International Journal of Chemistry and Applications.
ISSN 0974-3111 Volume 5, Number 2 (2013), pp. 73-81

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A Study on the Synthesis and Antibacterial Evaluation of Certain Copolyesters Containing Bischalcone Moiety in the Main Chain

M. Chitra[1], D. Reuben Jonathan[2]*, Y.C. Rajan[3] and V. Duraipandian[4]

[1]Department of Chemistry, Panimalar Institute of Technology, Chennai–600 123, India.
[2]Department of Chemistry, Kings Engineering College, Sriperumbudur–602 117, India.
[3]Department of Material Science and Engineering, National Chiao Tung University, Hsinchu–300, Taiwan.
[4]Department of Botany and Microbiology, College of Science, King Saud University, Riyadh–11451, Kingdom of Saudi Arabia.
E-mail: rechem_2010@yahoo.com

Abstract

Four copolyesters were synthesized by making use of succinyl chloride, and azelaic acid dichloride with the common diol (diol-I) 1,1'-methylene dinaphthol and the varying diol (diol-II) namely 3,3'-(1,4-phenylene)bis(1-(4-hydroxyphenyl)prop-2-en-1-one) (THAP) and 3,3'-(1,4-phenylene)bis(1-(4-hydroxy-3-methoxyphenyl)prop-2-en-1-one) (TMAP) by phase transfer catalyzed polycondensation. Acid catalyzed Claisen-Schmidt reaction was employed to synthesize the two varying diols. These copolyesters were characterized by solubility data and viscosity values. The microstructure of the repeating unit present in the copolyester backbone was confirmed by FT-IR, ^{1}H-NMR and ^{13}C-NMR spectra. These copolyesters exhibited prospective antibacterial activity against certain pathogenic bacteria.
Keywords: Chalcones, copolyesters, polycondensation, inherent viscosity, antibacterial.

Introduction

Macromolecular materials are found to be biologically active [1, 2] when biocidal moieties are incorporated in the polymer main chain or side chain. Chalcones and their derivatives are well-known for their biological effects [3]. Literature survey evidently indicates that numerous chalcones and their derivatives have been found to display a diverse array of pharmacological activities such as anti-inflammatory [4], anti-fungal [5], anti-oxidant [6] anti-malarial [7] antituberculosis [8], analgesic [9], anti-human immuno syndrome [10]. Certain chalcone-based complexes of ruthenium (II) were found to be dynamic against bacteria such as *E. coli*, *S. typhi* and fungi *Aspergillus niger* [11]. Sumathi and coworkers [12] synthesized a series of chalcone-based co-ordination compounds and reported their biocidal behaviour. Some new 3-(aryl)-1-(4-(quinolin-8-ylamino)phenyl)prop-2-en-1-ones were generated, characterized by usual methods, and their antibacterial activity were reported [13]. Chitra *et al* [14] have reported the synthesis of certain copolyesters having biocidal properties involving bischalcone and naphthalene moieties in the main chain.

However, there are no reports on the investigation of the synthesis of copolyesters containing bischalcone and dinaphthalene moieties in the main chain and their antibacterial activity. Consequently, we represent here in this paper the synthesis and the bactericidal efficacy of certain copolyesters possessing bischalcone and dinaphthalene moiety in the main chain. Copolyesters [15, 16] are a category of polymeric materials that involve ester linkages and are generated by the copolymerization of diacid, diol-I and diol-II in the ratio 2:1:1.

Experimental

Methanol was used as solvent for the preparation of the two bischalcone diols and as non-solvent for the precipitation of all the copolyesters. Merck LR samples of methanol and chloroform and SD fine AR sample of N, N-dimethylacetamide (DMAc) were purified as reported [17] and utilized Aldrich samples of 4-hydroxyacetophenone, 4-hydroxy-3-methoxyacetophenone and terephthaldehyde were used as received to synthesize the bischalcone diols. Aldrich samples of succinyl chloride and azelaic acid dichloride were used as such. Merck samples of sodium hydroxide, 1,1'-methylenedinaphthol and tetra-n-butylammoniumbromide were used as such for polycondensation process. Double-distilled water was used in the copolymerization process. Spectral grade DMSO-d6 (Aldrich) containing TMS as internal standard was involved in recording NMR spectra.

