Chemistry International 3(3) (2017) 240-243

International Scientific Organization
http://iscientific.org/
Chemistry International
www.bosaljournals.com/chemint/

Efficient synthesis of biscoumarins using zinc acetate as a catalyst in aqueous media

Vishvanath D. Patil, Ketan P. Patil, Nagesh R. Sutar* and Prathamesh V. Gidh*

Organic Chemistry Research Laboratory, Department of Chemistry, C.K.Thakur A.C.S. College New Panvel, Raigad, Maharashtra, India
*Corresponding author's E. mail: ketanpatil999@rediffmail.com

ARTICLE INFO

Article type:
Research article
Article history:
Received June 2016
Accepted December 2016
July 2017 Issue
Keywords:
bis-(4-hydroxycoumarin)methanes
Zinc acetate
Aldehyde
Aqueous media

ABSTRACT

Bis-(4-hydroxycoumarin)methanes derivatives (**1-9)** were synthesized via one pot condensation reaction of various aromatic aldehyde and 4-hydroxycoumarin using zinc acetate as a catalyst in presence of water as a solvent. This mediated reaction of various aromatic and hetero-aromatic aldehydes using catalytic amounts of zinc acetate avoids the use of expensive, corrosive reagents, toxic solvents and provides operational simplicity.

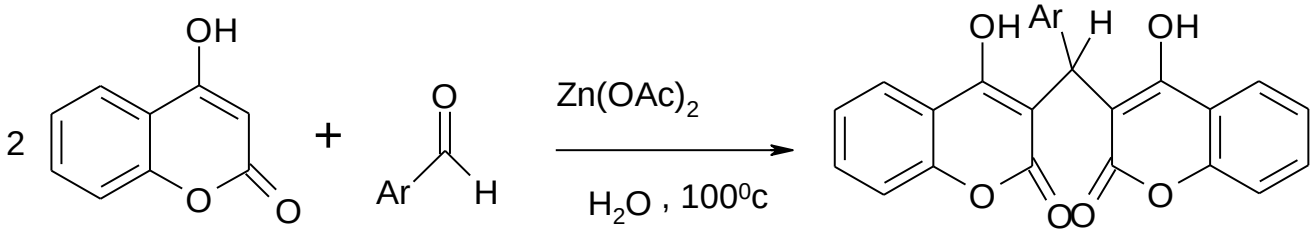
Capsule Summary: bis-(4-hydroxycoumarin)methanes derivatives were synthesized via one pot condensation reaction of various aromatic aldehyde and 4-hydroxycoumarin using zinc acetate as a catalyst in aqueous media.

Cite This Article As: Vishvanath D. Patil, Ketan P. Patil, Nagesh R. Sutar and Prathamesh V. Gidh. Efficient synthesis of biscoumarins using zinc acetate as a catalyst in aqueous media. Chemistry International 3(3) (2017) 240-243.

INTRODUCTION

Heterocyclic compounds with oxygen containing moieties are industrially very important as they serve as precursors. Coumarin **1** derivatives are biologically active chemical compounds found in many plants, notably in high concentration in the tonka bean, woodruff and bison grass (Hinman et al., 1956) and they have various biological activities such as anticoagulant, insecticidal, antihelminthic, hypnotic, antifungal, phytoalexinand as HIV protease inhibiters (Lee et al., 2007; Raghunathan et al., 2007; Burke et al., 1997) Several biscoumarins **3** were isolated from plants[5-11]. (Murray, 1995; Banerji et al., 1998, Riaz and Malik, 2001abc; Franke et al., 2002; Hao et al., 2003).Dimeric coumarin derivatives (phebalin, thamnosin, toddasin) were also identified from Rutacea and synthesized through expedites method (Smyth et al., 2000).Coumarin and its derivatives are widely used as additives to food, cosmetics, and optical brightening agents(Thomes, 1997; Zahradnik 1992). Although various procedures are reported for the synthesis of bis-(4-hydroxycoumarin)methanes, disadvantages including low yields, prolonged reaction time, use of an excess of reagents or catalysts, and use of toxic organic solvents necessitate the development of an alternative route for their simple and economic synthesis.

