Electron Affinities, Solvation Energies and Redox Potentials of Some Chalcones: Substituents' Effect and Correlation with Semi-Empirical MO Energies

Abdur RAHMAN*, **Rumana QURESHI, Mehvish KIRAN, Farzana Latif ANSARI**
Department of Chemistry, Quaid-i-Azam University, Islamabad-PAKISTAN
e-mail: chemabdpk@yahoo.co.uk

Experimental and theoretical investigations were carried out on 2 sets of chalcones. **Set 1** has an OH group on ring A and **Set 2** does not, and both have different substituents on ring B at different positions. The experimental investigations comprised cyclic voltammetric (CV) studies to determine the reactivity in terms of redox potentials in DMF at room temperature (23 ± 1 °C). Electrochemical parameters from cyclic voltammograms were used to evaluate the reversibility of electron transfer, standard reduction potentials, solvation energies, electron affinities, diffusion coefficients, critical scan rates and heterogeneous electron transfer rate constants. Heterogeneous electron transfer rate constants were determined experimentally by Gileadi's method for the **Set 2** chalcones only. Computational studies included the use of MO theory with *semi-empirical* AM1 and PM3 approximations for the determination of optimized geometries and the energies of lowest unoccupied molecular orbital (E_{LUMO}). An attempt was also made to correlate the experimental and theoretical parameters.

Introduction

Chalcones belong to a class of α, β–unsaturated ketones and are important and interesting compounds due to their vast applications in pharmaceuticals, agriculture and industry. A large number of chalcones and their derivatives are important pharmaceuticals and are widely used due to their antitumor, anticarcinogenic, antibacterial, antiulcer and anti-inflammatory activities[1−3]. We have reported the synthesis and biological screening of chalcones used in this study and a number of chalcones have been found to possess significant activity against inhibitors of acetylcholinesterase (AChE), butylcholinesterase (BChE), α-glucosidase and urease enzymes[4]. In agriculture certain chalcones are used to destroy phytopathogenic organisms, whereas in industry they are used in controlling corrosion of steel[5], as dyes and as UV absorbers in cosmetics[6].

Chalcones possess conjugated double bonds and a completely delocalized π-electron system on both benzene rings. Molecules possessing such a system have relatively low redox potentials and have a greater probability of undergoing electron transfer reactions. Cyclic voltammetric (CV) studies involving reduction or oxidation of the compounds may be used to study the ease of electron transfer and to determine quantities

---

*Corresponding author

such as redox potentials and electron transfer rate constants. Hence CV studies on both sets of chalcones were carried out to determine the half-wave potentials ($E_{1/2}$). Subsequently electron affinities (A) values were calculated[7-9] from $E_{1/2}$ using Eq. (1)

$$A = E_{1/2} - S + \chi + 0.53 \tag{1}$$

where A is the electron affinity of the molecule in the gas phase, S is the free energy of solvation of the anion of the molecule, and χ is the work function of the electrode. The solvation energy was calculated using Born's model of ionic solvation[10]

$$S = -\left(\frac{z^2 e^2}{2r}\right)\left(1 - \frac{1}{\varepsilon}\right)\left(\frac{1}{4\pi\varepsilon_\circ}\right)\frac{1}{1.6 \times 10^{-19}}eV \tag{2}$$

where ε is the dielectric constant and r is the radius. The radius for each compound was calculated[11] using Eq. (3)

$$\frac{4}{3}\pi r^3 = \frac{M}{Nd} \tag{3}$$

where M, N and d are molecular weight, Avogadro's constant and density of the compound, respectively. The radii of all compounds were calculated from the experimentally measured densities.

