

## A Green Synthesis of a Novel Calix[4]Resorcinarene from 7-Hydroxycitronellal Using Microwave Irradiation

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### ABSTRACT

A new versatile macromolecule cyclic C-3,7-dimethyl-7-hydroxycalix[4]resorcinarene (CDHHK4R) has been synthesized from a fragrance agent, 7-hydroxycitronellal, via microwave irradiation. The reaction utilized a domestic microwave oven at various irradiation time and power to yield an optimum condition. As a comparison, the conventional heating method was also employed for the synthesis of the same calix[4]resorcinarene. Compared to the conventional method, microwave-assisted reaction effectively reduced the reaction time, the amount of energy consumption and the waste production. It is found that the synthesis of CDHHK4R by microwave irradiation yielded 77.55% of product, higher than by conventional heating which was only 62.17%.

**Keywords:** calix[4]resorcinarene; 7-hydroxycitronellal; microwave irradiation

### ABSTRAK

Suatu makromolekul siklik baru, yaitu C-3,7-dimetil-7-hidroksikaliks[4]resorcinarena (CDHHK4R) telah disintesis dari 7-hidroksisitronellal menggunakan radiasi gelombang mikro. 7-Hidroksisitronellal merupakan salah satu komponen minyak sereh, dan merupakan bahan pembuat parfum yang dikenal sebagai "king of perfume". Reaksi dilakukan menggunakan oven gelombang mikro pada berbagai daya dan waktu radiasi untuk memperoleh kondisi optimum. Sebagai perbandingan, metode pemanasan konvensional juga dilakukan untuk memperoleh kaliks[4]resorsinarena yang sama. Hasil penelitian menunjukkan bahwa sintesis yang menggunakan gelombang mikro dapat mengurangi secara signifikan waktu reaksi, jumlah energi yang diperlukan, dan limbah yang dihasilkan. Hasil sintesis CDHHK4R dengan radiasi gelombang mikro juga lebih tinggi, yaitu sebanyak 77,55%, dibandingkan dengan pemanasan konvensional yang menghasilkan hanya 62,17%.

**Kata Kunci:** kaliks[4]resorsinarena; 7-hidroksisitronelal; radiasi gelombang mikro

### INTRODUCTION

Calix[4]resorcinarene is a class of cyclic tetramer composed of resorcinol which are linked by methine bridge to form a cavity-shaped [1]. This cavity may act as a host molecule for certain guest molecules in a host-guest system. Type of guest molecule can be varied (cations, anions or neutral molecules), depends on the functional group and the size of this cyclic tetramer [2]. Calix[4]resorcinarenes are one of the calixarene macrocycles which were synthesized from resorcinol and an aldehyde [3]. Calixarene firstly synthesized by Adolf von Baeyer from formaldehyde and phenol in acidic condition [4]. In its progress, the use of other variants of both of aliphatic and aromatic aldehydes was reported [5-7]. Calixarenes have been used in many fields [8], such as liquid crystals [9], extractions [10], sensors [11-12], membranes [13-14], catalysts [15-16], adsorbents [17-18], stationary phases of

chromatography [19-20], dyes [21], fluorescent materials [22], or semiconductors [23-25].

Synthesis of calix[4]resorcinarene was generally carried out by reflux using ethanol as a solvent in abundance. This reaction gives product in good yield [26-28]. Unfortunately, it requires long reaction times (20-24 h), so this method is not considered as environmentally friendly reaction. A new method considered more environmentally friendly was developed [29-30], including microwave irradiation method [31-32]. It was reported that the microwave-assisted irradiation can reduce the time of reaction, amount of energy consumption, waste production, hence offers many benefits for environmental protection [33]. The microwave assisted syntheses of calix[4]resorcinarene from resorcinol and aldehyde (ethanaldehyde, pentanaldehyde, hexanaldehyde, octanaldehyde, nonanaldehyde, decanaldehyde, dodecanaldehyde, benzaldehyde, and *p*-*t*-

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butylbenzaldehyde) have been done using 12-tungstophosphoric acid Keggin-type  $H_3PW_{12}O_{40} \cdot 13H_2O$  and concentrated HCl as catalyst. Excellent isolated yields (up to 90%) were attained within short reaction times (typically, 3–5 min) when the reaction was performed under microwave irradiation [34]. Unfortunately, the catalyst used by Hedidi has a complex structure, expensive, and not easily available. Moreover, the capability of the catalyst in synthesis of calix[4]resorcinarene from other aldehydes has not been yet known. Therefore, it is necessary to develop methods of synthesis of calixresorcinarene that use catalysts which are more simply and easily obtained.

