Indian Journal of Chemistry
Vol. 47B, September 2008, pp. 1447-1450

Note

The structure of Hantzsch coumarin

P Ramesh*, Anoop T Das, P Mohandass & R Nagasathya

Department of Natural Products Chemistry, School of Chemistry, Madurai Kamaraj University, Madurai 625 021, India

E-mail: npc_ramesh@yahoo.co.in

Received 15 November 2007; accepted (revised) 10 June 2008

The dimethyl dicoumarin prepared by Hantzsch and Zurcher has been characterized as 4,6-dimethyl-2*H*,8*H*-benzo[1,2-*b*:4,5-*b*']dipyran-2,8-dione by unambiguous synthesis of both angular (**2a**) and linear (**2b**) pyranocoumarins by Wittig reaction promoted by clay and comparing them with authentic Hantzsch coumarin prepared as described in literature. This is the first record of synthetic proof for the structure of Hantzsch coumarin.

Keywords: Dimethyl dicoumarin, Hantzsch coumarin, Wittig reaction

As early as 1871, Hantzsch and Zurcher[1] performed a double Pechmann condensation involving one mole of resorcinol and two moles of ethyl acetoacetate in the presence of conc. H_2SO_4 and obtained in low yield what they called dimethyl dicoumarin (Hantzsch coumarin) having either angular **2a** or linear **2b** structure (**Scheme I**).

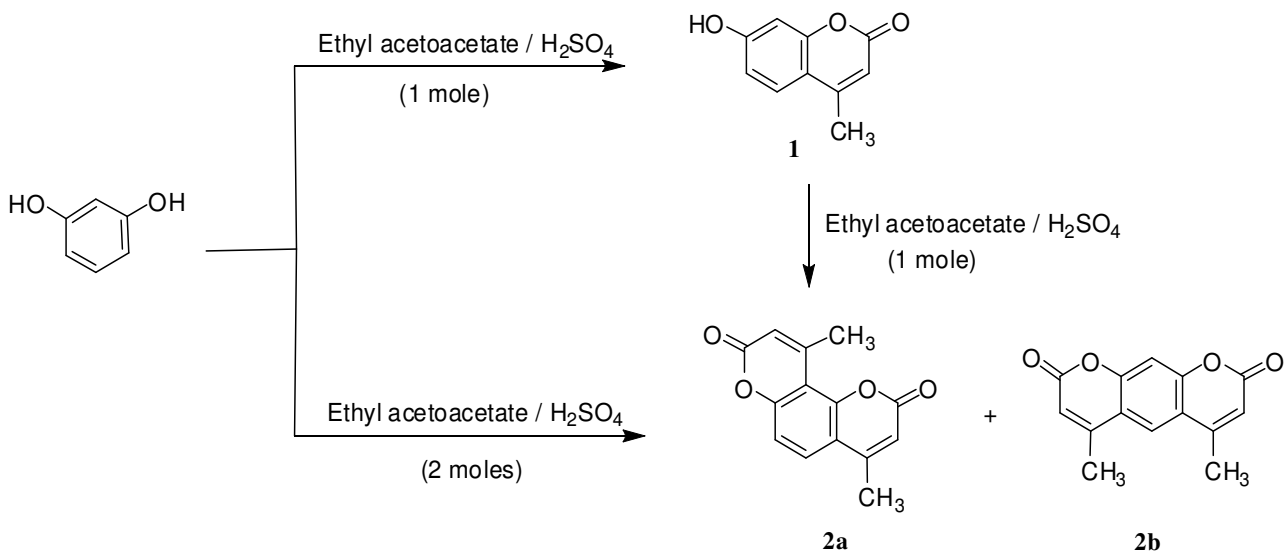
Sen and Chakravarthy[2] claimed to have prepared the same compound in 30% yield by condensing the 7-hydroxy-4-methylcoumarin **1** with one mole of ethyl acetate in the presence of conc. H_2SO_4. A choice between the structures **2a** or **2b** could not be made even by oxidation with $KMnO_4$. Later, Rangasamy and Seshadri[3] obtained a coumarino-α-pyrone by Pechmann condensation between resorcinol and ethyl acetoacetate in the presence of conc. H_2SO_4 and assigned an angular structure **2a** to it based on their earlier observation on the products of Pechmann reaction of 7-hydroxycoumarin and 7-hydroxy-4-methylcoumarin with malic acid for which they assigned angular structures. The constitution of these products as angular isomers was inferred from their synthesis from 7-hydroxycoumarin-8-aldehyde and 7-hydroxy-4-methylcou-marin-8-aldehyde by Perkin condensation.

