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Spectroscopic Studies on the Utility of Charge Transfer Interactions for Determination of Phenytoin Sodium[1]

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Abstract—Electron donor acceptor complexes (EDA) of the phenytoin sodium (Pyn) as a rich donor with different π-acceptors like *p*-chloranil (*p*-CHL), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), tetracyanoquinodimethane (TCNQ), chloranilic acid (CLA), *N*-bromosuccinimide (NBS) and picric acid (PA) have been synthesized. Spectroscopic and physical data such as formation constant (K_{CT}), molar extinction coefficient (ε_{CT}), standard free energy (ΔG^0), oscillator strength (f), transition dipole moment (μ), resonance energy (R_N) and ionization potential (I_p) have been determined. Based on the elemental analysis and photometric titrations the CT-complexes were found to have 1 : 1 stoichiometry.

Keywords: phenytoin sodium; charge transfer complexes; *p*-CHL, DDQ, TCNQ, CLA, PA

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INTRODUCTION

Phenytoin (Pyn; Fig. 1) is a hydantoin-derivative anticonvulsant drug used primarily in the treatment of complex partial seizures and generalized tonic-clonic seizures. Phenytoin is believed to protect against seizures by causing voltage-dependent block of voltage-gated sodium channels [1]. Phenytoin also can be used as an antiarrhythmic [2].

Charge-transfer complexes are known to take part in many chemical reactions like addition, substitution and condensation [3, 4]. These complexes have great attention for non-linear optical materials and electrical conductivities [5–8]. Electron donor-acceptor CT-interaction is also important in the field of drug-receptor binding mechanism [9], in solar energy storage [10] and in surface chemistry [11] as well as in many biological fields [12]. On the other hand, the CT reactions of certain π- acceptors have successfully been utilized in pharmaceutical analysis [13]. For these wide applications extensive studies on CT-complexes of π-acceptors have been performed [14]. Charge-transfer complexes of organic species are intensively studied because of their special type of interaction, which is accompanied by transfer of an electron from the donor to the acceptor [15, 16]. Also, protonation of the donor from acidic acceptors are general route for the formation of ion pair adducts [17–19]. The π-acceptors have numerous applications as analytical reagents for ex., they have been used for the spectrophotometric determination of many drugs in pharmaceutical formulations [20–26]. To the best of our knowledge, no wide spectroscopic studies have been performed on the interactions between phenytoin

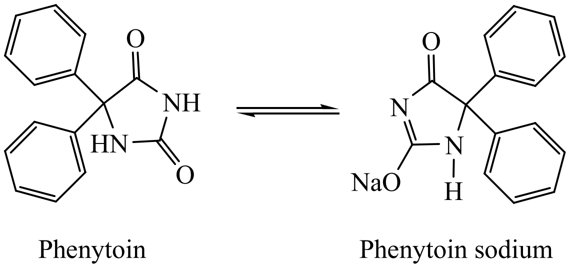

Fig. 1. Structures of phenytoin and its sodium salt.

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[1] The text was submitted by the authors in English.

2,3,5,6-Tetrachlorocyclohexa-2,5-diene-1,4-dione
(*p*-Chloranil; CHL)

2,3-Dichloro-5,6-dicyano-1,4-benzoquinone
(DDQ)

2,4,6-Trinitrophenol
(Picric acid; PA)

Tetracyanoquinodimethane
(TCNQ)

2,5-Dichloro-3,6-dihydroxy-1,4-benzoquinone
(Chloroanilic acid; CLA)

N-Bromosuccinimide
(NBS)

Fig. 2. Structures of π-acceptors.

sodium and different classes of π-acceptors. This paper describes spectrophotometric determination of phenytoin sodium based on the charge transfer interaction between π-acceptors (Fig. 2) and the sp^3 nitrogen atom of secondary amine group of Pyn as a good π-electron donor to form charge-transfer complexes.

EXPERIMENTAL

Phenytoin sodium was received from Egyptian International Pharmaceutical Industries Company (EIPICO). *p*-Chloranil (*p*-CHL), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), tetracyano quinodimethane (TCNQ), chloranilic acid (CLA), *N*-bromosuccinimide (NBS) and picric acid (PA) were obtained from Aldrich and Fluka. All chemicals were of analytical grade and were used without further purification.

The elemental analyses of carbon, hydrogen and nitrogen contents were performed using a Perkin Elmer CHN 2400 instrument. The molar conductivities of freshly prepared 1.0×10^{-3} M DMSO solutions were measured using Jenway 4010 conductivity meter. The electronic absorption spectra were recorded in methanol within 900-200 nm range using a Perkin-Elmer Precisely Lambda 25 UV-Vis double beam Spectrometer fitted with a quartz cell of 1.0 cm path length. Infrared spectra in the 4000–400 cm^{-1} range were recorded in KBr discs using a Shimadzu FT-IR Spectrometer with 30 scans and $2 cm^{-1}$ resolution, while Raman laser spectra of samples were measured on the Bruker FT-Raman instrument with 50 mW laser. ^1H NMR spectra were recorded on a Bruker 600 MHz spectrometer using TMS as the internal standard. DTG-TG thermograms were obtained on a Shimadzu TGA-50H. Samples in solid form were placed in platinum pans with a pierced lid, and heated at 30°C min^{-1} rate under nitrogen flow. Scanning electron microscopy (SEM) images and Energy Dispersive X-ray Detection (EDX) were taken on a Joel JSM-6390 equipment, with an accelerating voltage of 20 KV. The X-ray diffraction patterns were recorded on Bruker Advanced 8 X-ray powder diffraction machine; target CuK_α radiation, step scan mode with step = 0.05° and counting time 3.0 s/step.

