Reaction of α,β-Unsaturated Ketones with Guanidine. Substituent Effects on the Protonation Constants of 2-Amino-4,6-diarylpyrimidines

Farouk H. Al-Hajjar (1) and Salim S. Sabri (2)

Petroleum Technology Department, Kuwait Institute for Scientific Research,
P. O. Box 24885, Safat, Kuwait

Received September 15, 1981
Revised June 16, 1982

1,3-Diaryl-2-propen-1-ones, I, reacted with guanidine hydrochloride (II) in the presence of 3 moles of sodium hydroxide to give the corresponding 2-amino-4,6-diarylpyrimidines, III. The structure and configuration of the products are based on chemical and spectroscopic evidence.

The protonation constants of these compounds (series A and series B) have been determined in 50 volume percent ethanol-water medium. Excellent linear correlations are obtained when pK_a values of the two series of 2-amino-4,6-diarylpyrimidines, IIIa-j and IIIk-r, are plotted against the substituent constant, σx, and the polar substituent constant, $\sigma^* xC_6H_4$, for substituted phenyl groups.

The pK_a values have also been correlated with the extended Hammett equation. The correlation follows the equations:

$$\text{Series A; } pK_a = 3.273 - 0.820\sigma_{I,X} - 0.662\sigma_{R,X}$$

$$\text{Series B; } pK_a = 3.169 - 0.424\sigma_{I,X} - 0.137\sigma_{R,X}$$

J. Heterocyclic Chem., **19**, 1087 (1982).

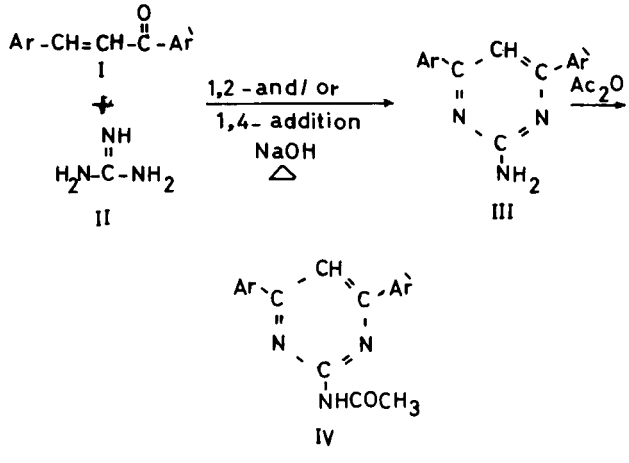
The reaction of acetylenic ketones with guanidine has been reported to give the corresponding 2-aminodiarylpyrimidines (3-8). The present investigation is intended to study the reaction of 1,3-diaryl-2-propen-1-ones, I, with guanidine and to account for the manipulated methods and, reasoning in establishing the mechanism of the reaction, the structure and configuration of the products as well as the effect of introducing a methyl group on the planarity of the molecule. The protonation constants of two series of these compounds (Ar' = C_6H_5 and p-$CH_3C_6H_4$) were correlated with extended Hammett equations [1] and [2] respectively.

$$pK_a = -\rho\sigma X + h \quad \ldots\ldots [1]$$

$$pK_a = \alpha\sigma_{I,X} + \beta\sigma_{R,X} + h \quad \ldots\ldots [2]$$

Two series of 2-aminopyrimidines, IIIa-j (Series A: Ar' = C_6H_5) and IIIk-r (Series B: Ar' = p-$CH_3C_6H_4$) were prepared by refluxing of 1,3-diaryl-2-propen-1-ones (1 mole), Ia-r, with an alcoholic solution of guanidine hydrochloride (1 mole) (II) containing an aqueous sodium hydroxide solution (3 moles) for 10 hours. The reaction of either 1-phenyl-3-(*p*-tolyl)-2-propen-1-one or 3-phenyl-1-(*p*-tolyl)-2-propen-1-one with guanidine hydrochloride (II) in the presence of 3 moles of sodium hydroxide solution gave the same product-type 2-amino-4-phenyl-6-(*p*-tolyl)pyrimidine (IIIb). The reaction proceeds either by 1,2-addition and/or 1,4-addition of the amino group of guanidine to the ketone, followed by cyclization to give the corresponding 2-aminopyrimidine derivatives III, according to the mechanism suggested for the thiourea reaction (9) (Scheme I). 1,4-Addition seems more likely by analogy to the reaction of α,β-unsaturated ketones with nitrogen compounds (10) and active methylene group (11,12).

