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SYNTHESIS AND CHARGE TRANSFER COMPLEX STUDIES OF CARBAZOLE SUBSTITUTED PYRIDOPYRIMIDINE WITH SOME Π-ACCEPTORS

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ABSTRACT

Carbazole Substituted Pyridopyrimidine (CSPP) was synthesized and Charge transfer complexes with some acceptors such as tetracyanoquinomethane (TCNQ) and 2,3-dichloro-5,6-dicyano-p-benzoquinone (DDQ) have been studied spectrophotometrically in acetonitrile at 21°C. The stoichiometries of the complexes were found to be 1:1 ratio by the Job method between donor and acceptors with the maximum absorption band at a wavelength of 715 nm for DDQ and 593 nm for TCNQ. The formation constants of the complexes were determined by Benesi-Hildebrand equation. The thermodynamic parameters were calculated by Van't Hoff equations and found spontaneous and exothermic.

Keywords: Spectrophotometer, charge transfer complexes, pyrimidine, TCNQ, DDQ

INTRODUCTION

Pyridopyrimidines and their derivatives have been using for many reasons because of their pharmacological properties. Dihydropyrimidines (DHPMs) have occupied an important place due to calcium channel modulators, antihypertensive agents, α_{1a}-adrenergic receptor antagonists[1,2,3], antiviral, anti-tumor, antibacterial and anti-inflammatory activities[4,5]. Among the family of heterocyclic compounds, the nitrogen-containing five and six-membered heterocycles have received a great deal of attention in the literature because of biological properties. Especially, pyridine and pyrimidine containing compounds have been the subject of expanding research efforts in heteroaromatic and biological chemistry and also, the compounds have great interest because of the wide variety of interesting biological activities[6,7,8]. The pyrido-[2,3-d] pyrimidine heterocycles are clinically important compounds due to their wide range of biological[9] and pharmaceutical applications such as bronchodilators, vasodilators and their anti-allergic, antihypertensive, cardiotonic, and hepatoprotective activities[10].

In pharmacokinetics, investigation of the physicochemical properties and mechanism of action of drug compounds in solution are very important. Spectroscopic and thermodynamic investigations lead to a measure of the strength of binding of the drug compounds to other substances present in living systems[11].

Electron Donor-Acceptor (EDA) complexes are an important phenomenon in biochemical and bioelectrochemical energy transfer processes[12]. Electron transfer between molecules was defined first by Mulliken [13]. Molecular interactions between electron donors and acceptors are generally associated with the formation of intensely colored charge transfer complexes (CTC) in which absorb radiation in the visible region[14]. In general, Electron Donor-Acceptor complexation occurs as an ionic band (radical ion-pairs).

Ionic interactions and structural recognition are very important processes in biological systems. For instance; drug action, enzyme catalysis and ion transfer through lipophilic membranes involve complexation[15]. The features of ionic interactions are the primary directors of specificity, rate control and reversibility in many biochemical systems[16].

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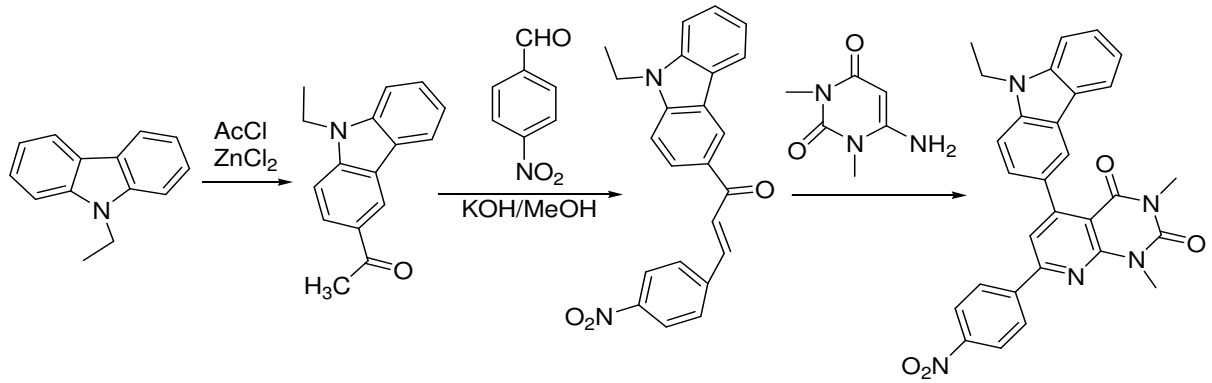
Reported methods for analysis of many drugs and charge transfer complex studies are studied mostly by direct UV-spectrophotometry[17-25], colourimetry[26] and HPLC[27]. And also, our previous works showed that the EDA complexes have good non-linear optical properties and electrical conductivities[28-30].
This paper reports synthesis of CSPP and simple, direct and sensitive spectrophotometric method for the determination of CSPP with TCNQ and DDQ. Stoichiometries, equilibrium constants and thermodynamic parameters of the complexes were determined.

