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Synthesis and Spectral Study of R,R',4,4'-Cyclohexylidene Diphenyloxy Acetic acids with Antimicrobial Activity

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ABSTRACT

Synthesis of R,R',4,4'-cyclohexylidene diphenyloxy acetic acids (R,R'= H,$CH_3$and Cl) by dissolving 0.1 mole bisphenols in 0.4 mole sodim hydroxide with drop wise addition of 0.2 mole chloroacetic acid. The reaction mixture refluxed for 4h at 60°C. Phenoxy acids have been confirmed by IR and NMR spectral characterization. The acids are also characterized by their antimicrobial and antifungal activities. The activities have been interpreted in light of bisphenol structures and the nature of substituent(s). The wide scale uses of bisphenol bioactive agents have brought many advantages to the agricultural industries.

Key words: Bisphenol, Phenoxy acetic acids, IR, NMR, Antimicrobial screening.

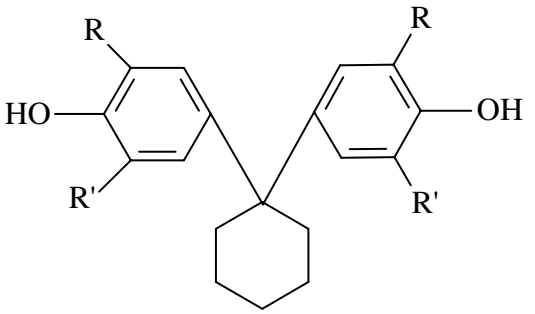
INTRODUCTION

Bisphenols are most widely useful as intermediates for dyes, drugs, varnishes, for the preparation of thermally stable polymers and epoxy resins. Various bisphenols have been found to be effective fungicides, antibacterial and cocciadal.[1,2,3] Phenoxy acids are most widely useful in the field of agriculture as herbicides as well as insecticides.[4] Bisphenols synthesized chloro derivatives possess antimicrobial and antifungal activity against different microbes.[5]

EXPERIMENTAL

Cyclohexanone (0.05mole) was treated with phenol or o-cresol (0.1mole) in the presence of mixture of hydrochloric acid and acetic acid (2:1 v/v) at 55-60°C for 3 h.[6,7] The product was filtered and treated with 2N sodium hydroxide solution. The solution was acidified with dilute sulfuric acid. Bisphenol-C and Methyl Bisphenol-C were recrystallized from Benzene.

Section 1: Synthesis of bisphenol-C



(I)

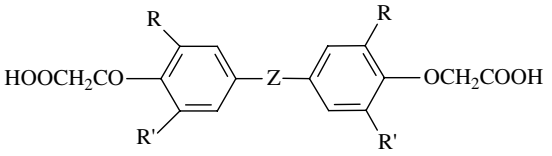
BC: R=R'=H MeBC: R= CH_3 and R'=H

Section 2: Synthesis of bisphenol-C derivatives

(II)

ClBC: R=R'=Cl
ClMeBC: R=CH_3 and R'=Cl
Z = Cyclohexyl

Section 3: Synthesis of phenoxy acetic acids of bisphenols



(III)

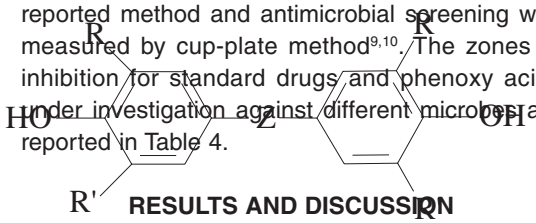
PAAC-1 : R=R'=H PAAC-2 : R= CH_3 and R'=H
PAAC-3 : R=R'=Cl PAAC-4 : R= CH_3 and R'=Cl
Z = Cyclohexyl

Bisphenol-C or Methyl Bisphenol-C were suspended in 90ml of carbon tetrachloride containing sodium sulfide (0.4g) and 10ml of thionyl chloride was added drop by drop.[8] The reaction mixture was reflux at 55°C for 3 h and 70°C for 1 h. The excess of thionyl chloride and carbon tetrachloride were distilled off. The products were carbonized in methanol solution and were further repeatedly recrystallized from methanol-water system prior to their use.

