

# Condensation reaction of benzil with resorcinol and the establishment of the spectral data as well as cytotoxicity study

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## Abstract

Condensation of benzil, **1** with resorcinol in the presence of potassium carbonate at 110-120°C gave the mixture of the compounds. Using various kinds of separation technique only five types of the polymeric products, **a1**, **a2**, **a3**, **a4** and **a5** were isolated. The compounds **a1**, **a4** showed high cytotoxic activity and the compounds **a2**, **a3** and **a5** showed relatively low cytotoxic activity against the brine shrimp lethality bioassay.

## Introduction

Various types of substituted heterocyclic compounds were synthesized and cytotoxic activity of these compounds have been found by screening tests (Islam et al., 2001a; Islam et al., 2001b; Lingcon et al., 2001). To compare the cytotoxic activity of the titled compounds in scheme 1 have been isolated and sent for screening tests whether they can show reasonable lethal effect on brine shrimp (Anderson et al., 1999) or not. The compounds that are mentioned have been furnished in Scheme 1 with Flow-chart 1.

## Materials and Methods

Melting points were not corrected. IR spectra were recorded on a Shimadzu DR 8001 FT-IR spectrometer, NMR spectra on a WP 200 spectrometer using TMS as internal standard and mass spectra on an MS Kratos mass spectrometer.

### Reaction

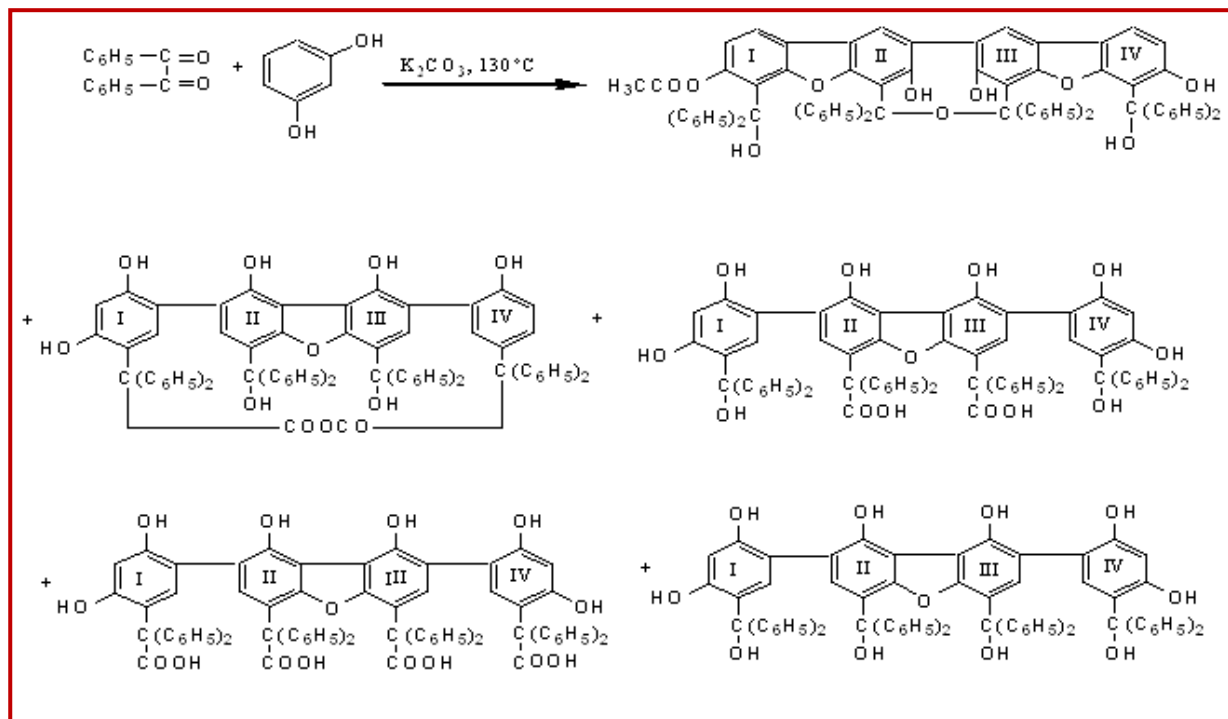
Benzil (0.01 moles or 2.10 gm), resorcinol (0.005 moles or 0.55 gm) and potassium carbonate (0.015 moles or

