Est. 1984

ORIENTAL JOURNAL OF CHEMISTRY
An International Open Free Access, Peer Reviewed Research Journal

www.orientjchem.org

ISSN: 0970-020 X
CODEN: OJCHEG
2018, Vol. 34, No.(4):
Pg. 2106-2113

Microwave Synthesis, Characterization and Antimicrobial activity of some Chromene derivatives

R. NANDHIKUMAR[1,2]* and K. SUBRAMANI[1,3]

[1]R&D Centre, Bharathiar University Coimbatore, Tamilnadu, India.
[2]Department of Chemistry, The Kavery Engineering College, Salem, Tamilnadu, India.
[3]PG & Research Department of Chemistry Islamiah College, Vaniyambadi, Tamilnadu, India.
*Corresponding author E-Mail: nandhikumar@gmail.com

http://dx.doi.org/10.13005/ojc/3404051

(Received: April 14, 2018; Accepted: June 25, 2018)

ABSTRACT

In the present study the synthesis of Chromene derivatives 7-ethyl-2, 3, 4, 4a-tetrahydro-1H-xanthen-1-one (3a), 7-bromo-2, 3, and 4, 4a-tetrahydro-1 H-xanthen-1-one (3b), 5-ethoxy-2, 3, and 4, 4a-tetrahydro-1 H-xanthen-1-one (3c),7-ethyl-3, 3a-dihydrocyclopenta[b]Chromen-1(2H)-one (4a), 7-bromo-3, 3a-dihydrocyclopenta[b]Chromen-1(2H)-one (4b),and 5-ethoxy -3, 3a-dihydrocyclopenta[b]Chromen-1(2H)-one (4c) have been reported by the reaction of substituted Salicylaldehyde with 2-cyclopenten-1-one/2-cyclohexen-1-one in the presence of ammonium acetate with ethanol using microwave-irradiation. The Microwave synthesized complexes have been categorized via IR, ^{1}H-NMR, ^{13}C-NMR, Mass Spectroscopy then elemental analysis. In this Microwave irradiation method contains two scheme, in the Scheme 2 gives high yield compare to Scheme 1.In the antibacterial and anti-fungal study the compounds 3b, 4a shows good and 4b shows very good activity against *Escherichia coli, Pseudomonas aeruginosa* and *Staphylococcus aureus* and 3b, 3c shows good activity against *Aspergillus Niger*, *Penicillium species* and *Candida albicans*, compare to others. Short reaction time, environment friendly products, high economical, excellent yield and good microbial activity are the highest benefits of this technique which create high commercial value than the other methods.

Keywords: Microwave, 2-Cyclohexen-1-one, Cyclopenten-1-one, antibacterial, antifungal.

INTRODUCTION

Eco-friendly synthetic procedure is a novel and promptly developing methods of medicinal chemistry. It's very fast growing importance is used for medicinal chemistry research fields because these methods are constructed to avoid the chemical waste and save the time. Microwave irradiation[1-3] method is the greatest changes for traditional chemical synthetic root. Through applying the eco-friendly synthetic technique, we can eliminate the use of poisonous thinners, hazardous producing substances and also the elimination of by-product. Gedye with Giguere (1986) stated for the paramount

period that a natural organic synthesis might be directed precisely quickly under microwave synthesis methods. In the medicinal chemistry and natural products field 2H-Chromenes (2H-1-Benzopyrans) are acting as an important intermediate[4-5] for many organic synthesis. Generally some Chromene containing compound used for the intermediates of positive logically arising product, such as Miroestrol compound. Coumarins compounds act as a very good antioxidant[6] and equally fluorescent methods, pointers for custom in evaluating, stabilizers, besides with medicinal usage for their, diuretic, anticoagulant, anti HIV[7], antitumor, anti-inflammatory[8-10], anticanser[11], anti-Alzheimer's[12-13], central nervous system activity[14] anti-leukemic, anti-bacterial[15-25], anti-malarial events[26], emetic[27]. Furthermore, they can be working as grease, paints, colors and used as possible eco-friendly agrochemicals. It has been reported[28-32] that poly functional vinylic compounds can be prepared by using Ammonium acetate substrates. The structures of microwave synthesized Chromene derivatives assumed from their elemental analysis (C, H, O, N, and Br) and IR, ^{1}H, ^{13}C -NMR, Mass spectra and tested the antimicrobial activity. In our knowledge this tecnique is the best methods for microwave synthesis and microbial activity of Chromene derivatives because this is eco-friendly simple method, good yield, short time and more economical.

