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Substituent effect on the electron acceptor property of 1,4-benzoquinone towards the formation of molecular complex with sulfamethoxazole

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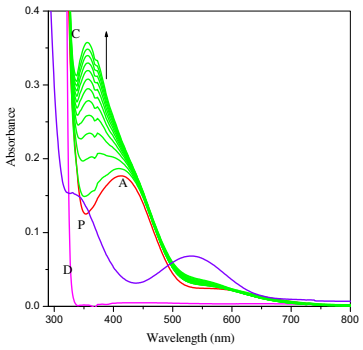
HIGHLIGHTS

- Novel substituted 1,4-benoquinones were employed as acceptors in the CT interaction with a drug.
- The mechanism of the interaction was studied using various spectral techniques.
- Progressive replacement of —Cl (–I effect) by —OMe (+M effect) makes the acceptor weaker.

GRAPHICAL ABSTRACT



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ABSTRACT

UV–Vis, ^{1}H NMR, FT-IR, LC–MS and fluorescence spectral techniques were employed to investigate the mechanism of interaction of sulfamethoxazole with varying number of methoxy/chloro substituted 1,4-benzoquinones (MQ_{1-4}) and to characterize the reaction products. The interactions of MQ_{1-4} with sulfamethoxazole (SULF) were found to proceed through the formation of a donor–acceptor complex, containing radical anion and its conversion to the product. Fluorescence quenching studies showed that the interaction between the donor and the acceptors are spontaneous. The results indicated that the progressive replacement of chlorine atom (–I effect) by methoxy group (+M effect) in the quinone decreased the electron acceptor property of the quinone. The results of the correlation of experimentally measured binding constants with electrochemical data and *ab initio* DFT calculations supported these observations.

Introduction

Charge transfer (CT) or electron donor acceptor (EDA) complexes constitute a very promising field of study due to its interesting optical and electronic properties [1]. CT is undoubtedly of fundamental importance in nature and governs a number of pivotal processes such as photosynthesis and vision [2]. The fascination of electron donor–acceptor architectures has been widely recognized in the design of organic optoelectronic materials for organic light emitting diodes [3], organic photovoltaics [4], sensors [5], organic field effect transistor [6], non-linear optics [7], magnetic materials [7], organic solar cells [8] and xerogel nanoparticles [9]. EDA reactions of certain σ and π acceptors have successfully utilized in pharmaceutical analysis of drugs [10]. Drug-receptor mechanism could be explained by means of CT phenomenon in addition to weak forces of non-covalent interactions [11]. As a primary step to determine whether CT phenomenon at any level involved, the ability of the donor drugs and related compounds to form charge transfer complexes with acceptors should be studied.

Quinones are important class of organic molecules which notably plays an essential role in redox reactions such as respiration and photosynthesis [12]. The key electron acceptors in the

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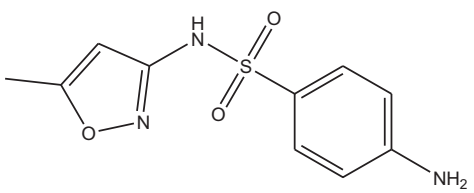
photosynthetic processes are menoquinones, plastoquinones and ubiquinones [13,14]. The biological activity of the quinones is reportedly due to the redox chemistry of the quinone system [15]. Quinones are capable of accepting one or two electrons to form the corresponding radical anion ($Q^{\cdot-}$) and hydroquinone dianion (Q^{2-}). Since quinones actively participate in electron transfer processes, the study of their structural properties is important. It is well known that any change in the substituent attached to the quinone ring alters its capability to accept electrons and consequently changes its biological reactions [16–18]. The presence of methoxy substituent is known to substantially influence the electron affinity and vibrational spectroscopy of benzoquinones and has been suggested to be important in determining the function of ubiquinone as a redox cofactor in bioenergetics [19]. Hence, a case study of CT interaction between 1,4-benzoquinones possessing varying the number of chloro/methoxy substituents with a chosen donor drug has been attempted.

The mechanism of interaction of quinone with drugs, in general, is a research topic of significant interest and hence the present study. The objective, therefore, of the present article is to study the spectral, thermodynamic and kinetic aspects of the interaction of 1,4-benzoquinones possessing varying number of methoxy/chloro substituents as electron acceptors (MQ_{1-4}) with sulfamethoxazole (SULF) drug with an aim to investigate the mechanism of these interactions and to characterize the structure of the products formed in these interactions. In general, drugs are poly-functional organic molecules and the present study aims at to investigate the actual site of attack during the formation of charge transfer interaction. Such a study would undeniably shed some light on the mechanism of the drug action in real pharmacokinetic study. Sulfamethoxazole is chemically known as 4-amino-N-(5-methylisoxazol-3yl)-benzene sulfonamide which is used as an antibacterial agent and to treat urinary tract infections [20]. It is also used in the treatment of sinusitis, toxoplasmosis and pneumocystis pneumonia which affects primarily patients with HIV. Though these 1,4-benzoquinones are known to organic chemists as intermediates, it is the first systematic attempt to utilize them as acceptors in the study of CT complexes with the drug. Such a structural variation of the quinones would certainly helps to tune the redox chemistry of them and hence its biological activity.

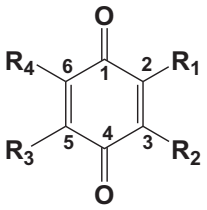
Experimental

Material and methodology

The electron acceptors viz. varying number of methoxy/chloro substituted 1,4-benzoquinones were synthesized and purified by the reported method [21]. The electron donor drug sulfamethoxazole was obtained as gift sample from a locally available pharmaceutical company and was used as received. The purity of the drug was checked by its melting point (observed 169 °C; literature 169 °C), ^{1}H NMR and FT-IR spectra. Commercially available spectroscopic grade solvents (Merck, India) were used without further purification. The structures of the drug and the acceptors are shown below.



Chemical structure of sulfamethoxazole



Acceptor	R_1	R_2	R_3	R_4
MQ_1	OCH_3	Cl	Cl	Cl
MQ_2	OCH_3	Cl	OCH_3	Cl
MQ_3	OCH_3	OCH_3	OCH_3	Cl
MQ_4	OCH_3	OCH_3	OCH_3	OCH_3

Solutions for the spectroscopic measurements were prepared by dissolving accurately weighed amounts of donor (D) and acceptor (A) in the appropriate volume of solvent immediately before running the spectra. The electronic absorption spectra were recorded on a JASCO (V 630, Japan) UV–Vis double beam spectrophotometer using 1 cm matched quartz cells by using corresponding pure solvent as reference. The temperature of the cell holder was controlled with a water flow (±0.2 °C). The steady state fluorescence spectra were obtained on a JASCO (FP 6200, Japan) spectrofluorimeter. The emission slit width (5 nm) and the scan rate (250 nm) was kept constant for all of the experiments. FT-IR spectra were recorded in a JASCO (FT-IR 460 Plus, Japan) spectrometer. ^{1}H NMR spectra were recorded at Madurai Kamaraj University, Madurai in a Brucker NMR spectrometer (300 MHz, Switzerland). The LCMS spectra were obtained from University of Hyderabad in a Shimadzu LCMS 2010 with ionization potential at 70 eV (LCMS 2010, Japan).