SCHEME 1



series A (Ar = C_6H_5)

a) Ar = C_6H_5
b) Ar = p-$CH_3C_6H_4$
c) Ar = m-ClC_6H_4
d) Ar = p-ClC_6H_4
e) Ar = p-$CH_3OC_6H_4$
f) Ar = 3,4-$OCH_2OC_6H_3$
g) Ar = m-$NO_2C_6H_4$
h) Ar = p-FC_6H_4
i) Ar = m-BrC_6H_4
j) Ar = p-$NO_2C_6H_4$

series B (Ar = p-$CH_3C_6H_4$)

k) Ar = p-$CH_3C_6H_4$
l) Ar = m-ClC_6H_4
m) Ar = p-ClC_6H_4
n) Ar = m-$CH_3OC_6H_4$
o) Ar = p-FC_6H_4
p) Ar = 3,4-$OCH_2OC_6H_3$
q) Ar = m-BrC_6H_4
r) Ar = m-$NO_2C_6H_4$

The structure of the products, IIIa-r, was established spectroscopically and chemically. Thus, their ir spectra (*cf.*, Table 1) show two bands in the ranges 1640-1610 cm^{-1}

Table I

Infrared Nuclear Magnetic Resonance Spectral Data of 2-amino-6-aryl-4-phenylpyrimidines (IIIh, IIIk-r)

	Infrared values (a) (in potassium bromide) ν (cm^{-1})		Assignments	Nuclear Magnetic Resonance Values (b) (in deuteriochloroform) δ	Assignments (No. of Protons)
IIIh	3490	(m)	NH_2	8.02-6.97 (m)	(10) ArH + =CH-
	3325	(br)		5.40 (br)	(2) NH_2
	3200	(br)			
	1635	(s)	C=N		
	1565	(s)	C=C		
IIIk	3478	(m)	NH_2	7.97-6.85 (m)	(9) ArH + =CH-
	3280	(m)		5.37 (br)	(2) NH_2
	3162	(br)		2.40 (s)	(3) Ar-CH_3
	1610	(s)	C=N		
	1578	(s)	C=C		
IIIℓ	3320	(br)	NH_2	7.97-7.27 (m)	(9) ArH + =CH-
	3100	(br)		5.33 (br)	(2) NH_2
	1635	(s)	C=N	2.38 (s)	(3) Ar-CH_3
	1560	(s)	C=C		
IIIm	3325	(br)	NH_2	8.03-6.87 (m)	(9) Ar + =CH-
	3205	(m)		5.33 (br)	(2) -NH_2
	1640	(s)	C=N	2.40 (s)	(3) Ar-CH_3
	1560	(s)	C=C		
IIIn	3460	(m)	NH_2	7.97-7.03 (m)	(9) ArH + =CH-
	3310	(m)		5.37 (br)	(2) -NH_2
	3190	(m)			
	1624	(s)	C=N		
	1568	(s)	C=C		
IIIo	3330	(br)	NH_2	8.00-7.23 (m)	(9) ArH + =CH-
	3200	(br)		5.37 (br)	(2) -NH_2
	1640	(s)	C=N	2.40 (s)	(3) Ar-CH_3
	1565	(s)	C=C		
IIIp	3485	(m)	NH_2	8.17-6.80 (m)	(8) ArH + =CH-
	3300	(m)		4.0 (s)	(2) OCH_2O
	3185	(m)		5.47 (br)	(2) -NH_2
	1635	(s)	C=N	2.40 (s)	(3) Ar-CH_3
	1570	(s)	C=C		
IIIq	3490	(m)	NH_2	8.00-7.17 (m)	(9) ArH + =CH-
	3300	(m)		5.30 (br)	(2) -NH_2
	3180	(m)			
	1620	(s)	C=N	2.40 (s)	(3) -Ar-CH_3
	1570	(s)	C=C		
IIIr	3460	(w)	NH_2	8.33-7.21 (m)	(9) ArH + =CH-
	3290	(br)		5.89 (br)	(2) -NH_2
	3200	(m)			
	1610	(m)	C=N	2.40 (s)	(3) Ar-CH_3
	1570	(s)	and		
	1530	(m)	C=C		

Abbreviations (a) br = broad, m = medium, s = strong, w = weak. (b) br = broad, s = sharp, m = multiplet.