In CV studies if the reverse peak does not appear then the heterogeneous electron transfer rate constant (k^0) can be calculated by analyzing the variation of peak position as a function of scan rate. Scan rate is related to the rate constant by Eq. (4) derived by Gileadi[12]

$$\log k^o = -0.48\alpha + 0.52 + \log\left[\alpha n F v_c D / RT\right]^{1/2} \tag{4}$$

where k^0 is the heterogeneous electron transfer rate constant, α is a dimensionless parameter known as the transfer coefficient, F is the Faraday constant, D is the diffusion coefficient, R is the universal gas constant, T is temperature, n is the number of electrons transferred from the electrode surface, and v_c is the critical scan rate. At critical scan rate the reaction changes from reversible to irreversible or from *quasi* reversible to irreversible as the scan rate is increased. Critical scan rate was calculated by plotting peak potential against the log of scan rate, whereas the diffusion coefficient D was calculated by using the Randle Sevick[13,14] equation:

$$i_p = 2.69 \times 10^5 n^{3/2} A C D^{1/2} v^{1/2} \tag{5}$$

where i_p is peak current, A is the electrode area, C is the concentration of the species, and v is the scan rate.

The present work describes studies carried out on 2 sets of chalcones, i.e. chalcones with and without a hydroxyl group on ring A and a number of substituents on ring B. Molecular orbital calculations using semi-empirical AM1 and PM3 approximations were carried out on all chalcones. An attempt was made to correlate the energies of the lowest unoccupied molecular orbital (E_{LUMO}) and Hammett constants (σ) with the half-wave reduction potentials ($E_{1/2}$) and electron affinity (A) values, respectively. Moreover, heterogeneous electron transfer rate constants (k^0) were calculated for **Set 2** only using Gileadi's method.

Experimental

Materials The chalcones studied in this work were used without further purification. Their synthesis, along with their biological activities, was recently reported by one of the authors[4]. A total of 19 compounds comprising a list of ortho, meta, para and di substituents were studied as shown in Schemes 1 and 2. The choice of solvent is dictated primarily by the solubility of the 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 at least over a wide range of potential. Spectrograde N,N-dimethylformamide (DMF) (BDH Chemicals Ltd., Poole, UK) was used as a solvent without further purification.

In controlled potential experiments a variable amount of the supporting electrolyte was used in order to decrease the resistance of the solution and to eliminate electromigration effects. Tetrabutylammoniumperchlorate (TBAP) from Fluka was used as the supporting electrolyte. TBAP was purified by recrystallization using methanol as the solvent.

Removal of dissolved oxygen As electrochemical reduction of oxygen usually proceeds via 2 well-separated, 2-electron steps, it was necessary to remove the dissolved oxygen before carrying out electrochemical studies. A variety of methods are available in the literature, the most common being the purging of inert gas such as nitrogen through the system under study. However, commercially available nitrogen contains a certain amount of oxygen as well. The purification of commercial nitrogen was done by passing it through a series of traps including $CrCl_3.6H_2O$ solution, pyrogallol, conc. H_2SO_4, $CaSO_4$ crystals and DMF before passing it through the sample under study.

Instrumentation A DMA 48 Digital Density Meter was used for measuring the densities of the chalcones. CV studies were carried out on a Polarographic Analyzer 174 A, Potentiostat/Galvanostat 173, Universal Programmer 175 (all EG & G Princeton Applied Research) in conjunction with an X-Y Recorder VP-65423A, Storage Oscilloscope Tektronix model 564 and Electrometer Probe Model 178. An Electrochemical Cell (model K64 PARC) connected to the circulating thermostat LAUDA model K-4R was used. A Hanging Mercury Drop Electrode (HMDE) was used as the working electrode. It consists of gold wire of 1.5 mm thickness, sealed into a glass tube at one end by means of araldite while the other end is kept covered with a small quantity of mercury. A copper wire is dipped into the mercury pool for external connection. A small mercury drop sticks to the open smooth surface of the gold wire. A thin platinum wire of thickness 0.5 mm with an exposed end of 10 mm and the remaining sealed in a glass tube was used as the counter electrode. A Saturated Calomel Electrode (SCE) from Fisher Scientific Company (Cat No. 13-639-51) in conjunction with an Electrometer Probe Model 178 was used as a reference electrode.