Synthesis and characterization of substituted quinones

1,4-Benzoquinones possessing varying number of chloro and methoxy substituents were synthesized and purified as reported elsewhere [21]. An excess amount of sodium methoxide was added into a stirred solution of chloranil in methanol at RT under N_2 atm. The reaction mixture was stirred for 12 h at 70 °C and cooled to room temperature. Then the reaction mixture was added into 200 ml of water and stirred for 1 h at RT. The crude material formed was filtered through a filter paper and residue was purified using column chromatography (Silica gel 60–120 by using 5–10% ethyl acetate pet ether mixture). The percentage yields of various quinones obtained by this method are shown in Scheme 1. For the preparation of MQ_4, four equivalents of sodium methoxide were added into MQ_1 under the same preparation condition.

2,3,5-Trichloro-6-methoxycyclohexa-2,5-diene-1,4-dione (MQ_1)

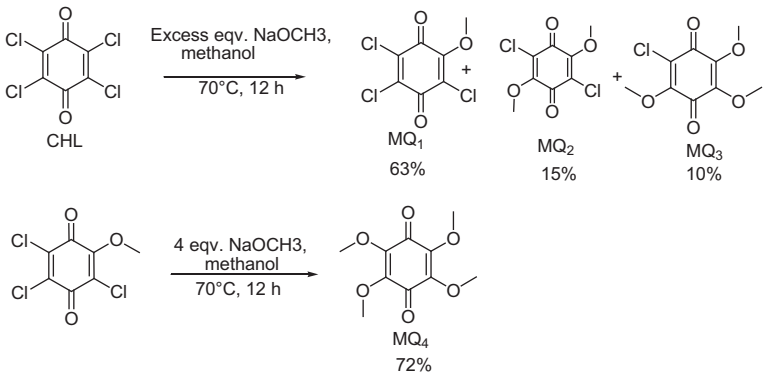
^{1}H NMR (DMSO-d^6, 300 MHz), δ(ppm) 4.19 (s, 3H), FT-IR (cm^{-1}): 1680 (C=O), 1668 (C=O), 1567 (C=C), UV–Vis in ethanol (λ_{max}): 410 nm (n–π^*), log ε 2.50, Anal. Calcd. for $C_7H_3Cl_3O_3$: C, 34.82; H, 1.25; found: C, 36.17; H, 1.74; m.p. 172 °C.

2,5-dichloro-3,6-dimethoxycyclohexa-2,5-diene-1,4-dione (MQ_2)

^{1}H NMR (DMSO-d^6, 300 MHz), δ(ppm) 4.07 (s, 3H), 4.12 (s, 3H) FT-IR (cm^{-1}): 1668 (C=O), 1568 (C=C), UV–Vis in ethanol (λ_{max}): 412 nm (n–π^*), log ε 2.50, Anal. Calcd. for $C_8H_6Cl_2O_4$: C, 40.54; H, 2.55; found: C, 41.24; H, 2.66; m.p. 141 °C.

2-chloro-3,5,6-trimethoxycyclohexa-2,5-diene-1,4-dione (MQ_3)

^{1}H NMR (DMSO-d^6, 300 MHz), δ(ppm) 3.92 (s, 3H), 4.07 (s, 3H), 4.12 (s, 3H); FT-IR (cm^{-1}): 1666 (C=O), 1568 (C=C), UV–Vis in



Scheme 1. Preparation method for methoxy/chloro substituted quinones (MQ_{1-4}).

ethanol (λ_{max}): 413 nm (n–π^*), log ε 2.51, Anal. Calcd. for $C_9H_9ClO_5$: C, 46.47; H, 3.90; found: C, 46.17; H, 3.78; m.p. 83 °C.

2,3,5,6-Tetramethoxycyclohexa-2,5-diene-1,4-dione (MQ_4)

^{1}H NMR (DMSO-d^6, 300 MHz), δ(ppm) 3.92 (s, 12H), FT-IR (cm^{-1}): 1668 (C═O), 1568 (C═C), UV–Vis in ethanol (λ_{max}): 416 nm (n–π^*), log ε 2.50, Anal. Calcd. for $C_{10}H_{12}O_6$: C, 52.63; H, 5.30; found: C, 53.12; H, 5.58; m.p. 134 °C.

Kinetic procedure

The kinetics of the interaction of SULF with the acceptors (**MQ_{1-4}**) different quinones was followed at three different temperatures in ethanol solvent under pseudo-first-order conditions, keeping [D] ≫ [A]. The increase in absorbance of the new peak at 340 nm for (SULF–MQ_1) and 350 nm for (SULF–MQ_2, SULF–MQ_3, SULF–MQ_4) with elapse of time were recorded. The pseudo-first-order rate constants (k_1) were calculated from the gradients of log (A_∞–A_t) against time plots, where A_∞ and A_t represent the absorbance at infinity and time t, respectively. The second order rate constants were calculated by dividing k_1 by [D] [22].

Results and discussion

Stoichiometry of the interaction

The stoichiometry of the CT complex formed, in all the cases, was determined by applying Job's continuous variation method [23]. In all the cases (SULF–MQ_{1-4}) the symmetrical curve with a maximum at 0.5 mole fraction indicated the formation of a 1:1 (D:A) CT complex (Fig. 1). The photometric titration measurements were also performed for the determination of the stoichiometry in these interactions. The results of the photometric titration studies (Fig. 2) confirmed the observed stoichiometry of the interaction [24]. The stoichiometry of the SULF–MQ_{1-4} systems is further confirmed by Jobs continuous variation method using emission studies also [25] [(Fig. 1Sa) Supplemental information].

Characterization of reaction products

In all the cases, the reaction products were obtained by allowing the reactants (4 mmol of SULF and 4 mmol of MQ_{1-4} in ethanol) to react for 24 h under stoichiometric conditions and subjected to MPLC separation. The FT-IR spectra of the pure SULF, MQ_{1-4} and their products were recorded and the peak assignments for important peaks for SULF–MQ_{1-4} systems are given in Tables 1–4. The results indicated that the shifts in positions of some of the peaks could be attributed to the symmetry and electronic structure

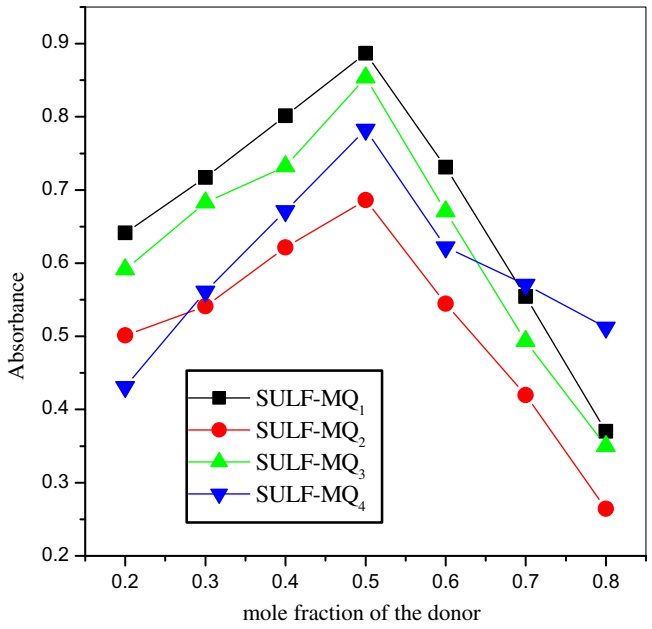


Fig. 1. Job's continuous variation plots for SULF with MQ_1, MQ_2, MQ_3 and MQ_4 in ethanol at 298 K.

modifications in both donor and acceptor units in the formed product relative to the free molecules.