Table II

Ultraviolet Spectral Data of 2-Amino-4,6-diarylpyrimidines (IIIa-r)

Compound	Ultraviolet maxima Neutral form (a) λ nm (log ε)	Protonated form (b) λ nm (log ε)
IIIa	332 (4.07)	347 (4.23)
	252 (4.37)	288 (4.21)
IIIb	333 (4.13)	353 (4.32)
	255 (4.32)	298 (3.99)
IIIc	335 (4.15)	348 (4.24)
	257 (4.46)	282 (4.23)
IIId	337 (4.19)	348 (4.31)
	258 (4.47)	296 (4.28)
IIIe	336 (4.30)	364 (4.45)
	252 (4.36)	~286-270 (4.10)
IIIf	342 (4.27)	374 (4.36)
	238 (4.40)	296 (4.02)
IIIg	338 (4.11)	348 (4.18)
	245 (4.60)	247 (4.48)
IIIh	332 (4.09)	347 (4.24)
	253 (4.38)	292 (4.19)
IIIi	336 (4.17)	350 (4.29)
	259 (4.45)	298 (4.26)
IIIj	350 (4.05)	358 (4.18)
	268 (4.40)	274 (4.38)
IIIk	334 (4.20)	356 (4.39)
	264 (4.36)	308 (4.26)
IIIe	336 (4.15)	352 (4.31)
	254 (4.35)	282 (4.19)
IIIm	340 (4.31)	366 (4.45)
	262 (4.38)	301 (4.20)
IIIn	335 (4.10)	354 (4.27)
	~262-250 (4.21)	296 (4.11)
IIIo	333 (4.10)	352 (4.30)
	257 (4.28)	296 (3.19)
IIIp	342 (4.29)	374 (4.42)
	264 (4.20)	~316-304 (4.06)
IIIq	336 (4.21)	358 (4.31)
	255 (4.41)	305 (4.28)
IIIr	334 (4.11)	352 (4.50)
	~262-240 (4.29)	~270-250 (4.56)

(a) In 50 volume %, ethanol-water *p*H 7.0. (b) In 50 volume %, ethanol-water, *p*H 2.0.

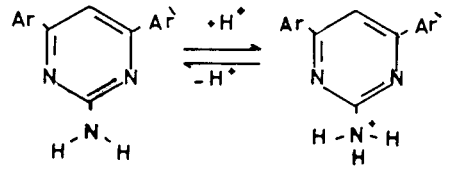
characteristic of the pyrimidine system (3-5), and three bands in the regions, 3490-3460 cm^{-1}, 3325-3280 cm^{-1}, and 3200-3100 cm^{-1} (νNH_2: free and H-bonded) (3).The nmr

spectra of these compounds gave further support for the aminopyrimidine structure, since they show a broad signal at δ 5.47-5.30 (NH_2) which disappeared when the deuteriochloroform solution was shaken with deuterium oxide. The ultraviolet spectra of III in 50% water-ethanol at *p*H's 2 and 7 gave two absorption maxima related to $'L_a$ and $'L_b$ bands, characteristic of the pyrimidine system (3). The values of the ultraviolet spectra for these compounds are shown in Table II. These results show a hypsochromic shift in going from *p*H 2 to *p*H 7 indicating that the auxochromic character of the amino group is not observed. Similar behaviour was reported for 2-aminopyrimidine (13), and 2-aminopyrimidine and their derivatives (14,15).

Acetylation of compounds, IIIa-f,g,i and j with acetic anhydride gave the corresponding acetyl-derivatives, IVa-f,g,i and j (3-5). The structure of these compounds was confirmed by their ir, uv and nmr spectra as well as their mp and mixed mp with authentic samples prepared as previously reported [*cf.*, references (3-5)].

Determination of the Protonation Constants of Two Series of 2-Amino-4,6-diarylpyrimidines IIIa-j and IIIk-r.

The acid-base equilibria of the two series of 2-aminopyrimidine derivatives, III, in 50% volume ethanol-water medium may be represented as follows:



The protonation constants (pK_a's) of the two series, IIIa-j and IIIk-r, were determined in 50% volume ethanol-water medium (25° ±0.1) using the spectrophotometric method at different *p*H values. Figure 1 shows the spectra of 2-amino-4,6-diphenylpyrimidine (IIIa) at different *p*H values. The dependence of absorbance on *p*H is shown in Figure 2 for the compound IIIa at 352 nm. The value of pK_a was calculated for each reading using the following equation [3].

$$pK_a = pH_x + \log(A_b - A_x)/(A_x - A_a) \quad \ldots\ldots [3]$$

Where A_x is the absorbance at pH_x; A_a and A_b are the absorbance values of the strongly acid and alkaline solutions of III, respectively. The results are summarized in Table III.

