

## Synthesis of Resorcin[4]arenes Using Microwave Irradiation and Conventional Heating

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Resorcin[4]arenes (**3a-h**) were synthesized by reacting of an aromatic or aliphatic aldehyde, resorcinol, hydrochloric acid and methanol using both microwave irradiation and conventional heating methods in good yields. It has been found that synthesis of resorcin[4]arenes using microwave irradiation, comparative to conventional heating method is more convenient and easily controlled.

**Key Words:** Resorcarene, Microwave irradiation, Resorcinol.

### INTRODUCTION

The acid catalyzed cyclocondensation reaction of a phenol with an aldehyde generally produces an amorphous mixture of products with high molecular weights. However it is well known that the acid catalyzed cyclocondensation reaction of resorcinol, a phenolic compound with some aliphatic aldehyds<sup>1-6</sup> such as acetaldehyde or the reaction of resorcinol with acetylene using mercuric salts<sup>3,4</sup> as a catalyst to produce crystalline high melting products. Nieder and Vogel<sup>4</sup> obtained only a single product from the reaction of resorcinol with acetaldehyde in aqueous sulfuric acid. The mass spectrum of the octamethylether, prepared by Erdman *et al.*<sup>6</sup> was in agreement with molecular structure. However, Högberg<sup>7</sup> has reinvestigated the acid catalyzed reaction of resorcinol and acetaldehyde by <sup>1</sup>H NMR spectroscopy. He found that under acid condition two stereoisomeric macrocyclic products could be obtained from the reaction of resorcinol with acetaldehyde<sup>7</sup> or *p*-bromobenzaldehyde<sup>8,9</sup>. Only one product was obtained when a mixture of ethanol, water and conc. hydrochloric acid was used. In view of these points, in present work the synthesis of some resorcin[4]arenes using microwave irradiation and conventional heating is reported.

### EXPERIMENTAL

All chemicals were of reagent grade quality and used without further purification. <sup>1</sup>H NMR spectra were recorded on a Bruker 500 MHz spectrometer. IR spectra were performed on a Galaxy FT-IR 500 spectrophotometer. Reaction progress was routinely monitored by thin layer chromatography on silica gel plates. Reactions were performed in a domestic Samsung microwave oven with a 230 V-50 Hz power source, 900 W output and 2450 MHz operating frequency.

**General procedure for preparation of 3a-h using conventional method:** A mixture of appropriate aldehyde (0.01 mmol), resorcinol (0.01 mmol), hydrochloric acid (37 %, 0.01 mmol) and ethanol (10 mL) in 100 mL Pyrex beaker was heated in a water bath at 75 °C for 1 h. Upon completion of the reaction, as monitored by TLC, the reaction mixture was cooled to precipitate the crude product, which was filtered and washed with warm ethanol (50 mL) and warm water (50 mL), respectively.

**General procedure for preparation of 3a-h using microwave irradiation:** A mixture of appropriate aldehyde (1 mmol), resorcinol (0.01 mmol), ethanol (2 mL) and 3-4 drops of hydrochloric acid (37 %) in a 50 mL Pyrex beaker was stirred for 2 min. The beaker was put inside a larger container filled with potsherd as a heat sinker and subjected to microwave irradiation at 50 % power level for 90 s. Upon completion of the reaction, as monitored by TLC, the reaction mixture was cooled to precipitate the crude product which was filtered and washed with warm ethanol (50 mL) and warm water, respectively.

**Phenyl-resocarene (3a):** Yield 90 %, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3600-3160, 3080, 2750, 1600.  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ ):  $\delta$  = 5.52-5.62 (4H, m,  $\text{CH}_{\text{benzyl}}$ ), 6.13-6.97 (28H, m,  $\text{CH}_{\text{arom}}$ ), 8.46 (4H, s, OH), 8.57 (4H, s, OH). Anal. calcd. for  $\text{C}_{52}\text{H}_{40}\text{O}_8$ : C, 78.79; H, 5.05 %. Found: C, 79.01; H, 5.32 %.

