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A Facile an Efficient Synthesis of Coumarin Derivatives via Pechmann Condensation under Grind-Stone Method Using Succinamide-N-Sulphonic Acid at Room Temperature

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ABSTRACT

A rapid and efficient solvent free synthesis of coumarin derivatives by Pechmann condensation reactions of substituted phenols with β-keto ester using succinamide-N-sulphonic acid (SuSA) as a catalyst under grinding techniques. Key advantages of this grinding method includes short reaction time, eco-friendly, good to excellent yield, non toxic and easy to handle.

Keywords: Coumarin, solvent free, SuSA, grinding technique.

I. INTRODUCTION

Coumarin is oxygen containing heterocyclic compound which are the parent chemical structure for a class of phytochemicals naturally occur in various plant species. Coumarin are represents the core structure of several molecules of pharmaceutical importance, such as novobiocin, coumaromycin and chartesium. The structural diversity found in this family of compounds led to the division into different categories, from simple coumarins to many other kinds of polycyclic coumarins, such as furocoumarins and pyranocoumarins. Simple coumarin is better known for the resemblance of its aroma to that of the vanilla [1]. Thus, the synthesized or artificially prepared coumarins have been mainly used in the manufacture of fragrances and essences. Nowadays, coumarins are considered to be a significant group of organic compounds.

They are associated with various biological activities viz. antiviral [2, 3], antibacterial [4, 5], antimicrobial [6], anticoagulant [7], anti-inflammatory [8, 9], anticancer [10, 11], anticonvulsant [12], antioxidant [13], antifungal [14, 15], and anti-HIV [16]. They also possess the properties like inhibition of platelet aggregation [17] and inhibition of steroid 5α-reductase [18]. Besides, they are attracting consider-able attention of chemists due to their wide range of applications such as optical brighteners [19], photosensitizers [20], fluorescent and laser dyes [21], and additives [22] in food, perfumes, cosmetics, and pharmaceuticals. The novel compounds are also utilized in drug and pesticidal preparations [23] considering these multifarious activities of coumarins, synthetic chemists are actively engaged in developing

new and superior methods for the isolation of coumarin derivatives. The most widely used method for their synthesis is Pechmann reaction [24–27], which involves the condensation between phenols and β-keto esters, in the presence of an acid catalyst. This method employs both homogeneous catalysts such as concentrated H_2SO_4[24, 25] etc

II. METHODS AND MATERIAL

All chemicals were purchased from Merck, Aldrich, or Spectrochem Chemical Companies and were used without further purification. Products were characterized by their physical constants and comparison with reported samples. The purity of the substrates and reaction monitoring were performed by thin-layer chromatography (TLC). In all the cases, ^{1}H NMR spectra were recorded with a Bruker Avance 400 MHz instrument. All chemical shifts are given in parts per million (ppm) relative to TMS using a deuterated solvent.

Preparation Succinimide-N-sulfonic acid:

SuSA was easily prepared by addition of an equivalent amount of cholorosulfonic acid to succinimide[28].

General procedure for the synthesis of coumarins:

A mixture of substituted phenols (1 mmol) and ethyl acetoacetate (1 mmol) was ground with succinamide-N-sulphonic acid (15 mol %) in a mortar by pestle for few minutes until the color of the reaction mixture has been taken place. The reaction mixture was kept at room temperature for half hours. The completion of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was poured into the ice cold water. The solid separated out was filtered, washed with water and recrystallized from ethanol to afford compound.