Merchant *et al.*[4] reported the formation of a neutral substance during the reaction of 7-hydroxy-4-methylcoumarin **1** with ethyl acetate in the presence of conc. H_2SO_4; from its chemical and spectral data, the neutral compound was considered to have either angular or linear structure. Since the m.p. of this neutral compound was different from that of the so called angular pyranocoumarin reported by Rangasamy and Seshadri[3], a linear structure was tentatively assigned to it. The NMR spectrum of this product could not be recorded due to its low solubility in common deuterated solvents.

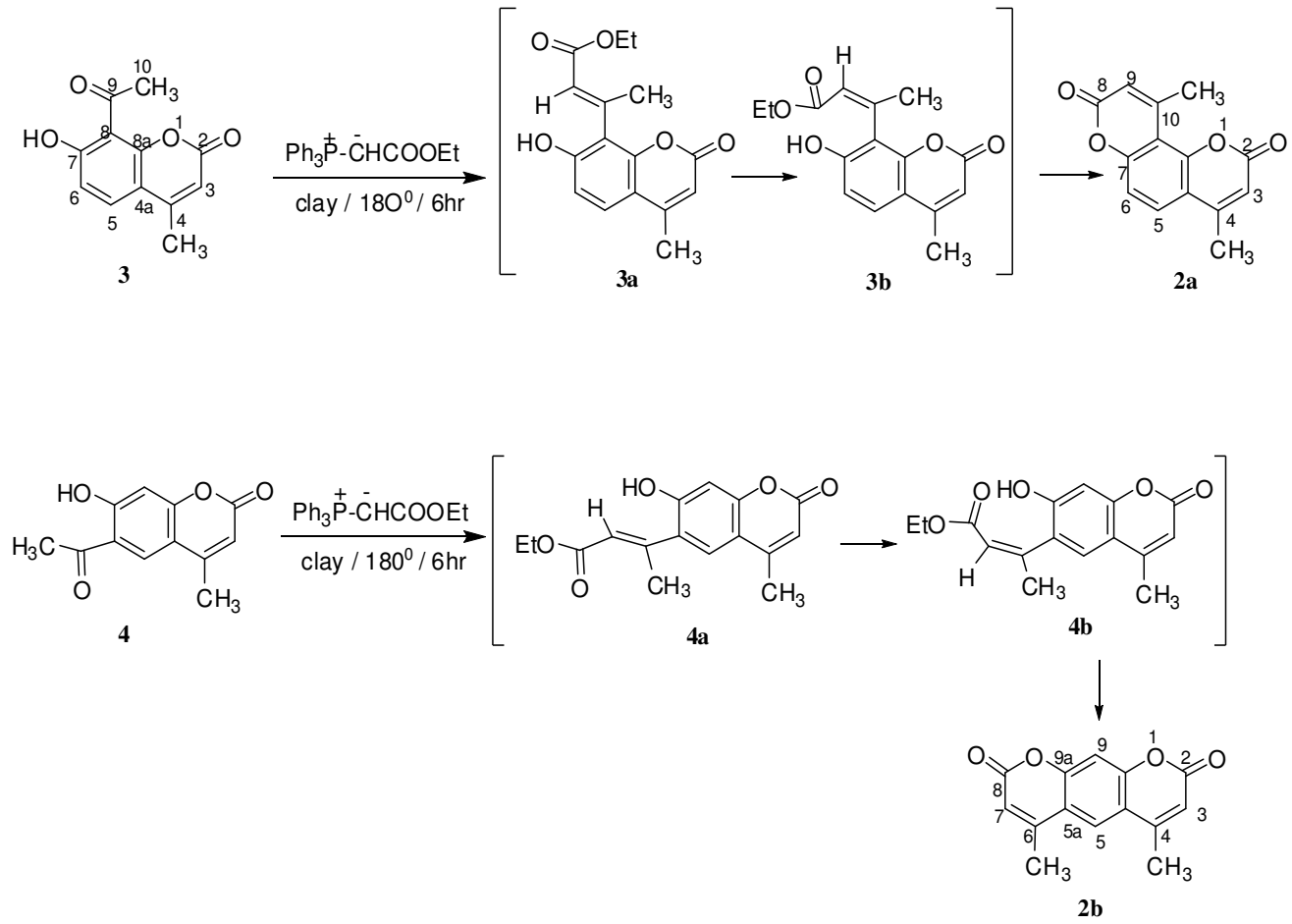
Osbrone[5] has suggested a linear structure for Hantzsch coumarin based on ^{1}H and ^{13}C NMR spectral evidence; however, no further evidence in support of the linear structure was put forward.

