December 2009 Volume 5 Issue 4

Trade Science Inc.

Organic CHEMISTRY

An Indian Journal

Short Communication

OCAIJ, 5(4), 2009 [449-451]

EPZ 10 as a reusable heterogeneous catalyst for the synthesis of coumarins

Omprakash B.Pawar[1], Fulchand R.Chavan[2], Narayan D.Shinde[1,*]

[1]Department of Chemistry, Shri Chhatrapati Shivaji College, Omerga – 413 606, (INDIA)

[2]Department of Chemistry, Vasantrao Naik College, Aurangabad – 431 003, (INDIA)

E-mail: drnds09@rediffmail.com

Received: 21st August, 2009 ; Accepted: 31st August, 2009

ABSTRACT

Coumarins have been synthesized by one-pot two-component Pechmann condensation in the presence of the EPZ 10, as an effective catalyst in excellent yields. The reaction work up is simple and the catalyst can be easily separated from the product and reused in several times.

KEYWORDS

Coumarins;
Pechmann condensation;
Solvent-free reaction;
Envirocats;
Green chemistry.

INTRODUCTION

Coumarins continue to be investigated because of their importance to medicinal chemists due to a variety of biological activity. Associated with the coumarin scaffold are antibacterial[1a], antiviral[1b], anticancer[1c], activities as well as inhibition of platelet aggregation[2a], and inhibition of steroid 5a-reductase[2b]. Coumarins are used in drug and pesticidel preparations[3], they have also found applications as photosensitizers, fluorescent and laser dyes[4].

Coumarins have been synthesized by several routes including Pechmann[5a,b], Perkin[6], Knoevenagel[7], Reformatsky[8] and Wittig reactions[9a,b]. A valuable method for the synthesis of coumarins is the Pechmann reaction, of phenols using concentrated sulphuric acid as the catalyst[5a,b]. this process causes formation of by products, required long reaction times, and introduces corrosion problems. For these reasons, there have been several attempts in the literature to find alternative and environmentally benign synthesis routes. Various catalyst systems such as montmorillonite clay[10]. Alum[11]. nano-crystalline sulfated-zirconia[12], ionic liquid[13] and other solid acids[14a,b,cl] have been employed for these purpose in the Pechmann condensation. Although these methods are suitable for certain synthetic applications, many of these procedures are associated with one or more disadvantages such as corrosive reagents, long reaction times, harsh reaction conditions, unsatisfactory yield, tedious work-up procedure and recovery of catalyst was not possible during work up processes. Therefore, the search continues for a better catalyst for the synthesis of coumarins in terms of milder reaction conditions, better yields, free of organic solvents, easy synthetic procedure and reusability. Recently, significant progress has been made in the application of EPZ 10 in catalytic processes. EPZ 10 is recyclable solid acid catalyst[15], which is prepared by supporting $ZnCl_2$ on clay. EPZ 10 contains predominantly strong Lewis acid sites as well as weak Bronsted acid sites[16]. EPZ 10 has been used as a catalyst for Friedel-Crafts alkylation, aromatic bromination, benzylation[17].

Short Communication

EXPERIMENTAL

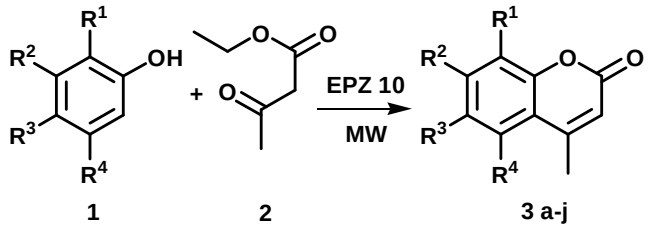
General consideration: Melting points were taken in open capillary and are uncorrected. ^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature on a 300 MHz Varian Inova Spectrometer in $CDCl_3$ using TMS as internal standard. Reactions were monitored by TLC on aluminum sheets recoated with silica gel $60F_{254.}$ A Whirlpool, (800T, 2450Mz) domestic microwave oven was used for all the experiments. Column chromatography was performed using silica gel (60-120 mesh size). All the products are known compounds and characterized by comparing there IR, ^{1}H NMR, ^{13}C NMR and melting point with those reported in literature.

