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# A facile synthesis of 2*H*-chromen-2-ones via Pechmann condensation under solvent free conditions using grinding technique

**Abstract:** A simple and highly efficient procedure for the synthesis of 2*H*-chromen-2-ones via von Pechmann condensation, involving the grinding of different phenols and β-ketoesters in the presence of silica supported sulfuric acid at room temperature, under solvent free conditions, has been described.

**Keywords:** 2*H*-chromen-2-ones; grinding technique; silica supported sulfuric acid; solvent free condition; von Pechmann condensation.

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## 1 Introduction

2*H*-Chromen-2-ones, commonly known as coumarins, are naturally occurring oxygen heterocyclic compounds which have a distinct and important place in natural and synthetic organic chemistry, as they have been found to exhibit varying degrees of biological activities, namely, antibacterial, antiviral, anticancer and anti HIV [1–3]. These have been reported to display activity against several types of animal tumors [4], prostate cancer and metastatic renal cell carcinoma [5] and have also been used as additives in food, cosmetics [6], optical brighteners [7], dispersed fluorescent and laser dyes [8].

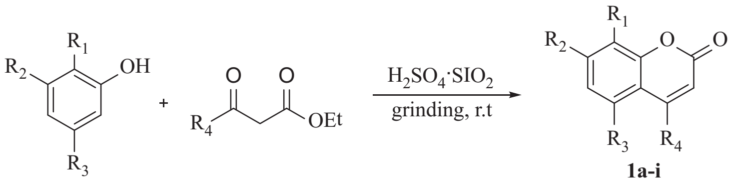
Due to the importance of the 2*H*-chromen-2-ones, continuous efforts have been made to simplify the procedures for the synthesis of these compounds, which include use of Pechmann and Duisberg [9], Perkin and Henry [10], Knoevenagal [11], Reformatsky [12] and Wittig [13] reactions. Among these, the Pechmann condensation is considered to be one of the most important, as it requires simple starting materials. A large number of condensing agents such as strong acids $H_2SO_4$, HCl, $H_3PO_4$, $F_3CCOOH$, solid super acid [9, 14–16], Lewis acids such as $ZnCl_2$, $FeCl_3$, $AlCl_3$, $BF_3{\cdot}2H_2O$, $ZnCl_2/Al_2O_3$, $ZrCl_4$ [14–18] and ion exchange resins [19] have been used in the Pechmann condensation. Recently, the use of microwaves [20], ionic liquid as a Lewis acid [21], $Zn/I_2$ [22], $Yb(OTf)_3$ [23], LiBr [24], $I_2$ [25], $CoPy_2Cl_2$ [26], p-TSA [27], $BTSA/SiO_2$ [28] and polyvinyl sulfonic acid [29] has also been reported.

Some of the above mentioned reagents possess limitations, such as the use of harsh or hazardous chemicals, mainly organic solvents, expensive and large amount of reactants, a longer reaction time, elevated temperature and the formation of side products. The shortcomings led us to develop a safe and more efficient method for the Pechmann condensation.

A survey of the literature reveals that silica supported sulfuric acid has been used as a versatile solid acid catalyst for various types of reactions [30–34]. The grinding technique has been considered to be an important tool to carry out the reactions under solvent free conditions, with maximum yield and minimum cost, and it has got much attention due to its operational simplicity [35–37]. In continuation of our work to develop simple green procedures for the synthesis of heterocyclic compounds using acid catalysts [27], we report a highly efficient method for the synthesis of 2*H*-chromen-2-ones via Pechmann condensation, using silica supported sulfuric acid under solvent free conditions using the grinding technique.

## 2 Experimental part

Melting points were determined in open capillaries using a Thiele tube. A mortar and pestle of porcelain was used for all the experiments. Silica gel (>99%), ethyl acetoacetate (>99%), 1-chloroethylacetoacetate (95%), benzoyl acetoacetate (90%), resorcinol (99%) and phloroglucinol (>99%) were purchased from Sigma-Aldrich Chemicals, New Delhi, India. Pyrogallol with >98% purity was also purchased from Sigma-Aldrich Chemicals. 1-Naphthol (>99%), 2-naphthol (>99%), ethyl acetate (99.9%) and sulfuric acid with 98% purity were received from Merck, Mumbai, India. Silica supported sulfuric acid was prepared by the procedure as reported in the literature [38].



