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Short Communication

$FeCl_3$-catalysed ultrasonic-assisted, solvent-free synthesis of 4-substituted coumarins. A useful complement to the Pechmann reaction

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ABSTRACT

The catalytic activity of $FeCl_3$ for the synthesis of a variety of 4-substituted coumarins using high energy techniques has been investigated. The ultrasonic-assisted conditions provide a useful complement to the Pechmann reaction, affording the coumarin derivatives in excellent yields, under solvent-free conditions, in short reaction times using an inexpensive, mild and benign Lewis acid catalyst.

1. Introduction

3-Oxo-3*H*-benzopyrans, commonly designated as coumarins, are widely encountered in nature [1]. These compounds find application in pharmaceuticals, fragrances, agrochemicals, and insecticides [2–4] since they possess a wide range of pharmacological activities including anticancer [5], antioxidant [6,7], anti-inflammatory, anti-HIV, anticoagulant, antibacterial, analgesic and immunomodulatory [8]. In addition, they represent one of the most sensitive and widely employed category of reagents for fluorescent derivatization [9–11].

The widespread biological activities of coumarin derivatives have aroused great interest in the development of new methods for their synthesis. Coumarins and their derivatives can be synthesized by various methods, such as the Pechmann [12,13], Perkin [14], Knoevenagel [15], Reformatsky [16], and Wittig reactions [17]. More specifically, the Pechmann reaction is widely used for preparing 4-substituted coumarins and involves the coupling of phenols and β-ketoesters, in the presence of acid catalysts including sulfuric acid [18], trifluoroacetic acid [19], P_2O_5 [20], or Lewis acids such as $ZnCl_3$, $AlCl_3$, gallium triiodide [21], AgOTf [22] and $SnCl_2{\cdot}2H_2O$ [23].

Further modifications involve the use of solid acid catalysts or exchange resins as alternatives to conventional acid catalysts, such as sulphamic acid [24], pentafluorophenylammonium triflate [25], sulphated zirconia [26], nanocrystalline ZnO/pyridine dicarboxylic acid [27], nafion resins [28] or cation exchange resins [29] however, very often they require high temperatures, long reaction times and in some cases result in lower yields. Recently, metal–organic frameworks (MOFs) Fe- and Cu-benzene-1,3,5-tricarboxylate (Fe- and CuBTC) have been investigated as solid acid catalysts for the synthesis of coumarins using the Pechmann reaction [30].

A number of literature reports have focused on the synthesis of heterocycles, including coumarins, under solvent-free conditions as an eco-friendly strategy since it significantly reduces waste production and precludes the use of organic solvents [31]. More, specifically for the solvent-free Pechmann reaction a variety of catalysts (Brønsted, Lewis or solid acids) have been employed which include samarium(III) nitrate hexahydrate [32], boron trifluoride dihydrate [33], $BiCl_3$ [34], $Bi(NO_3)_3{\cdot}5H_2O$ [35], $Sc(OTf)_3$ [36], LiBr [37], $BaCl_2$ [38], $TiCl_4$ [39], $ZrCl_4$ [40,41], silica gel supported zirconyl chloride octahydrate [42], $HClO_4{\cdot}SiO_2$ [43], alumina sulfuric acid [44], poly(4-vinylpyridine)-supported copper iodide [45], PEG-SO_3H [46], Zirconium(IV) Phosphotungstate and 12-Tungstophosphoric acid supported onto ZrO_2 [47]. In addition, the use of ionic liquids has also been explored in the solvent-free Pechmann reaction of coumarins [48].

The search of environmentally friendly and efficient synthetic approaches represents a new trend in organic synthesis during

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the last years. Synthetic chemists are increasingly paying attention to enabling technologies aiming at achieving high efficiency and meeting the green criteria of energy savings and the absence of dangerous or harsh reagents. In this respect there is a tendency to employ microwaves and/or ultrasound to accelerate organic reactions. The use of microwaves has emerged as a powerful tool for organic transformations since it reduces considerably the reaction time providing remarkable rate enhancement in a number of classical organic reactions, thus, leading to the high-speed construction of versatile chemical entities [49].