Computational Studies Molecular orbital calculations using Hyperchem 7.5 were carried out on all chalcones using AM1 and PM3 methods to calculate the energies of lowest unoccupied molecular orbital (E_{LUMO}). For substituted chalcones, the starting point was the optimized structure of unsubstituted chalcone; then substituents were added and their geometries were optimized by molecular mechanics. The geometries of these molecules were further optimized with AM1 and PM3.

We were interested in knowing whether there is a linear correlation between experimentally determined half-wave potentials ($E_{1/2}$) and E_{LUMO} values calculated through the semi-empirical AM1 and PM3 methods. Likewise, it was also considered worthwhile to know whether a similar correlation between electron affinities (A) and E_{LUMO} values exists.
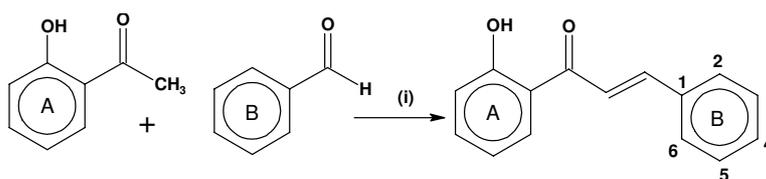
Scheme 1

Set 1	Substituents on ring B
1	H
2	4-Me
3	4-OMe
4	4-F
5	3,4-OMe
6	4-NMe$_2$
7	4-NO$_2$
8	4-Cl
9	3,4-[OCH$_2$O]

(i) EtOH, aq. 4 M NaOH, 3 h.
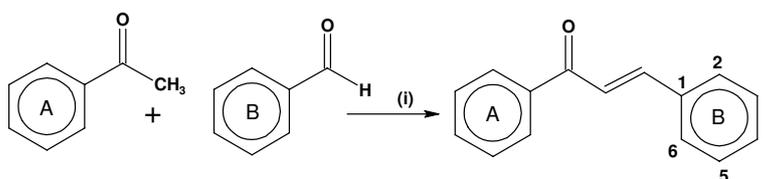
Scheme 2

Set 2	Substituents on ring B
10	H
11	4-Me
12	4-OMe
13	4-NMe$_2$
14	4-F
15	4-Cl
16	4-Br
17	4-NO$_2$
18	3-NO$_2$
19	2-Cl

(i) EtOH, aq. 4 M NaOH, 3 h.

Results and Discussion

Reduction potentials of chalcones were measured in DMF containing 0.1 M tetrabutylammoniumperchlorate (TBAP) as supporting electrolyte at room temperature. In general, all compounds undergo one electron reduction and exhibit no anodic peak except for nitro compounds (7, 17 and 18). This clearly indicates that the initial radical anion is short lived on the time scale of the voltammogram.

The values of (E$_{1/2}$) and [E$_P$−E$_{P/2}$] at 50 and 100 mVs^{-1} scan rates are listed in Table 1. Considering the reversibility criteria, i.e. [E$_P$−E$_{P/2}$] ≈ 60 ± 5 mV, it can be seen that all chalcones of **Set 1** exhibit irreversible behavior, while only compounds 17, 18 and 19 of **Set 2** show irreversibility at high scan rate.

Table 1. Half-wave potential ($E_{1/2}$) and reversibility (E_p-$E_{p/2}$) of chalcones at 50 and 100 mVs^{-1}.

