

Ring Transformations of 4*H*-Pyrans. Pyridines from 2-Amino-4*H*-Pyrans (1)

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Ring transformations of 4*H*-pyrans into pyridines are reported. Treatment of 2-amino-4,6-diaryl-3,5-dicyano-4*H*-pyrans (I) with nitrosylsulfuric acid brings about their transformation into 3,5-dicyano-4,6-diaryl-2-pyridones (VI) which can also be obtained from α -benzoylcinnamitriles (IX) and cyanoacetamide. Similarly, 2-amino-4,6-diaryl-5-carbomethoxy-3-cyano-4*H*-pyrans (II) lead to 4,6-diaryl-5-carbomethoxy-3-cyano-2-pyridones (VII). Treatment of both series of pyrans with sulfuric acid results in the formation of the corresponding 3,4-dihydro-2-pyridones (IV and V). Reaction of pyrans II with ammonium acetate in acetic acid yields 2-amino-4,6-diaryl-5-carbomethoxy-3-cyanopyridines (XII). Pyrans I undergo an entirely different type of reaction upon treatment with this reagent leading to 2,4,6-triaryl-3,5-dicyano-1,4-dihydropyridines (XV).

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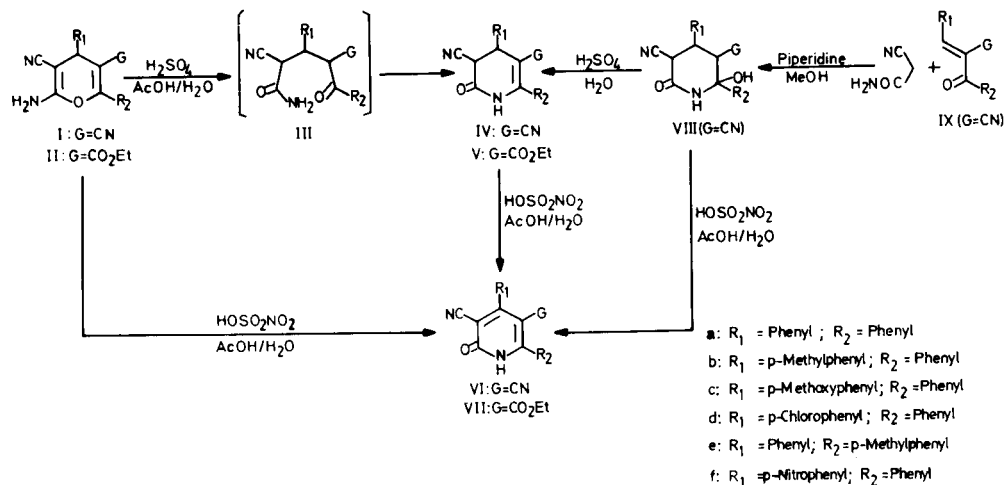
The study of ring transformations of heterocycles has deserved a good deal of work in recent years (2). The transformations of six-membered oxygen heterocycles, such as pyrylium salts (3) and pyrones and related compounds (4-6), into pyridines have been widely studied and have synthetic interest. However, the instability and difficulty of preparation of the 4*H*-pyran ring (7) are responsible for a rather scarce work on the chemistry of these compounds (8,9). In particular, studies on the chemistry of 2-amino-4*H*-pyrans are lacking in the chemical literature.

As reported in previous papers (10-13), we have developed synthetic procedures for the preparation of substituted 2-amino-4*H*-pyrans (I and II) which are reasonably stable. This paper deals with the ring transformations of these pyrans into pyridones and pyridines by

treatment with suitable reagents.

Transformation of 2-amino-4*H*-pyrans I and II into the corresponding 2-pyridones VI and VII is achieved when the pyrans are allowed to react with nitrosylsulfuric acid in acetic solution (Scheme I). The reaction can be understood by assuming the formation of an open chain intermediate (III) due to the nucleophilic attack of water to the protonated pyran ring. Cyclization of III in the reaction medium gives 3,4-dihydropyridones IV or V, whose spontaneous aromatization affords a series of 4,6-diaryl-3,5-dicyano-2-pyridones (VI) from pyrans I or 4,6-diaryl-5-carbomethoxy-3-cyano-2-pyridones (VII) from pyrans II.

