Int J Pharm Bio Sci 2014 Oct; 5(4): (P) 528 - 533

Research Article **Polymer Science**

International Journal of Pharma and Bio Sciences **ISSN 0975-6299**

SYNTHESIS, CHARACTERIZATION AND ANTIBACTERIAL STUDY OF CERTAIN COPOLYESTERS CONTAINING BISCHALCONE MOIETY IN THE MAIN CHAIN

T.S. PERUNDEVI[1] , D. REUBEN JONATHAN[2] AND S. KOTHAI*[1]

[1]PG & Research Department of Chemistry, Ethiraj College, Chennai – 600 008, India.
[2]Department of Chemistry, Madras Christian College, Chennai – 600 059, India.

ABSTRACT

Four novel random copolyesters were synthesized from a common diol (diol I) namely 2,5 ditertiarybutyl hydroquinone 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-methoxy phenyl)prop-2-en-1-one) (TMAP) and succinyl and glutary chloride by solution polycondensation. The two varying diols were synthesized using Acid catalyzed Claisen-Schmidt reaction. The copolyesters obtained were characterized by qualitative solubility tests and viscosity values. Their structure was confirmed by FTIR, ^{1}H and ^{13}C NMR spectra. These copolyesters displayed potential antimicrobial activity against bacterial strains.

KEYWORDS: **Bischalcone, Polycondensation, Copolyester, Bactericidal**

S. KOTHAI
PG & Research Department of Chemistry,
Ethiraj College, Chennai – 600 008, India.

INTRODUCTION

Chalcones (trans-1,3-diaryl-2-propen-1-ones)[1], belonging to flavonoid family are precursors of open chain flavonoids and isoflavonoids which are abundant in edible plants. Chalcones and its derivatives have attracted increasing attention due to numerous pharmacological applications. They have displayed a broad spectrum of pharmacological activities among which antimalarial[1-4], anticancer[5-9], antiprotozoal (antileishmanial and antitrypanosomal)[10], anti-inflammatory[11,12], antibacterial[13,14], antifilarial[15], antifungal[16,17], antimicrobial[18], larvicidal[19], anticonvulsant[20], antioxidant[21-23] activities have been reported Rahman[24] and Prasada Rao et al.[25] have synthesized and reported the antibacterial activity of few chalcones. Senthamizh Selvi and coworkers[26] have synthesized certain chalcone based random copolyesters and reported their biocidal behavior. Chitra et al.[27] have reported the synthesis of certain copolyesters having biocidal properties involving bischalcone and naphthalene moieties in the main chain. Abdullah et al.[28] has synthesized and reported antibacterial activities of a bischalcone derived from thiophene and its derivatives. The objective of the present investigation is to synthesize four copolyesters by incorporating the bischalcone moieties in the copolyester main chain by polycondensation process, then characterizing them by using appropriate analytical techniques and finally studying their bactericidal activity.

EXPERIMENTAL

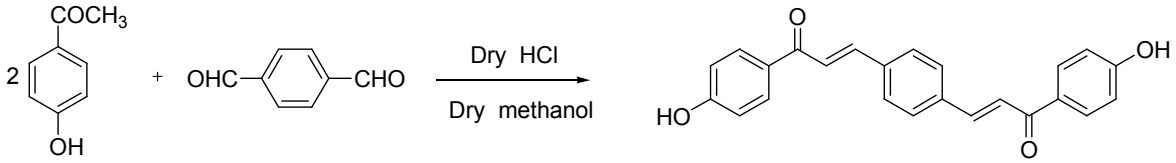
Aldrich samples of terepthaldehyde, 4-hydroxy acetophenone and 3-methoxy-4-hydroxy acetophenone were used as received. 2,5 Ditertiary butyl hydroquinone was used as received. Aldrich samples of succinyl and glutaryl chloride were purchased and used for the copolymerization process. SD-Fine AR sample of dimethyl acetamide (DMAc) was used as such solvent for finding out the inherent viscosity of the copolyester in solution. Spectral grade DMSO-d_6 (Aldrich) was used as internal standard for recording NMR Spectra.

Synthesis of Bischalcone Diols

The monomer diols 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) were synthesized by the process reported by Chitra and coworkers[29] .

