Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. *84* (4) 355–364 (2019)
JSCS–5189
UDC 547.814.1–41+537.5–962:615.28
Original scientific paper

Microwave-assisted synthesis of 2,8-di(alkyl/aryl)-4,6-dichloro--2*H*,8*H*-pyrano[3,2-*g*]chromene-3,7-dicarbaldehydes and their antimicrobial activity

RUPIREDDY VENKATARAMANA[1], VENKATA RAMANA REDDY CHITTIREDDY[1]*, DONGAMANTI ASHOK[2] and KUDLE KARUNAKAR RAO[3]

[1]*Department of Chemistry, Jawaharlal Nehru Technological University Hyderabad, Kukatpally, Hyderabad, Telangana, 500 085, India;* [2]*Department of Chemistry, Osmania University, Hyderabad, Telangana, 500 007, India and* [3]*Department of Biochemistry, Osmania University, Hyderabad, Telangana, 500 007, India*

(Received 27 January; revised 26 October 2018; accepted 5 February 2019)

Abstract: A series of 2,8-di(alkyl/aryl)-substituted bischromanone derivatives were synthesized in one pot from 4,6-diacetylresorcinol and aliphatic/aromatic aldehydes in the presence of pyrrolidine/piperidine under conventional heating and microwave irradiation. The 2,8-di(alkyl/aryl)-substituted bischromanones were converted into a new series of 4,6-dichloro-3,7-diformyl-2,8-di(alkyl/aryl)--substituted bischromenes using the Vilsmeier–Haack reagent. The structures of the compounds were established based on elemental analysis, IR, ^{1}H-NMR, ^{13}C--NMR and LC–MS spectral data. All the synthesized compounds were evaluated for their antimicrobial activity. Some of the compounds showed very good activity compared to standard drugs against all the tested pathogenic bacteria and fungi.

Keywords: bischromanone; bischromene; Vilsmeier–Haack reagent; microwave irradiation; antimicrobial activity.

INTRODUCTION

Chromene derivatives are an important class of heterocyclic ring systems consisting of benzene fused to a pyran ring, which appears as an important structural component in natural products[1–3] and synthetic drugs[4–6] with interesting biological activity. Several chromene derivatives possess important biological activities, such as anticancer,[7] antitumor,[8] anti-inflammatory,[9] antidiabetic,[10] antimicrobial,[11] antiviral,[12] antitubercular,[13] anti-HIV,[14] *etc.* In particular, various chromene derivatives of 2*H*-chromenes have been reported with important medicinal applications.[15–17] Some of them are currently used as drugs, such as bimakalim as an opener of KATP-channels,[18] cannabichromene (CBC) and some

*Corresponding author. E-mail: vrr9@yahoo.com
https://doi.org/10.2298/JSC180127011V

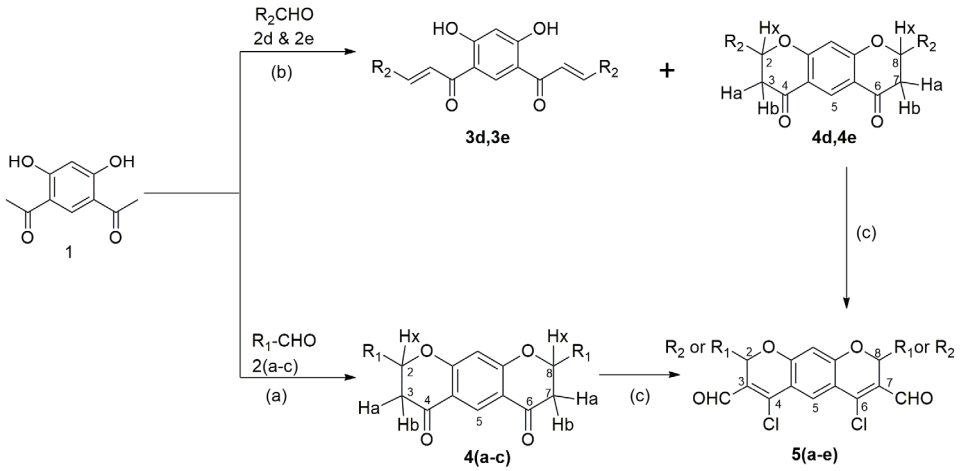
of its analogs with therapeutic potential for the treatment of anti-inflammatory diseases.[19] Acronycine isolated from the bark of *Acronychia baueri* exhibits anti-tumor[20] activity. Erysengalenseins B and C isolated from the stem bark of the Cameroonian medicinal plant are used for the treatment of stomach pain, female infertility and gonorrhea.[21]