The ir spectra of both series of pyridones show, in addition to the cyano stretching band at 2225-2240 cm^{-1} , a broad band at 2500-3200 cm^{-1} typical of 2-pyridones



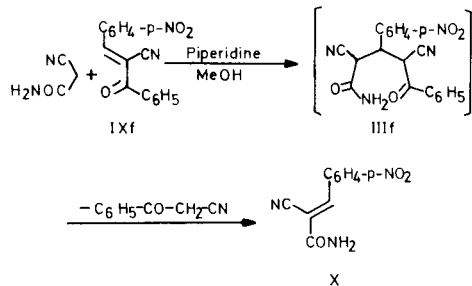
Scheme I

(14-16) and a C=O band at 1640-1650 cm^{-1} . Series VII show also the ester carbonyl band at 1720 cm^{-1} .

If pyrans I and II are treated with sulfuric acid in acetic solution in the absence of nitrosylsulfuric acid, the reaction proceeds also by ring cleavage and subsequent cyclization but the aromatization does not take place and the 3,4-dihydro-2-pyridones (IV and V) are isolated.

A confirmation of the structure of dihydropyridones IV was obtained by the independent synthesis of these compounds from cyanoacetamide and α -benzoylcinnamionitriles (IX) (17). In dry methanol and in the presence of piperidine, cyanoacetamide reacts with α -benzoylcinnamionitriles by Michael's addition followed by cyclization to give 6-hydroxy-2-piperidones (VIII, G = CN). Their nmr spectra show a complex multiplet at 3.7-4.8 ppm due to the three hydrogens of the ring, and a broad singlet at 9-9.1 ppm due to the NH group. The peak of the hydroxyl group appears within the aromatic multiplet (6.8-7.9 ppm) and can be identified by addition of trifluoroacetic acid.

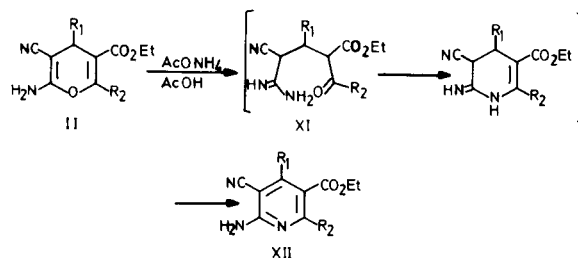
It must be pointed out that this reaction does not take place with α -benzoyl-*p*-nitrocinnamionitrile (IXf). In this instance, α -cyano-*p*-nitrocinnamamide (X), resulting from the elimination of ω -cyanoacetophenone from the Michael adduct, is isolated instead of the corresponding 6-hydroxy-2-piperidone (Scheme II).



Scheme II

Treatment of hydroxypiperidones VIII with 50% sulfuric acid (17a) results in their dehydration to 3,4-dihydropyridones IV. As revealed by the nmr spectra, these compounds are a *cis-trans* mixture. The multiplet at 4.3-5.3 ppm due to the hydrogens located at positions 3 and 4 consists of two pairs of doublets ($J = 7$ Hz and $J = 12$ Hz). From integration of signals formation of equal amounts of *cis* and *trans* isomers is inferred. Dihydropyridones IV can be aromatized to pyridones VI with nitrosylsulfuric acid and the same result is achieved starting from 6-hydroxy-2-piperidones VIII (Scheme I).

The transformation of 2-amino-4*H*-pyrans into pyridines containing the same ring substituents can be carried out with ammonium acetate in glacial acetic acid. Thus, 2-amino-4,6-diaryl-5-carbethoxy-3-cyanopyridines (XII) result from 2-amino-4,6-diaryl-5-carbethoxy-3-cyano-4*H*-pyrans (II) (Scheme III). The reaction involves nucleo-

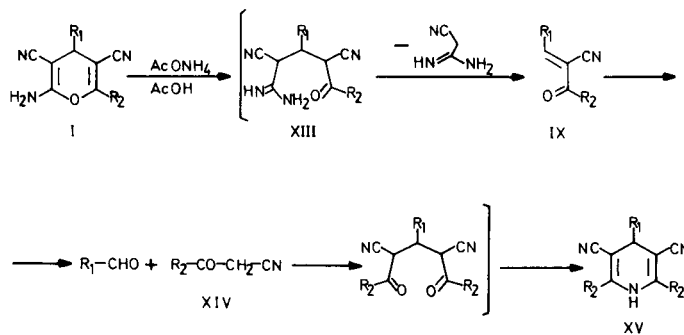


- a: $R_1 = \text{Phenyl}$; $R_2 = \text{Phenyl}$
 b: $R_1 = p\text{-Methylphenyl}$; $R_2 = \text{Phenyl}$
 d: $R_1 = p\text{-Chlorophenyl}$; $R_2 = \text{Phenyl}$
 f: $R_1 = p\text{-Nitrophenyl}$; $R_2 = \text{Phenyl}$