Recent reports have demonstrated acceleration of the Pechmann reaction by microwave irradiation catalysed by H_2SO_4 [50], TSA [51], wet phosphoric acid imidazolium dihydrogen phosphate [52], P_2O_5/molecular sieves 3 Å [53], mesoporous zirconium phosphate [54], dipyridine copper chloride [55], and graphite:montmorillonite K10 [56].

Ultrasound irradiation has been increasingly used in organic synthesis in the last three decades. Ultrasonic-assisted organic synthesis (UAOS) is a powerful and green approach which is becoming popular for accelerating organic compound synthesis [57]. Comparing with traditional methods, this method is more conveniently and easily controlled. A large number of organic reactions have been carried out in higher yield, shorter reaction times and milder conditions under ultrasound irradiation.

Recently, there is increasing interest in the application of ultrasound in the Pechmann reaction in the presence of various catalysts including $BiCl_3$ [58], poly(4-vinylpyridinium) hydrogen sulphate as solid catalyst [59], copper perchlorate [60], and acid zeolites [61].

In the context of our work on bioactive heterocyclic compounds [62–64] we set out to investigate the microwave- and ultrasound-assisted synthesis of 4-substituted coumarins under solvent-free conditions using $FeCl_3$ as catalyst. The development of environmentally benign protocols has received impressive attention during the last years and in this context iron can be considered as a desirable alternative, due to its non toxicity, low price and eco-friendly properties. Under this scope a number of iron-mediated organic transformations have appeared in the literature [65].

To the best of our knowledge, this is the first report of the effect of this eco-friendly Lewis acid in the Pechmann reaction using high energy techniques and solvent-free conditions.

2. Results and discussion

The reaction of phloroglucinol (**1a**) (1 mmol) with ethyl acetoacetate (**2a**) (2 mmol) was selected as a model for the optimization of the reaction parameters (Scheme 1). Initially, we set out to select the best conditions using sealed-vessel microwave processing and 10 mol% catalyst. As can be seen in Table 1 use of microwave irradiation for 10 min at 100 °C using 150 W, afforded the highest yield (99%) (Table 1, entry 2). Reduction of the temperature led to a decrease in the yield of product **3a** (84%) (Table 1, entry 1) while, increase in temperature decreased the yield even further (55%) (Table 1, entry 3).

Table 1
Optimisation of the Pechmann reaction conditions using microwave irradiation.

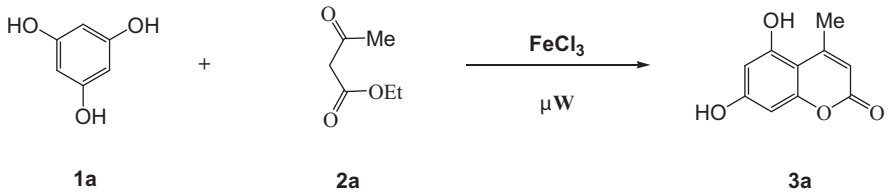
Entry	Reaction conditions microwave irradiation	Yield of **3a** (%)
1	80 °C/150 W 20 min[a]	84
2	100 °C/150 W 10 min[a]	99
3	120 °C/150 W 10 min[a]	55

[a] The disappearance of phloroglucinol, checked by TLC, determined the reaction time in each case.

Subsequently, we set out to optimize the amount of catalyst and we observed that the highest yield is obtained with 10 mol% $FeCl_3$ for both the microwave- and ultrasound-assisted Pechmann reaction (Table 2, entry 2). Use of 5 mol% $FeCl_3$ resulted in a lower yield of **3a** (Table 2, entry 1) and increase of catalyst amount to 20 mol% led to a more pronounced reduction of the obtained product **3a** (Table 2, entry 3), while no product formation was observed in the absence of catalyst (Table 2, entry 4).

