CHEMICAL KINETIC PARAMETERS BY TLC VIDEO DENSITOMETRY IN THE SYNTHESIS OF 4-FLUOROACRIDIN-9(10*H*)-ONE UNDER SONOCHEMICAL ACTIVATION

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Abstract

The present work highlights the synthesis of 4-fluoroacridone by intramolecular condensation of 2'-fluorodiphenylamine-2-carboxylic acidunder sonochemical activation. The kinetic parameters of reaction synthesis were determined by TLC video densitometry. In the synthesis, the effect of sonochemical activation on reaction rate and kinetic parameters such as time, temperatures, rate constants and activation energies were studied. The experimental results of traditional condition and sonochemical activation revealed the different kinetic parameters. The results indicated that activation energy of reaction decreased and the reaction rate greatly enhanced in sonochemical activation.

Keywords: Acridone, sonochemical activation, kinetic parameters, TLC video densitometry

Introduction

Derivatives of diphenylamine-2-carboxylic acid (2-(phenylamino) benzoic acid) and acridine-9(10*H*)-ones (acridones) possess important practical significance. Some of them having a broad spectrum of pharmaceutical activities are investigated as pharmaceuticals drug. Diphenylamine-2-carboxylic acids are basic intermediates products for synthesis of acridone derivatives. Based on these compounds, various dyes, indicators and biologically active compounds which possess as antitumor, anti-malarial, anti-viral and anti-bacterial action(Thorarense*etal*.,2007). In particular, acridone is commercially have been synthesized from diphenylamine-2-carboxylic acid and then from which 2-(9-oxoacridine-10(9H) -yl) (acridone acetic) is synthesized. Salts of this compounds are included in the list of life-saving drugs(Ершов *et al*., 1999). Therefore, improving the technology of synthesis of diphenylamine-2-carboxylic acids and acridones remains as an important task.

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At the current movement, much attention is given in the chemical research for the development of new energy-saving, cost-effective technologies and saving environmental hazardous processes. In this regard, great importance to search for new ways by activating chemical processes. During the last twenty years, most interesting process has been shown for chemical reactions which carried under ultrasonic radiation. Uses of this alternative sonochemical activation method in many cases have been shown significantly better results than that reaction performed under the traditional condition (Htun Yar Zar and Kudryavtseva 2013a, 2013b). However, in the scientific literature the practical experiment for the effect of sonochemical activation on the synthesis of diphenylamine-2-carboxylic acids has not been reported. Therefore, to study the effect of sonochemical activation and kinetic parameters on the synthesis of acrid one derivatives is an urgent task.

Materials and Methods

Preparation of TLC chromatogram to study the chemical kinetic

The quantity of samples were analyzed by TLC video densitometry. To calculate the content of substances in the analyzed samples, calibration was performed for each of the components of the mixture. For this purpose, standard solutions were prepared containing all possible components of the reaction mixture in known quantities in ethanol.

Firstly the pure micro samples of reactants and products were dissolved in ethanol or *N*, *N*-dimethylformamide, the concentration of each component being in the range of 0.001 to 0.050 M. The presence in the selected samples of phosphoric acid during dissolution with *N*, *N*-dimethyl for mamide does not affect the characteristics of chromatograms. Then the diluted samples were alternately placed with a microcapillaryonto a chromatographic plate. The spots of the samples were placed in order, depending on the reaction time (0, 10, 20, second or min).The volume of the applied sample on TLC plate was 1 ± 0.2 μL. Then the TLC plate was placed in a prepared chromatography chamber for elution. The special mobile or eluent carried out the spot of the analyzed samples. When eluent reached to the top of the TLC plate, the plate was dried in an oven at a temperature of 80 ± 5 °C for 5 min.

The chromatogram was processed on a video densitometer with UV ray at the wavelength of 254 nm.

Analytical methods used

The progress of the reaction was monitored by TLC (Sorbfil plates of PTSX-P-V-UV, Eluent: toluene, ethanol, acetone in various ratios). FT-IR spectra were recorded on IR-200 Nicolet and FSM 1201 "Monitoring" FT-IR spectrometers, in KBr tablets. Elemental analysis was performed by using a CHO 1109 analyzer (Carlo Erba), ^{1}H NMR spectra recorded on a Bruker AV-600 spectrometer and shifts measured relative to tetramethylsilane, solvent DMSO-d6. Mass spectra were recorded with the ACQUITY UPLC H-Class system with UV/mass-detectors ACQUITY SQD Waters (electrospray ionization), and a Chromatography-mass spectrometer Varian, detector Saturn-2000 (electron impact ionization). UV spectra were obtained on a spectrometer UV-1800 Shimadzu (solvent ethanol).