Preparation of THAP

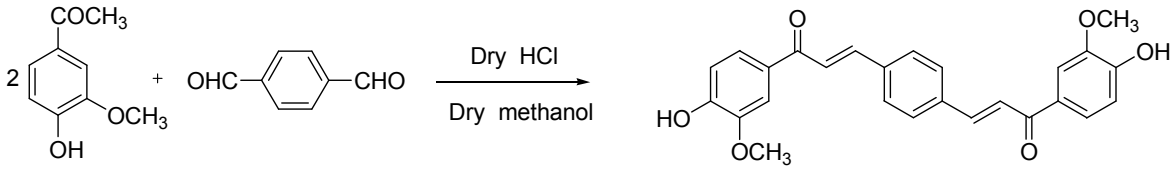
Dry HCl gas was passed through a well-cooled and stirred solution of 4-hydroxyacetophenone (60 mmol) and terephthaldehyde (30 mmol) in 50 mL of dry methanol. When ice cold water added yellow precipitate of THAP separated out. It was washed with double-distilled water and then re-crystallized from hot methanol. Yield: 89% m.p.: 262–264°C; IR(KBr) 3597 (b, O–H), 1652(s, C=O) cm-1; 1H NMR (DMSO-d6) δ 9.1 (s, 2H, –OH), δ 7.5–8.2 (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 was passed through a well-cooled and stirred solution of 4-hydroxy-3-methoxyacetophenone (60 mmol) and terephthaldehyde (30 mmol) in 50 mL of dry methanol. When ice cold water added yellow precipitate of TMAP separated out. It was washed with double-distilled water and re-crystallized from hot methanol. Yield: 82% m.p.: 239°C; IR(KBr) 3508 (b, O–H), 1642(s, C=O) cm^{-1}; ^{1}H NMR (DMSO-d6) δ 9.8 (s, 2H, –OH), δ 7.2–8.3 (m, 7H, 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 procedure[30] for the synthesis of a typical aliphatic diacid chloride-based copolyester is given here. The diols THAP (1mmol.) and 2,5 ditertiary butyl hydroquinone (1mmol.) were taken in a 100mL round-bottomed flask to which 15ml of o-dichlorobenzene was added. The reaction mixture was stirred at room temperature for 15 minutes in inert atmosphere. Then succinyl chloride (2mmol.) was added with constant stirring. Then the temperature was raised to 120°C and maintained at this temperature with continuous stirring for a span of 12 hours. At last the reaction mixture was cooled then poured into 100ml of hexane when the copolyester PSDH was precipitated. It was filtered, washed with dry methanol and dried in vacuum. Similar method was adopted to synthesize the copolyesters PSDM, PGDH and PGDM. The diacid chlorides, diol-I and diol-II used and the copolyester code of the four copolyesters are presented in Table 1.

Table-1
Monomers used and the copolyester code of the four copolyesters Together with Percentage of yield and inherent viscosities (η_{inh})

Diol-I: 2,5-ditertiarybutyl hydroquionone		**Copolyester code**	**Yield (%)**	**η_{inh} (dL/g)**
Diol-II	**Diacid chloride**			
THAP	Succinyl chloride	PSDH	78	1.1
TMAP	Succinyl chloride	PSDM	70	0.61
THAP	Glutaryl chloride	PGDH	80	0.61
TMAP	Glutaryl chloride	PGDM	74	0.61

Antibacterial Activity (Minimum Inhibitory Concentration Method)

Antibacterial activity of polymer sample was determined by minimum inhibitory concentration method (MIC). The polymer solution of 10mg/mL was used as the initial concentration. This was serially diluted repeatedly to obtain the dilutions of 5mg/mL, 2.5mg/mL, 1.25mg/mL, 0.625mg/mL, 0.3125 mg/mL, 0.15625mg/mL and finally 0.078125mg/mL. The antibiotic Streptomycin was used as the positive control. Each concentration was inoculated with 0.01mL of 24 hours bacterial cell suspension and incubated at 37^{o}C for about 24 hours. The presence of cloudiness or turbidity of the broth indicates positive growth. The concentration which inhibits the bacterial growth was taken as the MIC.

RESULTS AND DISCUSSION

Solubility of the four copolyesters were determined in various organic solvents qualitatively. The inherent viscosity (η_{inh}) of the copolyesters was determined using DMAc solution with Ubbelohde viscometer at a concentration 0.1 gdL^{-1} in which the pure solvent had a flow rate of 104 seconds at 30°C. The FT-IR spectrum of the random copolyesters was recorded using Shimadzu FT-IR instrument. The ^{1}H and ^{13}C-NMR spectra were recorded with BRUKER AV III 500 MHz NMR instrument in DMSO-d6 solvent.

Solubility

The copolyesters reported here were soluble in highly polar solvents such as DMAc and dimethyl formamide, partially soluble in moderately polar solvents like tetrahydrofuran and acetone but thoroughly insoluble in least polar solvents like benzene and hexane.

