

SYNTHESIS AND REACTION OF 3-CYANO 2-(1H)-PYRIDONES

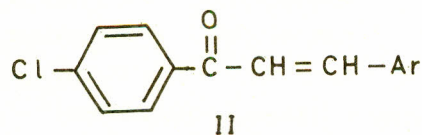
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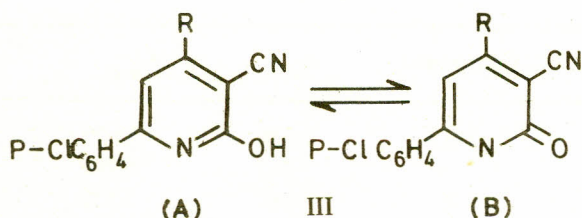
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Abstract. Ethyl cyanoacetate condenses with unsaturated Ketones (II) at 150° to give 3-cyano-4,6-diaryl-2-pyridones (III). The reactions of these compounds (III) with alkylating agents. Phosphorus oxychloride, amines and Grignard reagents has been investigated.

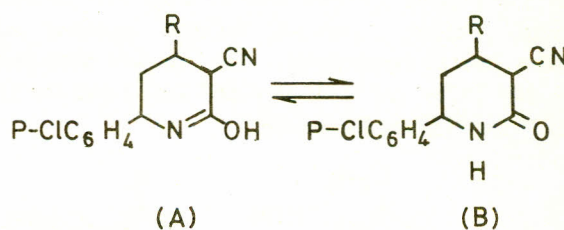
Ethyl cyanoacetate condenses with chalcones (IIa - g) in the presence of ammonium acetate to give (IIIa - g), (IV a - e) and (V a - e)¹⁻³. The condensation was carried out by heating a mixture of ethyl cyanoacetate, chalcone and ammonium acetate (molar ratio 1:1:0.8) at 150° for 6 hr. Treatment of the reaction mixture with ethanol yielded two parts: the ethanol-insoluble part afforded 3-cyano-4,6-diaryl-2-pyridones (III a - g), and the ethanol-soluble part which on fractional crystallization gave 3-cyano-4,6-diaryl-hexahydro-2-pyridones (IV a - e) and ethyl-2-amino-4,6-diaryl-nicotinic acids (V a - e)



- Ar
- | | |
|---|--|
| a | C ₆ H ₅ |
| b | C ₄ H ₃ O-2 |
| c | C ₆ H ₄ N(CH ₃) ₂ (p)- |
| d | C ₆ H ₃ O ₂ CH ₂ -(3,4)- |
| e | C ₆ H ₄ OCH ₃ (p)- |
| f | C ₆ H ₅ .CH=CH- |
| g | C ₆ H ₄ NO ₂ (m)- |

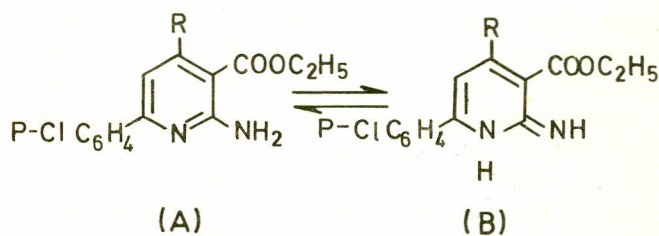


- | | | |
|-----|---|-----|
| (A) | III | (B) |
| a | C ₆ H ₅ | |
| b | C ₄ H ₃ O-2 | |
| c | C ₆ H ₄ N(CH ₃) ₂ (P)- | |
| d | C ₆ H ₃ O ₂ CH ₂ (3,4)- | |
| e | C ₆ H ₄ OCH ₃ (P)- | |
| f | C ₆ H ₅ .CH=CH- | |
| g | C ₆ H ₄ NO ₂ (m)- | |



(IV)

- | | |
|---|---|
| R | |
| a | C ₆ H ₅ - |
| b | C ₄ H ₃ O-(2) |
| c | C ₆ H ₄ N(CH ₃) ₂ (p)- |
| d | C ₆ H ₅ .CH=CH- |
| e | C ₆ H ₄ NO ₂ (m)- |



(V)

- | | |
|---|---|
| R | |
| a | C ₄ H ₃ O-(2) |
| b | C ₆ H ₄ N(CH ₃) ₂ (p)- |
| c | C ₆ H ₃ O ₂ CH ₂ (3,4)- |
| d | C ₆ H ₄ OCH ₃ |
| e | C ₆ H ₄ NO ₂ (m)- |

The products (III a - g) were shown beyond doubt to be 3-cyano-2-pyridones by the following evidence:

(i) The compound (IIIa) was identical with that formed by reaction of benzoyl-*p*-chloroacetophenone with cyanoacetamide.

(ii) Boiling (III a) with conc hydrochloric acid hydrolysed the cyano group and gave 4-phenyl-6-*p*-chlorophenyl-2-pyridone-3-carboxylic acid (VI).

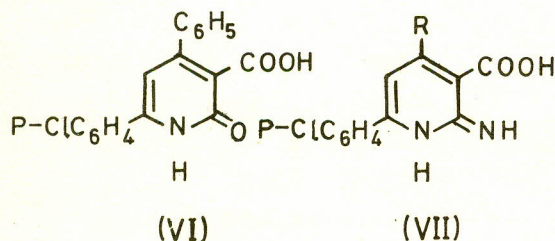
(iii) Their IR spectra showed the C≡N frequency at

2227 cm^{-1} and the carbonyl stretching frequency in the range 1706-1649 cm^{-1} , NH and OH frequencies in the range 3080-2725 cm^{-1} , characteristic of 2-pyridones^{4,9,14} (iv) Their UV spectra showed absorptions at $\lambda_{\text{max}}^{\text{ACOH}}$ 346 $\text{m}\mu$ (ϵ 7900) and $\lambda_{\text{max}}^{\text{ACOH}}$ 261 $\text{m}\mu$ (ϵ 7700).