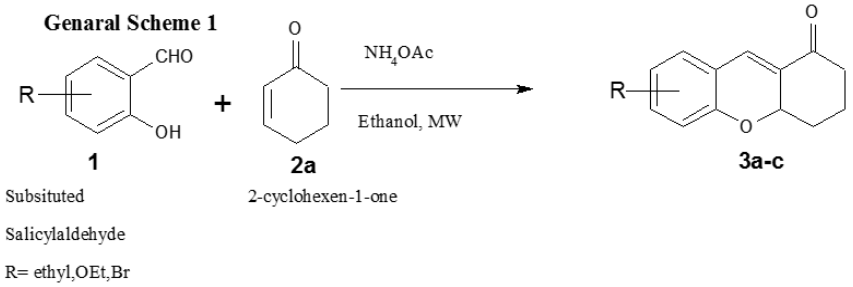
EXPERIMENTAL

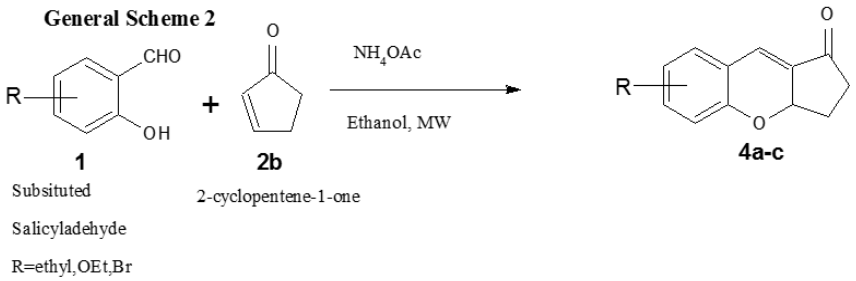
Use the open capillary tube to find out the compound melting points. FT-IR spectra data (KBR) were taken on Perkin-Elmer1300 FT IR spectrometer and Bruker WM-400 instruments (FT NMR400 MHz) recorded ^{1}H NMR &^{13}C NMR (Internal standard-TMS), GC-MS spectra were recorded on GC-Mass spectrometer instruments. Total products presented suitable small analytical report. Cleanliness of the product was tested by thin layer chromatography methods.

Scheme 1

Synthesis of 7-ethyl-2, 3, 4, 4a-tetrahydro-1H-xanthen-1-one (3a)

With a mixture of 5 mm 5-ethyl-2-hydroxybenzaldehyde in ethanol (few ml) and 20 mole% of ammonium acetate followed by of 2-cyclohexen-1-one (10 mm) added and the constant stirring continued on Microwave irradiation for 5 minute. Then the reaction compound was converted into an acid medium with a few ml of concentrated HCl and the bottom level was detached, wash the aqueous level with DCM. The compound deposit was dehydrated and, after the distillation process, providing the Chromene compound 7-ethyl-2, 3, 4, 4a-tetrahydro-1H-xanthen-1-one (3a) and in good yield (Table 1, Scheme 1).





7-Ethyl-2, 3, 4, 4a-tetrahydro-1H-xanthen-1-one (3a): (Scheme-1). m.p. of the product is 172 ºC yield 58 %. IR (KBr,λmax, cm^{-1}): 3116, 2995 (Ar-CH, str), 2860 (C-H str for CH3), 2846-2816 (C-H str for CH2), 1647 (C=O, str), 1534, 1575 (C=C, str), 1421, 1460 (C-C single bond str), 1220, 1290 (C-O single bond str). ^{1}HNMR (DMSO-H_2O) : 8.15 (1H , s), 7.55 (1H , s), 7.03-7.04 (1H , d), 6.66-6.67 (1H , d), 5.03-5.04 (1H, t), 3.28-3.34 (2H ,t), 2.22-2.36 (2H , q),1.67-1.74 (2H , m), 1.65-1.68 (2H , m),1.51-1.53(3H,t).^{13}NMR (DMSO-H_2O): 17.73,23.84,30.52,35.13,42.74,59.14,99.29,107.01,126.22,127.21,128.33,131.93, 144.83, 148.28, 165.31. GC-Mass: m/z = 228 M+.

