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3-Aryl-1-phenyl-2-propen-1-ones Ia-f and aroylphenylacetylenes Va-d reacted under reflux for 3 hours with cyanoacetamide in the presence of sodium ethoxide to give the corresponding 4-aryl-3-cyano-6-phenyl-2-(1*H*)pyridones VI. However, when ketones Ia-e were refluxed with cyanoacetamide for one hour in the presence of sodium ethoxide or piperidine, they gave the corresponding 4-aryl-3-cyano-3,4-dihydro-6-phenyl-2-(1*H*)pyridones IIIa-e, which upon heating with selenium gave the corresponding 2-pyridones VII. The structures of the products are based on chemical and spectroscopic evidence.

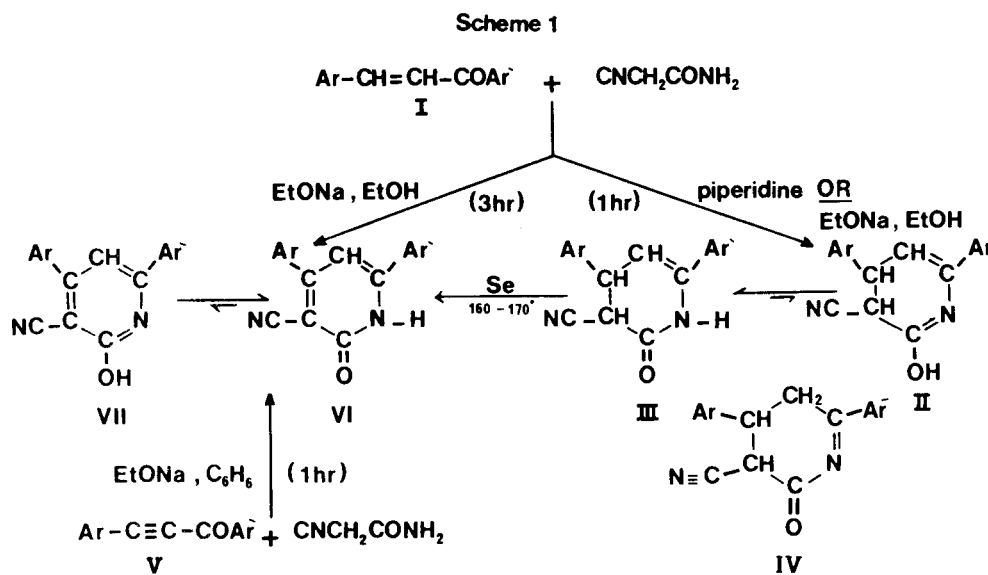
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The reactions of  $\alpha,\beta$ -unsaturated ketones with cyanoacetamide in the presence of sodium ethoxide (2-5) and piperidine (3-5) have been reported. In addition to the lengthy and laborious procedures employed, some of these reports contained erroneous structural assignments. In the present work, the reaction of cyanoacetamide with a series of  $\alpha,\beta$ -unsaturated ketones is studied in detail, and numerous new products are obtained. More efficient reaction procedures are introduced, and the spectroscopic as well as chemical properties of the products are used to deduce their structures. The initial reaction is deduced to be a simple 1,4-addition of the enolate anion to the conjugated system.

When 3-aryl-1-phenyl-2-propen-1-ones Ia-e were refluxed with cyanoacetamide in the presence of sodium ethoxide for one hour, they gave the corresponding 4-aryl-3-cyano-3,4-dihydro-6-phenyl-2-(1*H*)pyridones IIIa-e and not

4-aryl-3-cyano-6-phenyl-2,3,4,5-tetrahydropyridine IV as described previously by Barat (3). Similar treatment of If gave 4-*p*-chlorophenyl-3-cyano-6-phenyl-2-(1*H*)pyridone VI. However, when reflux was continued for 3 hours, the corresponding 4-aryl-3-cyano-6-phenyl-2-(1*H*)pyridones VIa-e were obtained. Products IIIb-e were also obtained in good yields when piperidine was substituted for sodium ethoxide (*cf.* Scheme 1).

