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POTENTIOMETRIC TITRATION OF SOME IMIDAZOLE DERIVATIVES IN NONAQUEOUS SOLVENT

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ABSTRACT

The acidity constants of 4,5-diphenyl imidazole, 2,4,5-triphenyl imidazole, and 2,4,5-triphenyl imidazole derivatives in nitrobenzene, acetonitrile and glacial acetic acid were determined. Perchloric acid, prepared in 1,4-dioxane, was used as the titrant for the measurement which were done in acetonitrile; perchloric acid, prepared in nitrobenzene, was used as the titrant for the measurements that were done in nitrobenzene and perchloric acid, prepared in glacial acetic acid, was used as the titrant for the measurements which were done in glacial acetic acid. The pKa values were obtained from the half neutralization potentials which were obtained from an analysis of the potentiometric titrations. The ranging of the increasing acidic strengths were determined by considering whether the compounds had a substituent on 4, 5 position or not.

INTRODUCTION

Potentiometric titration in non-aqueous media yield valuable information about basicity or acidity of compounds (Latinen and Harris, 1975). The aim of this work is to determine the acidity constants (i.e. pKa values) of 4,5 diphenyl imidazole, 2,4,5 triphenyl imidazole and the derivatives of 2,4,5-triphenyl imidazole. These compounds are active constituents of the certain antibacterial, antihelmintic and antirheumatic (Lombardina, 1974; İstanbullu and Şafak, 1982; Jaiswal, et.al., 1979; Maxwell, et.al., 1984). However, since these compounds are weak bases their titrations need great care. On the other hand for the weak bases, the utility of nitrobenzene, acetonitrile and glacial acetic acid are well known as titration medium (Kılıç and Gündüz, 1986; Fritz, 1953). Therefore pKa

values of 4,5-diphenyl imidazole, 2,4,5-triphenyl imidazole and the derivatives of 2,4,5-triphenyl imidazole were determined in these solvent.

EXPERIMENTAL METHODS

A Crison Micro pH 2001 model pH meter equipped with a glass electrode (Ingold model) was used. A magnetic stirrer, a 0.01 cm^3 calibrated semimicroburet and 50 cm^3 beaker were used for the titrations. The beaker was kept in a water bath wihch was thermostated at 20±0.1°C with a Braun Thermomix-1460 thermostat.

The imidazole derivatives used were synthesized and provided kindly by Uçucu and Işıkdağ (Işıkdağ and Uçucu, 1991). Nitrobenzene (Merck), acetonitrile (Merck), glacial acetic acid (Merck), and 1-4 dioxan (Merck) were reagent grade and used as received. Anhydrous perchloric acid in nitrobenzene (0.028 mol dm^{-3}) was used as titrant. For the titrations in nitrobenzene, anhydrous perchloric acid in nitrobenzene was prepeared as follows:

With a micro-pipette, 0.72 cm^3 of % 70 perchloric acid was added dropwise to 5 cm^3 of ice-cooled pure acetic anhydride. The light yellow solution was left for 5-6 hours at room temperature, then a 1 cm^3 of this solution was introduced into 50 cm^3 calibrated flask and diluted with nitrobenzene. The concentration of this solution was determined against primary standard of sodium carbonate in glacial acetic acid.

Perchloric acid prepared in 1,4-dioxane (0.181 mol dm^{-3}) was used as the titrant for the titration in acetonitrile, while perchloric acid prepared in glacial acetic acid (0.107 mol dm^{-3}) was used for the titration in glacial acetic acid.

For the titrations 10 mol^{-3} dm^{-3} solutions of compounds were used. Before potentiometric titrations, the pH meter was calibrated according to the instructions supplied by the manufacturer of the pH meter. During the titrations, the titrant was added in increments of 0.02 or 0.01 cm^3. The pH and emf values were read after they were stabilized. From the half neutralization potential of S-shaped titration curves, the pKa values were determined.

RESULTS AND DISCUSSION

Typical titration curves of 2-(3′-methoxy-4′-hydroxyphenyl)-4,5-di-(4′-methoxyphenyl) imidazole in acetonitrile with perchloric acid in

1,4-dioxane (Figure 1); in nitrobenzene with perchloric acid in nitrobenzene (Figure 2) and in glacial acetic acid with perchloric acid in glacial acetic acid (Figure 3) are given. All titrations resulted with S-shaped curves having 200-350 mV shifts at the equivalence points.