The pK_a values of the two series of 2-aminopyrimidine derivatives, IIIa-j and IIIk-r, were correlated with the simple Hammett equation {1} by two ways. In the first case,

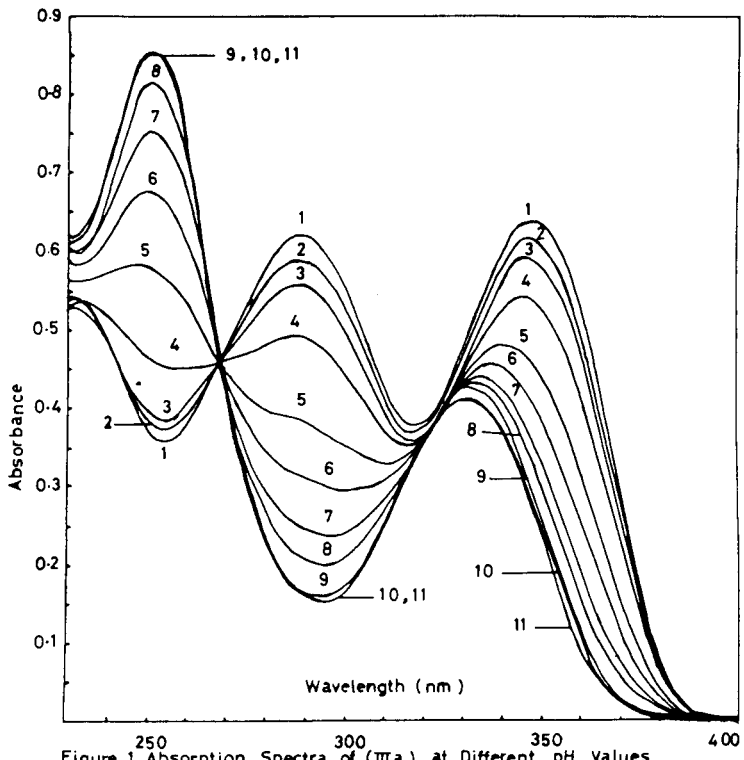


Figure 1. Absorption Spectra of (IIIa) at Different pH Values (3.485×10^{-5} M ; in 50 vol % ethanol - water, 25°)

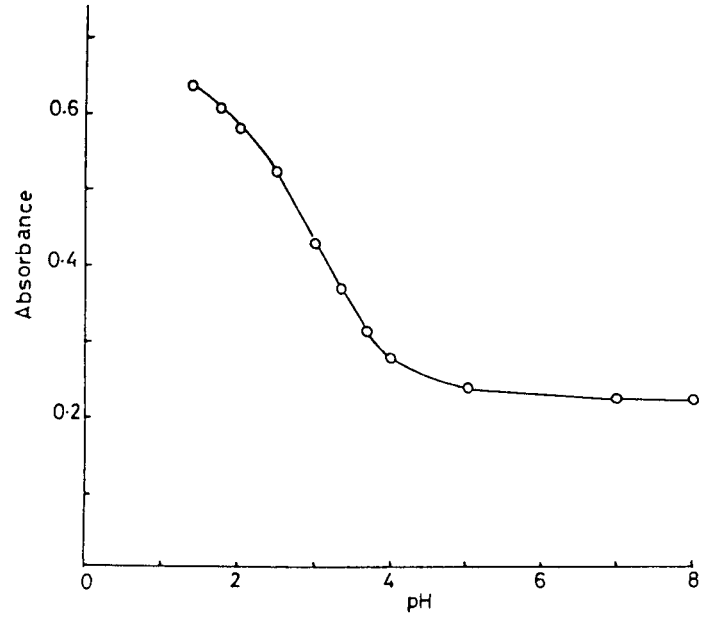


Figure 2. Absorbance as Function of pH for (IIIa) at 352 nm.

the pK_a values were plotted *vs.* the Hammett substituent constant σ_x of the X-substituent, Figures (3C and 4E). In the second case, we included the phenyl group with the substituent, and plotted the pK_a values against the polar substituent constant $\sigma^*xC_6H_4$ for substituent phenyl