The structures of the products were established both by spectroscopic and chemical evidence. Thus, the infrared spectra (potassium bromide) of compounds IIIa-e (Table I) were devoid of  $\nu$  OH, which excluded structure II. This conclusion is further supported by examining the infrared spectrum of IIIa in chloroform which shows a sharp band at  $3410\text{ cm}^{-1}$  (free NH) (6). These compounds also failed to give a color test with alcoholic ferric chloride solution. The proposed structure is also consistent with the



Compounds I, III and VI

a: Ar = C <sub>6</sub> H <sub>5</sub>	} Ar' = C <sub>6</sub> H <sub>5</sub>	e: Ar = 3,4-OCH <sub>2</sub> OC <sub>6</sub> H <sub>3</sub>	} Ar' = C <sub>6</sub> H <sub>5</sub>			
b: Ar = <i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>		f: Ar = <i>p</i> -Cl-C <sub>6</sub> H <sub>4</sub>		a: Ar = C <sub>6</sub> H <sub>5</sub>	} Ar' = C <sub>6</sub> H <sub>5</sub>	
c: Ar = <i>m</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>		g: Ar = C <sub>6</sub> H <sub>5</sub> ; Ar' = <i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>		b: Ar = <i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>		} Ar' = C <sub>6</sub> H <sub>5</sub>
d: Ar = <i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>				c: Ar = <i>p</i> -Cl-C <sub>6</sub> H <sub>4</sub>		
		d: Ar = C <sub>6</sub> H <sub>5</sub> ; Ar' = <i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>				

Compound V

a: Ar = C <sub>6</sub> H <sub>5</sub>	} Ar' = C <sub>6</sub> H <sub>5</sub>		
b: Ar = <i>p</i> -CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>		} Ar' = C <sub>6</sub> H <sub>5</sub>	
c: Ar = <i>p</i> -Cl-C <sub>6</sub> H <sub>4</sub>			} Ar' = C <sub>6</sub> H <sub>5</sub>
d: Ar = C <sub>6</sub> H <sub>5</sub> ; Ar' = <i>p</i> -CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>			

presence of a broad band in the region  $3220-3210\text{ cm}^{-1}$  ( $\nu$  NH) (6), and two strong bands in the regions  $1695-1690\text{ cm}^{-1}$  and  $1665-1650\text{ cm}^{-1}$ , which are attributed to the unconjugated carbonyl and the  $>C=C<$  stretching frequencies of the 2-pyridones (7). Further support for the assigned structures comes from the nmr spectra (Table I). They

show a multiplet in the region  $\delta$  4.33-3.33 and a doublet in the region  $\delta$  5.50-5.23 which correspond to the protons at carbons 3 and 4 and carbon 5, respectively. The spectra also show a broad signal in the region  $\delta$  9.90-8.13 attributed to the NH proton which disappears on the addition of deuterium oxide (8). The uv spectra of compounds

Table I

Infrared and Nuclear Magnetic Resonance Spectral Data of 4-Aryl-3-cyano-3,4-dihydro-6-phenyl-2(1H)pyridones (IIIa-e)

Compound No.	Infrared Bands (Potassium Bromide)		Nuclear Magnetic Resonance Values (Deuteriochloroform + DMSO- $d_6$ )	
	$\nu$ ( $\text{cm}^{-1}$ )	Assignments	$\delta$	Assignments (No. of Protons)
IIIa	3210 (br)	NH	9.90 (br)	(1) NH
	2220 (m)	C $\equiv$ N	7.67-7.17 (m)	(10) ArH
	1690 (s)	pyridone	5.4 (d)	(1) -CH= /
	1658 (s)	system	4.2-3.83 (m)	(2) >CH-CH \
IIIb	3215 (br)	NH	8.13 (br)	(1) NH
	2220 (m)	C $\equiv$ N	7.67-6.93 (m)	(9) ArH
	1695 (s)	pyridone	5.50 (d)	(1) -CH= /
	1660 (m)	system	4.27-3.43 (m)	(2) >CH-CH \
IIIc	3210 (br)	NH	8.17 (br)	(1) NH
	2220 (m)	C $\equiv$ N	7.50-6.67 (m)	(9) ArH
	1690 (s)	pyridone	5.43 (d)	(1) -CH= /
	1665 (s)	system	4.33-3.47 (m)	(2) >CH-CH + -OCH <sub>3</sub> \
IIId	3215 (br)	NH	9.40 (br)	(1) NH
	2220 (m)	C $\equiv$ N	8.0-6.77 (m)	(9) ArH
	1690 (s)	pyridone	5.40 (d)	(1) -CH= /
	1655 (m)	system	3.93-3.57 (m)	(5) >CH-CH + -OCH <sub>3</sub> \
IIIe	3220 (br)	NH	9.43 (br)	(1) NH
	2210 (w)	C $\equiv$ N	7.4 (s), 6.8 (s)	(8) ArH
	1690 (s)	pyridone	5.97 (s)	(2) OCH <sub>2</sub> O
	1650 (s)	system	5.23 (d)	(1) -CH= /
			4.17-3.33 (m)	(2) >CH-CH \

(a) In chloroform.