EXPERIMENTAL

Synthesis of carbazole substituted pyridopyrimidine (CSPP) : A mixture of nitrochalcone (the product was prepared according to the literature[31]) (2.16 g, 5.84 mmol) and 6-amino-1,3-dimethyluracil (0.89 g, 5.74 mmol) in 50 mL absolute ethanol in presence of sodium hydroxide (0.22 g, 5.5 mmol) were stirred at 80 °C for 8 hours, quenched with water, filtered and recrystallized from ether to give the compound and shown in Scheme-1.



Scheme-1: Synthesis of Carbazole Substituted Pyridopyrimidine compound

5-(9-Ethyl-9H-carbazol-3-yl)-1,3-dimethyl-7-(4-nitro-phenyl)-1H-pyrido[2,3-d]pyrimidi-ne -2,4-dione (CSPP): Yield 90 %, m.p. 320.5 °C.; IR(KBr, υ, cm^{-1}) : 1701 (C=O), 1663 (NO_2), 1348 (C-N), 748 (C-H, aromatic) ; ^{1}HNMR (300 MHz, $CDCl_3$, δ, ppm) : 8.84 (1H, s, =CH), 8.15-8.18 (1H, d, =CH), 7.29-7.59 (9H, m, - Ar-H), 7.25-7.27 (1H, t, = CH), 4.37-4.44 (2H, q, - CH_2), 3.93 (3H, s, - CH_3), 3.37 (3H, s, - CH_3), 1.45-1.49 (3H, t, - CH_3). Anal. Calcd. for $C_{29}H_{23}N_5O_4$: C, 68.90; H, 4.59; N, 13.85. Found : C, 68.86; H, 4.454; N, 13.76.

Preparation of Standard Solutions

Acceptors: the stock solutions of acceptors (TCNQ, DDQ) at a concentration of 5.10^{-3} M were freshly prepared in chloroform inappropriate volumetric flask. A standard solution (5.10^{-3} M) of the donor (CSPP) was prepared in a 10 ml volumetric flask using chloroform. Absorption Spectra were recorded on Shimadzu 2401 UV-Visible spectrophotometer.

Stoichiometries of the Complexes

The stoichiometries of the complexes were determined using Job's method of continuous variations[32]. Equimolar concentrations of CSPP and acceptor in the solvent were used to calculate for the experiment. The amount of donor and acceptor was varied from 0.2 ml to 0.8 ml to hold the total volume at 1 mL in the cuvette. The electronic absorption spectra in the wavelength range 350-800 nm were recorded for the complex solutions of the studied CSPP with TCNQ and DDQ in chloroform.

Determination of Equilibrium Constants

The equilibrium constants of the complexes were calculated by using Benesi-Hildebrand equation [33]. 4.08 mg of TCNQ and 4.54 mg of DDQ was weighed in the cuvette and added in 2 ml of 3.10^{-4} M donor solution. Then, each time 0,2 ml of 3.10^{-4} M CSPP solution was added in the cuvette and maximum absorptions were determined at indicated wavelengths for ten times.

Thermodynamic Constants

The thermodynamic constants of the complexes between donor and acceptor were evaluated from the spectral measurements at the five different temperatures such as 7, 14, 21, 28 and 35 °C. The constants were determined by plotting $\ln(Abs)/\varepsilon - \ln(D_o\text{-}Abs/\varepsilon)(A_o\text{-}Abs/\varepsilon)$ versus 1/T(K).

RESULTS AND DISCUSSION

Charge transfer complex formation between donor and acceptors exhibits new absorptions at a different wavelength than either donors or acceptors alone. The spectra of CSPP, TCNQ, and DDQ in chloroform were shown in Fig.-1.