Table III

Protonation Constants, pK_a, of Two Series of Substituted 2-Amino-2,4-diarylpyrimidines IIIa-j and IIIk-r, at 25°, μ = 0.10 *M* Hydrochloric Acid/-Sodium Chloride in 50 Volume % Ethanol-Water Solution

Series A		Series B	
Compound No.	pK_a	Compound No.	pK_a
IIIa	2.89	IVb	3.09
IIIb	3.09	IVk	3.18
IIIc	2.40	IVℓ	2.90
IIId	2.59	IVm	2.96
IIIe	3.26	IVn	3.04
IIIf	3.10	IVo	3.06
IIIg	1.97	IVp	3.17
IIIh	2.81	IVq	2.89
IIIi	2.39	IVr	2.72
IIIj	1.87		

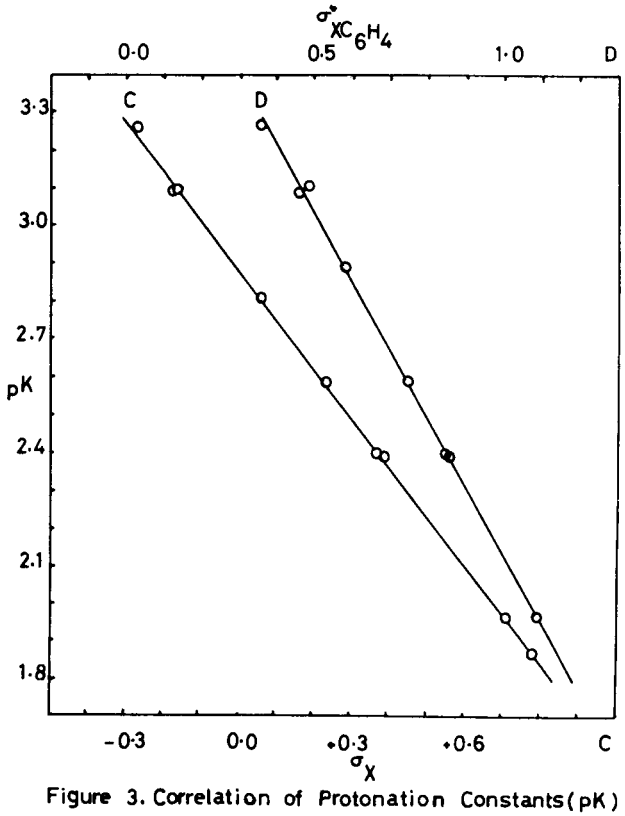


Figure 3. Correlation of Protonation Constants(pK) of 2-Amino-4,6-diaryl-pyrimidines(IIIa-j; series A) with the Substituents, σ_X(C) and $\sigma^*_{XC_6H_5}$ (D).

groups (16), Figures (3D and 4F). Excellent linear relations were obtained from the two series in both cases and may be represented by the equations:

Series A.

pK_a = (2.889 ±0.004) - (1.304 ±0.011) σx [4] and

PK_a = (3.924 ±0.018) - (1.787 ±0.026) σ^*xC_6H_4 [5], respectively.

Series B.

pK_a = (3.090 ±0.003) - (0.510 ±0.008) σx [6] and

pK_a = (3.536 ±0.011) - (0.762 ±0.015) $\sigma^*C_6H_4$ [7], respectively.

The pK_a values have also been correlated with the extended Hammett equation [2] by multiple regression analysis (17). The data used in the correlation are given in Table (IV) and the results are shown in Table (V). The results indicate that both the resonance and inductive parameters are linearly correlated with substituents when Ar' is a phenyl group (Series A). However, there is very poor correlation with the resonance parameter when Ar' is a tolyl group (Series B). This is manifested in the large standard deviation (greater than 2 times) obtained for this parameter (β) (Table V). Also, the values of α and β, thus obtained indicate that the composition of the electrical effect E, defined as the ratio β/α have the values 0.81 (Series A) and 0.32 (Series B), respectively, *i.e.*, the electrical effect of series B is 0.40 of that of the series A. It seems that the presence of the methyl group might affect the planarity of the aromatic ring with respect to the heteroaromatic ring.