Synthesis of 7-Bromo-2, 3, and 4, 4a-tetrahydro-1H-xanthen-1-one (3b)

With a mixture of 5 mm 5-Bromo-2-hydroxybenzaldehyde in ethanol (few ml) and 20% per mole of ammonium acetate followed by of 2-Cyclohexen-1-one (10 mm) added and the constant stirring continued on Microwave irradiation for 5 minute. Then the reaction compound was converted into an acid medium with a few ml of concentrated HCl and the bottom level was detached, wash the aqueous level with DCM. The compound deposit was dehydrated and, after the distillation process, providing the Chromene compound 7-bromo-2, 3, and 4, 4a-tetrahydro-1 H-xanthen-1-one (3b)) and in good yield (Table 1, Scheme 1).

7-Bromo-2, 3, and 4, 4a-tetrahydro-1 H-xanthen-1-one (3b): (Scheme-1): m.p. of the product is 213ºC yield 56 %. IR (KBr, λmax, cm^{-1}): 3135, 3014 (Ar-CH str), 2859, 2843 (C-H str for CH2), 1702 (C=O group Str), 1560,1527 (C=C group str), 1384,1365 (single bond C-C str), 1221,1279 (C-O str.),1869 (overtone for halide substitution) ^{1}HNMR (DMSO-H_2O): 8.299 (1H ,s), 7.89 (1H, s),7.348-7.378 (1H ,d) 5.272-5.283 (1H, t), 3.972-3.983 (2H , t), 2.37-2.39 (2H, multiplet), 1.66-1.78(2H, m). ^{13}NMR (DMSO-H_2O) 17.76,23.61,32.88,59.21,98.85,112.68,121.07,128.15,129.94,131.17, 143.76, 148.65, 165.17. GC-Mass: m/z = 227. M+.

Synthesis of 5-Ethoxy-2,3,4,4a-tetrahydroxanthen-1-one (3c)

With a mixture of 5 mm 3-Ethoxy-2-Hydroxybenzaldehyde in ethanol (few ml) and 20 mole% of Ammonium acetate followed by of 2-cyclohexen-1-one (10 mm) added and the constant stirring continued on Microwave irradiation for 5 minute. Then the reaction compound was converted into an acid medium using a few ml of concentrated HCl and the bottom level was detached, wash the aqueous level with DCM. The compound deposit was dehydrated and, after the distillation process, providing the Chromene compound 7-Ethyl-2, 3, 4, 4a-tetrahydro-1H-xanthen-1-one (3a) and in good yield (Table 1, Scheme 1).

5-Ethoxy-2, 3, 4, 4a-tetrahydroxanthen-1-one (3c): (Scheme-1): m.p. of the product is 197 °C yield 62 %. IR (KBr, λmax, cm^{-1}): 3186, 3070 (Ar-CH str.), 2955, 2830 (C-H str, CH_2), 1688 (aromatic C=O Str), 1526, 1474 (C=C group str), 1347, 1316 (C-C group str), 1266, 1223 (C-O str). ^{1}HNMR(DMSO-H_2O):7.98 (1H,s), 7.396-7.399 (1H, d), 7.376-7.393(1H, q), 7.265-7.271 (1H, d), 5.181-5.253(1H, t) , 4.512-4.588 (2H, q),3.172-3.381 (2H),2.476-2.599 (2H,m), 2.453-2.589 (2H, m),2.211-2.232 (3H,t).^{13}HNMR (DMSO-H_2O):17.68, 23.29,29.05,33.65,53.28,59.05,112.29,116.26,118.46,121.16, 134.25, 147.50, 149.65, 152.25, 165.46. Mass spectra: m/z = 244 M+ (base peak).