Indonesia is one of the largest essential oil producers for a particular commodity. One of the essential oils produced in Indonesia is citronella oil. The important components that contained in citronella oil is 7-hydroxycitronellal, well known as The King of Perfume. Consisting of aldehyde group, this fragrance compound can also be used as a raw material for synthesizing a novel calix[4]resorcinarene.

In this article, we report synthesis of a new tetramer cyclic, i.e. C-3,7-dimethyl-7-hydroxycalix[4]resorcinarene (CDHHK4R) from 7-hydroxycitronellal and resorcinol (Fig. 1). In this synthesis, the complex catalyst used by Hedidi was replaced with the simple one, i.e. *p*-toluenesulfonic acid. The synthesis carried out in two methods of heating, that are microwave irradiation and conventional heating. Therefore, expecting to yield a green synthesis, we employ microwave irradiation method and compare in its effectiveness with conventional heating.

## EXPERIMENTAL SECTION

### Materials

Synthesis and purification were carried out using a set of reflux apparatus, and domestic microwave oven (Electrolux EMM-2007X). The reagents consist of

resorcinol (Merck), 7-hydroxycitronellal (Aldrich), and *p*-toluenesulfonic acid pro analysis (Merck).

### Instrumentation

Equipments used for characterization were melting point apparatus, Fourier Transform Infrared (FTIR) Shimadzu 8400, Mass Spectrometry (MS) Waters LCT Premier X6, Proton and Carbon Nuclear Magnetic Resonance ( $^1H$ -NMR and  $^{13}C$ -NMR) JEOL ECA 500-500 MHz.

### Procedure

#### Synthesis of CDHHK4R using conventional heating

Into a 40 mL solution of resorcinol (0.330 g; 3 mmol) and 7-hydroxycitronellal (0.516 g; 3 mmol) in 70% ethanol, 5 mL of hydrochloric acid was added. The mixture was stirred under at 76 °C and was monitored by Thin Layer Chromatography (TLC). After 20 h, the reaction was completed. The orange solid was recrystallized with methanol and dried in an oven for 24 h to produce peach-colored solid (62.17%, m.p: 125 °C).

#### Synthesis CDHHK4R using microwaves irradiation

Into a 4 mL solution of resorcinol (0.330 g; 3 mmol) and 7-hydroxycitronellal (0.516 g; 3 mmol) in 70% ethanol, *p*-toluenesulfonic acid (0.008 g; 1%) was added. The mixture was stirred for 5 min at room temperature. Homogenic mixture was introduced into the microwave oven and irradiated for a certain period (irradiation was set at a certain power). The reaction progress was monitored by TLC. Various experimental conditions were optimized for the irradiation time (3, 4, 5, 6 and 7 min) and irradiation power (100, 182, 264, 300 and 400 W). After the completion reaction, orange solid was washed with distilled water, recrystallized with methanol and dried in an oven for 24 h to yield pale brown solid. The optimum result was achieved by 5 min irradiation time and 264 W irradiation power (77.55%, m.p: 130-132 °C).