The following facts are recorded in support of the structure V.

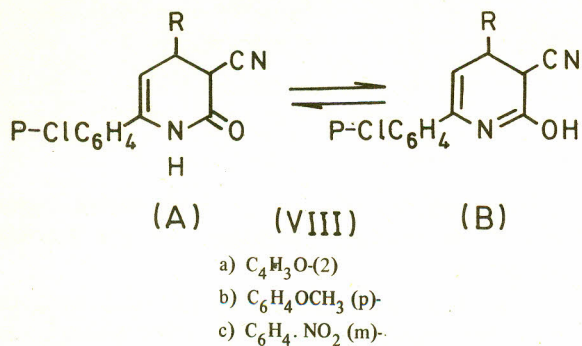
(i) The IR spectra showed well defined absorption bands at (3289 cm^{-1} broad), (1684 cm^{-1}) and (1613-1557 cm^{-1}) attributable to NH, C=O and C \equiv N respectively.

(ii) Hydrolysis of (Va and b) with 10% alcoholic potash yielded 2-amino-4, 6-diaryl nicotinic acids (VII a and b) respectively. The showed absorptions for NH (3289 cm^{-1}), C=O (1667 cm^{-1}) and for C=N (1577 cm^{-1}) in the IR spectra.

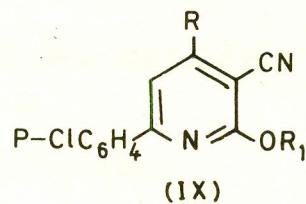


- (VI) (VII)
 a) R = C₆H₅
 b) R = C₆H₃O₂CH₂(3,4)

The reaction with chalcones, when carried in benzene gave only the 3-cyano-4, 6-diaryl-2-oxo-1,2,3,4-tetrahydropyridine derivatives (VIII a-c). This involved most probably the Michael addition and cyclization without dehydrogenation. In favour of this assumption is the fact that (III b) can be prepared from (VIII a) by heating at 120 - 150° or by action of bromine via aromatization. The IR spectrum of (VIIIa) exhibited characteristic absorption bands for NH and OH (3106 - 2985 cm^{-1}), C \equiv N (2227 cm^{-1}) and CO (1692 cm^{-1})



Reactions with 3-Cyano-2-(1H)-Pyridones: Alkylation: Treatment of the sodium or potassium or potassium salts of (III a-g) with dimethyl sulphate, diethyl sulphate, allyl chloride, benzyl chloride, ethylbromacetate and or ethyl bromomalonate gave (IX a-p).



	R	R ₁
a	C ₆ H ₄ OCH ₃ (p)	CH ₃
b	C ₆ H ₃ O ₂ CH ₂ (3,4)	CH ₃
c	C ₆ H ₅	C ₂ H ₅
d	C ₆ H ₅	-CH ₂ CH=CH ₂
e	C ₆ H ₄ OCH ₃ (p)	-CH ₂ .CH=CH ₂
f	C ₆ H ₃ O ₂ CH ₂ (3,4)	-CH ₂ .CH=CH ₂
g	C ₆ H ₅	-CH ₂ -C ₆ H ₅
h	C ₆ H ₄ NO ₂ (m)	-CH ₂ -C ₆ H ₅
i	C ₆ H ₄ OCH ₃ (p)	-CH ₂ -C ₆ H ₅
j	C ₄ H ₃ O(2)	-CH ₂ -C ₆ H ₅
k	C ₆ H ₄ N(CH ₃) ₂ (p)	-CH ₂ -C ₆ H ₅
l	C ₆ H ₅	-CH ₂ COOC ₂ H ₅
m	C ₆ H ₄ OCH ₃ (p)	-CH ₂ COOC ₂ H ₅
n	C ₆ H ₃ O ₂ CH ₂ (3,4)	-CH ₂ COOC ₂ H ₅
o	C ₆ H ₅ -CH=CH-	-CH ₂ COOC ₂ H ₅
p	C ₆ H ₅	-CH(COO C ₂ H ₅) ₂

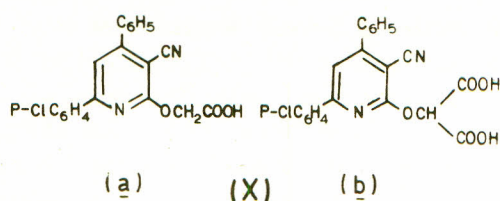
The structure of (IX) was confirmed from:

i) *Spectroscopically.* (a) The IR spectra showed bands attributable for C \equiv N (2227 cm^{-1}), C=N (1608 - 1592 cm^{-1}), C=C (1584 - 1567 cm^{-1}) The ester group (1757 - 1692 cm^{-1}) and ether linkage group (1242 cm^{-1}) and showed the absence of OH, NH, and CO groups. (b) The UV spectra of IXf, l and m showed the following results (Table 1) in C₂H₅OH delete.

TABLE 1.

