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EQUILIBRIA AND STRUCTURES OF SOME BARBITURATE COMPOUNDS

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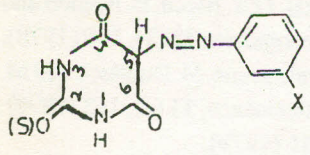
Some azobarbiturate and benzylidene barbiturate compounds were prepared. The structural chemistry was investigated based on different spectral and pH-metric methods. The tautomeric equilibria were explained. The electronic character of the substituents affects the mode of dissociation of the organic compounds.

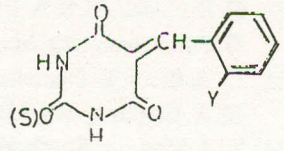
Key words. Barbiturates, Structures, Equilibria, pK's.

Introduction

Barbiturate compounds were studied in different fields [1-16]. It is interesting to study the mode of ionization of some azo barbiturate (I) benzylidene and salicylidine barbiturates and their thio-analogues (II) from the dissociation constant values obtained from pH-metric and spectrophotometric measurements. The data were explained based on the electronic character of the substituents.



(I)



(II)

a) H; b) CH_3; c) OH; d) Cl; e) NO_2; f) CO_2H; g) CHO; h) CH=NOH; i) CH=N $(CH_2)_2$ OH

Experimental

Synthesis of the organic compounds. The azo compounds were prepared following the diazotization process. The oxime compounds (I-h) was prepared by refluxing the corresponding aldehydo compound with NH_2OH. The Schiff base (I-i) was prepared by refluxing 2-aminoethanol with the corresponding aldehyde. Their C, H and N contents were given in Table 1. The condensation products (II) were prepared by refluxing the corresponding acid with the aldehyde dissolved in 30 ml dioxane. The products were filtered and washed with water, then dried in a vacuum desiccator over P_4O_{10}.

The KBr-ir spectra were recorded on SP 2000 Pye Unicam spectrophotometer. The ^{1}H-nmr data were obtained in ^{6}d-DMSO on EM-390 90MHz spectrometer. The electronic spectra were measured using Pye Unicam Model SP 1750. Unicam pH Meter Model 291 MK-2 was applied to evaluate the dissociation constants of the organic compounds. The measured pH values recorded in 50% V/V dioxane water solutions were corrected.

Results and Discussion

^{1}H-nmr. Barbituric acid gave signals at 3.3 and 10.95 due to CH_2 and -NH be the keto structure. Thiobarbituric acid gave both at 2.31 and 11.9 due to thione structure. The variation in the data (Table 2) is due to the difference in the electronegativity of -O and -S atoms. However, compounds having the keto structure are those of I-a, I-b, I-f, I-g, I-h, IIa and II-b; while compounds having a keto = enol euqilibrium are derived from I-c, I-e, I-g, I-h, I-i, II-a and II-b.

Infrared spectra. Barbituric acid (Table 3) gave the keto structure which is distorted from planarity where the methylene part had a boat configuration. Strong bands appeared at 3550-3470 and 3190 - 3100 cm^{-1}, are due to the existence of a hydrogen bonding [8], where the NH and C=O groups are in positions 3 and 4, respectively.

Thiobarbituric acid gave broad bands at 3640-3100 cm^{-1}, due to hydrogen bonding of the type NH...O. The medium band at 2840 cm^{-1} assigned to υCH_2. No band at 2500 cm^{-1} to exclude SH [8]. The carbonyl group was identified in the range 1740-1645 cm^{-1}. The thioamide group (NH-C=S) gave fundamental bands at 1240-1165 and 1260 cm^{-1} (υC-N and υC=S). The strong band at 1620 cm^{-1} was due to υC=N. The data indicated the existence of the thiobarbituric in thio-enol form.