Characterization of compounds:

7-hydroxy-4-methyl-2H-1-benzopyran-2-one (Table 2, Entry 1)

IR (KBr): 3280 (OH), 1715 (C=O), 1380 (C-CH_3) ^{1}HNMR ($CDCl_3$) : 2.35 (s, 3H, C4 - CH_3); 6.04 (s, 1H, C3 - H); 6.78 (s, 1H, C8 - H); 6.81 (d, J = 8.5 Hz, 1H, C5 -H), 7.52 (d, J = 8.5 H z, 1H, C6-H

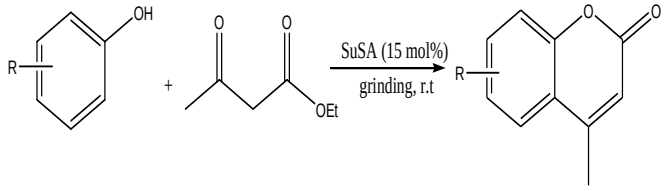
5, 7 - dihydroxy-4 methyl-2H-1- benzopyran-2-one (Table 2, Entry 2)

IR (KBr): 3320 (OH), 1690 (C = O), 1375 (C-CH_3) ^{1}HNMR ($CDCl_3$): 2.38 (s, 3H, C4 -CH_3); 6.01 (s, 1H, C3 -H) 6.65 (s, 1H, C8 -H); 6.75 (s, 1H, C6 -H)

III. RESULT AND DISCUSSION

To explore the SuSA used as the catalyst for the synthesis of coumarin derivatives. At the initially of this study, resorcinol and ethyl acetoacetate (EAA) were employed as model reaction. The model reaction was tried out using different concentration of catalyst under grinding technique as well as the solvent-free system. The results are summarized in Table 1. During this study, we have observed that yield of the product decreases with decreasing the amount of catalyst. When 15 mol% catalyst was added, the reaction yield was 86% (Table 1, entry 4), and when 10 mol% catalyst was added, the reaction yield decreased to 65% (Table 1, entry 3). Interestingly, no reaction took place in the absence of catalyst after 45 min (Table 1, entry 1). After this study, we observed that, 15 mol% catalysts proved to be an efficient catalyst to carry out the reaction smoothly.The Pechmann condensation reaction of substituted phenols and ethyl acetoacetate in the presence of SuSA was accomplished under the optimized reaction conditions (Scheme 1).

Encouraged by these results, we build the generality of reaction the reaction worked well with phenols containing electron-donating and electron-withdrawing substituents on the aromatic ring.



Scheme 1 synthesis of coumarin derivatives in presence of SuSA under grinding techniques

Table 1 Optimization of the catalyst[a]

Entry	Catalyst (mol %)	Yield[b] %
1	---	No reaction
2	5	35
3	10	65
4	15	86
5	20	86

[a]**Reaction Condition:** Resorcinol (1 mmol), ethyl acetoacetate (1 mmol) in presence of 15 mol% SuSA under grinding technique. [b]Isolated Yield.

Table 2 synthesis of coumarin derivatives in the presence of SuSA under solvent-free conditions.[a]

Entry	Phenol	β-keto ester	Time (min)	Yield[b] %	M. P. °C
1	1,3-$(OH)_2$–C_6H_4	EAA	15	86	184-186
2	1,3,5-$(OH)_3$–C_6H_3	EAA	10	88	286-288
3	3-CH_3O-1,5-$(OH)_2$–C_6H_3	EAA	15	85	122-124
4	C_6H_5–OH	EAA	25	65	78-80
5	4-NO_2–	EAA	15	78	151-154
	C_6H_4–OH				
6	1,2,3-$(OH)_3$–C_6H_3	EAA	15	82	242-244
7	2-naphthol	EAA	25	75	185-187

[a]**Reaction Condition:** Substituted phenol (1 mmol), ethyl acetoacetate (1 mmol) in presence of 15 mol% SuSA under grinding technique. [b]Isolated Yield.

IV. CONCLUSION

We have developed a new protocol based on the grinding technique for the synthesis of substituted coumarin in eco-friendly manner. The special advantages of this method provide a one pot synthesis strategy, eco-friendly mechanism, easy and simple work up of the products.