2.07 gm) were mixed and heated in three necked quick-fit round bottom flask in the oil bath at 110-120°C. Heat was continued until all the solids were melted to liquid and this liquid was heated for half an hour. CO<sub>2</sub> was evolved and this liquid was converted into colored solid mass. This solid contains mixture of compounds (Hans et al., 1905), P<sub>M</sub> that was examined on TLC.

### Extraction of the compound (a1)

Chloroform was mixed to the water-soluble portion and shaken half an hour. Two layers were formed. Lower layer was organic layer and upper layer was aqueous layer. Thus yellow organic layer was collected in several times and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. This organic layer was evaporated and it gives a single product, **a1**, m.p. 110 - 13°C. Its color is red. IR:  $\nu_{\text{Nujol}}$  (cm<sup>-1</sup>) 3500-2500 (b, H bonded OH of COOH); 2955, 2926 ( $\nu_{\text{C-H}}$ ); 1605 (b,  $\nu_{\text{C=O}}$ ); 1207 (b,  $\nu_{\text{C-O}}$  stretching). <sup>1</sup>H-NMR (DMSO):  $\delta$  10.20-9.80 (b, COOH),  $\delta$  8.50-8.20 (b, OH), 8.00-6.00 (m, C-H, aromatic protons). <sup>13</sup>C-NMR (DMSO):  $\delta$  195.20 (C-1);  $\delta$  135.93 (C-10),  $\delta$  132.59 (C-8),  $\delta$  131.11 (C-7),  $\delta$  129.97 (C-11), d 129.89 (C-3), d 129.62 (C-15), d 129.33 (C-6), d 129.21 (C-4), d 128.90 (C-5), 128.00 (C-12) and  $\delta$  70.56 (C-9). Mass: m/z (% of relative





Scheme 1

intensity) 1256.0 ( $M^+$ , 2%), 873.0 (15%), 677.0 (55%), 225.1 (6%), 154.0 (10%) and 105.0 (100%). The molecular ion peak appears at  $m/z$  1256 due to  $C_{80}H_{56}O_{15}$ .

#### Separation of the product (a2)

The product, **a2** was dried in desiccator and gave single spot on TLC examination, m.p. 258 - 60°C. The color of the compound was light brick red. **IR:**  $\nu^{Nujol}$  ( $cm^{-1}$ ) 3200-3600 (s, b,  $\nu OH$ ); 3087, 3056 (s,  $\nu C-H$ , aromatic); 1732, 1600 ( $\nu C=O$ ); 1565, 1547 ( $\nu C=C$ , aromatic rings); 1212 ( $\nu C-O$ ).

#### Isolation of the compound (a3)

After collecting the  $P_{LDM}$  product, this portion was separated by column chromatography on silica gel using pet ether and ethyl acetate. 0.639 gm was taken for separation. Different fractions were recorded and then later were evaporated. TLC examinations were shown in Table I.

#### Identification of the 4<sup>th</sup> fraction

This portion was orange yellow in color yielded 0.080 gm and m.p 140 - 42°C. This was designated as **a3**. **IR:**  $\nu^{Nujol}$  ( $cm^{-1}$ ) 3600-3200 (b,  $\nu OH$ ); 3025 ( $\nu C-H$ , aromatic); 1684, 1672 ( $\nu C=C$ , aromatic rings); 1277 (b,  $\nu C-O$ ).