Scheme III

philic attack by ammonia to the protonated pyran ring, leading to the amidine intermediate XI. The cyclization of this species followed by imino-enamino tautomerization and aromatization leads to the 2-aminopyridines XII. The nmr spectra of these compounds show, together with the aromatic and carbethoxyl peaks, the amino group as a broad signal at 7.3 ppm in deuteriodimethylsulfoxide or at 5.5 ppm in deuteriochloroform. In the ir spectra, the amino group gives rise to three stretching bands at 3150-3480 cm^{-1} and a bending band near 1620 cm^{-1} . The cyano group stretching band appears at 2210-2220 cm^{-1} and the carbonyl band at 1720 cm^{-1} .

However, this simple "oxygen-nitrogen exchange" by reaction with ammonium acetate/acetic acid has proved to be exclusive of pyrans II. When the same treatment is applied to pyrans I, an entirely different reaction takes place, bringing about the transformation into 2,4,6-triaryl-3,5-dicyano-1,4-dihydropyridines (XV). The reaction course can be described as shown in scheme IV. The amidine species XIII, resulting from ring cleavage, undergoes a retro-Michael elimination leading to an α -benzoylcin-



- a: $R_1 = \text{Phenyl}$; $R_2 = \text{Phenyl}$
 b: $R_1 = p\text{-Methylphenyl}$; $R_2 = \text{Phenyl}$
 f: $R_1 = p\text{-Nitrophenyl}$; $R_2 = \text{Phenyl}$

Scheme IV

namonitrile (IX) which decompose into aldehyde and ω -cyanoacetophenone (XIV). The reaction in 1:2 molar ratio of these compounds, followed by ammonia promoted cyclization affords the 1,4-dihydropyridines XV. The independent synthesis of XV by reaction of ω -cyanoacetophenone (XIV) with an aromatic aldehyde in the presence of ammonium acetate (18), and the reaction of α -benzoylcinnamonitriles (IX) with ammonium acetate/acetic acid that yields also dihydropyridines XV (Scheme V), corroborates this two-step decomposition of the pyran ring. On the other hand when a pyran in which the substituent at position 4 is different of the one located at position 6 ($R_1 \neq R_2$) the dihydropyridine obtained has R_1 at position 4 and R_2 at positions 2 and 6 (Scheme IV).

On support of this proposed interpretation is also the fact that 3,5-dicyano-1,4-dihydropyridine XVa resulted from 2-amino-3-carbethoxy-5-cyano-4,6-diphenyl-4*H*-pyran (XVI) (Scheme V) from which the carbethoxy group located at position 3 is lost in the retro-Michael elimination.

The different behaviour of pyrans I and pyrans II towards ammonium acetate in acetic acid can be attributed to the much higher electron attracting ability of the cyano group with respect to the carbethoxyl group, as shown by the pK_a of ω -cyanoacetophenones (19) and ethyl benzoylacetates (20). In consequence, if the starting pyran has a cyano group at position 5 (pyrans I), the retro-Michael decomposition of the intermediate XIII is favoured and the reaction leads to the 2,4,6-triaryl-3,5-dicyano-1,4-dihydropyridines XV (Scheme IV). On the other hand, if the pyran has a carbethoxyl group at position 5 (pyrans II), this decomposition is more difficult and the cyclization of the intermediate (XI) to 2-aminopyridine XII is the preferred reaction course (Scheme III).

EXPERIMENTAL

Melting points were determined with a Buchi apparatus (in capillar) and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 257 spectrophotometer in potassium bromide pellets. The 1H nmr spectra were determined on a Varian T-60A; chemical shifts are quoted in δ values, using TMS as internal standard. Mass spectra were recorded on a Varian MAT 711 spectrometer. The reactions were monitored by TLC performed on silica gel plates. Microanalysis were performed by the "Centro Nacional de Química Orgánica" of Madrid.

2-Amino-4*H*-pyrans (I).

2-Amino-4,6-diaryl-3,5-dicyano-4*H*-pyrans (I) and 2-amino-3-carbethoxy-5-cyano-4,6-diphenyl-4*H*-pyran (XVI) were prepared by the method described in (11) and 2-amino-4,6-diaryl-5-carbethoxy-3-cyano-4*H*-pyrans (II) were obtained as described in (12).

α -Benzoylcinnamonitriles (IX).

