

Investigation of Resonance Effect, Inductive Effect, Solvation Energies and Electron Affinities of Some Thiosemicarbazides, Hydrazides and Carboxylic Acids through Linear Scan Voltammetry

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Summary: Electrochemical measurements have been carried out for three sets of compounds. Set 1 comprising fourteen 4-(4-substitutedphenyl)-1-(isomericpyridoyl)thiosemicarbazides, Set 2 comprising three isomeric pyridine carboxylic acid hydrazides and Set 3 comprising three isomeric pyridine carboxylic acids. In all these compounds substituents on phenyl group are bromo, chloro, fluoro, methyl and methoxy group. All these compounds were studied in non-aqueous solvent DMF at 293K using linear scan voltammetry (LSV) as measuring techniques. LSV reveals a single reversible peak for all compounds. Effects of substituents on halfwave potential ($E_{1/2}$) values were explained on the basis of resonance and inductive effects. $E_{1/2}$ values were used for the evaluation of solvation energies (S) and electron affinities (A). Moreover, correlations of energies of lowest unoccupied molecular orbitals (E_{LUMO}) and Hammett constants (σ) with halfwave potentials ($E_{1/2}$) and electron affinities (A) were also studied.

Introduction

A number of thiosemicarbazides have been prepared and subjected to intensive screening for their useful and diverse activities. Many thiosemicarbazide derivatives have been found active as antitubercular drug [1], others show fungicidal, herbicidal, bactericidal, rodenticidal, anticonvulsant, anticholinesterase and hypoglycemic activities and some have been used commercially as dyes, photographic films and in textile industry [2]. A number of them have also shown plant growth promoting activities [3].

Electrochemical reversibility is an important intrinsic property of an electron transfer reaction. A reversible electrochemical reaction can be represented as



where O and R are oxidized and reduced species and n is the number of electron involved. Halfwave potential ($E_{1/2}$) can be related to the energy of highest occupied molecular orbital (E_{HOMO}) in case of oxidation and to lowest unoccupied molecular orbital (E_{LUMO}) in case of reduction. Thus, $E_{1/2}$ is useful in the investigations of molecular energy levels. Such studies have been made on ketones, quinones and nitroaromatic compounds [4]. In addition Hoihtink

[5], Streitwieser [6], Pysh and Yang [7], Neikana and Desmond [8], B. Pullman [9] and A. Maccolo [10] have also described similar correlations for a number of organic compounds.

Reduction potential is defined as the potential at which a species X in solution is reversibly reduced. In such a process, the electron enters into the shell of electroactive species.

When $E_{1/2}$ is taken as positive the relationship reported is [11-13]

$$E_{1/2} = \chi - A - S \quad (2)$$

where A is electron affinity, S is solvation energy and χ is work function of working electrode. Its value for glassy carbon electrode is 4.39 eV [14].

Solvation free energy of an ionic species can be calculated from the Born's equation [15].

$$S = \left(\frac{NZ^2e^2}{2r} \right) \left(1 - \frac{1}{\epsilon} \right) \quad (3)$$

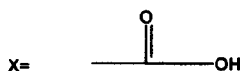
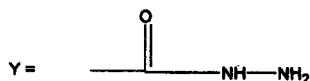
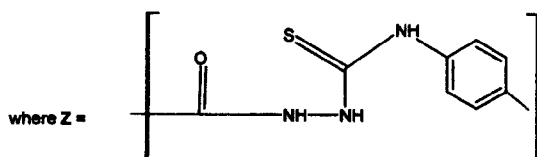
where N is Avogadro's number, Z is the charge, e is the electronic charge (in e.s.u), r is radius of the ionic species and ϵ is dielectric constant of medium.

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Radius of molecule is an important factor in calculating solvation energy. It can be estimated from the density using the equation [16].

$$\frac{4}{3} \pi r^3 = \left(\frac{1}{N} \right) \left(\frac{M}{d} \right) \quad (4)$$

where r is radius, d is density and M is molecular weight.



and

Set-1

Compounds	Formula
1	2-ZH-Pyridine
2	3-ZH-Pyridine
3	4-ZH-Pyridine
4	2-ZBr-Pyridine
5	3-ZBr-Pyridine
6	4-ZBr-Pyridine
7	2-ZCl-Pyridine
8	3-ZCl-Pyridine
9	4-ZCl-Pyridine
10	2-ZF-Pyridine
11	3-ZF-Pyridine
12	4-ZF-Pyridine
13	3-ZCH ₃ -Pyridine
14	3-ZOCH ₃ -Pyridine

Set-2

15	2Y-Pyridine
16	3Y-Pyridine
17	4Y-Pyridine

Set-3

18	2X-Pyridine
19	3X-Pyridine
20	4X-Pyridine

Scheme-1: Structural overview of compounds used in this study.