Thus, we proceeded to investigate the scope of the reaction using our optimized conditions and a series of phenols and polyphenols with a variety of β-ketoesters (Scheme 2). The results of the comparative study between microwave and ultrasonic irradiation are described in Table 3. In addition, to investigate the effect of the two high energy techniques we compared the results with conventional heating at 70 °C. This temperature was selected in order to compare directly our results with the previously reported method by Kumar et al. [66] who employed 20% mol anhydrous $FeCl_3$, as a Lewis acid in an ionic liquid medium at 70 °C. Furthermore, aiming at obtaining a direct comparison with our microwave-assisted conditions, we performed the Pechmann reaction between phloroglucinol and ethyl acetoacetate in the presence of 10% mol anhydrous $FeCl_3$ with heating at 100 °C and the desired product **3a** was formed in 3 h in 98% yield (data not shown). In the absence of $FeCl_3$ no product formation was observed with heating either at 70° or 100 °C. As illustrated in Table 3 the yields obtained were good to excellent. It is clear that the reaction time is reduced from several hours (5–12 h) to only a few minutes by using microwave or ultrasonic irradiation. However, the effect of ultrasound is more pronounced on the reaction outcome, resulting in high yields and in several occasions (Table 3, entries 5, 7, 9 and 10) higher than with the other two techniques.

The highest yields were obtained with phloroglucinol (**1a**) and resorcinol (**1b**) and ethyl acetoacetate (Table 3, entries 1 and 4) due to the presence of three and two hydroxyl groups, respectively, which resulted in activation of the benzene ring for hydroxyl alkylation. The yield of the corresponding reaction with pyrogallol (**1e**) (Table 3, entry 10) was lower, probably due to steric hindrance and/or oxidation to a quinone. The dialkoxyphenol **1c** bearing two methoxy groups at the meta position of the hydroxyl group gave the corresponding 4-substituted coumarins in very good to excellent yields without observing any dealkylation products (Table 3, entries 6–8). The reaction of phenol and nitrophenols with ethyl acetoacetate failed to give the corresponding coumarin derivatives under our conditions (data not shown).



Scheme 1. Microwave-assisted synthesis of 5,7-dihydroxy-4-methyl-2*H*-1-benzopyran-2-one (**3a**) catalysed by $FeCl_3$.

Table 2
Optimisation of $FeCl_3$ amount under microwave or ultrasound irradiation.

Entry	Catalyst (mol%)	Yield of **3a** (%)[a]	Yield of **3a** (%)[b]
1	$FeCl_3$ (5)	79	82
2	$FeCl_3$ (10)	99	99
3	$FeCl_3$ (20)	54	60
4	$FeCl_3$ (0)	0	0

[a] Microwave irradiation, 100 °C/150 W, 10 min.
[b] Ultrasound 20 kHz, nominal power 130 W, 18 min.

Our reaction conditions can be applied for the Pechmann reaction using phenols substituted by electron donating groups and β-keto esters bearing either electron donating (Table 3, entries 1, 2, 4, 5, 6, 7, 9 and 10) or electron withdrawing substituents (Table 3, entries 3 and 8). In addition, the previously reported method using 20% mol anhydrous $FeCl_3$, as a Lewis acid in an ionic liquid medium at 70 °C [66] suffered from lower yields, with longer reaction times and twice the amount of catalyst, as compared to our sonochemical reaction.

The Pechmann reaction is exergonic but does not take place in measurable amounts at room temperature and thus, requires initialisation through various sources including microwave and ultrasound. A recent theoretical study on the mechanism of the Pechmann reaction [67] suggests that three possible routes featuring (A) trans-esterification; electrophilic attack; water elimination (B) electrophilic attack; water elimination; trans-esterification (C) electrophilic attack; trans-esterification; water elimination, operate simultaneously. Furthermore, the oxo form of the β-keto-ester can perform the electrophilic attack to the phenolic substrate in an energetically more favourable way, thus precluding the participation of its enolic form in the reaction mechanism.