Typical procedure for the synthesis of 7-hydroxy-4-methyl-2*H*-chromen-2-one (3a): A mixture of resorcinol (10 mmol) and ethyl acetoacetate (10 mmol) in the presence of EPZ 10 (10 % w/w) was irradiated in microwave oven for 1.5 min. The reaction was monitored by TLC. After completion of the reaction, the mixture was diluted with ethyl acetate (5 mL); the catalyst was filtered off and washed with ethyl acetate (3×5 mL). The combined filtrates were concentrated under reduced pressure to afford the crude product **(3a)**, which was further purified by column chromatography (silica gel) with ethyl acetate and n-hexane as the eluent.

RESULTS AND DISCUSSION

Herein we report the synthesis of coumarins **(3)** promoted by the EPZ 10 catalysts under microwave irradiation, in excellent yield with shorter reaction time.

In the present work, we achieved a one-pot two-component condensation of phenol **(1)** ethyl acetoacetate **(2)** in the presence of EPZ 10 under the influence of microwave irradiation as a new efficient method to produce coumarins **(3)** (Scheme 1). Encouraged by this success, we extended the reaction of ethyl acetoacetate with a range of other substituted phenol under similar conditions. The optimized results are summarized in TABLE 1.



Scheme 1

TABLE 1: EPZ 10 catalyzed synthesis of coumarins (3a-j)

Entry	R^1	R^2	R^3	R^4	Product	Time Min	Yield (%)[a]
1	H	OH	H	H	3a	1.5	96
2	H	OH	H	OH	3b	2	94
3	OH	H	H	H	3c	2	85
4	OH	OH	H	H	3d	2	94
5	CH_3	OH	H	H	3e	2.5	88
6	H	OH	H	CH_3	3f	2.5	89
7	H	CH_3	H	H	3g	2	84
8	H	NH_2	H	H	3h	3	78
9	H	OMe	H	H	3i	2	90
10	H	H	OMe	H	3j	2	86

[a]**Isolated yields**

The reaction proceeds cleanly without formation of side product. The protocol of the process offers advantages in terms of simple procedure and work up, mild reaction conditions and excellent yields. The EPZ 10 catalyst used for reaction was recovered and reused with identical results. Thus, the recyclability was confirmed (TABLE 2). As shown in TABLE 3, the reaction of resorcinol and ethyl acetoacetate also carried out in the presence of protic solid acid (Montmorillonite K 10), liquid acid (H_2SO_4) and Lewis acid ($ZnCl_3$). The best yield was obtained with EPZ 10.

TABLE 2: EPZ 10 catalyst recovered in synthesis of coumarins (3a, 3j)

Entry	R^1	R^2	R^3	R^4	Product	Yield (%)[a]		
						Cycle 1	Recycle 1	Recycle 2
1	H	OH	H	H	3a	96	94	93
2	H	H	OMe	H	3j	86	85	83

[a]**Isolated yields.**

TABLE 3: Activity of catalysts in the synthesis of 7-hydroxy-4-methyl-2*H*-chromen-2-one (3a)

Entry	Catalyst	Reaction time	Yield (%)[a]
1[b]	--------	30 min.	Trace
2	H_2SO_4	10 min.	64
3	$ZnCl_2$	7 min.	88
4	Montmorillonite K 10	3 min.	78
5	EPZ 10	1.5 min.	96

[a]**Isolated yields.** [b]**In the absence of the catalyst**

To illustrate the need of the EPZ 10 for these reactions an experiment was conducted in the absence of EPZ 10. The yield in this case was trace after 30 min (TABLE 3, Entry 1). Obviously, EPZ 10 is an important component of the reaction.

CONCLUSION

In summary, we introduced a mild, convenient, and efficient method for the synthesis of coumarins by the reaction of phenol with β-ketoester using EPZ 10 as recyclable solid catalyst. The simple experimental procedure, short reaction time, mild reaction condition, and ease of recovery and reuse of catalyst are advantages of this method.