Compound	λ_{max}	ϵ_{max}
1 X F	326	6100
	267	5280
1 X l	357	3300
	330	3500
	260	500
1 X m	325	5200
	266	4900

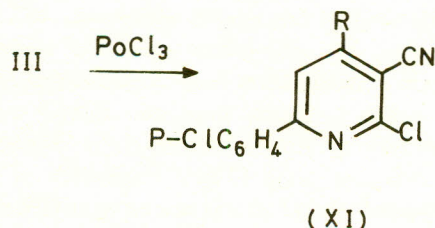
ii) *Chemically.* It has been found that the esters (IX l and p) are easily hydrolysed under alkaline conditions to give the expected acid products (X a and X b) respectively.



The structure of (Xa) was proved from: Correct analytical values, solubility in Sodium bicarbonate solution and showed a band for carboxylic group at (1700 cm^{-1}) and at (2950 cm^{-1}) for hydroxyl group.

The structure of (Xb) was proved from solubility in sodium bicarbonate solution and was decarboxylated to give (Xa) identified by melting point and mixed melting points.

Action of phosphorousoxychloride on-(III). The products (III a - g) on treatment with POCl_3 gave 2-chloro-4, 6-diaryl nicotinonitriles (XI a - g).

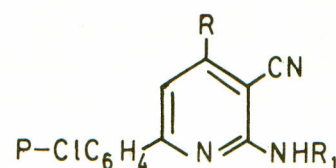


	R
a	C_6H_5 -
b	$\text{C}_4\text{H}_3\text{O}$ -(2)
c	$\text{C}_6\text{H}_4\text{N}(\text{CH}_2)_2$ (p)-
d	$\text{C}_6\text{H}_3\text{O}_2\text{CH}_2$ (3,4)-
e	$\text{CH}_3\text{OC}_6\text{H}_4$ -(p)
f	$\text{C}_6\text{H}_5\text{-CH=CH-}$
g	$\text{NO}_2\text{C}_6\text{H}_4$ -(m)

The structure of compounds (XI) has been confirmed by the following: (i) IR spectra showed different characteristic bands for $\text{C}\equiv\text{N}$ and $\text{C}=\text{N}$ groups (2227 cm^{-1} , $1608\text{-}1577\text{ cm}^{-1}$) respectively. (ii) UV spectrum of (XI c and f) shows $\text{EtOH}\lambda_{\text{max}}$ $360\text{ m}\mu$ (ϵ 6350) and $\text{EtOH}\lambda_{\text{max}}$ $325\text{ m}\mu$ (ϵ 800) respectively. (iii) Treatment of the tetrahydropyridone derivatives (VIII a - c) with POCl_3 resulted in the replacement of the hydroxyl group by chlorine accompanied by dehydrogenation and formation of (XI b,e and g) that were identified by melting point and mixed melting point.

Treatment of XIa with sodium methoxide,⁹ sodium ethoxide and sodium allyloxide gave (IX a, c and d) identical with that obtained by alkylation of (IIIa,c and d). as shown by IR spectra of the compounds.

The easily-replaceable chlorine at position 2, in products (XI a - g) was reacted with various amines and 2-amino derivatives (XIII) thus obtained are as follows:

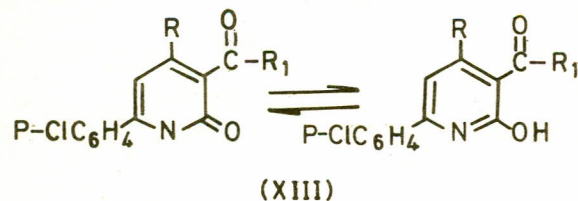


	R	R ₁
a	C_6H_5 -	CH_3
b	C_6H_5 -	C_4H_9 -n
c	C_6H_5	$\text{CH}_2\text{-CH}_2\text{OH}$
d	C_6H_5	C_6H_{11}
e	C_6H_5	$\text{C}_6\text{H}_4\text{COOH(o)}$
f	C_6H_5	$\text{C}_6\text{H}_4\text{C}_6\text{H}_4\text{NH}_2$
g	C_6H_5	$\text{C}_6\text{H}_4\text{SO}_2\text{NH-C-NH}_2$ NH
h	$\text{C}_6\text{H}_4\text{OCH}_3$ (p)-	CH_3
i	$\text{C}_6\text{H}_4\text{OCH}_3$ (p)-	C_4H_9 -n
j	$\text{C}_6\text{H}_4\text{OCH}_3$ (p)-	$\text{CH}_2\text{C}_6\text{H}_5$
k	$\text{C}_6\text{H}_4\text{OCH}_3$ (p)-	$\text{CH}_2\text{C}_4\text{H}_3\text{O}$ (2)
l	$\text{C}_6\text{H}_4\text{OCH}_3$ (p)-	C_{10}H_7 (α)-
m	$\text{C}_6\text{H}_4\text{OCH}_3$ (p)-	$\text{C}_6\text{H}_4\text{SO}_2\text{NH}_2$ (p)-
n	$\text{C}_6\text{H}_4\text{OCH}_3$ (p)-	$\text{C}_6\text{H}_4\text{-SO}_2\text{NH}$
o	$\text{C}_6\text{H}_4\text{NO}_2$ (m)-	C_4H_9 -n
p	$\text{C}_6\text{H}_4\text{NO}_2$ (m)-	$\text{CH}_2\text{-CH}_2\text{-OH}$
q	$\text{C}_6\text{H}_4\text{NO}_2$ (m)-	$\text{CH}_2\text{-CH}_2\text{CH}_3$
r	$\text{C}_6\text{H}_4\text{NO}_2$ (m)-	$\text{C}_6\text{H}_4\text{Cl}$ (p)-
s	$\text{C}_6\text{H}_4\text{NO}_2$ (m)-	$\text{CH}_2\text{-C}_6\text{H}_5$
t	$\text{C}_6\text{H}_4\text{NO}_2$ (m)-	$\text{CH}_2\text{C}_4\text{H}_3\text{O}$ (2)
u	$\text{C}_6\text{H}_4\text{NO}_2$ (m)-	C_{10}H_7 (α)-
v	$\text{C}_6\text{H}_4\text{NO}_2$ (m)-	$\text{C}_6\text{H}_4\text{CH}_3$ (p)-
w	$\text{C}_6\text{H}_3\text{O}_2\text{CH}_2$ (3,4)-	$\text{-CH(CH}_3)_2$
x	$\text{C}_6\text{H}_3\text{O}_2\text{CH}_2$ (3,4)-	$\text{C}_6\text{H}_4\text{SO}_3\text{H}$ (p)-
y	$\text{C}_6\text{H}_3\text{O}_2\text{CH}_2$ (3,4)-	$\text{C}_6\text{H}_4\text{SO}_3\text{H}$ (p)-
z	$\text{C}_6\text{H}_3\text{O}_2\text{CH}_2$ (3,4)-	C_{10}H_7 (α)-
a	$\text{C}_4\text{H}_3\text{O}$ -2	C_4H_9 -n
b	$\text{C}_6\text{H}_4\text{N}(\text{CH}_3)_2$ (p)-	C_4H_9 -n

