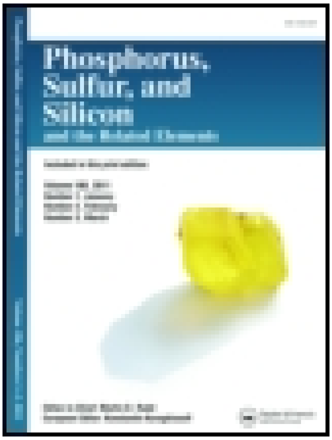

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Silica Sulfuric Acid: A Versatile and Reusable Catalyst for Synthesis of Coumarin-3-carboxylic Acids in a Solventless System

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Silica Sulfuric Acid: A Versatile and Reusable Catalyst for Synthesis of Coumarin-3-carboxylic Acids in a Solventless System

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Synthesis of substituted coumarin-3-carboxylic acid via Knoevenagel condensation of meldrum's acid with ortho-hydroxyaryl aldehydes in solventless system is described.

Keywords Coumarine-3-carboxylic acids; Knoevenagel condensation; silica sulfuric acid

INTRODUCTION

Coumarin-3-carboxylic acid (2-oxo-2H-chromene-3-carboxylic acid) subunit appears in a vast range of natural products and, due to the high levels of biological activity exhibited by many such compounds,[1] has been duplicated in numerous synthetic compounds exhibiting pharmaceutical activity.[2]

Coumarin-3-carboxylic acids are traditionally prepared via Knoevenagel condensation of ortho-hydroxyaryl aldehydes with malonic acid,[3,4] malonic ester,[4,5] or cyanoacetic acid and cyanoacetic ester using agents such as piperidine,[6,7] piperidinium acetate,[8] and ammonium acetate.[9,10] Knoevenagel himself described the solution phase condensation of 2-hydroxybenzaldehydes with malonic acid more than 100 years ago.[11] In 1988, a two-step method for the synthesis of coumarin-3-carboxylic acids was reported. 2-Methoxybenzaldehydes were condensed with Meldrum's acid in DMF, followed by cyclization in the presence of sulfuric acid.[12] Several one-pot procedures have been

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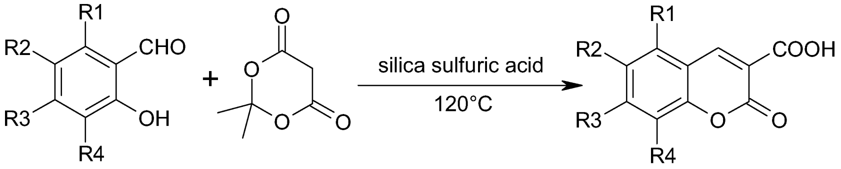


1a-h 2 3a-h

FIGURE 1 One-pot synthesis of coumarin-3-carboxylic acid.

reported using Meldrum's acid as the condensation reagent.[13–16] The reaction is catalyzed by sodium hydroxide,[14] clays,[15] or lithium salts.[16] A solid-phase approach has also been described.[17]

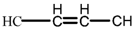
Our laboratory has been engaged in the exploration of practical green chemistry that eliminates or minimizes the use of volatile solvents that are dangerous to human life and the environment. We have found that coumarin-3-carboxylic acids can be readily prepared from 2-hydroxybenzaldehyds (1a–h) and Meldrum's acid (2) under classic conditions for Knoevenagel condensation (Figure 1). 2-Hydroxybezaldehyd and silica sulfuric acid were mixed and then equal molars of Meldrum's acid (2) was added and the mixture was heated without using any solvent at 120°C for the time indicated in Table I.

EXPERIMENTAL

Chemical and Apparatus

IR spectra were recorded (KBr disc) on a Philips PU 9800 FT-IR spectrometer. ^{1}H NMR and ^{13}C NMR spectra were run on an FT-NMR

TABLE I Yields and Physical Data Related to Products

Entry	R_1	R_2	R_3	R_4	Reaction time (min)	Yields[a] (%)	mp. (°C)	mp. Lit. (°C)
3a	H	H	H	H	45	80	190–191	191–192[15]
3b	H	H	H	MeO	40	85	209–210	—
3c	H	H	MeO	H	45	83	193–194	192–194[15]
3d	H	MeO	H	H	32	84	204–206	—
3e	H	NO2	H	H	30	82	233–234	234–235
3f	H	Br	H	H	35	92	194–196	195–196
3g		 $HC-\overset{H}{C}=\overset{H}{C}-CH$	H	H	40	86	235–236	236–237
3h	H	Cl		H	33	90	120	121

[a] Isolated yields.

