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**INTERNATIONAL JOURNAL OF  
 ADVANCED RESEARCH (IJAR)**

Article DOI: 10.21474/IJAR01/5399  
 DOI URL: <http://dx.doi.org/10.21474/IJAR01/5399>



### RESEARCH ARTICLE

## VOLTAMMETRIC STRUCTURE-ACTIVITY QUANTIFICATION OF REGIO-ISOMERS OF DIHYDROXYBENZOIC ACID: ELUCIDATION OF STERIC CONSTRAINTS DURING RAPID IODINATION BY AQUEOUS SOLUTIONS DEVOID OF IODIDE IONS.

R. P. Yadav, B. B. Bahule, V. T. Borkar and \*V. T. Dangat.

Post-Graduate Department of Chemistry, NowrosjeeWadia College, Affiliated to the SavitribaiPhule University, Pune- 411001, India.

#### Manuscript Info

##### Manuscript History

Received: 11 July 2017  
 Final Accepted: 13 August 2017  
 Published: September 2017

##### Key words:-

Dihydroxybenzoic Acid, Molecular Iodine, Electro-reduction, Diffusion Current.

#### Abstract

The reactivity of three regio-isomers of dihydroxybenzoic acid in aqueous medium has been assessed on a quantitative scaffold by voltammetry. The rapid iodination kinetics of these isomers by aqueous molecular iodine solutions devoid of iodide ions has been investigated and the data invoked to elucidate the steric compulsions in the dynamics of these reactions.

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#### Introduction:-

Halo products of aromatic compounds often are antiseptic, antiviral, and antibacterial and are of significance in pharmacodynamics. The reactivity of these substrates stems from a host of factors like their nucleophilicity, substituents present, reagent type and solvent nature<sup>1</sup>. The qualitative prediction of activity of these substrates is not a rarity but quantitative confirmation is needed.

Dihydroxybenzoic acids (DHBA) are a type of phenolic acids. There are six main compounds, having all the same molecular formula  $C_7H_6O_4$ . These are as follows:

1. 2-Pyrocatechuic acid or hypogallic acid
2.  $\beta$ -Resorcylic acid
3. Gentisic acid
4.  $\gamma$ -Resorcylic acid
5. Protocatechuic acid
6.  $\alpha$ -Resorcylic acid

Of these we have studied the fast iodinations kinetics of  $\alpha$ ,  $\beta$  and  $\gamma$  resorcylic acids by molecular aqueous iodine<sup>2</sup>.

3,5-dihydroxybenzoic acid is a biomarker and is quantified in human urine and for whole grain wheat intake.

2,4-dihydroxybenzoic acid is a metabolite detected in human plasma after consuming cranberry juice<sup>3</sup>.  $\beta$ -Resorcylic acid is prepared from resorcinol and  $KHCO_3$  in water<sup>4</sup>. The derivatives of dihydroxy benzoic acids have shown significant anti-Parkinson and anti-oxidant activity<sup>5</sup>.  $\beta$ -Resorcylic acid does not shows antioxidant activity but its ester derivative shows moderate antioxidant activity<sup>6</sup>. In Tri-hydroxy benzoic acid (Gallic acid) there are three hydroxyl groups are present gives potent antioxidant activity. Gallic acid derivatives possess ability against

**Corresponding Author:- R. P. Yadav, B. B. Bahule.**

Address:-Post-Graduate Department of Chemistry, NowrosjeeWadia College, Affiliated to the SavitribaiPhule University, Pune- 411001, India.

antibacterial, antifungal and anti-malarial diseases <sup>7</sup>. Iodination of 2,4-dihydroxy benzoic acid in presence of iodine in water : tetra furan (1:1) at pH 9-10 gave sterically crowded 2,4 dihydroxy-3-iodobenzoic acid <sup>8</sup>.

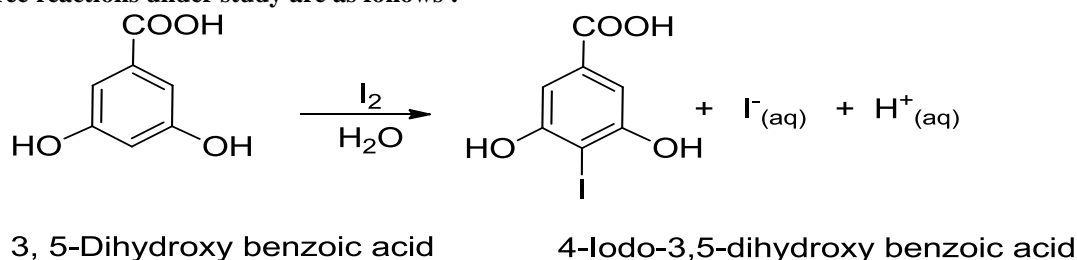
2,6-Dihydroxybenzoic acid is secondary metabolite of salicylic acid and it hydrolysed by liver enzyme during phase I Metabolism.