The IR spectra of the (XIIc and p) showed well defined absorption bands attributable to the NH_2 grouping (3030 cm^{-1}) and in (XIIe) to carboxylic grouping (1700 cm^{-1}) and to hydroxyl grouping (2950 cm^{-1}). The UV. absorption spectra of (XIIg, X and b) showed $\text{EtOH}\lambda_{\text{max}}$ $265\text{ m}\mu$, $318\text{ m}\mu$ and $456\text{ m}\mu$, (ϵ_{max} 9400 6400 and 9600) respectively.

Reaction of Grignard Reagents with III. 3-Cyano-2-(1 H)-pyridones(III) reacted with Grignard reagents namely methyl magnesium iodide, ethyl magnesium

iodide, phenyl magnesium bromide and benzyl magnesium chloride and give 3-acyl-2(1H)-pyridones (XIII a-j)^{12,13} Best results were obtained by using four moles of the Grignard reagent to one mole of the pyridone.



	R	R ₁
a	C ₆ H ₅	CH ₃
b	C ₆ H ₅ -	C ₂ H ₅
c	C ₆ H ₅ -	CH ₂ C ₆ H ₅
d	C ₄ H ₃ O-(2)	CH ₃
e	C ₄ H ₃ O-(2)	C ₆ H ₅
f	C ₆ H ₄ OCH ₃ (p)-	C ₆ H ₅
g	C ₆ H ₃ O ₂ CH ₂ (3,4)-	CH ₃
h	C ₆ H ₃ O ₂ CH ₂ (3,4)-	C ₆ H ₅
i	C ₆ H ₄ NO ₂ (m)-	CH ₃
j	C ₆ H ₄ NO ₂ (m)-	C ₂ H ₅

The IR spectra (Table 2) noted for the compounds (XIII) supports the structure assigned to them.

TABLE 2.

Compound	C=N cm ⁻¹	C=O cm ⁻¹	Amide C=O cm ⁻¹
XIII a	1650	1678	1660
b	1625	1680	1660
c	1628	1675	1658
d	1632	1680	1650
e	1624	1670	1660
g	1620	1672	1658
i	1630	1675	1658

The UV Spectra of (XIII d and i) showed the following absorption bands at $\text{EtOH} \lambda_{\text{max}}$ 313 m μ (ϵ_{max} 3200) and $\text{EtOH} \lambda_{\text{max}}$ 257 m μ (ϵ_{max} 7800) respectively.

Experimental

The IR absorption spectra were determined with a Unicam sp. 1200 spectrophotometer using KBr wafer Technique. The UV absorption spectra were determined with a unicam sp. 8000 UV recording spectrophotometer. All melting points are uncorrected.

The Reaction of Ethyl-cyano-acetate with Chal-

cones without a Solvent. A mixture of ethyl cyanoacetate (0.04 mole), the unsaturated Ketone II (0.04 mole), and ammonium acetate (0.03 mole) was heated at 150° for 6 hr and then allowed to cool. The yellowish red oil obtained was washed with ethanol. It was divided into two parts, an ethanol soluble part and ethanol insoluble part. The ethanol solution was concentrated after standing it overnight at room temperature. Colourless crystals separated which on recrystallizing from ethanol gave (V) (Table 5). The oil separated after addition of water to the ethanol filtrate, was dissolved in ether. The ethereal solution after standing overnight at room temperature gave crystals which after crystallization from ethanol gave (IV) (Table 4). The ethanol-insoluble part, was crystallized from glacial acetic acid and it afforded (III) as coloured crystals (Table 3).

Hydrolysis of (III a): Formation of 2-Hydroxy-6-(p-Chlorophenyl)-4-Phenyl-nicotinic Acid (VI). The comp. (III a) (1 g) was heated with conc. HCl (20 ml) for (10 hrs). The pale-yellow solid was washed with water. On crystallization from acetic acid it gave (VI) as pale yellow crystals, m.p. and mixed m.p. 270°

Hydrolysis of Ethyl 2-Amino-6-(p-Chlorophenyl)-4-Furyl Nicotinic Acid (Va): Formation of (VII a). The compound (Va) (1 g) was heated with 10% alcoholic potassium hydroxide (20 ml) for 3 hr, after the mixture has stood overnight, a crystalline compound was separated.

