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MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Synthesis and antimicrobial activity of some bisoctahydroxanthene-1,8-dione derivatives

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Abstract The bisoctahydroxanthen-1,8-dione derivatives were synthesized effectively via *p-dodecylbenzene* sulfonic acid the catalysed cyclocondensation of cyclic 1,3-dicarbonyl compounds with 1,3- or 1,4-benzene dicarboxaldehydes in water. The products were obtained with yield ranged from 75 to 95%. The structures of compounds were characterized by FT-IR, ^{1}H-NMR and elemental analysis. The antimicrobial properties of compounds against pathogens were investigated by the disc-diffusion method. These compounds were evaluated for potential antimicrobial activity against Gram-positive (*Staphylococcus aureus*, *Bacillus cereus*, *S. epidermidis* and *Nocardia canis*), Gram-negative bacteria (*Escherichia coli, Proteus vulgaris* and *Pseudomonas aeroginosa)*, yeasts (*Candida albicans* and *Rhodotorula rubra*) and mold (*Aspergillus niger*). The growth of *S. aureus*, *B. cereus*, *S. epidermidis*, *E. coli*, *C. albicans*, *R. rubra* and *A. niger* were inhibited by **3f** and **3g** compounds. All compounds were resistant against Gram-negative bacteria (*Proteus vulgaris* and *Pseudomonas aerginosa*) and results were upon comparison with reference discs.

Keywords Bisoctahydroxanthen-1,8-diones · Antibacterial activity · Antifungal activity

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Introduction

Xanthene-based compounds are important because of their use in medicine as they possess antimicrobial activities (Krasnoff *et al.*, 1999; Wang *et al.*, 2006; Qiao *et al.*, 1998; Limsuwan *et al.*, 2009). These compounds have also been investigated for agricultural bactericidal activity (Krasnoff *et al.*, 1999), photodynamic therapy, anti-inflammatory effects (Poupelin *et al.*, 1980) and antiviral activity (Jamison *et al.*, 1990). In particular, octahydroxanthene constitutes a structural unit in several natural products (Hatakeyama *et al.*, 1998) and they are valuable synthons because of the inherent reactivity of the inbuilt pyran ring (Shchekotikhin and Nikolaeva, 2006). A number of xanthene-based compounds are also available from natural sources. Santalin pigments, as they are popularly known, have been isolated from a number of plant species (Kinjo *et al.*, 1995). The wide-ranging biological activities associated with xanthenes, both naturally occurring and synthetic, ensure that the synthesis of these compounds remains a topic of current interest. Many methods are available to synthesize octahydroxanthene derivatives (Horning and Horning, 1946; Jin *et al.*, 2004, 2005, 2006; Odabasoglu *et al.*, 2008). There is a continuous and urgent need to discover new antimicrobial compounds with novel mechanisms of action because there has been an alarming increase in the incidence of new and re-emerging infectious diseases. Another big concern is the development of resistance to the antibiotics in current clinical use (Rojas *et al.*, 2003).

The purpose of this study was to evaluate the potential antimicrobial activities of the ten compounds. Several functionalized bisoctahydroxanthenes were prepared from various ketones and aromatic dialdehydes (Table 1). The reactions were easily worked up with short time, high yield and environmental friendliness. The structures of the