Recently Xiaoyi Wei and co-workers described the isolation of six derivative of lactones obtained from  $\beta$ -Resorcylic acid named Paecilomycins (A-F) <sup>9</sup>.

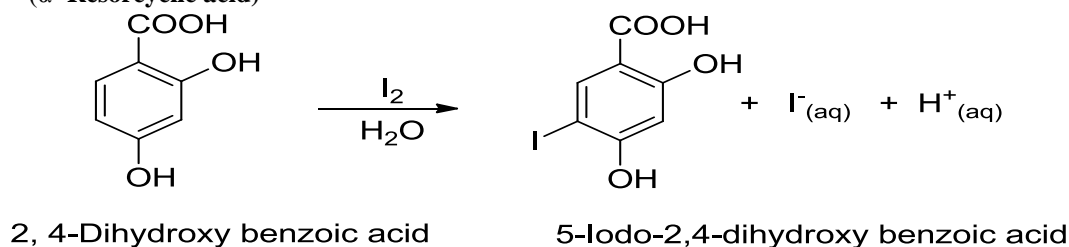
The three reactions studied herein are all fast hence we have adopted the hydrodynamic voltammetry technique to quantitatively assess the reactivity of three regioisomers ( $\alpha$ ,  $\beta$  and  $\gamma$ ) of dihydroxybenzoic acid in aqueous medium in iodination reactions using molecular iodine devoid of iodide ions.

The initial reactant concentrations in all the three reactions is kept the same to compared the half lives and hence the relative rapidity of these three reactions. The results of the present study are estimated quantitatively and route of mechanism discussed.

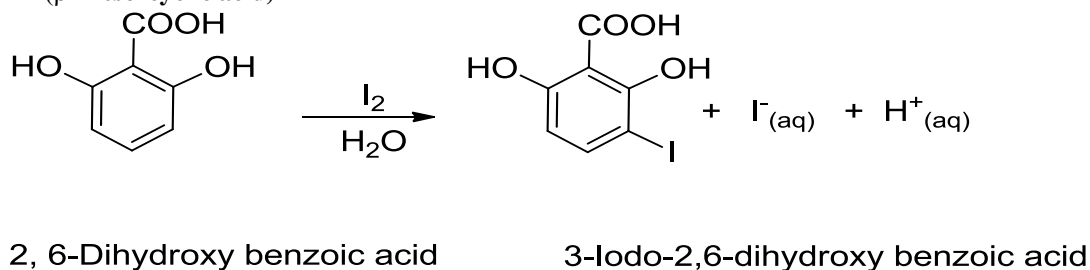
The three reactions under study are as follows :-



( $\alpha$ - Resorcylic acid)



( $\beta$ - Resorcylic acid)



( $\gamma$ - Resorcylic acid)

In these reactions, only iodine is electro reduced at the cathode and nano diffusion current due to it recorded. The reference electrode is the saturated calomel electrode SCE.

**Experimental:-**

**Materials and Instruments:-**

Stock solution of the supporting electrolyte was prepared in conductivity water using AR grade potassium nitrate

The regioisomers ; 3,5-dihydroxy benzoic acid, (  $\alpha$  ) ; 2,4-dihydroxybenzoic acid, (  $\beta$  ) ; and 2,6-dihydroxybenzoic acid, (  $\gamma$  ) were prepared in conductivity water using AR grade chemicals. Aqueous iodine solution was prepared by keeping  $I_2$  crystals overnight in conductivity water devoid of iodide ions and was standardized iodimetrically.

#### Electrodes:-

The positive electrode was a platinum micro-cathode (RPE) rotating at 600 rpm. The negative electrode was the saturated calomel electrode (SCE).

#### Calibration of diffusion current:-

Diffusion currents at the RPC for different concentrations of iodine solutions containing a hundredfold concentration of the supporting electrolyte were determined. [Table 1].The plot of diffusion current Vs concentration was linear at all temperatures [Fig.1 ].