Formation of the desired compounds was accelerated by microwave irradiation (10 min) albeit in lower yields as compared with the conventional heating method. Only in the case of phloroglucinol and ethyl acetoacetate we had comparable high yields. Apparently, the microwave intrinsic effects which were not influenced by solvents (solvent-free conditions), were less pronounced than the thermal effects, may be due to the predominating reaction pathway, as mentioned above. Conversely, our results underline the positive effect of ultrasound on the reaction outcome. Ultrasonication is linked to the cavitation phenomenon which causes high speed impinging liquid jets and strong hydrodynamic shear-forces. It is well known that when ultrasound irradiation is applied to a mixture, it generates alternating low-pressure and high-pressure waves in liquids, leading to the formation and violent collapse of small vacuum bubbles. When these bubbles burst, it results in high temperature and high pressure and drive high-speed jets of the β-keto ester into the $FeCl_3$ surface which in turn, exposes fresh surface of the Lewis acid catalyst, resulting in the enhancement of its efficiency. Furthermore, the cavitation effect via the energy input and material transfer between the reactants facilitates the intermolecular reaction between the phenol and the β-keto ester. Using the synthesis of compound **3a** as a model reaction we compared the results obtained by our method to others reported in the literature, focusing mainly on solvent-free conditions in the presence of homo or heterogeneous catalysts (Table 4).

Overall, as can be seen our reaction conditions afford the desired product **3a** either in higher yields, or in shorter reaction times, or both in comparison to literature reports.

3. Experimental section

3.1. General remarks

^{1}H NMR spectra were recorded at 600 or 300 MHz, and ^{13}C NMR spectra at 75 MHz. ^{1}H and ^{13}C NMR spectra are internally referenced to residual solvent signals ($CDCl_3$, DMSO-d_6, CD_3OD-d_4). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, dd = doublet of doublet, m = multiplet), coupling constant and integration. Data for ^{13}C NMR are reported in terms of chemical shift (δ ppm). Melting points (°C) are uncorrected. Microwave-assisted reactions were performed in a microwave reactor CEM Discover LabMate. The ultrasound-assisted reactions were carried out using a Sonics & Material INC. Vibra-Cell VCX-130 Titanium alloy Ti-6Al-4V probe (20 kHz, 130 W) with a Stepped Micro Tip 3 mm diameter. The HR-MS spectrum was obtained using a UHPLC-MS^n Orbitrap Velos-Thermo mass spectrometer.

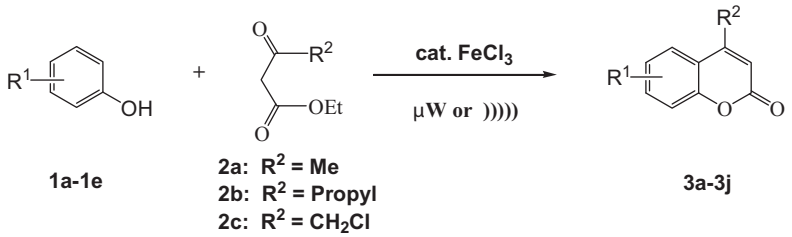
3.2. General procedure for the Pechmann reaction

3.2.1. Ultrasound method

A mixture of the appropriate phenol **1a–e** (3.73 mmol), β-keto-ester **2a–c** (7.46 mmol) and anhydrous $FeCl_3$ (0.373 mmol, 81 mg) was placed in a 10 mL glass tube and was sonicated (20 kHz, 130 W nominal power) for 1–20 min until completion of the reaction checked by TLC. The tube during sonication was immersed in a cooling bath set at 20 °C. For compounds **3a, 3b, 3c, 3f, 3j** the reaction mixture solidified upon completion of the reaction, due to product precipitation. Subsequently, ethanol (5 mL) was added, and the product **3a–j** crystallized upon dropwise addition of water (15 mL). The solid was filtered washed with water and was recrystallized from ethanol/water. The final product was then dried under high vacuum over P_2O_5.

