Montmorillonite Clay Catalysis. Part 7.[1] An Environmentally Friendly Procedure for the Synthesis of Coumarins *via* Pechmann Condensation of Phenols with Ethyl Acetoacetate†

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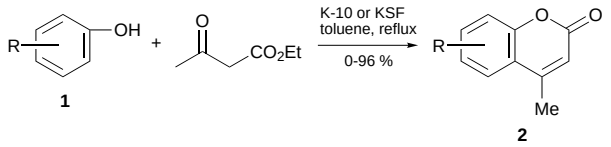
Coumarins are synthesised *via* Pechmann condensation of phenols with ethyl acetoacetate catalysed by montmorillonite clay in satisfactory yields; the scope and limitation of the method have been investigated.

Coumarins occupy a special place in the realm of natural and synthetic organic chemistry because many products which contain this subunit exhibit useful and diverse biological activity such as molluscacides,[2] have anthelmintic, hypnotic and insecticidal properties,[3] or serve as anticoagulant agents[4] or fluorescent brighteners.[5] These compounds can also be used for the synthesis of other products such as furocoumarins, chromenes, coumarones and 2-acylresorcinols.[6]

There have been many synthetic routes to the coumarins[7] including the Pechmann,[8] Perkin,[9] Knoevenagel,[10,11] Reformatsky[12] and Wittig[5,13] reactions. However, the Pechmann reaction has been the most widely applied method for preparing coumarins since it proceeds from very simple starting materials and gives good yields of coumarins substituted in either the pyrone or benzene ring or in both. The course of the reaction depends on the substituents on the phenol, on the catalyst used and on the nature of the β-oxo ester. The Pechmann reaction has been studied with homogeneous acid catalysts such as sulfuric, hydrochloric, phosphoric[8] and trifluoroacetic acid,[14] and with Lewis acids such as zinc chloride, iron(III) chloride, tin(IV) chloride, titanium chloride and aluminium chloride.[8] However, these conventional catalysts



1 2

Scheme 1

have to be used in excess, and they are subject to increasing environmental pollution and are non-recoverable. Consequently, there is a need for efficient and heterogeneous catalytic methods for this reaction by using inexpensive, easily handled and non-polluting catalysts. Cation-exchange resins,[15] Nafion-H,[16] zeolite-HBEA and other solid acids[17] have been employed for this purpose. More recently, microwave irradiation was applied to accelerate this reaction.[18]

Montmorillonite clays have been used as efficient catalysts for a variety of organic reactions.[19] They are inexpensive nontoxic powders which can be filtered easily from reaction mixtures and may be reused. However, syntheses of coumarins directly catalysed by montmorillonite clays have not been reported. In connection with our work on montmorillonite clays catalysis,[20] herein we describe an environmentally friendly procedure for the synthesis of coumarins *via* Pechmann reaction catalysed by montmorillonite K-10 and KSF.

As shown in Table 1, in the presence of montmorillonite clays, several phenols (**1a**, **1b 1f**) and ethyl acetoacetate were

Table 1 Synthesis of coumarin from phenols with ethyl acetoacetate catalysed by montmorillonite clays

