

## Qualitative Analysis of Two Phenolic isomers of Carvacrol and Thymol by using Briggs-Rauscher Oscillator System

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A new technique for identification of two phenolic isomers between carvacrol and thymol was discussed by using their different perturbation effect on Briggs-Rauscher oscillation system. In such system, a macrocyclic complex of  $[\text{NiL}](\text{ClO}_4)_2$  was used as catalyst, which ligand L is 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradeca-4,11-diene. Experimental results proved that the perturbation of equal amount of same concentration two isomers separately into B-R system could temporarily quench the oscillation for period of time prior and regeneration of oscillation. The inhibition is directly proportional to the concentration of isomers. The carvacrol causes inhibition time, while no effect of thymol on the active B-R oscillation is measured. We identified the two phenolic isomers in the range from  $1.25 \times 10^{-6}$  to  $3.23 \times 10^{-5}$  mol/L, and correlation coefficient is 0.98755. The FCA mechanism based on  $\text{HOO}^\bullet$  radical has been proposed.

**Keywords:** Phenolic Isomers; Briggs-Rauscher; Perturbation; Inhibitory effect; FCA mechanism

### 1. INTRODUCTION

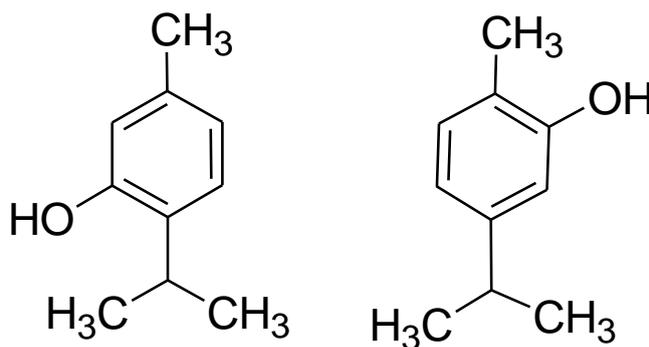
Isomers have equal number of atoms, but the arrangement of atoms is different. Or an atom group has two or more than two atomic cores having same atomic number and mass number but have different energy position. Isomers have difference kind of function, so everyone wants to prepare different kind of isomers to assist in numerous medical treatments. For example, L-DOPA and D-DOPA are isomers but both have different purpose. Levodopa is used for treatment of Parkinson's disease, and it is gold standard treatment for Parkinson's. The condition of Parkinson's disease is slow movements, muscle stiff and impaired speech. It is very common neurodegenerative disorder disease

worldwide [1]. While isomer of D-dopa causes the deficiency of white blood cell and the deficiency of white blood cell are easily influenced or vulnerable to diseases. Similarly the D-ethambutol is anti-tuberculosis drugs while L- ethambutol causes blindness. The identification of isomers is greatly appreciated in the field of analytical chemistry.

For the identification of different isomers, different instrumental techniques, such as GC-MS [2, 3], LC-MS [4], MS [5,6] and mass spectrometric-molecular statistic [7], were used. The GC-MS having some draw-backs, such as highly working temperature, not easy to operating and very expensive technique. LC-MS is also used for identification of drugs and isomers. The disadvantage of LC-MS is different limitation factor such as selection of appropriate mobile phase. MS is direct technique to identify samples and it sometimes couple with other technique to identify samples. Therefore, a new method was developed to identify the isomers, drugs and medicine to avoid this disadvantage. Thus we developed a new technique (oscillating chemical system) which is good detection limitation and easy to setup.

For the nonlinear chemical dynamic oscillator, Fechner discover electrochemical oscillator in 1828, for the first time. The passage of time the homogenous chemical oscillators were discovered, i.e. Bray- Liebafsky (BL oscillator) [8, 9], Briggs-Rauscher (BR oscillator) [10, 11], Belousov-Zhabotinsky (BZ oscillator) [12, 13,14]. Among this, Briggs-Rauscher (BR oscillator) and Belousov-Zhabotinsky (BZ oscillator) involvement of metal ion catalyst such as,  $Ce^{4+}$ ,  $Mn^{2+}$ ,  $Ru(bipy)_3^{2+}$ , and  $Fe(phen)_3^{2+}$  were studies. In 1982 Yatimirskii reported macrocyclic complex (Cu, Ni) catalyst [15]. The macrocyclic complexes of Cu, Ni were determine many organic compound, antioxidants, drugs, species and ions [16-24]. This chemical oscillator has much application like pattern formation [25], wave propagation and chaos [26].