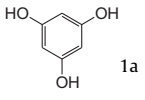
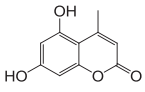
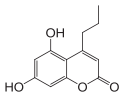
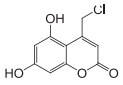
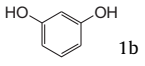
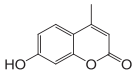
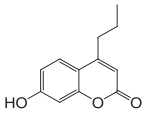
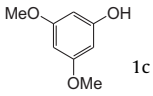
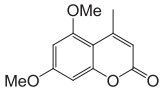
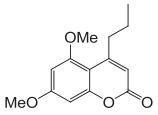
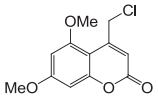
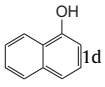
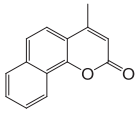
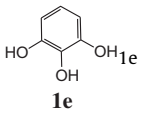
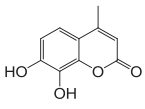
3.2.2. Microwave method

A mixture of the appropriate phenol **1a–e** (3.73 mmol), β-keto-ester **2a–c** (7.46 mmol) and anhydrous $FeCl_3$ (0.373 mmol, 81 mg) were added to a thick-wall borosilicate glass tube 10 mL. The tube was sealed, was placed in a CEM Discover LabMate microwave reactor and was irradiated 100 °C (150 W) for 10 min. After cooling to room temperature, ethanol (5 mL) was added, and the product **3a–j** crystallized upon dropwise addition of water (15 mL). The solid was filtered washed with water and was recrystallized from ethanol/water. The final product was then dried under high vacuum over P_2O_5.



Scheme 2. Synthesis of coumarins catalysed by $FeCl_3$ under solvent-free conditions, using microwave or ultrasound irradiation.

Table 3
Pechmann synthesis of 4-substituted coumarins in the presence of cat. amount $FeCl_3$ under microwave or ultrasonic irradiation, or conventional heating.

Entry	Phenol	β-Keto ester	Product	Ultrasonic irradiation[a]		Microwave irradiation[b]		Coventional heating[c]	
				Time (min)	Yield (%)[d]	Time (min)	Yield (%)[d]	Time (h)	Yield (%)[d]
1	 **1a**	**2a**	 **3a**	18	99	10	99	12	98
2		**2b**	 **3b**	15	60	10	62	12	99
3		**2c**	 **3c**	1	75	10	68	5	95
4	 **1b**	**2a**	 **3d**	20	97	10	76	12	99
5		**2b**	 **3e**	20	81	10	44	12	75
6	 **1c**	**2a**	 **3f**	11	80	10	52	12	97
7		**2b**	 **3g**	20	87	10	31	12	64
8		**2c**	 **3h**	20	96	–	–	–	–
9	 **1d**	**2a**	 **3i**	20	87	10	40	12	54
10	 **1e**	**2a**	 **3j**	12	55	10	39	12	36

[a] Reaction conditions: phenol, 1.0 mmol;, β-keto ester 2.0 mmol, solvent-free, ultrasonic probe 3 mm diameter, 20 kHz, 130 W nominal power.
[b] Reaction conditions: phenol, 1.0 mmol;, β-keto ester 2.0 mmol, solvent-free, μW, 150 W, 100 °C.
[c] Reaction conditions: phenol 1.0 mmol;, β-keto ester 2.0 mmol, solvent-free, heated at 70 °C.
[d] Isolated yield.

3.2.3. Conventional heating method

A mixture of the appropriate phenol **1a–e** (3.73 mmol), β-keto-ester **2a–c** (7.46 mmol) and anhydrous $FeCl_3$ (0.373 mmol, 81 mg) was heated at 70 °C. After completion of the reaction (TLC), ethanol (5 mL) was added, and the product **3a–j** crystallized upon drop-wise addition of water (15 mL). The solid was filtered washed with water and was recrystallized from ethanol/water. The final product was then dried under high vacuum over P_2O_5.