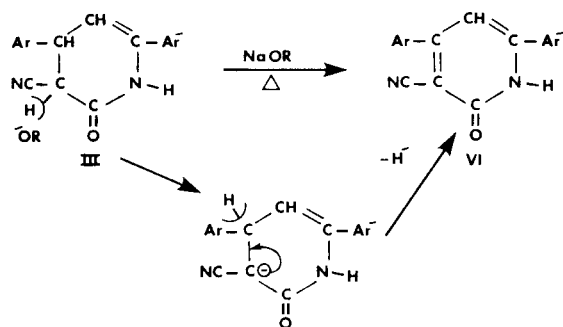
Table II

Ultraviolet Absorption Bands of Substituted 2(1H)pyridones (IIIa-e)

Compound No.	$\lambda$ max (nm) (log $\epsilon$ ) (a)		
	Carbon Tetrachloride	Ethanol	0.1N Sodium Hydroxide
IIIa	362 (3.13)	362 (3.32)	352 (3.47)
	262 (3.74)	280-254 (sh) (3.91)	251 (4.13)
IIIb	362 (3.12)	360 (3.31)	352 (3.39)
	266 (3.90)	266 (4.04)	249 (4.10)
IIIc	364 (2.92)	364 (2.98)	352 (3.53)
	277 (3.92)	275 (3.92)	250 (4.21)
IIId	360 (3.21)	360 (3.34)	354 (3.47)
	274 (3.84)	270 (3.95)	252 (4.12)
IIIe	358 (3.12)	358 (3.21)	364-340 (sh) (3.52)
	286 (3.86)	286 (3.98)	316 (3.71)
			236 (4.20)

(a) Abbreviation: sh = shoulder.

Scheme 2



IIIa-e lend further support to the proposed structures (Table II). These spectra show absorption bands attributable to  $\pi-\pi^*$  transition of the styrene moiety (9). The effect of solvent polarity (Table II) is exhibited as a red shift that varies inversely with the polarity of the solvent. This may be explained as due to the stabilizing

Scheme 3

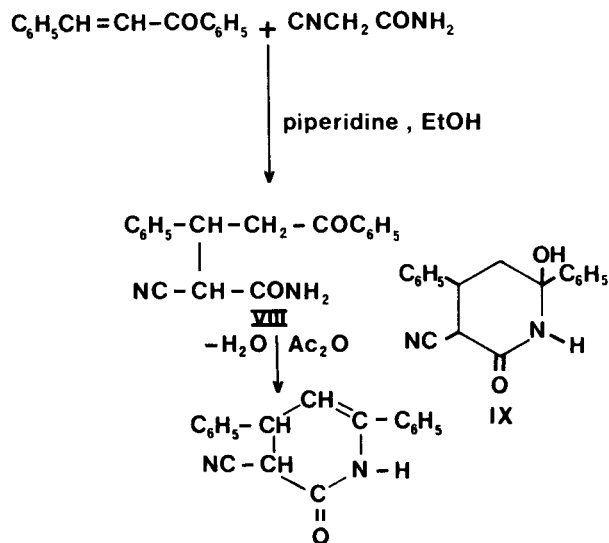


Table III

Infrared and Nuclear Magnetic Resonance Spectral Data of 4-Aryl-3-cyano-6-phenyl-2-(1H)pyridones (VIa-g)