Synthesis of solid phenytoin sodium charge transfer complexes. The six solid phenytoin sodium charge transfer complexes were synthesized as a yellow, red, brownish red, greenish blue, orange and white solids for the PA, DDQ, CLA, TCNQ, *p*-CHL, and NBS complexes, respectively, by mixing 0.275 g (1 mmol) of phenytoin sodium in 20 mL of methanol with 1 mmol of each acceptor dissolved in 20 mL of chloroform. All mixtures were stirred for 1 h at room temperature and the solid products were filtered off, washed with minimum amounts of chloroform and dried under vacuum over anhydrous $CaCl_2$.

Analytical data. **[(Pyn)(PA)].** M_W = 503.35; Calculated, %: C 50.11; H 2.80; N 13.91, Found, %: C, 49.79; H 2.72; N 13.84. **[(Pyn)(DDQ)].** M_W = 501.25; Calculated, %: C 55.11; H 2.21; N 11.18, Found, %: C, 55.03; H 2.12; N 11.14. **[(Pyn)(CLA)].** M_W = 483.23; Calculated, %: C 52.20; H 2.71; N 5.80, Found, %: C, 51.95; H 2.62; N 5.72. **[(Pyn)(TCNQ)].** M_W = 478.44; Calculated, %: C 67.78; H 3.16; N 17.57, Found, %: C, 67.55; H 3.09; N 17.33. **[(Pyn)(*p*-CHL)].** M_W = 520.12; Calculated, %: C 48.49; H 2.13; N 5.39, Found, %: C, 48.35; H 2.11; N 5.18. **[(Pyn)(NBS)].** M_W = 452.23; Calculated, %: C 50.46; H 3.34; N 9.29, Found, %: C, 50.12; H 3.28; N 9.11.

RESULTS AND DISCUSSIONS

Spectrophotometric titrations at 440, 421, 527, 743, 403, and 302 nm were performed for the reactions of Pyn with PA, DDQ, CLA, TCNQ, *p*-CHL, and NBS, respectively, using the Jenway 6405 spectrophotometer as follows: A 0.25, 0.50, 0.75, 1.00, 1.50, 2.00, 2.50, and 3.00 mL aliquot of a standard solution (5.0×10^{-4} M) of the appropriate acceptor (PA, DDQ, CLA, TCNQ, *p*-CHL, and NBS) in methanol was added to 1.00 mL of 5.0×10^{-4} M phenytoin sodium solution in methanol. The total volume of the mixture was 5 mL. The concentration of Pyn (C_d^0) in the reaction mixture was thus fixed at 1.0×10^{-4} M while the concentration of π-acceptors (C_a^0) varied from 0.25×10^{-4} M to 3.00×10^{-4} M. These concentrations produce [donor]:[acceptor] ratios from 3 : 1 to 1 : 3. The absorbance of each charge transfer complexes was measured and plotted (Fig. 3) as a function with the ratio of (C_d^0) : (C_a^0) according to a known method [27]. It was of interest to observe that the solvent has a pronounced effect on the spectral intensities of the formed CT complexes. To study this solvent effect in a quantitative manner, it was necessary to calculate the values of the equilibrium constant, *K*, the molar absorptivity ε, and the oscillator strength, *f*, of the Pyn complexes in the respective solvent. The 1 : 1 modified Benesi–Hildebrand equation [28] was used in the calculations:

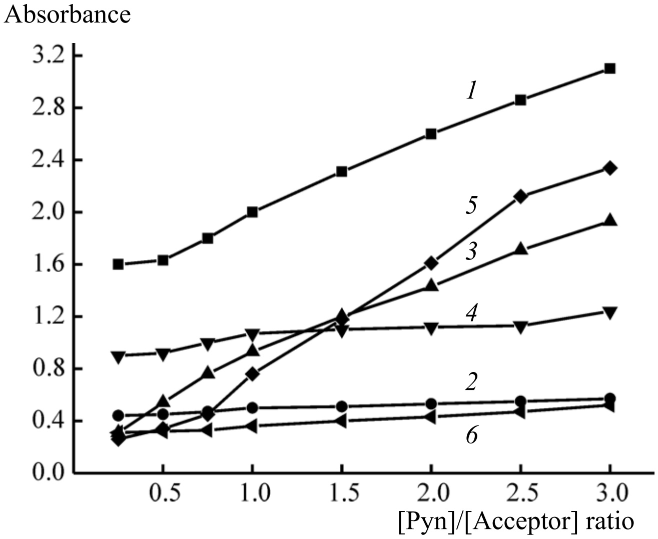


Fig. 3. Absorbance of phenytoin sodium CT complexes: (*1*) PA, 440 nm, (*2*) DDQ, 421 nm, (*3*) CLA, 527 nm, (*4*) TCNQ, 743 nm, (*5*) *p*-CHL, 403 nm, and (*6*) NBS, 302 nm.

$$\frac{C_a^0 C_d^0 l}{A} = \frac{1}{K\varepsilon} + \frac{C_a^0 + C_d^0}{\varepsilon}, \qquad (1)$$

where C_a^0 and C_d^0 are the initial concentrations of the acceptor (PA, DDQ, CLA, TCNQ, *p*-CHL, and NBS) and the donor phenytoin sodium, respectively, and A is the absorbance of the charge transfer bands at 440, 421, 527, 743, 403, and 302 nm for PA, DDQ, CLA, TCNQ, *p*-CHL, and NBS, respectively. When the $C_a^0 C_d^0/A$ values for each 1 : 1 charge transfer complex are plotted against the corresponding $C_a^0 + C_d^0$ values, straight lines are obtained with a slope of 1/ε and intercept of 1/*K*ε.