Table 1 Effect of the **3a–j** compounds on the growth of microorganisms

Test Microorganisms	Concentrations (μg/disc)	**3a**	**3b**	**3c**	**3d**	**3e**	**3f**	**3 g**	**3 h**	**3i**	**3j**	Tetracycline 10 μg/disc	Nystatin 100 U/disc
S. aureus	20	–	–	–	–	–	8	8	–	–	–		
	40	–	–	–	–	–	10	10	–	–	–	40	
	140	–	–	–	–	–	15	14	–	–	–		
B. cereus	20	8[a]	8[a]	–	–	–	8	8	8[a]	–	–		
	40	10[a]	11[a]	–	–	–	9	9	10[a]	–	–	28	
	140	10[a]	12[a]	–	–	–	9	8	8	7	7		
S. epidermidis	20	–	–	–	–	–	–	–	–	–	–		
	40	–	–	–	–	–	8[a]	–	–	–	–	15	
	140	–	–	–	–	–	10	7	–	–	–		
N. canis	20	–	–	–	–	–	–	–	–	–	–		
	40	–	–	–	–	–	7	–	–	–	–	14	
	140	–	–	–	–	–	8	–	–	–	–		
E.coli	20	–	–	–	–	–	7	–	–	–	–		
	40	–	–	–	–	–	8	–	–	–	7	25	
	140	–	–	–	–	–	9	–	–	–	8		
P. aeroginosa	20	–	–	–	–	–	–	–	–	–	-		
	40	–	–	–	–	–	–	–	–	–	–	13	
	140	–	–	–	–	–	–	–	–	–	–		
P. vulgaris	20	–	–	–	–	–	–	–	–	–	–		
	40	–	–	–	–	–	–	–	–	–	–	15	
	140	–	–	–	–	–	–	–	–	–	–		
C. albicans	20	7	7	–	7	–	8[a]	7	–	–	–		
	40	8[a]	8[a]	7	7	–	9	8	7	9	7		20
	140	8	8	7	7	–	9	8	7	9	7		
R. rubra	20	–	–	–	–	–	8[a]	8[a]	–	–	–		
	40	–	–	–	–	–	9[a]	9[a]	7	–	–		21
	140	7	7	–	–	–	12	10	9	9	7		
A.niger	20	–	–	–	–	–	–	–	–	–	–		
	40	–	–	–	–	–	–	–	–	–	–		22
	140	–	–	–	7	7	7	7	7	–	–		

[a] Cloudiness

Zone of inhibition in mm, discs Ø 6 mm

prepared compounds were established from their spectral (IR, ^{1}H NMR and elemental analyses) data. Synthesis of octahydroxanthene-1,8-dione is generally achieved by the condensation of 5,5-dimethyl-1,3-cyclohexanedione (dimedone) with aldehydes using Lewis acid catalysts. We have performed the synthesis using the following method recently reported in the literature by Jin *et al.* (2004) and Odabasoglu *et al.* (2008). We have observed that octahydroxanthene-1,8-dione derivatives can easily undergo the condensation with aromatic dialdehydes in the presence of p-dodecylbenzene sulfonic acid (DBSA) form 1,3-diketones (Scheme 1). The mixture of 1,3-cyclohexanediones **1** and aromatic dialdehydes **2** was refluxed in distilled water using this heterogeneous catalyst.

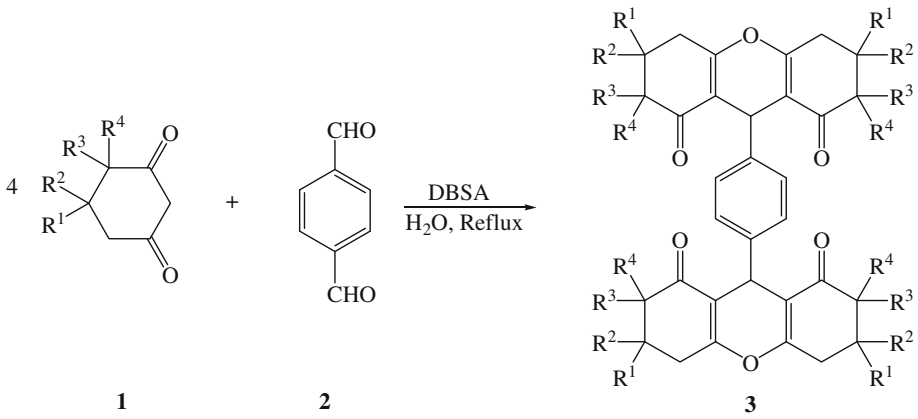
Result and discussions

Chemistry

In this study, ten bisoctahydroxanthene derivatives were prepared by one-pot reaction in distilled water for utilizing DBSA as a heterogeneous catalyst. The structures of the synthesized bisoctahydroxanthene derivatives, **3a–j**, were confirmed by IR, ^{1}H NMR spectra and elemental analysis data.

The IR spectra of all of the bisoctahydroxanthenes 3 were showed the sharp peaks for the carbonyl groups in region between 1666 and 1655 cm^{-1}. The other ν_{max} values at 3071–3025 cm^{-1} (aromatic C–H), 2964–2929 cm^{-1} (aliphatic C–H) were recorded.