Copolyesters containing methoxy substituent in the benzene ring of the bischalcone moiety had better solubility which might be attributed to their ability to disrupt the macromolecular chain. Similar explanation was offered by Sidharthan and coworkers[31] in a series of copolyester.

Viscosity Measurements

The η_{inh} value of all the four copolyesters was determined in DMAc solution at 30°C using Ubbelohde viscometer. The inherent viscosity values were found to be in the range of 0.61–1.10dL/g and are presented in table 1. The data shows that these copolyesters are reasonably of high molecular weight.

Spectral Studies

The FT-IR spectrum of all the four copolyesters showed characteristic absorption in the range of 1753–1762cm^{-1} due to ester C=O stretching frequency. Similar observations were made by Samuel and coworkers[32] in a series of copolyesters. The NMR spectra were recorded with BRUKER AV III 500 MHz NMR instrument in DMSO-d6 solvent to identify the structural units present in the copolyester chain. The aromatic protons were observed in the range of 7.3–8.3ppm. The vinyllic protons attached to the carbonyl carbon were observed in the range of 6.3–6.9ppm. The methoxy protons in the chalcone moiety are represented in the range of 3.0–3.3ppm. The methylene protons were observed in the range of 2.0–3.0ppm. Similar remarks were made Chitra and coworkers[27] in a series of copolyesters derived from bischalcones. The signals in the range of 192ppm and 142ppm 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.

Bactericidal Study

The antibacterial activity of the four copolyesters PSDH, PSDM, PGDH and PGDM were assayed against *Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumonia* and *Micrococcus luteus* by minimum inhibitory concentration[33-36].

Table 2

Inhibition effects of the four copolyesters on the growth of Staphylococcus aureus, Pseudomonas aeruginosa, Klebsiella pneumonia and Micrococcus luteus

Test Material	Minimum Inhibitory Concentration (In mg/ml)			
	K. pneuomoniae	*P. aeruginosa*	*S. aureus*	*M. luteus*
PGDH	0.0781	0.0781	0.0781	0.0781
PGDM	0.0781	1.2500	0.0781	2.5000
PSDH	0.0781	1.2500	0.0781	2.5000
PSDM	0.0781	0.3125	0.0781	2.5000
Antibiotic	1.2500	2.5000	10.0000	0.0781

The antibacterial efficacy of the copolyesters is very significant. The lowest concentration of MIC recorded against *S. aureus* and *K. pneumonia* was 0.0781mg/ml for all the four copolyesters. The lowest concentration of MIC recorded against *P. aeruginosa* was1.25mg/ml for copolyesters PGDM and PSDH, 0.3125 mg/ml for PSDM, 0.0781 mg/ml for PGDH. The lowest concentration of MIC recorded against *M. luteus* was 2.5mg/ml for copolyesters PGDM, PSDH and PSDM, 0.0781mg/ml for PGDH. The results indicate that the copolyester PGDH exhibits good bactericidal efficacy when compared with other copolyesters as well as the standard.

CONCLUSION

The four copolyesters are synthesized using a diol-I namely 2,5-ditertiarybutyl hydroquionone, diol-II namely (3,3'-(1,4-phenylene)bis(1-(4-hydroxyphenyl)prop-2-en-1-one) and 3,3'-(1,4-phenylene)bis (1-(4-hydroxy-3-methoxy phenyl)prop-2-en-1-one) and diacid chloride namely glutaryl chloride and succinyl chloride. The copolyesters PSDH, PSDM, PGDH and PGDM are highly soluble in polar organic solvents. These random copolyesters are characterized by solubility studies, viscosity measurements and spectroscopic techniques. These copolyesters exhibited significant bactericidal activity against pathogenic bacteria and are well documented.

ACKNOWLEDGEMENT

We express our gratitude to the Instrumentation Centre of Ethiraj College for Women, Chennai for providing spectral data.