In order to settle the prevailing controversy on the structure of Hantzsch coumarin, the authors have unambiguously prepared both the angular **2a** and linear **2b** pyranocoumarins by Wittig reaction in the presence of clay (montmorillonite KSF as promoter, **Scheme II**) and compared them with an authentic sample of Hantzsch coumarin prepared as described in the literature[1]. It was found that it is the linear isomer **2b** that agreed in all respects (m.m.p., co-TLC and co-IR) with authentic Hanztsch coumarin. Hence, it is concluded that dimethyl dicoumarin (Hantzsch coumarin) is 4,6-dimethyl-2*H*,8*H*-benzo[1,2-*b*:4,5-*b*']dipyran-2,8-dione. This is the first record of synthetic proof for the structure of Hantzsch coumarin.

Both the synthesized isomers (angular **2a** and linear **2b**) were characterized beyond doubt by spectral methods (IR, ^{1}H NMR, ^{13}C NMR and MS). A comparative study of the spectral data of the starting materials, 7-hydroxy-8-acetyl-4-methylcoumarin **3** and 7-hydroxy-6-acetyl-4-methylcoumarin **4** and those of the products **2a** and **2b** revealed the absence of one proton signals for chelated hydroxyls (at δ 11.50 and 12.02) and acetylmethyl signals (at δ 2.83, 2.80 and 29.6, 29.0) in the ^{1}H and ^{13}C NMR spectra of the products, thus confirming the formation of the pyranocoumarin. The linear structure for **2b** is inferred from its ^{1}H NMR spectrum which exhibited two one proton singlets at δ 7.64 and 7.27 assigned to C-5 and C-9 protons respectively. The ^{13}C NMR spectrum of **2b** revealed only eight carbon signals in agreement with the symmetrical structure expected



Scheme I



Scheme II

for a linear isomer. Thus, based on the above spectral data, compound **2b** is characterized beyond doubt as 4,6-dimethyl-2*H*,8*H*-benzo[1,2-*b*:4,5-*b*']dipyran-2,8-dione.

It is interesting to note that Wittig reaction involving stabilized ylides usually yields the thermodynamically more stable *trans* olefins. For the cyclisation to give coumarin, the initially formed *o*-hydroxy-*trans*-α,β-unsaturated ester **4a** must undergo isomerisation to give the *cis* isomer **4b**. This isomerisation is usually effected either thermally or photochemically. Heating the reaction mixture above 200°C led to considerable decomposition of the material. In this context, it was found that use of montmorillonite KSF clay as promoter facilitated the formation of the coumarin even at oil bath temperature in 40% yield. With aldehydes, clay mediated coumarin formation by Wittig reaction was found to proceed even at water bath temperature[6]. In conclusion, clay catalysed Wittig reaction is an attractive method for the preparation of coumarins by Wittig reaction involving stabilised ylides.

Experimental Section

Melting points were determined on sulphuric acid bath and are uncorrected. Mass spectra were recorded on FINNIGANMAT 8430 mass spectrometer operating at an ionization potential of 70 eV. IR spectra were recorded on a Shimadzu IR 470 spectrometer. ^{1}H and ^{13}C NMR spectra were scanned on a 300 MHz Bruker (Avance) spectrometer operating at 300 and 75 MHz respectively.

8-Acetyl-7-hydroxy-4-methylcoumarin[7], 3: Yield 70%; m.p.148ºC (EtOH); UV-Vis (MeOH): 243, 311, 342, 371 nm; IR (KBr): 3210, 1715 (C=O of coumarin), 1620 (C=O of ketone), 1560, 1480, 1440, 1380, 1270, 980 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.45 (s, 3H, CH_3), 2.83 (s, 3H, -$COCH_3$), 6.07 (s, 1H, H-3), 6.87 (d, 1H, *J*=8.5Hz, H-6), 7.60 (d, 1H, *J*=8.5Hz, H-5), 11.50 (s, 1H, 7-OH); ^{13}C NMR ($CDCl_3$): δ 21.2 (4-CH_3), 29.6 (C-10), 112.5 (C-3 & C-6), 113.6 (C-4a), 117.4 (C-8), 132.6 (C-5), 149.3 (C-8a), 152.8 (C-4), 160.3 (C-7), 199.8 (C-9).

6-Acetyl-7-hydroxy-4-methylcoumarin,[8] 4: Yield 60%; m.p., 211ºC (EtOH); UV-Vis (MeOH): 257, 297, 342 nm; IR (KBr): 3300, 1720 (C=O of coumarin), 1650 (C=O of ketone), 1600, 1430, 1350, 1250, 950 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.57 (s, 3H, CH_3), 2.80 (s, 3H, -$COCH_3$), 6.22 (s, 1H, H-3), 6.86 (s, 1H, H-8), 8.00 (s, 1H, H-5), 12.02 (s, 1H ,7-OH); ^{13}C NMR ($CDCl_3$): δ 21.2 (4-CH_3), 29.0 (C-10), 109.0 (C-8), 112.0 (C-3), 113.6 (C-4a), 118.6 (C-6), 127.0 (C-5), 152.8 (C-4), 156.0 (C-8a), 160.3 (C-7), 199.8 (C-9).