Scheme 1 Synthesis of bis octahydroxanthene derivatives **3a–j**



The ^{1}H NMR spectra of all of the corresponding compounds **3** showed that the tertiary allylic proton (CH) resonates at relatively low-field singlet δ 4.6 ppm approximately because this proton is deshielded by the combined effects of the adjacent double bond and the aromatic ring. Methyl group protons of compounds **3e**, **3f** showed singlet between δ 0.84 and 1.36 ppm. Methoxy group protons of compounds **3c**, **3d** showed singlet between δ 3.68 and 3.74 ppm. The remaining aliphatic protons generally appeared as a broad multiple δ 3.55 and 1.71 ppm. Signals for the aromatic protons showed in the range δ 6.64–7.74 ppm.

The yield, melting points and reaction time values of compounds **3a–j** are given in Table 2.

Antimicrobial activity

All the compounds have been screened for antimicrobial activity by the disc-diffusion method. Antimicrobial activity was measured for 40, 80 and 140 μg/disc concentrations against tested microorganisms (*S. aureus*, *B. cereus*, *S. epidermidis*, *N. canis*, *E. coli*, *P. aeroginosa*, *P. vulgaris*, *C. albicans*, *R.rubra* and *A. niger*) and reported in Table 1. Ten compounds showed antibacterial activity against some of the tested Gram-positive, Gram-negative bacterial strains with the diameters of zone inhibition ranging between 7 and 15 mm and antifungal activity against some of the tested yeast and mould strains with the diameters of zone inhibition ranging between 7 and 12 mm (Table 1). **3a**, **3b** and **3h** showed antibacterial activity only against *B. cereus.* **3f** and **3g** showed antibacterial activity against *S. aureus*, *B. cereus*, *S. epidermidis* and *E.coli.* **3f** and **3g** compounds were exhibited high antimicrobial activity (defined as perfectly clear zone) against *S. aureus*, respectively, 15 and 14 mm and yeast isolate (*R. Rubra*), respectively, 12 and 10 mm, at the concentration of 140 μg/disc. Furthermore, it appeared that the activity of the tested compounds increases as the concentration increases. Five compounds (**3a**, **3b**, **3c**, **3d** and **3e**) did not show antimicrobial activity against *S. aureus*, *S. epidermidis*, *N.canis*, *E. coli*, *P. aeroginosa* and *P. vulgaris* at three concentrations. Five compounds (**3a**, **3b**, **3f**, **3g** and **3h**) showed antimicrobial activity (defined as perfectly clear and cloudiness) against *B. cereus* with the diameters of zone inhibition ranging between 7 and 12 mm at three concentrations. Ten compounds did not show antibacterial activity against *Proteus vulgaris* and *Pseudomonas aeroginosa* at three different concentrations. The results were

Table 2 Preparation of compounds **3a-j** promoted by *p-dodecylbenzene* sulfonic acid in water

Compounds	R^1	R^2	R^3	R^4	Aldheyde (2)	Time (h)	Yield (%)
3a	C_6H_5	H	H	H	1,4-(OHC)C_6H_4	1	95
3b	C_6H_5	H	H	H	1,3-(OHC)C_6H_4	2	92
3c	3,4-(Dimethoxy)C_6H_4	H	H	H	1,4-(OHC)C_6H_4	2	94
3d	3,4-(Dimethoxy)C_6H_4	H	H	H	1,3-(OHC)C_6H_4	2	89
3e	H	H	CH_3	CH_3	1,4-(OHC)C_6H_4	1	92
3f	H	H	CH_3	CH_3	1,3-(OHC)C_6H_4	2.5	75
3g	H	H	H	H	1,4-(OHC)C_6H_4	1	90
3h	H	H	H	H	1,3-(OHC)C_6H_4	2	92
3i	CH_3	CH_3	H	H	1,4-(OHC)C_6H_4	1	95
3j	CH_3	CH_3	H	H	1,3-(OHC)C_6H_4	1	91

compared with reference discs (tetracycline for antibacterial and nystatin for antifungal). The compounds (**3a–j)** are more active against Gram-positive than Gram-negative bacteria, according to the inhibition zone. Gram-negative bacteria are generally more resistant compared to the Gram-positive ones. The lack of activity of tested compounds against Gram-negative bacteria could be attributed to the greater resistance of these bacteria, due to presence of an extra outer membrane in their cell wall acting as a barrier foreign for substances including antibiotics (Parekh and Chanda, 2007). **3f** compound showed good antifungal activity against *R. Rubra* (12 mm). **3a**, **3b**, **3c**, **3d**, **3f**, **3g**, **3h**, **3i** and **3j** compounds showed weak antifungal activity against *C. albicans* at 140 μg concentration. New compounds showed less or no antimicrobial activity against tested microorganisms when compared with standard antibiotics.