In recent years, the concept of the homodimer approach (combination into a single molecule of two identical structural units) has become a powerful tool in medicinal chemistry research either to improve the overall potency of the parent compounds or to obtain an entirely new biological activity.[22,23] Familiar reported examples are bisflavanones, biscoumarins and bischromones.[24]

Heterocyclic *β*-chloroaldehydes are mainly synthesized by the Vilsmeier–Haack ($POCl_3$ + DMF) reagent.[25] Vilsmeier–Haack chloroformylation reactions worked on keto methylene cyclic substrates, whereby heterocyclic chlorovinyl-aldehydes were synthesized.[26,27] The chloroaldehydes were important and versatile molecular building blocks for the synthesis of a variety of biologically active heterocyclic compounds.[28,29] This prompted the present synthesis of some new 2,8-di(alkyl/aryl)-substituted chloroaldehyde derivatives of bischromene.

EXPERIMENTAL

The synthetic route for the preparation of bischromenes **5a**–**e** is shown in Scheme 1.



Aliphatic and aromatic aldehydes: **2a**) pivalaldehyde, **2b**) isobutyraldehyde, **2c**) cyclohexanecarbaldehyde, **2d**) benzaldehyde and **2e**) 4-methylbenzaldehyde; $\mathbf{R_1}$ = a) *tert*-butyl, b) isopropyl and c) cyclohexyl; $\mathbf{R_2}$ = d) Ph and e) *para*-tolyl; reagents and conditions: a) pyrrolidine, 80 °C, 4–6 h and MWI, 8–12 min; b) piperdine, 80 °C, 5–6 h and MWI, 12 min; c) DMF/$POCl_3$, 0 to 50 °C, 1–2 h and MWI, 8–10 min

Scheme 1. Synthetic route for the preparation of bischromenes **5a–e**.

Materials

All solvents and chemicals were obtained commercially, mostly from Sigma–Aldrich, and were used without further purification.

Equipment

Melting points were determined in open capillaries and are uncorrected. Purity of the compounds was checked by TLC on silica gel 60 F_{254} (Merck). The ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance II 400 spectrometer (400 and 100 MHz, respectively) in $CDCl_3$ or DMSO-d_6 using TMS as the internal standard. Mass spectra were recorded on a Shimadzu LCMS-2020 mass spectrometer.

Analytical and spectral data of the synthesized compounds are given in Supplementary material to this paper.

*Conditions for LC-MS spectrum of compounds **3d**, **3e**, **4a**, **4b**, **4d**, **4e**, **5b**, **5d** and **5e***

Method of file is AF-KE-8.5.lcm. Tuning of file is D:\LCMS\Tuning files\Tuning-ESI--03022017.lct. Description: Kintex EVOC-18 (50×3.0 mm 2.6 μm). Mobile phase: A: 2.5 mM NH_4HCOO in water + 5 % acetonitrile. B: acetonitrile + 5 % 2.5 mM NH_4HCOO in water. T/B %: 0.01/5, 4/95, 5/95. Flow: 0.8 mL min^{-1} (gradient).

*Conditions for LC-MS spectrum of compounds **4c**, **5a** and **5c***

Column: kinetex EVO C-18 (50×3 mm, 2.6 μm). Mobile Phase: A: 2.5 mM aq NH_4OAc, B- acetonitrile. T/B %: 0.01/10, 4/90, 8/90. Flow rate: 0.8 mL / min (gradient).

Mass spectra for derivative **3d** were recorded in the negative ion mode. The IR spectra were recorded in KBr on a Shimadzu FTIR 8400S spectrophotometer. Elemental analysis was realized on a Vario-11 CHN analyzer. All the microwave irradiation experiments were performed in a CEM Discover microwave system and reaction temperatures were monitored by an equipped IR sensor.

*General procedure for the synthesis of (2,8-di-*tert*-butyl-2,3,7,8-tetrahydro-4*H*,6*H*-pyrano-[3,2-*g*]-chromene-4,6-dione (**4a**)*

Conventional heating method. To a stirred solution of 1,1′-(4,6-dihydroxy-1,3-phenylene)bis[ethanone] (**1**, 5.15 mmol) in ethanol were added pivalaldehyde (**2a**, 11.33 mmol) and pyrrolidine (5.15 mmol) at room temperature. The reaction mixture was refluxed for 6 h. The progress of the reaction was monitored by TLC (EtOAc/hexane 1/4). Upon completion of the reaction, the mixture was cooled to room temperature and poured into ice-cold water under stirring. The obtained solid was filtered off and washed with cold water (10 mL) then dried under high vacuum. The crude product was purified by column chromatography using a mixture of EtOAc/hexane to afford 2,8-di-*tert*-butyl-2,3,7,8-tetrahydro-4*H*,6*H*-pyrano[3,2-*g*]chromene-4,6-dione (**4a**) as a white solid in 60 % yield.