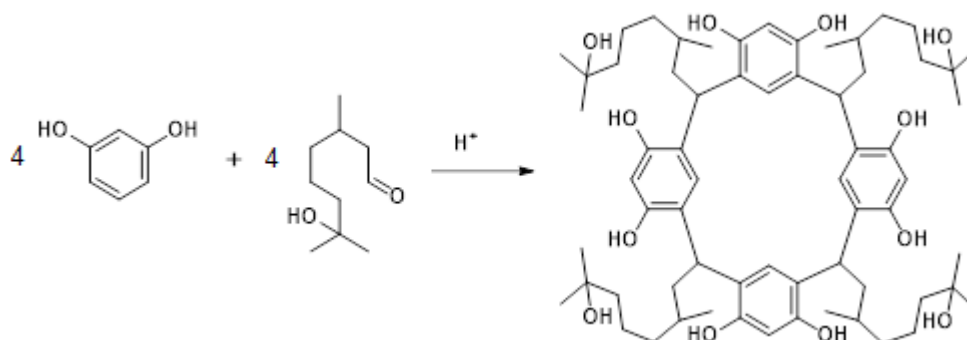


Fig 1. Reaction scheme of CDHHK4R

## RESULT AND DISCUSSION

### Synthesis of CDHKK4R

Synthesis of CDHKK4R using conventional heating resulted in 62.17% of peach colored solid as a product. Microwave irradiation has assisted CDHKK4R synthesis and gives 77.55% of product as pale brown solid. Monitoring product using TLC indicated that the reaction between resorcinol and 7-hydroxycitronellal yielding a new single compound.

FTIR spectrum of synthesis product shows absorption at wavenumber 1620, 1504 and 1458  $\text{cm}^{-1}$  that corresponds to the aromatic structure and supported by the absence of absorption at 1762.0 and 2715  $\text{cm}^{-1}$  that corresponds to the aldehyde group. This indicates the complete condensation of resorcinol and 7-hydroxycitronellal to form cyclic tetramer CDHKK4R.

The formation of the desired product is also supported by the mass spectroscopy analysis. Mass spectrum of CDHKK4R is shown in Fig. 2. The spectrum gives molecular ion peak at  $m/z$  1057.7 that corresponds to the mass of CDHKK4R with an additional of hydrogen atom. Whereas peaks at  $m/z$  1079.7 and 1095.6 correspond to the mass of CDHKK4R that binds one sodium (22.989) and potassium (39.102), respectively. Sodium and potassium ions were added in mass measurement process.

$^1\text{H-NMR}$  spectrum indicates the rccc (crown- $\text{C}_{4v}$ ) and rctt (boat- $\text{C}_{2v}$ ) conformation, with the rccc product as a predominant isomer (Fig. 3). These two isomers can be identified from proton pattern in  $^1\text{H-NMR}$  aromatic region [35]. Isomer with crown- $\text{C}_{4v}$  conformation will arise two singlet peaks at region between 6.0 to 8.0 ppm. One singlet upfield proton is identified to the proton at ortho position from hydroxy group of benzene which is

shielding, whereas downfield proton corresponds to the proton at meta position which is deshielding. Boat- $\text{C}_{2v}$  isomeric will appear as four singlet signals with integrity 2H for each signal at 6.0–8.0 ppm.

$^1\text{H-NMR}$  spectrum shows overlapped proton signals at 6.2 ppm and 6.9 ppm. Therefore, conformation and ratio of its isomer could not be identified from this NMR spectrum. However, with one proton signal from hydroxy functional group appeared at 7.9 ppm, it is likely that the most predominant product of mixture yielded is an isomer with crown- $\text{C}_{4v}$  conformation, as described in the previous studies [19]. Protons from methine bridge in CDHKK4R structure arranged appeared at 4.6–4.7 ppm, while aliphatic proton appeared at 0.8–2.0 ppm.

$^{13}\text{C-NMR}$  spectrum of CDHKK4R gives carbon aromatic signal between 103.6 ppm to 157.5 ppm with oxyaryl carbon appeared at a region from 153.5 ppm to 157.5 ppm (Fig. 4). Aliphatic carbon signal appeared at