In SULF–MQ_1 system, some of the significant shifts are: the peaks due to asymmetric and symmetric vibrations of the aromatic ring —NH_2 group of the free SULF occurred at 3469 cm^{-1} and 3376 cm^{-1}, respectively and in SULF–MQ_1 product it appeared at 3249 cm^{-1} indicating the participation of N—H moiety in the product formation. The ν(C═O), ν(O—CH_3) and ν(C—Cl) stretching vibrations in the free MQ_1 species appeared at 1684, 1270 and 909 cm^{-1}, respectively. In the product these stretching vibrations occurred at 1671, 1265 and 896 cm^{-1}, respectively. Such a bathochromic shift could be indicative of a higher charge density on the carbonyl and chloro groups of the MQ_1 molecule [26]. These observations suggested that the NH_2 moiety of SULF participated in the product formation with MQ_1.

As a representative case, the ^{1}H NMR spectra of the donor SULF and its reaction product with MQ_1 were recorded in DMSO d_6 and are given in [(Figs. 3Sa and 3Sb), supplemental information] respectively. Using the proton NMR technique, we can identify the nature of interaction between the donor and acceptor in the resulted product. Pure SULF molecule exhibited the characteristic peak due to aromatic —NH_2 group of the aromatic ring at 6.087 ppm and in the product they appeared at 9.620 ppm as —NH group. This

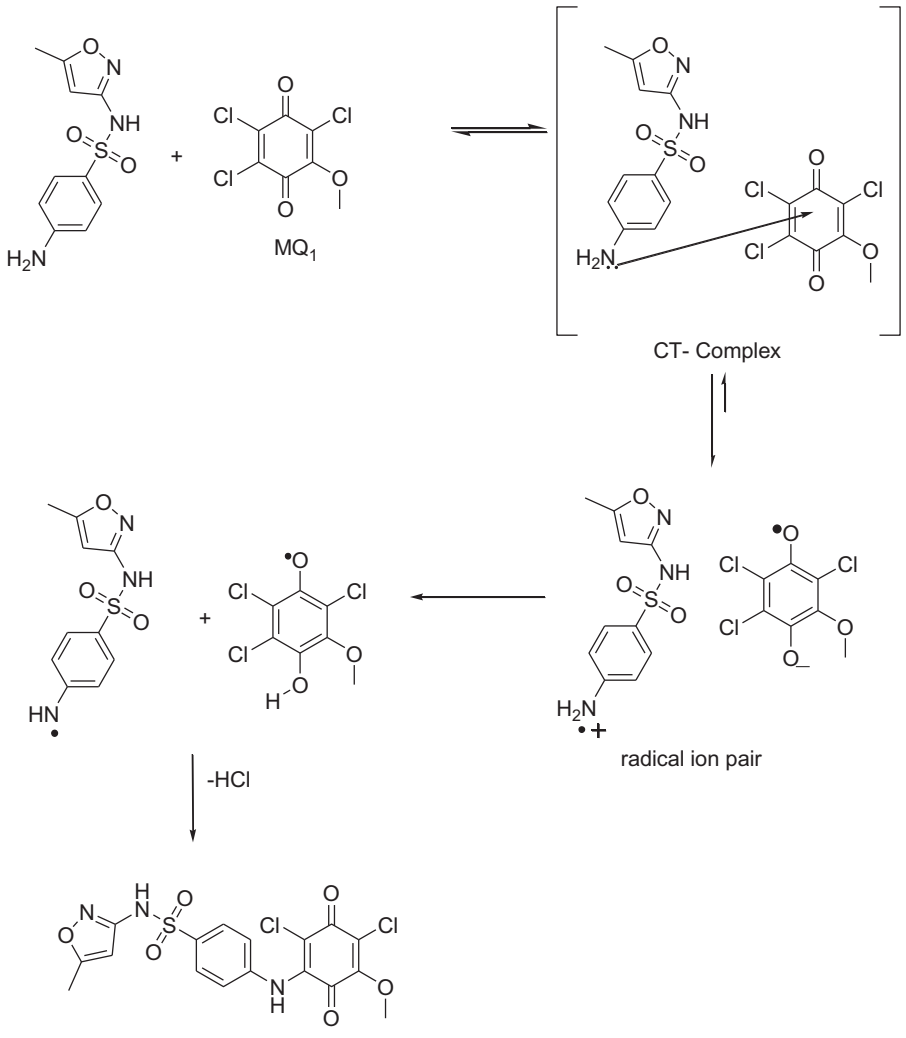
observation indicated that the product between SULF and MQ_1 is formed with the elimination of HCl molecule. The aromatic protons of pure SULF molecule lies in the range of 6.562–7.475 ppm and in the product/complex lie at 7.144–7.754 ppm. The —NH proton of the pure SULF occurs at 10.927 ppm and in the product/complex occurs at 11.339 ppm. The down field shifts of most of the signals are corresponding due to the interaction occurred between the donor and the acceptor [27,28].

In SULF–MQ_1 case, the liberation of HCl was qualitatively analyzed using litmus paper test (the reaction mixture turns blue litmus to red) and silver nitrate test (water extract of the reaction mixture gives white precipitate with silver nitrate solution). The LCMS spectrum, of SULF–MQ_1 product was recorded and it exhibited the molecular ion peak at m/z 458 [(Fig. 3Sc) supplemental information] which confirms the chemical reaction between the donor and acceptor leading to the product. In the SULF–MQ_{2-4} cases, the molecular ion peaks at m/z 492, 488, 484 confirm the adduct formation between SULF and the corresponding MQ_{2-4} [(Figs. 3Sd, 3Se, 3Sf) supplemental information].

Interaction of sulfamethoxazole with MQ_{1-4}

The electronic spectra of MQ_1 in the presence of large excess of donor, i.e. [D]/[A] > 100 were recorded as a function of time in ethanol (Fig. 3). Immediately after mixing ethanolic solutions of colorless SULF and pale yellow colored MQ_1, yields a pink colored solution whose electronic spectrum showed absorption band 460–600 nm range. This is the characteristic absorption bands of quinone radical ion [28,29]. It is observed that with elapse of time the intensity of these bands decreased (Fig. 3 inset) with a concurrent increase in intensity of the band at 415 nm. A clear isosbestic point is observed at 456 nm. The position of the absorption maximum of the peak at 415 nm has also been blue shifted with elapse of time. These observations indicated that the initial reactants were converted into final product via radical ion formation. For comparison the electronic spectrum of the product is also shown in Fig. 3. However, in the case of SULF–MQ_{2-4} systems, on mixing the ethanolic solutions of the reactants, the intensity of the λ_{max} of the acceptor increased with the elapse of time rather than the appearance of new peaks. A representative electronic spectrum is shown in Fig. 4. This indicated that the reactants associate through CT complexation to form an adduct rather than a permanent chemical reaction as occurred in the case of SULF–MQ_1 system.

The kinetics of interaction of SULF with MQ_{1-4} has been followed by monitoring the increase in absorbance of new peak in ethanol as a function of time under pseudo-first-order conditions, i.e. $[D] \gg [A]$. The pseudo-first-order rate constant (k_1) values for the formation of the product as a function of [D] and [A] are collected in Table 5. It is evident from the results in all the cases the rate is independent of initial concentration of A indicating first order



Mechanism of interaction of SULF with MQ_1

dependence on [A]. The plot of log k_1 versus log [D] is linear with a slope of unity ($r > 0.995$; slope range 0.007–0.0018) [(Fig. 4S) supplemental information] indicating unit order dependence on [D]. This was further supported by the constancy in k_2 values [28].