Scheme 2

Synthesis of 7-Ethyl-3, 3a-dihydrocyclopenta[b] Chromen-1(2H)-one (4a)

With a mixture of 5 mm 5-ethyl-2-hydroxy benzaldehyde in ethanol (few ml) and 20 mole% of Ammonium acetate followed by of 2-cyclopenten-1-one (10 mm) added and the constant stirring continued on Microwave irradiation for 5 minute. Then the compound was converted into an acid medium with a few ml of concentrated HCl and the bottom level was detached, wash the aqueous level with DCM. The organic compound deposit was dehydrated and, after the distillation process, providing the Chromene compound 7-Ethyl-3, 3a-dihydrocyclopenta[b]Chromen-1(2H)-one (4a) and in good yield. (Table 2, Scheme 2).

7-Ethyl-3, 3a-dihydrocyclopenta[b] Chromen-1(2H)-one (4a): (Scheme-II): m.p. of the product is 167 °C yield 66 %. IR (KBr, λmax, cm^{-1}): 3119, 3010 (Ar-CH str.), 2976 (C-H str for CH_3), 2904, 2816 (C-H str for CH_2) 1667 (aromatic C=O group str), 1544, 1450 (C=C group str), 1365 (C-C group str), 1223, 1173(C-O group str). ^{1}HNMR

(DMSO-H_2O): 7.751 (1H, s), 7.334-7.347 (1H, d), 7.269-7.279 (1H, d), 6.951 (1H, s), 5.133-5.247 (1H, t), 4.28-4.34 (2H, t), 3.118-3.166 (2H), 2.671-2.729 (2H,m),2.229-2.366 (3H, m).^{13}C NMR (DMSO-H_2O):17.74,23.74,31.92,34.83,59.94,103 .11,11.12,112.01,126.11,128.33,141.84, 144.89, 148.15,168.32.GC-Mass: m/z = 214 M+.

7-bromo-3, 3a-dihydrocyclopenta[b]Chromen-1(2H)-one (4b)

With a mixture of 5 mm 5-bromo-2-hydroxybenzaldehyde in ethanol (few ml) and 20% per mole of Ammonium acetate followed by of 2-cyclopenten-1-one (10 Mm) added and the constant stirring continued on Microwave irradiation for 5 minute. Then the compound was converted into an acid medium with a few ml of concentrated HCl and the bottom level was detached, wash the aqueous level with DCM. The organic compound deposit was dehydrated and after the distillation process, providing the Chromene compound 7-Bromo-3, 3a-dihydrocyclopenta[b]Chromen-1(2H)-one (4b) and in good yield. (Table 2, Scheme 2).

7-Bromo-3, 3a-dihydrocyclopenta[*b*]Chromen-1(2H)-one (4b)

(Scheme-II): m.p. of the product is 204°C yield 64 %. IR (KBr, λmax, cm^{-1}): 3157, 3021 (Ar-CH str), 2964, 2832 (C-H str, CH2), 171O (aromatic C=O group str), 1573, 1526 (C=C group str), 1465, 1391 (C-C group str), 1197, 1250 (C-O str.), 1895(overtone for halides). ^{1}HNMR (DMSO-H_2O): 8.061 (1H, s), 7.683 (1H, s), 7.511-7.578 (1H, d), 7.499-7.508 (1H, d), 5.371-5.379 (1H, t), 3.029-3.166 (2H, t), 2.265-2.389 (2H, t). ^{13}NMR (DMSO-H_2O): 33.06,36.00,73.12,106.88,11 2.55,115.18,128.33,128.65,123.88,133.06,148.89, 172.12.GC-Mass: m/z = 264 M+.

Synthesis of 5-Ethoxy-3, 3a-dihydrocyclopenta[b] Chromen-1(2H)-one (4c)

With a mixture of 5 mm 3-ethoxy-2-Hydroxybenzaldehyde in ethanol (few ml) and 20 mole% of Ammonium acetate followed by of 2-cyclopenten-1-one (10 mm) added and the constant stirring continued on Microwave irradiation for 5 minute. Then the compound was converted into an acid medium with a few ml of concentrated HCl and the bottom level was detached, wash the aqueous level with DCM. The organic compound deposit was dehydrated and after the distillation process, providing the Chromene compound 5-Ethoxy -3, 3a-dihydrocyclopenta[b]Chromen-1(2H)-one (4c) and in good yield. (Table 2, Scheme 2).