The physical spectroscopic data like formation constant (K_{CT}), molar extinction coefficient (ε_{CT}), standard free energy (ΔG^0), oscillator strength (*f*), transition dipole moment (μ), resonance energy (R_N) and ionization potential (I_p) were calculated for methanol solutions at 25°C, and the different acceptors were found to have a pronounced effect towards the interaction with phenytoin sodium. These calculations can be summarized as follows.

Table 1. Spectroscopic data for the phenytoin CT complexes.

Complex	λ_{max}, nm	E_{CT}, eV	K, L/mol	ε_{max}, L mol^{-1} cm^{-1}	f	μ	I_p	R_N	ΔG^0 (25°C), J/mol
PA	440	2.83	24000	12000	5.18	22	9.24	0.285	–24993
DDQ	421	2.95	33000	11000	4.75	21	9.39	0.281	–25782
CLA	527	2.36	42000	40000	17.28	44	8.66	0.435	–20674
TCNQ	743	1.67	52000	51500	22.24	59	7.82	0.335	–26909
p-CHL	403	3.09	22000	18000	7.77	26	9.59	0.397	–24777
NBS	302	4.12	48000	36000	15.55	32	10.08	0.730	–26710

Oscillator strength. The oscillator strength f was obtained from the approximate formula from [29].

$$f = (4.319 \times 10^{-9})\varepsilon_{max}\nu_{1/2}, \quad (2)$$

where $\nu_{1/2}$ is the band-width for half-intensity in cm^{-1} and ε_{max} is the maximum extinction coefficient of the CT-band. The oscillator strength values are given in Table 1. The data resulted reveals several aspects. (1) The [(Pyn)(A)] (where A= PA, DDQ, CLA, TCNQ, *p*-CHL and NBS) charge transfer systems show high values of both formation constant (K) and molar absorptivity (ε). This high value of (K) reflects the high stability of the phenytoin sodium charge transfer complexes as a result of the expected high rich donation of the Pyn which contains two nitrogen atoms; (2) the different values of the oscillator strength, f, increases with increasing in the dielectric constant (D) of the solvent. This result could be explained on the basis of competitive solvent interactions with the acceptors [30, 31].

Transition dipole moment. The transition dipole moment (μ) of the phenytoin sodium charge transfer complexes, Table 1, have been calculated from the equation 3 [32];

$$\mu(\text{Debye}) = 0.0958[\varepsilon_{max}\nu_{1/2}/\nu_{max}]^{1/2}. \quad (3)$$

The transition dipole moment is useful for determining if transitions are allowed, that the transition from a bonding π orbital to an antibonding π^* orbital is allowed because the integral defining the transition dipole moment is nonzero.

Ionization potential. The ionization potential (I_p) of the phenytoin sodium charge transfer complexes were calculated using empirical equation 4 derived by Aloisi and Piganatro [33, 34];

$$I_p(\text{eV}) = 5.76 + 1.53\times 10^{-4}\nu_{CT}, \quad (4)$$

where, ν_{CT} is the wavenumber in cm^{-1} corresponding to the charge transfer band formed from the interaction between donor and acceptor. The electron donating power of a donor molecule is measured by its ionization potential which is the energy required to remove an electron from the highest occupied molecular orbital.

Energy of the charge-transfer complexes. The energy of the charge-transfer complexes E_{CT} of the phenytoin sodium charge transfer complexes were calculated using Eq. (5) [35]:

$$E_{CT} = (h\nu_{CT}) = 1243.667/\lambda_{CT}\,(\text{nm}), \quad (5)$$

where, λ_{CT} is the wavelength of the complexation band.

Resonance energy. Determination of resonance energy (R_N) [36] theoretically derived from Eq. (6):

$$\varepsilon_{max} = 7.7 \times 10^{-4} / [h\nu_{CT}/[R_N] - 3.5], \quad (6)$$

where ε_{max} is the molar absorptivity of the phenytoin sodium charge transfer complexes at maximum CT band, ν_{CT} is the frequency of the CT peak and R_N is the resonance energy of the complex in the ground state, which, obviously is a contributing factor to the stability constant of the complex (a ground state property). The values of R_N for the CT complexes under study are given in Table 1.

Free energy. The standard free energy changes of complexation (ΔG^0) were calculated from the formation constants by the Eq. (7) [37];

$$\Delta G^0 = -2.303RT\log K_{CT}, \quad (7)$$

where ΔG^0 is the free energy change of the phenytoin sodium charge transfer complexes (kJ/mol), R is the gas constant (8.314 J mol^{-1} K), T is the temperature in Kelvin degrees (273°C) and K_{CT} is the formation constant of the complexes (L/mol) in different solvents at room temperature.