The melting point of compounds obtained was measured by using Electrothermal IA 9000 series instrument. The kinetic parameters of the reactions were studied by using a Denscan densitometer. To calculate the kinetic parameters, the programs "Sorbfil 1.8" and "Microsoft Office Excel" were used and the program "Sigma Plot 11.0" was used to create the kinetic diagrams. The influence of ultrasonic radiation on the course of processes was studied by using ultrasonic device IL100-6 /1laboratory apparatus.

Synthesis of 2'-fluorodiphenylamine-2-carboxylic acid ([2-((2-fluorophenyl) amino] benzoic acid)under sonochemical activation

12 mL of distilled water was introduced to a 250 mL round bottomed flask. 2.55 g (0.063mol) of sodium hydroxide was dissolved in it. After complete dissolution, 10 g (0.063mol) of 2-chlorobenzoic acid and 7.12 g (0.064mol) of 2-fluoroaniline were added. Sonotrode was immersed into the reactor. Then 0.5 g (0.005 mol) of copper(I) chloride was added to the reaction mixture and 6.37 g (0.076 mol) of sodium hydrogencarbonate was added by portion. The reaction mixture was heated for about 3 h by stirring at the temperature of 90 °C, the reaction progress was monitored by TLC. After 3 h the reaction mixture was poured into a beaker containing 100 mL of hot water and then sodium hydroxide solution and 5 g of activated charcoal were

added. The mixture solution was heated to boil and filtered. The resulting filtrate was acidified with concentrated hydrochloric acid. The precipitate was filtered and washed with hot water until neutral pH, then product was dried at 100 °C.

Yield = 46 %: T_{melt}= 185-186 °C. R_f = 0.22 (Sorbfil, toluene : acetone : ethanol = 10 : 3 : 2): UV-Visible (Ethanol) (λ nm): 304; FT-IR-spectrum (KBr),ῡ , cm^{-1}: O-H (3435): N-H (3321); =C-H (2800-3100); C=O (1651); C=C aromatic (1400-1600): Mass spectrum= $C_{13}H_{10}FNO_2$ m/z 231 $[M+H]^+$ (100%).

Acid-alkaline treatment of 2'-fluorodiphenylamine-2-carboxylic acid

10 % of diphenylamine-2-carboxylic acidsolution was prepared with water solvent and then 30% of sodium hydroxide solution was poured into the solution. 5 g of activated charcoal was added and boiled the solution. The hot solution was filtered by suction pump. The filtrate was acidified with 15% hydrochloric acid solution. The precipitate was filtered by suction, washed the residue with hot water. The product was dried at temperature 100 ºC in circulation oven. The yield percent of product was calculated.

Synthesis of 4-fluoroacridin-9(10*H*)-one

10 g (0.045 mol) of 2'-fluorodiphenylamine-2-carboxylic acid and 40 g of polyphosphoric acid (PPA)were mixed in the beaker. The mixture was stirred without heating to get homogeneous. Sonotrode was immersed into the reactor with the predetermined temperature and the reaction was carried out. After the reaction was completed, the reaction mixture was poured into beaker which contained 300 mL of boiled water. The residue was filtered by suction pump and then the residue was treated with sodium carbonate solution to remove trace amount of 2'-diphenylamine-2-carboxylic acid. After that the yellow colour precipitate was filtered and dried at 100°C. The yield % of 4-fluoroacridone was 97.82 %.

Yield = 97.82%: T_{melt} = 318°C. R_f = 0.76 (Sorbfil, toluene : acetone : ethanol = 10 : 3 : 2): UV-Visible (Methanol) (λ nm): 394, 376, 306, 294, 250,223,216. FT-IR-spectrum (KBr), ῡ , cm^{-1}: N-H (3437): C-H (2900-3300):

C=O (1641): C=C aromatic (1400-1600); C-F (Arylhalide) (1100-1250). Mass spectrum= $C_{13}H_8FNOm/z$: 213 $[M+H]^+$(100%).