#### Kinetic measurements:-

Equal concentrations of dihydroxybenzoic acid and iodine containing a hundredfold supporting electrolyte and the buffer solutions to maintain 7 pH, were mixed in a reaction vessel kept in a thermostat. The two electrodes were contained in this reaction vessel and the time of mixing was noted. At every 10 seconds, the decreasing diffusion current values were recorded for at least one half-life of the reaction.

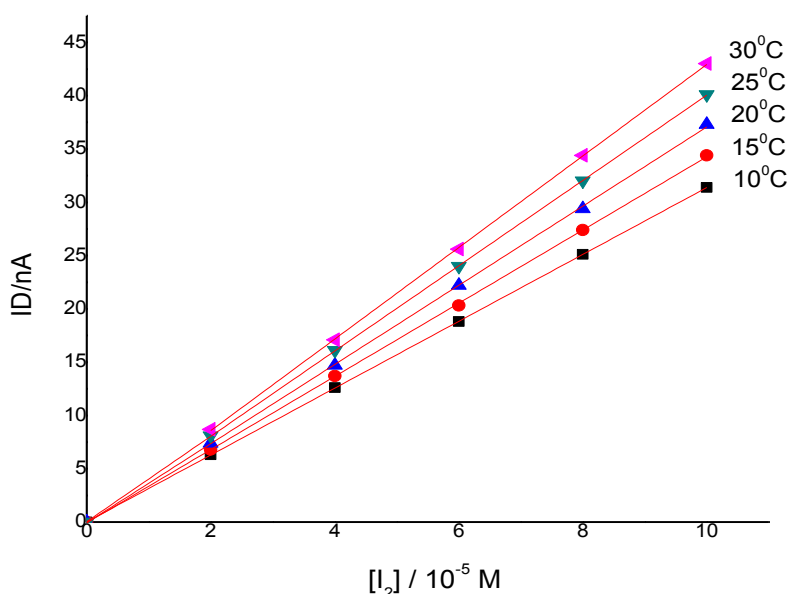
The plots of  $[I_2]^{-1}$  Vs time were found to be linear at all temperatures. The slopes of these plots are the specific reaction rates of the reactions under investigation.

#### Observation Table:-

**Table -1:-**Calibration of diffusion current for iodine.

[ $I_2$ ] / $10^{-5}$ M	Mean diffusion current / nA				
	10.0 <sup>0</sup> C	15.0 <sup>0</sup> C	20.0 <sup>0</sup> C	25.0 <sup>0</sup> C	30.0 <sup>0</sup> C
2.0	6.3	6.8	7.4	8.1	8.7
4.0	12.6	13.7	14.7	16.1	17.1
6.0	18.8	20.3	22.2	24.0	25.6
8.0	25.1	27.4	29.4	32.0	34.4
10.0	31.4	34.4	37.3	40.1	43.0

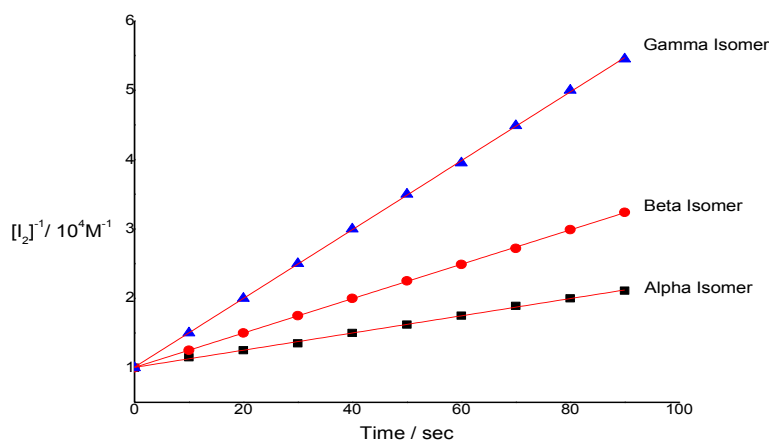
**Figure 1:-**Calibration of diffusion current for iodine at different temperatures.



**Table – 2:-**Kinetics of iodination of  $\alpha$ ,  $\beta$  and  $\gamma$  dihydroxybenzoic acid isomers at 25.0 °C Starting concentrations of reagents in 50 cm<sup>3</sup> = 10.0 x 10<sup>-5</sup>M.