Set 1		50 mVs^{-1}		100 mVs^{-1}	
Substituents on ring B		$E_{1/2}$(V)	Ep-$E_{p/2}$(mV)	$E_{1/2}$(V)	Ep-$E_{p/2}$(mV)
1	H	-1.742	82	-1.751	91
2	4-Me	-1.805	95	-1.811	96
3	4-OMe	-1.860	109	-1.869	128
4	4-F	-1.720	125	-1.736	129
5	3,4-OMe	-1.887	120	-1.902	121
6	4-NMe$_2$	-1.924	110	-1.929	109
7	4-NO$_2$	-1.301	174	-1.390	173
8	4-Cl	-1.687	77	-1.702	87
9	3,4-[OCH$_2$O]	-1.601	42	-1.690	45
Set 2					
10	H	-1.873	50	-1.878	55
11	4-Me	-1.917	50	-1.924	60
12	4-OMe	-1.944	50	-1.963	50
13	4-NMe$_2$	-2.061	62	-2.061	62
14	4-F	-1.801	40	-1.809	50
15	4-Cl	-1.791	40	-1.801	50
16	4-Br	-1.743	50	-1.753	50
17	4-NO$_2$	-1.260	70	-1.330	70
18	3-NO$_2$	-1.460	70	-1.540	80
19	2-Cl	-1.930	60	-1.940	70

Effect of Substituents on $E_{1/2}$

Schemes 1 and 2 show that chalcones I and 10 are unsubstituted; 2-4, 6-9 and 11-17 differ with respect to their substituents at the para position; 5 and 9 are disubstituted; and 18 and 19 are substituted at the meta and ortho positions, respectively. Values of $E_{1/2}$ and $[E_P-E_{P/2}]$ were determined from cyclic voltammograms. Generally compounds with electron withdrawing substituents were found to reduce more easily than those substituted with electron donating groups (Table 1). A comparison of the $E_{1/2}$ values of the chalcones shows that for electron donating substituents, e.g. CH_3, OCH_3 and NMe_2 (2, 3, 5 and 6), $E_{1/2}$ values are more negative, thereby confirming that they hinder the reduction process. In contrast, chalcones containing electron withdrawing groups (4 and 7-9 in **Set 1**) undergo an easy reduction as is evident from their $E_{1/2}$ values. The same trend was observed in **Set 2** of chalcones, where compounds 11-13, having electron donating graphs, show more negative $E_{1/2}$ values, while chalcones 14-19, having electron withdrawing groups, have less negative $E_{1/2}$ values when compared to unsubstituted chalcone 10 (Table 1).

Correlation of Hammett Constant (σ) and MO Energies (E_{LUMO}) with Half-wave Potential ($E_{1/2)}$) and Electron Affinities (A)

According to Zuman's method, the plotting of reduction potential vs. Hammett substituent constants often leads to a linear correlation[15]. Such a correlation can be used to predict the reduction potentials of unknown compounds. However, this procedure has the following major limitations: (1) the synthesis of a number of compounds needs to be done prior to measuring their redox potential in order to establish a correlation; (2)

compounds having substituents capable of directing conjugation (e.g., nitro, alkoxy and amino) fall far from the correlation line. The same is true for o-substituted compounds.

Table 2. Half-wave potential ($E_{1/2}$), E_{LUMO} and Hammett constant (σ) of chalcones.

Set 1		$E_{1/2}$(V)	E_{LUMO} (eV)		Hammett constant (σ)[18]
Substituents on ring B			AM1	PM3	
1	H	-1.751	-0.829	-1.038	0.000
2	4-Me	-1.811	-0.810	-1.017	-0.170
3	4-OMe	-1.869	-0.803	-0.989	-0.270
4	4-F	-1.736	-1.025	-1.207	0.150
5	3,4-OMe	-1.902	-0.822	-1.028	-
6	4-NMe$_2$	-1.929	-0.684	-0.937	-0.320
7	4-NO$_2$	-1.390	-1.695	-1.841	0.780
8	4-Cl	-1.702	-1.016	-1.173	0.240
9	3,4-[OCH$_2$O	-1.690	-0.950	-1.117	-
Set 2					
10	H	-1.878	-0.701	-0.800	0.000
11	4-Me	-1.924	-0.684	-0.783	-0.170
12	4-OMe	-1.963	-0.653	-0.753	-0.27
13	4-NMe$_2$	-2.061	-0.546	-0.723	-0.320
14	4-F	-1.809	-0.905	-1.009	0.150
15	4-Cl	-1.801	-0.909	-0.978	0.240
16	4-Br	-1.753	-0.962	-1.009	0.260
17	4-NO$_2$	-1.330	-1.621	-1.704	0.780
18	3-NO$_2$	-1.540	-1.352	-1.437	0.710
19	2-Cl	-1.940	-0.799	-0.824	-