The disodium salt of bisphenols were prepared by dissolving 0.1 mole bisphenols in 0.4 mole sodium hydroxide solution and then 0.2 mole chloroacetic acid was added drop wise with vigorous stirring. The reaction mixture refluxed at 60°C for 4 h. The products were washed well with distilled water and dried at room temperature. They were recrystallized from benzene and methanol-water systems, to get shining crystals. The %yields and m.ps. are reported in Table:1.

Antimicrobial activity of phenoxy acids of bisphenol-c

In order to grow different micrograms, the nutrient agar media was prepared according to reported method and antimicrobial screening was measured by cup-plate method[9,10]. The zones of inhibition for standard drugs and phenoxy acids under investigation against different microbes are reported in Table 4.



RESULTS AND DISCUSSION

Physical data of phenoxy acids of bisphenol-C are reported in Table 1.

Information about the structure of a molecule could frequently be obtained from its absorption spectrum. The atomic and electronic configuration of a molecule is responsible for the position of absorption bands. The most structural information of organic molecules could be obtained from IR spectra. The IR spectra (KBr pellets) of phenoxy acids of bisphenol-C PAAC-1 to PAAC-4 were scanned on a Shimadzu (FTIR-8400) over the frequency range 4000-400 cm^{-1} and shown in Fig. 1 and data of IR frequencies are reported in Table 2.

To study a molecule by NMR spectroscopy enables to record differences in the magnetic

Table 1: Physical data on phenoxy acetic acids of bisphenols

Phenoxy acid	Z	R	R'	Yield%	m.p.°C
PAAC-1	Cyclohexyl	H	H	74	94
PAAC-2	Cyclohexyl	CH_3	H	71	208
PAAC-3	Cyclohexyl	Cl	Cl	73	215
PAAC-4	Cyclohexyl	CH_3	Cl	69	196

Table 2: The characteristic IR (KBr) absorption frequences of PAAC-1 to PAAC-4

Type	Group Vibration mode	Observed IR frequencies cm^{-1}				Expected IR frequencies cm^{-1}
		PAAC-1	PAAC-2	PAAC-3	PAAC-4	
Carboxylic	O-H (str)	3427.3	3593.1 3230.5	3591.2 3230.5	3381	3550-3500 3300-2500
	O-H (def)	1235	1236.3	1236.3	1236.3	1320-1210
	C-O (str)	1435	1448.4	1448.4	1448.4	1440-1395
	C=O(str)	1758.1	1755.4	1757.7	1760	1775-1750
Aromatic	P=C-H (str)	3041.5	3018.4	3018.4	3020.3	3080-3030
	C=C (str) 1,4 sub	1606.6	-	1610.4	1601.5	1616 ± 6 1520-1480
	C=C (str) 1,2,4sub	1510	1612.4	1612.4	1612.4	1616± 6
		-	1593.1	1593.1	1595	1577± 8
			1510.2	1510.2	1510.2	1510 ± 8
	C-H (i.p. def) 1,4 sub	1184 1112.9	1180.4	1180.4	1180.4	1175 ± 6 1117 ± 7
	C-H (i.p. def) 1,2,4 sub	1010.6	1107 1012.6	1107.1 1012.6	1109 1012.5	1175-1125 1070-1000
	C-H (o.o.p. def) 1,4 sub	823.5	819.7	819.7	821.6	817 ± 15
	C-H (o.o.p. def) 1,2,4 sub	-	896.8	-	-	900-860 860-800
Alkane	C-H (str) ψas	2933.5	2935.5	2935.5	2935.5	2975-2950(CH_3) 2940-2915(CH_2)
	C-H (str) ψs	2858.3	2858.3	2858.3	2858.3	2880-2860(CH_3) 2870-2845(CH_2)
	$-CH_3$ ψs	-	1448.4	-	1448.4	1470-1435
	$-CH_3$ ψas	-	1365.5	-	-	1385-1370
	$-CH_2$ δas	1434.9	1448.4	1448.4	1448.4	1480-1440
Ether	C-O-C (str)	1234.4	1236.3	1236.3	1236.3	1260-1200
Halogen	C-Cl(str)	-	-	731 640	725 650	800-600 ~ 650

properties of the various magnetic nuclei present and to deduce in large measure what the positions of these nuclei are within the molecule. It consists of measuring the energy that is required to change a spinning nucleus from stable orientation to a less orientation in the magnetic field. The NMR spectra of phenoxy acids PAAC-1 to PAAC-4 were scanned on a Bruker FT NMR (300MHz) spectrometer by using a mixture of $CDCl_3$-$DMSOd_6$ –TFA for PAAC-1 and $CDCl_3$-TFA for PAAC-2 to PAAC-4 as a solvent