The antimicrobial activities of some xanthenes have been reported previously (Krasnoff *et al.*, 1999; Wang *et al.*, 2006; Qiao *et al.*, 1998; Limsuwan *et al.*, 2009). However, up to the present, no systematic study has been undertaken to examine the antimicrobial properties of octahydroxanthen-1,8-dione dyes. For this reason, in the present investigation, different microorganisms have been chosen and the antimicrobial effect of bisoctahydroxanthen-1,8-diones dyes on these microorganisms under in vitro conditions has been studied.

Experimental

Chemistry

The chemicals used in the synthesis of all the ketones and aromatic dialdheydes were obtained from Aldrich Chemical Company. All chemicals and solvents used for the synthesis were spectroscopic reagent grade. Melting points were measured on a Bibby Stuart Scientific apparatus. FT-IR spectra were recorded from a Bruker Optics Vertex 70 ATR-FTIR spectrometer. ^{1}H NMR spectra were obtained with a Bruker DPX-400 FT-NMR instrument with deuterated chloroform ($CDCl_3$) and dimethyl sulfoxide (DMSO-d_6) as solvent with tetramethylsilane as the reference standard. Chemical shifts are expressed in δ units (ppm). The elemental analyses (C, H and N) were recorded on an Elemental Analyzer LECO CHNS-932.

*Typical procedure for preparation of bisoctahydroxanthene-1,8-diones (**3a–j**)*

A mixture of a cyclohexane-1,3-dione **1** (4.0 mmol), aromatic dialdehyde **2** (1.0 mmol) and DBSA (0.42 g) in water (40 ml) was stirred at refluxing for 1 h. The progress of the reaction was monitored by TLC. After completion of the reactions, the mixture was cooled to room temperature and solid filtered off and washed with water. The crude products were purified by recrystallization from ethanol. Compounds **3a–j** were prepared similarly from 5-phenylcyclohexane-1,3-dione, 5-(3,4-dimethoxyphenyl)cyclohexane-1,3-dione, 4,4-dimethylcyclohexane-1,3-dione, cyclohexane-1,3-dione, dimedone, benzene-1,4-carboxaldehyde and the benzene-1,3-carboxaldehyde.

*9-(4-(1,8-dioxo-3,6-diphenyl-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)phenyl)-2,7-diphenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8-(2H)-dione (**3a**)*

White crystal solid (ethanol); mp 227°C; IR (KBr) *v* 3060 (aromatic CH), 2938 (aliphatic CH), 1665 (C=O), 1588 and 1497 (aromatic C=C), 1180 (CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33–2.34 (m, 4H, 4× CH), 2.66–2.81 (m, 6H, 3× CH_2), 2.85–2.99 (m, 6H, 3× CH_2), 3.05–3.11 (m, 2H, CH_2), 3.50–3.55 (m, 2H, CH_2), 4.68 (s, 2H, 2× CH), 7.08 (s, 1H, ArH), 7.11–7.14 (m, 1H, ArH), 7.19–7.29 (m, 11H, ArH), 7.32–7.36 (m, 6H, ArH), 7.39–7.41 (m, 5H, ArH); $C_{56}H_{46}O_6$ requires: C, 82.53; H, 5.69; found: C, 82.48; H, 5.61.

*9-(3-(1,8-dioxo-3,6-diphenyl-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)phenyl)-2,7-diphenyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8-(2H)-dione (**3b**)*

White crystal solid (ethanol); mp 249–251°C; IR (KBr) *v* 3031 (aromatic CH), 2950 (aliphatic CH), 1660 (C=O), 1586 and 1496 (aromatic C=C), 1180 (CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33–2.34 (m, 4H, 4× CH), 2.64–2.76 (m, 6H, 3× CH_2), 2.86–3.02 (m, 6H, 3× CH_2), 3.05–3.18 (m, 2H, CH_2), 3.51–3.54 (m, 2H, CH_2), 4.70 and 4.73 (2× s, 2H, 2× CH), 7.19–7.29 (m, 12H, ArH), 7.31–7.41 (m, 7H, ArH), 7.43–7.49 (m, 2H, ArH), 7.62–7.74 (m, 3H, ArH); $C_{56}H_{46}O_6$ requires: C, 82.53; H, 5.69; found C, 82.44; H, 5.60.