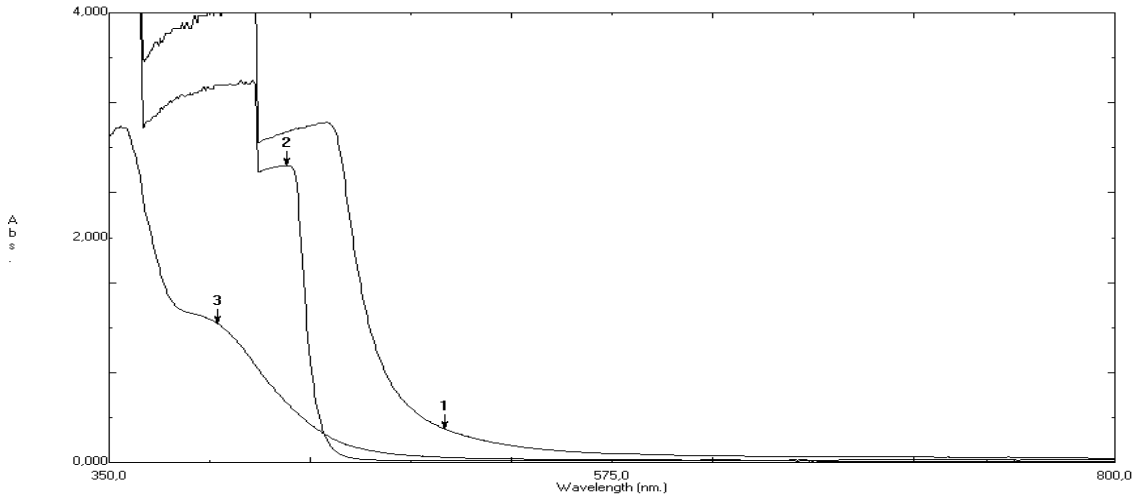


Fig.-1: The spectra of CSPP (1),TCNQ (2) and DDQ (3) alone in chloroform at 21 °C.

DDQ and TCNQ exhibit the most intense band and therefore are used commonly for many studies [19,21,22]. The indication complex formation of CSPP with TCNQ and DDQ is to form green and dark green colors while the solution of the donor was appeared to be colorless in chloroform. The spectra obtained for charge transfer (CT) shows maximum peaks at 715 for DDQ and 593 nm for TCNQ (Fig.-2).

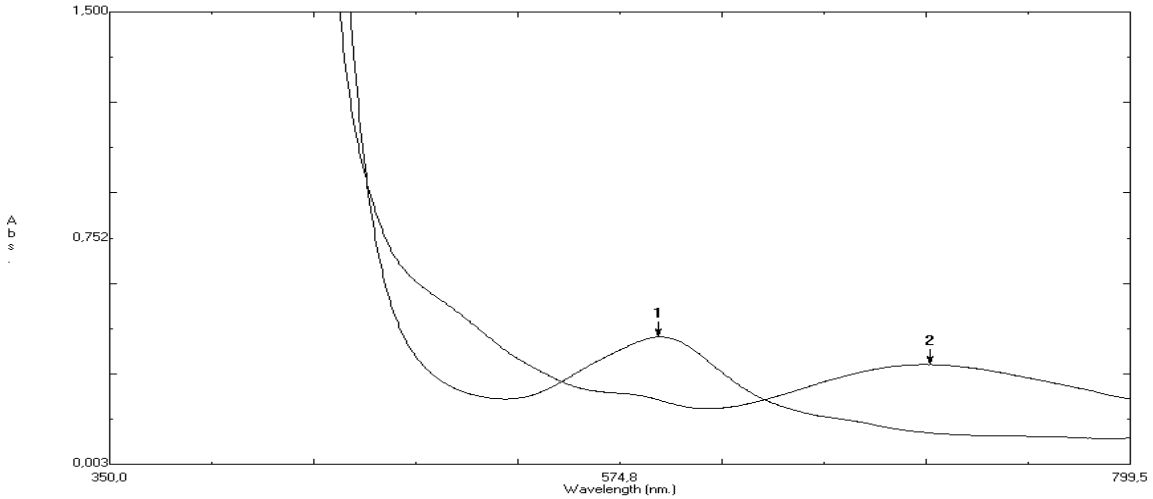
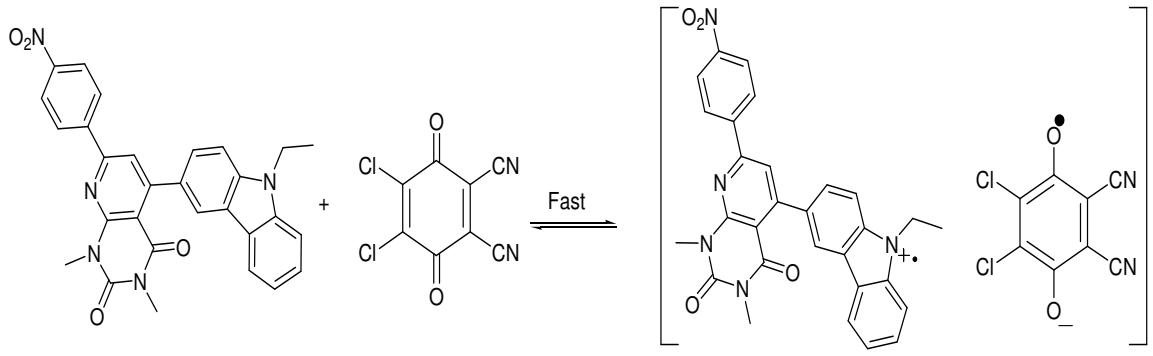