Phenol	Coumarin substituents	Catalyst/solvent/ temp. (T/°)	t/h	Yield(%)[a]		Mp (T/°C)	
				Found	Lit.	Found	Reported
Resorcinol (**1a**)	4-Me-7-OH	K-10/none/150	4	96	90[16]	188–188.5	184[16]
		K-10/toluene/reflux	8	94			
		KSF/none/150	5	88			
		KSF/toluene/reflux	10	90			
Phloroglucinol (**1b**)	4-Me-5,7-$(OH)_2$	K-10/toluene/reflux	8	85	49.1[15]	284–285	284.5–285[15]
		KSF/toluene/reflux	8	88			
Pyrogallol (**1c**)	4-Methyl-7,8-$(OH)_2$	K-10/toluene/reflux	10	66	56[16]	234–235	233[16]
m-Cresol (**1d**)	4,7-Me_2	K-10/none/150	8	69[b]	25[16]	131.5–132	134[16]
		KSF/none/150	12	61[b]			
p-Cresol (**1e**)	4,6-Me_2	K-10/none/150	12	61[b]	0[14]	149–150	150–151[24]
α-Naphthol (**1f**)	4-Me-7,8-benzo	K-10/none/150	8	80	85[21]	170.5–171	170[21]
Phenol (**1g**)	4-Me	K-10/none/150	10	65[b]	3[22]	83–84	83–84[23]
2-Naphthol (**1h**)	4-Me-6,7-benzo	K-10/none/150	12	68[b]	20[25]	182–183	183[25]
2-Nitrophenol (**1i**)	no reaction	K-10/none-150	12	—[c]			
3-Nitrophenol (**1j**)	no reaction	K-10/none/150	12	—[c]			
4-Nitrophenol (**1k**)	no reaction	K-10/none/150	12	—[c]			
2-Chlorophenol (**1l**)	no reaction	K-10/none/150	12	—[c]			
2,4-Dichlorophenol (1**m**)	no reaction	K-10/none/150	12	—[c]			
Hydroquinone (**1n**)	no reaction	K-10/none/150	12	—[c]			
Salicylaldehyde (**1o**)	no reaction	K-10/none/150	12	—[c]			
4-Hydroxybenzaldehyde (**1p**)	no reaction	K-10/toluene/reflux	12	—[c]			
2-Aminophenol (**1q**)	no reaction	K-10/toluene/reflux	12	—[c]			
4-Aminophenol (**1r**)	no reaction	K-10/toluene/reflux	12	—[c]			
4-(4-Nitrophenylazo)orcinol (**1s**)	no reaction	K-10/toluene/reflux	12	—[c]			

[a]Isolated yield. [b]Net yield, conversion rate of **1d** = 15%, conversion rate of **1e** = 4%, conversion rate of **1g** = 7%, conversion rate of **1h** = 5%. [c]100% of starting materials were recovered.

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heated in the absence of solvent or in refluxing toluene to give the corresponding coumarins in high yields. Pyrogallol (**1c**) afforded a good yield, *m*-cresol (**1d**), *p*-cresol (**1e**), phenol (**1g**) and *β*-naphthol (**1h**) provided poor conversion rates whereas nitrophenol (**1i**, **1j** and **1k**), 2-chlorophenol (**1l**), 2,4-dichlorophenol (**1m**), hydroquinone (**1n**), salicylaldehyde (**1o**), *p*-hydroxybenzaldehyde (**1p**), *o*-aminophenol (**1q**), *p*-aminophenol (**1r**) and 4-(*p*-nitrophenylazo)orcinol (**1s**) all failed to afford the corresponding coumarins. From the experimental results, it can be proved that phenols having electron-donating substituents in the position *meta* to the phenol hydroxy group promote the condensation. The $+E$ effects of these substituents support formation of the reactive polarised carbonation in the *ortho* position. An alkyl group is not strong enough to furnish the activation needed and thus gives a low yield (**1d**). In contrast, electron-withdrawing groups inhibit the reaction.

Generally speaking, K-10 worked better than KSF in term of reaction time and yield. The optimum amount of the catalyst used was between 25 and 30% by weight of the total reactants. Catalysts were easily regenerated by washing with ethanol, followed by drying at 110 °C for 12 h. The catalyst K-10 and KSF could be reused four times in the reaction with **1a** without significant loss of activity.

In conclusion, the use of montmorillonite clays as heterogeneous catalysts is a viable alternative to existing procedures. Furthermore, this method is advantageous because of easy separation, consistent yield, minimal environmental effects and recyclability of the catalyst.

Experimental

Melting points are uncorrected. Montmorillonite K-10 and KSF were purchased from Fluka and dried at 100 °C prior to use. Ethyl acetoaceate and all liquid phenols were distilled before use. The products were characterized by their melting points and/or IR and ^{1}H NMR spectra and by comparison with their literature data.

General Procedure for the Synthesis of Coumarins.—A mixture of the phenolic compound **1** (5 mmol), ethyl acetoaceate (5 mmol) and montmorillonite K-10 (or KSF) (30 wt% to **1** and ethyl acetoacetate) was refluxed in toluene (10 ml) using a Dean–Stark apparatus to remove water (or heated at 150 °C for those reactions in the absence of solvent) with constant stirring for 4–12 h as indicated in Table 1. The reaction was monitored by TLC. The montmorillonite was filtered off and washed with hot ethanol (2×5 ml). The solvent was removed under reduced pressure to afford the crude product. The crude product was purified by column chromatography on silica gel [light peroleum (bp 60–90 °C)–ethyl acetate as eluent] to give the pure coumarin **2**, yield 0–96% (Table 1).