**1a-i**

**1a:** $R_1$=$R_3$=H, $R_2$=OH, $R_4$=$CH_3$; **1b:** $R_1$=H, $R_2$=$R_3$=OH, $R_4$=$CH_3$; **1c:** $R_1$=$R_2$=OH, $R_3$=H, $R_4$=$CH_3$; **1d:** $R_1$=$R_3$=H, $R_2$=OH, $R_4$=$CH_2Cl$; **1e:** $R_1$=H, $R_2$=$R_3$=OH, $R_4$=$CH_2Cl$; **1f:** $R_1$=$R_2$=OH, $R_3$=H, $R_4$=$CH_2Cl$; **1g:** $R_1$=$R_3$=H, $R_2$=OH, $R_4$=Ph; **1h:** $R_1$=H, $R_2$=$R_3$=OH, $R_4$=Ph; **1i:** $R_1$=$R_2$=OH, $R_3$=H, $R_4$=Ph

**Scheme 1** Synthesis of 2*H*-chromen-2-ones under solvent free conditions using the grinding technique.

## 2.1 Preparation of $H_2SO_4$·$SiO_2$

To a dispersion of silica gel (10 g, 230–400 mesh) in diethyl ether (50 ml), 3 ml of conc. $H_2SO_4$ was added with shaking for 5 min. The solvent was removed under reduced pressure to get $H_2SO_4$·$SiO_2$, which was then dried at 110°C for 3 h.

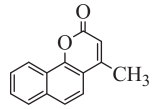
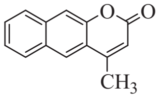
**Table 1** Effect of catalyst on model reaction.

| Sr. No. | Amount of catalyst (mg) | Time (min) | Yield (%) |
|---|---|---|---|
| 1 | 0 | – | No reaction |
| 2 | 50 | 5 | 82 |
| 3 | 100 | 5 | 95 |
| 4 | 150 | 5 | 92 |
| 5 | 200 | 5 | 91 |

## 2.2 General procedure for synthesis of 2*H*-chromen-2-ones 1a-i

A mixture of substituted phenol (1 mmol) and β-ketoester (1 mmol) was grounded with silica supported sulfuric acid (100 mg) in a mortar by pestle for 5 min, until a color change of the reaction mixture took place. The reaction mixture was kept at room temperature for about 10–20 min. The completion of the reaction was checked by thin layer chromatography. The reaction mixture was diluted with ethyl acetate and filtered to recover the catalyst. The filtrate was washed with water and concentrated. The residue obtained was recrystallized from ethanol to give pure 2*H*-chromen-2-ones in high yield.

**Table 2** Synthesis of 2*H*-chromen-2-ones via Pechmann condensation.

| Compound | $R_1$ | $R_2$ | $R_3$ | $R_4$ | Time (min) a+b | Yield (%)[1] | mp (°C) | lit. mp (°C) |
|---|---|---|---|---|---|---|---|---|
| **1a** | H | OH | H | $CH_3$ | 5+10 | 95 | 182–183 | 185 [26] |
| **1b** | H | OH | OH | $CH_3$ | 5+10 | 97 | 278–280 | 280 [26] |
| **1c** | OH | OH | H | $CH_3$ | 5+10 | 92 | 240–242 | 242 [26] |
| **1d** | H | OH | H | $CH_2Cl$ | 5+10 | 92 | 178–181 | 180 [26] |
| **1e** | H | OH | OH | $CH_2Cl$ | 5+10 | 90 | 185–187 | 187 [26] |
| **1f** | OH | OH | H | $CH_2Cl$ | 5+10 | 85 | 195–197 | 196–198 [25] |
| **1g** | H | OH | H | Ph | 5+10 | 90 | 255–257 | 257 [26] |
| **1h** | H | OH | OH | Ph | 5+10 | 82 | 244–246 | 244–246 [24] |
| **1i** | OH | OH | H | Ph | 5+10 | 80 | 195–197 | 196–198 [24] |
| **1j** | |  | | | 5+20 | 90 | 153–155 | 154–155 [25] |
| **1k** | |  | | | 5+20 | 86 | 180–182 | 183–184 [25] |

a, grinding time; b, time for which the reaction mixture was kept at room temperature; [1]Yield after purification.

**Table 3** Comparison of the results of the reactions carried out with different catalyst for the synthesis of coumarins with present method.