Microwave irradiation method. To a mixture of 1,1′-(4,6-dihydroxy-1,3-phenylene)bis-[ethanone] (**1**, 5.15 mmol) in ethanol (2.5 mL) were added pivalaldehyde (**2a**, 11.33 mmol) and pyrrolidine (5.15 mmol) in a glass vial equipped with a cap and then subjected to microwave irradiation for 10 min at 80 °C, at an irradiation power of 180 W. The progress of the reaction was monitored by TLC (EtOAc/hexane 1/4). Upon completion, the reaction mixture was cooled to room temperature and poured into ice-cold water under stirring. The solid obtained was filtered and washed with cool water (10 mL) then dried under high vacuum. The crude product was purified by column chromatography using a mixture of EtOAc/hexane to afford 2,8-di-*tert*-butyl-2,3,7,8-tetrahydro-4*H*,6*H*-pyrano[3,2-*g*]chromene-4,6-dione (**4a**) as a white solid in 85 % yield.

*General procedures for the synthesis of 2,8-di-*tert*-butyl-4,6-dichloro-2*H*,8*H*-pyrano[3,2-g]-chromene-3,7-dicarbaldehyde (**5a**)*

Conventional heating method. A round-bottom flask was charged with 2.5 mL of DMF and cooled to 0 °C. Phosphoryl chloride (1.51 mmol) was added dropwise under stirring, the mixture was stirred for 15 min at 0 to 5 °C, and a solution of 2,8-di-*tert*-butyl-2,3,7,8-tetrahydro-4*H*,6*H*-pyrano[3,2-*g*]chromene-4,6-dione (**4a**, 0.30 mmol) in 1.5 mL of DMF was added. The mixture was stirred for 15 min at 0 to 5 °C and the temperature increased to 50 °C and stirred for 1 h. The progress of the reaction was monitored by TLC (EtOAc/hexane, 1/5). Upon completion, the reaction mixture was cooled to room temperature, poured into ice water under stirring and then neutralized with a saturated aqueous $NaHCO_3$ solution. The obtained solid was filtered off and washed with water (30 mL) followed by *n*-pentane (15 mL) and then dried under high vacuum to afford 2,8-di-*tert*-butyl-4,6-dichloro-2*H*,8*H*-pyrano[3,2-*g*]chromene-3,7-dicarbaldehyde (**5a**) as a yellow solid in 65 % yield.

Microwave irradiation method. A round-bottom flask was charged with 2 mL of DMF and cooled to 0 °C. Then 1.51 mmol of phosphoryl chloride was added dropwise, the mixture was stirred for 15 min at 0 to 5 °C, and a solution of 0.3 mmol of 2,8-di-*tert*-butyl-2,3,7,8-tetrahydro-4*H*,6*H*-pyrano[3,2-*g*]chromene-4,6-dione (**4a**) in 1 mL of DMF was added. The mixture was maintained for 15 min at 0 to 5 °C, then transferred into a glass vial equipped with a cap and subjected to microwave irradiation for 8 min at 80 °C. The progress of the reaction was monitored by TLC (EtOAc/hexane, 1/5). Upon completion, the reaction mixture was cooled to room temperature, poured into ice water under stirring and then neutralized with saturated aqueous $NaHCO_3$ solution. The obtained solid was filtered off and washed with water (30 mL) and *n*-pentane (15 mL) then dried under high vacuum to afford 2,8-di-*tert*-butyl-4,6-dichloro-2*H*,8*H*-pyrano[3,2-*g*]chromene-3,7-dicarbaldehyde (**5a**) as a yellow solid in 83 % yield.

Biological assays

The bacterial and fungal strains obtained from the Department of Biochemistry, Osmania University, were used for evaluating the antimicrobial activity of the synthesized compounds.

Antibacterial activity. The bacterial cultures were incubated for 24 h at 37 °C on nutrient agar. The synthesized compounds were dissolved in DMSO, the antibacterial standard was diluted in sterile distilled water and the final volume was made with a concentration approximately 10^5–10^6 CFU mL^{-1}. For the agar disc diffusion method, Luria Bertani media was prepared, autoclaved and poured into sterilized Petri plates and then the plates were spread with Gram-positive bacterial strains and Gram-negative bacterial strains separately. Then sterile discs were kept and the synthesized compounds samples were added in two different concentrations (50 and 100 μg/mL) to the discs, which were incubated at 37 °C for 24 h. Then zone of inhibition was measured. All the experiments were performed in triplicate and the results are expressed as zone of inhibition (mm).