α -Benzoylcinnamonitrile (IXa), α -benzoyl-*p*-nitrocinnamonitrile (IXf) and α -benzoyl-*p*-methoxycinnamonitrile (IXc) were synthesized by Kaufman's method (21). α -Benzoyl-*p*-chlorocinnamonitrile (IXd) was obtained as described by Drapkina (22) and α -(*p*-methylbenzoyl)cinnamonitrile (IXe), as described in (11). The starting compounds for the synthesis of α -benzoylcinnamonitriles, ω -cyanoacetophenones (XIV), were prepared by the methods reported by Long (23) and Eby and Hauser (24).

4,6-Diaryl-3,5-dicyano-3,4-dihydro-2-pyridones (IV). General Procedure.

a) From 2-Amino-4,6-diaryl-3,5-dicyano-4*H*-pyrans (I).

To a suspension of 0.003 mole of the appropriate pyran in ca 10 ml. of acetic acid, cooled in an ice bath, are added 70 ml. of 80% aqueous sulfuric acid, dropwise and under stirring. The reaction mixture is stirred at 0° until total solution occurs (2-3 hours). After 12-24 hours at room temperature it is poured into crushed ice. The resulting solid was filtered off and washed with water until neutral pH. The dried product is recrystallized from an appropriate solvent.

b) From 4,6-Diaryl-3,5-dicyano-6-hydroxy-2-piperidones (VIII).

A suspension of 0.0015 mole of the corresponding 2-piperidone in 10 ml. of 50% sulfuric acid is stirred at room temperature for 24-48 hours. The reaction mixture is poured into ice water and the solid obtained is filtered off, washed with water and recrystallized.

3,5-Dicyano-4,6-diphenyl-3,4-dihydro-2-pyridone (IVa).

This compound was obtained in 87% yield by route a) and in 80% yield by route b), m.p. 193-194° (recrystallized from methanol); ir (potassium bromide): 3210, 3100, 3060, 3040, 2950, 2880, 2260, 2220, 1690, 1630, 1480, 1455, 1380, 1295, 1280, 1255, 1205, 1080, 1050, 1030, 1020, 1000 cm^{-1} ; nmr (DMSO- d_6): δ 10.82 (broad, 1H, NH), 7.10-7.56 (m, 10H, arom), 4.30-5.23 (m, 2H); ms: m/e 299 (M^+ , 49), 298 (43), 231 (42), 72 (23).

Anal. Calcd. for $C_{17}H_{13}N_3O$: C, 76.23; H, 4.37; N, 14.03. Found: C, 75.92; H, 4.30; N, 13.94.

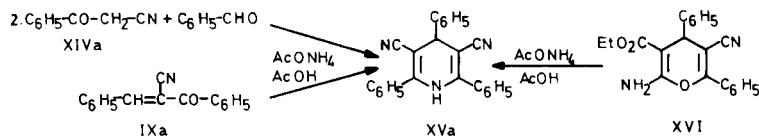
3,5-Dicyano-4-(*p*-methylphenyl)-6-phenyl-3,4-dihydro-2-pyridone (IVb).

This compound was obtained in 94% yield by route a) and in 93% yield by route b), m.p. 141-143° (recrystallized from benzene); ir (potassium bromide): 3230, 3120, 2960, 2880, 2260, 2220, 1700, 1630, 1480, 1370, 1270, 1250, 1175, 1060, 1030, 990 cm^{-1} ; nmr (DMSO- d_6): δ 10.90 (broad, 1H, NH), 7.00-7.50 (m, 9H, arom), 4.20-5.15 (m, 2H), 2.25 (s, 3H, CH_3).

Anal. Calcd. for $C_{20}H_{15}N_3O$: C, 76.67; H, 4.79; N, 13.41. Found: C, 76.31; H, 4.96; N, 13.24.

3,5-Dicyano-4-(*p*-methoxyphenyl)-6-phenyl-3,4-dihydro-2-pyridone (IVc).

This compound was obtained in 91% yield by route b), m.p. 170-171° (recrystallized from methanol); ir (potassium bromide): 3210, 3120,,



Scheme V

3000, 2940, 2210, 1690, 1615, 1585, 1520, 1500, 1470, 1365, 1250, 1190, 1170, 1115, 1055, 1030, 1020 cm^{-1} ; nmr (DMSO- d_6): δ 10.83 (broad 1H, NH), 6.73-7.60 (m, 9H, arom), 4.26-5.20 (m, 2H), 3.73 (s, 3H, CH_3O).