5-Ethoxy-3, 3a-dihydrocyclopenta[b]Chromen-1(2H)-one (4c)

(Scheme-II): m.p. of the product is 187°C yield 63 %. IR (KBr, λmax, cm^{-1}): 3179, 3094, 3027 (Ar-CH str.), 2988, 2931(C-H str for CH_3), 2887(C-H str for CH_2)1667 (aromatic C=O group str), 1594, 1532 (C=C group str), 1475, 1376 (C-C group str), 1189, 1275 (C=O group str). ^{1}HNMR (DMSO-H_2O): 7.555 (1H, s), 7.213 (1H, d), 6.813-6.935 (1H, q), 6.660-6.683 (1H, d), 4.86-4.91 (1H, t), 3.95-4.06 (2H, q), 3.53-3.61 (2H, t), 2.48-2.72(2H, m), 2.22, 2.24(3H, t). ^{13}NMR (DMSO-H_2O): 17.88,30.31,34.11,59.00,68.25,111.67,112.19,115 .55,116.05,12 9.46,138.26,141.76,144.73,169.96. GC-Mass: m/z = 230 M+.

RESULTS AND DISCUSSION

The green synthesis of all sequences of the final product was prepared by the reaction substituted salicylaldehyde and ammonium acetate followed by of 2-cyclohexen-1-one added in the presence of Microwave irradiation. Formation of 3a-3c was established by the occurrence of C-O-C extending peaks at 1279,1266&1290, λmax, cm^{-1} and aromatic C=O group stretching peaks at 1647,1702&1688, λmax, cm^{-1} in IR and aromatic group singlet at 7.75,8.29 & 7.98, λmax, cm^{-1} for the xanthene cyclic group in ^{1}HNMR spectra.

^{1}H-NMR spectrum valued showed a fine triplet at δ 5.03,5. &5.18 due to a xanthene group of their structure were found over spectral values and physical data (Table 1). FT-IR and ^{1}H NMR spectral records exposed carbonyl group absorption band at 1702,1688&1647, λmax, cm^{-1} of the aromatic -CO-C group, aromatic C-O extends band at 1290,1279 & 1266, λmax, cm^{-1} aliphatic group C-H and aromatic C-H group stretching at 2860, 2859 & 2830 and 3116, 31357 & 3186, λmax, cm^{-1} group of xanthene molecule. GC-Mass values also reinforced the planned structure through showing base peak at m/z = 228, 277 & 244M+.

In other methods, the reaction of Substituted Salicylaldehyde and ammonium acetate followed by of 2-Cyclopenten-1-one added in the presence of Microwave irradiation. Formation of 4a, 4b and 4c

was established by the occurrence of C-O-C group stretching peaks at 1223, 1275 & 1250, λmax, cm^{-1} and C=O is stretching peaks at 1667, 1667.41 & 1710, λmax, cm^{-1} in FT-IR and aromatic group singlet at 7.751, 8.06 & 7.55 cm^{-1} for the Chromene cyclic group in ^{1}HNMR spectra.

Table 1: Chromene compounds physical and analytical data (3a, 3b & 3c)

Compounds	Mol.F	Mol. W	Y(%)	m.p. (^{0}C)	Time (Min)	Found/calculated (%)			
						C	H	O	Br
3a	$C_{15}H_{16}O_2$	228	58	172	5	78.92	7.06	14.02	0
						(78.84	6.98	13.86	0.00)
3b	$C_{13}H_{11}BrO_2$	227	56	213	5.5	55.94	3.97	11.46	28.63
						(55.82	3.81	11.48	28.71)
3c	$C_{15}H_{16}O_3$	244	62	197	6	73.75	6.6	19.65	0
						(73.66	6.52	19.52	0.00)

Table 2: Chromene compounds physical and analytical data (4a, 4b & 4c)

Compounds	Mol. F	Mol.Wt	Y (%)	m.p. (^{0}C)	Time (Min)	Found/Calculated (%)			
						C	H	O	Br
4a	$C_{14}H_{14}O_2$	214	66	167	4	78.48	6.59	14.93	0
						(78.38	6.48	14.83	0.00)
4b	$C_{12}H_9BrO_2$	263	64	204	4.5	54.37	3.42	12.07	30.14
						(54.25	3.32	11.98	30.02)
4c	$C_{14}H_{14}O_3$	230	63	187	5	73.07	6.13	20.85	0
						(72.96	6.08	20.75	0.00)