Table IV

Substituent Constants used in the Correlation of Protonation Constants, pK_a, of 2-Amino-2,4-diarylpyrimidines IIIa-r

Substituent	σX	$\sigma^*XC_6H_4$	σI,X	σR,X
C_6H_5	0.00	0.58	0.00	0.00
p-$CH_3C_6H_4$	-0.17	0.46	-0.04	-0.13
m-Cl-C_6H_4	0.373	0.85	0.46	-0.09
p-Cl-C_6H_4	0.227	0.75	0.46	-0.23
p-$CH_3OC_6H_4$	-0.268	0.36	0.27	-0.54
3,4-$OCH_2OC_6H_3$	-0.16	0.48	—	—
m-$NO_2C_6H_4$	0.71	1.09	0.53	0.18
p-F-C_6H_4	0.062	—	—	—
m-Br-C_6H_4	0.39	0.86	0.49	-0.10
p-$NO_2C_6H_4$	0.778	1.50	0.65	0.62
m-$CH_3OC_6H_4$	0.115			

Table V

Results of Correlation with Equation [2]

Parameter	Series A Value	Series B Value
$-\alpha$	0.880	0.424
$-\beta$	0.662	0.137
h	3.273	3.169
R (a)	0.9998	0.9995
S_α (b)	0.254	0.196
S_β (b)	0.349	0.286
S_h (b)	0.202	0.168
n (c)	8	7

(a) Multiple correlation coefficient. (b) Standard errors of the estimates: α, β, and h, respectively. (c) Number of points.

Thus, reducing or eliminating the resonance contribution of Ar' ring leading to smaller pK_a values.

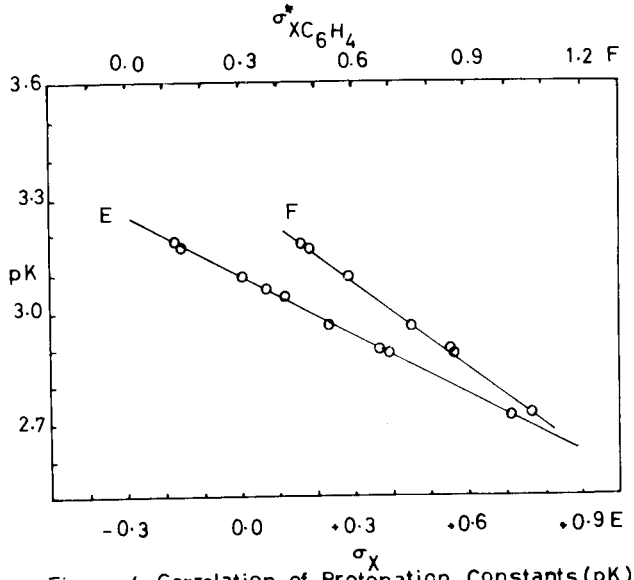


Figure 4. Correlation of Protonation Constants (pK) of 2-Amino-4,6-diaryl-pyrimidines (IIIk-l; series B) with the Substituents, σ_X (E) and $\sigma_{XC_6H_4}$ (F).

EXPERIMENTAL

The ir spectra were recorded using a Beckman IR 4260 Research Infrared Spectrophotometer. The ultraviolet spectra were measured on a Beckman Spectrophotometer ACTA using Scan speed ¼ nm/second and 10 nm/inch chart. The instrument was calibrated as previously described (18). The nmr spectra were measured on JEOL JNM-PM spectrometer using TMS as internal standard. Melting points are uncorrected. The purity of the analytical samples was checked by tlc (Silica gel). Microanalyses for C, H, N, Br, Cl and F were determined by Central Analytical Laboratory, KISR, Kuwait.

A Radiometer *p*H-meter model 63 fitted with a combined glass electrode type GK 2301C was used for determination of *p*H. The instrument was accurate to ± 0.01 *p*H unit. It was calibrated using two standard Radiometer buffer solutions at *p*H 4.01 and 7.00. The *p*H meter readings (B) recorded in 50 vol% ethanol-water solution were converted to hydrogen ion concentration $\{H^+\}$ by means of the widely known relation of Van Uitert and Hass (19),

$$-\log\{H^+\} = B \pm \log U_H$$

where U_H is the correction factor for the solvent composition and ionic strength for which B is used. For this purpose, readings were made on a series of solutions containing known amounts of hydrochloric acid and sodium chloride such that the ionic strength is equal to 0.10 in 50 vol% ethanol-water medium. The intercept, obtained from the linear plot of *p*H *vs.* B, corresponding to log U_H was found equal to 0.23 ± 0.01 at 25°.

