Indian Journal of Chemistry
Vol. 62, February 2023, pp. 121-125
DOI: 10.56042/ijc.v62i2.65632

Microwave assisted reaction, photophysical studies and antibacterial activities of simple sugar chalcone derivatives

Arasappan Hemamalini[a,*], Ayyavu Thirunarayanan[b] & Thangamuthu Mohan Das[c]

[a] Department of Chemistry, Government College of Engineering Srirangam, Thiruchirappalli 620 012, India

[b] Department of Chemical Engineering Biotechnology and Materials, FCFM, University of Chile, Av. Beauchef 851, Santiago, 600 025 Chile

[c] Department of Chemistry, School of Basic and Applied Sciences, Central University of Tamil Nadu, Thiruvarur 610 101, India

*E-mail: malininarayananchem86@gces.edu.in, thiruorgchem81@gmail.com, tmohandas@cutn.ac.in

Received 17 August 2022; accepted (revised) 12 January 2023

Aldol condensation is adopted for the synthesis of sugar chalcone derivatives from β-C-glycosidic ketones with various aromatic aldehydes under basic conditions with both conventional heating as well as microwave irradiation. Microwave assisted reaction gives excellent yields. Products obtained have been characterized using ^{1}H and ^{13}C NMR and elemental analysis. Sugar chalcone derivatives exhibit excellent antibacterial activity.

Keywords: Sugar chalcone, β-C-Glycosidic ketone, Conventional, Microwave, Antibacterial

Carbohydrates are the most abundant class of biomolecules on earth which are used to perform functions in life[1]. The main function of carbohydrate is to provide energy and play an important role in the structure and function of organs and nerve cells in the body[2]. It acts as a bioactive substance with regard to antibacterial, antiviral, antifungal, antiprotozoal, antineoplastic activity which was reported in literature[3].

Chalcones are well known intermediates for the synthesis of heterocyclic derivatives[4]. They are active lead molecules in medicinal chemistry for the new drug discovery[5]. Chalcones are valuable molecule of medicinal importance due to the presence of reactive ketoethylenic group[6]. Licochalcones segregated from the plant of licorice found to have a range of biological activities like antiplasmodic, chemopreventive, antimalarial, antitumor, antioxidant, anti-fungal, anti-inflammotory and antibacterial activities[7].

Microwave effect is an electromagnetic wave effect that influences many chemical reaction[8]. In recent time, microwave heating seems to be very effective and eco-friendly method of activation[9]. There are several advantages in adopting the microwave assisted method *viz*., shorter reaction times, high yield and low cost. The rate of the organic reaction will also be enhanced due to the superheating of solvents[10].

Synthesis of molecules having the sugar moiety incorporated with chalcone derivatives under microwave condition are under wide scope. In continuation of the ongoing research in the area of saccharide chemistry, the simple sugar chalcone derivatives were observed to give better results under microwave conditions. Furthermore, since both the saccharide moiety as well as the chalcone possess antimicrobial activity, the synthesized derivatives are the promising compounds to possess the antibacterial activity.

Results and Discussion

4,6-*O*-Butylidene-D-glucopyranose **1** was synthesized by adopting the literature procedure[11,12]. (4,6-*O*-Butylidene-β-D-glucopyranosyl) propan-2-one **2** was synthesized following the literature procedure[13-15]. The reaction of sugar protected propane-2-one, **2** with aromatic aldehydes using pyrrolidine as catalyst was carried out both with conventional as well as a microwave assisted reaction. Microwave assisted reaction comparatively reduced the time of the reaction from hours to minutes and additionally gave an excellent yield of about 85-90% of the corresponding α,β-unsaturated compounds, **3-7** (Fig. 1).

Normal conventional method needs longer reaction time and by products which limits the scope of its application. Aldol condensation is adopted for the synthesis of sugar chalcone from β-C-glycosidic ketones with various aromatic aldehydes under basic

condition using microwave technique. Microwave irradiation has been used to accelerate the organic reaction, due to high heat efficiency.