The pseudo first-order rate constants, for all the systems, were measured at three different temperatures and the thermodynamic parameters computed are collected in Table 6. A large negative value of entropy of activation indicates the involvement of polar transition state. This may be due to the fact that there is some charge separation in the transformation of reactants to product. Also the negative entropy of activation indicated a greater degree of ordering in the transition state than in the initial state, due to an increase in solvation during the activation process.

Based on the foregoing results and discussions the following plausible mechanism for the interaction SULF with MQ_{1-4} has been proposed.

Mechanism of interaction of SULF with MQ_1.

Mechanism of interaction of SULF with MQ_{2-4}.

Characterization of the interaction product

SULF–MQ_1 [3,6-dichloro-2-methoxy-5-(4-amino-N-(5-methylisoxazol-3-yl)-benzene sulfonamide)cyclohexa-2,5-diene-1,4-dione].

^{1}H NMR (DMSO-d^6, 300 MHz), δ(ppm) 2.29 (s, 3H), 4.17 (s, 3H), 6.14 (s, 1H), 7.14 (d, J = 8.7 Hz, 2H), 7.72 (d, J = 8.7 Hz, 2H), 9.62 (s, 1H), 11.33 (s, 3H). FT-IR (cm^{-1}, KBr): 3249 (NH), 1671 (C=O), 1265, 1037 (—OCH_3); LCMS: Calcd. For $C_{17}H_{13}Cl_2N_3O_6S$: 458.2; found: 458.4; *Anal.* Calcd. for $C_{17}H_{13}Cl_2N_3O_6S$: C, 44.55; H, 2.86;: N, 9.17; found: C, 45.75; H, 2.70;: N, 9.06.

Characteristics of the CT complexes

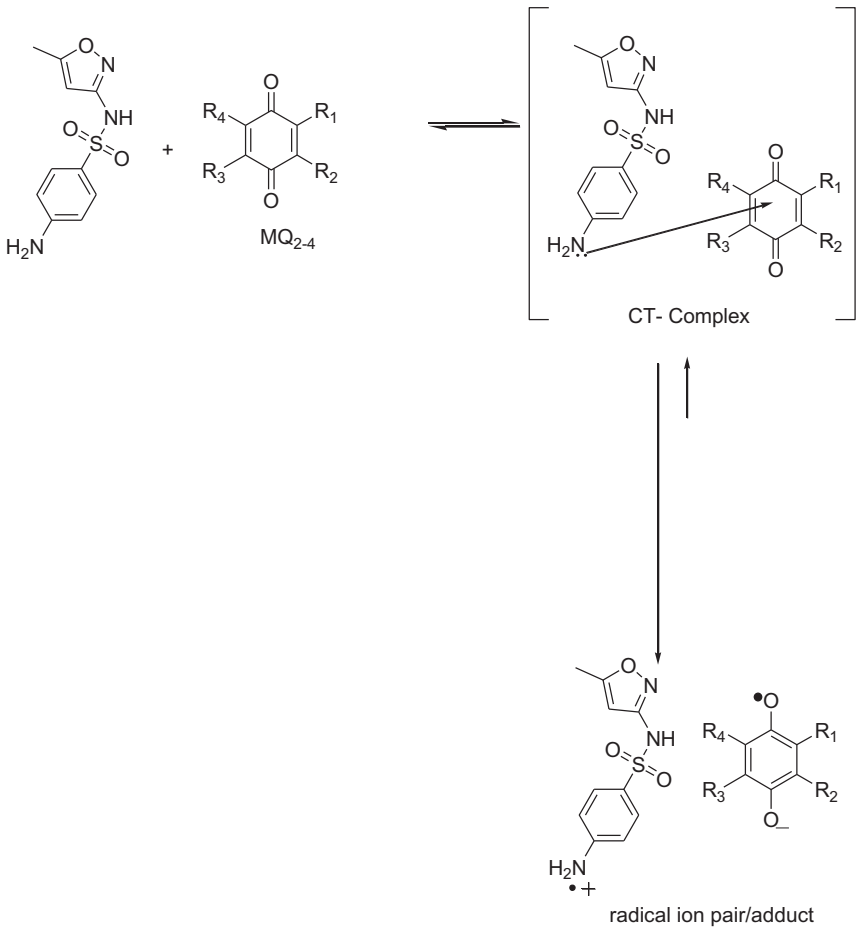
In all the SULF–MQ_{1-4} systems, an attempt was made to characterize the CT complexes formed in these reactions. For that the absorbance of the new bands were measured using constant acceptor concentration in ethanol and varying concentrations of the donor but always [D] ≫ [A]. A representative spectra is shown in Fig. 6S, [supplemental information]. The nature of the spectra indicated that the interactions between the donor and the acceptor are of CT type. The formation constants (K) and molar extinction coefficients (ε) of the CT complexes were determined spectrophotometrically using the Scott equation [30].

$$[D][A]/d = [D]/\varepsilon + (1/K\varepsilon) \quad (1)$$

where [D] and [A] are the initial molar concentrations of the donor and acceptor, respectively and d the absorbance. The values of K and ε are determined from the gradient and intercept of the linear plot of [D][A]/d against [D]. Representative Scott plots are shown in [(Fig. 5S) Supplemental information] and the values of K and ε thus determined are given in Table 7. The observed high values of K suggested that the formed CT complexes are of a strong type [28] and the linearity of the Scott plots further supported this result.

Fluorescence studies

The nature and magnitude of the interaction of drugs with receptors play an important role in the pharmacokinetics of the



Mechanism of interaction of SULF with MQ_{2-4}

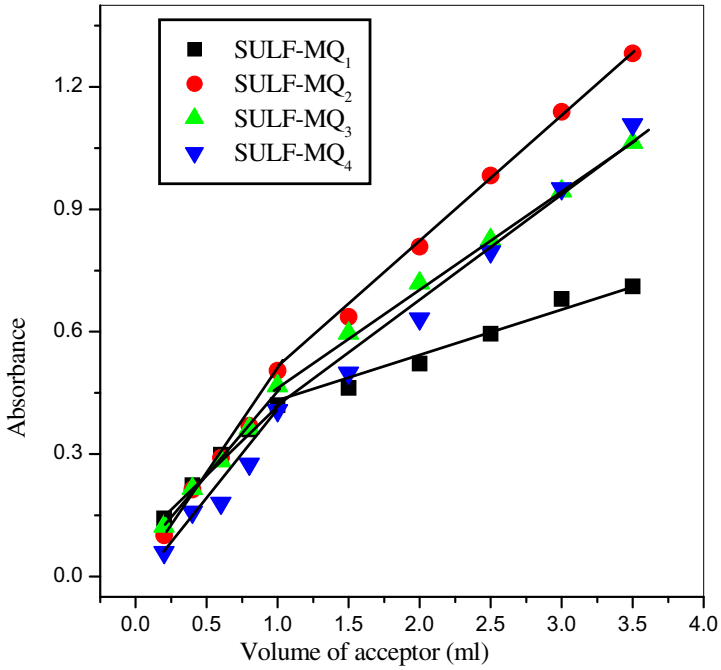


Fig. 2. Photometric titration plots for SULF with MQ_{1-4} in ethanol at 298 K.

