

## A study on the synthesis and bactericidal activity of certain copolyesters containing bischalcone moiety in the main chain

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### Abstract

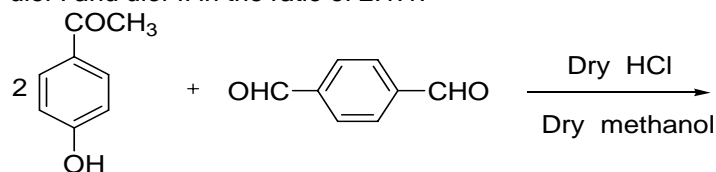
Four copolyesters were synthesized from 3,3-(1,4-phenylene)bis(1-(4-hydroxyphenyl)prop-2-en-1-one (THAP) and 3,3-(1,4-phenylene)bis(1-(4-hydroxy-3-methoxyphenyl)prop-2-en-1-one (TMAP) by phase transfer catalyzed polycondensation with adipoyl chloride and sebacoyl chloride and a common diol-I 1,5-dihydroxynaphthalene. These copolyesters were characterized by solubility data and viscosity values. The microstructure of the repeating unit was confirmed by IR, <sup>1</sup>H NMR and <sup>13</sup>C NMR. These copolyesters displayed potential bactericidal activity against pathogenic bacteria.

**Keywords:** Bischalcones, copolyesters, polycondensation, antibacterial.

### Introduction

Chalcones are known for their bactericidal activity (Rajakumar *et al.*, 2006). Several chalcones have been synthesized and their biocidal activity was investigated against some bacterial and fungal strains (Sohel *et al.*, 2006). Most of the chalcones are highly biologically active with a number of pharmacological and medicinal applications (Srivastava, 2008). Chalcones have been used as anti-HIV agents (Wu *et al.*, 2003), cytotoxic agents with antiangiogenic activity (Nem *et al.*, 2003), antimalarials (Wu *et al.*, 2002), anti-inflammatory (Tuchinda *et al.*, 2002) and anti-tumor agents (Xia *et al.*, 2000). Certain chalcone-coated cotton was tested against three organisms, namely *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa*. They were found to be bactericidal in nature (Sivakumar *et al.*, 2010). The chalcone 4,4',6'-trihydroxy-2'-methoxychalcone exhibited biocidal property (Morimoto *et al.*, 2000).

However, there are no reports on the study of the synthesis of random copolyesters and their bactericidal efficacy. So we report herein the synthesis and antibacterial activity of certain random copolyesters containing chalcones THAP and TMAP in the copolyester backbone. Copolyesters (Kannappan *et al.*, 2001) are a class of polymeric materials which contain ester linkages and are synthesized by the copolymerization of diacid, diol-I and diol-II in the ratio of 2:1:1.



### Experimental

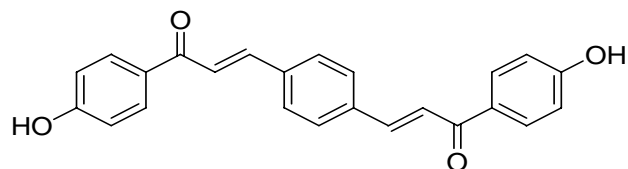
Aldrich samples of 4-hydroxyacetophenone, 4-hydroxy-3-methoxyacetophenone and terephthalaldehyde were used as received. Methanol was used as non-solvent for the polymers and as solvent for the preparation of the monomers. Merck, LR sample of methanol and SD fine AR sample of *N,N*-dimethylacetamide (DMAc) were purified as reported (Furniss *et al.*, 1997) and used. Spectral grade DMSO-d<sub>6</sub> (Aldrich) containing TMS as internal standard was used as received for recording NMR spectra.

The monomers, THAP and TMAP, were synthesized by the already reported method (Kannappan *et al.*, 2002).

#### Preparation of THAP

Dry HCl gas was passed through a well-cooled and stirred solution of 4-hydroxyacetophenone (60 mmol) and terephthalaldehyde (30 mmol) in 50 ml of dry methanol. Yellow crystals of THAP separated out. It was washed with double-distilled water and re-crystallized from hot methanol. Yield: 90% m.p.: 262-264°C; IR(KBr) 3597 (b, O-H), 1652(s, C=O) cm<sup>-1</sup>; <sup>1</sup>H NMR (DMSO-d<sub>6</sub>) 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]<sup>+</sup>.