#### Isolation of the compound (a4)

Further separation of the 6<sup>th</sup> fraction

The 6<sup>th</sup> fraction in Table I was taken for PTLC method for further separation and pet ether and ethyl acetate

were used as solvent (EA:PE=3:2). Three bands were found in Table II.

3<sup>rd</sup> band that collected was designated as **a4**. The product was solid (light pink color). **IR:**  $\nu^{Nujol}$  ( $cm^{-1}$ ) 3600 - 3200 (b,  $\nu OH$  (H bonded of COOH) group); 3060, 3028 ( $\nu C-H$ , aromatic); 1799, 1714 (b,  $\nu C=O$ ); 1601 ( $\nu C=C$ , aromatic rings); 1277 (b,  $\nu C-O$  stretching).

#### Isolation of the compound (a5)

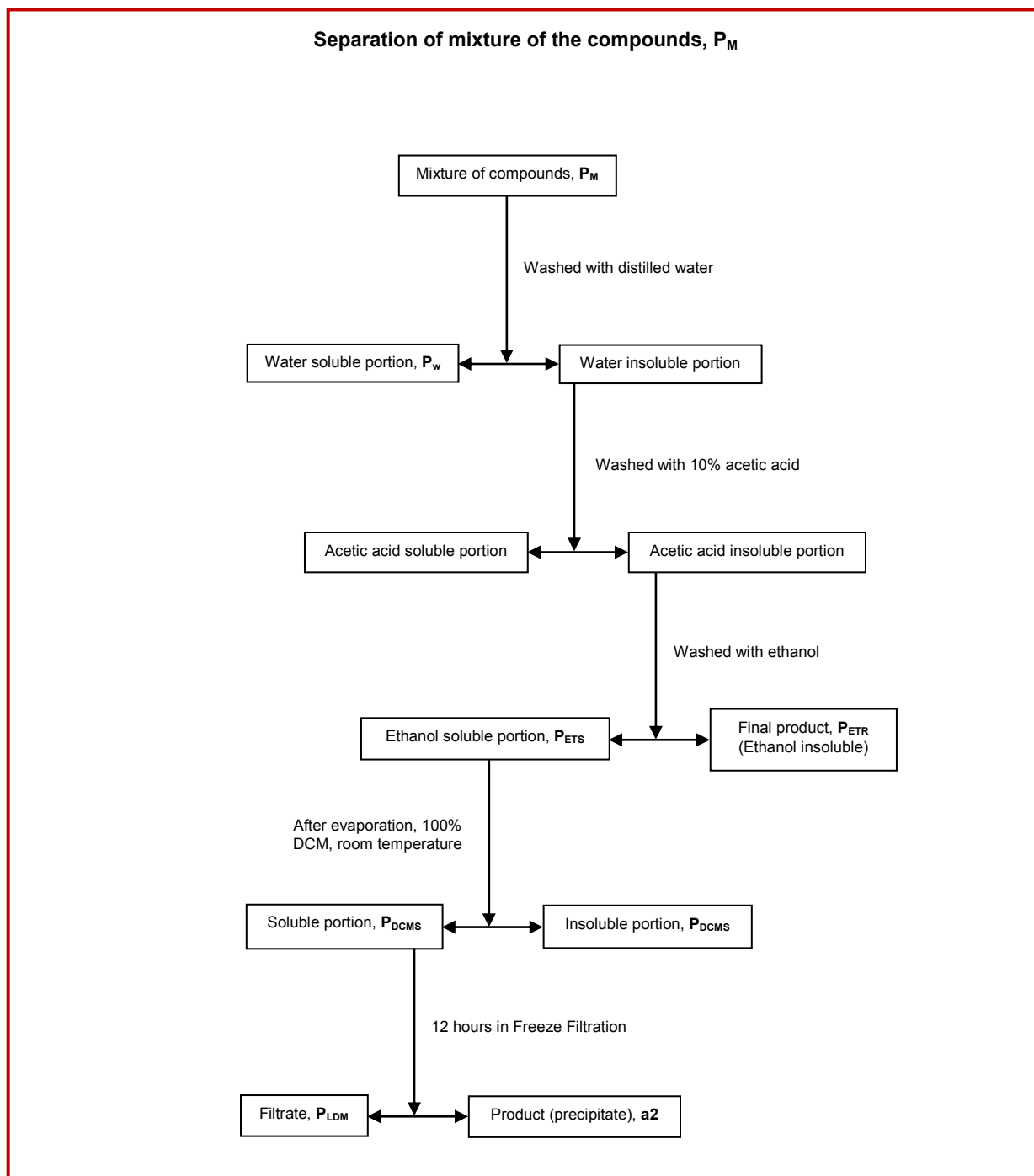
After getting the  $P_{ETR}$  product this portion was separated by column chromatography on silica gel using ethyl acetate and pet ether. 1.0 gm was taken for separation. Different fractions were collected and evaporated for the TLC examination, which were given in Table III.