*9-(4-(3,6-bis(3,4-dimethoxyphenyl)-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-yl)phenyl)-2,7-bis(3,4-dimethoxyphenyl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8-(2H)-dione (**3c**)*

White crystal solid (ethanol); mp 253°C (dec.); IR (KBr) *v* 3047 (aromatic CH), 2939 (aliphatic CH), 1664 (C=O), 1591 and 1518 (aromatic C=C), 1187 (CO) cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33–2.34 (m, 4H, 4× CH), 2.68–2.76 (m, 6H, 3× CH_2), 2.81–2.84 (m, 2H, CH_2), 2.88–2.90 (m, 2H, CH_2), 2.94–3.12 (m, 4H, 2× CH_2), 3.41–3.46 (m, 2H, CH_2), 3.68 and 3.71 (2× s, 24H, 8xOCH_3), 4.69 (s, 2H, 2× CH), 6.64–6.79 (m, 3H, ArH),

6.80–6.88 (m, 6H, ArH), 6.95–7.05 (m, 5H, ArH), 7.08–7.17 (m, 1H, ArH), 7.21–7.25 (m, 1H, ArH); $C_{64}H_{62}O_{14}$ requires: C, 72.85; H, 5.92; found C, 72.77; H, 5.89.

9-(3-(3,6–bis(3,4-dimethoxyphenyl)-1,8-dioxo-2,3,4,5,6,7,8,9-octahydro-1H-xanthen-9-Yl)phenyl)-2,7-bis(3,4-dimethoxyphenyl)-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8-(2H)-dione ***(3d)***

Yellow solid (ethanol); mp 293°C (dec.); IR (KBr) *v* 3071 (aromatic CH), 2936 (aliphatic CH), 1666 (C=O), 1591 and 1516 (aromatic C=C), 1183 (CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 2.33–2.34 (m, 4H, 4× CH), 2.67–2.77 (m, 8H, 4× CH_2), 2.84–2.98 (m, 6H, 3× CH_2), 3.16–3.20 (m, 2H, CH_2), 3.73 and 3.74 (2× s, 24H, 8× OCH_3), 4.65 and 4.67 (2× s, 2H, 2× CH), 6.75–6.77 (m, 2H, ArH), 6.84–6.89 (m, 6H, ArH), 6.99–7.07 (m, 5H, ArH), 7.11–7.17 (m, 2H, ArH), 7.21 (s, 1H, ArH); $C_{64}H_{62}O_{14}$ requires: C, 72.85; H, 5.92; found C, 72.72; H, 5.86.

9,9′-(1,4-phenylene)bis(2,2,7,7-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8-(2H)-dione) ***(3e)***

White crystal solid (ethanol); mp 269°C (dec.). IR (KBr) *v* 3049 (aromatic CH), 2964 (aliphatic CH), 1655 (C=O), 1578 and 1508 (aromatic C=C), 1183 (CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.86 (s, 12H, 4× CH_3), 0.99 (s, 12H, 4× CH_3), 1.71–1.85 (m, 8H, 4× CH_2), 2.59–2.78 (m, 8H, 4× CH_2), 4.61 (s, 2H, 2× CH), 7.42 (s, 4H, ArH); $C_{40}H_{46}O_6$ requires: C, 77.14; H, 7.44; found C, 77.04; H, 7.40.

9,9′-(1,3-phenylene)bis(2,2,7,7-tetramethyl-3,4,5,6,7,9-hexahydro-1H-xanthene-1,8-(2H)-dione) ***(3f)***

Yellow solid (ethanol); mp 131°C (dec.). IR (KBr) *v* 3032 (aromatic CH), 2929 (aliphatic CH), 1665 (C=O), 1581 and 1514 (aromatic C=C), 1149 (CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 0.84, 0.98, 1.27 and 1.36 (4× s, 24H, 8× CH_3), 1.71–1.86 (m, 8H, 4× CH_2), 2.22–2.65 (m, 8H, 4× CH_2), 4.47 and 4.52 (2× s, 2H, 2× CH), 6.79 (t, 1H, ArH), 6.90–7.05 (m, 3H, ArH); $C_{40}H_{46}O_6$ requires: C, 77.14; H, 7.44; found C, 77.10; H, 7.38.

9,9′-(1,4-phenylene)bis(3,4,6,7-tetrahydro-2H-xanthene-1,8-(5H,9H)-dione) ***(3g)***

Yellow solid (ethanol); mp °C (dec.) >300, 338–340 (Cremlyn and Shabbir, 2004).