On crystallization from ethyl alcohol it gave (VII a) as yellow crystals m.p. 126° (with decomposition), yield 80%.

Analysis. (Found : C,66.6;H,4.1;N,8.7; C₁₈H₁₃ClN₂O₂ 325.5; requires: C,66.6;H,4.00; N,8.7).

Hydrolysis of Ethyl-2-Amino-6-(p-Chlorophenyl)-4-(p-Dimethyl Aminophenyl) Nicotinic Acid (Vb): Formation of (VII b). The compound (Vb) (1 g) was heated with 10% alcoholic KOH (20 ml) for 3 hr, after the mixture had stood overnight, a crystalline compound was separated. On crystallization for methylalcohol it gave (VIIb) as greenish yellow crystals, m.p. 188°, yield 80%

Analysis. Found : C,61.8;H,3.50;N,7.6 C₁₉H₁₃ClN₂O₄ 368.5; requires: C,61.9;H,3.5;N,7.6

The Reaction of Ethylcyano Acetate with Chalcones in Benzene Formation of (VIII). A mixture of ethylcyanoacetate (5.65 g.) (0.05 mole), the chalcone (II) (0.05 mole), and ammonium acetate (3.08 g) (0.04 mole) in 40 ml of benzene was refluxed for 8 hr. Water was added to the reaction mixture and after standing overnight, a crystalline solid was precipitated.

It was treated with a small amount of dilute methanol to remove the unchanged chalcone, and crystallized from ethanol to give (VIII), yield 40% (Table 6)

TABLE 3. 3-CYANO-4, 6-DIARYL-2-PYRIDONES (III).

Compound No.	M.p.	Colour	Mol.wt	Yield %	Analysis%					
					Required			Found		
					C	H	N	C	H	N
IIIa	285	Yellow	C ₁₈ H ₁₁ ClN ₂ O 306.7	60	70.5	3.6	9.1	70.3	3.5	9.0
IIIb	300	Yellow	C ₁₆ H ₉ ClN ₂ O ₂ 296.7	65	64.7	3.1	9.4	64.8	3.2	9.5
IIIc	315	Orange	C ₂₀ H ₁₆ ClN ₂ O 351.8	65	68.3	4.6	8.00	68.20	4.4	7.8
IIId	252	Yellow	C ₁₉ H ₁₁ ClN ₂ O ₃ 350.8	62	65.1	3.2	7.9	65.0	3.0	7.8
IIIe	277	Yellow	C ₁₉ H ₁₃ ClN ₂ O ₂ 336.8	62	67.8	3.9	8.3	67.7	3.9	8.3
IIIf	218	Yellow	C ₂₀ H ₁₃ ClN ₂ O 332.8	60	72.2	3.9	8.4	72.1	3.8	8.5
IIIg	218	Brown	C ₁₈ H ₁₀ ClN ₃ O ₃ 351.8	61	61.5	2.9	11.9	61.4	2.8	11.9

TABLE 4. 3-CYANO-4, 6-DIARYL-HEXAHYDRO -2-PYRIDONES (IV).

Compound No.	M.p.	Colour	Mol.wt	Yield%	Analysis %				
					Required C	H	Found C	H	
IV a	261	Colourless	C ₁₈ H ₁₅ ClN ₂ O 310.8	28	69.6	4.8	69.4	4.8	
IV b	260	Orange	C ₁₆ H ₁₃ ClN ₂ O ₂ 300.70	25	63.9	4.4	63.8	4.4	
IV c	210	Orange	C ₂₀ H ₂₀ ClN ₂ O 339.8	24	70.7	5.9	70.7	6.0	
IV d	201	Paleyellow	C ₂₀ H ₁₇ ClN ₂ O 336.8	25	71.3	5.1	71.4	5.0	
IV e	330	Brown	C ₁₈ H ₁₄ ClN ₃ O ₃ 358.8	26	60.3	3.9	60.3	3.9	

Aromatization of 3-Cyano-4-Phenyl-6-(p-Chlorophenyl) -2-Oxo- 1,2,3,4,-Tetrahydro Pyridine (VIII a) to from 3-Cyano-4-Phenyl -6-(p-Chlorophenyl) -2-Pyridone (III a). (a) A solution of compound (VIII a) (2 g) in chloroform (20 ml) was treated with bromine solution in CHCl₃ (1m 20 ml).

The solution during addition, was chilled in an ice bath and stirred. Then it was warmed on a steam bath until evolution of hydrogen bromide ceased and the

volume was reduced to half pure ethanol was added and the solution chilled. The yellow solid was crystallized from acetic acid to give (III a) (65%) identified by m.p. and mixed m.p.

Analysis: Found: C,70.5; H,3.5; N,9.2; C₁₈H₁₁ClN₂O 306.; requires; C,70.5;H,3.6; N,9.1).

(b) Aromatization of (VIII a) was also accomplished by heating in an oil bath at 210° for 3 hr and crystallizing the resulting product.

TABLE 5. ETHYL-2-AMINO-4, 6-DIARYL NICOTINIC ACIDS (V).