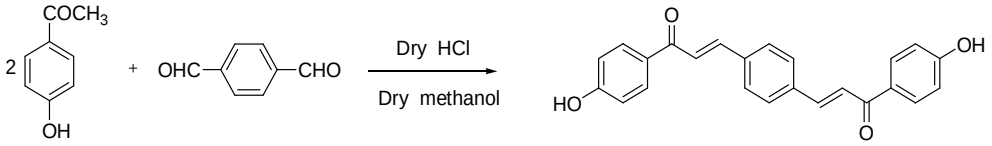
Synthesis of Bischalcone Diols

The bischalcone diols, THAP and TMAP, were synthesized by the already existing method [15].

Preparation of THAP

Dry HCl gas (generated as a result of the reaction between concentrated sulphuric acid and dry crystals of sodium chloride) was passed through a well-cooled solution

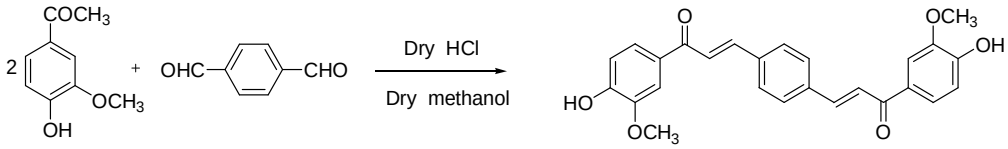
of 4-hydroxyacetophenone (100 mmol.) and terephthaldehyde (50 mmol.) in 100 mL of dry methanol taken in a 250-mL round-bottomed flask under stirring condition. The yellow-coloured solid of THAP got precipitated out which was washed with double-distilled water and re-crystallized from hot methanol. Yield: 92% m.p.: 262–264°C; IR(KBr) 3595 cm^{-1} (b, O–H), 1654 cm^{-1} (s, C=O); ^{1}H NMR (DMSO-d6) δ 9.1 (s, 2H, –OH), δ 7.4–8.3 (m, 12H, aromatic), δ 6.7–6.9 (dd, 2H, –CH=CH–) and MS (EI) m/z 370 [M]+.



3,3'-(1,4-phenylene)bis(1-(4-hydroxyphenyl)prop-2-en-1-one)

Preparation of TMAP

Dry HCl gas (generated as a result of the reaction between concentrated sulphuric acid and dry crystals of sodium chloride) was passed through a well-cooled solution of 4-hydroxy-3-methoxyacetophenone (100 mmol.) and terephthaldehyde (50 mmol.) in 100 mL of dry methanol taken in a 250-mL round-bottomed flask under stirring condition. The bright yellow-coloured solid of TMAP got precipitated out which was washed with double-distilled water and re-crystallized from hot methanol. Yield: 84% m.p.: 239°C; IR(KBr) 3506 cm^{-1} (b, O–H), 1644 cm^{-1} (s, C=O); ^{1}H NMR (DMSO-d6) δ 9.8 (s, 2H, –OH), δ 7.1–8.4 (m, 10H, aromatic), δ 6.7–6.9 (dd, 2H, –CH=CH–), δ 3.5 (s, 6H, $–OCH_3$) and MS (EI) m/z 430 [M]+.



3,3'-(1,4-phenylene)bis(1-(4-hydroxy-3-methoxyphenyl)prop-2-en-1-one)

Synthesis of Copolyesters

The usual procedure [18] involved in the synthesis of a typical aliphatic diacid-based copolyester is represented here.

The common diol (diol-I) 1,1'-methylenedinaphthol, (3 mmol.) and one of the varying diols (diol-II), (3 mmol.) were dissolved in double-distilled water (30 mL) containing dissolved sodium hydroxide (12 mmol.) taken in a 100-mL round-bottomed flask. This reaction mixture was stirred continuously at room temperature

for a span of 30 minutes in an inert nitrogen atmosphere. A solution of 2 mL of 2% tetra-n-butylammoniumbromide was added and stirred. About 30-mL solution containing the succinyl chloride (6 mmol.) in distilled chloroform was added using a pressure equalizer with constant stirring. The mixture was maintained at room temperature with continuous stirring for about 3 hours. Then the reaction mixture was poured into 300 mL of methanol when the copolyester was precipitated. The precipitated copolyester was filtered, washed with dry methanol, and then dried in vacuum.

The diacid chlorides, diol-I, and diol-II used and the copolyester code of the four copolyesters are represented in table 1.

Table 1: The diacid chlorides, the common diol and the varying diols used and the copolyester code of the four copolyesters together with percentage of yield (%) and inherent viscosities (η_{inh}).

