**Synopsis**

**STUDIES ON STRUCTURE-ACTIVITY RELATIONSHIPS OF SOME ACTIVATED ALKENES**

For a large number of organic compounds in solutions, rate constants and equilibrium constants have been measured. The volume of results available has become so large that it is now essential to find suitable procedures for summarizing and analyzing them. This involves the development and use of empirical correlations by which one set of results can be related to another. The data may thus also be analyzed to reveal the fundamental factors underlying organic reactivity. This general approach is called the correlation analysis. Organic compounds are capable of structural variation in the vicinity of a reaction center, permitting an almost continuous variation in its electrophilic or nucleophilic character. This capacity may then be used as a delicate probe into the effects which electronic perturbation produces upon reaction affinity and from which the electronic demands of the reaction may be inferred. The use of this information in deducing mechanism is a highly developed art, applicable to polar reactions in particular. Chapter 1 is confined to the introduction of this work with related literature survey; chapter 2, of experimental aspects; chapter 3 deals with the study of antibacterial activity to find out the substituent effect on 2-benzylidene-1,3-indandione and 5-benzylidenebarbituric acid; chapter 4 deals with the correlation of the chemical shift with Hammett substituent constant to study the nature of the effect of substituent in 5-benzylidenebarbituric acid and chapter 5 investigates the electron transfer reactions in the cyclic voltammetry study of 4′- substituted (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-one.

**Chapter 1**

**Introduction**

This chapter details the nature and scope of the present work. A brief account of the linear free energy relationships relevant to the present work is discussed. Correlation of the chemical shift with substituent constant (e.g. Hammett σ) has been widely used to investigate the nature of the effect of the substituent of the physical properties of compounds. Electron density around the nucleus of interest (C, H) is mostly affected by the electron donating and electron withdrawing ability of the substituent. Therefore, a correlation between the observed chemical shift and any parameter representing such ability seems to be well-founded, would indicate that the effect of any other rate would be satisfactorily predicted by simply measuring the chemical shift of a given derivative, and there are numerous reports on the subject. Correlation of these parameters has now been applied, originally proposed to equilibria and reaction rates, to spectroscopic properties such as 1H and 13C NMR substituent induced chemical shifts (SCS) in recent years.

Cyclic voltammetry, a popular tool in the last thirty-five years for studying electrochemical reactions has been employed by organic chemists in the study of biosynthetic reaction pathways and studies of electrochemically generated free radicals. An increasing number of inorganic chemists have been using cyclic voltammetry to evaluate the effects of ligands on the oxidation/reduction potentials of the central metal ion in complexes and multinuclear clusters. This type of information plays an integral part in many of the approaches directed toward solar energy conversion and in model studies of enzymatic catalysis. Knowledge of the electrochemistry of a metal complex can be useful in the selection of the proper oxidizing agent to put the metal complex in an intermediate oxidation state. The electrochemical methodology has also been exploited as a novel means of introducing functional groups and removing blocking agents.

Antibacterial activity studies have also been made and the zone of inhibition is used for correlation studies.

**Chapter 2**

**Experimental section**

The details of the preparation of 4′-substituted 2-benzylidene-1,3-indandiones, 4′-substituted 5-benzylidenebarbituric acids and 4′-substituted (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-ones are described in this chapter. In addition, the details of the characterization techniques UV, FT-IR, 1H NMR, and 13C NMR measurements are also given.

In 1H NMR spectrum of 2-benzylidene-1,3-indandione whose signals assignment were quite complicated, but the ethylene proton is well separated from the signals of the aromatic protons because of the β-proton nearest to the aromatic ring will experience a magnetic field from the induced circulation of π-electrons in the aromatic ring, which will augment the applied field and hence will lead to a down field shift. All the aromatic protons are deshielded because of the ring current effect. Assignment of the signals was based on splitting pattern and peak integration ratio.

13C NMR signals assigned for various carbons were based on the

1. Chemical shift exhibited by the signals.
2. Relative signal intensity.

13C chemical shifts of 4′-substituted 2-benzylidene-1,3-indandiones were assigned by intensity and SCS consideration. The proton-noise decoupled spectrum of parent compound contains 14 signals corresponding to 14 different carbon atoms. In all the spectra, the two carbonyl carbon signals were readily recognized from their low intensity and also well separated from other signals to the downfield extreme, since their assignment was not difficult.

In 1H NMR spectrum of 5-benzylidenebarbituric acid whose, signals assignment was not difficult and all signals well separated from each other. The two different NH-protons are expected to downfield than the -CH-proton of C7 carbon atom. The -CH-proton of C7 is well separated from all other protons signals. Hence, it’s assignment is not difficult.

13C NMR spectrum of 5-benzylidenebarbituric acid contains 9 signals corresponding to 9 different carbon atoms. In all the spectra, carbonyl carbon signal was readily recognized and also well separated from other signals to the downfield extreme, since its assignment was not difficult.

In 1H NMR spectra of 4′-substituted (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-ones whose signals assignment were not difficult and all signals were well separated from each other. The -CH- proton of furan C5 carbon atom is expected to downfield than -CH- proton of furan C3 carbon atom. The -CH- proton of furan C4  is well separated from all other protons signals, hence it’s assignment is not difficult. Two ethylenic protons C3 and C2 carbon atoms are well separated from each other. The α-ethylenic proton is expected to be downfield shift because of its proximity to the carbonyl group. Assignment of the signals was based on splitting pattern and peak integration ratio.

The proton noise decoupled spectrum of 13C NMR spectrum of (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-one contains 11 signals corresponding to 11 different carbon atoms. In all the spectra, carbonyl carbon signal was readily recognized from its low intensity and also well separated from other signals to the downfield extreme, since its assignment was not difficult.