      As the reactions at the surface of electrodes involve the transfer of electrons to the neutral molecule, the incoming electron should occupy the lowest unoccupied molecular orbital (LUMO). Hence, a linear correlation is also expected between $E_{1/2}$ and E_{LUMO}. Such correlations have indeed been observed for other compounds such as quinines[16]. E_{LUMO} were calculated using both AM1 and PM3 semi-empirical methods and plotted against experimentally determined $E_{1/2}$, whereby a linear correlation was observed in both sets of chalcones. However, the results were slightly better with the AM1 method (Figures 1 and 2). As $E_{1/2}$ is a measure of the ease of reduction or oxidation, a linear correlation of $E_{1/2}$ and Hammett constant (σ) is expected. A plot of experimentally determined $E_{1/2}$ values vs. σ gives a straight line with a correlation coefficient of 0.88 (Figure 3). Similar linear plots were obtained in the case of electron affinities (A) when plotted against Hammett constants (σ) (Figure 4) and against E_{LUMO} (Figure 5).

Solvation Energies

Solvation energies were calculated using Born's formula[10], Eq. (2), which utilizes the radii of solutes, which in turn were calculated using experimentally determined density values. Densities (d), radii (r) and solvation energies (S) of these compounds are listed in Table 3. The values of solvation energies depend upon the nature of the solvent and the substituents. From the data given in Table 3 it is clear that the values of solvation energies are higher for unsubstituted compounds. This is due to the fact that solvation energies

depend upon the size of substituents. The greater the size of the substituents, the larger would be the magnitude of solvation energy.
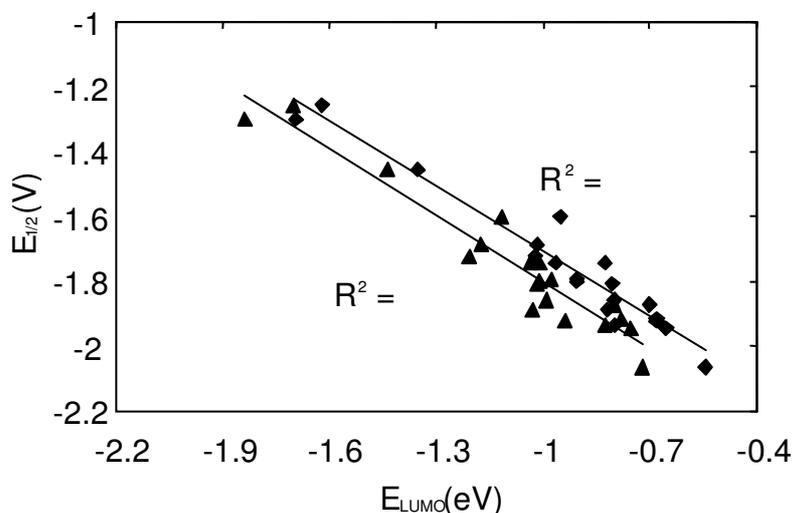
Figure 1. Plot of E_{LUMO} (calculated by AM1 ■ and PM3 ▲ methods) vs. $E_{1/2}$ measured at scan rate 50 mVs^{-1}.
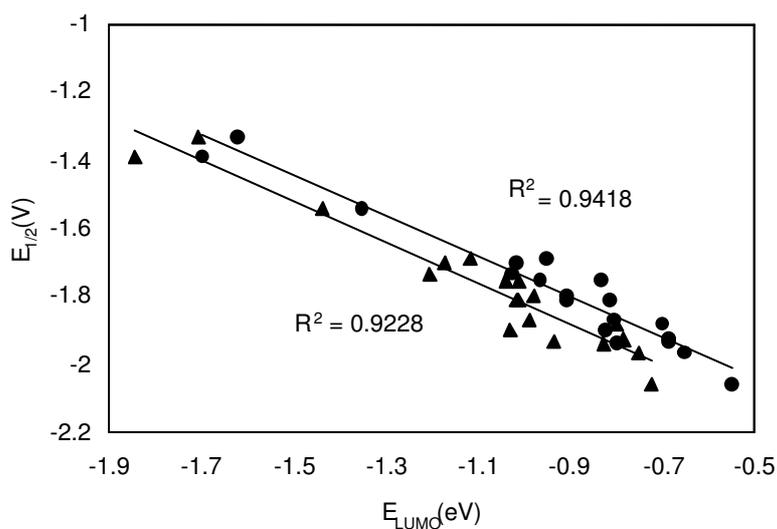
Figure 2. Plot of E_{LUMO} (calculated by AM1 ● and PM3 ▲ methods) vs. $E_{1/2}$ measured at scan rate 100 mVs^{-1}.