Compound No.	M.p.	Colour	Mol.wt.	Yield%	Analysis%				
					Required C	H	Found C	H	
V a	>300	Brown	C ₁₈ H ₁₅ ClN ₂ O ₃ (342.8)	20	63.1	4.4	63.0	4.4	
V b	320	Orange	C ₂₂ H ₂₂ ClN ₃ O ₂ (399.2)	21	66.3	5.6	66.3	5.5	
V c	>300	Yellow	C ₂₀ H ₁₅ ClN ₂ O ₄ (382.8)	18	62.8	3.9	62.8	3.9	
V d	269	Yellow.	C ₁₆ H ₁₉ ClN ₂ O ₃ (322.8)	19	59.5	5.9	59.5	5.8	
V e	310	White	C ₂₀ H ₁₆ ClN ₃ O ₄ (400.8)	20	59.9	4.0	59.8	4.1	

TABLE 6. 3-CYANO-4, 6-DIARYL -2-OXO-TETRAHYDROPYRIDINES (VIII).

Compound No.	M.p.	Colour	Mol. wt.	Required		Analysis %		Found	
				C	H	N	C	H	N
VIII a	169	Brown	C ₁₆ H ₁₁ ClN ₂ O ₂ 298.5	64.3	3.7	9.4	64.3	3.8	9.4
VIII b	128	Pale yellow	C ₁₉ H ₁₄ ClN ₂ O ₂ 337.5	67.6	4.1	8.3	67.5	4.1	8.2
VIII c	162	White	C ₁₈ H ₁₁ ClN ₃ O ₃ 352.749	61.6	3.1	11.9	61.6	3.2	11.8

Alkylation of 3-Cyano-4, 6-Diaryl -2-Pyridones (III): Formation of (IX). (a) Methylation: A hot solution of 3-cyano-4,6-diaryl-2- pyridones (III), (1 g.) in sodium hydroxide solution (50 ml, 20%) was treated with dimethyl sulphate (3 ml) and then warmed for 1 hr on steam bath. The crystalline solid that separated after cooling was crystallized from suitable solvent to give (IX a and b) as colourless needles, yield 70% (cf. Table 7).

(b) *Ethylation.* 3-Cyano-4, 6-diaryl-2- pyridone (III a) undergo ethylation by using diethyl sulphate in the same manner as above (cf. Table 7).

(c) *Allylation.* A mixture of the sodium or potassium salt of (III) (1 g), absolute ethanol (50 ml), and allylchloride (3 ml) was heated for 5 hr on water bath.

The crystals which separated upon cooling the reaction mixture were filtered off and recrystallized from suitable solvent to give (IXd, e and f) (Yield 60%), (cf. Table 7).

(d) *Benzylation.* A mixture of the sodium or potassium salt of (III) (1 g), absolute ethanol (50 ml), and benzyl chloride (3 ml) was refluxed for 5 hr. The colourless crystals which separated upon cooling the reaction mixture, were filtered off and recrystallized from suitable solvent to give (IX g - k) (yield 65%) (cf. Table 7).

(e) *Reaction with Ethyl Bromoacetate:* A mixture of the sodium or potassium salt of the appropriate (III) (1g), absolute ethanol (50 ml) and ethyl bromoacetate (0.6 gm) was refluxed for 5 hour. The crystals which separated on cooling were filtered off and re-

3-CYANO 2-(IH)-PYRIDONES

TABLE 7. 2-ALKOXY OR ALLYLOXY -3-CYANO-4, 6-DIARYL PYRIDONE (IX).

Compound No.	M.p.	Colour	Solvent of cryst	Mol.wt.	Analysis %			
					Required C	H	Found C	H
IX a	300	White	E	$C_{20}H_{15}ClN_2O_2$ 350.5	68.47	4.3	68.5	4.3
IX b	232	White	A	$C_{20}H_{13}ClN_2O_3$ 364.5	65.84	3.6	65.8	3.5
IX c	190	White	E	$C_{20}H_{15}ClN_2O$ 334.5	71.74	4.5	71.6	4.5
IX d	189	White	E/A	$C_{21}H_{15}ClN_2O$ 346.5	75.72	4.3	75.8	4.3
IX e	271	Yellow	D	$C_{22}H_{17}ClN_2O_2$ 376.5	70.11	4.5	70.2	4.4
IX f	195	Brown	A	$C_{22}H_{15}ClN_2O_3$ 390.5	67.60	3.8	67.7	3.9
IX g	278	White	E	$C_{25}H_{17}ClN_2O$ 386.8	75.00	4.3	75.1	4.2
IX h	300	White	E	$C_{25}H_{16}ClN_3O_3$ 441.8	67.95	3.6	67.9	3.8
IX i	252	White	E	$C_{26}H_{19}ClN_2O_2$ 426.5	73.15	4.5	73.0	4.7
IX j	303	White	E	$C_{23}H_{15}ClN_2O_2$ 386.5	71.41	3.9	71.5	3.8
IX k	300	White	E	$C_{27}H_{22}ClN_3O$ 439.5	73.72	5.00	73.7	5.1
IX l	300	White	M	$C_{22}H_{17}ClN_2O_3$ 392.5	67.26	4.3	67.3	4.4
IX m	230	White	M	$C_{23}H_{19}ClN_2O_4$ 422.5	63.19	4.5	63.2	4.5
IX n	280	Yellow	Ac	$C_{23}H_{17}ClN_2O_5$ 436.5	63.23	3.9	63.2	3.9
IX o	139	White	A	$C_{24}H_{19}ClN_2O_3$ 418.5	68.8	4.5	68.7	4.6
IX p	215	White	E	$C_{25}H_{21}ClN_2O_5$ 436.5	68.7	4.8	68.8	4.9

E = Ethyl alcohol, Ac=Acetic acid, M = Methyl alcohol, D = Dioxane, A=Acetone.

crystallized from suitable solvent to give (IX i-o) (yield 70%) (cf. Table 7).