Compound No.	Infrared Bands (Potassium Bromide)		Nuclear Magnetic Resonance Values (Deuteriochloroform + Deuterated Acetic Acid)	
	$\nu$ ( $cm^{-1}$ )	Assignments	$\delta$	Assignments (No. of Protons)
VIa	3100-2800 (br)	NH	8.00-7.33 (m)	(11) ArH + NH
	2218 (s)	C $\equiv$ N	6.8 (s)	(1) -CH=
	1640 (s)	>C=O		
VIb	3100-2800 (br)	NH	7.83-7.17 (m)	(10) ArH + NH
	2220 (s)	C $\equiv$ N	6.73 (s)	(1) -CH=
	1640 (s)	>C=O	2.43 (s)	(3) -CH <sub>3</sub>
VIc	3100-2800 (br)	NH	8.17-7.17 (m)	(10) ArH + NH
	2218 (s)	C $\equiv$ N	6.73 (s)	(1) -CH=
	1640 (s)	>C=O	3.87 (s)	(3) -OCH <sub>3</sub>
VI d	3100-2800 (br)	NH	7.83-6.93 (m)	(10) ArH + NH
	2220 (s)	C $\equiv$ N	6.77 (s)	(1) -CH=
	1645 (s)	>C=O	3.87 (s)	(3) -OCH <sub>3</sub>
VIe	3100-2800 (br)	NH	8.00-6.67 (m)	(9) ArH + NH
	2220 (s)	C $\equiv$ N	6.67 (s)	(1) -CH=
	1655 (s)	>C=O	6.07 (s)	(2) -OCH <sub>2</sub> O
VI f	3100-2800 (br)	NH	8.00-7.17 (m)	(10) ArH + NH
	2220 (s)	C $\equiv$ N	6.57 (s)	(1) -CH=
	1645 (s)	>C=O		
VIg	3100-2800 (br)	NH	7.83-7.17 (m)	(10) ArH + NH
	2226 (s)	C $\equiv$ N	6.7 (s)	(1) -CH=
	1635 (s)	>C=O	2.43 (s)	(3) -CH <sub>3</sub>

influence of hydrogen bonding on the amide form III; whereas the enol-form II is favored in the non-polar solvent. This situation is reminiscent of the behaviour of  $\beta$ -diketones (10) and a related series of pyrimidine derivatives (7,11).

The chemical behaviour of these compounds is also in good agreement with the assigned structures. Thus, upon

heating with 10% sodium hydroxide solution for 2 hours or with selenium at 160-170° for one hour, compounds IIIa-e gave the corresponding 4-aryl-3-cyano-6-phenyl-2-(1H)pyridones VI in good yields (Scheme 2). These last products are identical with the products obtained from the reaction of acetylenic ketones with cyanoacetamide in the presence of sodium ethoxide (*cf.* Scheme 1). The structures

Table IV

Ultraviolet Absorption Bands of 4,6-Diaryl-3-cyano-2-(1*H*)pyridone Derivatives (VIa-g) (a)

Compound No.	$\lambda$ max (nm) (log $\epsilon$ )		
	Chloroform	Ethanol	0.1 <i>N</i> Sodium Hydroxide
VIa	367 (4.15)	366 (4.10)	355 (4.16)
	290-278 (sh) (4.04)	292-278 (sh) (3.86)	254 (4.35)
	260 (4.34)	257 (4.24)	
VIb	367 (4.11)	365 (4.07)	354 (4.15)
	310 (3.97)	296 (3.90)	256 (4.33)
	259 (4.23)	257 (4.21)	
VIc	366 (4.14)	364 (4.10)	356 (4.37)
	292-280 (sh) (3.80)	294-282 (sh) (3.77)	252 (4.53)
	256 (4.32)	255 (4.30)	
VI d	370-354 (sh) (4.03)	366-348 (sh) (4.27)	356 (4.35)
	344 (4.08)	338 (4.28)	256 (4.51)
	257 (4.10)	256 (4.34)	
VIe	368 (4.21)	368 (4.14)	358 (4.29)
	298 (4.04)	296-282 (3.95)	258 (4.48)
	260 (4.32)	259 (4.31)	
VI f	360 (4.26)	357 (4.28)	355 (4.27)
	260 (4.28)	257 (4.33)	248 (4.31)
VIg	359 (4.09) (b)	370 (4.26)	357 (4.22)
	396-286 (sh) (3.97)	260 (4.29)	257 (4.31)
	261 (4.31)		

(a) Abbreviation: sh = shoulder. (b) In carbon tetrachloride.

of the latter series of compounds were established by studying their ir, nmr and uv spectra (*cf.* Tables III and IV). Thus, their ir spectra show a strong band in the region 1655-1635  $\text{cm}^{-1}$  (unsaturated pyridone system) and a broad band in the region 3100-2800  $\text{cm}^{-1}$  in addition to a strong band at 2226-2218  $\text{cm}^{-1}$  (conjugated  $\nu$  C $\equiv$ N) (8).