Table 1
FT-IR wave numbers (cm^{-1}), intensity[a] and tentative band assignments for the SULF and its product with MQ_1.

SULF	MQ_1	SULF–MQ_1 product	Assignments
3469s		3432b	
3376s		3249s	ν(N—H);
3299s			
3012m		3006w	ν(C—H); aromatic,
2927m		2923m	ν(C—CH_3)
2854m		2854	ν(C—H)
	1684s	1745m	ν(C=O)
		1671	
1621		1617	ν(C=N); isoxazole
1596s	1575s	1581	ν(C=C)
1502			
1471		1486w	δ(N—H)
1365		1363m	ν(C—N)
1310		1308	$\nu(SO_2)$
	1270m	1265m	ν(O—CH_3)
	1099s	1091m	
	909m	896w	ν(C—Cl)
	778m	769	
	722m		

[a] s, Strong; m, medium; w, weak; ν, stretching; δ, bending.

Table 2
FT-IR wave numbers (cm^{-1}), intensity[a] and tentative band assignments for the SULF and its product with MQ_2.

SULF	MQ_2	SULF–MQ_2 product	Assignments
3469s		3465m	
3378s		3378s	ν(N—H);
3300s		3296m	
3012m		3006w	ν(C—H); aromatic,
2927m		2925m	ν(C—CH_3)
2854m		2857	ν(C—H)
	1663s	1660m	ν(C=O)
1621		1619	ν(C=N); isoxazole
1596s	1568s	1597	ν(C=C)
1502		1504w	δ(N—H)
1471		1471	
1365		1365m	ν(C—N)
1310		1313	$\nu(SO_2)$
	1270m	1267m	ν(O—CH_3)
	1060s	1062m	
	908m	887w	ν(C—Cl)
	734m	734	

[a] s, Strong; m, medium; w, weak; ν, stretching; δ, bending.

drugs. CT interaction is one of the non covalent binding forces in the drug–receptor mechanism. In the present study, an attempt was made to study the CT interaction of SULF with MQ_{1-4} by means of fluorescence study. Fluorescence spectra were recorded at room temperature in ethanol in the range of 300–700 nm using an excitation at 270 nm for SULF. It was observed that the fluorescence of SULF was quenched by MQ_{1-4} as a result of formation of CT complex. The experimental results indicated that the quenching efficiency increased with increasing concentration of the electron acceptor (Figs. 5 and 6) [(Figs. 7Sa, 7Sb), supplemental information] and with increasing time. The fraction of acceptors bound to the donors was determined by using the following Eq. (2).

$$\theta = (F_0 - F)/F_0 \quad (2)$$

where F and F_0 denote the fluorescence intensities of donor in the presence of acceptor and in the absence of acceptor, respectively. From the resulting values of θ, the association constant K_f for SULF–MQ_{1-4} systems was computed using the method described by Ward [31]. It has been shown that for equivalent and independent binding sites (Eq. (3)):

$$1/(1-\theta)K_f = [A_T]/\theta - n[D_T] \quad (3)$$

where n is the number of binding sites $[A_T]$, is the total acceptor concentration and $[D_T]$ is the total donor concentration. The plot $1/(1-\theta)$ versus $[A_T]/\theta$ is linear ($r > 0.97$, for SULF–MQ_{1-4} systems) indicating that under the experimental conditions all the binding

Table 3
FT-IR wave numbers (cm^{-1}), intensity[a] and tentative band assignments for the SULF and its complex with MQ_3.

SULF	MQ_3	SULF–MQ_3 complex	Assignments
3469s		3465m	
3376s		3378s	ν(N—H);
3299s		3296	
3012m		3006w	ν(C—H); aromatic,
2927m		2927m	ν(C—CH_3)
2854m		2854	ν(C—H)
	1674s	1679m	ν(C=O)
	1662	1660	
	1634	1623	
1621		1617	ν(C=N); isoxazole
1596s	1595s	1581	ν(C=C)
1502 1471		1504w 1467	δ(N—H)
1365		1367m	ν(C—N)
1310		1308	$\nu(SO_2)$
	1277m	1280m	ν(O—CH_3)
	1052s	1091m	
		1029m	
	940m 747m	927w 730	ν(C—Cl)

[a] s, Strong; m, medium; w, weak; ν, stretching; δ, bending.

Table 4
FT-IR wave numbers (cm^{-1}), intensity[a] and tentative band assignments for the SULF and its complex with MQ_4.

SULF	MQ_4	SULF–MQ_4 complex	Assignments
3469s		3465s	
3376s		3365s	ν(N—H);
3299s		3301	
3012m		3006w	ν(C—H); aromatic,
2927m		2927m	ν(C—CH_3)
2854m		2854	ν(C—H)
	1666s	1621m	ν(C=O)
1621		1598	ν(C=N); isoxazole
1596s	1606s	1598	ν(C=C)
1502		1506	δ(N—H)
1471		1471w	
1365		1367m	ν(C—N)
1310		1311	$\nu(SO_2)$
	1276m	1267m	ν(O—CH_3)
	1059s	1025m	

[a] s, Strong; m, medium; w, weak; ν, stretching; δ, bending.

sites are equivalent and independent. The value of K_f obtained, from the plots, for SULF–MQ_1, SULF–MQ_2, SULF–MQ_3 and SULF–MQ_4 systems are found to be 3.6×10^3, 2.4×10^3, 2.2×10^3, and 0.9×10^3 mol L^{-1}, respectively. The standard Gibbs energy change ΔG° was calculated from K_f values using the relation $\Delta G^\circ = -2.303\,RT \log K_f$. The ΔG° values for SULF–MQ_{1-4} systems were found to be −19.6, −18.7, −18.4 and −16.4 kJ mol^{-1} respectively, indicating that the interaction between the drug and the acceptors is exothermic and spontaneous in nature.

Fluorescence quenching can occur by different mechanisms viz. static or dynamic or both. Stern–Volmer equation (Eq. (4)) is useful in understanding the mechanism of fluorescence quenching.

$$F_0/F = 1 + K_{SV}[Q] \quad (4)$$

where F_0 is the initial fluorescence intensity measured in the absence of quencher and F is that in the presence of quencher concentration [Q]. The Stern–Volmer constant K_{SV} is obtained by plotting F_0/F against [Q]. In all the cases, linear Stern–Volmer relationship observed (Fig. 7) indicated that either static or dynamic quenching is dominant [32,33].

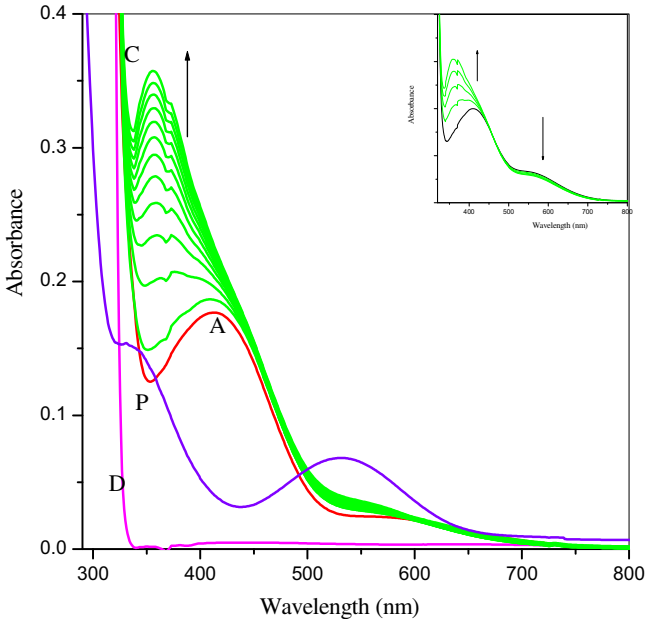


Fig. 3. Electronic absorption spectra of SULF with MQ_1 in ethanol at 298 K (D: Donor; A: Acceptor; C: complex; P: product) inset: clear isosbestic point at 456 nm.