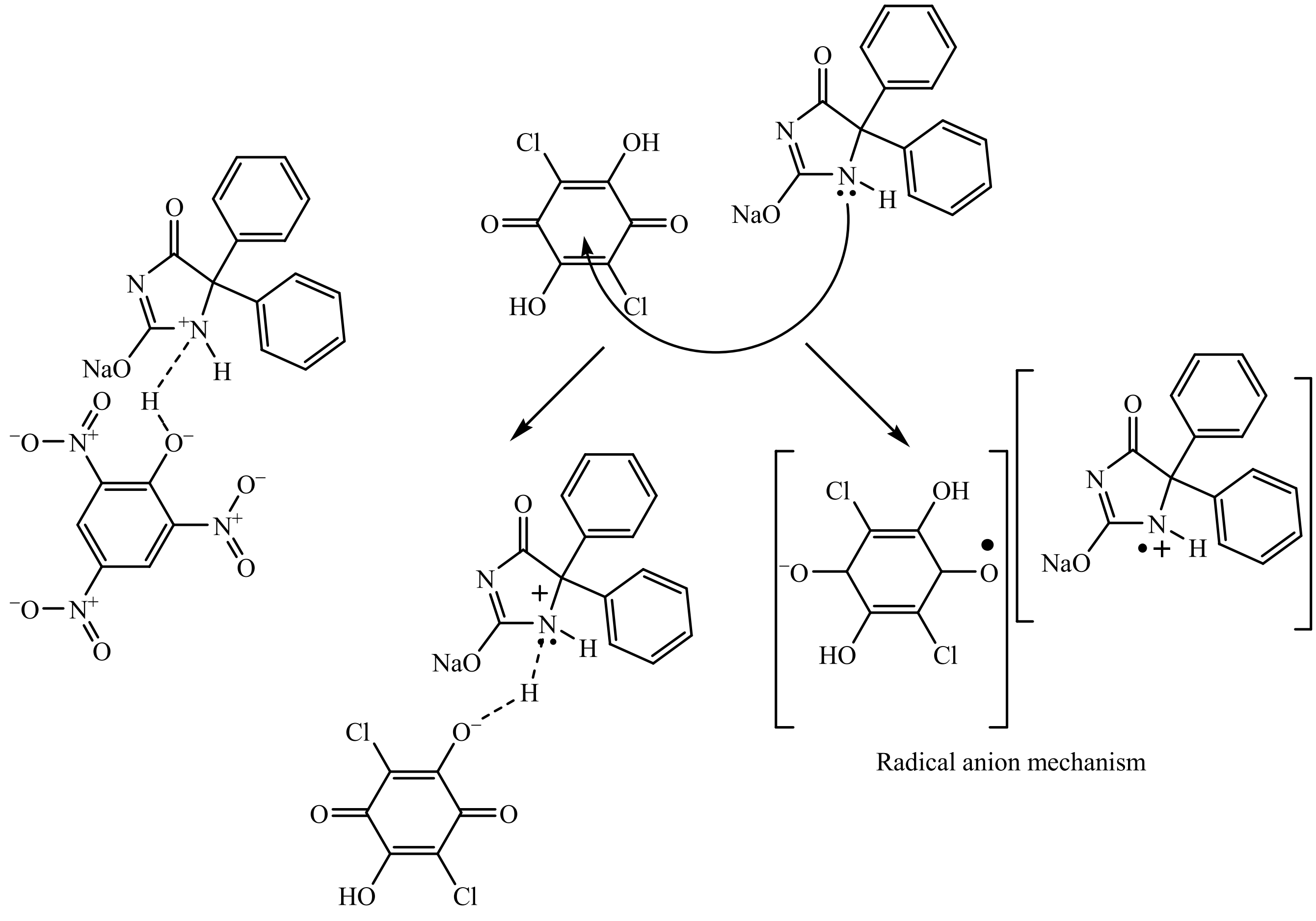
Table 2. Characteristic infrared and Raman frequencies (cm^{-1}) and tentative assignments of CLA, PA, and their Pyn charge transfer complexes

CLA	PA	Pyn	[(Pyn)(acceptor)]		Assignments
			CLA	PA	
–	–	–	3526, 3446	3612, 3544	Hydrogen bond
3235	2980, 2872	3309, 3059 3023, 2925	3216, 3272 3080, 3037 (3068)	3272, 3202 3086, (3068)	ν(O–H) + ν(N–H) ν(C–H)
1664, 1630	1861, 1632 1608	1690	1776, 1714	1776, 1738	ν(C=O) + ν(NO_2) ν(C=C)
–	–	1379	1367 (1353)	1342 (1353)	ν(C–N); –NH
752, 690	781, 732 703	761, 700	743, 700	793, 743	C–H out-of-plane

PA and CLA charge transfer complexes. The spectrum of the Pyn/CLA system shows strong absorption band at 527 nm with red shift due to the formation of [(Pyn)(CLA)] charge transfer complex, while the corresponding absorption bands associated with the formation of the complex [(Pyn)(PA)] is observed at 440 nm (red shift) in the spectrum of Pyn/PA system. Furthermore, photometric titration measurements based on the characteristic absorptions bands of the charge transfer complexes confirmed the molar ratios of the two mentioned complexes. Generally, these complexes show high values of both the formation constant (*K*) and the molar absorptivity (ε). These high values of *K* confirm the expected high stabilities of the formed charge transfer complexes as a result of the expected high donation of the phenytoin sodium. The equilibrium constants are strongly dependent on the nature of the used acceptor including the type of electron withdrawing substituents to it such as nitro and halogen groups.