The microwave reaction was carried out using various solvents as shown in Table 1. Since, dichloromethane has a low boiling point, it is not preferable in the microwave condition, though it worked in the conventional method. Dichloroethane which has a high boiling point compared to dichloromethane was found to be a better solvent compared to the others. Moreover, the yield of the product has increased and the reaction time got minimized by adopting the microwave assisted reaction (Table 2). Structure of the synthesized sugar chalcone derivatives, **3-7** were characterized using ^{1}H and ^{13}C NMR spectroscopy and elemental analysis. The appearance of two doublets at δ 7.55 and δ 6.82 corresponds to olefin proton and the *trans* form of the olefin was confirmed from the coupling constant which was found to be 16.2 Hz whereas the four aromatic protons appeared as multiplet in the range δ 7.71-7.62 in the ^{1}H NMR. It also notably exhibited a large coupling constant for the H-1 signal ($^{3}J_{H1,H2}$ ~ 9.6 Hz), indicating a *trans*-diaxial orientation of H-1 and H-2 as expected for a β-D-configured glucopyranose moiety[12]. The acetal proton appears as triplet at δ 4.53 with coupling constant 5.1 Hz which confirmed the protection of sugar. The α,β-unsaturated carbonyl carbon resonated at δ 197.3 and the cyanide carbon appeared around δ 140.8 in^{13}C NMR, which gave further confirmation for the formation of sugar-chalcone product, **6**.

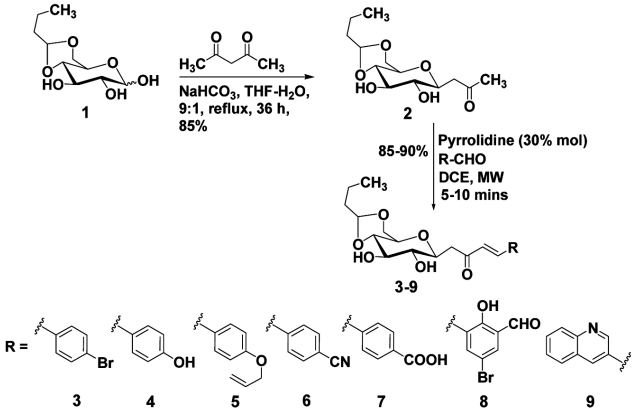

Fig. 1 — Microwave assisted synthesis of sugar chalcone derivatives

Table 1 — Different solvents used in microwave oven method for the synthesis of compound **3**

S. No.	Solvents used	Yield (%)
1	DMF	25
2	EtOH	38
3	MeOH	40
4	CH_3CN	20
5	DCE	85

Photophysical studies of simple sugar chalcone derivatives

Absorption studies was carried out for the synthesized sugar chalcone derivatives, **3-9** using acetonitrile as solvent. The absorption profile of the derivatives are shown in Fig. 2. Absorption spectrum of compounds, **3-9** shows the absorbance at 292, 318, 316, 297, 290, 256 and 338 nm wavelengths respectively. From the observation, it is found that the compound **9**, which possesses indole substituent, has the absorbance at higher wavelength. This may be due to the extension of the conjugation between the chalcone and the indole moiety. The sugar-chalcone compound, **8** though it possesses multi-functional groups did not show any prominent response.

Antibacterial studies

Antibacterial activity was studied for three different chalcones against three human pathogenic bacteria namely *Bacillus subtilis*, *Pseudomonas aeruginosa* and *Klebsiella pneumonia* by the agar diffusion method. All the three compounds **4**, **7**, **9** were tested for their efficacy in inhibiting the growth of the tested pathogens (see ESI). The antibacterial test revealed that all the chalcone derivatives **4**, **7** and **9** were active against all the three human pathogenic bacteria at a concentration of 75 µL. Hence, it was observed that the sugar derivative associated with chalcone possesses excellent

Table 2 — Reaction time and yield percentage in both conventional and microwave method