General procedure for preparation of 2a and 2b

An intimate mixture is prepared by grinding separately, 8-acetyl-7-hydroxy-4-methylcoumarin **3** (0.01 mole) and 6-acetyl-7-hydroxy-4-methylcoumarin **4** (0.01 mole), carboethoxytriphenylphosphorane (0.01 mole) and montmorillonite KSF (thrice the weight of starting materials) in a preheated glass mortar. The mixture was then quickly transferred into a R.B. flask fitted with an air condenser provided with a $CaCl_2$ guard tube and heated on an oil bath at 180ºC for 6 hr. The reaction mixture was extracted with hot chloroform and the solvent evaporated. The resulting residue was purified by column chromatography over silica gel.

4,10-Dimethyl-2*H*,8*H*-benzo[1,2-*b*:3,4-*b*']dipyran-2,8-dione, 2a: Yield 45%; m.p. 246-48ºC (EtOH); UV-Vis (MeOH): 271, 291 nm; IR (KBr) : 1715 and 1690 (C=O of coumarin), 1580, 1430, 1310, 1260, 1170, 980 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.45 (s, 3H, CH_3), 2.80 (s, 3H,-CH_3), 6.20 (s, 1H, H-3 and H-9), 7.15 (d, 1H, *J*=9.0Hz, H-6), 7.60 (d, 1H, *J*=9.0Hz, H-5); ^{13}C NMR ($CDCl_3$): δ 21.2 (4- and 10-CH_3), 112.5 (C-3 and C-9), 117.8 (C-4a), 118.4 (C-6), 119.7 (C-8a), 126.4 (C-5), 145.9 (C-11), 149.0 (C-7), 152.8 (C-4 and C-10), 160.9 (C-2 and C-8); MS: *m/z* (%) 243 (M+1, 15), 242 ($M^{+\cdot}$, 100), 214 (M-CO,80), 215, 186 (214-CO), 185, 158 (186-CO), 157, 130 (158-CO), 127, 115.

4,6-Dimethyl-2*H*,8*H*-benzo[1,2-*b*:4,5-*b*']dipyran-2,8-dione, 2b: Yield 40%; m.p. >300ºC ($CHCl_3$); UV-Vis (MeOH): 221, 267, 300 nm; IR (KBr): 1760 and 1710 (C=O of coumarins), 1615, 1370, 1300,1130, 1210, 1045 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 2.30 (s, 3H, CH_3), 2.48 (s, 3H, -CH_3), 6.30 (s, 2H, H-3 and 7), 7.27 (s, 1H, H-9), 7.64 (s, 1H, H-5); ^{13}C NMR ($CDCl_3$): δ 24.6 (4- and 6-CH_3), 109.0 (C-3), 113.0 (C-9), 124.7 (C-5), 125.5 (C-4a), 150.0 (C-9a), 153.0 (C-4 and C-6), 162.0 (C-2 and C-8); MS: *m/z* (%) 243 (M+1, 15), 242 ($M^{+\cdot}$, 100), 214 (M-CO, 80), 215, 186 (214-CO), 185, 158 (186-CO), 157, 130 (158-CO), 127, 115.

Acknowledgement

The authors wish to thank Dr. V. Narayanan, former Professor and Head, Department of Natural Products Chemistry, School of Chemistry, MKU for

his interest in this work and NMR facility under IRHPA-DSA and GC-MS under UGC-DRS programmes for NMR and mass spectral data.

References

1 Hantzsch A & Zurcher H, *Ber Dtsch Chem Ges*, 20, **1887**, 1328.
2 Sen R N & Chakravarthi B, *J Indian Chem Soc*, 6, **1929**, 793.
3 Rangaswamy S & Seshadri T R, *Proc Indian Acad Sci*, 6A, **1937**, 112.
4 Merchant J R, Patel J R & Thakkur S M, *Indian J Chem*, 12, **1974**, 657.
5 Osborne A G, *Tetrahedron*, 9, **1983**, 1523.
6 Ramesh, unpublished results.
7 *Organic Synthesis Coll Vol* (John Wiley and Sons, London), 3, **1955**, 283.
8 Setna S & Ragini P, *Organic Reactions*, edited by A H Blatt & F C McGrew (John Wiley and Sons, London), VII, **1953**, 22.