^{1}H-NMR range presented a fine triplet peaks at δ 5.13,5.37 & 4.86 due to Chromene compounds of their structure were found over spectral and physical data (Table 2). FT-IR and ^{1}H-NMR spectral data exposed carbonyl group absorption band at 1667, 1710 & 1667 cm^{-1} of the aromatic-CO-C group, aromatic C-O is stretching band at 1223,12791250 & 1250 cm^{-1} aliphatic group C-H and aromatic group C-H stretching at 2816, 2832 & 2887 and 3119, 3157 & 31863179 cm^{-1} group of Chromene molecule. GC-Mass data also reinforced the planned structure by showing base peak at m/z = 214,264 & 230M+.

Antibacterial activity

Novel synthesized Chromene derivatives are selected for their anti-bacterial behavior *in vitro* beside the species of *Escherichia coli* (*Gram –ve*, micro-organism), Pseudomonas aeruginosa (*Gram –ve*, micro-organism) and *Staphylococcus aureus* (*Gram +ve*, micro-organism) by agar well (disk) diffusion techniques. Ciprofloxacin is used as a standard drug and the outcomes are

Table 3: Antibacterial activity for Chromene compounds (3a-3c &4a-ac)

Antibacterial activity for (3a-3c &4a-4c)mm			
Compounds	*Escherichia coli* (mm)	*Staphylococcus aureus*(mm)	*Pseudomonas aeruginosa*(mm)
3a	6	6	5
3b	7	6	4
3c	8	7	4
4a	7	4	5
4b	16	14	12
4c	5	4	4

shown in Table-3 and Fig.1. In the antibacterial study the compounds 3b, 4a shows good and 4b shows very good activity against *Escherichia coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa*, compare to others.

Anti-fungal activity

Novel green synthesized Chromene compounds are selected for their antifungal behavior in vitro beside the micro-organism of Penicillium species, Aspergillus Niger and Candida albicans, by agar well (disk) diffusion techniques. The experiment products are liquefied in DMSO.

Commercial Amphotericin-B is used as a standard and the outcomes are displayed in Table 4 and Fig. 2. In the anti-fungal study the compounds 3b and 3c shows very good activity against *Aspergillus Niger*, *Penicillium species*, *Candida albicans* and, compare to others.

Table 4: Anti-fungal activity for (3a-3c &4a-4c)

Anti-fungal activity for (3a-3c & 4a-4c)mm			
Compounds	*Penicillium sps* (mm)	*Aspergillus niger* (mm)	*Candida albicans* (mm)
3a	-	-	-
3b	8	4	-
3c	4	5	5

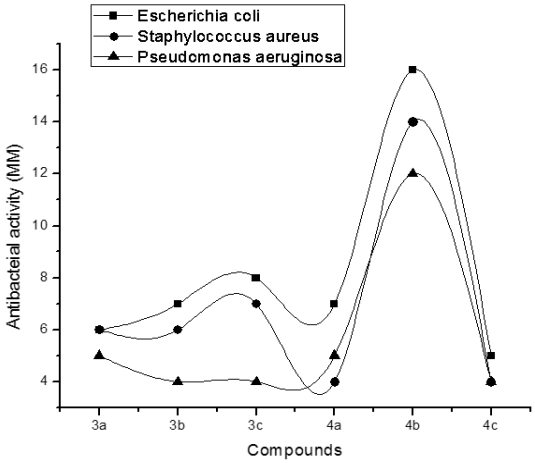


Fig.1. Antibacterial study for compounds (3a-3c & 4a-4c)

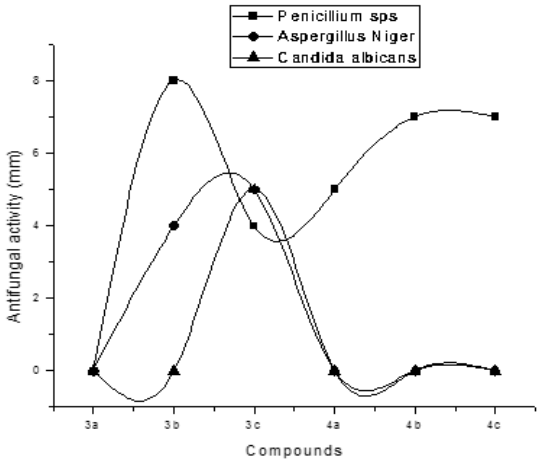


Fig. 2. Anti-fungal study for compounds (3a-3c &4a-4c)