Antifungal activity. Two types of fungi cultures were incubated in potato dextrose agar (PDA) medium at 25±1 °C for 5 days to obtain new mycelium for antifungal assay, then a mycelia as discs of approximately 0.45 cm diameter cut from the culture medium were picked out with a sterilized inoculation needle and inoculated in the center of a PDA plate. The test compounds were dissolved in DMSO at a concentration of 100 μg mL^{-1} and 0.1 mL of was added to the potato dextrose agar medium (PDA) plate. The inoculated plates were incubated at 25 °C for 5 days. Acetone was diluted with sterilized distilled water and used as the control, while amphotericin B (100 μg mL^{-1}) was used as the standard control. Three replicates of each experiment were performed. The radial growth of the fungal colonies was measured on the 5^{th} day.

RESULTS AND DISCUSSION

In previous approaches, 4,6-diacetylresorcinol (**1**) was condensed with different aromatic aldehydes in 1 % ethanolic sodium hydroxide to give the corresponding chalcones,[30–32] which were further converted to bisflavanones.[33] There was no evidence of the formation of bisflavanones in a single step. The intention was therefore to develop a fast and efficient one-pot method for the preparation of such bisflavanone and bischromanone derivatives, which could be further converted to the corresponding bischromenes. Initially 2,8-dialkyl-substituted bischromanone **4a**–**c** derivatives were synthesized in one pot from 4,6-diacetylresorcinol (**1**) and aliphatic aldehydes (**2a**–**c**) in the presence of pyrrolidine under conventional and microwave irradiation conditions, as shown in Scheme 1 and the results are summarized in Table I. Under the same reaction conditions, only 15–25 % of 2,8-diphenyl-2,3,7,8-tetrahydro-4*H*,6*H*-pyrano[3,2-*g*]chromene-4,6--dione (**4d**) and 2,8-di-*p*-tolyl-2,3,7,8-tetrahydro-4*H*,6*H*-pyrano[3,2-*g*]chromene-4,6-dione (**4e**), and 10–20 % of 1,1′-(4,6-dihydroxy-1,3-phenylene)bis[3-phenylprop-2-en-1-one] (**3d**) and 1,1′-(4,6-dihydroxy-1,3-phenylene)bis[3-*p*-tolylprop--2-en-1-one] (**3e**) were formed. It was therefore decided to screen other bases in an effort to improve the yields of **4d** and **4e**.

TABLE I. Comparison of the yields of compounds **4a**–**e** and **5a**–**e** under different synthetic conditions

Compound	Melting point, °C	Conventional heating		Microwave irradiation	
		Time, h	Isolated yield, %	Time, min	Isolated yield, %
4a	150–152	6	60	10	85
4b	142–144	4	65	10	81
4c	120–122	5	68	10	82
4d	182–184	6	45	12	51
4e	165–167	5	40	12	53
5a	145–147	1	65	08	83
5b	130–131	1	68	08	80
5c	170–171	2	62	10	79
5d	200–201	2	59	08	75
5e	189–191	2	66	10	81

A set of different bases, *i.e.*, morpholine, DIPEA, piperazine, piperidine and KOH, were tested with **2d** and **1** in ethanol using microwave (MW) irradiation for 12 min and conventional methods for 5 h at 80 °C. The results are summarized in Table II.

From Table I, the base piperidine under microwave irradiation was found to be the most effective for this transformation furnishing 51 % yield of the desired product 2,8-diphenyl-2,3,7,8-tetrahydro-4*H*,6*H*-pyrano[3,2-*g*]chromene-4,6--dione (**4d**) and a smaller amount of 1,1′-(4,6-dihydroxy-1,3-phenylene)bis[3--phenylprop-2-en-1-one] (**3d**, 12 % yield) was also isolated. Thus, this optimized

condition was applied for the synthesis of 2,8-di-*p*-tolyl-2,3,7,8-tetrahydro--4*H*,6*H*-pyrano[3,2-*g*]chromene-4,6-dione (**4e**) in 55 % yield, and 10 % of 1,1′--(4,6-dihydroxy-1,3-phenylene)bis[3-*p*-tolylprop-2-en-1-one] (**3e**) was also isolated. Furthermore, compounds **4a**–**e** were converted to **5a**–**e** in the presence of Vilsmeier–Haack reagent (DMF+$POCl_3$) at 0–50 °C under conventional and microwave irradiation methods, as shown in Scheme 1 and the results are summarized in Table II.