#### Further separation of the 4<sup>th</sup> fraction

The 4<sup>th</sup> fraction was taken for PTLC method for further separation and pet ether and ethyl acetate were used as solvent (EA:PE=5:95). Three bands were found in Table IV.

2<sup>nd</sup> band was collected and was designated as **a5**. The product was solid, m.p. 287 - 88°C.

**IR:**  $\nu^{Nujol}$  ( $cm^{-1}$ ) 3600-3300 (b,  $\nu OH$ , stretching); 3063, 3050 ( $\nu C-H$ , aromatic); 2980 ( $\nu C-H$ , aliphatic); 1809, 1740 (b,  $\nu C=O$  asymmetric and symmetric stretching); 1597, 1581 ( $\nu C=C$ , aromatic rings); 1211 ( $\nu C-O$ ). **<sup>1</sup>H-NMR** (DMSO):  $\delta$  8.20-8.00 (b, OH, phenol),  $\delta$  7.90-7.10 (m, C-H, aromatic protons),  $\delta$  6.40-6.20 (s, OH, alcohol),



Flow Chart

$\delta$  2.30 (s, 3H, CH<sub>3</sub>, aliphatic). **Mass:** m/z (% of relative intensity) 677.0 (18%), 483.1 (25%), 307.1 (22%) and 154.0 (100%). The molecular ion peak appears at m/z 1150 due to C<sub>78</sub>H<sub>54</sub>O<sub>10</sub>.

## Results and Discussion

The mixture of the products,  $P_M$  was washed with

water and then this water soluble portion was extracted by chloroform and TLC examination of the product, **a1** showed the single spot. In the IR spectrum of the compound **a1**, the broad band at 3500 - 2500 cm<sup>-1</sup> points out the presence of H-bonded OH of COOH (i.e., presence of COOH group and OH group of aromatic in H-bonding). The signal at 2955 cm<sup>-1</sup> indicates the presence of C-H group in aromatic ring. The value of  $d_H$  is lowered due the H-bonded. The weak band at 1605

Table I		
Several fractions that were recorded during column chromatography		
Fractions	Color	TLC examination and R <sub>f</sub> value
1 <sup>st</sup> fraction (1-5)	----	----
2 <sup>nd</sup> fraction (6-13)	Light yellow	One spot, 0.73, benzil (reactant)
3 <sup>rd</sup> fraction (14-18)	Light orange	Three spots having reactant
4 <sup>th</sup> fraction (19-29)	Orange yellow	One spot, 0.35
5 <sup>th</sup> fraction (30-34)	Light green	One spot with tailing
6 <sup>th</sup> fraction (35)	Slightly yellow	Two spot, 0.35, 0.81
7 <sup>th</sup> fraction (36-42)	Yellow orange	Three spots with tailing
8 <sup>th</sup> fraction (43-48)	Light yellow orange	Three spots having too much tailing