I-a gave a medium band at 3120 cm^{-1} where one of the NH groups was tautomerized to N=C-OH. The azo compound was confirmed by the weakness of υCH_2 required for the diazotization process. The strong bands 1530 and 1430 were due to υN=N while the bands 1600 and 1330 were due to υC=N, to suggest keto-enol euqilibrium. Different types of hydrogen bonding are possible. i) Intramolecular between the nitrogen atom of the azo-group and the-OH group formed from the enolized -CH-CO system. ii) Intermolecular to form cyclic dimer through N-H....O=C (3320-3240 cm^{-1}). iii) O-H....O type (3500-3100 cm^{-1}), where NH and OH were proton donors and both -N and -O atoms were proton acceptors. Both intra - and intermolecular O-H...N and NH...O bonds may lead to a number of structures in simultaneous equilibrium [9-11]. The angular nature of the NH...O bond removes the stretching effect of the H atom between the N and O atoms to weaken the attraction interaction. The terminal OH in an intramolecular NH...OH system absorbs at a slightly lower frequency than a free OH, whereas a terminal OH in an intramolecualr OH...OH

system with a similar geometry did not. The OH dipole fluctuation during vibration would be accompanied by changes in the oxygen lone pair dipole which may induce charge fluctuation N lone pair orbital [11], to exercise a damping effect of the terminal OH and thus lowering its frequency. In general, the lower frequencies of υNH and υC=O were due to association throughcis and trans forms and the hydrogen bond existed through the keto ⟺ enol tautomerism.

The fundamental IR of the $-NO_2$ (I-e) and the -Cl (I-d) compounds (Table 3) illustrated that the former predominated in the imino-keto-azo structure beside the latter is subjected to tautomerism.

The carboxy compounds (I-f), existed in a dimeric structure through hyrogen bond with a medium band at 920 cm^{-1} mainly in the keto-azo structure. Some of the bands were splitted due to (a) hydrogen bonding effect, (b) double minimum potential for the bonded proton and (c) harmonicity considerations.

However, the hydrogen bond of I-a was at a lower position than the free acid with the tautomerism between the keto and the enol structures. The IR bands of I-g compound were at a lower position than the corresponding barbituric acid, due to the electronegativity difference between -O and -S atoms. The thio compound (I-g-S) (Tabel 3) existed mainly in the keto-thione skeleton. The I-i compound existed in different dynamic structures in euqilibrium to each other e.g. keto, enol, zwitter ion. The data of I-h (Table 3) indicated: (i) hyrogen bond between υNH and υOH, (ii) υC=O, υCH=N , υC=N and υN=N were identified, i.e., I-h existed in the azo-oxime structure with minimum contribution of the enol tautomer. The

TABLE 1. ANALYTICAL DATA OF THE PREPARED (Ia-ı) AND (IIa, b) COMPOUNDS.

Compound	Colour	Formula	%Found / (%Calculated)		
			C	H	N
I-a) Arylazo [O]	Yellow	$C_{10}H_8N_4O_3$	51.6 (71.7)	3.3 (3.4)	24.2 (24.1)
I-b) Tolyl [O]	Yellow	$C_{11}H_{10}N_4O_3$	53.5 (53.6)	4.1 (4.1)	22.4 (22.7)
I-c) Hydroxy [O]	Brown	$C_{10}H_8N_4O_4$	48.9 (48.3)	3.0 (3.2)	22.0 (22.5)
I-d) Chloro [O]	Yellow	$C_{10}H_7N_4O_3Cl$	45.1 (45.0)	2.6 (2.6)	21.0 (21.0)
I-e) Nitro [O]	Yellow	$C_{10}H_7N_5O_5$	43.0 (43.3)	2.2 (2.5)	25.0 (25.2)
I-f) Carboxy [O]	Orange	$C_{11}H_8N_4O_5$	48.1 (47.8)	3.4 (2.9)	20.3 (20.3)
I-g) Aldehydo [O]	Orange	$C_{11}H_8N_4O_4$	50.9 (50.7)	3.2 (3.1)	21.7 (21.5)
I-g) Aldehydo H_2O [S]	Orange	$C_{11}H_8N_4O_4$	44.2 (44.9)	3.3 (3.4)	18.7 (19.0)
I-h Aldoxime $2H_2O$ [O]	Yellow	$C_{11}H_{13}N_5O_6$	42.6 (42.4)	4.5 (4.2)	22.3 (22.5)
I-h) Aldoxime $3H_2O$ [S]	Orange	$C_{11}H_{15}N_5O_6S$	38.0 (38.3)	4.3 (4.3)	19.5 (20.3)
I-i) Schiff base [O]	Orange	$C_{13}H_{13}N_5O_4$	51.6 (51.5)	4.0 (4.3)	22.8 (23.1)
II-a) Benzylidene $3H_2O$ [O]	Pale Yellow	$C_{11}H_{14}N_2O_6$	49.1 (48.9)	3 (5.2)	10.2 (10.4)
II-a Benzylidene H_2O [S]$^{+++}$	Yellow	$C_{11}H_{10}N_2O_3S$	53.1 (52.8)	3.8 (4.0)	11.0 (11.2)
II-b) Salicylidene [O]	Orange	$C_{11}H_8N_2O_4$	57.1 (56.8)	3.1 (3.4)	12.0 (12.1)
II-b) Salicylidene [S}$^{+++}$	Pale Yellow	$C_{11}H_8N_4O_3S$	53.4 (53.2)	3.7 (3.2)	11.6 (11.3)