**4-Dimethylaminophenyl-resocarene (3b):** Yield 60 %, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3600-3200, 3100-3050, 2950, 1610.  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ ):  $\delta$  = 3.07 (24H, s,  $\text{NCH}_3$ ), 5.60-5.77 (4H, m,  $\text{CH}_{\text{benzyl}}$ ), 6.20-7.72 (28H, m,  $\text{CH}_{\text{arom}}$ ), 8.89-9.67 (8H, s, OH). Anal. calcd. for  $\text{C}_{60}\text{H}_{60}\text{O}_8\text{N}_4$ : C, 74.69; H, 6.22, N, 5.81 %. Found: C, 75.05; H, 6.56, N, 5.98 %.

**4-Methylphenyl-resocarene (3c):** Yield 65 %, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3600-3150, 3100-3000, 2980, 1660.  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ ):  $\delta$  = 1.71 (12H, s,  $\text{CH}_3$ ), 5.64-5.66 (4H, m,  $\text{CH}_{\text{benzyl}}$ ), 5.90-6.83 (24H, m,  $\text{CH}_{\text{arom}}$ ), 8.41-8.72 (8H, bs, OH). Anal. calcd. for  $\text{C}_{56}\text{H}_{48}\text{O}_8$ : C, 79.25; H, 5.66 %. Found: C, 79.58; H, 5.85 %.

**2,5-Dimethoxyphenyl-resocarene (3d):** Yield 80 %, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3600-3200, 3100-3050, 2950, 1610.  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ ):  $\delta$  = 3.17, 3.46 (24H, s,  $\text{OCH}_3$ ), 5.77-5.80 (4H, m,  $\text{CH}_{\text{benzyl}}$ ), 6.08-6.41 (24H, m,  $\text{H}_{\text{arom}}$ ), 8.16-4 (4H, bs, OH), 8.30 (4H, bs, OH). Anal. calcd. for  $\text{C}_{60}\text{H}_{56}\text{O}_{16}$ : C, 69.77; H, 5.42 %. Found: C, 70.10; H, 5.71 %.

**2,4-Dimethoxyphenyl-resocarene (3e):** Yield 90 %, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3600-3100, 3050, 2950, 2760, 1620.  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ ):  $\delta$  = 3.36, 3.70 (24H, s,  $\text{OCH}_3$ ), 5.33-5.63 (4H, m,  $\text{CH}_{\text{benzyl}}$ ), 5.74-6.45 (24H, m,  $\text{CH}_{\text{arom}}$ ), 8.08-8.28 (8H, bs, OH). Anal. calcd. for  $\text{C}_{60}\text{H}_{56}\text{O}_{16}$ : C, 69.77; H, 5.42 %. Found: C, 70.12; H, 5.69 %.

**2-Hydroxyphenyl-resocarene (3f):** Yield 55 %, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3600-3150, 3050, 2750, 1600.  $^1\text{H}$  NMR (500 MHz, DMSO- $d_6$ ):  $\delta$  = 5.77-5.84 (4H, m,  $\text{CH}_{\text{benzyl}}$ ), 6.01-6.73 (24H, m,  $\text{CH}_{\text{arom}}$ ), 8.13-8.39 (8H, bs, OH), 8.39-8.42 (bs, OH). Anal. calcd. for  $\text{C}_{52}\text{H}_{40}\text{O}_{12}$ : C, 72.90; H, 4.18 %. Found: C, 73.16; H, 4.38 %.

**4-Methoxyphenyl-resocarene (3g):** Yield 85 %, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3500-3100, 3080, 2960, 1640.  $^1\text{H NMR}$  (500 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  = 3.63-3.9 (12H, m,  $\text{OCH}_3$ ), 5.45-5.57 (4H, m,  $\text{CH}_{\text{benzyl}}$ ), 6.11-6.61 (24H, m,  $\text{CH}_{\text{benzyl}}$ ), 8.40-8.50 (8H, bs, OH). Anal. calcd. for  $\text{C}_{56}\text{H}_{48}\text{O}_{12}$ : C, 73.68; H, 5.26%. Found: C, 73.98; H, 5.50%.