Table II		
Different bands in TLC		
Name	Amount	R <sub>f</sub> value
1 <sup>st</sup> band	Trace amount	Discarded
2 <sup>nd</sup> band	3 mg	Three spots with tailing
3 <sup>rd</sup> band	4 mg	One spot, 0.81

Table III				
Different fractions that were recorded during column chromatography				
Fraction no	Test tube no	Color	Amount	TLC exam. & R <sub>f</sub> value
1 <sup>st</sup> fraction	1-4	----	----	----
2 <sup>nd</sup> fraction	5-10	Light yellow	0.05 g	0.95, it may reactant (benzil)
3 <sup>rd</sup> fraction	11-18	Reddish	0.08 g	0.95, 0.90
4 <sup>th</sup> fraction	19-21	Brown	0.03 g	0.90, one spot with tailing
5 <sup>th</sup> fraction	22-28	Red	0.10 g	Too many spots
6 <sup>th</sup> fraction	29-50	Deep red	0.15	Too many spots
7 <sup>th</sup> fraction	51-70	Yellow	0.17	Too many spots
8 <sup>th</sup> fraction	71-90	Yellow	0.21	Too many spots

Table IV		
Different bands in TLC		
Name	Amount	R <sub>f</sub> value
1 <sup>st</sup> band	Trace amount	Discarded
2 <sup>nd</sup> band	8 mg	0.90 (one spot)
3 <sup>rd</sup> band	5 mg	0.90, 0.88 tailing

cm<sup>-1</sup> identifies C=O group in COOH and the value at 1288 cm<sup>-1</sup> indicates the presence of C-O group. In <sup>1</sup>H-NMR spectrum, the broad signal (hum) at δ 10.2 - 9.8 is assigned for COOH and the other broad value at δ 8.5 -

8.2 indicates the presence of OH group in aromatic. The multiplet at 8.0 - 6.0 shows the presence of the rest of C-H protons in aromatic ring. In <sup>13</sup>C-NMR spectrum, the peak at δ 195.20 (C-1) is assigned for the carbonyl

group, C=O in COOH. The aromatic carbons are designated by the following values  $\delta$  135.93 (C-10),  $\delta$  132.59 (C-8),  $\delta$  131.11 (C-7),  $\delta$  129.97 (C-11),  $\delta$  129.89 (C-3),  $\delta$  129.62 (C-15),  $\delta$  129.33 (C-6),  $\delta$  129.21 (C-4),  $\delta$  128.90 (C-5),  $\delta$  128.00 (C-12) and  $\delta$  70.56 (C-9). In the mass spectrum, molecular ion peak ( $M^+$  2%) appears at  $m/z$  1256 that corresponding to the molecular formula  $C_{80}H_{56}O_{15}$ . In this spectrum the base peak is formed at  $m/z$  105.

The product, **a2** was obtained from the cold precipitate of DCM soluble portion and this DCM soluble portion was found from ethanol soluble portion of **P<sub>M</sub>**. This product gave the single spot on TLC examination. In the IR spectrum of the compound, **a2** the broad band at 3600 - 3200  $cm^{-1}$  indicates the presence of OH group. The signals at 3087  $cm^{-1}$ , 3056  $cm^{-1}$  indicate the presence of C-H group in aromatic ring. The values at 1732  $cm^{-1}$ , 1600  $cm^{-1}$  show the presence of C=O group in CO-O-CO. The bands at 1565  $cm^{-1}$  and 1547  $cm^{-1}$  indicate the presence of C-H group of aromatic ring. The weak band at 1212  $cm^{-1}$  also identifies the existence of C-O group.