In this work, we reported analytical tool for identification of two isomers, (carvocrol and thymol) by using B-R oscillator which is based on macrocyclic Ni complex catalyst, where ligand L is 5,7,7,12,14,14-hexamethyl-1,4,8,11-tetraazacyclotetradeca-4,11-diene. Experimental results proved that the perturbation of equal amount of same concentration two isomers separately into B-R system could cause different effects: the carvocrol temporarily quench the oscillation for period of time prior and regeneration of oscillation (cause inhibition time), while no influence of thymol was notice. The inhibition is directly proportional to the concentration of isomer. The identification the two phenolic isomers over the range from  $1.25 \times 10^{-6}$  to  $3.23 \times 10^{-5}$  M, with correlation coefficient is 0.98755.

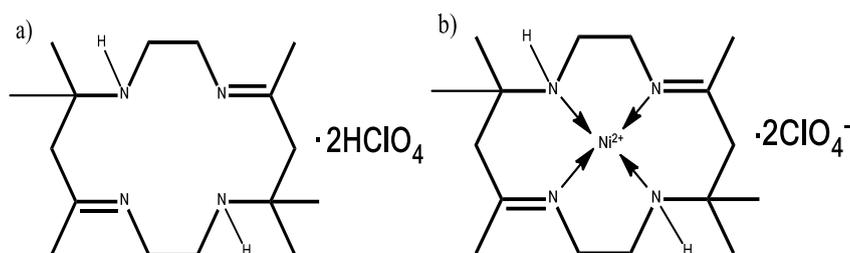


**Scheme 1.** Structure of Thymol and Carvocrol

## 2. EXPERIMENTAL

### 2.1. Reagents

The reagents, such as sulfuric acid (Aldrich, 98%), malonic acid (MA) (Sinopharm Chemical Reagent, China),  $\text{KIO}_3$  (Sinopharm Chemical Reagent, China) and  $\text{H}_2\text{O}_2$  (30%) (Sinopharm chemical reagent, China) and carvocrol and thymol are commercial purchased expect  $[\text{NiL}](\text{ClO}_4)_2$  catalyst. Catalyst was prepared according to references [27, 28] and it was confirmed by IR spectrum and elemental analyses. The structure of  $[\text{NiL}](\text{ClO}_4)_2$  is shown in Scheme 2. The 2.00 mol/L malonic acid,  $1.73 \times 10^{-2}$  mol/L  $[\text{NiL}](\text{ClO}_4)_2$ ,  $1.4 \times 10^{-1}$  mol/L  $\text{KIO}_3$ , and 4.00 mol/L  $\text{H}_2\text{O}_2$  were prepared with  $2.5 \times 10^{-2}$  mol/L  $\text{H}_2\text{SO}_4$  solution.



**Scheme 2.** Structure of macrocyclic Ni-Complex catalyst

### 2.2. Apparatus

In the BR experiment, a glass container (50 ml) was used with Model (79-3) magnetic stirrer (Jiangsu, China), which was applied to standardize the reaction solution. In the glass reactor, the stirring rate was kept at 500 rpm. Two electrode, Model 217 platinum electrode (Shanghai, China) which acts as working electrode connected to saturated calomel electrode (SCE) (Model 217 Shanghai, China) which called reference electrode using a salt bridge containing 1 mol/L  $\text{Na}_2\text{SO}_4$ . They were utilized to screening the change in potential. These two electrodes were connected to an amp (Vernier Software Technology, U.S.A) and GO-Link sensor interface, and these two electrodes is connected to personal computer (PC) to use Logger Lite data-acquisition program to record potential verus time.