Reaction with Ethyl Bromomalonate. The Compound (III) was reacted with ethyl bromomalonate in the same manner as above to give IXp, (cf. Table 7).

Hydrolysis of 2-Alkoxy Derivatives (IX l and p) to give the Corresponding mono and Dicarboxylic acids A mixture of (IX l and p) (0.01 mole and KOH (0.01 mole) was dissolved in a mixture of ethanol (50 ml) and water (30 ml), and heated under reflux for three hours cooled acidified with dilute hydrochloric acid, extracted with ether, washed with water and dried over anhydrous calcium chloride. The ethereal layer was evaporated, and the residual oil was crystallized from ethyl alcohol to give (Xa and b) as a colourless crystals. The results are given in Table 8.

Action of Phosphorus Oxychloride on 2-Pyridones III or (VIII) Formation of XI A suspension of each of (III a-g) (1 g) and phosphorus oxychloride (5 ml) was heated on a water bath for 2 hour. The reaction mixture was poured gradually into crushed ice. The solid which separated, was filtered off and crystallized from acetic acid to give (XI). The details of these products are summarized in Table 9.

The reaction was carried out as described above using each of (VIII a, b and c); the products proved to be identical with (XI b, e and g), respectively.

Reaction of 2-Chloro-3-Cyano-4, 6-Diaryl Pyridine (XI a) with Sodium Methoxide, Sodium Ethoxide and Sodium Allyloxide. Formation of (IX a, c, and d). A solution of (XI a) (1g.) in alcohol (20 ml) was treated with sodium alkoxide refluxed for 5 hours, then

TABLE 8.

Compound. No.	M.p.	Yield%	Mol.wt.	Analysis %			
				Required		Found	
				C	H	C	H
X a	210	60	$C_{20}H_{13}ClNO_2$ 334.5	71.7	3.9	71.8	3.8
X b	260	50	$C_{21}H_{13}ClNO_4$ 378.5	66.6	3.4	66.5	3.5

TABLE 9. 2-CHLORO-3-CYANO-4, 6-DIARYL PYRIDINES (XI).

Compound. No.	M.p.	Colour	Yield%	Mol.wt.	Analysis %			
					Required		Found	
					C	H	C	H
XI a	215	Yellow	75	$C_{18}H_{10}Cl_2N_2$ 325	66.5	3.1	66.5	3.1
XI b	260	Yellow	70	$C_{16}H_8Cl_2N_2O$ 315	61.0	2.5	60.9	2.5
XI c	298	Yellow	70	$C_{20}H_{15}Cl_2N_3$ 369	65.0	4.1	65.0	4.1
XI d	237	Brown	70	$C_{19}H_{10}Cl_2N_2O_2$ 369	61.8	2.7	61.8	2.8
XI e	210	Brown	75	$C_{19}H_{10}Cl_2N_2O$ 353	64.6	2.8	64.6	2.8
XI f	180	Grey	80	$C_{20}H_{12}Cl_2N_2$ 351	68.4	3.4	68.3	3.4
XI g	230	Yellow	82	$C_{18}H_9Cl_2N_3O_2$ 370	58.4	2.4	58.4	2.5

TABLE 10. 3-CYANO-2-ALKYL OR ARYLAMINE-4, 6-DIARYL PYRIDIME (XII).

Compound No.	M.p.	Colour	Solvent of cryst.	Mol.wt.	Analysis %					
					Required			Found		
XII a	237	Pale yellow	A	$C_{19}H_{14}CIN_3$ 319.5	71.4	4.38	3.1	71.4	4.4	13.1
XII b	138	White	E	$C_{22}H_{20}CIN_3$ 361.5	73.0	5.53	11.6	73.1	5.5	11.9
XII c	284	White	A	$C_{20}H_{16}CIN_3O$ 349.5	68.7	4.57	12.0	68.7	4.6	12.1
XII d	263	White	A	$C_{24}H_{22}CIN_3O$ 387.5	74.3	5.67	10.8	74.4	5.6	10.9
XIII e	241	Buff	A	$C_{25}H_{16}CIN_3O_2$ 225.8	70.50	3.76	9.9	70.6	3.8	9.9
XII f	244	Yellow	A	$C_{30}H_{21}CIN_4$ 472.6	76.2	4.44	11.9	76.2	4.4	11.8
XII g	242	Pale yellow	A	$C_{25}H_{19}CIN_6O_2S$ 502.9	59.7	3.78	16.7	59.7	3.8	16.8
XII h	236	Pale yellow	E	$C_{20}H_{16}CIN_3O$ 349.8	68.7	4.57	12.0	68.8	4.6	12.0
XII i	146	White	E	$C_{23}H_{22}CIN_3O$ 391.5	70.5	5.61	10.7	70.5	5.5	10.7
XII j	134	White	E	$C_{26}H_{20}CIN_3O$ 425.5	73.3	4.7	9.8	73.3	4.8	9.8
XII k	>300	White	E	$C_{24}H_{18}CIN_3O_2$ 415.5	69.3	4.33	10.10	69.5	4.4	10.2
XII l	270	Buff	E	$C_{29}H_{20}CIN_3O$ 461.5	75.40	4.33	9.10	75.5	4.3	9.1
XII m	238	White	A	$C_{25}H_{19}CIN_4O_3S$ 476.5	63.0	3.98	11.8	62.9	3.8	11.9
XII n	235	White	A	$C_{30}H_{20}CIN_6O_3S$ 577.5	62.3	3.46	14.54	62.4	3.5	14.6
XII o	225	White	E	$C_{22}H_{19}CIN_4O_2$ 406.5	64.9	4.7	13.8	64.9	4.6	14.0
XII p	190	Black	Ac	$C_{19}H_{15}CIN_4O_3$ 382.5	59.6	3.9	14.6	59.7	3.8	14.6
XII q	291	Yellow	Ac	$C_{21}H_{17}CIN_4O_2$ 392.5	64.20	4.3	14.3	64.2	4.3	14.2
XII r	181	White	E	$C_{24}H_{14}CIN_4O_2$ 425.5	67.7	3.3	13.2	67.7	3.3	13.2
XII s	248	White	E	$C_{25}H_{17}CIN_2O_2$ 412.5	72.7	4.2	6.8	72.7	4.2	6.8