Electron Affinities

Electron affinities were calculated from solvation energies and half-wave potentials. These values fall in the range 1.5-2.2 eV. These are comparable with the electron affinities (A) of simple aromatic hydrocarbons (1-2 eV)[11,17]. The greater values of electron affinities for chalcones may be attributed to the presence of conjugated carbonyl groups.

A comparison of the electron affinity values of substituted chalcones with those of the unsubstituted one show that electron donating substituents lower the electron affinity and electron attracting substituents increase it. The capability of a para substituent to increase the electron affinity in the order $-NO_2 > -Br = -Cl > -F$ can be related to the decreasing value of the Hammett constant (σ) (Table 3).
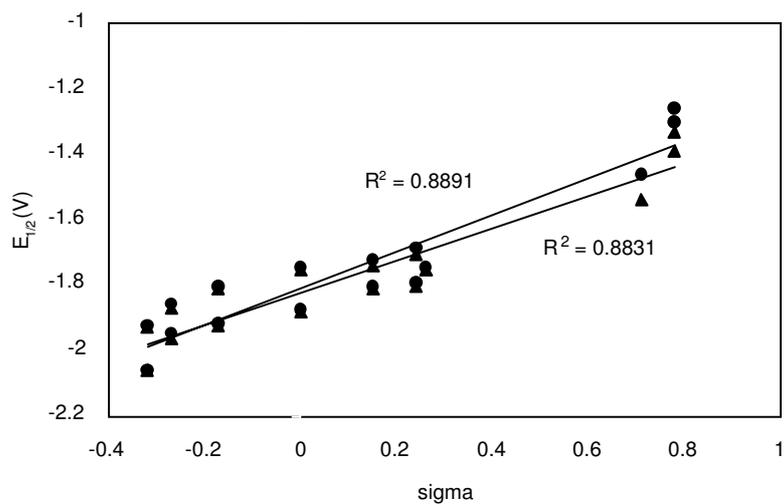
Figure 3. Plot of σ vs. $E_{1/2}$ measured at scan rate 50 ● and 100 ▲ mVs^{-1}.
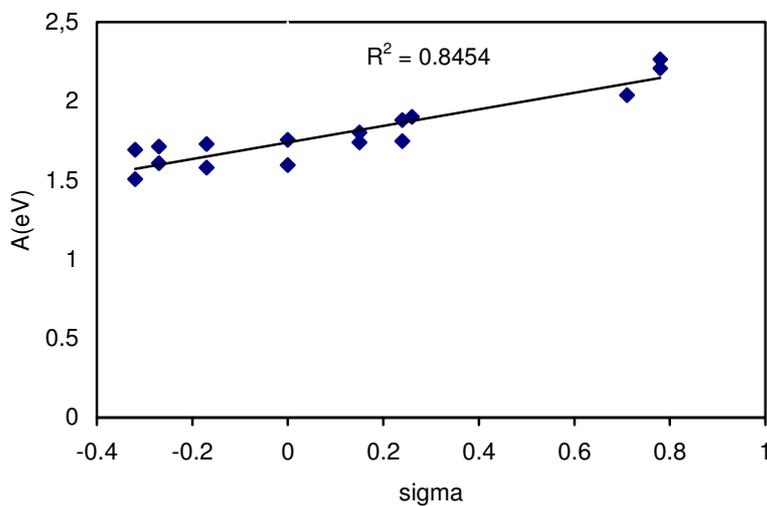
Figure 4. Plot of Hammett substituent constant (σ) vs. electron affinity (A).
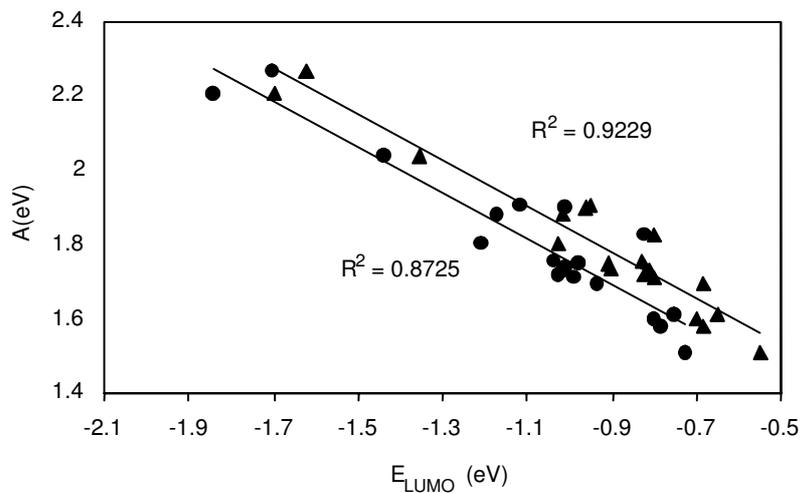
Figure 5. Plot of E_{LUMO} (calculated by PM3 ▲ and AM1 ● methods) vs. electron affinity A.