The band assignments of infrared and Raman laser spectra of the donor (Pyn) as well as the formed charge transfer complexes Pyn/CLA and Pyn/PA are reported in Table 2. However, the appearance of a group of IR and Raman spectral bands in the spectra of the charge transfer complexes supports the conclusion that a deformation of the electronic environment of phenytoin sodium is occurred by accepting protons from CLA or PA acceptors. The infrared spectra of both charge transfer complexes are characterized by a group of bands appearing in the region >3400 cm^{-1}, which are not appearing in the spectra of the free donor and acceptors. The blue shifts of stretching vibration bands of both –NH and C–N to lower wavenumbers from 3309 and 1379 cm^{-1} in case of Pyn free donor to 3272–3203 cm^{-1} and 1367–1342 cm^{-1} are assigned to the involvement of –NH group in the charge transfer complexation. These bands are attributed to the stretching vibration of the intermolecular hydrogen bond [38]. These results caused by the protonation of the $^{+}$NH group of the donor through proton transfer from the acidic center on the PA or CLA acceptor. The shift of the IR bands of the acceptor part to lower wavenumbers and those of the donor part to higher values reflects a donor to acceptor charge transfer of *n*–π* interaction, $D_{\mathrm{HOMO}} \rightarrow D_{\mathrm{LUMO}}$ transition [39]. The equivalent conductance values at 1.0 × 10^{-4} molar concentrations indicated that these complexes have a small limit of conductivity. The data of conductivity confirms that these complexes have a positive ($^{+}$NH) and negative charge (O^{-} of acidic in chloranilic or picric acid) resulted from charge transfer transition. The low conductivity values for the two CT-complexes may be due to intermolecular hydrogen bond formation. Reaction mechanism is based on the reaction of the basic nitrogen of phenytoin sodium base as *n*-donor with the CLA π-acceptor to form charge transfer complex which subsequently dissociate into radical anions depending on the polarity of the solvent used. In polar solvents, such as methanol, complete electron transfer from the donor to the acceptor moiety takes place with the formation of intensely colored radical anions [40]. Raman laser spectra of both PA and CLA charge transfer complexes supported infrared assignments which are recorded the lower shift in the stretching vibration modes of –NH and C–N at 3068 and 1353 cm^{-1} due to charge transfer chelation in presence of nitrogen atom of secondary –NH group.

Scheme 1. Suggested structures of [(Pyn)(PA)] and [(Pyn)(CLA)] charge transfer complexes.



Hydrogen bonding

Radical anion mechanism

In ^{1}H NMR spectra of the CLA and PA Pyn complexes, generally, the protons of the donor are shifted to a lower field. The aromatic protons of the phenytoin sodium and PA acceptor are shifted to a lower field (7.29–7.76 ppm). In the complexes, the proton of –NH is shifted to a lower field (8.86–9.03 ppm). In both complexes, there is a new band appeared at 10.67 and 10.82 ppm for PA and CLA complexes, respectively, it could be deduced that the charge-transfer may proceeds from the association of intermolecular hydrogen bond.

Accordingly, the hydrogen bonding and radical anions between Pyn donor and the (PA and CLA) acceptors can be formulated as shown in Scheme 1.

***p*-CHL Charge transfer complex.** For this system, the charge transfer band appears at 403 nm. The observation of this band can be assigned to the formation of radical anions arising from the complete transfer of *n*-electrons (-NH group) from donor to acceptor moiety in methanol. In order to obtain the stoichiometry of the resulting complex, the molar ratio method [27] was performed. The photometric plot clearly indicates the formation of a 1 : 1 (donor: acceptor) complex. The formation constant (*K*) and molar absorptivity (ε) were calculated using the relationship summarized in Eq. (1).

The infrared and Raman spectral data of phenytoin, *p*-CHL and its [(Pyn)(*p*-CHL)] charge transfer complex are presented in Table 3. The stretching of both C=O *p*-CHL and phenytoin show a drastic shift to higher frequencies different intensities rather than free Pyn donor upon radical anions arising from the complete transfer of n-electrons from donor to acceptor moiety in methanol as a polar solvent. These

Table 3. Characteristic infrared and (Raman) frequencies (cm^{-1}) and tentative assignments of Pyn, *p*-CHL, and [(Pyn$^{\cdot+}$)(*p*-CHL$^{\cdot-}$)] CT complex

p-CHL	Pyn	[(Pyn$^{\cdot+}$)(*p*-CHL$^{\cdot-}$)]	Assignments
–	3309, 3059 3023, 2925	3272, 3204, (3069)	ν(N–H) + ν(C–H)
1680, 1583 1555, 1528	1690	1771, 1716, 1616 (1758,1683, 1610)	ν(C=O) ν(C=C)
–	1379	1318 (1278)	ν(C–N); –NH
–	761, 700	744, 697	C–H out-of-plane

shifts are resulted from the building of higher charge density on the carbonyl groups of the *p*-CHL acceptor in the complex formation. Moreover, the –NH and C–N stretching vibrations of the phenytoin sodium moiety were observed at (3272 and 3204) cm^{-1} and 1318 cm^{-1} regions, these considerably affected by lower shift of bands upon complex formation. According to these observations, the following scheme is suggested for the interaction of Pyn and *p*-CHL with 1 : 1 molar ratios.

$$\text{Pyn} + p\text{-CHL} = \text{Pyn}^{\cdot+}\ p\text{-CHL}^{\cdot-}$$

The conductivity data of Pyn in the presence of *p*-CHL was measured and recorded small increases. This slightly increasing in conductance after complexation supported that the charge transfer complex is formed from the formation of dative ion pairs. The spectral features of the [(Pyn$^{\cdot+}$)(*p*-CHL$^{\cdot-}$)] complex is wholly consistent with Mulliken's formulation of weak complexes in which the new UV-Vis absorption relates to the electronic transition ($h\nu_{\mathrm{CT}}$) corresponding to [41].