In continuation of our on-going research for the development of simple and efficient methods for the synthesis of various heterocyclic compounds(Kokare et al., 2007; Bahekar and Shinde, 2004), herein we wish to report a



1 **2** **3**

Scheme I: Synthesis of bis-(4-hydroxycoumarin)methanes (**3**) using 4-hydroxycoumarin (**1**) and aromatic ketone (**2**).

Table 1: Investigation of catalytic effect of anhy. $Zn(OAc)_2$ on synthesis of bis-(4-hydroxycoumarin)methanes

Entry	Anhydrous Zn(OAc)2	Time	Yield[b]
	mmol	min	%
1	0.01	45	52
2	0.05	40	58
3	0.1	45	98
4	0.2	40	98

[b]Isolated yields

simple, economic, and efficient one-pot method for the synthesis of bis-(4-hydroxycoumarin)methanes **1-9** in water using Zinc acetate as the catalyst.

MATERIAL AND METHODS

Chemical and reagents

All reagents were purchased from Merck and Loba and used without further purification. The reaction was monitored by TLC using 0.25 mm E-Merck silica gel plates, which were visualized in Iodine Chamber. Melting points were taken in open capillaries. ^1H NMR in d_6 on 300 MHz using TMS as internal standard.

General procedure for synthesis of bis-(4-hydroxycoumarin)methanes

A mixture of 4-hydroxycoumarin (2 mmol), aromatic and heteroaromatic aldehydes (1 mmol), and Zinc acetate (0.1mmol) in 25 ml of water was stirred under heating at 100^0C for the appropriate time mentioned in Table 2. The completion of reaction was monitored by Thin Layer Chromatography System, solvent system ethyl acetate: hexane (4:6). After completion of the reaction, the reaction mixture was cooled and poured over ice water (50 ml). The solid crude product, which separated out, was filtered, washed with water and dried to give the desired compound.

RESULTS AND DISCUSSION

The optimum condition for the synthesis of bis-(4-hydroxycoumarin)methanes derivatives **3** was established by considering a reaction between benzaldehyde **2** and 4-hydroxycoumarin **1** as model reaction. It was performed in the presence of anhydrous Zn $(OAc)_2$ as a catalyst by using water as a solvent **(Scheme 1).**

It was observed that catalyst concentration also plays a vital role in the synthesis of bis-(4-hydroxycoumarin) methanes. After varying the concentration of $Zn(OAc)_2$, we got optimum yield with 0.1mmol of catalyst. On further increasing the amount of catalyst, the yield of corresponding product remain same.

Thus, the most appropriate loading amount for anhydrous $Zn(OAc)_2$ as a catalyst was found to be 0.1 mmol as per results summarized in Table 1.

In order to understand the wide utility of Zinc acetate, the optimized system was used for the synthesis of a variety of bis-(4-hydroxycoumarin)methanes (Table 2). Having established reaction conditions, various aldehydes reacted smoothly with 4-hydroxycoumarin under similar reaction conditions to afford the corresponding bis-(4-hydroxycoumarin)methanes derivative in good to excellent yields in relatively short reaction times (entries 1-9 Table 2). It should be noted that this method is suitable for the preparation of bis-(4-hydroxycoumarin)methanes derivatives with electron donating (entries 2, 3, 5, 6, Table 2) as well as electron withdrawing (entries 4 Table 2) and heteroaromatic aldehydes (entries 7-9, Table 2) and 4-hydroxycoumarin derivatives with fine results.

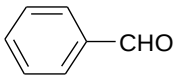
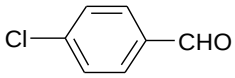
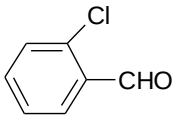
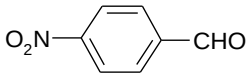
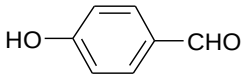
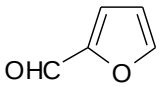
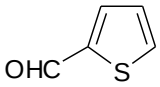
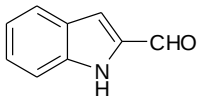
The categorization data of various (1H NMR, Infrared and Mass spectroscopy) achieved for various representive compounds are given below

3-((phenyl)(4-hydroxy-2-oxo-2H-chromen-3-yl)methyl)-4-hydroxy-2H-chromen-2-one (3a)

IR (KBr) 3057, 1676, 1608, 1568, 1492, 1350, 759 cm^{-1}; ^1H NMR ($CDCl_3$): δ (ppm) = 11.53 (s, 1H, OH), 11.32 (s, 1H, OH), 8.09-7.24 (m, 13H, 13 × CH), 6.11 (s, 1H, CH).