| Entry | Catalysts | Time | Temp. (°C) | Yield (%) | Ref. |
|---|---|---|---|---|---|
| 1 | $H_2SO_4$ | 24 h | Room temp. | 20–82 | [20] |
| 2 | $CoPy_2Cl_2$ | 1.5–3.0 min | MW | 58–96 | [26] |
| 3 | $I_2$ | 4–8 h | Room temp. | 60–75 | [25] |
| 4 | LiBr | 15–90 min | 75 | 54–92 | [24] |
| 5 | $FeCl_3$/ionic liquid | 10–13 h | 70 | 65–85 | [39] |
| 6 | $ZrCl_4$ | 5.0–60 min | 70 | 56–95 | [15] |
| 7 | $BTSA{\cdot}SiO_2$ | 1.0–90 min | 85 | 75–95 | [28] |
| 8 | $SnCl_2{\cdot}2H_2O$/EtOH | 1.15–6 h | 80 | 34–60 | [40] |
| 9 | $GaI_3/CH_2Cl_2$ | 0.7–100 h | Room temp. | 65–96 | [41] |
| 10 | $Sc(OTf)_3$ | 1–20 h | 80 | 74–97 | [42] |
| 11 | CAN | 10–15 min | 110 | 93–96 | [43] |
| 12 | $ClSO_3H$ | 10–25 min | 10 | 50–98 | [44] |
| 13 | W-$ZrO_2$/toluene | 6 h | 110 | 50–80 | [45] |
| 14 | $BF_3{\cdot}2H_2O$ | 20 min | 60 | 98–99 | [17] |
| 15 | $Sm(NO_3)_3{\cdot}6H_2O$ | 15–90 min | 80 | 45–98 | [46] |
| 16 | Oxalic acid | 45–105 min | 80 | 78–96 | [47] |
| 17 | $H_2SO_4{\cdot}SiO_2$/grinding[1] | 5 min | Room temp. | 80–97 | – |

[1] Present method.

## 3 Results and discussion

In order to study the efficiency of the catalyst, a mixture of resorcinol and ethyl acetoacetate was grounded in the presence of silica supported sulfuric acid ($H_2SO_4{\cdot}SiO_2$) in a mortar by a pestle (Scheme 1), which was taken as the model reaction. The progress of the reaction was checked by thin layer chromatography. The reactants were found to have reacted almost completely in 5 min and had to be kept at room temperature for another 10–20 min for the completion of the reaction. The optimum conditions of the reaction were achieved by using varying amounts of catalyst and best yields were obtained by using 100 mg of $H_2SO_4{\cdot}SiO_2$. No reaction was found to take place in the absence of a catalyst. Further, it was observed that lower concentrations of the catalyst gave lower yields and higher concentrations of the catalyst were found to be of no use, as the reaction was not improved in terms of yield and time (Table 1). This indicates that the best results were obtained by using 100 mg of catalyst in standard reaction under solvent free conditions.

To check the reusability of the catalyst, a recycle study was carried out. The catalyst was used for three recycles in a model reaction. In the 1st, 2nd and 3rd recycles, the yields were obtained as 95%, 92% and 88%, respectively. Thus, the recycle results showed no appreciable loss in yields.

The scope of the method was further studied by reacting differently substituted phenols with ethyl acetoacetate, 1-chloroethylacetoacetate and benzoyl acetoacetate, to give corresponding coumarins in excellent yields under solvent free conditions at room temperature. The identity of the products (Table 2) was confirmed by their IR, $^1$H NMR, $^{13}$C NMR and mass spectral data and by comparison with authentic samples. Moreover, to illustrate the efficiency and generality of the present protocol, some of the results of our method compared with the literature methods as shown in Table 3. Thus, it is evident that the present protocol is superior to the reported methods in terms of time and yield of the product using the grinding technique.

## 4 Conclusion

In conclusion it can be stated that the present protocol for the synthesis of 2*H*-chromen-2-ones via Pechmann condensation, using silica supported sulfuric acid, is simple and highly efficient under solvent free conditions using the grinding technique. This is a mild, rapid and superior method.