+ The % sulphur content: Found/ (Calculated): 10.4/(10.8) ; ++ The % Sulphur content: Found/ (Calculated): 12.3/(12.8) +++ The % Sulphur content: Found/ (Calculated): 12.9/(12.9) ;[O] Stands for compounds derived from barbituric acid. [S] Stands for compounds derived from thiobarbituric acid.

TABLE 2. ^{1}H-NMR SPECTRA FOR THE ORGANIC COMPOUNDS d^6 -DMSO.

Compound	Signals (δ, ppm)	Assignments
Barbituric acid	3.3	CH_2
	10.95	NH
Thiobarbituric acid	2.31	CH_2
	11.90	NH
I-a) 5-arylazobarbituric acid	7.0-7.7	C_6H_4, CH
	11.0-13.2	NH
I-b) 5-m-tolylazobarituric acid	2.3	CH_3
	6.9	CH
	7.3	C_6H_4
I-c) 5-m-hydroxyarylazo-barbituric acid	5.7-7.7	C_6H_4
	9.65	Phenolic OH
	11.2	NH
	13.9	OH
I-d) 5-m-chloroarylazo-baribituric acid	7.0-7.9	C_6H_4, CH
	10.7	NH
I-e) 5-m-nitroarylazo-barbituric acid	5.7	C_6H_4
	6.8-8.5	OH
	11.5-12.6	NH
I-f) 5-m-carboxyarylazo-barbituric acid	7.3-7.8	C_6H_4, CH
	8.1-8.2	COOH
	10.7-12.2	NH
I-g) 5-m-aldehydoarylazo-barbituric acid	7.4-8.1	C_6H_4, CH
	10.0	CHO
I-g) 5-m-aldehydoarylazo-thiobarbituric acid	7.0-8.3	C_6H_4, CH
	9.9	CHO
	12.35	NH
	14.1	Enolic OH
I-H) 5-m-(arylazobarbituric acid)-3'aldoxime	7.3-8.3	C_6H_4, 2CH
	11.3	NH
	14.0	OH
I-h) 5-m-(phenylazothio-barbituric acid)-3'-aldoxime	7.2-8.5	C_6H_4, CH
	11.2-12.0	OH
	12.2-12.8	NH
	14.2	Phenolic acid
I-i) 5-m-(arylazobarbituric acid)-3'-schiff base	7.4-8.0	C_6H_4, CH
	9.9	Alcoholic OH
	11.3	NH
	14.0	Enolic OH
II-a) 5-Benzylidene barbituric acid	7.2-8.6	C_6H_5, CH
	11.25	NH
II-a) 5-Benzylidene thiobar-bituric acid	6.8--8.2	C_6H_5, CH
	11.5	OH
	12.2	NH
II-b) 5-Salicylidene barbituric acid	4.65	CH
	6.8-7.4	C_6H_5
	11.0	OH
II-b) 5-Salicylidene thio-barbituric acid	4.9	NH
	6.7-7.3	C_6H_4, CH
	11.3-12.6	NH, OH

(Table 2 contd...)

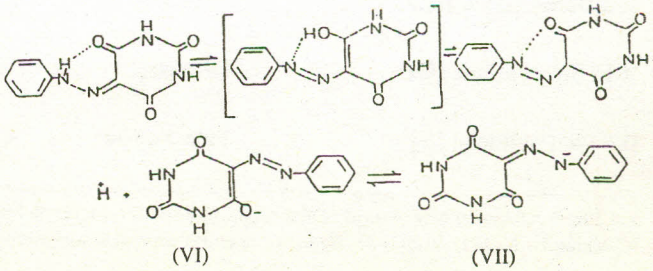
strong band at 1065 cm^{-1} was due to υN-OH of oxime-oximate interaction [8] in the thione structure (υC=S: 795 cm^{-1}; δC=S : 700 cm^{-1}). The 1430, 1265, 1100 and 795cm^{-1} were due to thioamide group [8-11]. The lowering of the υC-S was indicative of the reduced double bond character of the C=S bond. The bands at 1620 and 1605 cm^{-1} were due to C=N of medium and weak appearance, respectively, due to CH=N-OH and the tautomerism accompanied with conjugation and reduction of the double bond character of the C=N as a result of the increased polarity, respectively.