3-((4-chloro-phenyl)(4-hydroxy-2-oxo-2H-chromen-3-yl)methyl)-4-hydroxy-2H-Chromen-2-one (3b)

Table 2: Synthesis of bis-(4-hydroxycoumarin)methanes catalysed by zinc acetate[a]

Entry	Aldehydes	Product[b]	Time (min)	Yield[c] (%)	M.P. (^{0}C)	
1		3a	25	98	228-230[r*]	226-228[f*]
2		3b	20	98	252-254	254-256
3		3c	35	90	224-226	224-226
4		3d	15	98	232-234	236-237
5		3e	30	94	224-224	220-224
6		3f	25	96	242-244	244-246
7		3g	25	95	202	199-201
8		3h	20	94	210	212
9		3i	25	93	240-242	241

[a]Aldehyde (1 mmol),4-hydroxycoumarin (2mmol) and Zn(OAc)2 (0.1 mmol) water (25ml) was stirred magnetically at 100 ^{0}C, [b]All products were identified by their IR and 1H NMR spectra, [c]Isolated Yield, r* reported and f* found (recorded in present investigation)

IR (KBr) 3076, 1668, 1602, 1566, 1491, 1450, 1350, 1270, 1215, 767 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ (ppm) = 11.54 (s, 1H, OH), 11.32 (s, 1H, OH), 8.09-7.17 (m, 12H, 12 × CH), 6.04 (s, 1H, CH).

3-((2-chloro-phenyl)(4-hydroxy-2-oxo-2H-chromen-3-yl)methyl)-4-hydroxy-2H-chromen-2-one (3c)

IR (KBr) 3057, 2719, 1660, 1568, 1494, 1437, 1352, 1309, 758 cm$^{-1;}$ ^{1}H NMR ($CDCl_3$): δ (ppm) = 11.63 (s, 1H, OH), 10.93 (s, 1H, OH), 8.03-7.22 (m, 12H, 12 × CH), 6.14 (s, 1H, CH).

3-((4-methoxy-phenyl)(4-hydroxy-2-oxo-2H-chromen-3-yl)methyl)-4-hydroxy-2H-chromen-2-one (3d)

IR (KBr) 3070, 3001, 1668, 1604, 1466, 1510, 1452, 1352, 1309, 1259, 769 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ (ppm) = 11.5 (s, 1H, OH), 11.29 (s, 1H, OH), 8.05-6.87 (m, 12H, 12 × CH), 6.05 (s,1H,CH), 3.80 (s, 3H, CH_3O).

3-((2-methoxy-phenyl)(4-hydroxy-2-oxo-2H-chromen-3-yl)methyl)-4-hydroxy-2H-chromen-2-one (3e)

IR (KBr) 3076, 1666, 1604, 1568, 1487, 1454, 1350, 763 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ (ppm) = 11.58 (s, 1H, OH), 11.28 (s, 1H, OH), 8.05-6.77 (m, 12H, 12 × CH), 6.08 (s, 1H, CH), 3.75(s,3H,CH_3O).

3-((4-nitro-phenyl)(4-hydroxy-2-oxo-2H-chromen-3-yl)methyl)-4-hydroxy-2H-chromen- 2-one (3f)

IR (KBr) 3080, 1660, 1616, 1600, 1566, 1518, 1450, 1348, 765 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ (ppm) =11.57 (s, 1H, OH), 11.37 (s, 1H, OH), 8.22-7.26 (m, 12H, 12 × CH), 6.13 (s, 1H, CH).

3-((4-hydroxy-phenyl)(4-hydroxy-2-oxo-2H-chromen-3-yl)methyl)-4-hydroxy-2H-chromen-2-one (3g).

IR (KBr) 3452, 3072, 1668, 1608, 1566, 1514, 1433, 1348, 1307, 763 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ (ppm) = 11.49 (s, 1H, OH), 11.29 (s, 1H, OH), 8.05-6.77 (m, 12H, 12 × CH), 6.04 (s, 1H, CH), 3.73 (q, 3H, OH)

3-((3,4,5-trimethoxy-phenyl)(4-hydroxy-2-oxo-2H-chromen-3-yl)methyl)-4-hydroxy-2H-chromen-2-one (3h).