For spectrophotometric determination of the protonation constants of compounds IIIa-r, an aliquot of the stock solution made by dissolving a known weight of 2-amino-4,6-diarylpyrimidine, III, in ethanol to give a $1.0 \times 10^{-2}M$ solution, was diluted with aqueous hydrochloric acid and ethanol. The final solution contains accurately about $3 \times 10^{-5}M$ of the compound III and 0.10 *M* hydrochloric acid in 50 vol% ethanol-water solution.

The absorption spectra of the solution at constant temperature, (25° ± 1) were taken at different *p*H's by adding carbonate-free sodium hydroxide and/or hydrochloric acid in small amounts. Since the total change in volume did not exceed 1.0%, no correction was made for the concentration of the compounds. The ionic strength was kept constant at 0.10 *M* hydrochloric acid/sodium chloride. Each compound was subjected to three pK_a determinations, and the average values given in Table III are within ± 0.01-0.03 pK_a units.

Reaction of 1,3-Diaryl-2-propen-1-ones with Guanidine.

General Procedure.

A mixture of the 1,3-diaryl-2-propen-1-one (0.05 mole) and guanidine hydrochloride (4.5 g) in ethanol (100 ml) was refluxed while a solution of sodium hydroxide (0.15 mole) in water (15 ml) was added portionwise during 4 hours. Refluxing was continued for a further 6 hours. The solvent was evaporated and the residue was diluted with water (200 ml) and extracted with benzene. Evaporation of benzene yielded white products which were crystallized from suitable solvents to give the corresponding 2-amino-4,6-diarylpyrimidines III.

2-Amino-4,6-diphenylpyrimidine (IIIa).

This compound had mp 138-139° (3).

Table VI

2-Amino-4,6-diarylpyrimidines (IIIh,k-IVr)

Compound	Yield (%)	Mp °C	Formula	Calcd. (%) C	H	N	X	Found (%) C	H	N	X
							F				F
IIIh	91	145-146 (b)	$C_{16}H_{12}FN_3$	72.74	4.56	15.84	7.16	72.51	4.58	15.99	7.01
IIIk	85	172-173 (a)	$C_{18}H_{17}N_3$	78.52	6.22	15.26	—	78.49	6.31	15.37	—
							Cl				Cl
IIIℓ	83	160-161 (a)	$C_{17}H_{14}ClN_3$	69.03	4.77	14.21	11.99	69.22	4.80	14.12	12.22
IIIm	86	168-169 (a)	$C_{17}H_{14}ClN_3$	69.03	4.77	14.21	11.99	69.11	4.75	14.02	12.18
IIIn	84	143-144 (a)	$C_{18}H_{17}N_3O$	74.20	5.88	14.42	—	74.33	5.98	14.67	—
							F				F
IIIo	89	159-160 (a)	$C_{17}H_{14}FN_3$	73.10	5.05	15.04	6.80	73.25	5.01	15.17	6.75
IIIp	94	218-219 (b)	$C_{18}H_{15}N_3O_2$	70.81	4.95	13.76	—	70.99	5.10	13.88	—
							Br				Br
IIIq	81	166-167 (b)	$C_{17}H_{14}BrN_3$	60.00	4.15	12.35	23.51	60.24	4.20	12.25	23.69
IVr	88	182-182 (b)	$C_{17}H_{14}N_4O_2$	66.66	4.61	18.29	—	66.51	4.67	18.51	—

(a) Crystallized from cyclohexane. (b) Crystallized from benzene.

2-Amino-4-phenyl-6-(*p*-tolyl)pyrimidine (IIIb).

This compound had mp 127-128° (3).

2-Amino-6-(*m*-chlorophenyl)-4-phenylpyrimidine (IIIc).

This compound had mp 132-133° (3).

2-Amino-6-(*p*-chlorophenyl)-4-phenylpyrimidine (IIId).

This compound had mp 157-158° (3).

2-Amino-6-(*p*-methoxyphenyl)-4-phenylpyrimidine (IIIe).

This compound had mp 161-162° (3).

2-Amino-6-(3,4-methylenedioxyphenyl)-4-phenylpyrimidine (IIIf).

This compound had mp 201-202° (3).

2-Amino-6-(*m*-nitrophenyl)-4-phenylpyrimidine (IIIg).

This compound had mp 185-186° (5).