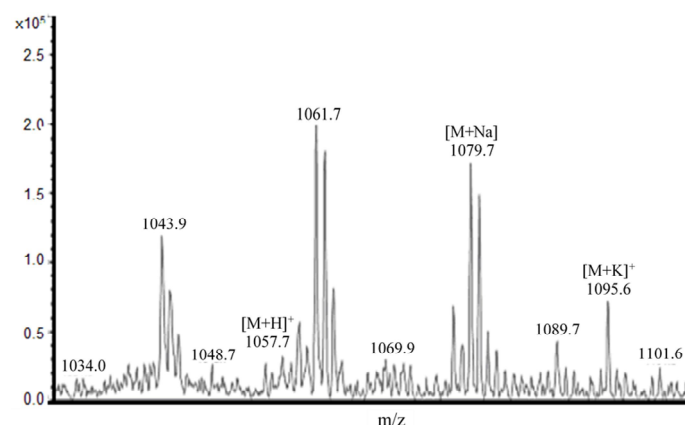


Fig 2. Mass spectrum of CDHKK4R

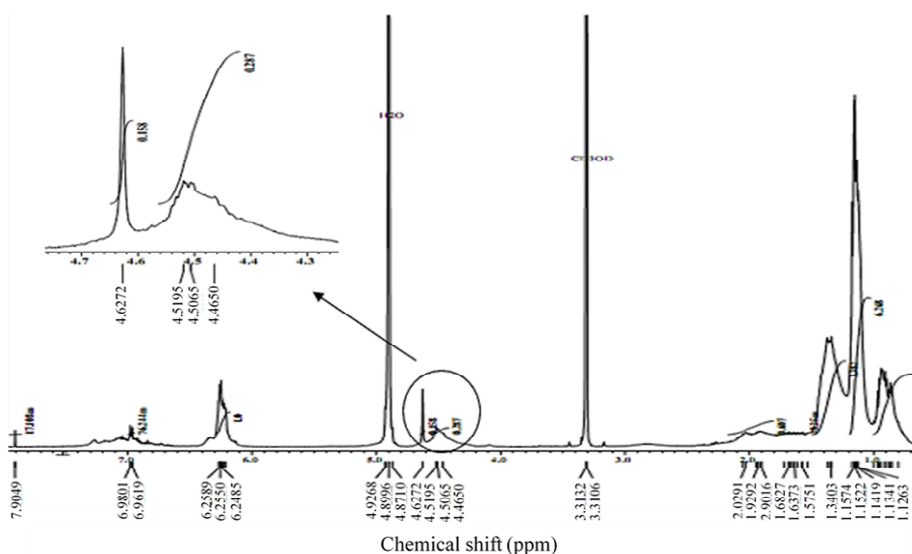


Fig 3.  $^1\text{H-NMR}$  spectrum of CDHKK4R

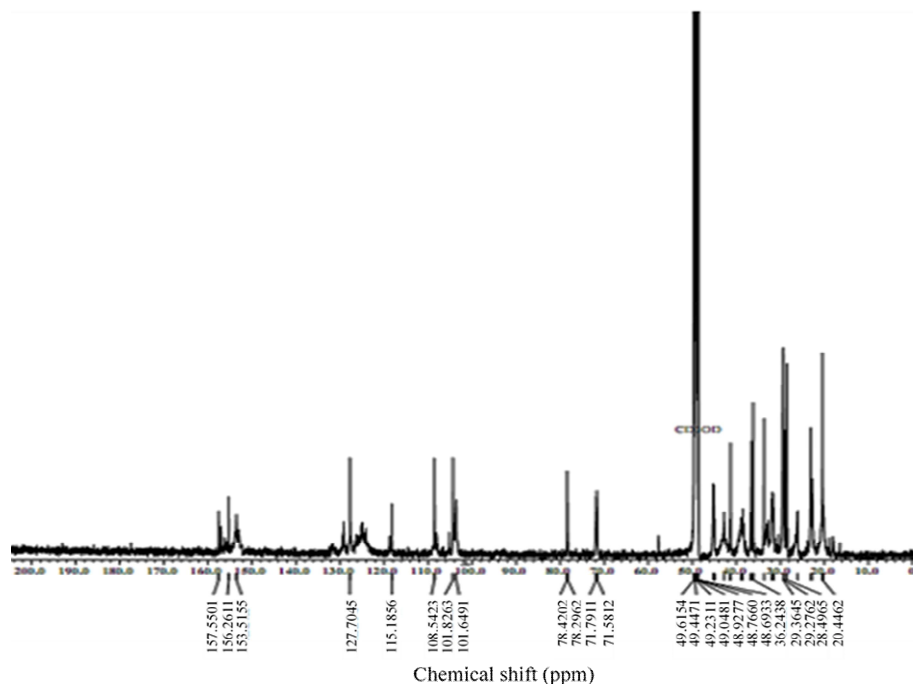


Fig 4.  $^{13}\text{C}$ -NMR spectrum of CDHHK4R

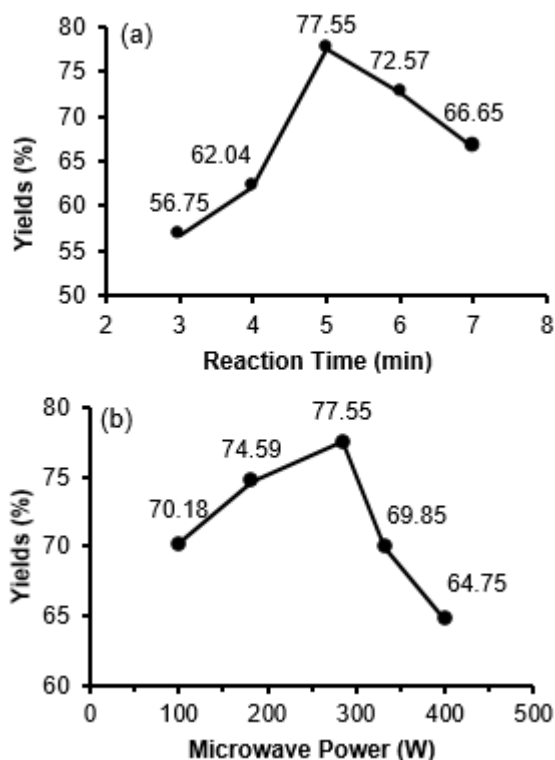


Fig 5. Percentage of CDHHK4R resulted from synthesis in various reaction time (a) and power of microwave oven (b)

20.0-50.0 ppm with aliphatic carbon binds oxygen signal appeared at 71.5–78.4 ppm. FTIR,  $^1\text{H}$ -NMR,  $^{13}\text{C}$ -NMR and MS indicated that CDHHK4R was successfully synthesized.

The effect of different factor on synthesis of CDHHK4R, i.e. reaction time and microwave power is reported. The percentage of products resulted in various reaction time (3, 4, 5, 6 and 7 min) at 264 W of irradiation power and mole ratio of 1:1, was given in Fig. 5(a). Optimal reaction was performed for 5 min reaction time, yielding 77.55% of product after recrystallization. The product percentage then decreased at longer reaction time, due to more induce side reactions.

The best result of variation microwave power experiment was yielded from reaction with ratio mole of reactant 1:1, irradiated for 5 min at power of microwave oven 264 W. Increasing of irradiation power above 264 W (Fig. 5(b)) decreased the percentage of product because of the random movement of the reactant particles in the excess of irradiation.

Several parameters such as environment acceptability, atom economy, atom efficiency, mass efficiency and electrical energy efficiency can be used as a benchmark in determining how greener a reaction were performed. The comparison between two methods of heating in CDHHK4R synthesis was shown in Table 1.

**Table 1.** Comparison between synthesis of CDHHK4R using microwave (MA) and conventional heating (Reflux)

Parameter	MA	Reflux
Reaction Time (min)	5	1200