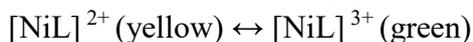
### 2.3. Procedure

The sequence of all reagent in the glass reactor is following, 14.8 ml of  $2.5 \times 10^{-2}$  mol/L  $\text{H}_2\text{SO}_4$  solution, 6.8 ml of  $1.4 \times 10^{-1}$  mol/L  $\text{KIO}_3$  solution, 3.4 ml of 2.00 mol/L MA solution, 2 ml of  $1.73 \times 10^{-2}$  mol/L  $[\text{NiL}](\text{ClO}_4)_2$  solution and 13 ml of 4.00 mol/L  $\text{H}_2\text{O}_2$  solution. The electrode was dipped into reactor, and  $\text{H}_2\text{O}_2$  was put into crystal glass reactor. The glass reactor was retained in ice bath and the temperature was precise to use the reaction temperature at  $4.0 \pm 0.5$  °C. The oscillations are started after short induction of time and potential versus time were noted in the PC.

### 3. RESULTS AND DISCUSSION

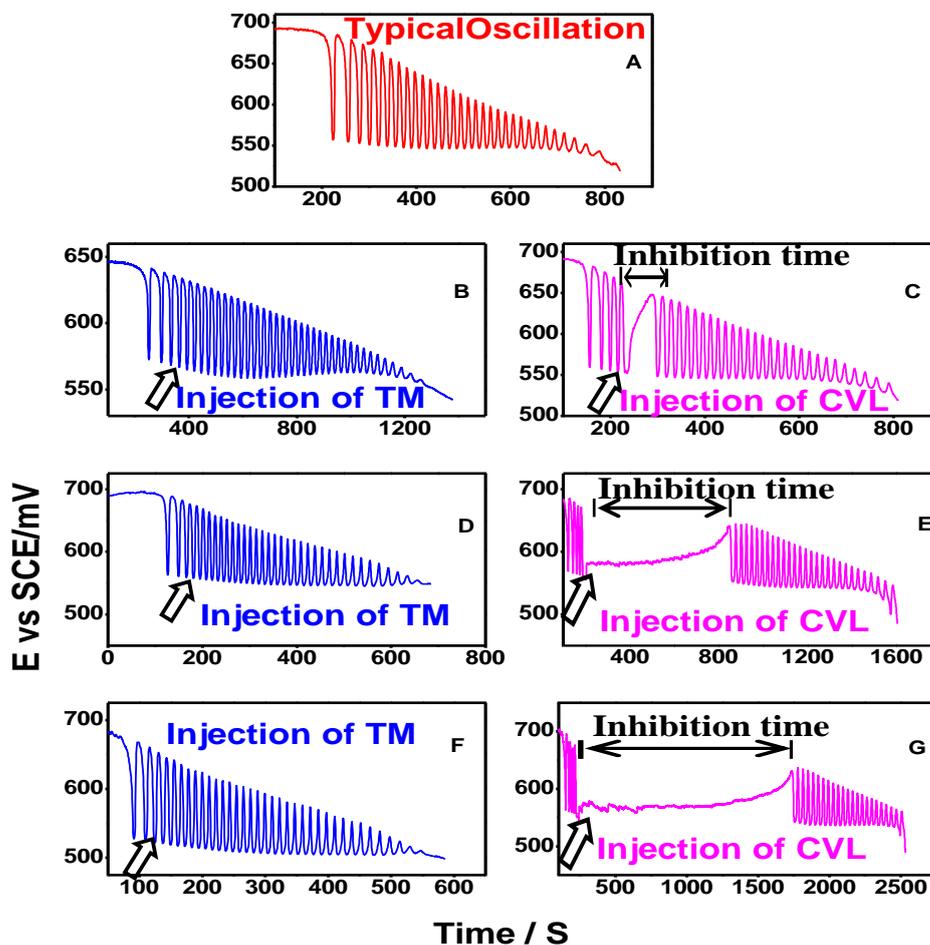
#### 3.1. Typical oscillation for B-R reaction