V. REFERENCES

[1]. Borges F, Roleira F, Milhazes N, et al.Simple coumarins and analogues inmedicinal chemistry: occurrence,synthesis and biological activity.Curr Med Chem 2005;12(8):887-916

[2]. Zembower DE, Liao S, Flavin MT, Xu ZQ , Stup TL, Buckheit RW, et al. Structural analogues of the calanolide anti-HIV agents. Modification of the trans-10,11-dimethyldihydropyran- 12-ol ring (ring C). Journal of Medicinal Chemistry. 1997;40:1005-1017. DOI: 10.1021/jm960355m

[3]. Završnik D, Muratović S, Makuc D, Plavec J, Cetina M, Nagl A, et al. Benzylidene-bis-(4-hydroxycoumarin) and benzopyrano-coumarin derivatives: Synthesis, 1H/13C-NMR conformational and X-ray crystal structure studies and in vitro antiviral activity evaluations. Molecules. 2011;16:6023-6040. DOI: 10.3390/molecules16076023

[4]. Nawrot-Modranka J, Nawrot E, Graczy K. In vivo antitumor, in vitro antibacterial activity and alkylating properties of phosphorohydrazine derivatives of coumarin and chromone. European Journal of Medicinal Chemistry. 2006;41:1301-1309. DOI: 10.1016/j.ejmech.2006.06.004

[5]. EI-Saghier AMM, Naili MB, Rammash BK, Saleh NA, Kreddan KM. Synthesis and antibacterial activity of some new fused chromenes. ARKIVOC. 2007; 2007:83-91. DOI: 10.3998/ ark.5550190.0008.g09

[6]. Creaven BS, Egan DA, Kavanagh K, McCann M, Mahon M, Noble A, et al. Synthesis and antimicrobial activity of copper(II) and silver(I) complexes of hydroxynitrocoumarins: X-ray crystal structures of [Cu(hnc)2(H2O)2].2H2O and [Ag(hnc)] (hncH = 4-hydroxy-3- nitro-2H-chromen-2-one). Polyhedron. 2005; 24:949-957. DOI: 10.1016/j. poly.2005.03.006

[7]. Golfakhrabadi F, Abdollahi M, Ardakani MRS, Saeidnia S, Akbarzadeh T, Ahmadabadi AN, et al. Anticoagulant activity of isolated coumarins (suberosin and suberenol) and toxicity evaluation of Ferulago carduchorum in rats. Pharmaceutical Biology. 2014;52:1335-1340. DOI: 10.3109/13880209.2014.892140

[8]. Ronad P, Dharbamalla S, Hunshal R, Maddi V. Synthesis of novel substituted 7-(benzylideneamino)- 4-methyl-2H-chromen-2-one derivatives as anti-inflammatory and analgesic agents. Archiv der Pharmazie: Chemistry in Life Sciences. 2008;341:696-700. DOI: 10.1002/ ardp.200800057

[9]. Lin CM, Huang ST, Lee FW, Sawkuo H, Lin MH. 6-Acyl-4-aryl/ alkyl-5,7-dihydroxycoumarins as anti-inflammatory agents. Bioorganic & Medicinal Chemistry. 2006;14:4402- 4409. DOI: 10.1016/j.bmc.2006.02.042

[10]. Wang CJ, Hsieh YJ, Chu CY, Lin YL, Tseng TH. Inhibition of cell cycle progression in human leukemia HL-60 cells by esculetin, Cancer Letters. 2002; 183:163-168. DOI: 10.1016/ S0304-3835(02)00031-9

[11]. Dexeus FH, Logothetis CJ, Sella A, Fitz K, Amato R, Reuben J.M, et al. Phase II study of coumarin and cimetidine in patients with metastatic renal cell carcinoma. Journal of Clinical Oncology. 1990;8:325-329. DOI: 10.1200/JCO.1990.8.2.325

[12]. Bhat MA, Siddiqui N, Khan SA. Synthesis of novel thioureido derivatives of sulfonamides and thiosemicarbazido derivatives of coumarin as potential anticonvulsant and analgesic agents, Indian Journal of Pharmaceutical Sciences, 2006; 68:120-124. DOI:10.4103/0250-474X.22984