Table 3: The chemical shifts of PAAC-1 TO PAAC-4

Phenoxy acids	Chemical shift, δ ppm	Types of proton(s)
PAAC-1	7.546	-COOH (s)
	7.125-7.096	Ar-H(m)
	4.542	$-OCH_2$-(s)
	2.176	α $-CH_2$-(s)
	1.505	$\beta+\gamma$ $-CH_2$-(s)
PAAC-2	7.201-7.172	Ar-H(m)
	6.827-6.788	Ar-H(m)
	4.754	$-OCH_2$-(s)
	2.231	α-CH_2 - + $-CH_3$(s)
	1.526	$\beta+\gamma$ $-CH_2$-(s)
PAAC-3	7.212-7.183	Ar-H(m)
	6.834-6.795	Ar-H(m)
	4.765	$-OCH_2$-(s)
	2.240	α-CH_2-(s)
	1.564	$\beta+\gamma$ $-CH_2$-(s)
PAAC-4	7.203-7.174	Ar-H(m)
	6.827-6.788	Ar-H(m)
	4.750	$-OCH_2$-(s)
	2.232	α $-CH_2$ - + $-CH_3$(s)
	1.527	$\beta+\gamma$ $-CH_2$-(s)

Table 4: The zone of inhibition for phenoxy acids and standard drugs

Compound	Zone of inhibition (mm) Antibacterial			Antifungal	
	E.coli	***B.mega***	***S.typhosa***	***S.albus***	***A.niger***
Griseofulvin	10	19	22	17	20
Chloramphenicol	20	28	20	24	14
Ampicillin	20	25	19	22	18
Benzyl penicillin	15	17	20	18	15
DMF	09	09	09	09	09
PAAC-1	10	12	12	20	17
PAAC-2	12	10	13	19	15
PAAC-3	11	12	11	16	12
PAAC-4	12	12	10	22	14