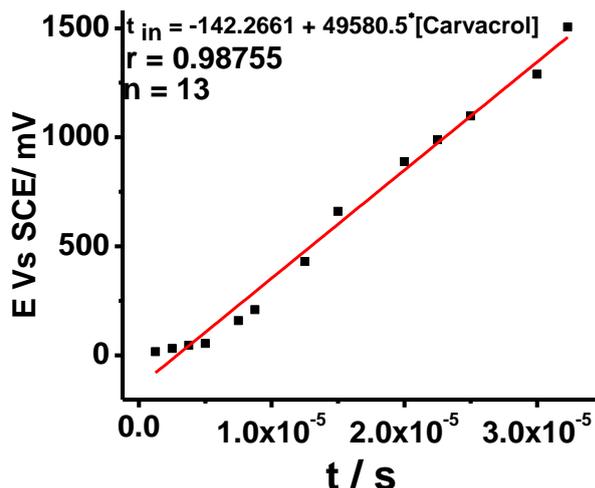
Typical oscillation for B-R reaction was obtained as shown in Fig. 1a, by the mixing of all reagents in order. We measured that the color of the solution is continuously change from yellow to brown and from brown to yellow, due to one electron transfer process among  $[\text{NiL}]^{2+}$  to  $[\text{NiL}]^{3+}$  as listed below. During the reaction of  $\text{I}_2$  with low concentration was generated, due to  $\text{I}_2$  the appearance color was notice brown relatively green.



#### 3.2. Perturbation of B-R potential oscillation

For identification of two isomers (carvocrol and thymol) from each other's, the same amount of equal concentrations of isomers was used to perturbate in BR system. The concentration over range of these two isomers was investigated from  $1.25 \times 10^{-6}$  to  $3.23 \times 10^{-5}$  mol/L.





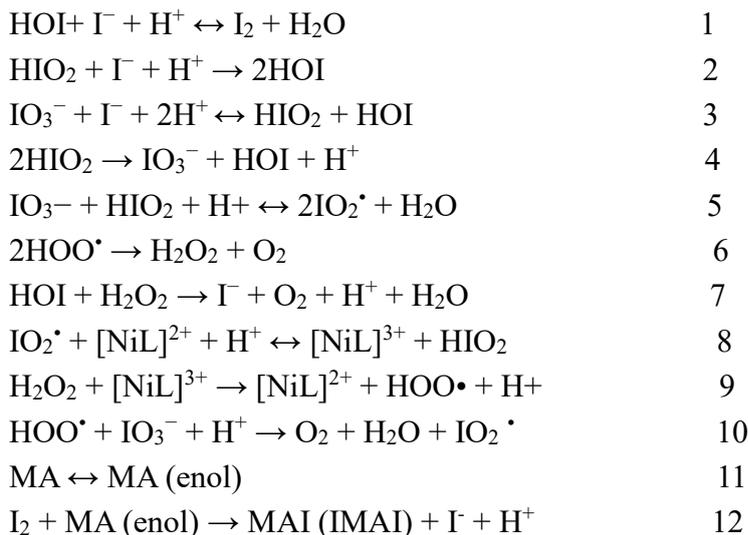
**Figure 1.** a) Typical oscillation for proposed system; b). Perturbation of  $7.5 \times 10^{-6}$  mol/L [Carvacrol]; c). Perturbation of  $7.5 \times 10^{-6}$  mol/L [thymol]; d). Perturbation of  $1.50 \times 10^{-5}$  mol/L [carvacrol]; e). Perturbation of  $1.50 \times 10^{-5}$  mol/L [thymol]; f). Perturbation of  $3.25 \times 10^{-5}$  mol/L [carvacrol]; g). Perturbation of  $3.25 \times 10^{-5}$  mol/L [thymol]; h) Linear relationship between  $t_{in}$  and concentration of carvacrol; Common condition;  $[H_2SO_4] = 2.25 \times 10^{-2}$  mol/L;  $[KIO_3] = 2.27 \times 10^{-2}$  mol/L;  $[[NiL](ClO_4)_2] = 8.21 \times 10^{-4}$  mol/L;  $[MA] = 1.75 \times 10^{-1}$  mol/L;  $[H_2O_2] = 1.25$  mol/L;  $t = 5$  °C.

The perturbation of both isomers were obtained, the inhibition time cause by Carvacrol are listed in Fig.1b, although the perturbation of same amount of concentration in thymol had no influence in B-R system as shown in Fig. 1c. As the concentration increases, we observed that the inhibition time is higher as shown in Fig. 1(d, f), while no effect on thymol in high concentration (as shown in Fig. 1 (e, g)). The linear regression curves were obtained against  $t_{in}$  and concentration range ( $1.25 \times 10^{-6}$  to  $3.23 \times 10^{-5}$  mol/L) with correlation coefficients of 0.98755 as shown in Figure 4.1h. We notice the different behaviors of two isomers (carvacrol and thymol). We successfully identified two isomers by their perturbation effect on B-R oscillation system. We proposed a novel method for identification of isomers. This technique is suitable for identification isomers as well as analytical methods such as wide range of detection, recovery of analyst and easy to setup.

