



SYNTHESIS OF AURONES (2-BENZYLIDENE BENZOFURAN-3(2H)-ONES) DERIVATIVES USING CHOLINE CHLORIDE/TIN(II) CHLORIDE DEEP EUTECTIC SOLVENT AND Fe_3O_4/λ -CARRAGEENAN/ZN(II)

Sanjeev Kumar

Research Scholar, Dept. of Chemistry, Kurukshetra University,
Kurukshetra, Haryana(India)

ABSTRACT :

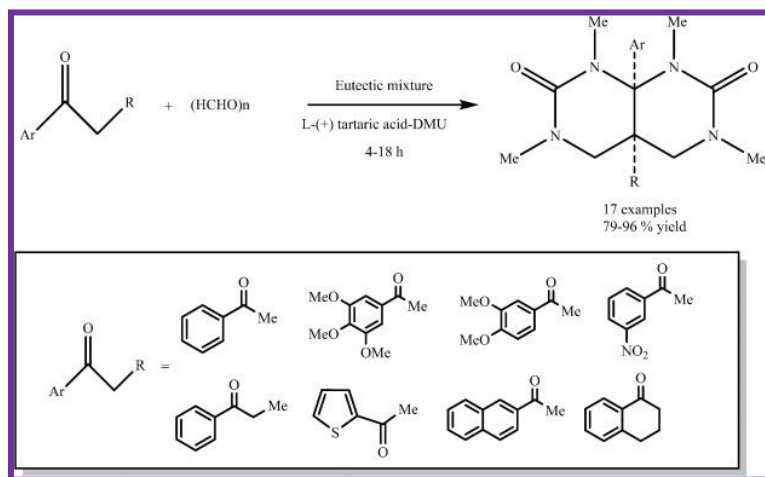
In this study, various Aurones (2-benzylidenebenzofuran-3(2H)-ones) derivatives have prepared efficiently through a simple method using choline chloride/tin(II) chloride ($ChCl \cdot 2SnCl_2$) deep eutectic solvent (DES), alone, or in the presence of Fe_3O_4/λ -carrageenan/Zn(II) magnetic bionanocatalyst. In the employed procedure, 2-chloro-1-(2,4-dihydroxyphenyl)ethanone have mixed with aromatic aldehydes and the reactions have been completed in the presence of DES at 90 °C in 1.5 h. In addition to, using DES/ Fe_3O_4/λ -carrageenan/Zn(II), the reaction time was reduced to 30 min. DES has been recycled four times without important loss of its activity to make a greener method for preparation of Aurones.

Keywords

Aurones, Condensation, DES, Nanocomposite, Catalyst.

INTRODUCTION

Aurones (2-benzylidenebenzofuran-3(2H)-ones) derivatives are important organic compounds which are structural isomers of flavones that contain an exocyclic carbon-carbon double bond bridging the benzofuranone and phenyl rings [1,2], and they exhibit useful biological activities, such as antimicrobial [3], antiparasitic [4-7], antiviral [8], anti-inflammatory [9], For synthesis point of view Aurones (2-benzylidenebenzofuran-3(2H)-ones) are very important in organic synthesis, due to their wide biological and pharmacological properties. However, the literature has several methods for the

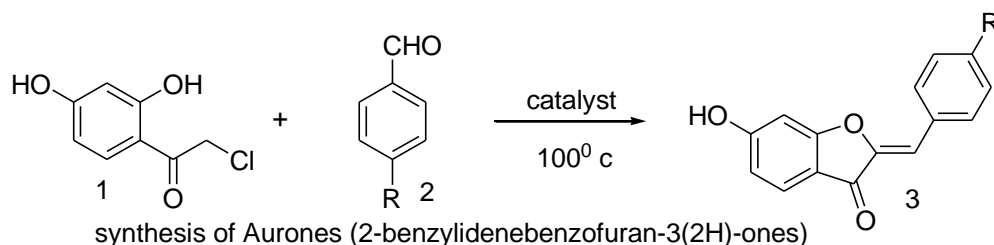


synthesis of Aurones derivatives has been reported.