Compd	R	Conventional method		Microwave method	
		Reaction time (h)	Yield (%)	Reaction time (min)	Yield (%)
3	4-Br	1.0	68	5	85
4	4-OH	1.5	58	5	87
5	4-allyl	0.5	45	5	90
6	4-CN	1.5	59	10	88
7	4-COOH	1.5	59	10	87
8	2-OH 5-Br	1.0	65	5	89
9	-indole	1.0	75	15	86

antibacterial activity. Additionally, due to the substituent attached to the aromatic moiety, there was a significant difference in the activity. The sugar chalcone derivative, **4** which possesses the electron donating hydroxyl group was found to exhibit higher activity in all the three bacteria compared to the sugar chalcone derivative **7** whereas the compound which possesses the indole moiety **9**, exhibited excellent antibacterial activity. Hence, it is observed that not only the sugar and chalcone but also the substituents that are present in the aromatic moiety are also responsible for the activity against bacteria. The antibacterial activity of sugar chalcone derivatives are represented by the percentage of inhibition against various bacterial strains (Table 3).

Antibacterial assay

The *in vitro* antibacterial activity of the sugar chalcone derivatives **4**, **7**and **9** were determined by the well diffusion method described by Perez *et al*. Luria Bertani agar was used for the preparation of plates. The medium was poured on to the sterile Petri-dishes of 90 mm diameter. The agar was allowed to set at ambient temperature. Fresh bacterial cultures of four human pathogenic bacteria such as *Bacillus subtilis* MTCC121 (Gram positive), *Pseudomonas aeruginosa* MTCC424 (Gram negative) and *Klebsiella pneumoniae* MTCC3384 (Gram negative) were spread as a thin film on the surface of the Luria Bertani agar plates. After incubation using a sterile cork borer, wells were cut from the agar in the plate. The compounds were weighed and dissolved in dimethyl sulfoxide (DMSO 10 mg mL^{-1}). Aliquots of 75 µL (1%) of the test solution (compound **4**, **7** and **9**) were poured in to the wells using a sterile micropipette. The inoculated plates were initially incubated for 15 min at RT, and they were incubated at 37°C for 24 h. Turbidity was adjusted with sterile broth so as to correspond to 0.5 McFarland standard. Then the plates were examined for any zone of growth inhibition. Inhibition zones were recorded as the diameter of growth-free zones including the diameter of the well in mm at the end of the incubation period. 75 µL of chloroform served as the control.

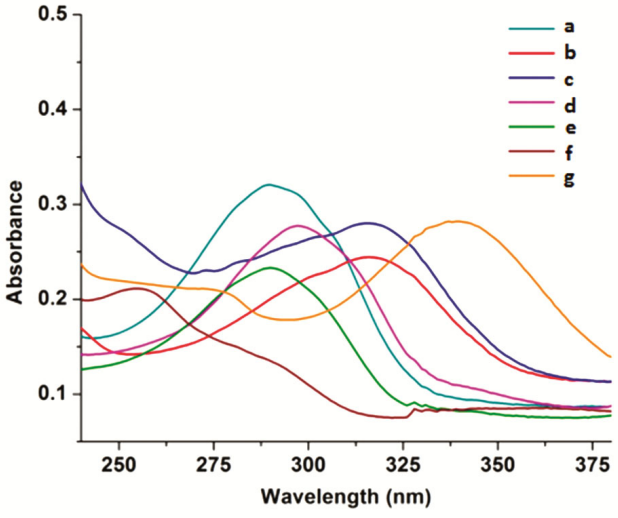

Fig. 2 — Absorption spectra of sugar chalcone derivatives using acetonitrile solvent (1×10^{-5} M), a-g [a = compound 3, b=compound 4, c=compound 5, d=compound 6, e=compound 7, f=compound 8, g=compound 9]

Experimental Details

Synthesis of sugar-chalcone derivatives using microwave oven method (3-9)

To a solution of β-C-glycosidic ketone (1 mmol) in dichloroethane (5 mL) were added pyrrolidine (30%) and aldehyde (1.2 mmol) under microwave conditions. The reaction mixture was concentrated under reduced pressure and extracted using ethyl acetate-water mixture. The ethyl acetate layer was dried over anhydrous sodium sulphate and concentrated to dryness. The product thus obtained was purified through column chromatography.