CONCLUSIONS

Microwave assisted synthesis of Substituted Salicylaldehyde with 2-cyclopenten-1- /2-cyclohexen-1-one in the presence of ammonium acetate with ethanol gives a good yield of some novel Chromene compounds (3a-3c and 4a-4c). In this synthetic Microwave irradiation method the compound 4a-4c (Table 1) gives high yield. Total compounds are lively against all the verified bacterial and fungal strains. Compound 3a-3c and 4a-4c are medium or more active against antibacterial and fungal strains for standard drug and antibacterial activity. In the antibacterial and anti-fungal study the compounds 3b, 4a shows good and 4b shows very good activity against *Staphylococcus aureus*, *Pseudomonas aeruginosa* and *Escherichia coli* and 3b, 3c shows very good activity against *Aspergillus Niger*, *Penicillium species* and *Candida albicans*, compare to others. This research work has high economic, because used available and simple catalyst, simple reaction methods, need less time and get ecofriendly nature.

ACKNOWLEDGEMENT

The authors are thankful to the Director, Bharathiyar University R&D center for giving the

opportunity to complete the research and for their constant encouragement to write the article in good form and Dr. G. Sarawathi, HOD of chemistry. Government Engineering College Bargur, Tamilnadu, India for their encouragement and providing necessary research facilities.