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References

1 Part 6, Z.-H. Zhang, F. Yang, T.-S. Li and C.-G. Fu, *Synth. Commun*., 1997, **27**, 3823.
2 A. Schonberg and N. Latif, *J. Am. Chem. Soc*., 1954, **76**, 6208.
3 A. Mitra, S. K. Misra and A. Patra, *Synth. Commun*., 1980, **10**, 915.
4 L. A. Singer and N. P. Kong, *J. Am. Chem. Soc*., 1966, **88**, 5213.
5 N. S. Narasimhan, R. S. Mali and M. V. Barve, *Synthesis*, 1979, 906.
6 S. M. Sethna and N. M. Shah, *Chem. Rev*., 1945, **36**, 1.
7 S. Wawzoek, in *Heterocyclic Compounds*, ed. R. C. Elderfield, Wiley, New York, 1951, vol. 2, p. 173.
8 S. Sethna and R. Phadka, *Org. React*., 1953, **7**, 1.
9 J. R. Johnson, *Org. React*., 1942, **1**, 210.
10 G. Jones, *Org. React*., 1967, **15**, 204.
11 G. Brufola, F. Fringuelli, O. Piermatti and F. Pizzo, *Heterocycles*, 1996, **43**, 1257.
12 R. L. Shirner, *Org. React*., 1942, **1**, 1.
13 R. S. Mali, S. N. Yeola and B. K. Kulkarni, *Indian J. Chem*., 1983, **22B**, 352.
14 L. L. Woods and J. Sapp, *J. Org. Chem*., 1962, **27**, 3703.
15 E. V. O. John and S. S. Israelstam, *J. Org. Chem*., 1961, **26**, 240.
16 D. A. Chaudhari, *Chem. Ind. (London)*, 1983, 568.
17 (*a*) A. J. Hoefnagel, E. A. Gunnewegh, R. S. Downing and H. van Bekkum, *J. Chem. Soc*., *Chem. Commun*., 1995, 225; (*b*) E. A. Gunnewegh, A. J. Hoefnagel, R. S. Downing and H. van Bekkum, *Recl. Trav. Chim. Pays-Bas*, 1996, **115**, 226.
18 V. Singh, J. Singh, K. Preet and G. L. Kad, *J. Chem. Res. (S)*, 1997, 58.
19 T.-S. Li and T.-S. Jin, *Youji Huaxue*, 1996, **16**, 385.
20 (*a*) T.-S. Li, Y.-T. Yang and Y.-L. Li, *J. Chem. Res. (S)*, 1993, 28; (*b*) T.-S. Li, H.-Z. Li, J.-L. Guo and T.-S. Jin, *Synth. Commun*., 1996, **26**, 2497; (*c*) T.-S. Li, S.-H. Li, J.-T. Li and H.-Z. Li, *J. Chem. Res. (S)*, 1997, 26; (*d*) T.-S. Li and S.-H. Li, *Synth. Commun*., 1997, **27**, 2299; (*e*) Z.-H. Zhang, T.-S. Li and C.-G. Fu, *J. Chem. Res. (S)*, 1997, 174; (*f*) T.-S. Li, Z.-H. Zhang and C.-G. Fu, *Tetrahedron Lett*., 1997, **38**, 3285; (*g*) A.-X. Li, T.-S. Li and T.-H. Ding, *Chem. Commun*., 1997, 1389.
21 A. Robertson, W. F. Sandrock and C. B. Hendng, *J. Chem. Soc*., 1931, 2426.
22 H. von Peckmann and C. Duisberg, *Ber. Dtsch. Chem. Ges*., 1883, **16**, 2119.
23 E. H. Woodruff, *Org. Synth*., 1944, **24**, 69.
24 R. N. Lacey, *J. Chem. Soc*., 1954, 854.
25 K. S. Murty, P. S. Rao and T. R. Seshadri, *Proc. Indian Acad. Sci*., 1937, **6A**, 316 (*Chem. Abstr*., 1938, **32**, 3362).