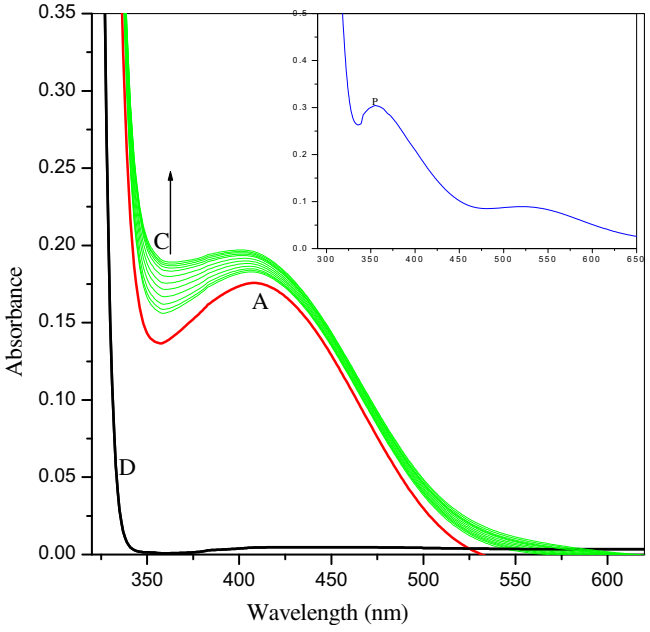


Fig. 4. Electronic absorption spectra of SULF with MQ_3 in ethanol at 298 K (D: Donor; A: Acceptor; C: complex; P: product).

The relationship between the fluorescence quenching intensity and the concentration of quenchers can be described by the following equation.

$$\log(F_0 - F)/F = \log K_A + n \log[Q] \quad (5)$$

where K_A is the binding constant and n is the number of binding sites per donor molecule [34]. In the present study, in all the cases, a plot of log $(F_0–F)/F$ versus log [Q] is linear [(Fig. 8S Supplemental information 10, $r > 0.98$)] and the binding constant values computed are collected in Table 8. The results indicated that, the

Table 5
Effect of concentration of the donor and acceptors on the rate of the interaction at 298 K.

[D] (10^{-2} M)	[A] (10^{-4} M)	k_1 (10^{-4}), s^{-1}				k_2 s^{-1} mol^{-1} dm^3			
		SULF–MQ_1	SULF–MQ_2	SULF–MQ_3	SULF–MQ_4	SULF–MQ_1	SULF–MQ_2	SULF–MQ_3	SULF–MQ_4
0.5	5.5	1.65	1.24	0.92	0.66	3.4	2.5	1.8	1.3
0.7	5.5	2.45	1.84	1.35	0.85	3.5	2.6	1.9	1.2
0.9	5.5	3.12	2.42	1.69	1.02	3.4	2.6	1.8	1.2
1.1	5.5	3.76	2.94	2.03	1.32	3.4	2.6	1.8	1.2
1.1	4.4	3.06	2.14	1.53	1.17				
1.1	3.3	3.06	2.14	1.53	1.17				
1.1	2.2	3.06	2.14	1.53	1.17				

Table 6
Kinetic and thermodynamic parameters for the interaction of SULF with MQ_{1-4} in ethanol.

Systems	λ	k_1 (10^{-4}) s^{-1}			$\Delta H^{\#}$	$-\Delta S^{\#}$	$\Delta G^{\#}$
	(nm)	298	305	313 K			
SULF–MQ_1	346	3.76	4.70	5.60	17	250	93
SULF–MQ_2	355	2.98	3.42	3.78	18	253	93
SULF–MQ_3	355	2.03	2.46	3.03	19	255	94
SULF–MQ_4	355	1.32	1.92	2.12	22	246	94

$\Delta H^{\#}$ kJ mol^{-1}; $\Delta S^{\#}$ J K^{-1} mol^{-1}; $\Delta G^{\#}$ kJ mol^{-1}.

Table 7
Formation constants of the CT complexes formed between SULF and MQ_{1-4} in ethanol at 298 K.

Property	SULF–MQ_1	SULF–MQ_2	SULF–MQ_3	SULF–MQ_4
K (dm^3 mol^{-1}) Absorption method	2980	2390	1810	1220
ε (dm^3 mol^{-1} cm^{-1}) Absorption method	6410	5550	3215	1404
K_f (mol L^{-1}) Emission method	3615	2441	2207	939
Stern–Volmer constant K_{SV} Emission method	3891	2577	2148	1918

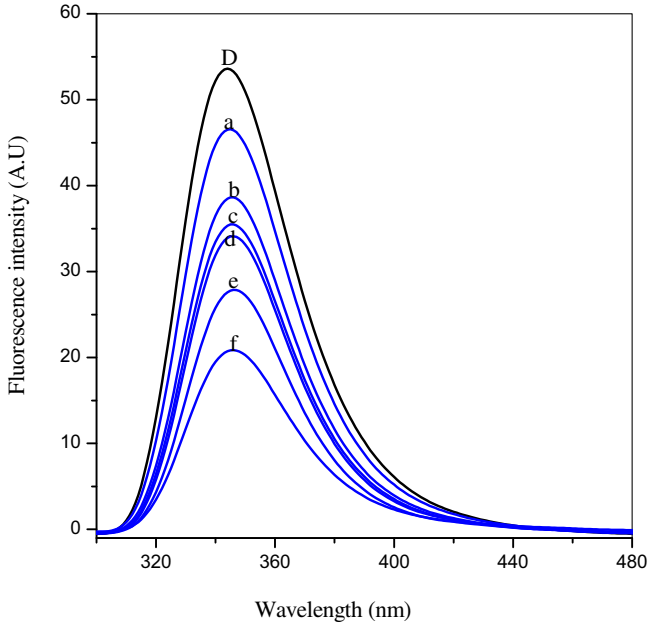


Fig. 5. Variation of fluorescence spectra of SULF–MQ_1 system in ethanol at fixed concentration [D] = {2.8125×10^{-3} (curve D)} and variable concentration of [A] $\times$ 10^{-4} = {1.3875 (curve a)}, 2.775 (curve b), 4.1625 (curve c), 5.55 (curve d), 6.9375 (curve e), 8.325(curve f) mol L^{-1} at 298 K.