continued

XII t	200	White	E	$C_{23}H_{14}ClN_4O_3$ 429.5	64.3	3.3	13.0	64.3	3.3	13.1
XII u	290	White	E	$C_{28}H_{17}ClN_4O_2$ 476.5	70.6	3.6	11.8	70.5	3.5	11.8
XII v	257	Brown	E	$C_{24}H_{14}Cl_2N_4O_2$ 461	62.5	3.3	12.0	62.5	3.03	12.1
XII w	153	Brown	Ac	$C_{22}H_{18}ClN_3O_2$ 391.5	67.4	4.5	10.6	67.5	4.59	10.6
XII x	239	White	A	$C_{25}H_{16}ClN_3O_5S$ 545.5	54.8	3.0	8.9	54.9	2.93	8.9
XII y	251	White	A	$C_{26}H_{19}ClN_6O_4S$ 546.5	57.1	3.5	13.4	57.1	3.47	13.4
XII z	245	White	A	$C_{29}H_{18}ClN_3O_2$ 475.5	73.2	3.8	8.8	73.2	3.8	8.8
XII a	145	Yellow	E	$C_{20}H_{18}ClN_3O$ 351.5	68.3	5.1	11.4	68.3	5.2	11.9
XII b	287	Yellow	E	$C_{24}H_{25}ClN_4$ 304.5	94.6	8.2	18.4	94.6	8.3	18.3

E = Ethyl alcohol Ac = Acetic acid, M = Methyl alcohol, D = Dioxane, A = Acetone.

TABLE 11. 2-HYDROXY-4, 6-DIARYL-3-PYRIDYL ALKYL, BENZYL AND/OR PHENYL KETONES (XIII).

Compound No.	M.p.	Colour	Mol. wt.	Analysis %			
				Required	Found		
XIII a	195	Yellow	$C_{19}H_{14}ClNO_2$ 323.5	70.6	4.5	70.5	4.3
XIII b	210	Yellow	$C_{20}H_{16}ClNO_2$ 337.5	71.1	4.7	71.1	4.7
XIII c	198	White	$C_{25}H_{18}ClNO_2$ 399.5	75.1	4.5	75.1	4.5
XIII d	258	Green	$C_{17}H_{11}ClNO_3$ 312.5	65.3	3.6	65.3	3.5
XIII e	281	Yellow	$C_{22}H_{13}ClNO_3$ 374.5	70.1	3.4	70.5	3.5
XIII f	277	Yellow	$C_{25}H_{18}ClNO_3$ 415.5	72.3	4.3	72.2	4.3
XIII g	265	Green	$C_{20}H_{14}ClNO_4$ 367.5	65.3	3.8	65.30	3.80
XIII h	250	Yellow	$C_{25}H_{16}ClNO_4$ 429.5	69.7	3.6	69.8	3.7
XIII i	128	Brown	$C_{19}H_{13}ClN_2O_3$ 352.5	64.9	3.6	64.7	3.7
XIII j	300	Yellow	$C_{20}H_{15}ClN_2O_3$ 366.5	65.5	4.1	65.5	4.1

allowed to cool? On diluting the reaction mixture with water the solid filtered off and crystallized from ethanol or acetone, and proved to be identical with (IX a, c and d) respectively.

Reaction of 2-Chloro-3-Cyano-4, 6-Diaryl Pyridines (XI) with Amines: Formation of (XII). A suspension of (XI a - g) (0.05 mole) and the appropriate amine (methylamine, n-butylamine, ethanol amine, cyclohexyl amine, anthranilic acid, benzidine, sulphaguanidine n-propylamine, p-chloro-aniline, benzyl amine, furfuryl amine, 1-naphthyl-amine, p-toluidine, sulphaniilic acid) (0.1 mole) was refluxed for 2 hour, and allowed to cool. The reaction mixture was triturated with cold ethanol and the solid was crystallized from suitable solvent to give (XII a - b). The details of these products are summarized in Table 10.

Action of Grignard Reagents on III: Formation of (XIII). To a suspension of III (2 g.) in dry benzene (50 ml) was added an ethereal solution of alkyl and or aryl magnesium halide prepared from 0.9 g magnesium 7.0 g alkylhalide, benzyl chloride or 8.0 g bromobenzene and 40 ml dry ether. The reaction mixture was refluxed (steam-bath) for 2 hour, set aside room temperature, and then decomposed with a cold solution of hydrochloric acid (10 %). The coloured solid was crystallized from acetic acid or ethanol (yield 80%), (the results are summarized in Table 11).

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