I-c gave a series of bands at 3570, 3510, 3210, 3090, 2850, 2150, 2120 and 1880 cm^{-1}, due to extensive hydrogen bond. The carbonyl bands in I-b were more resolved than that of I-c. The reverse was for the υC=N bands. In general, I-b and I-c compounds predominated in the keto and the enol tautomers, respectively.

II-a showed the presence of intramolecular hydrogen bond of the N-H...O type with the elucidation of υN-H, δN-H, γNH, υC=N, amide and thioamide I.δC-O(s), δ (S) O-H, υδC-N, δ C-O (S), δ C=O (s), γNH, υC=O (S) where the keto (or thione) and enol or (thiol) were in equilibrium to each other. The later tautomer existed in low concentration as controlled from the relative intensity of the bands. Bands of II-b were at a lower position than that of II-a due to hydrogen bonding, leading to increased degree of association. The thio system gave characteristic bands due to C-N and C=S, to assign the existence of the thione structure with the absence of υS-H bands. These compounds are centrosymmetric and exist in different conformations. The point of symmetry was lost, i.e. in an assymmetric nature.

Effect of pH on the electronic absorption spectra. Barbituric acid at different pH's gave three UV bands at λ_{max}, 240, 270 and 280 nm due to the existence of keto (pH < 1; 235 and 285 nm), enol (pH > 1; 245 and 265 nm) and and ionized species (pH > 7 ; 235, 260 and 285 nm) [15].

I-a (5 x 10^{-5}M) gave three bands at λ_{max} 200, 265 and 392 nm. The first two's were intense (n- π*) while the later one was of medium intensity due to the azo electronic transition (π -π*) in tautomers III and IV. In strong acidic media, the



(VI) (VII)

TABLE 3. SOME FUNDAMENTAL INFRARED BANDS (cm^{-1}) OF THE ORGANIC COMPOUNDS.