Physicochemical and spectral data of (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-bromophenyl) -but-3-en-2-one, 3: m.p.228-230°C. Yield 0.30 g (68%). ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 7.65-7.45 (m, 5H, Alk-H, Ar-H), 6.77 (d, *J*= 16.2 Hz, 1H, Alk-H), 5.09 (s, 1H, Sac-OH), 4.87(s, 1H, Sac-OH), 4.53 (t, *J*= 5.0 Hz, 1H, Sac-H), 4.05 (dd, *J*= 3.0 Hz, *J*= 10.1 Hz, 1H,Sac-H), 3.86 (t, *J*= 8.9 Hz, 1H, Sac-H), 3.60 (t, *J*= 9.0 Hz, 1H, Sac-H), 3.39 (t, *J*=9.8

Table 3 — Inhibition effect of compounds **4**, **7** and **9** on growth of bacteria at 75 µL concentration

S. No.	Bacteria	Zone of inhibition of compounds (diameter in mm)		
		Comp. **4**	Comp. **7**	Comp. **9**
1	*Bacillus subtilis*	10	7	13
2	*Pseudomonas aureginosa*	6	2	11
3	*Streptococcus*	12	5	13
4	Control	NI	NI	NI

NI: No Inhibition

Hz, 1H, Sac-H), 3.31-3.27 (m, 1H, Sac-H), 3.40-3.10 (m, 2H, Sac-H), 3.12-3.09 (m,1H, -CH_2), 2.82 (dd, *J*= 9.0 Hz, *J*= 15.9 Hz, 1H, -CH_2), 1.65-1.57 (m, 2H, -CH_2), 1.42(q, *J*= 7.2 Hz, 2H, -CH_2), 0.90 (t, *J*= 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ +DMSO-d_6): δ 202.7, 146.2, 138.3, 136.9, 134.6, 131.9, 129.2, 106.9, 85.5, 81.6, 79.5,79.3, 75.4, 73.0, 48.3, 41.0, 22.1, 18.8. Anal. Calcd for $C_{20}H_{25}BrO_6$: C, 54.43; H, 5.71. Found: C, 54.47; H, 5.75%.

Physicochemical and spectral data of (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-hydroxyphenyl) -but-3-en-2-one, 4: m.p.188-190°C. Yield 0.22 g (58%). ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 9.50 (s, 1H, Ph-OH), 7.53-7.40 (m, 3H, Ar-H), 6.86 (d, *J* = 8.4 Hz, 2H, Ar-H), 6.60 (d, *J* = 15.9 Hz, 1H, Alk-H), 4.76 (s, 1H, Sac-OH), 4.53 (t, *J* = 5.0 Hz, 1H, Sac-H), 4.10-4.07 (m, 1H, Sac-H), 3.89 (t, *J* = 7.8 Hz, 1H, Sac-H), 3.64 (t, *J* = 7.8 Hz, 1H, Sac-H), 3.40 (t, *J* = 9.6 Hz, 1H, Sac-H), 3.32-3.21 (m, 3H, Sac-H), 3.15-3.09 (m, 1H, -CH_2), 2.80-2.77 (m, 1H, -CH_2), 1.64-1.61 (m, 2H, -CH_2), 1.40 (q, *J* = 7.2 Hz, 2H, -CH_2), 0.90 (t, *J* = 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 192.6, 154.8, 138.1, 124.9, 120.4, 118.1, 110.9, 96.9, 75.3, 71.0, 69.8, 69.5, 65.3, 63.1, 37.9, 31.0, 12.1, 8.6. Anal. Calcd for $C_{20}H_{26}O_7$: C, 63.48; H, 6.93. Found: C, 63.53; H, 6.97%.