TABLE II. Screening of the bases under conventional and microwave irradiation conditions

Entry	Base	Conventional heating		Microwave irradiation	
		Yield of **4d**, %	Yield of **3d**, %	Yield of **4d**, %	Yield of **3d**, %
1	Pyrrolidine	15	10	25	20
2	Morpholine	10	12	14	21
3	DIPEA	38	10	45	15
4	Piperazine	12	15	15	18
5	Piperidine	45	15	51	12
6	KOH	–	91	5	92

The structures of compounds **4a**–**e** and 5**a**–**e** were characterized by IR, ^{1}H-NMR, ^{13}C-NMR and mass spectroscopy, as well as elemental analysis. The IR spectrum of compound **4b** contained the absorption of carbonyl groups at 1741 cm^{-1}. The ^{1}H-NMR spectrum of **4b** showed three characteristic signals due to the protons of the 2-CH, 8-CH groups and the 3-CH_2, 7-CH_2 group at the chiral carbon atom of the chromanone pyran ring, which formed an ABX system (H_a, H_b and H_x). The H_a proton, which is in the *cis* position relative to the H_x proton, resonated from 2.57 ppm as a doublet of doublets *(dd)* with coupling constants $J_{vicinal}$ = 7.3 Hz and $J_{geminal}$ = 16.8 Hz, while the H_b proton, which is in the *trans* position relative to the H_x proton, was shifted downfield to 2.73 ppm as a doublet of doublet *(dd)* with coupling constants $J_{vicinal}$ = 12.8 Hz and $J_{geminal}$ = = 16.8 Hz. The H_x proton appeared at 4.25–4.38 ppm with vicinal coupling constants 7.3 and 12.8 Hz had matching vicinal spin–spin interaction constants of H_{ax} and H_{bx}. The proposed structure of compound **4b** was further supported by the ^{13}C-NMR spectrum, in which the C-2 and C-3 carbons of the pyrane ring resonated at 31.26 and 82.42 ppm respectively and carbonyl carbons signal appeared at 190.47 ppm and in the LCMS spectrum 302.9 $[M+H]^+$ appeared as the base peak.

Based on the spectral data, compounds **5a**–**e** were identified as 4,6-dichloro--2,8-dialkyl/aryl-2*H*,8*H*-pyrano[3,2-*g*]chromene-3,7-dicarbaldehyde (Fig. 1). In the IR spectrum of compound **5b**, a characteristic peak appeared at 1742 cm^{-1}, corresponding to the aldehyde group. The signals at δ 5.16–5.19 ppm (H2 and H8) in the ^{1}H-NMR spectrum and the signals at δ 80.26 ppm (C2 and C8), 125.63–125.76 ppm (C3 and C7) and the carbonyl carbon at 187.98 ppm in the

^{13}C-NMR spectrum of compound **5b** confirmed the formation of the 2*H*-chromene skeleton and in the LC-MS spectrum two molecular ion peaks appeared as 395.0 $[M+H]^+$ and 397.0 $[M+2+H]^+$ in 3:1 ratio due to the chloro group of chromene **5b**.