Bruker AVANCE 300 MHz spectrometer in DMSO-d_6 and chemical shifts are indicated in δ ppm. Melting points (uncorrected) were measured on an Electrothermal 9100 apparatus and chemicals were obtained from Merck.

Different 2-hydroxybenzaldehydes (1a–h) bearing various substituents were used in our study. All of them react readily with Meldrum's acid in presence of a catalytic amount of silica sulfuric acid. Silica sulfuric acid was prepared by following the literature procedure.[18]

General Procedure

Silica sulfuric acid (0.02 g) was added to 2-hydroxybenzaldehydes (1a–h) (1 mmol) and the mixture was stirred sufficiently and was kept under stirring until 2-hydroxybenzaldehyde and the reagents were completely mixed. Finally, Meldrum's acid (1 mmol) was added and heated at 120°C.The progress of the reaction was monitored by TLC using petroleum ether and ethyl acetate (1:1) as eluent. The times needed for reactions to complete are given in Table I. Upon the completion of the reaction, the organic substance was extracted with chloroform. After evaporating the solvent, crude products recrystallized from aqueous ethanol. The crystallized product was filtered and dried under vacuum.

Coumarin-3-carboxylic acids (3a–h) (Figure 1) were obtained in high yields and purity. The purity of product was confirmed by melting point, ^{1}H NMR, ^{13}C NMR, and FT-IR spectroscopy.

RESULTS AND DISCUSSION

We have developed a very simple synthesis method of coumarin-3-carboxylic acids utilizing the Knoevenagel condensation between Meldrum's acid and ortho-hydroxyarylaldehydes.

Meldrum's acid has $pK_a = 5$ and because it is sensitive to heat, decyclization occurs at high temperatures according to the suggested mechanism (Figure 2).[18]

Therefore, in this study we tried to eliminate high temperature and heat in order to avoid Meldrum's acid decomposition. If Meldrum's acid decomposes, a ketene with carbon hybridization of Sp is produced that is significantly less reactive than Meldrum's acid itself and according to the suggested mechanism some side products may also be produced. It is obvious that the production of coumarine should be done under mild conditions to minimize Meldrum's acid decomposition. One other advantage of our suggested reaction is solventless conditions to overcome

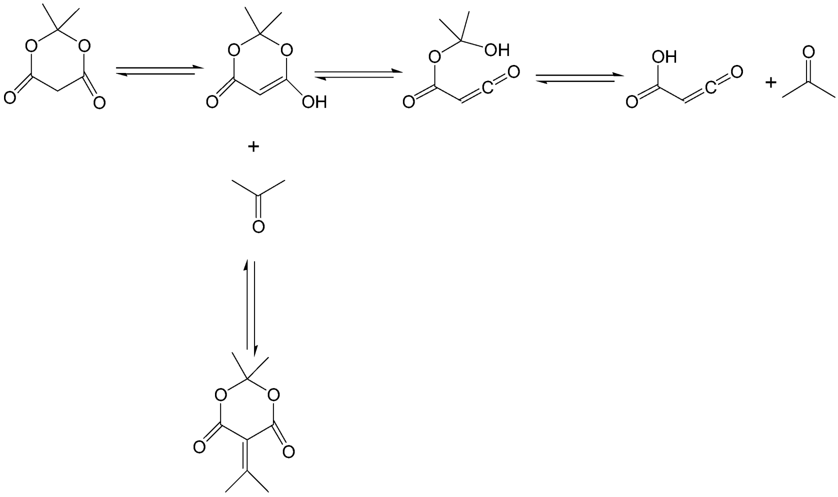


FIGURE 2 Decyclization of Meldrum's acid.

the harmful effect of volatile solvents on environment. Reasonable reaction times and yields are also advantageous (Table I).

We investigated the reusability and recycling of silica sulfuric acid. The recycled catalyst could be washed with chloroform and subjected to a second run of the reaction process.

The comparison of the efficiency of silica sulfuric acid in synthesis of 3f after four times is shown in Table II.