Physicochemical and spectral data of (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-allyloxyphenyl)-but-3-en-2-one, 5: m.p.204-208°C. Yield 0.19 g (45%); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 7.86-7.80 (m, 3H, Alk-H, Ar-H), 7.24 (d, *J*= 8.7 Hz, 1H, Ar-H), 6.96 (d, *J*= 15.9 Hz, 1H,Alk-H), 6.40-6.30 (m, 1H, Alk-H), 5.73 (d, *J*= 17.1 Hz, 1H, Alk-H), 5.62 (d, *J*= 10.5Hz, 1H, Alk-H), 5.28 (d, *J*= 4.5 Hz, 1H, -OCH_2), 5.05 (d, *J*= 3.0 Hz, 1H, Sac-OH), 4.89(d, *J*= 5.1 Hz, 1H, -Sac-OH), 4.84 (t, *J*= 5.0 Hz, 1H, Ace-H), 4.38 (dd, *J*= 3.9 Hz, *J*=9.9 Hz, 1H, Sac-H), 4.19 (t, *J*= 4.5 Hz, 1H, Sac-H), 3.93 (t, *J*= 4.2 Hz, 1H, Sac-H), 3.71(t, *J*= 9.6 Hz, 1H, Sac-H), 3.63-3.45 (m, 4H, Sac-H, -CH_2), 3.12 (dd, *J*= 9.0 Hz, *J*= 15.9Hz, 1H, -CH_2), 1.95-1.89 (m, 2H, -CH_2), 1.73 (q, *J*= 7.5 Hz, 2H, -CH_2), 1.21 (t,*J*= 7.4Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 202.7, 165.3, 147.6,137.5, 134.8, 131.9, 129.1, 122.7, 119.9, 107.0, 85.4, 81.5, 79.7, 79.4, 75.3, 73.5, 73.1,48.0, 41.0, 22.1, 18.7. Anal. Calcd for $C_{23}H_{30}O_7$: C, 66.01; H, 7.23. Found: C, 66.06; H, 7.27%.

Physicochemical and spectral data of (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-cyanophenyl)-but-3-en-2-one, 6: m.p.172-174°C. Yield 0.23 g (59%); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 7.71-7.62 (m, 4H, Ar-H), 7.55 (d, *J*= 16.2 Hz, 1H, Alk-H), 6.82 (d, *J*= 15.9 Hz, 1H, Alk-H),4.53 (t, *J*= 5.1 Hz, 1H, Ace-H), 4.12 (dd, *J*= 3.9 Hz, *J*= 9.6 Hz, 1H, Sac-H), 3.97-3.90(m, 1H, Sac-H), 3.72 (t, *J*= 8.9 Hz, 1H, Sac-H), 3.44-3.30 (m, 3H, Sac-H), 3.23 (t, *J*=9.0 Hz, 1H, Sac-H), 3.15 (dd, *J*= 3.3 Hz, *J*= 16.2 Hz, 1H, -CH_2), 2.92 (dd, *J*= 7.8 Hz, *J*= 16.1 Hz, 1H, -CH_2), 1.66-1.59 (m, 2H, -CH_2), 1.42 (q, *J*= 7.8 Hz, 2H, -CH_2), 0.92 (t, *J*= 7.2 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 197.3, 140.8, 138.7,132.7, 129.1, 128.7, 118.3, 113.7, 102.5, 80.4, 76.0, 75.3, 74.3, 70.6, 68.3, 43.7, 36.2,17.5, 13.9. Anal. Calcd for $C_{21}H_{26}O_7$: C, 64.60; H, 6.71. Found: C, 64.65; H, 6.74%.