IR (KBr) 3072, 3003, 1662, 1618, 1602, 1566, 1508, 1450, 1348, 1126, 761 cm^{-1}; ^1H NMR ($CDCl_3$): δ (ppm) =11.55 (s, 1H, OH), 11.28 (s, 1H, OH), 8.04-6.42 (m, 10H, 10 × CH), 6.07 (s, 1H, CH), 3.85-3.72 (s, 9H, 3 × CH_3O).

CONCLUSIONS

Results revealed that zinc acetate is a highly efficient catalyst for the synthesis of bis-(4-hydroxycoumarin) methanes derivatives by using various substrates as aldehyde and 4-hydroxycoumarin in presence of water as a solvent. The advantages include low cost, ease of catalyst handling, requirement of a very small amount of catalyst as 0.1 mmol and remarkable selectivity under mild and neutral conditions of this commercially available inexpensive catalyst is an attractive feature of this method.

ACKNOWLEDGEMENTS

The authors acknowledged the partial support of this work by Prof. B. P. Bandgar, Ex. Vice Chancellor, University of Solapur, India and Dr. G. A. Meshram, Associate Professor, Department of Chemistry, University of Mumbai, India. The authors are thankful to Dr. S. T. Gadade, Principal, C. K. Thakur ACS College for providing laboratory and other facilities.

REFERENCES

Lee, J.H., Bang, H.B., Han, S.Y., Jun, J.G., 2007, An efficient synthesis of (+)-decursinol from umbelliferone, Tetrahedron Letters 48, 2889.

Manian, R.D.R.S., Jayashankaran, J., Raghunathan, R., 2007, A rapid access to indolo[2,1-a] Pyrolo[4',3':4,5] pyrano[5,6,-C] Coumarin/[6,5,-C] derivatives by domino knovenagal intramolecular heteroDiels-Alder reactions, Tetrahedron Letters 48, 1385.

Zhao, H., Neamati, N., Hong, H., Mazumder, A., Wang, S., Sunder, S., Milne, G.W.A., Pommier, Y., Burke, T.R., 1997, Coumarin based inhibitors of HIV integrase, Journal of Medicinal Chemistry 40, 242.

Murray, R.D.H., 1995, Coumarins, Natural Product Reports 12, 477.

Banerji, J., Saha, M., Mukherjee, P., Mondal, S., Joshi, P.C., 1998, A new dimeric coumarin from boenninghausenia albiflora Reichband Meissner (Rutaceae), Indian Journal of Chemistry 37B, 523.

Riaz, M., Malik, A., 2001a, Novel Coumarin glycosides from Daphne oleoides, Helvetica Chimica Acta 84, 656.

Riaz, M., Malik, A., 2001b, Structure determination of daphjamilin, a new biscoumarin glycoside by NMR spectroscopy, Magnetic Resonance in Chemistry 39, 641.

Riaz, M., Malik, A., 2001c, Daphsaifnim admeric Coumarin glycoside from Daphne oleoides, Heterocycles 55, 769.

Franke, K., 2002, Flavone-coumarin hybrids from Gnidia socotrana, Journal of Phytochemistry 61, 873.

He, H.P., Chen, S.T., Shen, Y.M., Zhao, Y.B., Hao, X., 2003, A novel dimeric coumarin from clausena lenis, Chinese Chemical Letters 14, 1150.

Concannon, S.M., Ramachandran, V.N., Smyth, W.F., 2000, A study of the homonuclear Diels-Alder dimerizations of hydroxybutenyl and pentadienyl Coumarins, Tetrahedron Letters 41, 9909.

Okenne, R., Thomes, R.D., 1997. Coumarins. Biology application and modes of action. Wiley & Sons.

Zahradnik, M., 1992, Comarins: Biology, applications and mode of action. Wiley & Sons.

Kokare, N.D., Nagawade, R.R., Rane, V.P., Shinde, D.B., 2007. The production and application of flouorescent brightening agent, Synthesis 4, 766-772.

Bahekar, S.S., Shinde, D.B., 2004, Samarium(III) catalysed one-pot construction of Coumarin. Tetrahedron Letters 45, 7999-8001.