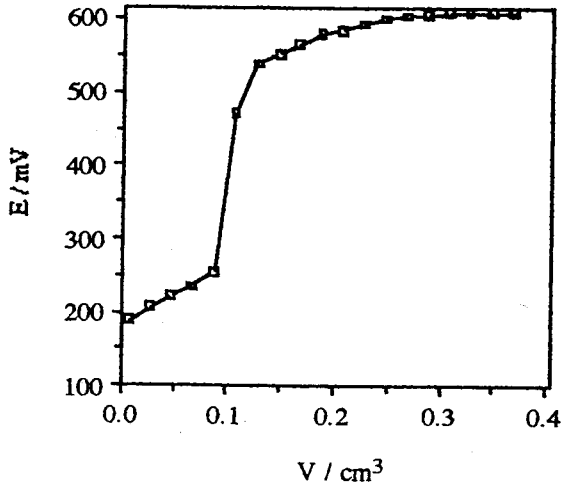


Fig. 1. Titration curve of compound IX using acetonitrile as solvent and perchloric acid prepared in 1,4-dioxane as titrant.

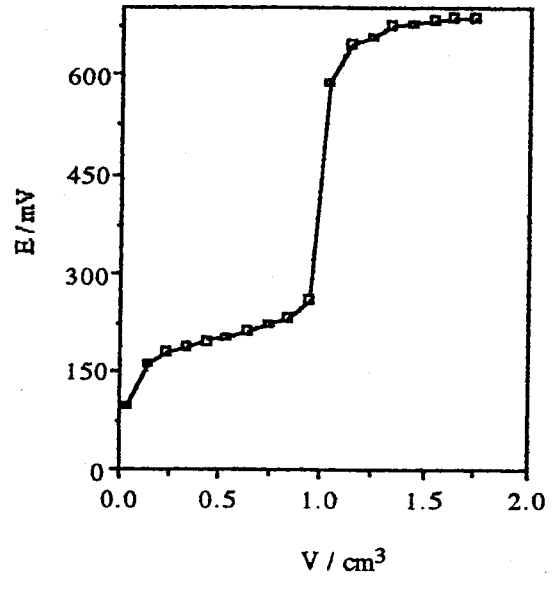


Fig. 2. Titration curve of compound IX using nitrobenzene as solvent and perchloric acid prepared in nitrobenzene as titrant.

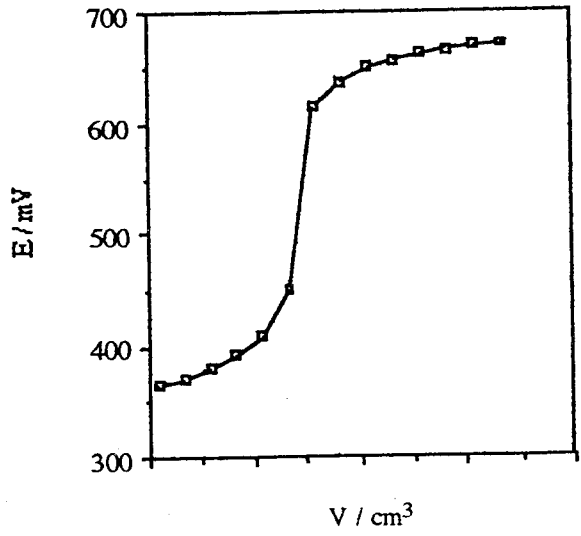


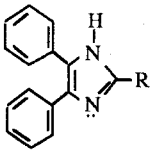
Fig. 3. Titration curve of compound IX using glacial acetic acid as solvent and perchloric acid prepared in glacial acetic acid as titrant.