Compound	νO-H	νN-H	νC-H	νC=O	νC=N	νC-O	νC-N	νN-N
Barbituric acid (BA)	3550(s), 3470(s)	3190(s), 3100(s)	2880(s)	1760(m), 1750(m), 1720(m), 1700(m)	1630(m), 1365(m), 1350(s)	1285(s)	1235(s)	
Thiobarbituric acid (SBA)	3640(w), 3500(b)	3125(b)	2875(m)	1740(w), 1725(s), 1690(m), 1645(m)	1620(s), 1610(w)		1240(s), 1165(s)	
I-a) 5- (arylazo)-BA	3280(m)	3120(m)	2860(w), 2380(w)	1750(w), 1730(m), 1680(m)	1610(s), 1365(s)	1210(m)	1180(s), 1135(m)	1180(s), 1480(s)
I-b) m- (Tolylazo) - BA	3460(b)	3160(w)	3000(sh)	1735(m), 1680(m), 1650(s)	1600(w)	1300(s)	1250(s), 1160(s) 1065(m)	1570(s), 1500(b), 1410(sh)
I-c) m- (Hydroxyarylazo)-BA	3570(m), 3510(w)	3210(m), 3090(m)	2850(m), 2120(w), 1880(w)	1740(s), 1750(sh), 1680(sh)	1620(s)	1320(m), 1290(s)	1250(m), 1170(w), 1150(s), 1085(m), 1060(m)	1540(s), 1450(b)
I-d) m- (Chloroarylazo) - BA		3500(b)		1770(m), 1670(s)	1600(w)	1300(m)	1260(s)	1515(s), 1470(m), 1450(m)
I-e) m- (Nitroarylazo) - BA	3460(m)	3280(s), 3220(s), 3100(m)	2860(m)	1775(s), 1750(m), 1735(m), 1695(s)	1650(m), 1610(m)	1295(s), 1265(s)	1215(m)	1550(s), 1500(s), 1470(s), 1450(s)
I-f) m- (Carboxyarylazo)-BA	3380(w)	3120(sh)	2860(w) 2700(w), 1680(m)	1810(s), 1780(m), 1740(m), 1710(m)	1630(m), 1610(s)	1280(m)	1360(m), 1330(w), 1215(m)	1550(s), 1500(s), 1450(s)
I-g) m- (Aldehydoarylazo)-BA	3520(b)	3230(sh), 3080(w)	2860(w), 2200(s)	1760(s), 1710(w)	1620(w), 1600(m)	1300(m), 1265(s)	1350(w), 1170(w), 1150(m)	1550(s), 1480(m), 1440(m)
I-g) m- (Aldehydoarylazo)-SBA	3500(b)	3280(w), 3100(m)		1715(s), 1670(m)	1600(w)	1290(w)	1185(w), 1150(s)	1525(s), 1470(m), 1435(m)
I-h) m- (Arylazo)- BA-3-aldoxime	3320(m), 3220(m)	3100(m)	2880(w)	1750(w), 1725(s) 1685(s)	1625(m)	1290(m), 1260(s)	1165(m), 1130(m)	1550(s), 1510(s), 1480(s), 1440(s)
I-h) m- (Arylazo)- SBA aldoxime		3240(b)		1710(m), 1675(s)	1620(m), 1605(w)	1365(w)	1285(m), 1265(s)	1540(s), 1430
I-i) m- (Arylazo)-BA-3-aldoethanol amine	3520(b)	3230(m), 3100(m)	2870(m)	1765(s), 1710(s)	1625(w), 1605(m)	1285(s), 1270(w)	1175(w), 1155(m) 1040(m)	1550(s), 1485(m), 1440(s)
II-a) 5-Benzylidene-BA	3540(b)	3240(s), 3100(w)	2870(m), 1850(w)	1770(s), 1700(s)	1600(s), 1350(s)	1080(m), 1040(m)	1210(s)	
II-a) 5-Benzylidene-SBA	3100(b) 2920(w), 2360(w)	3100(b), 2920(w), 2360(w)	1715(m)	1715(m), 1670(s)	1585(m), 1545(s), 1445(s)	1305(m)	1230(m), 1205(s)	
II-b) 5-Salicylidene-SBA	3520(b)	3100(sh),	2850(m), 1830(w)	1740(s)	1675(sh), 1370(s), 1330	1280(s)	1235(s), 1155(s) 1135(m)	
II-b) 5-Salicylidene-SBA	3300(w)	3160(m)		1695(w), 1670(m)	1615(m)	1285(s)	1210(m), 1180(m)	

Abbreviations: strong (s); medium (m); broad (b); weak (w); shoulder (sh)

S = Strong (s); medium (m); broad (b); weak (w); shoulder (sh).

TABLE 4a. pK VALUES OF THE ORGANIC COMPOUNDS SPECTROPHOTOMETRICALLY (25°C, 0.5 M-KCl).

Compound		Half height	Modified limited absorption	Colleter
Barbituric acid (BA)	pk_1	5.30	5.25	5.35, 5.14
	pk_2	8.20	8.30	8.41, 7.33
Thiobarbituric acid (SBA)	pk_1	9.75	9.75	9.62, 9.71, 10.65
I-a) Arylazo-BA	pk_1	3.40	3.40	3.22, 3.50, 4.14
	pk_2	7.50		
I-b) Tolylazo-BA	pk_1	9.90	9.80	8.50, 9.00, 10.17, 9.34
I-c) Hydroxy-arylazo-Ba	pk_1	8.60	8.50	9.0, 8.74, 9.0, 9.49
	pk_2	12.20	12.00	12.95, 12.66, 12.19
I-d) Chloro-arylazoBA	pk_1	3.80	3.80	3.81, 3.65
	pk_2	7.25	7.00	6.65, 6.85, 6.42
I-e) Nitro-arylazo-BA	pk_1	7.50	7.35	6.37, 7.64, 7.68
	pk_2	11.30	11.30	11.72, 11.60
I-f) Carboxy-arylazo-BA	pk_1	8.30		
I-g) Aldehydoarylazo-BA	pk_1	9.00	9.00	8.34, 8.74, 8.42, 10.31, 9.44
I-g) Aldehydoarylazo-SBA	pk_1	6.2	6.2	4.50, 5.66, 5.50, 6.35
	pk_2	10.50	10.50	10.66, 10.50, 10.34
I-h) m-(Arylazo-BA)-	pk_1	7.80	7.80	8.19, 7.80
3'-aldoxime	pk_2	11.70	11.60	12.38
I-h) m-(Arylazo-SBA)-	pk_1	8.20	8.10	8.55, 9.23, 8.70, 8.25
3'-aldoxime	pk_2	12.00	12.00	12.55, 12.52, 12.52, 12.15
I-i) m-(arylazo-BA)-	pk_1	7.90	7.85	7.24, 4.85, 8.44
3'-schiff base	pk_2	11.30	11.30	10.77
II-a)5-Benzylidene-BA	pk_1	3.50	3.80	2.84, 4.65, 3.85
	pk_2	11.50	11.60	10.27, 11.79, 12.16
II-a)5-Salicylidene-BA	pk_1	6.20	6.15	5.66, 5.50, 7.57, 6.26
	pk_2	10.10	10.15	9.30, 9.91, 10.50, 10.75
II-b) 5-Benzylidene-SBA	pk_1	6.10	6.20	5.32, 6.16, 6.43, 6.85
II-b)5-Salicylidene	pk_1	6.50	6.75	5.89, 6.93, 7.74