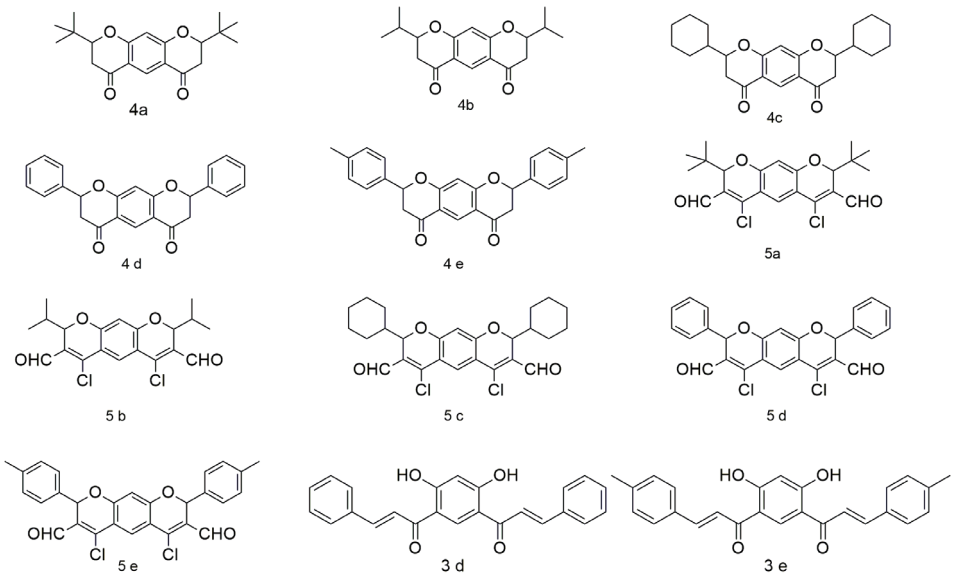


Fig. 1. The synthesized 2,8-dialkyl/aryl-substituted bischromanones (**4a**–**e**), bischromenes (**5a**–**e**) and 1,1′-(4,6-dihydroxy-1,3-phenylene)bis[3-arylprop-2-en-1-one] (**3d** and **3e**).

Antibacterial activity

All the synthesized compounds **4a**–**e** and **5a**–**e** were screened for their antibacterial activity against the Gram-negative bacterial strains *Escherichia coli* (MTCC 43) and *Raoultella planticola* (MTCC 530) and the Gram-positive bacterial strains *Bacillus subtilis* (MTCC 121) and *Staphylococcus aureus* (MTCC 96) at the concentrations 50 and 100 μg mL^{-1} and gentamycin used as the reference. The agar well-diffusion method[34,35] was used to assay the antibacterial activity against the test strains. The results obtained as zone of inhibition in mm are presented in Table III. All the compounds showed relatively better activity against the Gram-negative bacteria than against the Gram-positive bacterial strains. The compounds having a cyclohexyl substituent, **4c** and **5c**, showed better activity against both the Gram-negative and Gram-positive bacterial strains. The compounds with a *para*-tolyl substituent, **4e** and **5e**, showed good activity against the both types of bacterial strains at both 50 and 100 μg ml^{-1} concentrations. The compounds **4b**, **4d** and **5b** showed moderate activity against Gram-positive and Gram-negative bacterial strains. The compounds having *tert*-butyl group (**4a** and **5a**) showed poor activity against all bacterial strains. How-

ever, in the case of the chromenes of chloroaldehydes derived from chromanone, the activity did not depend greatly on the chloro and aldehyde substitutions, as evidenced by the fact that **4c**, **5c**, **4e** and **5e** all had approximately the same level of activity.

TABLE III. Antimicrobial activity (zone of inhibition, mm) of 2,8-dialkyl/aryl-substituted bischromanones **4a**–**e** and bischromenes **5a**–**e**

Compound	Gram negative bacteria				Gram positive bacteria				Fungal strains	
	E. coli		*R. planticola*		*B. subtilus*		*S. aureus*		*C. albicans*	*A. niger*
	Concentration of compounds **4a**–**e** and **5a**–**e**, μg mL^{-1}									
	50	100	50	100	50	100	50	100	100	100
4a	7.5	12.3	8.1	14.9	7.8	10.2	9.0	13.3	7.2	10.0
4b	9.2	13.5	8.9	14.1	9.0	11.3	9.7	14.5	9.2	10.5
4c	**10.5**	**17.8**	**10.0**	**14.5**	**11.2**	**17.2**	**12.9**	**17.6**	**13.0**	**12.0**
4d	8.1	13.5	8.3	13.8	9.5	17.0	8.5	14.7	12.8	11.2
4e	9.3	14.7	10.5	15.3	12.6	18.0	10.7	16.3	11.6	8.9
5a	8.1	12.5	8.0	14.0	8.1	11.5	8.2	13.7	9.9	9.5
5b	9.8	14.1	9.0	13.7	8.6	13.2	11.3	14.6	8.8	9.2
5c	**13.2**	**18.6**	**11.5**	**16.9**	**9.6**	**17.9**	**12.6**	**17.0**	**13.5**	**12.6**
5d	9.0	13.4	9.6	13.5	8.8	14.7	9.5	15.8	12.4	10.6
5e	10.0	17.1	10.0	16.2	10.4	16.2	10.3	16.0	13.2	9.9
Gentamicin	12.6	18.5	11.2	16.4	12.0	18.0	13.2	17.5	–	–
Amphotericin B	–	–	–	–	–	–	–	–	14.5	13.2

Antifungal activity

All the synthesized compounds were screened for their antifungal activity against two pathogenic fungi, *Aspergillus niger* and *Candida albicans* using amphotericin B as the reference and the results obtained as zone of inhibition in mm are presented in Table III. All the compounds showed moderate antifungal activity against the tested fungal strains. Compounds **4c** and **5c** showed good activity against *Candida albicans*.