Fig.-2: The complexes of CSPP with TCNQ (1) and DDQ (2) in chloroform at 21 °C.

Charge transfer transitions generally occur through partial electron transfer from HOMO of the CSPP to LUMO of the acceptors which are TCNQ and DDQ in this study. EDA complexes absorb light in a manner different than either donor or acceptor and when the ground state of an EDA complex absorbs light that

matches the excitation energy of the complex, the excited state is formed. In this excited state, one electron is transferred from the lowest energy CT transition will involve promotion of one electron residing in the highest occupied molecular orbital (HOMO) of CSPP to the TCNQ or DDQ to form radical anion and radical cation. We elucidate the plausible structure of the CT complex. Charge transfer transition between CSPP and acceptors is shown in Scheme-2.



Scheme-2: Charge transfer transition between donor and acceptor

Job's method of continuous variation[32] was used to define the stoichiometry of the complex formation. The 1:1 complex formation ratio (figure 3) mentions that CSPP has only one strong basic and electron containing center which gives electron easily to TCNQ and DDQ.

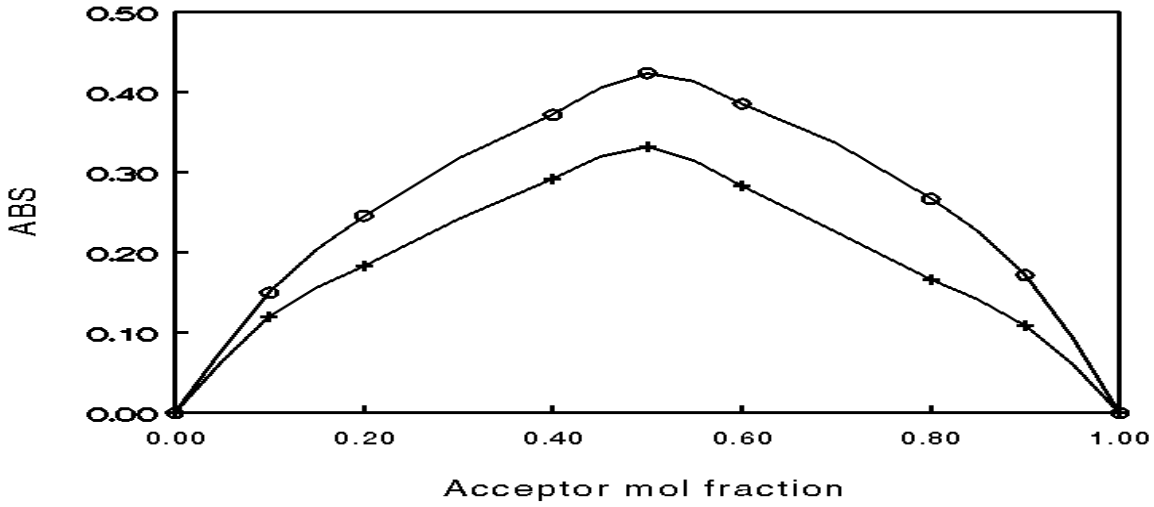


Fig.-3: The plot of Job's method for CSPP with DDQ (+) and TCNQ(◊).