TABLE 4b. pK VALUES OF THE ORGANIC COMPOUNDS POTENTIOMETRICALLY, 0.5 M-KCl, 50% v/v DIOXANE/H_2O, 25°C.

Compound	$\bar{n}_A$ - pH		Point-wise method		Algebraic method	
	pk_1	pk_2	pk_1	pk_2	pk_1	pk_2
BA*	3.80	-	3.90	-	3.89	-
BA**	4.35	-	4.40	-	4.35	-
BA***	5.40	-	5.30	-	5.31	-
SBA*	4.15	9.25	4.20	9.20	4.20	9.25
SBA**	4.65	11.30	4.70	11.35	4.48	-
I-a) 5-(Arylazo)-BA**	-	10.35	-	10.40	-	10.57
I-e) m-(Nitroarylazo)-BA**	9.75	-	9.80	-	9.80	-
I-f) m-(Carboxyarylazo) BA**	5.60	10.30	5.60	10.30	5.59	-
II-a) 5-Benzylidene-BA**	5.80	7.10	5.80	7.10	5.69	7.25
II-a) 5-Benzylidene-SBA**	6.50	11.40	6.80	11.40	6.52	-
II-b) 5-Salicylidene-BA**	5.00	6.90	5.00	6.90	4.93	6.87
II-b) 5-Salicylidene-SBA***	5.60	7.60	5.60	7.70	5.40	7.70

* Aqueous media; **50% v/vDioxane/water; ***75% v/v Dioxane/water.

tautomer (III) exists. In alkaline media, two main intense bands appeared with λ_{max} at 269 and 330 nm, where the CT bands mostly vanished with the creation of a new $n \rightarrow \pi$ band at 330 nm, as in tatutomer (V). The following equilibria exist. I-c (5 x 10^{-5}M) in the pH range (1.78-7.76), showed three electronic spectral bands at λ_{max} 226 (π–π^{α}), 262 (π–π^{α}) and 402 (n-π^{α}) nm. On increasing the pH, the second band was increased in intensity with a red shift, while the third one was decreased in intensity. Three isobestic points were observed at λ_{max} 262, 370 and 426 nm. The azo ==== hyrazo tautomerism is excluded due to the absence of the Q-band [19]

However, 5 x 10^{-5} M of I-b in the pH range (1.76-9.76) showed two bands: 230nm, week, K-band) and (390 nm, intense, R- band). So, the methyl group is of minor importance to affect the azo electronic requirements. In solutions with pH range 9.76-11.76, the K-band disappeared, and the R-band decreased in intensity accompanied with a blue shift due to

Compound	pH	322 nm (medium)	270 nm (weak)	378 nm (strong)
I-e	1.76-5.78	n ⟶ π*		n ⟶ π*
	7.76-9.76	decreased	increased with a slight blue shift of λ_{max}	decreased
	10-76-12.73			gradual increase with a slight red shift of λ_{max}
I-f I-g I-d	shows similar trend as I-e with two isobestic points at. 320 and 420 nm shows only one isobestic point at 362 nm shows different unresolved isobestic points			
	218 nm	246 nm	349 nm	
I-g	π ⟶ π* due to C=S increased with increase of pH		n ⟶ π* decreased with increase of pH with a blue shift of λ_{max}	

intramolecular hydrogen bonding between -OH and the -N=N- groups. Two isobestic points were at 232 and 362 nm. The mode of ionization of this compound follows I-a.