2-Amino-6-(*m*-bromophenyl)-4-phenylpyrimidine (IIIi).

This compound had mp 116-117° (5).

2-Amino-6-(*p*-nitrophenyl)-4-phenylpyrimidine (IIIj).

This compound had mp 232-233° (4).

The other analytical and physical data for the balance of the compounds are reported in Table VI.

Acetylation of 2-Amino-4,6-diarylpyrimidines (IIIa-g, i and j).

The pyrimidine III (1.0 g) was heated with acetic anhydride (3 ml) on a boiling water-bath for one hour. The product which precipitated on addition of cold 50% ethanol (20 ml) was worked up as previously reported (3) to give the corresponding 2-acetamido-4,6-diarylpyrimidine (IV).

2-Acetamido-4,6-diphenylpyrimidine (IVa).

This compound had mp 224-225° (3).

2-Acetamido-4-phenyl-6-(*p*-tolyl)pyrimidine (IVb).

This compound had mp 150-151° (3).

2-Acetamido-6-(*m*-chlorophenyl)-4-phenylpyrimidine (IVc).

This compound had mp 174-175° (3).

2-Acetamido-6-(*p*-chlorophenyl)-4-phenylpyrimidine (IVd).

This compound had mp 185-186° (3).

2-Acetamido-6-(*p*-methoxyphenyl)-4-phenylpyrimidine (IVe).

This compound had mp 163-164° (3).

2-Acetamido-6-(3,4-methylenedioxyphenyl)-4-phenylpyrimidine (IVf).

This compound had mp 145-146° (3).

2-Acetamido-6-(*m*-nitrophenyl)-4-phenylpyrimidine (IVg).

This compound had mp 170-171° (5).

2-Acetamido-6-(*m*-bromophenyl)-4-phenylpyrimidine (IVi).

This compound had mp 170-171° (5).

2-Acetamido-6-(*p*-nitrophenyl)-4-phenylpyrimidine (IVj).

This compound had mp 232-233° (4).

REFERENCES AND NOTES

(1) To whom all correspondence should be addressed.

(2) On Sabbatical leave from the University of Jordan, Amman, Jordan.

(3) F. G. Baddar, F. H. Al-Hajjar, and N. R. El-Rayyes, *J. Heterocyclic Chem.*, **13**, 257 (1976).

(4) N. R. El-Rayyes and F. H. Al-Hajjar, *ibid.*, **14**, 257 (1977).

(5) Y. A. Al-Farkh, F. H. Al-Hajjar and H. S. Hamoud, *Chem. Pharm. Bull.*, **26**, 1298 (1978).

(6) G. Coispeau, J. Elguero, and R. Jacquier, *Bull. Soc. Chim. France*, 689 (1970).

(7) G. Coispeu and J. Elguero, *ibid.*, 2717 (1970).

(8) K. Bowden and E. R. H. Jones, *J. Chem. Soc.*, 953 (1946).

(9) F. H. Al-Hajjar, Y. A. Al-Farkh and H. S. Hamoud, *Can. J Chem.*, **57**, 2734 (1979).

(10) Y. Al-Farkh, F. H. Al-Hajjar, F. S. Al-Shamali and H. S. Hamoud, *Chem. Pharm. Bull.*, **27**, 264 (1979).

(11) R. Connor and D. B. Andrews, *J. Am. Chem. Soc.*, **56**, 2713 (1934).

(12) Y. Al-Farkh, F. H. Al-Hajjar and H. S. Hamoud, *J. Heterocyclic Chem.*, **16**, 1 (1979).

(13) M. M. Simson, *J. Am. Chem. Soc.*, **71**, 1470 (1949).

(14) E. A. Steck and J. W. Ewing, *ibid.*, **70**, 3397 (1948).

(15) K. B. DeRoss and C. A. Salemink, *Naturwissenschaften*, **56**, 1263 (1969).

(16) Y. Nagai, H. Matsumoto, J. Nakano, and H. Watanabe, *Bull. Chem. Soc. (Japan)*, **45**, 2560 (1972).

(17) M. R. Spiegel, "Theory and Problems of Statistics", Schaum Publishing Co, NY, 1961, p 269.

(18) M. S. El-Ezaby and N. Gayed, *J. Inorg. Nucl. Chem.*, **37**, 1065 (1975).

(19) L. G. Van Uitert and C. G. Haas, *J. Am. Chem. Soc.*, **75**, 451 (1953).