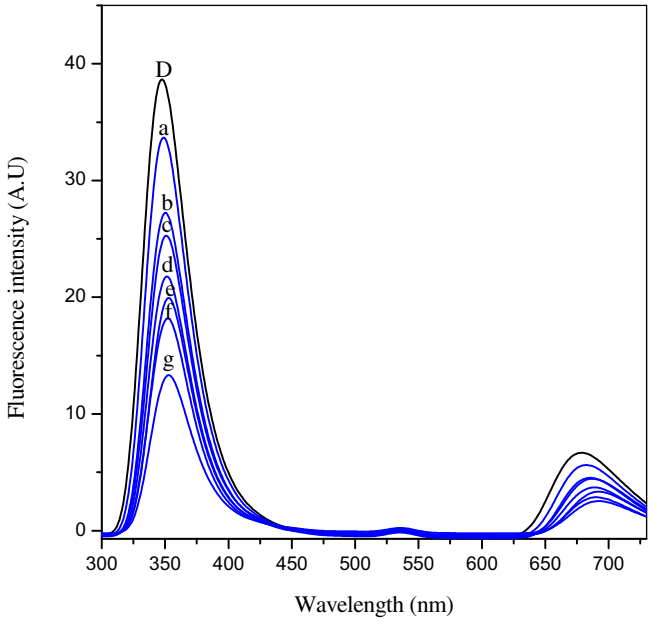


Fig. 6. Variation of fluorescence spectra of SULF–MQ_2 system in ethanol at fixed concentration [D] = {2.8125×10^{-3} (curve D)} and variable concentration of [A] $\times$ 10^{-4} = {1.3875 (curve a)}, 2.775 (curve b), 4.1625 (curve c), 5.55 (curve d), 6.9375 (curve e), 8.325 (curve f), 9.7125 (curve g) mol L^{-1} at 298 K.

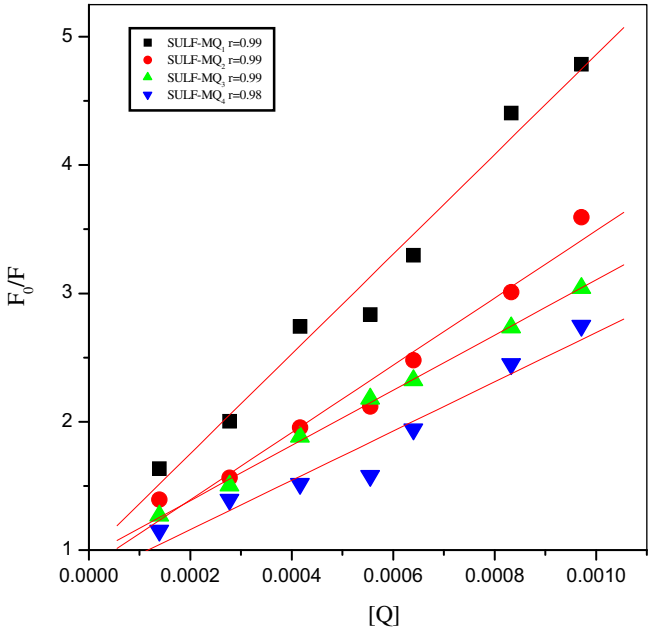


Fig. 7. Stern–Volmer plots for the fluorescence quenching of SULF with the acceptors MQ_{1-4} in ethanol at 298 K.

Table 8
Binding constants (K_A) and number of binding sites (n) for SULF–MQ_{1-4} systems in ethanol.

Acceptors	K_A (mol^{-1} L)	n
SULF–MQ_1	3.2×10^3	1.1
SULF–MQ_2	2.6×10^3	0.9
SULF–MQ_3	1.7×10^3	0.9
SULF–MQ_4	0.6×10^3	0.8

Table 9
Reversible voltammetric parameters for the acceptors.

Acceptor	E_{pc}	E_{pa}	$E_{1/2}$	i_{pa}/i_{pc}
MQ_1	−0.12	−0.02	−69	1.1
MQ_2	−0.29	−0.18	−232	0.9
MQ_3	−0.43	−0.33	−383	1.1
MQ_4	−0.62	−0.50	−556	1.1

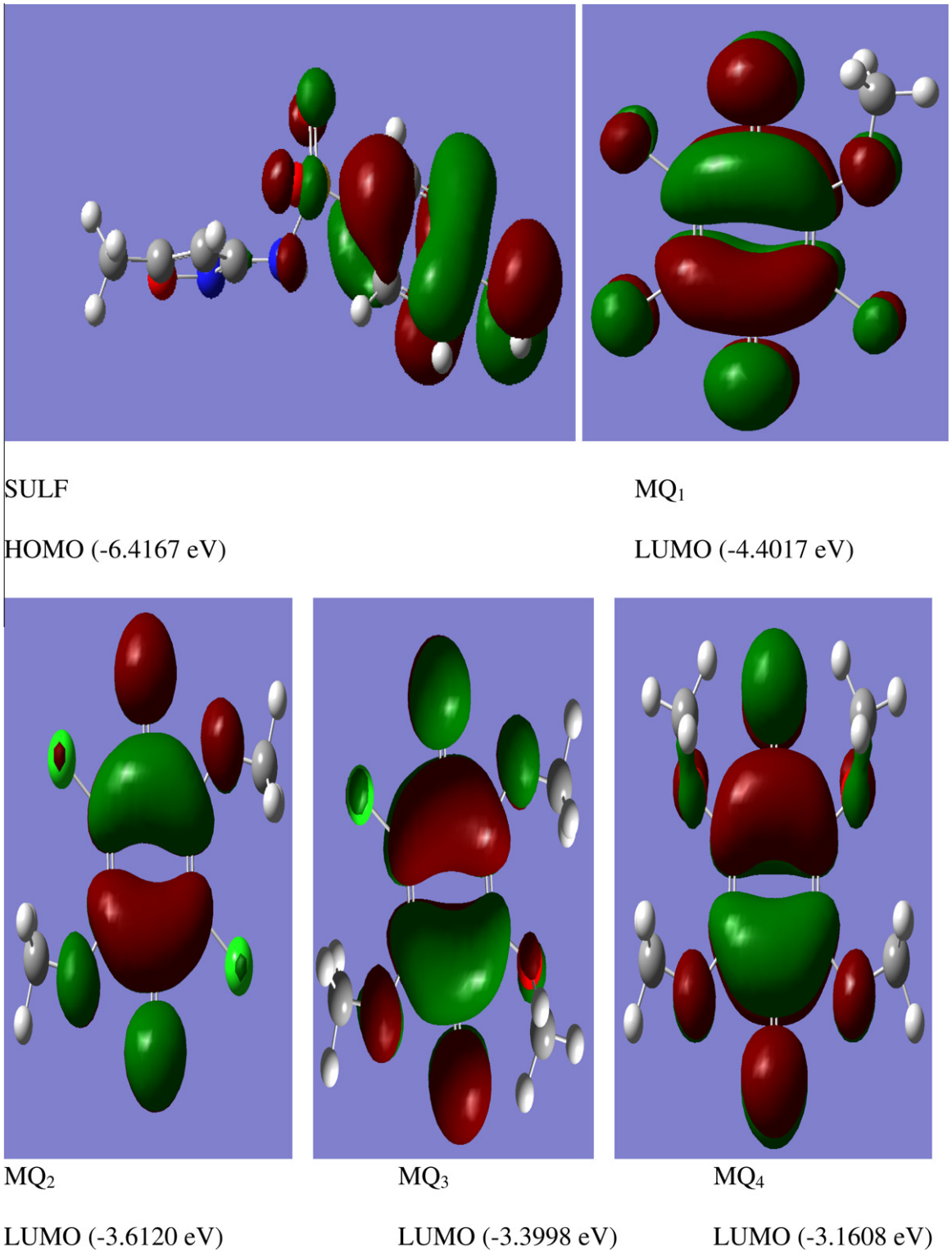


Fig. 8. The optimized structures of the SULF and MQ_{1-4} along with frontier orbitals.