^{1}HNMR (DMSO-d6) δ: 7.16 ppm (m,J=8.14Hz,^{1}H)7.29 ppm (m,J=11.1Hz,^{1}H), 7.22 ppm (t,J=7.96Hz, ^{1}H) 7.67 ppm (t,J=8.0Hz,^{1}H), 7.38 ppm (d,J=8.03Hz,^{1}H), 8.28 ppm (d,J=7.96Hz,^{1}H), 8.31 ppm (d,J=7.86Hz,^{1}H), 11.95 ppm (s,^{1}H).

Results and Discussion

Quantity of Substances in a Mixture of Samples Analyzed by Thin-Layer Chromatography with Video-densitometry

During the course of the study the quantitative analysis of samples of reaction mixtures was carried out by using video densitometry. The consumption of the initial components and the formation of the reaction products were monitored by taking the analyzed sample from reaction mixture at definite time intervals. The thin layer chromatography with video densitometry method was used to analyze the quantity of reactants and products from reaction mixtures and determined by comparing pure reactant 2'-fluorodiphenylamine-2-carboxylic acid and fluoroacridone samples products (Lundanes *et al*., 2013).

By analyzing the TLC chromatogram with video densitometry, a table of the relative areas of the peaks of the separated substances and the R_f values of each peak was obtained. To calculate the relative content of substances in the analyzed samples, a calibration was performed for each of the components of the mixture in accordance with the method of Маркович *et al*., (2008). According to the Table 1, the relative areas of the peaks of substances in standard solution and the known amount of each component in the standard solution, the ratio of the mass of the substance to its relative peak area K_i were determined by the equation (1).

$$K_i = \frac{m_i}{S_i} \quad (1)$$

where m_i is the mass of the each component in the standard mixture, S_i is the relative peak area of the each component. The average data for each component was calculated and that was used to convert the relative areas in the analyzed samples into mass fractions of W_i according to the equation(2).

$$W_i = K_i \frac{S_i}{\sum_{j=1}^{n} K_j S_j} \quad (2)$$

where n is the number of all components.

The actual amount of 2'-fluorodiphenylamine-2-carboxylic acid (FDPACA) in the first sample was taken as 100%, and the corresponding 4-fluoroacridone (4-FA) was 0%. Taking the amount of molecular masses of the substances and the mass fractions of all components were recalculated to the extent of accumulation or expenditure (in the case of FDPACA). Examples of processing experimental data are given in Tables 1 and 2.

Table 1: Ratios of the Mass of Substances in the Standard Solution Corresponding to the Area of Spots in the Mixture of 2'-Fluorodiphenylamine-2-carboxylic acid and 4-Fluorocridone

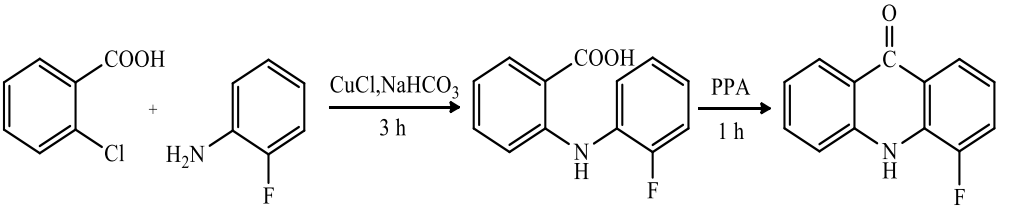
Components	**R_f**	**Relative peak area, S_i**	**Mass of component in solution m (g)**	**m/S_i**
FDPACA	0.28	4335	0.01	2.30×10^{-6}
4-FA	0.85	9488	0.01	1.05×10^{-6}

Table 2: The Degree of Accumulation of 4-Fluoroacridone and the Expenditure of 2'-Fluorodiphenylamine-2-carboxylic acid when it is Cyclized in PPA at 80 °□ under Sonochemical Activation

No.	**Time,s**	**Relative peak area, S_i**		**Mass fraction, W_i**		**Degree of expenditure**	**Degree of accumulation**
		FDPACA	**4-FA**	**FDPACA**	**4-FA**	**(FDPACA)**	**(4-FA)**
1	0	1	0	1	0	1	0
2	300	0.838	0.161	0.919	0.080	0.919	0.088
3	600	0.503	0.496	0.689	0.310	0.689	0.338
4	1200	0.456	0.543	0.648	0.351	0.648	0.384
5	1800	0.321	0.678	0.508	0.491	0.508	0.536
6	2400	0.238	0.761	0.360	0.679	0.370	0.708
7	3600	0.122	0.877	0.233	0.766	0.233	0.836
8	5400	0.072	0.927	0.146	0.853	0.146	0.932
9	7200	0.026	0.973	0.055	0.944	0.055	1.031