Anal. Calcd. for $\text{C}_{20}\text{H}_{15}\text{N}_3\text{O}_2$: C, 72.93; H, 4.59; N, 12.75. Found: C, 72.83; H, 4.60; N, 13.00.

3,5-Dicyano-4-(*p*-chlorophenyl)-6-phenyl-3,4-dihydro-2-pyridone (IVd).

This compound was obtained in 94% yield by route b), m.p. 171-172 (recrystallized from ethanol); ir (potassium bromide): 3450, 3330, 3200, 3130, 2950, 2260, 2210, 2190, 1705, 1610, 1600, 1590, 1490, 1410, 1370, 1305, 1290, 1280, 1250, 1200, 1090 cm^{-1} ; nmr (DMSO- d_6): δ 10.83 (broad 1H, NH), 7.16-8.00 (m, 9H, arom), 4.36-5.40 (m, 2H).

Anal. Calcd. for $\text{C}_{19}\text{H}_{12}\text{ClN}_3\text{O}$: C, 68.36; H, 3.59; Cl, 10.64; N, 12.59. Found: C, 68.41; H, 3.93; Cl, 11.01; N, 12.74.

3,5-Dicyano-6-(*p*-methylphenyl)-4-phenyl-3,4-dihydro-2-pyridone (IVe).

This compound was obtained in 89% yield by route b), m.p. 216-217° (recrystallized from ethanol); ir (potassium bromide): 3220, 3160, 2860, 2240, 2200, 1715, 1690, 1610, 1460, 1335, 1290, 1270, 1235, 1200 cm^{-1} ; nmr (DMSO- d_6): δ 10.86 (broad, 1H, NH), 7.03-7.50 (m, 9H, arom), 4.26-5.23 (m, 2H), 2.30 (s, 3H, CH_3).

Anal. Calcd. for $\text{C}_{20}\text{H}_{15}\text{N}_3\text{O}$: C, 76.67; H, 4.79; N, 13.41. Found: C, 76.89; H, 5.07; N, 13.79.

4,6-Diaryl-3,5-dicyano-6-hydroxy-2-piperidones (VIII). General Procedure.

To a suspension of 0.004 mole of the appropriate α -benzoylcinnamitrile (IX) in ca. 10 ml. of dry methanol a solution of 0.005 mole of cyanoacetamide in 5 ml. of dry methanol with a few drops of piperidine is added. The mixture is stirred at room temperature for about 10-12 hours. The solid that precipitates is filtered off and recrystallized. Since these piperidones decompose during normal purification procedures, the recrystallization must be carried out by dissolving the solid in methanol at room temperature and cooling the solution at -20°.

3,5-Dicyano-6-hydroxy-4,6-diphenyl-2-piperidone (VIIIa).

This compound was obtained in 91% yield, m.p. 147-148° (recrystallized from methanol); ir (potassium bromide): 3500, 3340, 3110, 3030, 2920, 2250, 2220, 1690, 1615, 1490, 1450, 1385, 1360, 1335, 1265, 1245, 1125, 1100, 1070 cm^{-1} ; nmr (DMSO- d_6): δ 9.03 (broad 1H, NH), 7.00-7.70 (m, 11H, arom, OH), 3.76-4.70 (m, 3H).

Anal. Calcd. for $\text{C}_{19}\text{H}_{15}\text{N}_3\text{O}_2$: C, 71.90; H, 4.76; N, 13.24. Found: C, 71.73; H, 4.47; N, 13.27.

3,5-Dicyano-6-hydroxy-4-(*p*-methylphenyl)-6-phenyl-2-piperidone (VIIIb).

This compound was obtained in 91% yield, m.p. 133-134° (recrystallized from methanol); ir (potassium bromide): 3470, 3280, 3090, 2920, 2260, 2240, 1670, 1510, 1480, 1450, 1410, 1365, 1285, 1270, 1240, 1220, 1190, 1070 cm^{-1} ; nmr (DMSO- d_6): δ 8.93 (broad, 1H, NH), 6.90-7.60 (m, 10H, arom, OH), 3.73-4.60 (m, 3H), 2.23 (s, 3H).

Anal. Calcd. for $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_2$: C, 72.48; H, 5.17; N, 12.68. Found: C, 72.18; H, 4.88; N, 12.62.

3,5-Dicyano-6-hydroxy-4-(*p*-methoxyphenyl)-6-phenyl-2-piperidone (VIIIc).