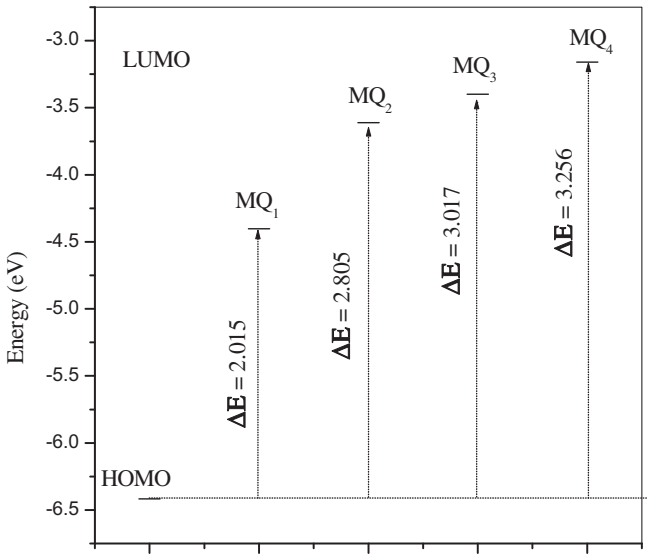


Fig. 9. Energy of HOMO of the donor and LUMO of the acceptors.

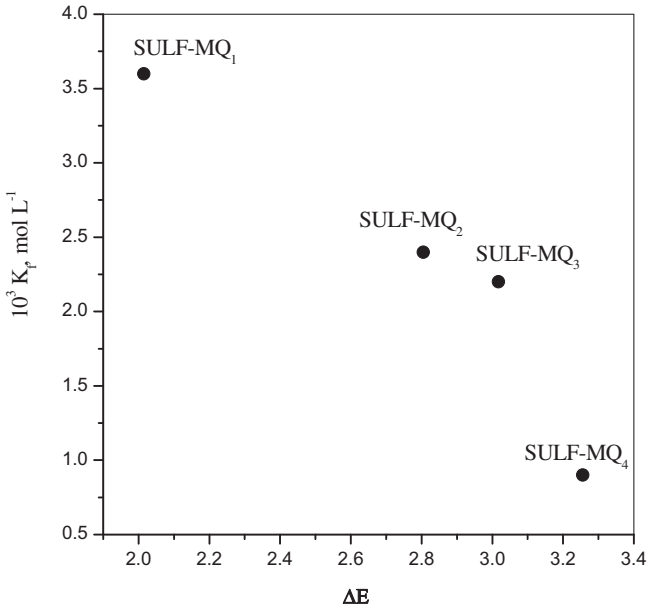


Fig. 10. Correlation between association constant K_f and ΔE.

binding constant value decreased from MQ_1 to MQ_4, i.e. the magnitude of binding constant is in the order of SULF–MQ_1 > SULF–MQ_2 > SULF–MQ_3 > SULF–MQ_4. These observations are in corroboration with the results of absorption spectral studies as enumerated earlier in this paper. That is the formation constant computed using absorption spectral data follows the same order (Table 6). Also, the rate constant for the interaction, in these cases, decreased with an increase in methoxy groups in the acceptor (Tables 6 and 8). The value of *n*, for the systems, is nearly constant in ethanol indicating the presence of equivalent binding sites.

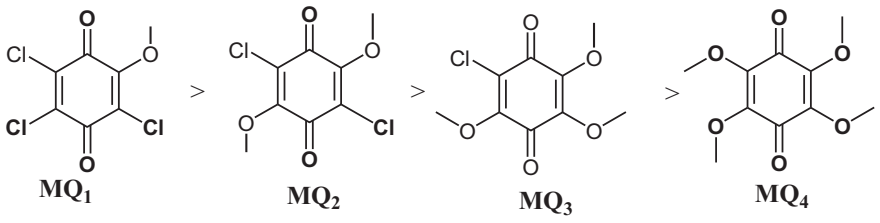
Electrochemical studies

The redox potentials of the acceptors were measured by cyclic voltametry at room temperature using a conventional two-compartment three electrode cell with a 3 mm Glassy Carbon (GC) disk as working electrode and 0.1 M tetrabutylammonium perchlorate as the electrolyte in acetonitrile. For all the acceptors, the voltagrams, recorded in the potential range from +1.5 V to −0.8 V versus Ag/AgCl are shown in [(Fig. 9S) Supplemental information]. To compare the electron accepting properties of these acceptors the electrochemical data of the first wave alone has been considered here. The half wave potential values ($E_{1/2}$) were evaluated from the voltammograms obtained at a sweep rate of 100 mV s^{-1}, $E_{1/2} = (E_{pa} + E_{pc})/2$, where E_{pa} and E_{pc} correspond to anodic and cathodic peak potentials, respectively. In all the cases, the ratio of i_{pa}/i_{pc}, was found to be nearly unity (Table 9) indicating reversible nature of the systems [15,16]. The results obtained indicated that the $E_{1/2}$ values become more negative from MQ_1 to MQ_4. That is the electron accepting property (reduction) of MQ_4 is relatively low when compared to MQ_1 or in other words MQ_4 is comparatively a weaker acceptor. This may be due to the fact that progressive replacement of electron withdrawing chlorine atom (−I effect) by electron releasing methoxy group (+M effect) rendered the quinone increasingly electron rich and consequently make it as a weak acceptor. This observation corroborates well with the results obtained in the spectral and kinetic studies enumerated above.

Theoretical calculations

To understand the foregoing experimental observations on the CT complex formed between SULF and the acceptors, we have performed the optimization of SULF, MQ_{1-4} using Density Functional Theory with the Backle3LYP hybrid functional, by using a basis set of 6-31G. Computations have been performed using the Gaussian 03 Revision D.01 program package [35]. The optimized geometry of the donor along with HOMO and the acceptors along with LUMO are depicted in Fig. 8. In the case of SULF, the HOMO is concentrated on the —NH_2 group and in the case of the acceptors the LUMO resides on the quinone ring.

The energies of the frontier orbitals of the donor and the acceptors along with the energy corresponds to the CT transition, ΔE(=$HOMO_{SULF}$–$LUMO_{acceptor}$) [36,37], for all the systems are shown in Fig. 9. It is evident from the figure that the ΔE depends on the nature of the substituent present in the quinone. Also, a good linear correlation obtained between the theoretical energy gap values and the experimentally determined stability constant values (Fig. 10) indicated that the strength of the acceptor decrease in the order:



Conclusions

The charge transfer properties of 1,4-benzoquinones possessing varying number of chloro and methoxy substituents were, for the first time, investigated. Various spectral techniques have been employed to characterize the final product of these interactions. In all the cases, the stoichiometry of the CT interaction was found to be 1:1. The trends in the rate constants and formation constants showed that the strength of the complex formation is in the order of SULF–MQ_1 > SULF–MQ_2 > SULF–MQ_3 > SULF–MQ_4. The half wave potential values ($E_{1/2}$) for the one electron reduction of these acceptors indicated that the electronegativity of the acceptors increased from MQ_1 to MQ_4. The observed equilibrium, kinetic and electrochemical properties of these acceptors were found to be well supported by *ab initio* DFT calculations.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.saa.2013.01.016.

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