When the ir spectrum of VIb was run in chloroform solution, a sharp band at 3410  $\text{cm}^{-1}$  (free NH) was obtained. The nmr spectra of these compounds show a singlet in the region  $\delta$  6.80-6.67 attributable to the olefinic proton (7,8). Further support for the proposed structures of compounds VIa-f comes from their uv spectra which show strong resemblance to the spectra of substituted 2-pyridones (12) (Table IV). The ultraviolet spectra of compounds VIa-g in polar and non-polar solvent are listed in Table IV. A pattern of behaviour similar to that of series III is observed, and indicates that these compounds exist in the amide from VI rather than structure VII assumed by Sakurai and Midorikawa (8).

The reaction seems to proceed by 1:4-addition initiated by the enolate ion of cyanoacetamide. This assumption is supported by the separation of  $\delta$ -benzoyl- $\alpha$ -cyano- $\beta$ -phenylbutyramide (VIII) from the reaction of 1,3-diphenyl-2-propen-1-one (Ia) with cyanoacetamide in the presence of piperidine (Scheme 3). That this is the structure of the product, and not the hydroxy-piperidone structure IX assumed by Barat (3), is confirmed by chemical and

Table V

4-Aryl-3-cyano-3,4-dihydro-6-phenyl-2-(1*H*)pyridones (IIIa-e,g)

Compound No.	Yield (%)	M.p. °C	Formula	Calcd. %			Found %		
				C	H	N	C	H	N
IIIa (a)	90	234-235	C <sub>18</sub> H <sub>14</sub> N <sub>2</sub> O	78.81	5.14	10.21	78.93	5.25	10.17
IIIb	95	219-220	C <sub>19</sub> H <sub>16</sub> N <sub>2</sub> O	79.17	5.56	9.72	79.03	5.62	9.68
IIIc	92	170-171	C <sub>19</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	75.00	5.26	9.21	75.06	5.11	9.25
III d	88	216-217	C <sub>19</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	75.00	5.26	9.21	74.85	5.31	9.20
IIIe	90	231-232	C <sub>19</sub> H <sub>14</sub> N <sub>2</sub> O <sub>3</sub>	71.70	4.40	8.81	71.60	4.30	8.80
IIIg (3)	89	187-188	C <sub>19</sub> H <sub>16</sub> N <sub>2</sub> O	79.17	5.56	9.72	79.03	5.66	9.82

(a) Reported in m.p. 220-222° (3).

Table VI

4-Aryl-3-cyano-6-phenyl-2-(1*H*)pyridones (VIa-g)

Compound No.	Yield %	M.p. °C	Formula	Calcd. %			Found %		
				C	H	N	C	H	N
VIa	77	340 sub.	C <sub>18</sub> H <sub>12</sub> N <sub>2</sub> O	79.41	4.41	10.29	79.59	4.46	10.12
VIb	80	334 sub.	C <sub>19</sub> H <sub>14</sub> N <sub>2</sub> O	79.72	4.89	9.97	79.82	4.98	9.73
VIc	81	335 sub.	C <sub>19</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	75.49	4.64	9.27	75.87	4.86	9.01
VI d	83	234-235	C <sub>19</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	75.49	4.64	9.27	75.48	4.67	9.30
VIe	78	334 sub.	C <sub>19</sub> H <sub>12</sub> N <sub>2</sub> O <sub>3</sub>	72.15	3.80	8.86	72.08	3.83	8.60
VI f	88	330 sub.	C <sub>18</sub> H <sub>11</sub> N <sub>2</sub> OCl	70.47	3.59	9.14	70.48	3.63	9.00
VIg	79	274-275 (a)	C <sub>19</sub> H <sub>14</sub> N <sub>2</sub> O	—	—	9.97	—	—	9.83

(a) Reported m.p. 268° (4).

spectroscopic results. Thus, when this compound is heated with acetic anhydride, it gave 3-cyano-3,4-dihydro-4,6-diphenyl-2-(1*H*)pyridone (IIIa), identical with the product already separated from the reaction of Ia with cyanoacetamide in the presence of sodium ethoxide. Furthermore, the infrared spectrum (potassium bromide) shows two broad bands at 3180  $\text{cm}^{-1}$  and 3240  $\text{cm}^{-1}$  in addition to a sharp band at 3410  $\text{cm}^{-1}$  (free and bonded NH). In chloroform, two sharp bands at 3460  $\text{cm}^{-1}$  and 3410  $\text{cm}^{-1}$  appear and are attributed to free amino group (6).