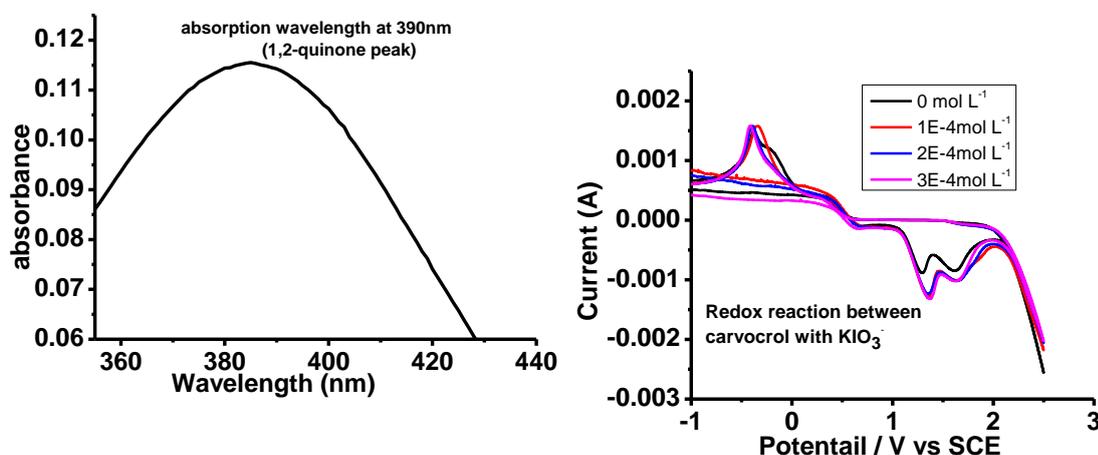
### 3.3. Proposed mechanism for B-R oscillating system

The mechanism of B-R oscillation system is complex due to various kinetic steps involved in sovereign variables. For the first time, in 1982, Noyes and Furrow (NF model) proposed skeleton of mechanism, which was able to generate some basic feature of oscillation system [29]. The similar mechanism was developed by De Kepper and Epstein (DE model) in the same time [30]. The more detail mechanism was proposed in 1996 by Sorensen and his co-workers, and the mechanism is well presented and varied range for the experimental results in batch reactors [31]. Furrow [32, 33] proposed a new FCA mechanism for NF and DE models. Hydroperoxyl radical  $HOO^\bullet$  radical (intermediate species which generate oscillation reactions) play an importance role in FCA

mechanism. The FCA model, based on Ni-complex catalyzed system, involving 12 basic oscillatory reactions, are following.



The reaction 1-5 called oxyiodine reaction involvement, the same reaction in NF model [34]. The reaction 6 – 7 which involves oxygen in NF model [34], Catalyst involvement reaction showed the reaction 8-9, same in NF model [34].



**Figure 2.** (a) UV spectrum of carvocrol in the presence and absence of  $\text{H}_2\text{SO}_4$ ,  $\text{KIO}_3$ : Condition;  $[\text{carvocrol}] = 1.25 \times 10^{-2} \text{ mol/L}$ ,  $[\text{H}_2\text{SO}_4] = 2.25 \times 10^{-2} \text{ mol/L}$ ;  $[\text{KIO}_3] = 2.27 \times 10^{-2} \text{ mol/L}$ . (b) CV of  $\text{KIO}_3$  with carvocrol. Common condition:  $[\text{KIO}_3] = 2.27 \times 10^{-2} \text{ mol/L}$ ,  $[\text{H}_2\text{SO}_4] = 2.25 \times 10^{-2} \text{ mol/L}$ . Scan rate = 100 mV/s.

In this reaction  $\text{Mn}^{2+}$  replaced with tetraazamacrocyclic Ni-complex catalyst. The reaction 10, by the involvement reduction of oxyiodine, which is analogous in the reaction (12) in FCA model [35].