3.2.4. 5,7-Dihydroxy-4-methyl-2H-1-benzopyran-2-one (*3a*)

Starting from phloroglucinol (**1a**) (3.73 mmol, 0.470 g) and ethyl 3-oxobutanoate (**2a**) (7.46 mmol, 0.971 g) the title compound **3a** was obtained as a beige solid. Mp: 293–295 °C (lit: 289–290 °C dec.) [72]. ^{1}H NMR (600 MHz, DMSO-d_6): δ 2.48 (3H, d, J = 1.2 Hz), 5.85 (1H, s), 6.16 (1H, d, J = 2.4 Hz), 6.25 (1H, d, J = 2.4 Hz), 10.30 (s, 1H), 10.53 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 23.5, 94.6, 99.1, 102.1, 108.9, 155.1, 156.6, 158.0, 160.2, 161.1.

Table 4
Comparison of the results obtained in this work for compound **3a** to those reported by other groups.

Entry	Catalyst	Reaction conditions	Time	Yield (%)	Refs.
1	Sulphated zirconia	Neat/80 °C	24 h	52	[26]
2	$Sm(NO_3)_3{\cdot}6H_2O$	Neat/80 °C	25 min	95	[32]
3	$Bi(NO_3)_3{\cdot}5H_2O$	Neat/80 °C	20 min	92	[35]
4	$BaCl_2$	Neat/100 °C	25 min	90	[38]
5	$HClO_4{\cdot}SiO_2$	Neat/130 °C	60 min	97	[43]
6	P4VPy–CuI	Neat/80 °C	10 min	92	[45]
7	PEG–SO_3H	Neat/80 °C	15 min	89	[46]
8	3-methyl-1-sulfonic acid imidazolium hydrogen sulfate	Neat/40 °C	22 min	96	[48]
9	Phosphoric acid imidazolium dihydrogenphosphate	MW heating oven/140 W	25 min	78	[52]
10	$BiCL_3$	Neat/ultrasonic bath (33–35 kHz, 85 W)	15 min	92	[58]
11	Poly(4-vinylpyridinium) hydrogen sulfate	Neat/US (35KHz, 200 W)	3 min	91	[59]
12	[BMIM] [Tf_2N], $FeCl_3$	Neat/70 °C	10 h	77	[66]
13	p-TsOH	Neat/60 °C	10 min	81	[68]
14	Wells–Dawson heteropolyacid $H_6P_2W_{18}O_{62}{\cdot}24H_2O$	Neat/130 °C	48 min	98	[69]
15	$KAl(SO_4)_2{\cdot}12H_2O$	Neat/80 °C	2 h	90	[70]
16	$Yb(OTf)_3$	Neat/85 °C	1 h	91	[71]
17	$FeCl_3$	Neat/US (20 kHz, 130 W)	18 min	99	This work

*3.2.5. 5,7-Dihydroxy-4-propyl-2H-1-benzopyran-2-one (**3b**)*

Starting from phloroglucinol (**1a**) (3.73 mmol, 0.470 g) and ethyl 3-oxohexanoate (**2b**) (7.46 mmol, 1.18 g) the title compound **3b** was obtained as a beige solid. Mp: 241–243 °C (lit: 244 °C) [73]. ^{1}H NMR (600 MHz, DMSO-d_6): δ 0.94 (3H, t, J = 7.2 Hz), 1.56–1.62 (2H, m), 2.85 (2H, t, J = 7.2 Hz), 5.82 (1H, s), 6.17 (1H, d, J = 2.4 Hz), 6.26 (1H, d, J = 2.4 Hz), 10.26 (s, 1H), 10.54 (s, 1H). ^{13}C NMR (75 MHz, DMSO-d_6): δ 13.9, 22.6, 37.3, 94.8, 99.3, 101.4, 108.3, 156.9, 157.5, 158.5, 160.2, 160.9.