Table 3. Densities (d), radii (r), solvation energies (S) and electron affinities (A) of chalcones.

Set 1		d (g.mL^{-1})	r (A°)	S (eV)	A (eV)
Substituents on ring B					
1	H	0.955	4.530	1.543	1.756
2	4-Me	0.950	4.630	1.510	1.729
3	4-OMe	0.931	4.766	1.467	1.714
4	4-F	0.972	4.620	1.512	1.802
5	3, 4-OMe	1.039	4.766	1.467	1.720
6	4-NMe$_2$	0.901	4.897	1.428	1.693
7	4-NO$_2$	0.906	4.900	1.426	2.207
8	4-Cl	0.947	4.765	1.467	1.881
9	3,4-[OCH$_2$O]	0.960	4.800	1.455	1.905
Set 2					
10	H	0.949	4.435	1.576	1.596
11	4-Me	0.949	4.526	1.545	1.581
12	4-OMe	0.951	4.730	1.478	1.609
13	4-NMe$_2$	0.948	4.720	1.481	1.508
14	4-F	0.909	4.549	1.537	1.739
15	4-Cl	0.956	4.655	1.502	1.747
16	4-Br	0.952	5.007	1.396	1.901
17	4-NO$_2$	0.912	4.805	1.455	2.265
18	3-NO$_2$	0.958	4.749	1.472	2.038
19	2-Cl	0.940	4.727	1.479	1.828

Heterogeneous Electron Transfer Rate Constants

Heterogeneous electron transfer rate constants (k^0) determined experimentally using Gileadi's methods are listed in Table 4. The rate constants were of the same order of magnitude (10^{-4}cms^{-1}) as those of quasi-reversible reactions. However, no conclusion regarding a possible correlation between the electronic effect of substituent and molecular size with k^0 could be drawn.