CONCLUSIONS

Novel 2,8-dialkyl/aryl-substituted bischromanones and bischromenes were synthesized in one pot under microwave and conventional synthetic methods. The green synthetic method of microwave irradiation synthesis was established to be an efficient method over conventional method. All the titled compounds were screened for their *in vitro* antimicrobial activity. It was observed that compounds **4c**, **4e**, **5c** and **5e** exhibited potent antibacterial activity and compounds **4c** and **5c** showed good antifungal activity against all the tested strains compared to the standard drugs at their respective concentrations.

SUPPLEMENTARY MATERIAL

Spectral and analytical data of the synthesized compounds are available electronically at the pages of journal website: http://www.shd.org.rs/JSCS/, or from the corresponding author on request.

Acknowledgments. The authors are grateful to the Head of Department of Chemistry JNTU-H, for providing laboratory facilities and the Director, Central Facilities for Research and Development (CFRD), Osmania University, Hyderabad, for providing the spectral analysis facilities. The authors are thankful to the Department of Biochemistry Osmania University, Hyderabad, for providing the biological activity facilities.

ИЗВОД

СИНТЕЗА 2,8-ДИ(АЛКИЛ/АРИЛ)-4,6-ДИХЛОР-2*H*,8*H*-ПИРАНО[3,2-*g*]ХРОМЕН-3,7-ДИКАРБАЛДЕХИДА ПОД МИКРОТАЛАСНИМ ЗРАЧЕЊЕМ И ИСПИТИВАЊЕ ЊИХОВЕ АНТИМИКРОБНЕ АКТИВНОСТИ

RUPIREDDY VENKATARAMANA[1], VENKATA RAMANA REDDY CHITTIREDDY*[,1], DONGAMANTI ASHOK[2] и KUDLE KARUNAKAR RAO[3]

[1]Department of Chemistry, Jawaharlal Nehru Technological University Hyderabad, Kukatpally, Hyderabad, Telangana, 500 085, India, [2]Department of Chemistry, Osmania University, Hyderabad, Telangana, 500 007, India и [3]Department of Biochemistry, Osmania University, Hyderabad, Telangana, 500 007, India

Серија деривата 2,8-ди-(алкил/арил) супституисаних бисхроманона синтетисана је у једном реакционом кораку, полазећи од 4,6-диацетилрезорцинола и алифатичних/ароматичних алдехида, у присуству пиролидина/пиперидина, загревањем традиционалним поступком или микроталасима. Добијени 2,8-ди-(алкил/арил) супституисани бисхроманони су даље преведени у серију нових 4,6-дихлор-3,7-дидиформил-2,8-ди(алкил/арил) супституисаних бисхромена, употребом Филсмајер–Хаковог (Vilsmeier–Haack) реагенса. Структуре добијених производа одређене су на основу елементалне анализе и IR, ^{1}H-NMR, ^{13}C-NMR спектралних и LC–MS података. Испитана је антимикробна активност свих синтетисаних једињења. Неки од деривата показују веома добре активности према патогеним бактеријама и гљивицама, у поређењу са стандардним лековима.

(Примљено 27. јануара, ревидирано 26. октобра 2018, прихваћено 5. фебруара 2019)

REFERENCES

1. J. H. G. Lago, C. S. Ramos, D. C. C. Casanova, A. A. Morandim, D. C. B. Bergamo, A. J. Cavalheiro, V. S. Bolzani, M. Furlan, E. F. Guimarães, M. C. M. Young, M. J. Kato, *J. Nat. Prod.* **67** (2004) 1783
2. D. C. Baldoqui, M. J. Kato, A. J. Cavalheiro, V. S. Bolzani, M. C. M. Young, M. Furlan, *Phytochemistry* **51** (1999) 899
3. J. Kjer, V. Wray, R. Edrada-Ebel, R. Ebel, A. Pretsch, W. Lin, P. J. Proksch, *Nat. Prod.* **72** (2006) 2053
4. W. Sun, L. D. Cama, E. T. Birzin, S. Warrier, L. Locco, R. Mosley, M. L. Hammond, S. P. Rohrer, *Bioorg. Med. Chem. Lett.* **16** (2006) 1468
5. A. V. Stachulski, N. G. Berry, A. C. L. Low, S. Moores, E. Row, D. C. Warhurst, I. S. Adagu, J. F. Rossignol, *J. Med. Chem.* **49** (2006) 1450
6. C. Garino, F. Bihel, N. Pietrancosta, Y. Laras, G. Quelever, I. Woo, P. Klein, J. Bain, J. L. Boucher, J. L. Kraus, *Bioorg. Med. Chem. Lett*. **15** (2005) 135
7. M. K. Aliaa, M. K. Manal, K. A. Eman, A. H. E. Heba, *Int. J. Pharm. Res. Dev.* **4** (3) (2012) 310