In the present work, we are concerned with the investigation of reduction potential ($E_{1/2}$), solvation energies (S) and electron affinities (A) of fourteen 4-(4-substitutedphenyl)-1-(isomericpyridoyl) thiosemicarbazides, three isomericpyridine carboxylic acid hydrazides and three isomeric pyridine carboxylic acids. In all these compounds substituents on phenyl group are bromo, chloro, fluoro, methyl and methoxy group. All these compounds (Scheme 1) were studied in non-aqueous solvent DMF at 293K using linear scan voltammetry (LSV) as measuring technique. In the end correlations of energies of lowest unoccupied orbitals (E_{LUMO}) and Hammett's constant (σ) with halfwave potential ($E_{1/2}$) and electron affinities (A) were also studied.

Results and Discussion

Substituents Effect on Halfwave Potential ($E_{1/2}$)

Halfwave reduction potential ($E_{1/2}$) values for all these compounds under study are summarized in Table-1. A comparison of reduction potentials of compounds 1, 2 and 3 shows that substitution of Z-H group at *meta* position of pyridine ring causes the reduction potential to be more negative as compared to *ortho* and *para* substituted ring. Phenomenon of resonance can be used to account for more negative halfwave potential value of *meta* substituted ring as compared to *ortho* and *para* substituted positions. Substituents that do not form fully conjugated system cannot conjugate themselves with the ring. Thus, electron density of ring is completely localized on it and it seems difficult for an electron to access the pyridine ring, which is most probable reduction site. This difficulty shifts reduction potential to more negative side. In case of *ortho* and *para* position of the substituents delocalization of electron density occurs with substituents, whereas, delocalization decreases in case of *meta* substituents. A comparison of reduction potentials of Z-X substituted pyridines where X = F, Cl or Br (*i.e.*, compounds 4-12) shows some interesting results. As F is more electronegative atom than Cl and Br atoms, its I-effect is more pronounced than +R effect. Considering the size of F atom irrespective of its higher electronegativity, it behaves like H atom. In compound 14, CH₃ group of (13) is replaced by the OCH₃ group. It has +R and -I effect which result in negative σ_p value due to +R > -I. Thus, its resultant character is electron donating, which causes reduction to be more difficult, hence,

Table-1: Densities (d), Radii (r), Halfwave Potential ($E_{1/2}$), Solvation Energies (S) and Electron Affinities (A) of compounds under study.

Compound ID	D (g/cm ³)	r (Å)	- $E_{1/2}$ (V)	S (eV)	A (eV)
1	1.420	4.150	2.706	1.686	1.026
2	1.342	4.229	2.768	1.655	0.995
3	1.871	3.786	2.725	1.648	1.045
4	1.706	3.982	2.664	1.657	1.097
5	1.761	4.224	2.595	1.656	1.167
6	1.571	4.358	2.602	1.640	1.222
7	1.502	4.248	2.687	1.647	1.084
8	1.604	4.156	2.636	1.683	1.099
9	1.529	4.222	2.602	1.657	1.159
10	1.548	4.124	2.672	1.696	1.050
11	1.589	4.089	2.630	1.671	1.117
12	1.425	4.240	2.599	1.650	1.169
13	1.522	4.142	2.698	1.689	1.031
14	1.554	4.141	2.730	1.690	0.998
15	1.428	3.363	2.371	2.080	0.967
16	1.454	3.342	2.418	2.093	0.907
17	1.420	3.369	2.123	2.077	1.218
18	1.526	3.173	2.816	2.105	0.497
19	1.358	3.227	2.841	2.135	0.442
20	1.490	3.198	2.792	2.110	0.516

causing a cathodic shift in peak reduction potential of compound 14 as compared to compound 13, although, compound 14 has a slightly higher value of σ_p than compound 13.

In all cases of compounds mentioned and discussed above, inductive effect tends to be in the electron withdrawing sense (-I) since most of the substituents available are more electronegative than carbon atom (except for CH₃ group). The *ortho* and *para* position substituents are capable of exerting an electron donating resonance effect but capacity for sharing their n-electrons falls off with increasing electronegativity. Sometime +I effect leaves σ_p negative for OCH₃ and CH₃, but positive for halogens as the effect changes from +R > -I to +R < -I.