Yield (%)	77.55	62.17
Environment Acceptability	4.28	42.06
Atom Economy (%)	93.36	23.11
Atom Efficiency (%)	72.40	14.37
Mass Efficiency (%)	71.92	16.24
Electrical Energy Efficiency (%)	$2.6 \times 10^{-4}$	$1.8 \times 10^{-6}$

Microwave assisted in synthesis of CDHHK4R was proven to effectively reduce the time of reaction, from hours to minutes by the thermal and non-thermal combination effect that performed in microwave irradiation. When irradiated, particle of reactant molecules will rotate along the electrical field applied. This rotation increasing the energy of particles to collide to each other results in a friction which produces heat. This effect is known as a thermal effect.

Introduction of microwave irradiation into a chemical reaction is direct, without heat absorption of the container, which can yield shorter reaction time. Short reaction time can induce reduction of amount of solvent used, energy used and waste production. Besides, with short reaction time, possibility of product decomposition is minimal.

This can be inferred that the use of microwave-assisted reaction is a greener option due to the shorter reaction time, lower environmental acceptability, lower amount of waste produced, higher atom economy, atom efficiency and mass efficiency with higher yield. Lower energy consumption is identified by higher energy efficiency which may help the energy saving for world today.

## CONCLUSION

A novel calix[4]resorcinarene, CDHHK4R, has been synthesized from 7-hydroxycitronellal by using microwave irradiation and conventional methods. Compared to the conventional method, microwave irradiation effectively reduces of reaction time, amount of energy consumption, and waste production. In addition, the microwave irradiation gives higher percentage of product than conventional one.

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