Table 4. Diffusion coefficient (D), critical scan rate (ν_c) and heterogeneous electron transfer rate constants (k^0) of chalcones (**Set 2**).

Set 2		D × 10^8(cm^{2}s^{-1})	ν_c(Vs^{-1})	k^0× 10^{-4} (cms^{-1})
Substituents on ring B				
10	H	1.463	0.912	6.404
11	4-Me	0.959	0.912	5.186
12	4-OMe	1.790	0.955	7.248
13	4-NMe$_2$	0.246	0.871	2.568
14	4-F	3.233	0.759	8.684
15	4-Cl	1.635	0.398	4.475
16	4-Br	2.356	0.501	6.624
17	4-NO$_2$	0.366	0.977	3.314
18	3-NO$_2$	0.959	1.000	5.431
19	2-Cl	0.670	0.575	4.472

Conclusion

From the $E_{1/2}$ values of both sets of chalcones it was found that the presence of OH on ring A facilitates the reduction of these compounds due to the formation of hydrogen bonding between an oxygen atom of the carbonyl group and a hydrogen atom of the OH group. From the behavior substituents present on ring B it is clear that electron withdrawing substituents facilitate reduction and lead to less negative reduction potential values, while the opposite trend was found for electron donating substituents. Fairly good linear correlations were observed for chalcones. As a whole, correlations involving $E_{(LUMO)}$ calculated by the AM1 method were better than those calculated by the PM3 method. Half-wave potentials, solvation energies and electron affinities followed the same trends, as expected.

References

1. H. Haraguchi, H. Ishikawa, K. Mizutanik, Y. Tamura and T. Kinoshita, **Bio. Org. Med. Chem. 6**, 339 (1998).

2. H. Silh, T.H. Lee, J.P. Wang, J.I. Wang and C.N. Lin, **Pharma. Res. 15**, 39 (1998).

3. T.W. Flechtener, **Carbohydr. Res. 77**, 262 (1997).

4. F.L. Ansari, S. Umbareen, L. Hussain, T. Makhmoor, S.A. Nawaz, M.A. Lodhi, S.N. Khan, F. Shaheen, M.I. Chaudhry and A. Rahman, **Chemistry and Biodiversity 2**, 487 (2005).

5. E.T. Oganesysan and A.S. Saraf, **Khim. Far. Zh. 18**, 22 (1991).

6. C.N. Reilley, **J. Chem. Edu. 39A**, 583 (1962).

7. E. Lyons, **Nature 166**, 193 (1950).

8. M. Mohammad, N.P. Dost, M. Jalil, R. Qureshi, M. Saleem, A.Y Khan and R. Iqbal, **Bul. Electrochem. 4**, 287 (1988).

9. R.N. Hedges and F.A. Matson, **J. Chem. Phys. 28**, 950 (1958).

10. J.O'M. Bockris and A.K.N. Reddy, "**Modern Electrochemistry**" Vol. 1, Plenum Press, New York, 1979.

11. M.E. Poever, **Electrochim. Acta 13**, 1079 (1969).

12. E. Gileadi and U. Eisner, **J. Electroanal Chem. 28**, 81 (1970).

13. J.E.B. Randles, **Trans Faraday Soc. 44**, 327 (1984).

14. A. Sevick, **Collec. Czech Chem. Commun. 13**, 349 (1984).

15. P. Zuman, "**Substituents Effect in Organic Polarography**" Plenum Press, New York, 1973.

16. M. Hamazian and P. Norouizi, **J. Electroanal. Chem. 49**, 573 (2004).

17. L.D. Hicks, A.J. Fry and V.C. Kurzweil, **Electrochimica. Acta. 50**, 1039 (2004).

18. N. Isaacs, "**Physical Organic Chemistry**" 2nd Edn. Longman Scientific and Technical, Burnt Mill, UK, 1995.