REFERENCE

1. Motta LF., Gaudio AC., Takahata Y. Quantitative structure-activity relationships of a series of chalcone derivatives (1,3-diphenyl-2-propen-1-one) as anti-*Plasmodium falciparum* agents (antimalaria agents). Internet Electronic Journal of Molecular Design, 5: 555-569, (2006).
2. Awasthi SK., Mishra N., Kumar B., Sharma M., Bhattacharya A., Mishra LC., Bhasin VK. Potent antimalarial activity of newly synthesized substituted chalcone analogs in vitro. Medicinal Chemistry Research, 18: 407-420, (2009).
3. Cheng MS., Shili R., Kenyon G. A solid phase synthesis of chalcones by Claisen-Schmidt condensations. Chinese Chemical Letters, 11(10): 851-854, (2000).
4. Lim SS., Kim HS., Lee DU. In vitro antimalarial activity of flavonoids and chalcones. Bulletin of the Korean Chemical Society, 28(12): 2495-2497, (2007).
5. Achanta G., Modzelewska A., Feng L., Khan SR., Huang P. A boronic-chalcone derivative exhibits potent anticancer activity through inhibition of the proteasome. Molecular Pharmacology, 70(1): 426-433, (2006).
6. Romagnoli R., Baraldi PG., Carrion MD., Cara CL., Cruz-Lopez O., Preti D. Design, synthesis and biological evaluation of thiophene analogues of chalcones. Bioorganic and Medicinal Chemistry, 16(10): 5367-5376, (2008).
7. Echeverria C., Santibanez JF., Donoso-Tauda O., Escobar CA., Tagle RR. Structural antitumoral activity relationships of synthetic chalcones. International Journal of Molecular Sciences, 10(1): 221-231, (2009).
8. Szliszka E., Czuba ZP., Mazur B., Sedek L., Paradysz A., Krol W. Chalcones enhance TRAIL-induced apoptosis in prostate cancer cells. International Journal of Molecular Sciences**,** 11(1): 1-13, (2010).
9. Ilango K., Valentina P., Saluja G. Synthesis and in-vitro anticancer activity of some substituted chalcone derivatives. Research Journal of Pharmaceutical, Biological and Chemical Sciences, 1(2): 354-359, (2010).
10. Lunardi F., Guzela M., Rodrigues AT., Corre R., Eger-Mangrich I., Steindel M., Grisard EC., Assreuy J., Calixto JB., Santos ARS. Trypanocidal and leishmanicidal properties of substitution-containing chalcones. Antimicrobial Agents and Chemotherapy, 47(4): 1449-1451, (2003).
11. Yadav HL., Gupta P., Pawar PS., Singour PK., Patil UK. Synthesis and biological evaluation of anti-inflammatory activity of 1,3-diphenyl propenone derivatives. Medicinal Chemistry Research, 20(4): 461-465, (2011).
12. Zhang XW., Zhao D., Quan YC., Sun LP., Yin XM., Guan LP. Synthesis and evaluation of anti-inflammatory activity of substituted chalcone derivatives. Medicinal Chemistry Research, 19(4): 403-412, (2010).
13. Hamdi N., Fischmeister C., Puerta MC., Valerga P. A rapid access to new coumarinyl chalcone and substituted chromeno[4,3-c]pyrazol-4(1*H*)-ones and their antibacterial and DPPH radical scavenging activities. Medicinal Chemistry Research, 20(4): 522-530, (2011).
14. Bhatia NM., Mahadik KR., Bhatia MS. QSAR analysis of 1,3-diaryl-2-propen-1-ones and their indole analogs for designing potent antibacterial agents. Chemical Papers, 63(4): 456-463, (2009).
15. Awasthi SK., Mishra N., Dixit SK., Singh A., Yadav M., Yadav SS., Rathaur S. Antifilarial activity of 1,3-diarylpropen-1-one: Effect on glutathione-*S*-transferase, a phase-II detoxification enzyme. American Journal of Tropical Medicine and Hygiene, 80(5): 764-768, (2009).
16. Bag S., Ramar S., Degani MS. Synthesis and biological evaluation of α,β-unsaturated ketone as potential antifungal agents. Medicinal Chemistry Research, 18(4): 309-316, (2009).
17. Lahtchev KL., Batovska DI., Parushev SP., Ubiyvovk VM., Sibirny AA. Antifungal activity of chalcones: A mechanistic study using various yeast strains. European Journal of Medicinal Chemistry, 43(10): 2220-2228, (2008).
18. Yayli N., Ucuncu O., Yasar A., Kucuk M., Akyuz E., Karaoglu SA. Synthesis and biological activities of *N*-alkyl derivatives of *o*-, *m*-, and *p*-nitro (*E*)-4-azachalcones and stereoselective photochemistry in solution with theoretical calculations. Turkish Journal of Chemistry, 30(4): 505-514, (2006).