The pKa values of compound 2,4,5-triphenyl imidazole derivatives which do not have any substituent at 4 and 5 positions are given in Table 1. The pKa values of imidazole having substituents at 4 and 5 positions are given in Table 2. Quantitative results of the titrations of 4, 5-diphenyl imidazole and 2,4,5-triphenyl imidazole derivatives in glacial acetic acid are given in Table 3. As it is seen from Table 1 the acidic strenghts of the compounds in nitrobenzene are in the following order: 4,5-diphenyl imidazole < 4,5-diphenyl-2-(3′,4′-dimethoxyphenyl) imidazole < 4,5-diphenyl-2-(4′-methoxyphenyl) imidazole < 4,5-diphenyl-2-(3′-methoxy-4′-hydroxyphenyl) imidazole < 2,4,5-triphenyl imidazole.

The acidity order of these compounds is affected by the inductive and mesomeric electron donating effect of the substituents and also by the hyperconjugation between methoxy and hydroxy groups. These are discussed below in detail:

The pKa value of the compound II is smaller than that of the compound I, due to the hindrance of protonation by the phenyl group which has mesomeric electron-withdrawing effect.

Table 1. pKa Values Compound Structure vs. Molecular Structure.



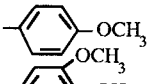
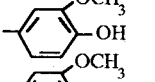
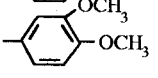
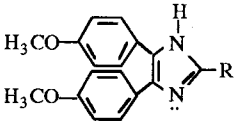
Designation	R	pKa		
		Nitrobenzene	Acetonitrile	Glacial acetic acid
I	−H	3.31	3.15	-0.41
II		2.57	2.17	-0.19
III		2.95	2.75	-0.11
IV		2.89	2.53	-0.16
V		3.22	2.62	-0.28

Table 2. pKa Values Compound Structure vs. Molecular Structure.



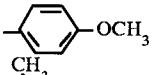
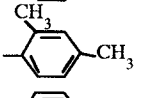
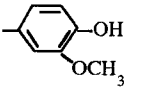
Designation	R	pKa		
		Nitrobenzene	Acetonitrile	Glacial acetic acid
VI		2.97	2.74	-0.57
VII		3.68	3.24	-0.15
VIII		3.36	3.03	-0.12
IX		3.55	3.25	-0.20

Table 3. Quantitative Results of the Titrations Obtained in Glacial Acetic Acid.

Compound of Number	Weighted Sample (mg)	Calculated amount of sample from titration data (mg)	Yield (%)
I	5.50	5.28	96
II	5.69	5.55	97
III	8.15	7.83	96
IV	8.55	8.21	96
V	8.90	8.55	96
VI	6.85	6.65	97
VII	7.40	7.21	97
VIII	9.60	9.22	96
IX	10.10	9.65	96

The pKa value of the compound II is found to be greater than that of the compound III due to electron-donating effect of methoxy group at 4 position.

An increase of pKa values of the compounds IV and V compared to the pKa value of the compound III was expected. However this situation was observed for the compound V but not for the compound IV. Presumably hyperconjugation between methoxy and hydroxy group decreases the pKa value of the compound IV. Acidic strenghts of second series of compounds (Table 2) in nitrobenzene are in the following order: 2,4,5-tri-(4′-methoxyphenyl) imidazole < 2-(3′-methoxy-4′-hydroxyphenyl)-4,5-di-(4′-methoxyphenyl) imidazole < 2-(2′,4′-dimethylphenyl)-4,5-di-(4′-methoxyphenyl) imidazole < 2-phenyl-4,5-di-(4′-methoxyphenyl) imidazole.

The order of acidities is affected by mesomeric and inductive electron donating effect of substituents as well as hyperconjugation between hydroxy and methoxy groups. From the comparison of the pKa values of the first group compounds (Table 1) with those of the second group of the compounds (Table 2) increase of pKa values due to electron-donating effect of methoxy groups at 4 and 5 positions of the phenyl ring is observed. Acidity order in acetonitrile and glacial acetic acid can not be explained by either inductive and mesomeric effect of substituents or hyperconjugation. Disorderliness of the acidic strengths found in acetonitrile might be due to homoconjugation taking place in acetonitrile (Gündüz et.al., 1990).

Quantitative results of the titrations given in Table 3 indicates that using glacial acetic acid as solvent is suitable for quantitative determinations of imidazole derivatives since yields of each titration is almost 96%.

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