Often it was observed that, the most of these methods suffer at least some disadvantages, such as a long reaction time, expensive reagents, use of toxic solvents or catalysts, harsh reaction conditions, environmental problems, undesirable wastes, unsatisfactory yield, non-recyclable catalyst, and tedious work-up procedures. Although, the synthesis of this class of heterocyclic compounds is particularly significant for researchers and in continuation of previous works on the use of DES in the synthesis of important compounds [10-11]. So in this research above said a new method for synthesis of Aurones (2-benzylidenebenzofuran-3(2H)-ones) derivatives is adopted.

RESULT AND DISCUSSION

In this report, researcher hope to present a simple and efficient method for the synthesis of Aurones (2-benzylidenebenzofuran-3(2H)-ones) derivatives (Scheme 1) by the reaction between 2-chloro-1-(2,4-dihydroxyphenyl)ethanone and aromatic aldehydes in the presence of DES, alone, or in the presence of $\text{Fe}_3\text{O}_4/\lambda$ -carrageenan/Zn(II) nanocatalyst.



(Scheme 1)

Initially, I chose the model reaction between 2-chloro-1-(2,4-dihydroxyphenyl)ethanone and benzaldehyde in the presence of catalyst (DES or DES and nanomagnetic) to optimize the reaction parameters and obtain the best conditions (Scheme 1). Different reaction conditions, such as the type of DES ($\text{ChCl}_2\cdot 2\text{SnCl}_2$, $\text{ChCl}_2\cdot 2\text{ZnCl}_2$ and $\text{ChCl}_2\cdot 2\text{Urea}$), the amount of DES (5, 10, 15 and 20 mol %), reaction temperature (r.t, 60, 90, 120 °C), and the reaction time (0.5, 1, 1.5, 2, 5 h), have employed to obtain the best reaction conditions. The results were listed in Table 1 which showed that the best yield of the product has observed in the reaction at 90 °C in the presence of 5 mol% $\text{ChCl}_2\cdot 2\text{SnCl}_2$ at 1.5 h. Moreover, to determine the catalytic or synergic effect of the prepared bionanocatalyst, different values of this catalyst were added to the reaction at its optimized conditions (Table 2) and the reaction time and its temperature has reoptimized. The results showed that this catalyst reduces the reaction time to 30 min.

Table 1: Optimization of reaction conditions for the model reaction

Entry	Cat. Type	Cat (mol%)	T(°C)	Time(h)	Yield(%)
1	$\text{ChCl}_2\cdot 2\text{SnCl}_2$	20	r.t	5	0
2	$\text{ChCl}_2\cdot 2\text{SnCl}_2$	20	60	2	20
3	$\text{ChCl}_2\cdot 2\text{SnCl}_2$	20	90	1.5	89
4	$\text{ChCl}_2\cdot 2\text{SnCl}_2$	5	90	1.5	91
5	$\text{ChCl}_2\cdot 2\text{ZnCl}_2$	20	90	2.5	38
6	$\text{ChCl}_2\cdot 2\text{Urea}$	20	90	2.5	61

Table 2: Optimization of reaction conditions for the model reaction

Entry	$\text{Fe}_3\text{O}_4/\lambda$ Carrageenan/Zn(II)(g)	T(°C)	Time(min)	Yield (%)
1	0.1	Rt	120	0
2	0.1	60	30	42
3	0.1	90	30	91
4	0.1	120	30	72
5	0.05	90	30	58

The optimized conditions were employed for the synthesis of other Aurones (2-benzylidenebenzofuran-3(2H)-ones) derivatives to show the versatility of this method. Therefore, the all reactions with different aldehydes are summarized in Table 3.

Table 3. Synthesis of some Aurones (2-benzylidenebenzofuran-3(2H)-ones) derivatives.