[13]. Tyagi YK, Kumar A, Raj HG, Vohra P, Gupta G, Kumari R, et al. Synthesis of novel amino and acetyl amino-4-methylcoumarins and evaluation of their antioxidant activity. European Journal of Medicinal Chemistry. 2005; 40:413-420. DOI: 10.1016/j.ejmech.2004.09.002

[14]. Sardari S, Mori Y, Horita K, Micetich RG, Nishibe S, Daneshtalab M. Synthesis and antifungal activity of coumarins and angular furanocoumarins. Bioorganic & Medicinal Chemistry. 1999;7:1933-1940. DOI: 10.1016/S0968-0896(99)00138-8

[15]. Stein AC, Alvarez S, Avancini C, Zacchino S, von Poser G. Antifungal activity of some coumarins obtained from species of Pterocaulon (Asteraceae). Journal of Ethnopharmacology. 2006;107:95-98. DOI: 10.1016/j.jep.2006.02.009

[16]. Chen Y, Zhang Q , Zhang B, Xia P, Xia Y, Yang Z-Y, et al. Anti-AIDS agents. Part 56: Synthesis and anti-HIV activity of 7-thia-di-O-(–)-camphanoyl-(+)- cis-khellactone (7-thia-DCK) analogs. Bioorganic & Medicinal Chemistry. 2004;12:6383-6387. DOI: 10.1016/j. bmc.2004.09.038

[17]. Cravotto G, Nano GM, Palmisano G, Tagliapietra S. An asymmetric approach to

coumarin anticoagulants via hetero- Diels–Alder cycloaddition. Tetrahedron: Asymmetry. 2001;12:707-709. DOI: 10.1016/S0957-4166(01)00124-0.

[18]. Fan GJ, Mar W, Park MK, Choi EW, Kim K, Kim S. A novel class of inhibitors for steroid 5α-reductase: Synthesis and evaluation of umbelliferone derivatives. Bioorganic & Medicinal Chemistry Letters. 2001; 11:2361-2363. DOI: 10.1016/ S0960-894X(01)00429-2

[19]. Zahradnik M. The Production and Application of Fluorescent Brightening Agents. Chichester: John Wiley & Sons; 1992

[20]. Hepworth JD, Gabbutt CD, Heron BM. In: Katritzky AR, Rees CW, Scriven EFV, editors. Comprehensive Heterocyclic Chemistry II. Vol. 5. Oxford: Pergamon Press; 1996. pp. 301-350

[21]. Green GR, Evans JM, Vong AK. In: Katritzky AR, Rees CW, Scriven EFV, editors. Comprehensive Heterocyclic Chemistry II. Vol. 5. Oxford: Pergamon Press; 1996. pp. 469-500

[22]. O'Kennedy R, Coumarins TRD. Biology, Applications and Mode of Action. Chichester: John Wiley & Sons; 1997

[23]. Meuly WC, Kirk-Othmer. Encyclopedia of Chemical Technology. 3rd ed. Vol. 7. New York: John Wiley & Sons; 1979. p. 196

[24]. von Pechmann H, Duisberg C. Ueber die Verbindungen der Phenole mit Acetessigäther. Berichte der Deutschen Chemischen Gesellschaft. 1883; 16:2119-2128. DOI: 10.1002/ cber.188301602117

[25]. Von Pechmann H, Duisberg C. Neue Bildungsweise der Cumarine. Synthese des Daphnetins. I. Berichte der Deutschen Chemischen Gesellschaft. 1884; 17:929-979. DOI: 10.1002/ cber.188401701248

[26]. Panetta A, Rapoport H. New syntheses of coumarins. The Journal of Organic Chemistry. 1982; 47:946-950. DOI: 10.1021/jo00345a009

[27]. Miyano M, Dorn CR. Mirestrol. I. Preparation of the tricyclic intermediate. The Journal of Organic Chemistry. 1972; 37:259

[28]. F. Shirini and N. Ghaffari Khaligh, succinimide-N-sulfonic acid: A mild, efficient and reusable catalyst for the chemoselective trimethylsilation of alcohols and phenols, Phosphorus, Sulfur, and Silicon, 186:2156–2165, 2011