Kinetic Parameters of Cyclization Reaction of 2’-Fluorodiphenylamine-2-carboxylic acid under Sonochemical Activations

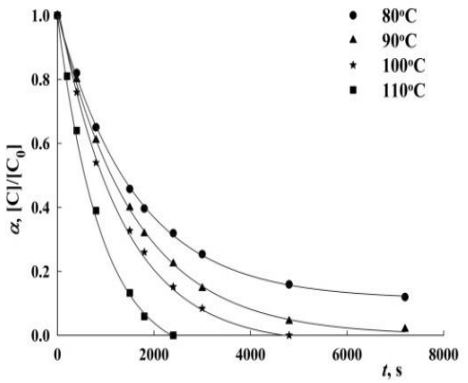
2’-fluorodiphenylamine-2-carboxylic acid was synthesized by condensation of 2-chlorobenzoic acid and 2-fluoroaniline in the presence of sodium hydrogencarbonate and copper(I) chloride. In polyphosphoric acid (PPA), 2-fluoroacridone was synthesized by intramolecular condensation of 2’-fluorodiphenylamine-2-carboxylic acid. The chemical equationis described in the following.



The kinetic parameters of intramolecular condensation of 2’-fluorodiphenylamine-2-carboxylic acid were determined by using numerical integration methods equation of reaction rate.

Determination of the kinetic parameters of cyclization of 2’-fluorodiphenylamine-2-carboxylic acid was carried out under conditions of sonochemical activation, but also under traditional conditions.

In the course of studies by using thin-layer chromatography with densitometry, kinetic curves for the consumption of 2’-diphenylamine-2-carboxylic acidvaries with temperature and time are illustrated in Figure 1.



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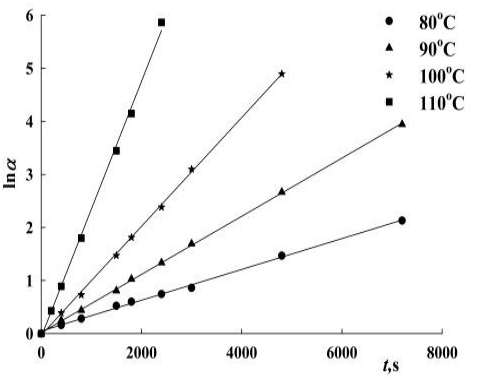

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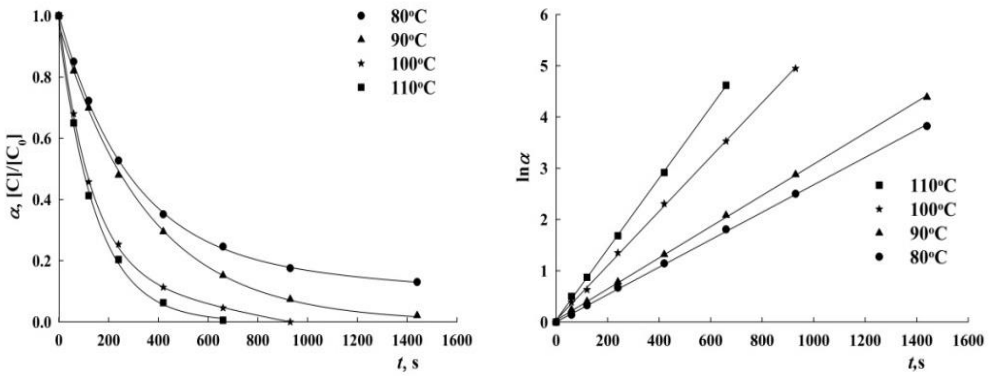


b b'

Figure 1: Kinetic curves for the consumption of 2'-diphenylamine-2-carboxylic acid in PPA under (a) thermal conditions and (b) sonochemical activations at different temperatures and their plots (a', b')

As can be seen from the curves shown in Figure 1 (b), under sonochemical activations, at the temperature of 80 °C the reaction time was 1 h and at 110 °C, only 15 min. In this case, under thermal conditions at a temperature of 80 °C, the reaction time was 4 h, and at 110 °C, 45 min. Thus, under sonochemical activations, the reaction time was greatly decreased. At the same time, it should be noted that the optimal reaction temperature can be considered at 100 °C to synthesis of acrid one derivatives. Since at lower temperatures the duration of the process was increased, and at 110 °C, according to chromatographic mass spectrometry data, traceamount of 2-fluorodiphenylamine was formed as by-product.