8. T. Raj, R. K. Bhatia, A. Kapur, M. Sharma, A. K. Saxena, M. P. Ishar, *Eur. J. Med. Chem.* **45** (2010) 790
9. Y. X. Tan, T. Gong, C. Liu, R. Y. Chen, D. Q. Yu, *Chem. Pharm. Bull.* **58** (2010) 579
10. S. Rapposelli, F. da Settiomo, M. Digiacomo, C. la Motta, A. Lapucci, S. Sartini, M. Vanni, *Arch. Pharm. (Weinheim, Ger.)* **344** (2011) 372
11. D. C. Mungra, M. P. Patel, D. P. Rajani, R. G. Patel, *Eur. J. Med. Chem*. **46** (2011) 4192
12. J. Mori, M. Iwashima, M. Takeuchi, H. Saito, *Chem. Pharm. Bull*. **54** (2006) 391
13. R. K. Nimesh, D. H. Dhaval, T. M. Prashant, K. P. Saurabh, *Med. Chem. Res.* **20** (2011) 854
14. C. K. Denish, K. P. Hetal. K. G. Nilesh, *Asian J. Biomed. Pharm. Sci.* **2** (2012) 126
15. A. Kobayashi, K. Takehira, T. Yoshihara, S. Uchiyama, S. Tobita, *Photochem. Photobiol. Sci.* **11** (2012) 1368
16. N. E. B. Saidu, S. Valente, E. Bana, G. Kirsch, D. Bagrel, M. Montenarh, *Bioorg. Med. Chem.* **20** (2012) 1584
17. A. Stefanachi, A. D. Favia, O. F. Nicolotti, L. Leonetti, L. Pisani, M. Catto. C, Zimmer, R. W. Hartmann, A. Carotti, *J. Med. Chem.* **54** (2011) 1613
18. S. Chandrasekhar, K. Vijeender, K. Venkatram Reddy, *Tetrahedron Lett.* **46** (2005) 6991
19. V. S. Moskvina, Y. L. Garazd, M. M. Garazd, A. V. Turov, V. P. Khilya, *Chem. Heterocycl. Compd. (N.Y., N.Y., U.S.)* **43** (2007) 421
20. D. Chaturvedi, A. K. Chaturvedi, N. Mishra, V. Mishra, *Org. Chem. Int.* **48** (2012) 2089
21. A. K. Tripathi, S. Koul, S. C. Taneja, *Indian J. Chem., B* **49** (2010) 1561
22. L. F. Tietze, H. P. Bell, S. Chandrasekhar, *Angew. Chem. Int. Ed*. **42** (2003) 3996
23. L. W. Deady, J. Desneves, A. J. Kaye, G. J. Finlay, B. C. Baguley, W. A. Denny, *Bioorg. Med. Chem.* **8** (2008) 977
24. M. Rahman, M. Riaz, U. R. Desai, *Chem. Biodiversity* **4** (2007) 2495
25. A. Vilsmeier, A. Haack, *Ber. Dtsch. Chem. Ges*. **60** (1927) 119
26. M. Weissenfel, H. Schurig, G. Huchsam. *Z. Chem. (Stuttgart. Ger.)* **6** (1966) 471
27. P. R. Giles, C. M. Marson, *Tetrahedron* **47** (1991) 1303
28. R. E. Khidre, B. F. Abdel-Wahab, F. A. R. Badria, *Lett. Drug Design Discovery* **8** (2011) 640
29. W. M. Abdou, R. E. Khidre, A. A. Kamel, *Arch. Pharm. (Weinheim, Ger.)* **345** (2012) 123
30. M. Vijaya Bhaskar Reddy, Y.-C. Shen, E. Ohkoshi, K. F. Bastowd, K. Qian, K.-H. Lee, T.-S. Wu, *Eur. J. Med. Chem.* **47** (2012) 97
31. D. Ashok, D. Shravnani, *Asian J. Chem.* **21** (2009) 808
32. M. Purushothaman, K. Loganathan, K. Sithick Ali, *Int. J. ChemTech. Res.* **4** (2012) 479
33. D. Ashok, M. Sarasija, A. Jeyanthi, D. Shravani, K. Sudershan, *Indian J. Heterocycl. Chem.* **25** (2016) 231
34. A. W. Bauer, W. M. M. Kirby, J. C. Sherris, M. Turck, *Am. J. Clin. Pathol.* **36** (1966) 493
35. C. Azoro, *World J. Biotechnol.* **3** (2002) 347.