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# References

[1] Maxwell A. *Mol. Microbiol*. 1993, 9, 681–686.
[2] Zembower DE, Liao S, Flavin MT, Xu Z-Q, Stup TL, Buckheit RW Jr, Khilevich A, Mar AA, Sheinkman AK. *J. Med. Chem*. 1997, 40, 1005–1017.
[3] Wang C-J, Hsieh Y-J, Chu C-Y, Lin Y-L, Tseng T-H. *Cancer Lett*. 2002, 183, 163–168.
[4] Maucher A, Von Agerer E. *J. Cancer Res. Clin. Oncol*. 1994, 120, 502–504.
[5] Marshall ME, Butler K, Fried A. *Mol. Biother*. 1991, 3, 170–178.
[6] O'Kennedy, R, Thornes, RD. In *Coumarins: Biology, Applications and Mode of Action*, Wiley & Sons: Chichester, 1997.
[7] Zabradnik, M. *The Production and Application of Fluorescent Brightening Agents*, John Wiley & Sons: New York, 1992.
[8] Murry RDH, Mendez J, Brown SA. *The Natural Coumarins: Occurrence, Chemistry and Biochemistry*, John Wiley & Sons: New York, 1982.
[9] Pechmann VH, Duisberg C. *Chem. Ber*. 1884, 17, 929–979.
[10] Perkin WH, Henry W Sr. *J. Chem. Soc*. 1875, 28, 10–11.
[11] Brufola G, Fringuelli F, Piematti O, Pizzo F. *Heterocycl*. 1996, 43, 1257–1266.
[12] Shirner RL. *Org. React*. 1942, 1, 15–16.
[13] Mali RS, Tilve SA. *Synth. Commun*. 1990, 20, 1781–1791.
[14] Wools LL, Sapp J. *J. Org. Chem*. 1962, 27, 3703–3705.
[15] Smitha G, Reddy CS. *Synth. Commun*. 2004, 34, 3997–4003.
[16] Jin T, Guo Y, Yin Y, Liu H, Li T. *Indian J. Chem*. 2003, 42B, 2612–2614.
[17] Stoyanov VE, Jochen M. *Molecule* 2005, 10, 762–766.
[18] Shockravi A, Valizadeh H, Heravi MM. *Phosphor. Sulfur Silic. Relat. Elem*. 2003, 178, 143–147.
[19] John EVO, Israelstam SS. *J. Org. Chem*. 1961, 26, 240–242.
[20] Singh V, Singh J, Kaur KP, Kad GL. *J. Chem. Res (S*). 1997, 2, 58–59.
[21] Potdar MK, Mohile SS, Salunkhe MM. *Tetrahedron Lett*. 2001, 42, 9285–9287.
[22] Chavan SP, Shivasankar K, Sivappa R, Kali R. *Tetrahedron Lett*. 2002, 43, 8583–8586.
[23] Wang L, Xia J, Tian H, Qian C, Ma Y. *Indian J. Chem*. 2003, 42B, 2097–2099.
[24] Kumar S, Saini A, Sandhu JS. *Arkivoc* 2007, 2007 (xv), 18–23.
[25] Parjapati D, Gohain M. *Catal. Lett*. 2007, 119, 59–63.
[26] Madhav JV, Kuarm BS, Someshwar P, Rajitha B, Reddy YRT, Crooks PA. *J. Chem. Res (S)*. 2008, 4, 232–234.
[27] Makrandi JK, Sharma D, Kumar S. *Green Chem. Lett. Rev*. 2011, 4, 127–129.
[28] Parhami A, Khalafi-Nezhad A, Haghighi SM, Bargebid R, Zare A, Moosavi-Zare AR, Nikrooz M. *Arkivoc*. 2012, 2012 (ix), 111–121.
[29] Kuarm BS, Crooks PA, Rajitha B. *Internat. J. Res. Pharms. Bio. Sc*. 2012, 3, 50–53.
[30] Heravi MM, Ajami D, Ghassemzadeh M. *Synth. Commun*. 1999, 29, 1013–1016.
[31] Oskooie HA, Heravi MM, Sadnia A, Jannati F, Behbahani FK. *Monatash. Chem*. 2008, 139, 27–29.
[32] Wu H, Shen Y, Fan L-Y, Wan Y, Zhang P, Chen C-F, Wang W-X. *Tetrahedron* 2007, 63, 2404–2408.
[33] Shaterian HR, Ghashang M, Feyzi M. *Appl. Catal. A Gen*. 2008, 345, 128–133.
[34] Mohammadpoor-Baltork I, Mirkhani V, Moghadam M, Tangestaninejad S, Zolfigol MA, Abdollahi-Alibeik M, Khosropour AR, Kargar H, Hojati SF. *Catal. Commun*. 2008, 9, 894–901.
[35] Aakeroy CB, Sinha AS, Epa KN, Spartz CL, Desper J. *Chem. Commun*. 2012, 48, 11289–11291.
[36] Sachdeva H, Saroj R, Khaturia S, Dwivedi D. *Green Process Synth*. 2012, 1, 469–477.
[37] Rahman AFMM, Ali R, Jahng Y, Kadi AA. *Molecules* 2012, 17, 571–583.
[38] Chen X, She J, Shang Z-C, Wu J, Zhang P. *Synth. Commun*. 2009, 39, 947–957.
[39] Kumar v, Tomar S, Patel R, Yousaf A, Parmar VS, Malhotra SV. *Synth. Commun*. 2008, 38, 2646–2654.
[40] Upadhyay KK, Mishra RK, Kumar A. *Catal. Lett*. 2008, 121, 118–120.
[41] Sun P, Hu Z. *Synth. Commun*. 2005, 35, 1875–1880.
[42] Jung K, Park Y-J, Ryu J-S. *Synth. Commun*. 2008, 38, 4395–4406.
[43] Reddy YT, Sonar VN, Crooks PA, Dasari PK, Reddy PN, Rajitha B. *Synth. Commun*. 2008, 38, 2082–2088.
[44] Kotharkar SA, Bahekar SS, Shinde DB. *Mendeleev Commun*. 2006, 16, 241–242.
[45] Reddy BM, Reddy VR, Giridhar D. *Synth. Commun*. 2001, 31, 3603–3607.
[46] Bahekar SS, Shinde DB. *Tetrahedron Lett*. 2004, 45, 7999–8001.
[47] Kokare ND, Sangshetti JN, Shinde DB. *Chinese Chem. Lett*. 2007, 18, 1309–1312.

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