A general trend was observed for the compounds under investigation thus:

The data suggest the following tautomerism:

$$\rangle C = S \rightleftharpoons \rangle C - SH$$

with intramolecular hydrogen bonding between OH and the azo groups.

For I-h and thio analogue, proton ionization slightly increases the basicity of the oxime nitrogen through resonance stabilization of the oxime conjugate base.

I-i gave bands at λ_{max} 222 and 382 nm with the presence of one isobestic point at 362 nm. The latter band was red shifted with the increase of pH, due to sucessive ionization, and the alcoholic radical of the elthanolamine moiety was not affected with pH while the barbiturate moiety is sensitive to pH.

II-a (O- or S-) give bannds at 210 ($\pi \rightarrow \pi^*$) and 248 nm ($n \rightarrow \pi^*$) affected by pH, due to the keto ⟷ enol and thione ⟷ thiol euqilibria. In general, the acidity of the condensed product is lower than that of the free barbituric acid and red shifted due to cojugation. II-b (O- or S-) are somehow different than II-a and its thio analogue due to the presence of hydrogen bond in the salicylidene series.

pH-metric titration and evaluation of pK values. Different methods were applied to evaluate the pK values pH-metrically: 1) n_A-pH, 2) Point-wise, (3) Algebraic method [12]. Also, some spectrophotometric methods were applied for the same purpose: (i) Half height [20], (ii) colleter [21], (iii) modified limiting absorption [20]. Based on the pK values, the following observations were made (Table 4).

(1) The pK value for n_A increases with increasing the concentration of dioxane, due to decreasing polarity of the medium.

(2) Two pK values are obtained for all the azo compounds except I-g, I-b and I-f, where only one value is deduced. pK_1 is assigned to the deprotonation of the enolized group and pK_2 is attributed to the ionization of the -OH group fromed by tautomerization of the C=O with the acidic CH group to form a chelate structure with the azo group. The pk_2 value of I-C is attributed to the ionization of the m-OH group. The strenght of the intramolecular hydrogan bond, found between the -OH and -N=N- groups represented by the pK_2 values is affected by the nature of the substituents. The increased pK values of the compounds containing -CH_3 and -OH groups are attributed to their electron donor property. The electron acceptor substituents (-Cl, -COOH and -NO_2) attached to the phenyl ring decreased the pK value of the -OH group formed by tautomerization to weaken the intramolecular hydrogen bond, since the electron density on the azo group is decreased.

(3) The pK_1 value for the nitro compound is attributed to the ionization of the tautomeric step while pK_2 is assigned to proton ionization of the imino group [8].

(4) The pK value of 8.3 for I-f is due to the different resonating structures mainly in the keto form to strengthen its attracting property and facilitate the proton ionization. More or less similar results are obtained for I-g but with a slight higher pK value than I-f.

(5) Thiobarbituric acid is less acids than barbituric acid, since S is less electronegative than -O. The -CHO (S) compound gives high pK value compare to the -CHO(O) compound.

(6) The electron attracting property of the oxime group leads to lower the pK value of the aldehydo derivatives of barbituric and thiobarbituric acids. The Pk_2 values can be attributed to the -OH ionization of the oxime.

(7) pK values of I-i were attributed to the ionization of the tautomeric step associated with the proton ionization of the ethanolamine moiety. Lowering in the pK_1 value from 9.0 to 7.9 in case of the -CHO, and the schiff base respectively, was probably due to the attracting property of the -CH=N group.

(8) Two pK values were obtained for IIa and IIb, while only one pK value was obtained for the corresponding thio-analogues, attributed to the electronegativity between - O and -S atoms, which leads to more conjugation in the former compounds. pK_2 was due to the proton ionization as a results of tautomerism.

By virtue of +M and -I effects of the -OH group, the pK_1 value (6.20) of II-b is higher than that of barbituric acid (5.30). The value of pKa was due to the ionization of the phenolic-OH.

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