Benesi-Hildebrand equation[33] shown below was used to calculate for the association constants of the complexes and data was obtained from Fig.-4.

$$\frac{[D_o]}{Abs} = \frac{1}{K\varepsilon[A_o]} + \frac{1}{\varepsilon} \; or \; \frac{[A_o]}{Abs} = \frac{1}{K\varepsilon[D_o]} + \frac{1}{\varepsilon} \qquad (1)$$

Where $[A_o]$, the initial concentration of the TCNQ or DDQ; $[D_o]$, the initial concentration of the CSPP; Abs, the absorbance of the complex; ε the molar absorptivity of the complex formed and K, the association constant of the charge transfer complex. The related constants given in Table 1 were obtained from slope and intercept of the regression lines (Fig.-4).

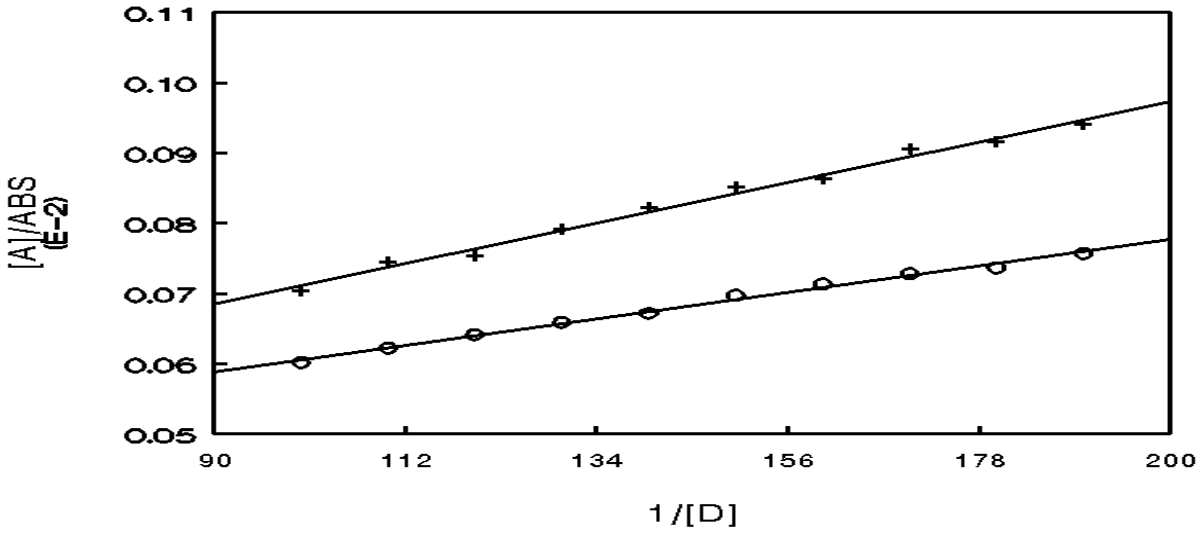


Fig.-4: Benesi-Hildebrand plots for CSPP with DDQ (+) and TCNQ(◊).

The results in Table-1 show that the K values of charge transfer complexes with TCNQ are bigger than the values with DDQ due to the higher electron accepting ability of TCNQ than that of DDQ. TCNQ has four strong electron withdrawing groups in conjugation with an aromatic ring which causes high delocalization leading to an increase in the Lewis acidity of the acceptor. The results are in good agreement with the literature[34].

Table-1: Formation constants of the complexes of CSPP with TCNQ and DDQ in chloroform at 21 °C.

Complexes	CSPP-DDQ	CSPP-TCNQ
λ_{max} (nm)	715	593
Stoichiometries	1:1	1:1
Concentrations	$2{,}6215.10^{-6}$	$1{,}7113.10^{-6}$
Intercept	0,00045	0,00038
r^2	99,5	99,7
ε($L.mol^{-1}\ cm^{-1}$)	2227,17	2597,40
K∈	381533,76	584453,53
K_{CT} ($L.mol^{-1}$)	171	225

The thermodynamic constants (ΔG, ΔH, ΔS) of the electron donor-acceptor complexes of CSPP with acceptors were evaluated from the spectral measurements at six different temperatures and calculated using by Van't Hoff and Beer-Lambert equations shown below:

$$\frac{\ln(Abs)}{\varepsilon} = \frac{-\Delta H}{RT} + \frac{\Delta S}{R} + \ln\left(D_o - \frac{Abs}{\varepsilon}\right)\left(A_o - \frac{Abs}{\varepsilon}\right) \quad (2)$$

The slope of the plot was used to calculate enthalpies. For the calculation of relative entropies, the intercept of the plot was used and obtained from Fig.-5.