19. Begum NA., Roy N., Laskar RA., Roy K. Mosquito larvicidal studies of some chalcone analogues and their derived products: structure-activity relationship analysis. Medicinal Chemistry Research, 20(2): 184-191, (2011).
20. Kaushik S., Kumar N., Drabu S. Synthesis and anticonvulsant activities of phenoxychalcones. The Pharma Research, 3(1): 257-262, (2010).
21. Vasil'ev RF., Kancheva VD., Fedorova GF., Batovska DI., Trofimov AV. Antioxidant activity of chalcones: The chemiluminescence determination of the reactivity and the quantum chemical calculation of the energies and structures of reagents and intermediates. Kinetics and Catalysis, 51(4): 507-515, (2010).
22. Sivakumar PM., Prabhakar PK., Doble M. Synthesis, antioxidant evaluation and quantitative structureactivity relationship studies of chalcones. Medicinal Chemistry Research, 20(4): 482-492, (2011).
23. Vogel S., Ohmayer S., Brunner G., Heilmann J. Natural and non-natural prenylated chalcones: Synthesis, cytotoxicity and anti-oxidative activity. Bioorganic and Medicinal Chemistry, 16(8): 4286-4293, (2008).
24. Rahman MA. Chalcone: A Valuable Insight into the Recent Advances and Potential Pharmacological Activities. Chemical Sciences Journal, 29: (2011).
25. Prasadarao K., Lusirani Susuma AJ., Mohan S. Synthesis, Characterisation and Antibacterial activity of few chalcones. International Journal of Pharma and Bio Sciences, 3(4): 781-788, (2012).
26. Senthamizh Selvi R., Nanthini R., Sukanyaa G. Synthesis, Characterization and Antimicrobial Activity of Certain Chalcone Based Random Copolyesters. Journal of Chemical and Pharmaceutical Research, 4(1): 393-397, (2012).
27. Chitra M., Rajendran T V., Duraipandiyan V., Rajan YC., Reuben Jonathan D. A study on the synthesis and bactericidal activity of certain copolyesters containing bischalcone moiety in the main chain. Indian Journal of Science and Technology, 3(8): 890-893, (2010).
28. Abdullah M A., Salman AK. Synthesis and Anti-bacterial Activities of a Bis-Chalcone Derived from Thiophene and its Bis-Cyclized Products. Molecules, 16: 523-531, (2011).
29. Chitra M., Reuben Jonathan D., Rajan YC., Duraipandiyan V. A Study on the Synthesis and Antibacterial Evaluation of Certain Copolyesters Containing BisChalcone Moiety in the Main Chain. International Journal of Chemistry and Applications, 5(2): 73-81, (2013).
30. Arumugasamy E., Baskar B., Kannappan V. Synthesis and Characterization of Certain Thermotropic Liquid Crystalline Random Copolyesters. Journal of Polymer Materials, 17: 4–9. (2000).
31. Sidharthan J., Reuben Jonathan D., Peter Amaladhas T. Synthesis and Characterization of Certain Thermotropic Liquid Crystalline Copolyesters Containing α,β- Unsaturated Ketone in the Main Chain. International Journal of Chemistry and Applications, 4(3): 241–250. (2012).
32. Sugaraj Samuel R., Reuben Jonathan D., Christurajan Y., Jayakumar S., Pichai R. Synthesis, Characterization and Ultrasonic Determination of Certain Copolyesters Containing Bis(Arylidene)Acetone Moiety in the Main Chain. Indian Journal of Science and Technology, 3(6): 696–701, (2010).
33. Tamilarasan K., Nanthini R., Prakash N., Rajkumar E., Ranganathan N.G, Udaya Prakash N.K. Synthesis, Characterization and Ultrasonic Determination of Certain Copolyesters Containing Bis(Arylidene)Acetone Moiety in the Main Chain. International Journal of Research in Pharmaceutical Sciences, 4(4): 604-607. (2013).
34. Anil Mayekar N., Hongqi Li., Yathirajan H.S., Narayana B., Suchetha Kumari N. Synthesis, Characterization and Antimicrobial Study of Some New Cyclohexenone Derivatives. International Journal of Chemistry, 2(2):114-123. (2010).
35. Mahesh Kumar MVS., Prasad Talluri VSSL., Raja Gopal SV. Studies on Phytochemical Constituents, Antimicrobial and Antioxidant Activities Of Some Medicinal Plants of North Coastal Andhra Pradesh. International Journal of Pharma and BioSciences, 5(3): 26-37. (2014).
36. Deepika S., Raja Gopal SV. Evaluation of Phytochemical and Bioactive Screening of Blepharis Molluginifolia Flower Extracts. International Journal of Pharma and BioSciences, 5(3): 204-211. (2014).