ACKNOWLEDGEMENTS

The authors are thankful to Dr. M. S. Shingare, Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad – 04. India. for encouragement during the process of carrying out this work and Prof. S. R. Pokharkar, Head, Department of Chemistry, Modern College, Shivajinagar, Pune - 05. India for providing the laboratory facility.

REFERENCES

[1] **(a)** A.Maxwell; Mol.Microbial., **9**, 681 **(1993)**.
(b) D.E.Zembower, S.Liao, M.T.Flavin, Z.-Q.Xu, T.L.Stup, R.W.Jr.Buckheit, A.Khilevich, A.A.Mar, A.K.Sheinkman; J.Med.Chem., **40**, 1005 **(1997)**.
(c) C.-J.Wang, Y.-J.Hsieh, C.-Y.Chu, Y.-L.Lin, T.-H.Tseng; Cancer Lett., **183**, 163 **(2002)**.

[2] **(a)** G.Cravotto, G.M.Nano, G.Palmisana, S.Tagliapietra; Tetrahedron: Asymmetry., **12**, 707 **(2001)**.
(b) G.M.Fan, W.Mar, M.K.Park, E.W.Choi, K.Kim, S.Kim; Bioorg.Med.Chem.Lett., **11**, 2361 **(2001)**.

[3] W.C.Meuly; 'Kirk – Othmer Encyclopedia of Chemical Technology', 3rd Ed., John Wiley and Sons; New York, **(1979)**.

[4] A.R.Katritzky, C.W.Rees, E.F.Scriven; 'Pyran and their Benzoderivatives Synthesis', 5th Ed., Pergamom Press, **(1996)**.

[5] **(a)** H.Von Pechmann, C.Duisberg; Ber.Dtsch.Chem.Ges., **16**, 2119 **(1883)**.
(b) H.Von Pechmann; Ber.Dtsch.Chem.Ges., **17**, 929 **(1884)**.

[6] J.R.Johnson; Org.React., **1**, 210 **(1942)**.

[7] G.Jones; Org.React., **15**, 204 **(1967)**.

[8] R.L.Shriner; Org.React., **1**, 1 **(1942)**.

[9] **(a)** W.M.Abdou, N.A.F.Ganoub, N.M.Abdel-Rahman; Phosphorus Sulphur Relat.Elem., **61**, 91 **(1991)**.
(b) J.Yavari, R.Hekmat-Shoar, A.Zonouki; Tetrahedral Lett., **39**, 2391 **(1998)**.

[10] S.Frere, V.Thiery, T.besson; Tetrahedron Lett., **42**, 2791 **(2001)**.

[11] Dabiri, Minnoo, Baghbanzadeh, Mostafa, Kiani, Shadi, Vakilzadeh, Yasimin; Chemical Monthly., **138**, 99 **(2007)**.

[12] B.Tyagi, M.K.Mishra, R.V.Jasra; J.Mol.Catal.A: Chem., **286**, 41 **(2008)**.

[13] M.K.Potdar, S.S.Mohite, M.M.Salunkhe; Tetrahedron Lett., **42**, 9285 **(2001)**.

[14] **(a)** L.L.Woods, J.Sapp; J.Org.Chem., **27**, 3703 **(1962)**.
(b) S.P.Chavan, K.Shivasankar, R.Sivappa, R.Kale; Tetrahedron Lett., **43**, 8583 **(2002)**.
(c) V.Alexander, R.P.Bhat, S.D.Samant; Tetrahedron Lett., **46**, 6957 **(2005)**.

[15] Envirocats catalysts are available from Contract Chemicals. England (www.contract-chemicals.com).

[16] S.J.Barlow, T.W.Bastock, J.H.Clark, S.R.Cullen; Tetrahedron Lett., **34**, 3339 **(1993)**.

[17] C.O.Kappe; J.Org.Chem., **62**, 7201 **(1997)**.