Time / s	Diffusion current / nA			[I <sub>2</sub> ] / 10 <sup>-5</sup> M			[I <sub>2</sub> ] <sup>-1</sup> / 10 <sup>4</sup> M <sup>-1</sup>		
	$\alpha$	$\beta$	$\gamma$	$\alpha$	$\beta$	$\gamma$	$\alpha$	$\beta$	$\gamma$
0	40.10	40.10	40.10	10.00	10.00	10.00	1.00	1.00	1.00
10	34.80	32.00	27.00	8.70	8.00	6.67	1.15	1.25	1.50
20	32.00	27.00	20.00	8.00	6.67	5.00	1.25	1.50	2.00
30	29.60	22.80	16.20	7.41	5.71	4.00	1.35	1.75	2.50
40	27.00	20.00	13.10	6.67	5.00	3.33	1.50	2.00	3.00
50	24.90	17.60	11.90	6.17	4.44	2.86	1.62	2.25	3.50
60	22.80	16.10	10.00	5.71	4.02	2.53	1.75	2.49	3.95
70	21.40	14.80	9.00	5.29	3.68	2.23	1.89	2.72	4.49
80	20.00	13.10	8.10	5.00	3.34	2.00	2.00	2.99	5.00
90	18.90	12.40	7.40	4.74	3.09	1.83	2.11	3.24	5.45

**Figure – 2:-**Kinetics of iodination of the isomers  $\alpha$ ,  $\beta$  and  $\gamma$  of dihydroxybenzoic acid at 25.0 °C.



### Results and Discussion:-

All the three isomers studied, undergo fast second order iodination kinetics. The products are mono-iodo compounds after iodination reactions.

**Table – 3:-**Specific reaction rates at 25.0 °C for the iodination of dihydroxybenzoic acid isomers.

Sr.No.	Isomer of dihydroxybenzoic acid	t <sub>1/2</sub> / s	k / M <sup>-1</sup> s <sup>-1</sup>
1.	Alpha ; 3,5-dihydroxy benzoic acid	80	125
2.	Beta ; 2,4-dihydroxy benzoic acid	40	250
3.	Gamma ; 2,6-dihydroxy benzoic acid	20	500

### Conclusion:-

The velocity constants are in the order  $\alpha < \beta < \gamma$  at 25 °C for the three isomers under study. This is explainable as follows :

The acid group being electron withdrawing, is meta orienting while the hydroxyl group is electron donating, hence is o and p directing<sup>10</sup>.

Steric hindrance is due to proximity of substituents causes hydrogen bonding to reduce the reactivity of  $\alpha$  isomer.

In the alpha isomer, the two -OH groups block the positions meta to the -COOH group resulting in the formation of the 4-iodo-3,5-dihydroxy benzoic acid. The position between the two -OH groups is not preferred for substitution due to steric hindrance.

In  $\beta$  isomer iodo-substituents attached to the 5<sup>th</sup> position because this position is activated unitedly by all the tree groups undergoes consideration.

In the gamma isomer, electron donating resonance effect of two hydroxyl groups at C<sub>2</sub> and C<sub>6</sub> activates C<sub>3</sub> position towards electrophile iodine. Hence 3-iodo-2,6, dihydroxy benzoic acid is formed as fastest rate among the three regioisomers studied.

### **Acknowledgement:-**

The authors are thankful to the Principal, NowrosjeeWadia College, Pune for providing the necessary infrastructure and constant encouragement during this research work.

### **References:-**

1. Borkar V.T., Bonde S.L and Dangat V.T., (2013) International Journal of Chemical Kinetics.,45,11,693-702.
2. Ross A.B., Kamal-Eldin A and Aman P., (2004).,Nutr Rev.,62(3),81-95.
3. Koskela A.,Linko-Parvinen A.M.,Hiisivuori P., Samaletdin A., Kamal-Eldin A.,Tikkanen M.J and Adlercreutz H.,(2007)., Clin Chem., 53(7), 1380.
4. Clibbens and Nierenstein.,(1915)., J.Am.Chem.Soc.,107,1494.
5. Mahajan S.K., Chaudhari R.Y and Wagh R.S.,(2011).,Journal of Pharmacy Research.,4(7),2285-2287.
6. Sroka Z and Ciwoski W.,(2003).,Department of Poland.,1,50-144.
7. Kubo I.,Xiao P and fujita K.,(2001).,Bioorganic Chemistry Letters.,11.347.
8. Thomsen I and Torssell K.B.,(1991).,Acta.Chem.Scand.,45,539-542.
9. LiangxiongXu., Zhengxing He.,JinghuaXue.,Xiaoping Chen andXiaoyi Wei.,(2010).,Journal of Natural Products.,73,5.
10. 10. Clayden J., Greeves N and Warren S.,(2012)., Organic Chemistry., 2<sup>nd</sup> edition., Oxford University Press., New York.