*3.2.6. 4-(Chloromethyl)-5,7-dihydroxy-2H-1-benzopyran-2-one (**3c**)*

Starting from phloroglucinol (**1a**) (3.73 mmol, 0.470 g) and ethyl 4-chloro-3-oxobutanoate (**2c**) (7.46 mmol, 1.23 g) the title compound **3c** was obtained as a beige solid. Mp: 251–253 °C, (lit: 246–248 °C) [72]; ^{1}H NMR (600 MHz, DMSO-d_6): δ 5.04 (2H, s), 6.22 (1H, s), 6.23 (1H, d, J = 2.4 Hz), 6.28 (1H, d, J = 2.4 Hz), 10.42 (s, 1H), 10.89 (s, 1H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 45.1, 94.9, 99.3, 99.9, 108.9, 152.0, 156.6, 157.2, 160.2, 161.6.

*3.2.7. 7-Hydroxy-4-methyl-2H-1-benzopyran-2-one (**3d**)*

Starting from resorcinol (**1b**) (3.73 mmol, 0.411 g) and ethyl 3-oxobutanoate (**2a**) (7.46 mmol, 0.971 g) the title compound **3d** was obtained as a beige solid. Mp 184–186 °C (lit: 185–187 °C) [36]. ^{1}H NMR (DMSO-d_6, 600 MHz): δ 2.37 (3H, d, J = 1.2 Hz), 6.13 (1H, s), 6.70 (1H, d, J = 2.4 Hz), 6.80 (1H, dd, J = 2.4, 8.4 Hz), 7.60 (1H, d, J = 3.0 Hz), 10.50 (1H, s), ^{13}C NMR (75 MHz, DMSO-d_6): δ 18.2, 102.2, 110.3, 112.0, 112.9, 126.6, 153.6, 154.9, 160.3, 161.2.

*3.2.8. 7-Hydroxy-4-propyl-2H-1-benzopyran-2-one (**3e**)*

Starting from resorcinol (**1b**) (3.73 mmol, 0.411 g) and ethyl 3-oxohexanoate (**2b**) (7.46 mmol, 1.18 g) the title compound **3e** was obtained as a beige solid. Mp 129–131 °C (lit: 127–128 °C) [74]. ^{1}H NMR (300 MHz, $CDCl_3$/DMSO-d_6): δ 0.95 (3H, t, J = 7.5 Hz), 1.56–1.67 (2H, m), 2.59 (2H, t, J = 7.5 Hz), 5.94 (1H, s), 6.68–6.71 (2H, m), 7.35 (1H, d, J = 3.6 Hz), 9.69 (1H, br s), ^{13}C NMR (75 MHz, $CDCl_3$/DMSO-d_6): δ 18.8, 21.4, 33.6, 103.1, 109.6, 111.7, 113.0, 125.3, 155.3, 156.6, 160.9, 161.8.

*3.2.9. 5,7-Dimethoxy-4-methyl-2H-1-benzopyran-2-one (**3f**)*

Starting from 3,5-dimethoxyphenol (**1c**) (3.73 mmol, 0.575 g) and ethyl 3-oxobutanoate (**2a**) (7.46 mmol, 0.971 g) the title compound **3f** was obtained as a beige solid. Mp 170–172 °C (lit: 171–173 °C) [41]. ^{1}H NMR (600 MHz, DMSO-d_6): δ 2.53 (3H, s), 3.85/3.86 (6H, 2s), 5.95 (1H, s), 6.29 (1H, d, J = 2.4 Hz), 6.44 (1H, d, J = 2.4 Hz); ^{13}C NMR (75 MHz, DMSO-d_6): δ 24.4, 55.80, 55.84, 93.4, 95.5, 105.0, 111.4, 154.6, 157.1, 159.2, 161.2, 162.9.