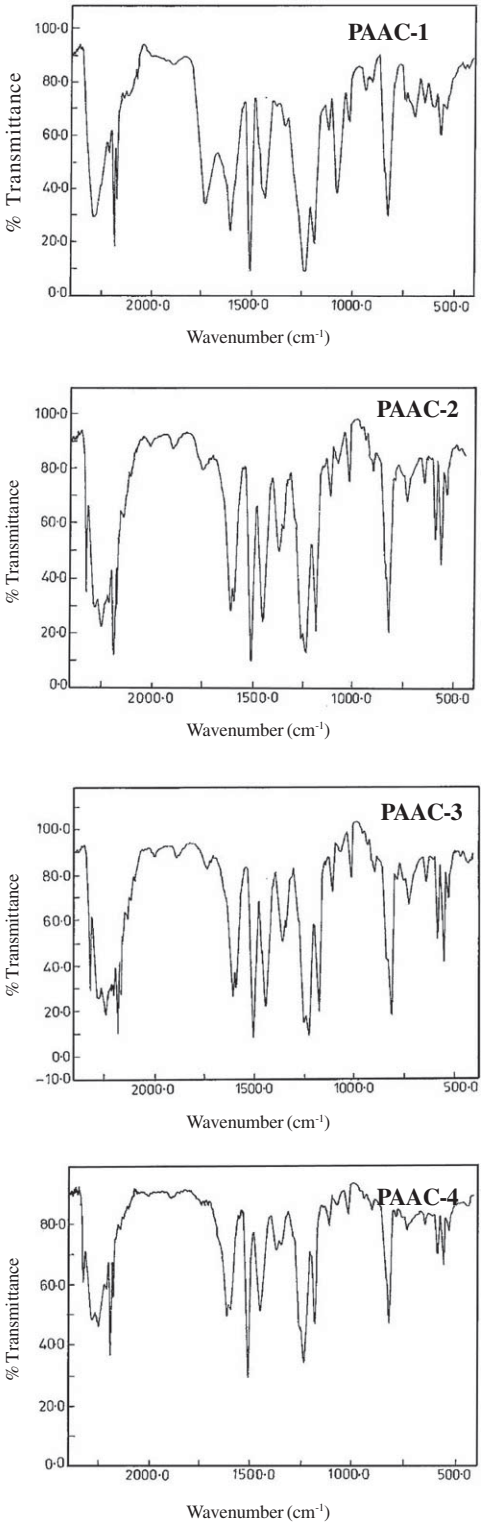


Fig. 1: The IR Spectrum of PAAC-1 to PAAC-4

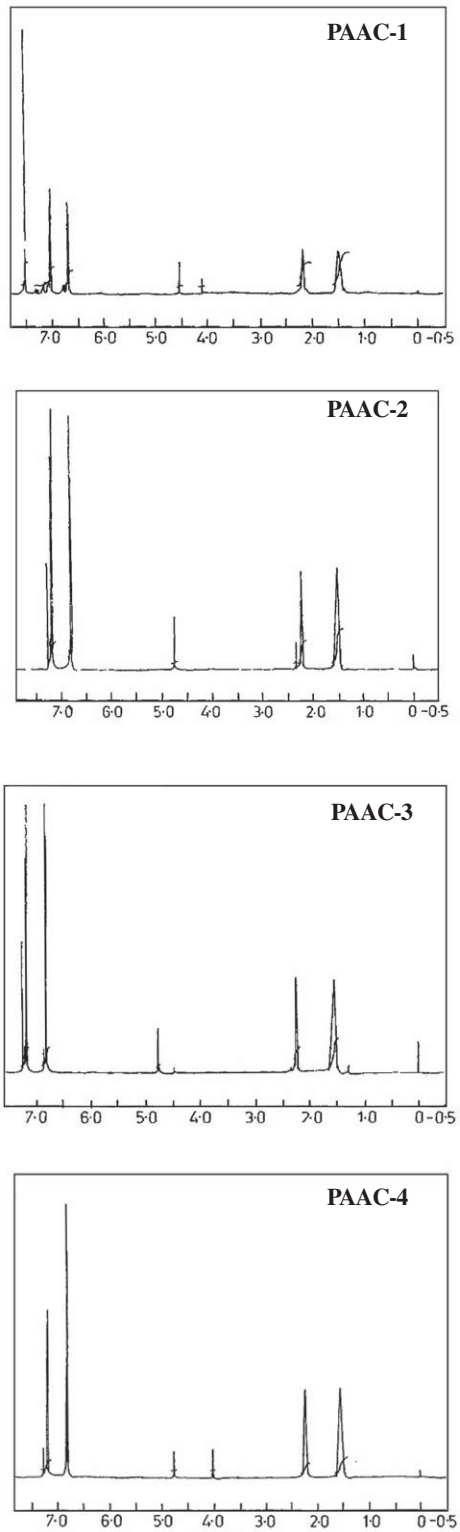


Fig. 2: The NMR Spectrum of PAAC-1 to PAAC-4

and TMS as an internal standard. NMR spectra are shown in Figure-2. Different types of protons, multiplicity and chemical shifts are reported in Table-3.

As antibacterial screening PAAC-1 to 4 are active with griseofulvin against *E.coli*. PAAC-1 to 4 are moderately active as benzyl penicillin against *B.mega*. PAAC-1 to 4 possess comparable activity with griseofulvin, ampicillin and benzyl penicillin against *S.albus*. As antifungal screening PAAC-1 active as ampicillin and PAAC-2 as benzyl penicillin against *A.niger*. PAAC-4 is comparable active with chloramphenicol against *A.niger*. In conclusion phenoxy acids of bisphenol-C possess moderate to superior activity against the selected microbes. The data of antibacterial and antifungal activity are reported in Table-4.

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