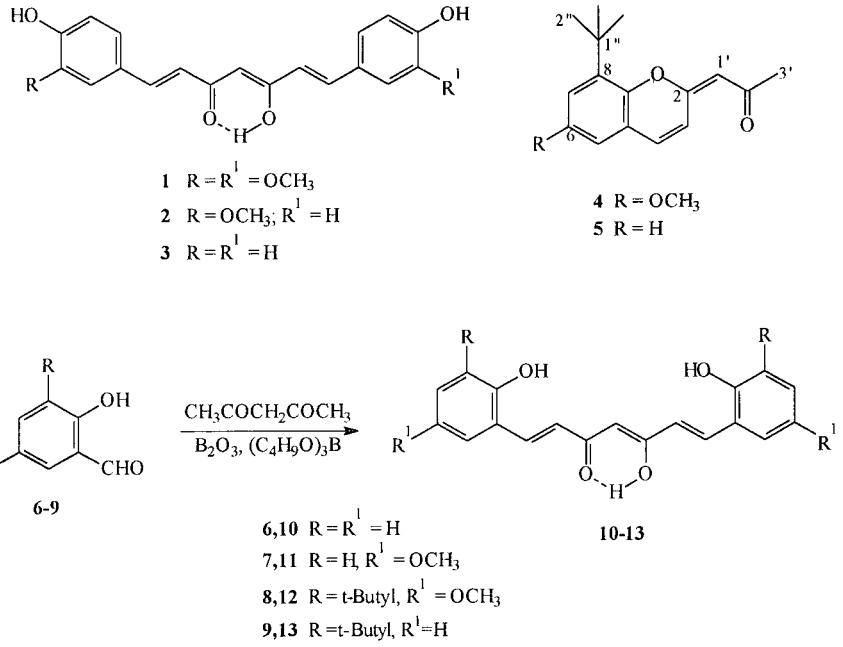
The reaction of 3-*t*-butyl-2-hydroxy-5-methoxybenzaldehyde **6** with acetylacetone resulted in the formation of an unusual product, 1-[8-(*t*-butyl)-6-methoxy-2H-chromem-2-ylidene] acetone **4**.

The role of antioxidants in disease prevention has been gaining increasing importance in recent years. Curcuminoids **1–3**, metabolites of *Curcuma* species have been reported, not only as safe and potent antioxidants,[1,2] but also to possess antibacterial,[3] antiinflammatory,[4] antitumour[5,6] and anti-HIV[7] activities. During limited SAR studies on curcuminoid analogues, Kuttan *et al*.[8] have found that salicylyl analogue **10** had a better antioxidant activity profile. As the antioxidant nature of butylated hydroxyanisole (BHA) has been well established, we planned to introduce BHA units into curcuminoids and attempted the synthesis of **12** via the condensation of **8** with acetylacetone. But we instead could isolate an unusual product **4**. To understand the factors responsible for the formation of **4**, we have carried out the condensations of salicylaldehyde **6**, 2-hydroxy-5-methoxybenzaldehyde **7** with acetylacetone. In both of these reactions, the expected products **10** and **11** have been obtained in 61 and 40% yield, respectively (Scheme 1). Therefore, it seems that the formation of **4** is influenced by the 3-*t*-butyl group in **8**. A fact supported further by the condensation of **9** with acetylacetone in which the unusual product, **13** was again isolated.

Formation of coumarin from salicylaldehyde under Perkins conditions is a well documented reaction. Such a sequence of monocondensation of acetylacetone with **8** followed by cyclization might, perhaps, lead to the formation of **4**.

1-[8-t-Butyl)-6-methoxy-2H-chromen-2-ylidene]acetone **4**: To a solution of boric oxide (350 mg, 5 mmol) in DMF (1 mL) at 60–70 °C was added acetylacetone (0.48 mL, 4.7 mmol) followed by tributyl borate (2.4 mL, 9 mmol). After 5 min, 3-*t*-butyl-2-hydroxy-5-methoxy benzaldehyde (**8**, 1.89g, 9 mmol) and a solution of 1,2,3,4-tetrahydroquinoline (0.1 mL) in glacial acetic acid (0.3 mL) and DMF (1 mL) were added and heating was continued for 4 h. After this period, aqueous acetic acid (20%, 50 mL) was added and stirring continued for a further 1 h. The reaction mixture was then cooled to room temperature and extracted with chloroform (2 × 25 mL). The chloroform layer was washed with water and brine, successively and dried over sodium sulfate. The residue obtained after the removal of solvent was chromatographed over silica gel column with hexane–chloroform (9:1) as eluent to give **4** (650 mg, 27%), mp 88–90 °C; UV (MeOH) λ_{max}(log ε) 221 (4.27), 271 (3.99), 303(4.26); IR



Scheme 1

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

(Neat) ν_{max} 2953, 1658, 1601, 1572, 1553, 1454, 1427, 1218, 1167, 1109, 956 cm^{-1}, ^1H NMR ($CDCl_3$, 90 MHz): δ 1.44 (9H,s, H-2′′), 2.20 (3H, s, H-3′), 3.80 (3H, s, 6-OCH_3), 5.84 (1H, s, H-1′), 6.58 (1H, d, *J* = 3.0 Hz, H-7), 6.97 (1H = d, *J* = 3.0 Hz, H-5), 7.08 (1H, d, *J* = 10.5 Hz, H-3), 8.06 (1H, d, *J* = 10.5 Hz, H-=4); ^{13} C NMR ($CDC1_3$, 22.5 MHz): δ 29.9, 31.7, 34.8, 55.6, 100.2, 107.3, 117.4, 119.3, 121.5, 134.6, 138.9, 145.0, 155.2, 161.9, 196.0; EIMS: *m/z* (rel. int.) 272 (M^+, 50), 257 (100), 242 (13), 230 (5), 215 (7), 120 (3); Found C, 74.19; H, 7.47%; calcd. for $C_{17}H_{20}O_3$: C, 75.00; H, 7.35%.

*1-[8-(Butyl)-2H-chromem-2-ylidene] acetone **5**:* Under the conditions described for the formation of **4**, 3-t-butyl-2-hydroxybenzaldehyde **9** gave the chromene derivative **5**, as light yellow solid, 25% yield, m.p. 98–100 °C; IR (Neat) ν_{max} 2968, 1654, 1617, 1569, 1540, 1471, 1420, 1220, 1165, 954, 741 cm^{-1}; ^1H NMR ($CDCl_3$, 90 MHz): δ 1.45 (9H, s, H-2′′), 2.21 (3H, s, H-3′), 5.87 (1H, s, H-1′), 7.06–7.42 (4H, m), 8.02 (1H, d, *J* = 10.1 Hz, H-4); ^{13} C NMR ($CDC1_3$, 22.5 MHz): δ 30.0, 31.8, 34.7, 100.7, 118.9, 121.2, 123.4, 125.7, 128.8, 134.5, 137.2, 161.7, 178.9, 196.2; EIMS: *m/z* (rel. int.) 242 (M^+, 29), 227 (100), 211 (11), 197 (3), 186(2), 185 (5), 141 (3), 128 (2), 92 (12); Found C, 78.65; H, 7.61% calcd. for $C_{16}H_{18}O_2$; C, 79.34; H, 7.43%.

We thank Sri G. Ganga Raju, Managing Director, Laila Impex for his encouragement, Prof. D. Bagchi, USA and Prof. V. Anjaneyulu, Andhra University for some of the spectral data and RSIC, CDRI, Lucknow for C, H-analysis.

Received 8 September 1999; accepted 8 March 2000
Paper 9/07209J

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