After collecting the cold filtrate, **P<sub>LDM</sub>** of DCM soluble portion that obtained from ethanol soluble portion of **P<sub>M</sub>** and this portion (**P<sub>LDM</sub>**) was separated by column chromatography on silica gel using pet ether and ethyl acetate. 0.639 gm was taken for separation. Different fractions were recorded and from these fractions, the 4<sup>th</sup> and 6<sup>th</sup> fractions were collected. The 4<sup>th</sup> portion was orange yellow colored and this portion was designated as **a3**. In the IR spectrum of the compound, **a3** the broad band at 3600 - 3200  $cm^{-1}$  indicates the presence of OH group. The signal at 3025  $cm^{-1}$  indicates the presence of C-H group in aromatic ring. The bands at 1684  $cm^{-1}$  and 1672  $cm^{-1}$  indicate the presence of C-H group in aromatic ring. The weak band at 1277  $cm^{-1}$  also identifies the existence of C-O group.

The 6<sup>th</sup> fraction was taken for PTLC method for further separation. Pet. ether and ethyl acetate were used as solvents (EA:PE=3:2). Here 3 bands were found. 3<sup>rd</sup> band that collected was designated as **a4**. The product was light pink color. In the IR spectrum of the compound **a4** the broad band at 3600 - 3200  $cm^{-1}$  indicates the presence of OH group. The signals at 3060  $cm^{-1}$ , 3028  $cm^{-1}$  indicate the presence of C-H group in aromatic ring. The values at 1799  $cm^{-1}$  and 1714  $cm^{-1}$  show the presence of C=O group in COOH. The band at 1601  $cm^{-1}$  indicates the presence of C-H group of aromatic ring. The weak band at 1277  $cm^{-1}$  also identifies the existence of C-O group.

After getting the ethanol insoluble portion, **P<sub>ETR</sub>** this portion was separated by column chromatography on silica gel using ethyl acetate and pet ether. 1.0 gm was taken for separation. Different fractions were recorded, from these fractions only 4<sup>th</sup> fraction was collected and

it was taken for PTLC method for further separation. Pet. ether and ethyl acetate were used as solvents (EA:PE=5:95). Here 3 bands were found. 2<sup>nd</sup> band was collected that designated as **a5**. In the IR spectrum of the compound, **a5** the broad band at 3600 - 3300  $cm^{-1}$  indicates the presence of OH group. The signals at 3063  $cm^{-1}$ , 3050  $cm^{-1}$  indicate the presence of C-H group in aromatic ring. The value at 2980  $cm^{-1}$  shows the presence of C-H in saturated aliphatic. The bands at 1809 and 1740  $cm^{-1}$  indicate the presence of C=O group (asymmetric and symmetric stretching). The values at 1597 and 1581  $cm^{-1}$  exhibit C=C group in aromatic ring. The sharp band at 1211  $cm^{-1}$  also identifies the existence of C-O group. In <sup>1</sup>H-NMR spectrum the broad peak shows the singlet at  $\delta$  8.2 - 8.0 which would be assigned for OH protons of phenol type compounds. The multiplet at  $\delta$  7.9 - 7.1 indicates the presence of C-H protons in aromatic rings. The two singlets at  $\delta$  6.3 and  $\delta$  6.2 indicate the presence of two OH groups. The singlet at 2.3 indicates the presence of CH<sub>3</sub> group in CH<sub>3</sub>-CO-O. In the MS spectrum of the compound, **a5** molecular ion peak ( $M^+$  1%) appears at  $m/z$  1150 that corresponding to the molecular formula  $C_{78}H_{54}O_{10}$ . In this spectrum the base peak is formed at  $m/z$  154.

#### Cytotoxicity

Cytotoxicity of all the compounds was measured by brine shrimp lethality bioassay method (Anderson et al., 1999) Cisplatin, a recognized anti-cancer drug was used as reference to compare the efficacy of the synthesized compounds. Compounds **a1**, **a2**, **a3**, **a4** and **a5** showed significant cytotoxicity. Compounds **a1** and **a4** showed high cytotoxicity. Compounds, **a2**, **a3** and **a5** showed relatively low cytotoxicity. So these compounds may show anti-microbial, anti-tumor etc. activity.

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