Spectral Data for Products

(**3a**) FT-IR: KBr ($\upsilon_{\max}$, cm^{-1}) 3471 (OH acid), 3055 (CH aromatic), 2930 (CH vinilic) 1744 (C=O ester),1679 (C=O acid), 1610, 1565 (C=C); ^{1}HNMR (DMSO-d_6), δ : 13.6 (H acid), 8.7(s), 7.88 (d, j = 8.3 Hz), 7.7 (dd, J = 8.3) 7.6 (d, J = 8.3); ^{13}CNMR (DMSO-d_6), 163.90 (COOH),

TABLE II Reuse of the Silica Sulfuric Acid for Synthesis of 3f

Entry	Time (min)	Yield (%)[a]
1	35	85
2	45	80
3	45	72
4	75	60

[a] Isolated yields.

156.60 (COO-), 154.40 (C—O), 148.20, 134.10, 130.11, 124.71, 118.20 (C aromatic ring), 117.90, 116.00 (C vinilic).

(**3b**) FT-IR: KBr ($\upsilon_{\max}$, cm^{-1}) 3420, (OH acid), 3050 (CH aromatic) 2912 (CH vinilic) 1754 (C=O ester), 1673 (C=O acid), 1607, 1565 (C=C); ^{1}HNMR (DMSO-d_6), δ : 13.2 (s, broad, H acid), 8.69 (s, 1H aromatic), 7.3 (m, 3H aromatic), 3.91 (s, O—CH3). ^{13}CNMR (DMSO-d_6), δ : 164.23 (COOH), 156.37 (COO-), 148 (C—OCH3), 146.74 (COC=O), 144.14, 131.67, 125.82, 121.32 (C aromatic ring), 118.57, 116.21 (C vinilic), 56.09 (O—CH3).

(**3c**) FT-IR: KBr ($\upsilon_{\max}$, cm^{-1}): 3421 (OH acid), 3044 (CH aromatic), 2986 (CH vinilic), 1735 (C=O ester), 1690 (C=O acid), 1617, 1559 (C=C aromatic); ^{1}HNMR (DMSO-d_6), δ : 12.99 (broad, s, COOH), 8.72 (H aromatic), 7.81 (H vinilic), 7.06, 6.18 (H aromatic), 3.74 (OCH3); ^{13}CNMR: 164.60 (COOH), 164.08 (COO-), 157.17 (C—OCH3), 156.80 (C—O), 149.01, 131.50 (C aromatic), 113.76, 113.20 (C vinilic), 111.56, 100.02 (C aromatic), 57.00 (OCH3).

(**3d**) FT-IR: KBr ($\upsilon_{\max}$, cm^{-1}): 3447 (OH acid), 3052 (CH aromatic), 2952 (CH vinilic), 1755 (C=O ester), 1686 (C=O acid), 1621, 1574 (C=C). ^{1}H NMR (DMSO-d_6), δ : 13.20 (H acid), 8.65 (s, H vinilic), 7.40–7.37 (m, 3 H, aromatic), 7.34 (1H aromatic), 3.79 (s, OCH3). ^{13}CNMR (DMSO-d_6), δ : 164.40 (COOH), 157.40 (OC=O), 156.10 (C—OCH3), 149.30 (C—O), 148.40, 122.40 (C aromatic), 119.10, 118.80 (C vinilic), 117.60, 112.20 (C aromatic), 56.20 (OCH3).

(**3e**) FT-IR: KBr ($\upsilon_{\max}$, cm^{-1}): 3450 (OH acid), 3096 (CH aromatic), 2949 (CH vinilic), 1742 (C=O ester), 1695 (C=O acid), 1617, 1569 (C=C). ^{1}H NMR (DMSO-d_6), δ : 13.3 (H acid) 8.80, 8.50 (H aromatic), 7.64 (H vinilic), 7.61 (H aromatic); ^{13}CNMR (DMSO-d_6): 163.56 (COOH), 157.99 (OC=O), 155.38 (C—O), 147.02 (C-NO2), 133.50, 128.20 (C aromatic), 125.80, 120.20 (C vinilic), 118.30, 117.60 (C aromatic).

(**3f**) FT-IR: KBr ($\upsilon_{\max}$, cm^{-1}): 3440 (OH acid), 3044 (CH aromatic), 2950 (CH vinilic), 1756 (C=O ester), 1690 (C=O acid), 1600, 1558 (C=C). ^{1}H NMR (DMSO-d_6), δ : 11.50 (Hacid), 8.64, 8.12 (H aromatic); 7.85 (H vinilic); 7.39 (H aromatic). ^{13}CNMR (DMSO-d_6): 164.20 (COOH), 156.50 (OC=O), 153.90 (O—C), 147.02, 136.70, 132.30, 120.30, 120.20 (C aromatic), 118.80, 116.60 (C vinilic).