Compounds 15, 16 and 17 are comparatively smaller than thiosemicarbazides. Less negative values of $E_{1/2}$ for these compounds are evidence of easy approach of electron to the lowest unoccupied molecular orbital. Considering *ortho*, *meta* and *para* substituted compounds similar trend is observed regarding the $E_{1/2}$ values. Carboxylic linkage present at *ortho* and *para* position of ring have electron withdrawing effect. This stabilizes the electron acceptance site in ring as compared to *meta* position of substituent. -CO-NH-NH₂ group cannot be considered as a single group because it does not completely conjugate with ring.

$E_{1/2}$ values of compounds 18, 19 and 20 are more negative reflecting the difficult reduction. σ_p and σ_m values of -COO- predict less negative $E_{1/2}$ for *ortho* and *para* substitution as compared to *meta* position. As observed experimentally they return the similar previous behavior of other molecules with respect to their *ortho*, *para* and *meta* position of substituent group.

Solvation Energy

The values of densities and radii of the neutral compounds and the corresponding solvation energies of their anions are summarized in Table-1. The magnitude of solvation energy shows a clear trend and some qualitative conclusion may be drawn from these data. The fact that solvation energy is always negative means that all ions prefer to exist in solvated state rather than in vacuum. However, it does not follow that all salts dissolve in all liquids, because in many cases the solvation energy is not great enough to overcome the lattice energy.

Secondly, smaller the ion, more negative is its solvation energy value. Thus an inverse relationship does exist between radius of anion and its solvation energy. From the data it is also seen that *p*-substituted pyridine ring has less solvation energy as compared to its *ortho* and *meta* substituted compounds. It is because of the fact that their radii are larger than other substituted positions. A broader line for the values of solvation energy also exists, which is predicted by their structures. Solvation energy of thiosemicarbazides is less than 2.0 eV and those of hydrazides and acids are greater than 2.0 eV.

A very few direct measurements of electron affinities for hydrocarbon are available in literature although it is possible to determine experimentally at least their relative order from the capture of thermal electrons [17]. From the extent that these hydrocarbons can form defined molecular complexes of charge transfer type in which they are electron acceptors, one can also calculate electron affinities from the wavelength of the new absorption bands of these complexes [18]. Electron affinities of all compounds under study were calculated using equation 3 and reported in Table-1. These results are of theoretical interest, since halfwave potential has been taken as a measure of energy states. Electron affinity is higher for those compounds which reduce at less negative potentials such as *p*-substituted thio-

semicarbazide. Electron affinity of acids is relatively low as compared to other classes of compounds as they reduce at more negative potentials.

Correlation of E_{LUMO} with $E_{1/2}$ and A

Molecular orbital theory continues to be one of the most important techniques for illustrating many quantum chemical quantities such as bond orders, electron densities and orbital energies [19]. Electron affinity (A) as Mulliken had reported [20] is related to E_{LUMO} values. Here also linear correlations were observed for E_{LUMO} (calculated by AM1 method) with $E_{1/2}$ and A with a correlation coefficient of 0.97 and 0.99 respectively as shown in Fig. 1 and 2. We have also observed similar linear correlation for chalcones [21].

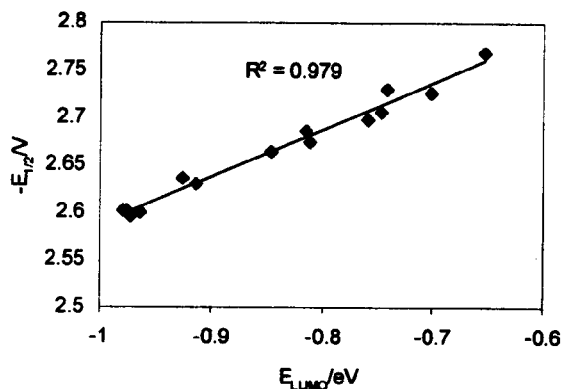


Fig. 1: Plot of E_{LUMO} calculated by AM1 method against halfwave potential ($E_{1/2}$) for Set 1 compounds.