Physicochemical and spectral data of (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(4-carboxy-phenyl)-but-3-en-2-one, 7: m.p.184-186°C. Yield 0.24 g (59%); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 8.04(d, *J*= 8.4 Hz, 2H, Ar-H), 7.64 (d, *J*= 8.4 Hz, 2H, Ar-H), 7.58 (d, *J*= 16.2 Hz, 1H, Alk-H), 6.85 (d, *J*= 16.2 Hz, 1H, Alk-H), 4.53 (t, *J*= 5.1 Hz, 1H, Sac-H), 4.05 (dd, *J*= 4.2Hz, *J*= 10.1 Hz, 1H, Sac-H), 3.87 (t, *J*= 9.2 Hz, 1H, Sac-H), 3.59 (t, *J*= 8.7 Hz, 1H,Sac-H), 3.26-3.13 (m, 5H, Sac-H, -CH_2), 2.84 (dd, *J*= 8.7 Hz, 1H, -CH_2), 1.65-1.57 (m,2H, -CH_2), 1.42 (q, *J*= 7.5 Hz, 2H, -CH_2), 0.90 (t, *J*= 7.4 Hz, 3H, -CH_3); ^{13}C NMR(75MHz, $CDCl_3$ + DMSO-d_6): δ 202.5, 146.1, 143.3, 137.3, 134.9, 133.2, 132.9, 106.8, 85.6,81.6, 79.6, 79.4, 75.4, 73.0, 48.4, 41.1, 22.2, 18.8. Anal. Calcd for $C_{21}H_{26}O_8$: C, 62.06; H, 6.45. Found: C, 62.10; H, 6.49%.

Physicochemical and spectral data of (*E*)-1-(4,6-*O*-butylidene-β-D-glucopyranosyl)-4-(5-bromo-2-hydro-xy-3-formylphenyl)-but-3-en-2-one, 8: m.p.81-82°C. Yield 0.23 g (56%); ^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ 10.3 (s,1H, Ph-OH), 8.20 (d, *J*= 16.2 Hz, 1H, Alk-H), 7.81 (s, 1H, Ar-H), 7.53 (d, *J*= 7.8 Hz,1H, Ar-H), 7.28 (d, *J*= 8.4 Hz, 1H, Ar-H), 7.21 (d, *J*= 15.9 Hz, 1H, Alk-H), 5.26 (bs, 1H, Sac-H), 5.01-4.93 (m, 2H, Sac-H), 4.50 (bs, 1H, Sac-H), 4.29 (bs, 1H, Sac-H), 4.02 (bs,1H, Sac-H), 3.80-3.51 (m, 2H, Sac-H), 3.30-3.20 (m, 2H, -CH_2), 2.02 (bs, 2H, -CH_2),1.86-1.81 (m, 2H, -CH_2), 1.32-1.30 (m, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6): δ 202.9, 160.6, 142.2, 135.7, 132.4, 131.8, 128.8, 127.8, 122.6, 107.0, 85.4, 81.3,80.0, 79.5, 75.4, 73.1, 48.0, 41.0, 22.1, 18.7. Anal. Calcd for $C_{21}H_{25}BrO_8$: C, 51.97; H, 5.19. Found: C, 52.03; H, 5.24%.

Physicochemical and spectral data of (*E*)-1-(4,6-*O*-butylidene- β-D-glucopyranosyl)-4-(3-indolyl)-but-3-en-2-one, 9: m.p.195-198°C. Yield 0.30 g (75%).^{1}H NMR (300MHz, $CDCl_3$): δ 7.86 (d, *J* = 16.2 Hz, 1H, Alk-H), 7.61 (s, 1H, Ind-H), 7.61 (s, 1H, Alk-H), 7.53-7.47 (m, 2H, Ar-H), 7.24-7.22 (m, 2H, Ar-H), 6.81 (d, *J* = 15.9 Hz, 1H, Alk-H), 4.91 (s, 1H, Sac-OH), 4.64 (s, 1H, Sac-OH), 4.55 (t, *J* = 5.1 Hz, 1H, Sac-H), 4.10 (dd, *J* = 3.3 Hz, *J* = 9.0 Hz, 1H, Sac-H), 3.93 (t, *J* = 7.5 Hz, 1H, Sac-H), 3.65 (t, *J* = 7.5 Hz, 1H, Sac-H), 3.43 (t, *J* = 9.6 Hz, 1H, Sac-H), 3.36-3.26 (m, 3H, Sac-H), 3.15 (dd, *J* = 3.0 Hz, *J* = 18.0 Hz, 1H, -CH_2), 2.84 (dd, *J* = 8.7 Hz, *J* = 15.6 Hz, 1H, -CH_2), 1.68-1.59 (m, 2H, -CH_2), 1.43 (q, *J* = 7.5 Hz, 2H, -CH_2), 0.91 (t, *J* = 7.4 Hz, 3H, -CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.8, 142.5 (2C), 135.9, 130.1, 127.6, 126.1, 125.9, 124.9, 117.5, 117.2, 107.0, 85.4, 78.0, 79.8, 79.6, 75.4, 73.1, 48.0, 41.0, 22.1, 18.7. Anal. Calcd for $C_{22}H_{27}NO_6$: C, 65.82; H, 6.78; N, 3.49. Found: C, 65.86; H, 6.81; N, 3.53%.