*3.2.10. 5,7-Dimethoxy-4-propyl-2H-1-benzopyran-2-one (**3g**)*

Starting from 3,5-dimethoxyphenol (**1c**) (3.73 mmol, 0.575 g) and ethyl 3-oxohexanoate (**2b**) (7.46 mmol, 1.18 g) the title compound **3g** was obtained as a beige solid. Mp 119–121 °C (lit: 117–119 °C) [75]. ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.99 (3H, t, J = 7.2 Hz), 1.53–1.64 (2H, m), 2.84 (3H, t, J = 7.5 Hz), 3.84/3.86 (6H, 2s), 5.96 (1H, s), 6.29 (1H, d, J = 2.4 Hz), 6.44 (1H, d, J = 2.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 14.1, 22.8, 38.5, 55.7, 55.8, 93.6, 95.5, 104.3, 110.7, 157.3, 158.2, 158.6, 161.3, 162.6.

*3.2.11. 4-(Chloromethyl)-5,7-dimethoxy-2H-chromen-2-one (**3h**)*

Starting from 3,5-dimethoxyphenol (**1c**) (3.73 mmol, 0.575 g) and ethyl 4-chloro-3-oxobutanoate **2c** (7.46 mmol, 1.23 g) the title compound **3h** was obtained as a beige solid. Mp 155–157 °C. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.86/3.90 (6H, 2s), 4.90 (2H, s), 6.33 (1H, d, J = 2.4 Hz), 6.46 (1H, s), 6.48 (1H, d, J = 2.4 Hz); ^{13}C NMR (75 MHz, $CDCl_3$): δ 45.5, 56.0, 56.3, 94.0, 96.0, 102.7, 111.4, 151.2, 157.1, 158.4, 160.9, 163.3; HRMS (ESI$^+$): $[M+H]^+$, found 255.04190. $C_{12}H_{12}Cl^{35}O_4$ requires 255.04186.

*3.2.12. 1-Methyl-3H-benzo[f]chromen-3-one (**3i**)*

Starting from 1-naphthol (**1d**) (3.73 mmol, 0.538 g) and ethyl 3-oxobutanoate (**2a**) (7.46 mmol, 0.971 g) the title compound **3i** was obtained as a beige solid. Mp 167–169 °C (lit: 152–154 °C) [52]. ^{1}H NMR ($CDCl_3$, 600 MHz): δ 2.54 (3H, s), 6.37 (1H, d, J = 2.4 Hz), 7.57–7.71 (4H, m), 7.84–7.88 (1H, m), 8.53–8.57 (1H, m); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 19.4, 114.5, 115.3, 120.4, 122.8, 123.3, 124.3, 127.3, 127.8, 128.7, 134.9, 150.7, 153.6, 161.1.

*3.2.13. 7,8-Dihydroxy-4-methyl-2H-1-benzopyran-2-one (**3j**)*

Starting from pyrogallol (**1e**) (3.73 mmol, 0.470 g) and ethyl 3-oxobutanoate (**2a**) (7.46 mmol, 0.971 g) the title compound **3j** was obtained as a beige solid. Mp 240–242 °C (lit: 242–244 °C) [72]. ^{1}H NMR (600 MHz, DMSO-d_6): δ 2.35 (3H, s), 6.09 (1H, s), 6.78 (1H, d, J = 8.4 Hz), 7.06 (1H, d, J = 8.4 Hz), 9.59 (br s, 2H). ^{13}C NMR (75 MHz, CD_3OD-d_4): δ 18.8, 111.1, 113.3, 114.5, 116.7, 133.4, 144.4, 150.6, 156.4, 163.5.

4. Conclusion

In conclusion, we have successfully demonstrated the catalytic activity of $FeCl_3$ for the synthesis of a variety of 4-substituted coumarins under ultrasound and microwave conditions. Moreover, the ultrasound-assisted conditions provide a useful complement to the Pechmann reaction and leads to excellent yields of the coumarin derivatives under mild conditions, in short reaction time using an

inexpensive, mild and benign Lewis acid catalyst, in the absence of solvents.

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