**Chapter 3**

**Substituent effects on the 1H and 13C NMR chemical shifts on the**

**4′-substituted 5-benzylidenebarbituric acid.**

In this chapter, the correlation of the chemical shift with substituent constant has been widely used to investigate the nature of the effect of the substituent on the physical properties of compounds. Electron density around the nucleus of interest (H, C) is mostly affected by the electron donating and electron withdrawing ability of the substituent. Therefore, a correlation between the observed chemical shift and any parameters representing such ability seems to be well-founded and there are numerous reports on the subject.

The substituent effect of 5-benzylidenebarbituric acid is analysed by correlating both 1H NMR and 13C NMR chemical shifts with Hammett substituent constants. The single substituent parameter (SSP) analysis was done by using the substituent constants σp, σpo,σp+, σp+/ σp, σp+/ σp-, σp+/ σp/ σp-  for the various substituents. For most of the correlations, it gives good correlations.

The DSP analysis was also performed for the chemical shift data and the correlations have been reported by using *σR, σRo*, *σR+, σR-*. The TSP analysis was also performed in which there is a separation of polar, resonance and steric effects.

**Chapter 4**

**Antibacterial activity: A structure-reactivity study**

In this chapter, the antibacterial activity of 4′-substituted 2-benzylidene-1,3-indandiones and 4′-substituted 5-benzylidenebarbituric acids was determined using agar well diffusion method.

In this study, for 4′-substituted 2-benzylidene-1,3-indandiones, five gram-negative bacteria (*Aeromonas hydrophilia, Escherichia coli, Pseudomonas aeruginosa, Proteus mirabilis, Vibrio paraheamolyticus*) and a gram-positive bacterium (*Staphylococcus aureus*) were used. The result of the present study showed a broad range of antimicrobial activity. The zone of inhibition for different substituents shows that the electron withdrawing substituents have higher values than the electron releasing substituents. The order of antibacterial activity is given by -OCH3<-CH3<- H <-Cl <-Br <-COOH. In order to express the effect of substituents quantitatively, it has been decided to correlate the logarithm of inhibition zone radius with the Hammett substituent constants for all the microorganisms.

For 4′-substituted 5-benzylidenebarbituric acids, one gram-positive bacterium (*Staphylococcus aureus*) and five gram-negative bacteria (*Escherichia coli, Klebsiella oxytoca, Proteus mirabilis, Pseudomonas aeruginosa and Shigella sonnei )* were used. The order of antibacterial activity of compounds for all the microorganism was in the following sequence:

-OCH3<-OH < -CH3< -H < -Cl < -Br< -NO2

For this study, the single substituent parameter (SSP) analysis was done using the Hammett constants σp, σpo, σp+, σp+/ σp, σp+/ σp-, σp+/ σp / σp- and the result shows a positive value of *ρ* indicating that electron withdrawing substituents increase the antibacterial activity and electron releasing substituents retard the antibacterial activity.

The DSP analysis has been performed for the resonance scale σR, σR+,σR- and the best fit is given in equation form. The analysis of results shows that for this study most of the bacteria show normal substituent effect.

Multiple regression analysis was also performed using Yukawa-Tsuno equation for all the microorganisms. This analysis shows the contribution of resonance and inductive effect. Most of the organisms for this compound show less contribution of resonance effect.

**Chapter 5**

**Substituent effects on the cyclic voltammetry reduction peak potentials of**

**4′-substituted (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-ones.**

This chapter gives an account of substituent effects on the voltammetry reduction peak potentials of various 4′-substituted (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-ones. Voltammetry reduction of 4′-substituted (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-ones in acetonitrile containing tetrabutylammonium tetrafluoroborate (TBATFB) as a supporting electrolyte has been carried out by employing glassy carbon electrode. Cyclic voltammetry reduction of (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-one gives a two separate irreversible one-electron peaks. A mechanism involving two separate addition of single electron has been suggested.

An attempt has been made to correlate the Ep and Ep1/2 of the first peak of 4’-substituted (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-ones with substituent constants separately. Better correlations are obtained with σp,σp/ σp+, σp+/ σp-, σp+/ σp/ σp- constants. A positive value of ρ is obtained showing that electron attracting substituents accelerate electrochemical reduction and electron donating substituents retard it. The Hammett correlation for the second reduction peak of 4′-substituted (E)-1-(furan-2-yl)-3-phenylprop-2-ene-1-ones is poor.

**List of publications**

1. [Synthesis and Antimicrobial Activity of 2-benzylidene-1,3 indandiones: A Structure-Reactivity Study](http://www.imedpub.com/articles/synthesis-and-antimicrobial-activity-of-2benzylidene13-indandiones-astructurereactivity-study.php?aid=18003).

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Der Chemica Sinica 7 (4), 1-7, 2016.

1. [Synthesis and Antibacterial Activity of 5- benzylidenebarbituric acids: A structure-reactivity Study](http://sphinxsai.com/2017/ch_vol10_no7/3/(1019-1027)V10N7CT.pdf).

K Radhakrishnan**, P Mohandass**, S Sankaralingam, S Chandra Mohan

International Journal of ChemTech Research 10 (7), 1019-1027,2017.

1. Effect of substituent on the 13C - NMR chemical shifts of substituted

5-benzylidenebarbituricacids.

**P.Mohandass**, K.Radhakrishnan, S.Manimekalai, V.Suriyanarayanan and S.Radhakrishnan. Asian Journal of Research in Chemistry (in press).