Conclusion

Thus, different sugar chalcone derivatives were synthesized both in conventional as well as under microwave condition. It was found that the reaction carried out under microwave condition seems to provide an excellent yield with less reaction time. The highly conjugated sugar chalcone found to exhibit higher shift in absorption studies and also found to exhibit excellent antibacterial activities with various human pathogens tested.

Supplementary Information

Supplementary information is available in the website http://nopr.niscpr.res.in/handle/123456789/58776.

Acknowledgement

Authors acknowledge and thank DST, New Delhi for the use of NMR facility under DST-FIST programme at the Department of Organic Chemistry, University of Madras, Guindy Campus, Chennai, India. AH thanks the Department of Chemistry, Government College of Engineering Srirangam, Trichy, India for providing the infrastructure facility.

References

1 Ferreira V F, *Quimica Nova*, 32(3) (2009) 623.
2 Asif H M, Akram M, Saeed T, Ibrahim Khan M, Akhtar N, Rehman R, Ali Shah S M, Ahmed K & Shaheen, *International Research Journal of Biochemistry and Bioinformatics*, 1(1) (2011) 1.
3 *Carbohydrate-Based Drug Discovery*, edited by C-H Wong (Wiley-VCH, Weinheim, Germany) (2003).
4 (a) Hemamalini A, Nagarajan S, Ravindar P, Subramanian V & Mohan Das T, *Synthesis*, 15 (2011) 2495; (b) Hemamalini A, Nagarajan S & Mohan Das T, *Carbohydrate Research*, 346 (2011) 1814; (c) Hemamalini A, Nagarajan S & Mohan Das T, *Carbohydrate Research*, 352 (2012) 12.
5 Rammohan A, Satyanarayana Reddy J, Sravya G, Narasimha Rao C & Zyryanov G V, *Environmental Chemistry Letters*, 18(2) (2020) 433.
6 Verma S, Srivastava A K & Pandey O P, *PharmaTutor*, 6(2) (2018) 22.
7 Salehi B, Quispe C, Chamkhi I, Omari N E, Balahbib A, Sharifi-Rad J, Bouyahya A, Akram M, Iqbal M, Docea A O, Caruntu C, Leyva-Gomez G, Dey A, Martorell M, Calina D, Lopez V & Les F, *Front Pharmacol*, (2021). doi: 10.3.3389/fphar.2020.592654
8 Grewal A S, Kumar K, Redhu S & Bharadwaj S, *International Journal of Pharmaceutical and Applied Sciences*, 3(5) (2013) 278.
9 Yadav A R & Mohite S K, *Research Journal of Pharmaceutical Dosage Forms and Technology*, 12(3) (2020) 191.
10 Mayo K G, Nearhoof E H & Kiddle, J, *Org Lett*, 4(9) (2002) 1567.
11 Mellis R L, Mehltretter C L & Rist C E, *J Am Chem Soc*, 73 (1951) 294.
12 Bonner T G, Bourne E J & Lewis D, *J Chem Soc*, 7453 (1965).
13 Bragnier N & Scherrmann M C, *Synthesis*, 5 (2005) 814.
14 Rodrigues F, Canac Y & Lubineau A, *Chem Commun* (*Cambridge*), 20 (2000) 2049.
15 Riemann I, Papadopoulos M A, Knorst M & Fessner W D, *Aust J Chem*, 55 (2002) 147.