Entry	Aldehyde	Product	Yield (%)	m.pt(^o C)
1	Ph	3a	87	224-225
2	4-OCH ₃ C ₆ H ₅	3b	70	252-252
3	4-CH ₃ C ₆ H ₅	3c	85	227-228
4	4-ClC ₆ H ₅	3d	70	238-239
5	4-BrC ₆ H ₅	3e	74	243-244

CONCLUSION

In summary, an environment friendly and green approach have presented for the synthesis of Aurones (2-benzylidenebenzofuran-3(2H)-ones) derivatives via the reaction between chloro-1-(2,4-dihydroxyphenyl)ethanone and aromatic aldehydes in the presence of $\text{ChCl}_2 \cdot \text{SnCl}_2$, alone, or in the presence of $\text{Fe}_3\text{O}_4/\lambda$ -carrageenan/ Zn(II) . This method offers several advantages, including using DES instead of toxic organic solvents or catalysts (or both), simple work-up procedure, excellent yields, short reaction time, easy synthesis, greener condition and non-chromatographic purification of products and reusability of DES.

EXPERIMENTAL SECTION

Chemicals were purchased from Merck and Sigma-Aldrich companies. Melting points were measured using the open capillary tube method with an electro thermal 9200 apparatus. ¹H NMR and ¹³C NMR spectra were recorded on Bruker AV-400 spectrometer at 400 and 100 MHz, respectively in DMSO-d₆. Coupling constant (J) are expressed in Hz. Chemical shifts (δ) of NMR are reported in parts per million (ppm) units relative to the solvent.

PREPARATION OF $\text{Fe}_3\text{O}_4/\lambda$ -CARRAGEENAN/ Zn(II)

Fe_3O_4 nanoparticles were prepared by chemical co-precipitation of 2:1 of a molar ratio of $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$ (1 g) and $\text{FeSO}_4 \cdot 6\text{H}_2\text{O}$ (0.65 g). Both iron salts were dissolved in 50 mL of deionized water and stirred to produce a clear solution. This solution has been sonicated for 30 min. Then, NH_4OH solution (25 %) was added to the solution. When the pH of the solution was reached to 10, a dark solution was appeared, indicating the formation of magnetic nanoparticles. The solution was allowed to stir at 80 °C under N_2 atmosphere for 2 h and the nanomagnetite was separated by a magnet, washed with water and acetone, and dried by air. Then, λ -carrageenan (0.25 g) was dissolved into 50 mL of distilled water to get the homogenous solution, magnetite nanoparticles were added, and the solution was stirred for 18 h at room temperature. The resulting coated nanomagnetite was separated by a magnet, washed with water and acetone, and dried by air. Finally, $\text{Fe}_3\text{O}_4/\lambda$ -carrageenan (1 g) was added to 25 mL aqueous solution of $\text{ZnCl}_2 \cdot 6\text{H}_2\text{O}$ (0.5 g) and the mixture was gently stirred at room temperature for 24 h. The resulting catalyst ($\text{Fe}_3\text{O}_4/\lambda$ -carrageenan/ Zn(II)) was separated by using external magnet, washed with water and acetone, and dried by air.[12]

General procedure for the synthesis of Aurones (2-benzylidenebenzofuran-3(2H)-ones) derivatives.

Chloro-1-(2,4-dihydroxyphenyl)ethanone (2 mmol) and aromatic aldehydes (1 mmol), and $\text{ChCl}_2 \cdot 2\text{SnCl}_2$ (5 mol%) (in some reactions, in the presence of 0.1 g of $\text{Fe}_3\text{O}_4/\lambda$ -carrageenan/ Zn(II)) were mixed in a 25 ml round-bottom flask equipped with a condenser on the top. The reaction mixture was stirred for 30 min, and during stirring, it was warmed slowly on oil bath to 90 °C. The progress of reaction was checked by TLC and after completion of the reaction, the mixture was

diluted with 5 ml water and 10 ml Et₂O. The nanomagnetic catalyst was separated by external magnet then the organic layer was separated by simple liquid-liquid extraction. The deep eutectic solvent was dried at 60–70 °C, where organic layer was dried over MgSO₄ and its solvent was evaporated. After all the crude product was recrystallized in ethanol to get pure product. The structure of all products was confirmed by melting point, ¹H and ¹³C NMR data compared with literature.