**Methyl-resocarene (3h):** Yield 95 %, IR (KBr,  $\nu_{\max}$ ,  $\text{cm}^{-1}$ ): 3550-3150, 3050, 2750, 1610.  $^1\text{H NMR}$  (500 MHz,  $\text{DMSO-}d_6$ ):  $\delta$  = 1.40 (12H, d,  $\text{CH}_3$ ), 4.25-4.2 (4H, m,  $\text{CH}_{\text{benzyl}}$ ), 6.20-6.70 (m, 8 $\text{H}_{\text{arom}}$ ), 8.60 (bs, OH). Anal. calcd. for  $\text{C}_{32}\text{H}_{32}\text{O}_8$ : C, 70.58; H, 5.88 %. Found: C, 70.90; H, 6.13 %.

## RESULTS AND DISCUSSION

The condensation reaction of resorcinol with different aldehydes in a mixture of acid and ethanol has been reinvestigated as shown in Fig. 1. Reactions were carried out using both microwave irradiation and conventional heating methods. Under these conditions we could isolate one isomer for each reaction. Yields of products using both methods were almost the same.

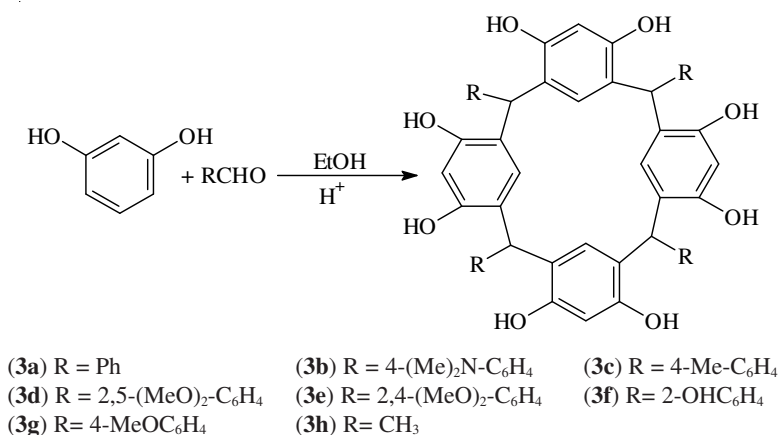


Fig. 1. Specifications of used RCHO and resorcin[4]arenes

$^1\text{H NMR}$  spectra of all the synthesized compounds are very similar and in agreement with the structures of resorcin[4]arenes. The aromatic protons resonate as multiple signals at 6.18-7.20 ppm range depend on the substituted R group. The benzylic proton for **3(a-g)** resonate as a singlet at 5.57-5.90 ppm. However for **3h** this proton resonates as a quartet at higher shift (4.50 ppm). The OH groups resonate as broad signals at 8.10-8.89 ppm.

Microwave irradiation is a non-conventional energy source, which has been of special interest in organic chemistry in recent years. Some of interesting features of this method are the rapid reaction rates, simplicity and cleaner reaction conditions<sup>10-16</sup>. In order to synthesize some resorcin[4]arenes in a clean and fast method it is decided to investigate the influence of microwave irradiation on acid-catalyzed cyclization of aldehyde with resorcinol.

Synthesis of resorcin[4]arenes from an aldehyde and resorcinol using conventional heating needs vigorous reaction conditions. However microwave irradiation promotes these reactions easily so that the reaction times are reduced to minutes rather than hours for conventional heating method. The ratio between the reaction times ( $t_c/t_{mv} = 40$ ) using conventional heating and microwave irradiation reflects the microwave heating effect.

### Conclusion

In summary, we have synthesized some new resorcin[4]arenes by reaction of an aldehyde, resorcinol, hydrochloric acid and methanol using both microwave irradiation and conventional heating methods in good yields. Synthesis of resorcin[4]arenes under microwave irradiation is a simple and environmentally friendly process. Reduction of reaction time and easy reaction set-up and work-up are the advantages of this method.

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