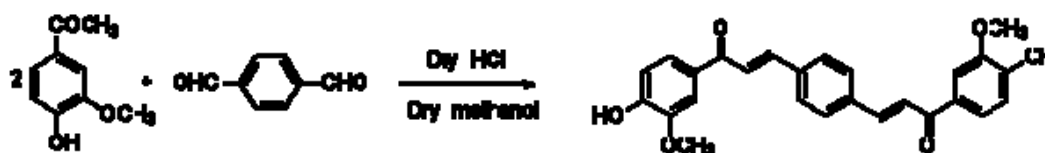
#### 3,3-(1,4-phenylene)bis(1-(4-hydroxyphenyl)prop-2-en-1-one



### Preparation of TMAP

Dry HCl gas was passed through a well-cooled and stirred solution of 4-hydroxy-3-methoxyacetophenone (60 mmol) and terephthalaldehyde (30 mmol) in 50 ml of dry methanol. Yellow crystals of TMAP separated out. It was washed with double-distilled water and re-crystallized from hot methanol. Yield: 85% m.p.: 239°C; IR(KBr) 3508 (b, O-H), 1642(s, C=O)  $\text{cm}^{-1}$ ;  $^1\text{H NMR}$  (DMSO-d<sub>6</sub>)  $\delta$  9.8 (s, 2H, -OH),  $\delta$  7.2-8.3 (m, 7H, aromatic),  $\delta$  6.7-6.9 (dd, 2H, -CH=CH-),  $\delta$  3.5 (s, 6H, -OCH<sub>3</sub>) and MS (EI) m/z 430 [M]<sup>+</sup>.

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



### Synthesis of copolyesters

The procedure (Samuel *et al.*, 2010) for the synthesis of a typical aliphatic diacid-based copolyester is given here.

The common diol (diol-I) 1,5-dihydroxynaphthalene, (2.5 mmol) and one of the varying diols (diol-II) (2.5 mmol) were dissolved in double-distilled water (25 ml) containing dissolved sodium hydroxide (10 mmol) taken in a three-necked 100 ml round-bottomed flask. The mixture was stirred continuously at room temperature for 30 minutes in nitrogen atmosphere. A solution of 2 ml of 2% tetra-n-butylammoniumbromide was added and stirred. About 25 ml solution containing the adipoyl chloride (5 mmol) in chloroform was added using a pressure equalizer with constant stirring. The mixture was maintained at room temperature with continuous stirring for 3 hours. The reaction mixture was poured into 300 ml of methanol when the copolyester was precipitated. It was filtered, washed with methanol and then dried in vacuum.

The monomer diols and diacid chlorides used and the copolyester code of the four copolyesters are represented in Table 1.

Table 1. Monomer diols and diacid chlorides used and the copolyester code of the four copolyesters

Common diol (diol-I) 1,5-dihydroxynaphthalene		Copolyester code
Varying diol (diol-II)	Diacid chloride	
THAP	Adipoly chloride	PDAA
TMAP	Adipoly chloride	PDBA
THAP	Sebacoyl chloride	PDAS
TMAP	Sebacoyl chloride	PDBS

### Bactericidal study

The antibacterial activity of the two bischalcone diols and the four copolyesters PDAA, PDBA, PDAS and PDBS was assayed against *Bacillus epidermidis*, *Staphylococcus aureus*, *Klebsiella pneumoniae* and *Micrococcus luteus* by disc diffusion method (Rajan *et al.*, 2008).

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 this 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  $\mu\text{g}$  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  $\mu\text{g}$ /disc) was used as the standard. A disc of 150  $\mu\text{l}$  of DMSO served as the control.

### Results and discussion

The copolyesters synthesized in the present work were characterized by solubility studies, viscosity measurements and spectral data.

#### Solubility

Solubility of all the copolyesters was determined in various solvents qualitatively. The copolyesters reported in this present work were soluble in highly polar solvents such as dimethyl sulphoxide (DMSO) and DMAc and insoluble in hexane and benzene. Copolyesters with methoxy substituent in the benzene ring had higher solubility because of their capacity to disrupt the chain which favors its solubility. Similar observation was reported in literature (Kannappan *et al.*, 2000) in a series of random copolyesters.

#### Viscosity measurements

The inherent viscosity ( $\eta_{\text{inh}}$ ) of the copolyesters was determined in DMAc solution at a concentration 0.1  $\text{gdL}^{-1}$  using Ubbelohde viscometer in which the pure solvent had a flow rate of 590 seconds. In each case, 25 mg of dry copolyester sample was dissolved in 25 ml of DMAc, kept aside for 12 hours with occasional shaking. The  $\eta_{\text{inh}}$  was calculated from the flow time measurement at 30°C. The inherent viscosity values of all the four copolyesters are presented in Table 2. It may be pointed out that the copolyesters synthesized from TMAP have higher  $\eta_{\text{inh}}$  values than those prepared from THAP. This may be due to the presence of methoxy substituent in the aromatic ring which gets involved in increasing the dipolar interaction and hence have higher viscosity values.