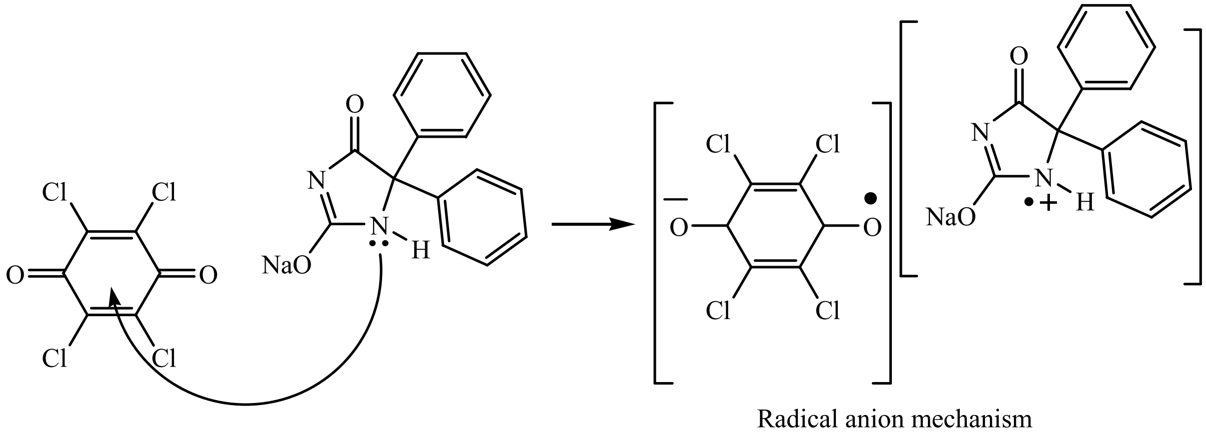
The ^{1}H NMR spectrum of the [(Pyn$^{\cdot+}$)(*p*-CHL$^{\cdot-}$)] complex also supports the formation of radical ions (Scheme 2).

DDQ and TCNQ complexes. The plot of absorbance vs. Pyn/DDQ mole ratio obtained at 421 nm shows a break at Pyn/DDQ= 1 and further confirms the suggested mechanism;

$$\text{Pyn} + \text{DDQ} \rightarrow \text{Pyn}^{\cdot+}\ \text{DDQ}^{\cdot-}$$

For evaluation of the equilibrium constant and the molar absorptivity of the resulting 1 : 1 [18C6] : [DDQ] complex [Eq. (1)] were calculated according to straight line produced. On the other hand, from the absorption spectrum of 1.0 × 10^{-4} M TCNQ in the absence of 1.0×10^{-4} M Pyn, over the range of 200–900 nm the intensity of TCNQ band at 743 nm within the [(Pyn)(TCNQ)] complex increases on comparison with the free TCNQ acceptor. Such observation is indicative of the formation of charge transfer complex through an equilibrium reaction. The formation of TCNQ$^{\cdot-}$ and

Scheme 2. Suggested structure of [(Pyn$^{\cdot+}$)(*p*-CHL$^{\cdot-}$)] charge transfer complex.



Radical anion mechanism

Table 4. Characteristic infrared frequencies (cm^{-1}) and tentative assignments of DDQ and [(Pyn$^{\cdot+}$)(DDQ$^{\cdot-}$)] CT complex

DDQ	Pyn	[(Pyn$^{\cdot+}$)(DDQ$^{\cdot-}$)]	Assignments
–	3309, 3059 3023, 2925	3272, 3211, 3062	ν(N–H) + ν(C–H)
2250, 2236	–	2238	ν(C≡N)
1680, 1555, 1430	1690	1772, 1744, 1723	ν(C=O) + ν(C=C)
–	1379	1237	ν(C–N); –NH
–	761, 700	744, 697	C–H out-of-plane

Table 5. Characteristic infrared frequencies (cm^{-1}) and tentative assignments of TCNQ and [(Pyn$^{\cdot+}$)(TCNQ$^{\cdot-}$)] CT complex

TCNQ	Pyn	[(Pyn$^{\cdot+}$)(DDQ$^{\cdot-}$)]	Assignments
3137, 3050, 2969 2851	3309, 3059 3023, 2925	3279, 3211, 3069 2975	ν(N–H) + ν(C–H)
2220	–	2177, 2122	ν(C≡N)
1670, 1539	1690	1772, 1724	ν(C=O) + ν(C=C)
–	1379	1325	ν(C–N); –NH
–	761, 700	750, 703	C–H out-of-plane

Pyn$^{\cdot+}$ radical anions have been recorded frequently [42–44]. Based on these observations it can be concluded that the molar ratio between [Pyn]: TCNQ is 1 : 1.

The IR spectral data of DDQ free acceptor and the 1 : 1 charge transfer complex are presented in Table 4, the CN and CO stretching of DDQ show a drastic shift to lower frequencies upon molecular complex formation with phenytoin sodium.

These shifts are indicative of a higher charge density on the cyano and carbonyl groups of the DDQ acceptor of its transfer complex. However, the ν(CN) stretching of the –NH group of Pyn observed within 1379 cm^{-1} region was shifted to 1237 cm^{-1} upon the complex formation. This is probably due to the participation of the secondary –NH group in the interaction with DDQ acceptor. Main band assignments for both TCNQ and its charge transfer complex appeared in the spectra are given in Table 5.

A comparison of the relevant infrared spectral bands of the Pyn free donor and TCNQ acceptor with the corresponding appeared in the IR spectrum of the isolated charge transfer complex clearly indicated that the characteristic bands of Pyn show some shift in the frequencies (Table 5), as well as some change in their bands intensities. This could be attributed to the expected symmetry and electronic structure changes upon the formation of the charge transfer complex. Moreover, in general, the IR spectrum of the molecular complex of TCNQ with Pyn indicate the ν(C≡N) and ν (C=C) of the free TCNQ are shifted to lower and higher wavenumbers values on complexation. Since TCNQ is deprived from any acidic centers, we may conclude that the molecular complexes are formed through *n*-π* charge migration from HOMO of the donor to the LUMO of the acceptor.