Common Diol (Diol-I):1,1'-Methylene Dinaphthol		**Copolyester Code**	**Yield (%)**	**η_{inh} (dL/g)**
Diacid Chloride	**Varying Diol (Diol-II)**			
Succinyl chloride	THAP	PMASu	65	0.22
Succinyl chloride	TMAP	PMBSu	70	0.70
Azelaic acid dichloride	THAP	PMAAz	74	0.41
Azelaic acid dichloride	TMAP	PMBAz	79	0.83

Bactericidal Study

The disc diffusion method [19] was employed to establish the antibacterial activity of the two bischalcone diols (THAP and TMAP) and the four copolyesters (PMAS, PMBS, PMAAz and PMBAz) against *Bacillus epidermidis, Staphylococcus aureus, Klebsiella pneumoniae* and *Micrococcus luteus.*

Disc Diffusion Method: The test bacteria were sub-cultured in Muller-Hinton broth from which 1 mL of cell suspension was taken and the optical density was adjusted to 0.5, after which it was spread as a thin film over the Muller–Hinton agar plates. The synthetic compounds were loaded onto the discs at 50, 100 and 150 µg concentrations and air-dried. These were placed on the inoculated Muller-Hinton agar plates and incubated at 37°C for 48 hours. After incubation, the zone of inhibition was measured. A streptomycin disc (10 µg/disc) was utilized as the standard. A disc of 150 µl of DMSO served as the control.

Results and Discussion

The copolyesters synthesized in the current work were characterized by solubility studies, viscosity measurements, and the usual spectral data. Disc diffusion method was utilized to evaluate the bactericidal activity of the copolyesters.

Solubility of all the copolyesters was determined qualitatively in various non-polar and polar solvents. They were found to be practically insoluble in non-polar solvents like hexane and benzene, but highly soluble in polar solvents such as dimethyl formamide, DMAc, and dimethyl sulphoxide. Copolyesters with methoxy substituent in the benzene ring of the bischalcone moiety had higher solubility which may be due to their competence to disrupt the chain which encourages its solubility. Related observation was made by Kannappan *et al* [20] in a series of random copolyesters containing potential mesogens.

The inherent viscosity (η_{inh}) of the copolyesters was determined in DMAc solution at a concentration 0.1 gdL^{-1} by making use of an Ubbelohde viscometer at 30°C. The η_{inh} values of all the four copolyesters are presented in table 1, which indicates that the outcome of the copolyester synthesis is successful. It may be pointed out that the copolyesters synthesized from TMAP have higher η_{inh} values than those prepared from THAP. This may be due to the existence of methoxy substituent in the aromatic ring of the bischalcone moiety which gets associated in escalating the dipolar interaction and hence have higher viscosity values.

FT-IR spectra of all the four copolyesters were recorded by making use of Nicolet 510 FT-IR instrument. The IR spectra of all the four copolyesters disclosed characteristic absorption in the range of $\bar{\upsilon}$ = 1724–1755 cm^{-1} which is due to ester C=O stretching frequency. Similar comments were made by Arumugasamy and coworkers [21] in a series of thermotrophic liquid crystalline random copolyesters.

The ^{1}H and ^{13}C NMR spectra were recorded by utilizing JEOL GSX-400MHz instrument in DMSO-d6 solvent to make out the structural units existing in the copolyester chain. The aromatic protons are observed in the range of 7.2–8.1 ppm, while the vinyllic protons attached to the carbonyl carbon are seen in the range of 6.7–6.9 ppm. The methoxy protons in the bischalcone moiety are indicated by a signal at 3.4 ppm. The signals due to the methylene protons obtained from diacid chloride were observed in the range of 1.5–2.4 ppm. The signals in the range of 182–205 ppm and 165–175 ppm in the ^{13}C NMR spectra of the copolyesters are owing to the carbonyl carbon of the α,β-unsaturated ketone and ester groups, respectively, which indicates the formation of copolyester. Similar observations were made by Sidharthan *et al* [22] in a series of thermotrophic liquid crystalline random copolyesters containing α,β-unsaturated ketone in the main chain.

Bactericidal Study

The bactericidal efficacy of the two bischalcone diols and the four copolyesters PMAS, PMBS, PMAAz and PMBAz was screened against *B. epidermidis, S. aureus, K. pneumoniae* and *M. luteus* using disc diffusion method [23, 24]. The outcomes are summarized in table 2.