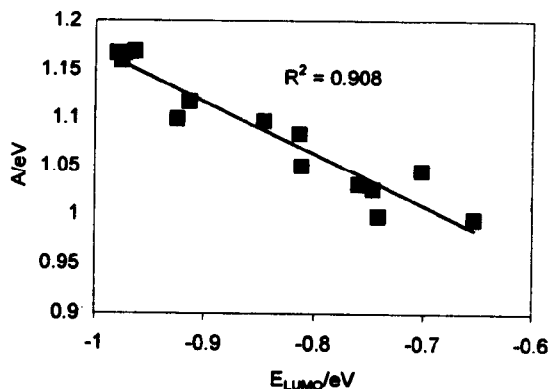


Fig. 2: Plot of E_{LUMO} calculated by AM1 method against electron affinities values (A) of Set 1 compounds.

Experimental

Chemicals

Dimethylformamide (DMF), BDH Chemicals Ltd., Poole, England was used as solvent and purified by the method reported in literature [19]. The choice of solvent is governed primarily by the solubility of analyte, its redox activity and by the solvent properties such as electrical conductivity, electrochemical activity and chemical reactivity. The solvent should not react with the analyte or product and should not undergo electrochemical reactions over a range of potentials used in the experiment.

In controlled potential experiments variable amount of supporting electrolyte was used in order to decrease resistance of the solution and to eliminate electro-migration effects. Tetrabutyl ammonium perchlorate (TBAP) from Fluka was used as supporting electrolyte. TBAP was purified by recrystallization using methanol as the solvent. Detail structures of the compounds used in this study are given in Scheme 1.

Instrumentation

For LSV measurements Polarographic Analyzer Model 364 (supplied by EG and G Princeton Applied Research) and National X-Y Recorder (VP-6423A) were used throughout the work. This model is capable of performing normal, simple DC polarography, differential pulse polarography and linear sweep voltammetry at stationary electrode system. Electrochemical cell (model K64 PRC) connected to the circulating thermostat LAUDA model K-4R was used. Glassy carbon was used as working or test electrode. Silver/silver nitrate electrode was used as reference electrode, which has a contact with the analyte via a porous vycor frit. Pt-wire of 5.4 cm length and a diameter of 0.5 mm was used as a counter electrode. Densities of all these compounds were determined by weight method [21].

Procedure for Electrochemical Measurement

0.1M, 10 ml solution of TBAP in DMF was transferred into electrolysis cell and N_2 gas was purged through the solution for 15-20 minutes to deoxygenate it. The system was then subjected to linear sweep voltammetry (LSV). Current voltage behavior of the system was examined in order to

check any impurity in the blank solution. 10^{-3} M solutions of relevant compounds were prepared by adding weighed amount in same blank solution. After purging again with N_2 gas, cyclic voltammograms were recorded at scan rate 50 mV/ sec for all compounds under study.

Removal of Dissolved Oxygen

As electrochemical reduction of oxygen usually proceeds via reversible one electron step, it is necessary to remove dissolved oxygen before carrying out electrochemical studies. Variety of methods are available in literature, the most common being the purging of inert gas such as nitrogen through the system under study. However, commercially available nitrogen contains certain amount of oxygen as well. Therefore, purification of commercial nitrogen was done by passing it through a series of traps including $CrCl_3 \cdot 6H_2O$ solution, pyro-gallol, conc. H_2SO_4 , $CaSO_4$ crystals and DMF before passing it through the sample under study.

Computational Studies

Molecular orbital calculations using Hyperchem 7.5 were carried out on all compounds using AM1 method to calculate the optimized geometries and energies of lowest unoccupied molecular orbital (E_{LUMO}). For substituted compounds, the starting point was the optimized structure of unsubstituted compounds, the substituents were added and their geometries were optimized by molecular mechanics. The geometries of these molecules were further optimized by semiempirical technique. By the application of single point energy calculations, E_{LUMO} of these compounds is calculated.

We were interested to know whether, there exist linear correlation between experimentally determined halfwave potentials ($E_{1/2}$) and E_{LUMO} values calculated through semiempirical AM1 method. Likewise, it is also considered worthwhile to know similar correlation of electron affinities (A) with E_{LUMO} values. High level calculations on such compounds involve hours of computer CPU time and to save time one would require carrying out calculation at the lowest level commensurate with good accuracy. Therefore, E_{LUMO} of all these compounds were calculated by using semiempirical method.

Conclusions

LSV studies of thiosemicarbazides, pyridine hydrazides and carboxylic acids show the effect of

ortho, *meta* and *para* substitution on $E_{1/2}$, S and A values. Pyridine carboxylic acids possess comparatively low A which may be explained on the basis of its higher reduction potentials. Linear correlation of E_{LUMO} with $E_{1/2}$ and A resulted in the correlation coefficient values close to one.

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