### 3.4. Cyclic voltammetry experiments for B-R

In the presence and absence of both isomers (carvocrol and thymol), the cyclic voltammetry experiments were performed into following media:

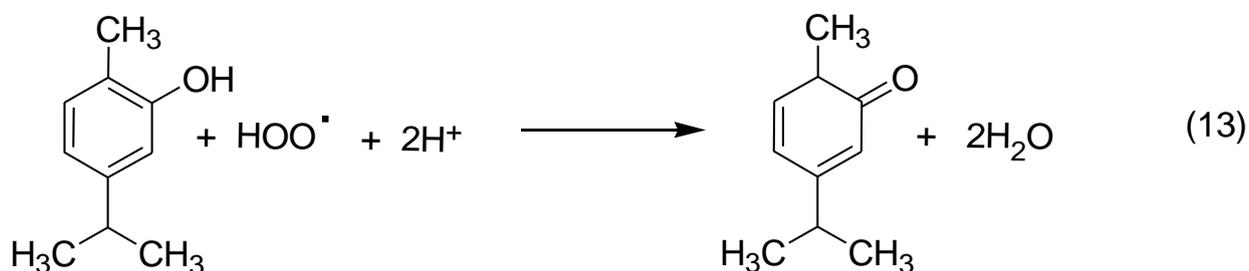
$\text{H}_2\text{SO}_4 + \text{KIO}_3$ ,  $\text{H}_2\text{SO}_4 + \text{MA}$ ,  $\text{H}_2\text{SO}_4 + \text{H}_2\text{O}_2$ ,  $\text{H}_2\text{SO}_4 + [\text{NiL}](\text{ClO}_4)_2$ .

We investigated that, the results of cyclic voltammetry (CV) experiments only react with carvocrol between potassium iodate ( $\text{KIO}_3$ ) seemed in Fig. 2.

### 3.5. Product identification in B-R system

For the UV spectrum experiments, the solution mixture made by the following: 50  $\mu\text{l}$  of 0.01 M solution of carvocrol, the solution of 34 ml of  $2.5 \times 10^{-2}$  mol/L,  $\text{H}_2\text{SO}_4$  (sulfuric acid) and 6 ml of  $2.27 \times 10^{-3}$  mol/L,  $\text{KIO}_3$  solution.  $[\text{NiL}](\text{ClO}_4)_2$ , MA,  $\text{H}_2\text{O}_2$  reagent didn't show redox reaction in (CV) experiments through carvocrol and thymol. The mixture of 1 ml solution was transferred into UV-cells for UV experiments to determine product in reagent mixture. Absorbance verses wavelength the product were determine approximately at wavelength of 390 nm, as shown in Fig.2 a. The UV spectrum for 1, 2 quinone is agreed in references [36, 37, 38, 39]. Thus we established that carvocrol was oxidized to 1, 2 quinone in B-R system.

### 3.6. Explanation of reaction (13) with carvocrol and $\text{KIO}_3$



The UV spectra confirm the product, which is 1-2-quinone in B-R system. The CV experiment confirms the redox reaction among carvocrol and  $\text{KIO}_3$ . But we propose  $\text{HOO}^\bullet$  instead of  $\text{KIO}_3$  as oxidation reagent because of the appearance of the inhibition time. The inhibition time is due to  $\text{HOO}^\bullet$  radical on B-R system, which was observed by Franz [40]. A Feanz phenomenon was experimentally confirmed by Cervellati et al [32]. This hypothesis have many publication based on  $t_{\text{in}}$  due to  $\text{HOO}^\bullet$  radical [41, 42, 43]. Currently our group publishes many articles regarding  $\text{HOO}^\bullet$  radical to produce  $t_{\text{in}}$  [38, 39,44].

## 4. CONCLUSIONS

We established a new technique for identification of two phenolic isomers between carvocrol and thymol by using their inhibitory effect on a B-R oscillator. The carvocrol and thymol were shown to identify from each other by depositing them into B-R system. We notice that carvocrol causes inhibition time, while thymol didn't show any influence toward B-R system. Therefore we identify two isomers in their inhibitory effect used as parameters.

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