9,9′-(1,3-phenylene)bis(3,4,6,7-tetrahydro-2H-xanthene-1,8-(5H,9H)-dione) ***(3h)***

White crystal solid (ethanol); mp 212°C (dec.). IR (KBr) *v* 3025 (aromatic CH), 2953 (aliphatic CH), 1654 (C=O), 1590 (aromatic C=C), 1176 (CO) cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 1.79–1.90 (m, 4H, 2× CH_2), 1.94–2.02 (m, 4H, 2× CH_2), 2.21–2.36 (m, 8H, 4× CH_2), 2.58–2.74 (m, 8H, 4× CH_2), 4.53 and 4.66 (2× s, 2H, CH), 6.93–6.96 (m, 2H, ArH), 7.00–7.05 (t, 1H, ArH), 7.45–7.69 (m, 1H, ArH); $C_{32}H_{30}O_6$ requires: C, 75.28; H, 5.92; found C, 75.20; H, 5.88.

9,9′-(1,4-phenylene)bis(3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2H-xanthene-1,8-(5H,9H)-dione) ***(3i)***

mp 273–275°C (dec.), 274–275 (Tu *et al.*, 2004; Cagulada *et al.*, 2009).

9,9′-(1,3-phenylene)bis(3,3,6,6-tetramethyl-3,4,6,7-tetrahydro-2H-xanthene-1,8-(5H,9H)-dione) ***(3j)***

mp 253–254°C (dec.), 252–253 (Tu *et al.*, 2004).

Antimicrobial activity

Test microorganisms

The antimicrobial activity of the synthesized compounds was evaluated against Gram-positive (*B. cereus* NRRL 3711, *Staphylococcus aureus* ATCC 25923, *S. epidermidis* ATCC 12228, *Nocardia canis*) and Gram-negative (*Escherichia coli* ATCC 25922, *Proteus vulgaris* NRRL-B-123, *Pseudomonas aeroginosa* ATCC 27853) bacterial strains, yeast cultures (*Candida albicans* ATCC 10231, *Rhodotorula rubra*) and mould culture (*Aspergillus niger* ATCC 10949). Bacterial and fungal cultures of test organisms were maintained on Nutrient agar slants at 4°C and were subcultured in petri dishes prior to use. Ten compounds were tested for their antimicrobial (antibacterial and antifungal) activities by disc-diffusion method (NCCLS, 1997) using Nutrient Agar medium for bacteria and fungi. The compounds were dissolved in DMSO. Antimicrobial activity was measured for three concentrations (40, 80 and 140 µg for each disc). Disc containing DMSO was used as control. Test bacteria were transferred to tubes containing 4 to 5 ml Nutrient Broth. The test cultures were incubated at 37°C until they were visibly turbid. The density of these cultures was adjusted to 0.5 Mc Farland (at 625 nm, 0.08–0.1 absorbance) with sterile saline. After autoclaving, Nutrient Agar was poured into petri dishes to give a uniform depth of approximately 4 mm and was allowed to a cool temperature.

A suspension containing approximately 10^8 CFU/ml for bacteria, 10^7 CFU/ml for yeasts and 10^5 CFU/ml for mould was spread on the plates of Nutrient Agar. The entire surface of the Nutrient Agar plates were inoculated by streaking with a sterile swab dipped into adjusted suspension. Then, the paper discs impregnated with the solutions of the compounds tested were placed on the surface of the media inoculated with the microorganisms. The plates were incubated at 37°C for 24 h for bacterial strains, 48 h for yeast and at room temperature for 72 h for fungi, after pre-incubation for 1 h at 4°C. After incubation, the growth inhibition zone around the disc were observed indicating that the examined compounds inhibits the growth of microorganisms. Each assay in this experiment was repeated three times. Tetracycline (10 μg/ml) for bacteria and Nystatin (100 U) for yeast and fungi were used as positive control.

Conclusions

In conclusion, novelty bisoctahydroxanthene derivatives were synthesized with higher yields. Afterwards, the antimicrobial activities of all synthesized compounds were determined by disc-diffusion method. In general, tested compounds showed antimicrobial activity against *S. aureus*, *B. cereus*, *C. albicans* and *R.rubra*. **3f** and **3g** compounds showed antimicrobial activity tested microorganisms except *P. aeroginosa* and *P. vulgaris* at tested concentration (140 μg/disc). The present study adds new data in the relationships of xanthenes and their antimicrobial activities.

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