Table 2. Percentage of yield and inherent viscosities ( $\eta_{inh}$ ) of the copolyesters

Copolyester code	Yield (%)	$\eta_{inh}$ (dL/g)
PDAA	70	0.32
PDBA	76	0.77
PDAS	78	0.45
PDBS	80	0.88

### Spectral studies

IR spectra of the four copolyesters were recorded using Nicolet 510 FT-IR instrument. The IR spectra of all the four copolyesters showed characteristic absorption in the range of  $1730-1745\text{ cm}^{-1}$  due to ester C=O stretching frequency.

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded with JEOL GSX-400MHz instrument in DMSO- $d_6$  solvent to identify the structural units present in the copolyester chain. The aromatic protons are observed in the range of 7.5-8.0 ppm. The methoxy protons in the chalcone moiety are indicated by a signal at 3.4 ppm. The signal in the range of 185-200 ppm and 168-172 ppm in the  $^{13}\text{C}$  NMR spectra of the copolyesters is due to the carbonyl carbon of the  $\alpha,\beta$ -unsaturated ketone and ester groups (Kannappan *et al.*, 2002) which indicates the formation of copolyester.

All the four test copolyesters and the two bischalcone diols were tested, each at 50, 100 and 150  $\mu\text{g}$  concentration for their efficacy in inhibiting the microbial growth. From Table 3, it is clear that the bischalcone diol THAP is less active towards the four bacteria than TMAP, indicating that the presence of ether group significantly enhances the bactericidal activity. The copolyesters PDAA, PDBA, PDAS and PDBS exhibited higher antibacterial activity than the bischalcone diols from which the copolyesters were deduced. Thus, the polymerization of bischalcone diols enhanced the antimicrobial activity. The activities of the copolyesters PDBA and PDBS are greater than those of PDAA and PDAS, which may be due to the presence of methoxy substituent. Similar observations were also reported earlier (Rajan *et al.*, 2008).

Streptomycin inhibited the growth 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-I, 1,5-dihydroxynaphthalene. The dicarboxylic acid chlorides and diol-II are varied. The dicarboxylic acid chlorides used are adipoyl chloride and sebacoyl

Table 3. Inhibition effects of the bischalcone diols and the copolyesters on the growth of *B. epidermidis*, *S. aureus*, *K. pneumoniae* and *M. luteus*

Test material	<i>Bacillus epidermidis</i>			<i>Staphylococcus aureus</i>		
	Zone of inhibition (mm)					
	50 $\mu\text{g/mL}$	100 $\mu\text{g/mL}$	150 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	100 $\mu\text{g/mL}$	150 $\mu\text{g/mL}$
THAP	2.7	3.3	4.3	3.2	3.8	4.9
PDAA	4.5	6.8	7.2	3.9	4.6	5.7
PDAS	3.1	4.3	5.4	3.2	4.2	5.4
TMAP	3.0	4.1	5.2	3.3	4.0	5.5
PDBA	7.4	9.2	10.3	6.2	7.8	9.8
PDBS	5.9	8.6	9.5	4.5	5.4	6.9
Test material	<i>Klebsiella pneumoniae</i>			<i>Micrococcus luteus</i>		
	Zone of inhibition (mm)					
	50 $\mu\text{g/mL}$	100 $\mu\text{g/mL}$	150 $\mu\text{g/mL}$	50 $\mu\text{g/mL}$	100 $\mu\text{g/mL}$	150 $\mu\text{g/mL}$
THAP	3.6	4.3	5.0	3.9	4.4	5.2
PDAA	4.9	7.7	9.4	5.5	6.7	8.3
PDAS	4.5	6.3	7.8	5.1	6.2	8.0
TMAP	4.0	4.8	5.5	4.0	4.8	5.9
PDBA	5.8	8.9	10.2	5.8	8.7	11.3
PDBS	5.6	8.7	9.4	5.4	8.3	10.4

### Bactericidal study

The antibacterial activity of the two bischalcone diols and the four copolyesters PDAA, PDBA, PDAS and PDBS was assayed against *B. epidermidis*, *S. aureus*, *K. pneumoniae* and *M. luteus*. The zone of inhibition for each concentration against all test bacteria is depicted in Table 3. A positive correlation exists between the concentration of the test materials and the zone of inhibition.

chloride. The diol-II used are 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). The copolyesters were characterized by viscometric and spectral studies. These copolyesters exhibited significant bactericidal activity against pathogenic bacteria.



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