Table 2: Inhibition effects of the bischalcone diols and the copolyesters on the growth of *B. epidermidis, S. aureus, K. pneumoniae* and *M. luteus.*

Test material	**Bacillus epidermidis**			**Staphylococcus aureus**		
	Zone of inhibition (mm)			**Zone of inhibition (mm)**		
	50 µg/mL	**100 µg/mL**	**150 µg/mL**	**50 µg/mL**	**100 µg/mL**	**150 µg/mL**
THAP	2.7	3.3	4.3	3.2	3.8	4.9
PMAS	4.7	7.1	7.6	4.1	4.9	6.1
PMAAz	3.4	4.9	6.3	3.3	4.5	5.9
TMAP	3.0	4.1	5.2	3.3	4.0	5.5
PMBS	7.6	9.5	10.7	6.4	8.1	10.2
PMBAz	5.9	8.9	10.0	4.6	5.7	7.4
Test material	**Klebsiella pneumoniae**			**Micrococcus luteus**		
	Zone of inhibition (mm)			**Zone of inhibition (mm)**		
	50 µg/mL	**100 µg/mL**	**150 µg/mL**	**50 µg/mL**	**100 µg/mL**	**150 µg/mL**
THAP	3.6	4.3	5.0	3.9	4.4	5.2
PMAS	5.1	8.0	9.8	5.6	7.0	8.7
PMAAz	4.6	6.6	8.3	5.2	6.5	8.5
TMAP	4.0	4.8	5.5	4.0	4.8	5.9
PMBS	5.8	9.2	10.6	6.0	8.9	11.6
PMBAz	5.6	8.8	9.5	5.3	8.5	10.8

A constructive parallel is existing between the concentrations of the test materials and that of the zone of inhibition. All the four test copolyesters and the two bischalcone diols were tested, each at 50, 100 and 150 µg concentration to assess their efficacy in inhibiting the growth of the tested pathogens.

From table 2, it is apparent that the bischalcone diol THAP is less vigorous towards the four bacteria than TMAP, indicating an important conclusion that the presence of ether group significantly enhances the bactericidal activity. A parallel interpretation was given by Rajan *et al* [23] in a series of bischromanones. When compared to the monomeric materials THAP and TMAP, the copolyesters PMAS, PMBS, PMAAz and PMBAz were found to be greater in its biocidal nature. Thus, the copolymerization of bischalcone diols significantly enhanced the antimicrobial activity of the polymeric materials. Similar observation was reported by Chitra *et al* [14] in a series of random copolyesters. The copolyesters proficiently subdued the growth of *M. luteus and K. pneumoniae* moderately inhibited the growth of *S. aureus* and feebly inhibited the growth of *B. epidermidis.* In general, the activities of the copolyesters PMBS and PMBAz are found to be superior to those of PMAS and PMBAz which may be due to the existence of methoxy substituent present in the phenyl rings. Streptomycin inhibited the escalation of *B. epidermidis* by 19 mm, *S. aureus* by 20 mm, *K. pneumoniae* by 18 mm, and *M. luteus* by 16 mm.

Conclusion

Four copolyesters are synthesized using a common diol (diol-I), 1,1'-methylenedinaphthol. The dicarboxylic acid chlorides and diol-II are varied. The dicarboxylic acid chlorides used are succinyl chloride and azelaic acid dichloride. The varying diol (diol-II) used are THAP and TMAP. The copolyesters were characterized by viscometric and spectral studies. It has also been established that these copolyesters exhibited considerable bactericidal efficacy against pathogenic bacteria.

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Biographical Sketch

[1] Dr. M. Chitra is an Associate Professor, Department of Chemistry; Panimalar Institute of Technology is a Ph. D., degree holder in the field of Polymer Chemistry from the University of Madras. She has 12 years of teaching experience at the collegiate level.

[2] Dr. D. Reuben Jonathan is an Associate Professor and Head, Department of Chemistry; Kings Engineering College, Irungattukottai, Sriperumbudur-602117 is a Ph. D., degree holder in the field of Synthetic Polymer Chemistry from the University of Madras. He has published and presented more than 12 papers at the international and national level. He was also involved in publishing 2 text books on Engineering Chemistry and an Engineering Chemistry Laboratory Manual for first year B.E. /B. Tech. students. He has a decade of teaching experience at the collegiate level. He is the member of Indian Spectrophysics Association. At present he is guiding researchers on synthetic organic and polymer chemistry and the study of their biological activities.

[3] Dr. Y. Christurajan is a Post Doctoral Fellow in Taiwan with more than four years of post doctoral research experience in the field of Supramolecular Chemistry. He has a Ph. D., degree to his credit in the field of Synthetic Organic Chemistry from the University of Madras. He has published and presented more than 15 papers at the international and national level.

[4] Dr. V. Duraipandian is an Assistant Professor, Department of Botany and Microbiology, College of Science, King Saud University; Riyadh 11451, Kingdom of Saudi Arabia is a Ph. D., degree holder in the field of Plant Chemistry & Biology from the University of Madras. He has published and presented more than 15 papers at the international and national level.