It is now possible to reconstruct the sequence of steps in the reaction of olefinic  $\alpha,\beta$ -unsaturated ketones with cyanoacetamide as follows: I  $\rightarrow$  VIII  $\rightarrow$  III and/or VI, with a corresponding sequence for the acetylenic counterparts.

#### EXPERIMENTAL

Melting points are uncorrected. The ir spectra were recorded using a Beckman IR 4260 Research Infrared Spectrophotometer. The nmr spectra were measured on JEOL JNM-PM Spectrometer using TMS as internal standard. The ultraviolet spectra were measured on a Beckman Spectrophotometer ACTA using scan speed 1/4 nm/second and 10 nm/inch chart. The purity of the analytical samples was checked by tlc (Silica gel). Microanalyses for N were determined by Central Analytical Laboratory (KISR), while C and H were determined by Alfred Bernhardt, West Germany.

Reaction of 3-Aryl-1-phenyl-2-propen-1-ones Ia-f with Cyanoacetamide.

a) In the Presence of Piperidine.

A mixture of cyanoacetamide (0.0125 mole) of 3-aryl-1-phenyl-2-propen-1-one (I, 0.0125 mole) in ethanol (150 ml.) was heated on a boiling water bath, in the presence of piperidine (1 ml.), for 1 hour. The reaction mixture was cooled and then poured into dilute hydrochloric acid (10%, 100 ml.). The solid product was crystallized from methanol to give the corresponding 4-aryl-3-cyano-3,4-dihydro-6-phenyl-2-(1*H*)pyridone III as colorless needles (*cf.* Table V). In the case of 1,3-diphenyl-2-propen-1-one (Ia), the product isolated was  $\delta$ -benzoyl- $\alpha$ -cyano- $\beta$ -phenylbutyramide (VIII) as colorless needles, m.p. 168-169° (methanol) (reported m.p. 177-178) (5), yield 82%.

*Anal.* Calcd. for  $\text{C}_{18}\text{H}_{16}\text{N}_2\text{O}$ : C, 78.24; H, 5.84; N, 10.14. Found: C, 78.11; H, 5.68; N, 10.34.

Heating of the later compound with acetic anhydride for 1 hour on a boiling water bath, led to 3-cyano-3,4-dihydro-4,6-diphenyl-2-(1*H*)pyridone (IIIa) in quantitative yield.

b) In the Presence of Sodium Ethoxide.

The ketone I (0.0125 mole), dissolved in absolute ethanol (150 ml.), was mixed with the sodium salt of cyanoacetamide (0.0125 mole) (prepared

from cyanoacetamide and sodium ethoxide in 1:1 mole ratio). A deep orange color appeared, and the mixture was refluxed for 1 hour on a boiling water bath. The reaction mixture was concentrated and then poured into cold dilute hydrochloric acid (10%; 100 ml.). The product was crystallized from methanol to give the corresponding 4-aryl-3-cyano-3,4-dihydro-6-phenyl-2-(1*H*)pyridone IIIa-e as colorless crystals (yields 87-90%) (Table V).

Heating of these compounds (IIIa-e) with 10% sodium hydroxide solution for 2 hours or with selenium at 160-170° for 1 hour gave the corresponding 4-aryl-3-cyano-6-phenyl-2-(1*H*)pyridones VI (*cf.* Table VI).

When the reaction mixture in b was heated for 3 hours instead of 1 hour (except for If which does not require the long period of heating), it gave the corresponding 3-cyano-2-(1*H*)pyridone derivatives VI (yield 79-88%). Mixtures of III and VI of variable composition were obtained when the reaction mixture was heated for periods of 1.5-2.5 hours, and were separated by boiling with methanol.

Reaction of Aroylphenylacetylenes Va-d with Cyanoacetamide.

Aroylphenylacetylene V (0.0125 mole) in dry benzene (50 ml.) was added to the sodium salt of cyanoacetamide (0.0125 mole) in dry benzene (150 ml.). The reaction mixture, which gradually acquired deep red color, was heated under reflux for 1 hour. The reaction product was poured into dilute hydrochloric acid (10%, 150 ml.) and the benzene layer was washed successively with water, sodium hydrogen carbonate and water, dried (sodium sulfate) and evaporated. Crystallization of the residual solid from methanol gave the corresponding 4-aryl-3-cyano-6-phenyl-2-(1*H*)pyridone VI as colorless needles (*cf.* Table VI).

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