In kinetic equation, the order of the process of intramolecular condensation of 2'-fluorodiphenylamine-2-carboxylic acid in polyphosphoric acid under thermal and sonochemical activations was described by the first-order reactions, that was evidenced by the linear dependence of ln α -*t*.

Thus, for the cyclization of 2'-diphenylamine-2-carboxylic acid under thermal conditions, the rate constants of the reaction at the appropriate temperatures were: k_{80}= (29.92 ± 1.19) x 10^{-4} s^{-1}, k_{90} = (58.53 ± 2.34) x 10^{-4} s^{-1}, k_{100} = (106.43 ± 4.25) x 10^{-4} s^{-1}, k_{110} = (245.34 ± 9.81) x 10^{-4} s^{-1}. Under the

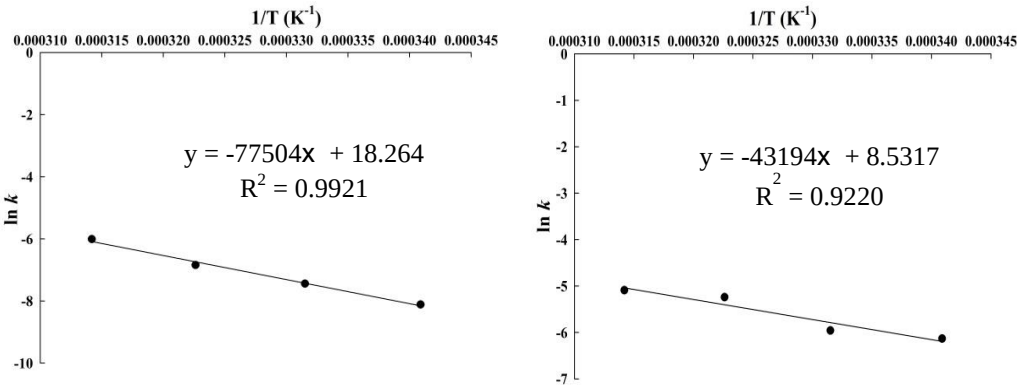
sonochemical activation, reaction rate constants was being as the following values: k_{80} = (21.69 ± 0.86) x 10^{-4} s^{-1}, k_{90} = (25.81 ± 1.03) x 10^{-4} s^{-1}, k_{100} = (52.89 ± 2.11) x 10^{-4} s^{-1}, k_{110} = (61.06 ± 2.46) x 10^{-4} s^{-1}.

To calculate the activation energy on the basis of the values of the rate constants of the reaction at different temperatures, the Arrhenius formula was used (Connors, 1990).

$$k = A \cdot e^{-\frac{E}{RT}} \quad (3)$$

$$\ln k = \ln A - \frac{E}{RT} \quad (4)$$

Figure 2 in the Arrhenius coordinates gives the dependence of the reaction rate constant on the temperature for the cyclization of 2'-fluorodiphenylamine-2-carboxylic acid.



a b

Figure 2: Arrhenius plot for the processes of cyclization of 2'-fluorodiphenylamine-2-carboxylic acidin PAA under (a) thermal conditions and (b) sonochemical activation

The points fitted well to a straight line, from which the activation energy of was calculated. Under sonochemical activation the activation energy was 43.19 ± 4 kJ/mol and 77.50 ± 4 kJ/mol under thermal conditions. The obtained results show that under sonochemical activations the required activation energy was very low.

Conclusion

In this research, 2'-fluorodiphenylamine-2-carboxylic acid was synthesized by condensation of 2-chlorobenzoic acid and 2-fluoroaniline in the presence of copper(I) chloride. In polyphosphoric acid, 4-fluoroacridone compound was synthesized by intramolecular condensation of 2'-fluorodiphenylamine-2-carboxylic acidunder sonochemical activation. The synthesized compounds were identified by FT-IR Spectroscopy, Mass Spectrometry and ^{1}HNMR Spectroscopy methods. The effect of sonochemical activation on the synthesis of 4-fluoroacridone, the kinetic parameters: time, reaction rate constants, temperatures and activation energies were studied by TLC video-densitometry. According to the kinetic parameters, in the synthesis of 4-fluoroacridone under sonochemical activation, the reaction time was reduced, decreased activation energy and increased reaction rate, that was compared by relating the results of thermal conditions.

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