The Gibbs free energy (ΔG^o) of the EDA complexes was calculated according to the equation:

$$\Delta G^o = -RT \ln K_{CT} \quad (3)$$

Where, K_{CT}, the equilibrium constant of charge transfer complexes ($L\ mol^{-1}$); R, the gas constant (1,987 cal $mol^{-1}\ ^oC$); T, the temperature (Kelvin degrees).

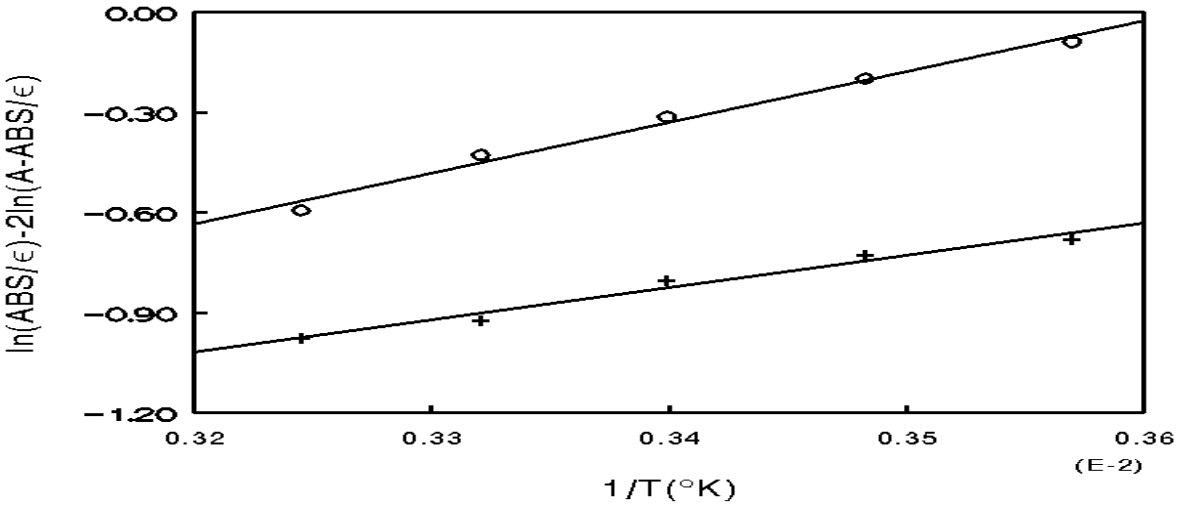


Fig.-5: Van't Hoff plot for CSPP with DDQ (+) and TCNQ(◊) at 7,14,21,28, and 35 °C.

The values of thermodynamic parameters (ΔS, ΔH and ΔG°) listed in Table-2 show that the CT complex formation process between the used donor and the acceptors is of exothermic in nature and spontaneous. There is a good agreement with the literature values of the constants[35].

Table-2: Thermodynamic parameters of the complexes of CSPP with TCNQ and DDQ in chloroform at 7, 14, 21, 28, 35 °C for ΔS, ΔH and 21 °C for ΔG°

Complexes	CSPP-DDQ	CSPP-TCNQ
ΔH (cal.mol $^{-1}$)	-1906	-3011
ΔS (cal.mol $^{-1}$)	-8,116	-10,89
ΔG (cal.mol $^{-1}$)	-3044	-3207
r^2	98,6	99,4

CONCLUSION

The methods used in this study can be used for the spectrophotometric determination of drug-disease interactions. The methods have many advantages such as simple, sensitive, accurate and are suitable for routine analysis. As a result, it is found that 1:1 EDA complexes were formed by using a heterocyclic compound by a single step reaction and single solvent system. This study indicates a possibility that new types of CT structures will be designed by devising the combination of donor and acceptor.

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