(**3g**) FT-IR: KBr ($\upsilon_{\max}$, cm^{-1}): 3421 (OH acid), 3056 (CH aromatic), 1747 (C=O ester), 1681 (C=O acid), 1597, 1569 (C=C). ^{1}H NMR (DMSO-d_6), δ : 13.30 (H acid), 9.36, 8.60, 8.32 (d $J = 9.3$), 8.25 (d $J = 9.3$), 8.01 (d $J = 9.3$), 7.91 (t, H aromatic), 7.61 (H vinilic). ^{13}CNMR (DMSO-d_6): 164.70 (COOH), 157.20 (OC=O), 155.50 (C—O), 144.02, 136.20 (C aromatic), 130.30 (C vinilic), 129.54, 129.48, 129.46, 126.89 (C aromatic), 122.80 (C vinilic), 117.80, 116.90, 112.60 (C aromatic).

(**3h**) FT-IR: KBr ($\upsilon_{\max}$, cm^{-1}): 3435 (OH acid), 3040 (CH aromatic), 2950 (CH vinilic), 1750 (C=O ester), 1695 (C=O acid), 1600, 1548 (C=C). ^{1}H NMR (DMSO-d_6), δ : 11.60 (H acid), 8.14, 7.80 (H aromatic), 7.71 (H vinilic), 7.42 (H aromatic).^{13}CNMR (DMSO-d_6): 163.68 (COOH), 157.43 (OC=O), 153.75 (C–O), 146.52 (C-Cl), 135. 78, 131.97, 120.40 (C aromatic), 120.35, 119.10 (C vinilic), 116.48 (C aromatic).

REFERENCES

[1] R. D. H. Murray, J. Mendez, and S. A. Brown, *The Natural Coumarins: Occurrence, Chemistry and Biochemistry* (John Wiley & Sons, New York, 1982).
[2] W. C. Meuly, *Kirk-Othmer Encyclopedia of Chemical Technology*, 3rd ed. (John Wiley & Sons, New York, 1979), pp. 7, 196.
[3] G. Jones, *Organic Reactions* (John Wiley & Sons, New York, 1967), pp. 15, 204.
[4] F. Bigi, L. Chesini, R. Maggi, and G. Sartori, *J. Org. Chem.*, **64,** 1033 (1999).
[5] E. Knoevenagel, *Chem. Ber.*, **37,** 4461 (1904).
[6] C. Wiener, C. H. Schroeder, and K. P. Link, *J. Am. Chem. Soc.*, **79,** 5301 (1957).
[7] B. S. Creaven, D. A. Egan, K. D. Kavanagh, M. McCann, A. Noble, B. Thati, and M. Walsh, *J. Inorg. Biochem.*, **101**(8), 1108 (2007).
[8] A. Song, X. Wang, and K. S. Lam, *Tetrahedron Lett.*, **44,** 1755 (2003).
[9] J. L. Scott and C. L. Raston, *Green Chem.*, **2,** 245 (2000).
[10] G. W. V. Cave, C. L. Raston, and J. L. Scott, *Chem. Comm.*, 2159 (2001).
[11] E. Knoevenagel, *Chem. Ber.*, **31,** 2585 (1898).
[12] V. Armstrong, O. Soto, J. A. Valderrama, and R. Tapia, *Synthetic Comm.*, **18,** 717 (1988).
[13] R. Maggi, F. Bigi, S. Carloni, A. Mazzacani, and G. Sartori, *Green Chem.*, **3,** 173 (2001).
[14] E. A. Shirokova, G. M. Segal, and I. V. Torgov, *Bioorg. Khim.*, **14,** 236 (1988).
[15] B. P. Bandgar, L. S. Uppalla, and D. S. Kurule, *Green Chem.*, **1,** 243 (1999).
[16] B. P. Bandgar, L. S. Uppalla, and V. S. Sadavarte, *J. Chem. Res. (S)*, **2,** 40 (2002).
[17] B. T. Watson and G. E. Christiansen, *Tetrahedron Lett.*, **39,** 6087 (1998).
[18] V. I. Tararov, A. Korostylev, G. Konig, and A. Borner, *Synth. Comm.*, **36,** 187 (2006).