Spectral data of some representative compounds

(Z)-5-Hydroxy-2-benzylidene-benzofuran-3(2H)-one (**5**) **3a**: yellow solid, m.pt 224-225 ¹H NMR (400 MHz, DMSO-d₆): δ=9.83(s, 1H, 5OH), δ=7.97 (d, j=7.2Hz, 2H, ArH), 7.41-7.52(m, 3H, ArH), 7.40(d, j=8.8Hz, 1H, ArH), 7.22(dd, j=8.8Hz, 1H, ArH), 7.03(d, j=2.8Hz, 1H, ArH), 6.88 (s, 1H,CH) ppm; ¹³C NMR (100 MHz, DMSO-d₆): d 184.4, 159.9, 154.4, 147.7, 132.6, 131.7, 130.4, 129.4, 126.3, 121.7, 114.3, 112.1, 108.3 ppm.

(Z)-5-Hydroxy-2-(4-methoxybenzylidene-benzofuran-3(2H)-one **3b**: yellow solid, m.pt 251-252 ¹H NMR (400 MHz, DMSO-d₆): δ=9.77(s, 1H, OH), δ=7.95 (d, j=8.8Hz, 2H, ArH), 7.38(d, 8.8Hz 1H, ArH), 7.21(dd, j=8.8Hz, 1H, ArH), 7.08(d, j=8.8Hz, 2H, ArH), 7.02(d, j=2.4Hz, 1H, ArH), 6.87 (s, 1H,CH), 3.83(s, 3H, OCH₃) ppm; ¹³C NMR (100 MHz, DMSO-d₆): d 184.0, 161.3, 159.6, 154.3, 146.6, 133.7, 126.4, 125.1, 122.0, 115.2, 114.2, 112.6, 108.2, 55.9 ppm.

(Z)-5-Hydroxy-2-(4-methylbenzylidene-benzofuran-3(2H)-one **3c**: pale yellow solid, m.pt 227-228 ¹H NMR (400 MHz, DMSO-d₆): δ=9.79(s, 1H, OH), δ=7.88 (d, j=8.0Hz, 2H, ArH), 7.40(d, 8.8Hz 1H, ArH), 7.32(d, j=8.0Hz, 2H, ArH), 7.22(dd, j=8.8Hz, 1H, ArH), 7.02(d, j=2.4Hz, 1H, ArH), 6.86 (s, 1H,CH), 2.36(s, 3H, CH₃) ppm; ¹³C NMR (100 MHz, DMSO-d₆): d 184.3, 159.7, 154.3, 147.2, 140.6, 131.8, 130.2, 129.8, 126.2, 121.8, 114.4, 112.4, 108.2, 21.6 ppm.

(Z)-5-Hydroxy-2-(4-chlorobenzylidene-benzofuran-3(2H)-one **3d**: yellow solid, m.pt 238-239(70%) ¹H NMR (400 MHz, DMSO-d₆): δ=9.82(s, 1H, OH), δ=7.99 (d, j=8.4Hz, 2H, ArH), 7.57(d, 8.4Hz 2H, ArH), 7.39(d, j=9.2Hz, 1H, ArH), 7.23(dd, j=8.8Hz, 1H, ArH), 7.03(d, j=2.4Hz, 1H, ArH), 6.90 (s, 1H,CH), ¹³C NMR (100 MHz, DMSO-d₆): 184.4, 159.8, 154.5, 147.8, 135.0, 133.3, 131.5, 129.6, 126.4, 121.6, 114.4, 110.8, 108.3 ppm

(Z)-5-Hydroxy-2-(4-bromobenzylidene-benzofuran-3(2H)-one **3e**: yellow solid, m.pt 243-244(77%) ¹H NMR (400 MHz, DMSO-d₆): δ=9.83(s, 1H, OH), δ=7.91 (d, j=8.4Hz, 2H, ArH), 7.71(d, 8.4Hz 2H, ArH), 7.40(d, j=9.2Hz, 1H, ArH), 7.23(dd, j=8.8Hz, 1H, ArH), 7.03(d, j=2.4Hz, 1H, ArH), 6.88 (s, 1H,CH), ¹³C NMR (100 MHz, DMSO-d₆): 184.4, 159.8, 154.5, 147.9, 133.5, 132.5, 131.8, 126.4, 123.9, 121.6, 114.4, 110.8, 108.3ppm.

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