It is noteworthy to say that the spectra of both [(Pyn$^{\cdot+}$)(TCNQ$^{\cdot-}$)] and [(Pyn$^{\cdot+}$)(DDQ$^{\cdot-}$)] complexes have a sharp broadening with distortion in the stretching vibration bands, this can be discussed under the knowledge that Raman analysis of fluorescent materials and compounds is a challenging task experimentally due to the overlap of fluorescence which, even when very weak, can overwhelm the inherently weak Raman scattering signal [45, 46].

^{1}H NMR spectra for the [(Pyn$^{\cdot+}$)(TCNQ$^{\cdot-}$)] and [(Pyn$^{\cdot+}$)(DDQ$^{\cdot-}$)] complexes showed two main signals around 8.94–8.92 ppm and 7.66–6.94 ppm due to –NH of Pyn and protons of aromatic moieties, respectively.

Scheme 3. Suggested structures of [(Pyn$^{\cdot+}$)(TCNQ$^{\cdot-}$)] and [(Pyn$^{\cdot+}$)(DDQ$^{\cdot-}$)] charge transfer complexes.

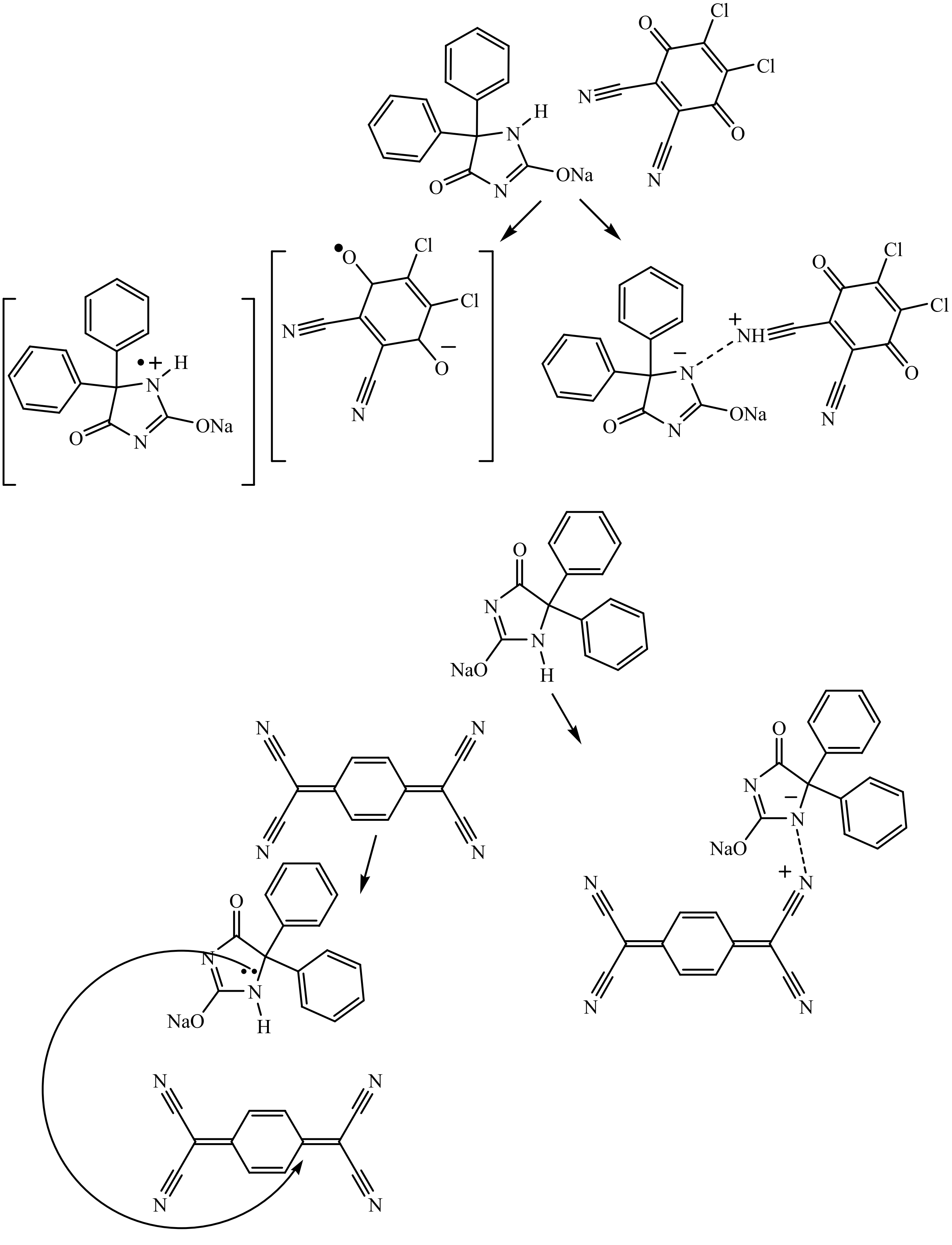


Table 6. Characteristic of infrared and (Raman) frequencies (cm^{-1}) and tentative assignments of NBS and [(Pyn$^{\cdot+}$)(NBS$^{\cdot-}$)] CT complex