REFERENCE

1. Vrushali Patil.; Ashish Asrondkar.; Anil Bobade.; Abhay Chowdhary.; *IJSR*. **2013**, 1688-1690.
2. Shivaputra, A.; Patil,Siddappa A Patil & Renukadevi Patil, *Future Med Chem.*, **2015**, *7.*
3. Abolghasem shameli akandi.; ebrahim balali.; talieh mosavat.; mohammad mehdi ghanbari.; and ali eazabadi. *Orient. J. Chem.*, **2014**, *30*(2), 587-591.
4. S.Arulmurugan, S.; Helen P. Kavitha and Venkatraman,B.R. *Rasayan J. Chem.*, **2010** *3*(3) 385-410.
5. Gudipudi Gopinath.; VenuSankeshi.; Shaymperugu.; Malini D.Alaparthi.; Srinivas Bandaru.; Vijay K.Pasala.;Prasad RaoChittineni.; David Krupadanam, G.L.; Someswar R. Sagurthi. *European J of Med Chem.*, **2016**, *124*(29), 750-762.
6. Jessica Elizabeth.; Philip Shanty.; Angamaly Antony Sneha.; Jose Eettinilkunnathi.; M.R. Prathapachandra Kurup,M.R .; Mohanan Puzhavoorparambi.;Velayudhan. *Inorganica Chimica Acta.*, **2018**, *469*(1), 87-97.
7. Nancy Thomas and Subin Mary Zachariah. *Asian J Pharm Clin Res.*, **2013**, *6*(2), 11-15.
8. Shu-Ting Chung.; Wen-Hsin Huang.; Chih-Kuo Huang.; Feng-Cheng Liu.; Ren-Yeong Huang.; Chin-Chen Wu.; An-Rong Lee.; *Research on Chemical Intermediates.*, **2016**, *42*(2), 1195–1215.
9. Vrushali Patil.; Ashish Asrondkar.; Anil Bobade.; Abhay Chowdhary.; *IJSR.*, **2013**, 2319-7064.
10. Bahubali M.Chougala.; S.Samundeeswari.; Megharaja Holiyachi.; Nirmala S.Naik.; Lokesh A.Shastri.; Suneel Dodamani.; SunilJalalpure .; Sheshagiri R. Dixit .; Shrinivas D. Joshi .; Vinay A. *European J of Med Chem.*, **2018**, *143*(1), 1744-1756.
11. Jawaid Akhtar Ahsan.; Ahmed Khan Zulphikar.; Ali Rafi Haider.; Shahar Yar, M. *European J of Med Chem.*, **2017**, *125*(5), 143-189.
12. Islam H. El Azab.; Mohamed M. Youssef and Mahmoud A. Amin. *Molecules.*, **2014**, *19*, 19648-19664.
13. Sujay Laskar and Goutam Brahmachari. Signpost Open Access *J. Organic & Biomol Chem.*, **2014**, *2*, 1-50.
14. Rupnar, B.D.; Rokade P. B.; Gaikwad, P. D and Pangrikar, P.P. *IJCEBS.*, **2014**, *2*(1), 2320–4087.
15. Jessica Elizabeth.; Philip Shanty.; Angamaly Antony Sneha .; Jose Eeettinilkunnathi.; Prathapachandra Kurup Mohanan, M.R.; Puzhavoorparambi.; Velayudhan. *Inorganica Chimica Acta.*, **2018**, *469*(1), 87-97.
16. Latha Rani, N.; Manasagangotri.;Mysuru.; Prashanth,T.; Sridhar, M.A.; Gurupadaswamy, H.D.; Shaukath Ara, K & N. K. Lokanath N.K. **2016**, *11*, 262-270.
17. Shweta Saxena.; Ratnesh das and Arti saxena. *Chem Sci Rev Let.*, **2015**, *4*(14), 688-694.
18. Lamia Dammak.;Mariem Kammoun.;Noureddine Allouche.; Houcine Ammar and Souhir Abid. *Org. Commun.*, **2017**, *10*, 1 32-39.
19. Nirav K Shah.; Nimesh M Shah., Manish P Patel.; Ranjan G Patel, *J of Chem Sci.*, **2013**, *125*(3), 525–530.
20. Aziz Behrami, *Orient. J. Chem.*, **2014**, *30*(4), 1747-1752.
21. Chetan B. Sangani.; Nimesh M. Shah.; Manish P. Patel and Ranjan G. Patel, *J. Serb. Chem. Soc.*, **2012**, *77* (9) 1165–1174.
22. Sharaish, P.; Sivasubramanian, N.; Bollywar Archana Devi.; Madhulatha, C.; Sushma, G.S and Maithri, P. *IJPLS.*, **2013**, *4*(3), 2458-2464.
23. Hoda Pasdar.; Naser Foroughifar.; Bahare Hedayati Saghavaz.; *J Med Microbiol Infec Dis.*, **2015**, *3*(3-4), 75-79.
24. Pankaj S. Chaudhari.; Shrikant S. Patil. *Int J of Chem Tech Res.*, **2017**, *10*(15), 126-134.
25. Venkataraman, S.; Meera,R.; Vidya Ramachandran.; Nagarajan,K.; Aruna,A.; Padma Thanga Parameswari, S and Devi,P.; *IJRPC.*, **2013**, *3*(4).
26. A.Parthiban, A.; Muthukumaran,J. AshanManhas.; Kumkum Srivastava.; Krishna, R.; Surya Prakash Rao,H.; *Bio & Med Chem Lett.*, **2015**, *25*(20), 4657-4663.

27. Islam H. El Azab.; Mohamed M. Youssef and Mahmoud A. Amin. *Molecules*., **2014**, *19*, 19648-19664.
28. Nirav.K.Shah.; Nimesh.M Shah.; Manish P Patel, Ranjan G Patel, *Chem. Sci*., **2013**, *125*, 525-530.
29. Jian-Feng Zhou.; Yuan-Zhi Song.; Jin-Shun Lv.; Gui-Xia Gong.; Shujiang Tu. *Int. J. of Rapid comm.syn org chem*., **2009**, *8*,112.
30. Jian-Feng Zhou.; Xiao-Jun Sun.; Feng-Wen Lou Meng Lv.; Lu-Lu Zhang.; *Res Chem Intermed*., **2013**, *39*, 1401–1408.
31. Kanakaraju, S.; Prasana Srinivas Basavoju, B.; Chandramouli, G. V. P. *Arb J chem*., **2017**, *10*(2), 2705-2713.
32. Ahmed Khodairy.; Ali, M.; Ali, T.; Mohamed, El-Wassimy. *J of Het Chem*., **2017**, *54*, 3342–3349.