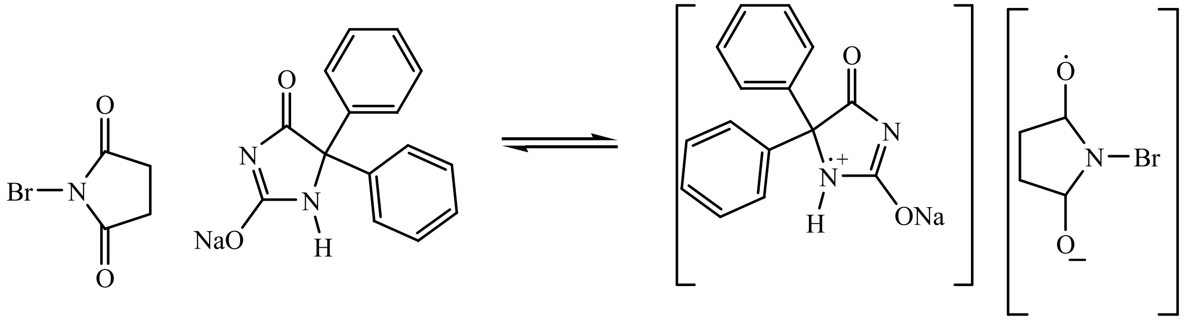
NBS	Pyn	[(Pyn$^{\cdot+}$)(NBS$^{\cdot-}$)]	Assignments
3079, 3052, 2954 2925, 2869, 2854	3309, 3059 3023, 2925	3279, 3211, 3062 2954, (3068, 2941)	ν(N–H) + ν(C–H)
1673	1690	1772, 1730, (1755)	ν(C=O) + ν(C=C)
–	1379	1366, 1311, 1238	ν(C–N); –NH
785, 845, 912	761, 700	743, 697, (773, 688)	C–H out-of-plane

All signals are lowerfield shifted compared to signals of free phenytoin sodium donor and acceptors. This shift is due to the ring current influence of the magnetic anisotropy of nitrogen atoms and the field effect of the electronic dipoles located on the nitrogen atom. Upon the assignments of electronic, infrared and proton NMR spectra, the suggested structures of both DDQ and TCNQ charge transfer complexes can be shown as in Scheme 3.

NBS charge transfer complex. The electronic absorption spectrum of the charge transfer complex formed from the reaction of Pyn donor and NBS acceptor in methanol demonstrates strong absorption band at 302 nm. The stoichiometry of the [Pyn][NBS] reaction was shown to be 1 : 1. This was concluded on the bases of the obtained elemental analysis data of the isolated solid charge transfer complex as indicated in the experimental section, as well as from the infrared spectrum of the solid NBS complex, which indicate the existence of the bands characteristic for both the [Pyn] and the respective NBS acceptor. The stoichiometry of 1 : 1 is also strongly supported by photometric titration measurements. Accordingly, the formed charge transfer complex upon the reaction of [Pyn] as a donor with the NBS as π-acceptor under investigation in methanol has the general formula [(Pyn)(NBS)]. This complex shows high values of both the formation constant (*K*) and the extinction coefficients (ε). These high values of *K* confirm the expected high stability of the formed charge transfer complex as a result of the expected high donation of the Pyn. The equilibrium constant is strongly dependent on the nature of the used acceptor including the type of electron withdrawing substituents to it such as bromo and carbonyl groups. For example, Table 1, the value of equilibrium constant for [(Pyn)(NBS)] is one of highest value rather than other complexes in respective solvent. The equilibrium constant value has equal to 48000 L/mol, that reflects the relatively higher electron acceptance ability for NBS. The number of donating atoms available is another important factor that affects the stability of charge transfer complexes [47]. Since in the process of molecular complexation, it is reasonably assumed that the charge density is donated from the donor to acceptor, the increased number of nitrogens in the ring is expected to increase the donor-acceptor interaction in solution. The effective overlapping of donor-acceptor orbitals involves the proper spatial positions of donor and acceptor molecules. This also needs specific conformation of donor. During complexation, some energy will consume for the conversion of most stable conformation of free donor to a conformation which is suitable for complex formation. This will act as a destabiliser factor in the whole process. Among the donor studied, Pyn has the most rigid structure. So, the variation of its conformation involves energy consumption. Based on this property, the observation of least stability for [(Pyn)(NBS)] (Table 1) is not unexpected. The conductance as a function of [Acceptor]/[Donor] mole ratios was measured and the results are shown that there is slightly increase of conductance upon acceptor addition thus, it can be concluded that the complex is completely ionic. The IR and Raman spectra of Pyn and their 1 : 1 [(Pyn)(NBS)] charge transfer complex are compared in Table 6. The bands generally show some shift upon complexation for the stretching vibrations of the –NH, and carbonyl group.

The ^{1}H NMR spectrum of this charge transfer complex was compared with the free phenytoin sodium donor, and the proton peak of –NH group was detected at 9.10 ppm, indicating the involvement of the nitrogen atom of –NH groups in complexation. The group of signals within 2.40–2.80 ppm and 6.40–8.80 ppm ranges are assigned to 4H of NBS and 12H of aromatic moieties of Pyn donor. These signals are shifted to lower field after complexation, these results

Scheme 4. Suggested structure of the [(Pyn$^{\cdot+}$)(NBS$^{\cdot-}$)] charge transfer complex.



are also supported the formation of radical ions between Pyn and NBS (Scheme 4).

The X-ray data of the synthesized phenytoin sodium charge transfer complexes showed significant change due to the effect of different acceptors on the complexation. The spectra of all Pyn charge transfer complexes containing a sharp-to-medium peak at 2θ = 11.40° which is assigned to the Pyn moiety with different intensities upon charge transfer complexation. The behavior of phenytoin sodium complexes is crystalline with well definite peaks and located in nano-scale range 50–150 nm [21, 24].

The results of EDX spectra confirm the presence of essential elements associate of phenytoin sodium CT complexes with different acceptors. The presence of some signals in the EDX spectra can be ignored as they arise from the analytical technique. On the other hand, the SEM images also depicts that each of *p*-CHL, TCNQ, CLA, DDQ, NBS, and PA acceptors is randomly distributed within the Pyn, having no surface contact between them but with good interfacial bonding.

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