This compound was obtained in 71% yield, m.p. 133-135° (recrystallized from methanol); ir (potassium bromide): 3460, 3280, 3080, 2925, 2880, 2840, 2250, 2205, 1675, 1610, 1580, 1515, 1365, 1310, 1260, 1180 cm^{-1} ; nmr (DMSO- d_6): δ 9.00 (broad, 1H, NH), 6.70-7.70 (m, 10H, arom, OH), 3.66-4.66 (m, 3H), 3.66 (s, 3H, CH_3O).

Anal. Calcd. for $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_3$: C, 69.15; H, 4.93; N, 12.09. Found: C, 68.68; H, 4.90; N, 12.42.

3,5-Dicyano-6-hydroxy-4-(*p*-chlorophenyl)-6-phenyl-2-piperidone (VIIId).

This compound was obtained in 38% yield, m.p. 201-202° (recrystallized from methanol); ir (potassium bromide): 3500, 3320, 3270, 3140, 2240, 2200, 1675, 1595, 1580, 1490, 1440, 1410, 1370, 1090, 1060, 1010 cm^{-1} ; nmr (DMSO- d_6): δ 9.06 (broad, 1H, NH), 7.13-8.03 (m, 10H, arom,

OH), 3.86-4.70 (m, 3H).

Anal. Calcd. for $\text{C}_{19}\text{H}_{14}\text{ClN}_3\text{O}_2$: C, 64.86; H, 3.98; Cl, 10.09; N, 11.94. Found: C, 64.48; H, 4.20; Cl, 10.39; N, 11.72.

3,5-Dicyano-6-hydroxy-6-(*p*-methylphenyl)-4-phenyl-2-piperidone (VIIIe).

This compound was obtained in 60% yield, m.p. 124-125° (recrystallized from methanol); ir (potassium bromide): 3500, 3310, 2220, 1680, 1425, 1370, 1270, 1085, 1020 cm^{-1} ; nmr (DMSO- d_6): δ 9.00 (broad, 1H, NH), 7.00-8.03 (m, 10H, arom, OH), 3.86-4.70 (m, 3H), 2.30 (s, 3H, CH_3).

Anal. Calcd. for $\text{C}_{20}\text{H}_{17}\text{N}_3\text{O}_2$: C, 72.48; H, 5.13; N, 12.68. Found: C, 72.01; H, 4.88; N, 12.60.

Reaction of α -Benzoyl-*p*-nitrocinnamitrile (IXf) with Cyanoacetamide.

Following the general procedure, after 10 hours stirring at room temperature a complex mixture of decomposition products is revealed by tlc. From this mixture α -cyano-*p*-nitrocinnamamide (X) is isolated in 10% yield, m.p. 233-234° (25).

4,6-Diaryl-3,5-dicyano-2-pyridones (VI). General Procedure.

a) From 4,6-Diaryl-3,5-dicyano-3,4-dihydro-2-pyridones (IV).

To a suspension of 0.0015 mole of the corresponding 3,4-dihydro-pyridone (IV) in 4 ml. of acetic acid is added, dropwise and under stirring at 0°, a solution of nitrosylsulfuric acid (26,27), prepared from 0.0019 mole of sodium nitrite, 36 g. of sulfuric acid and 6 ml. of water and maintained at 0°. The resulting slurry is stirred until total solution occurs (a few minutes). After 8-10 hours standing at room temperature, the reaction mixture is poured into crushed ice. The resulting solid is filtered off and washed with water until total elimination of acid residues. Further purification is achieved by recrystallization in a suitable solvent.

b) From 4,6-Diaryl-3,5-dicyano-6-hydroxy-2-piperidones (VIII).

The procedure was as above, using 0.00015 mole of the appropriate 2-piperidone as the starting compound, 0.00025 mole of sodium nitrite and 5 ml. of 50% sulfuric acid. The reaction time was 48-72 hours.

c) From 6-Amino-4,6-diaryl-3,5-dicyano-4H-pyrans (I).

The corresponding pyran (0.0058 mole) in acetic acid (ca 15 ml.) was treated at 0° with a solution of nitrosylsulfuric acid prepared from 0.0067 mole of sodium nitrite, 128 g. of sulfuric acid and 20 ml. of water. After 3-6 hours of stirring total solution was achieved and the reaction mixture was poured into crushed ice. The solid was filtered off and recrystallized.

3,5-Dicyano-4,6-diphenyl-2-pyridone (VIa).

This compound was obtained in 81% yield by method a), 87% yield by method b) and 26% yield by method c), m.p. 262-263° (recrystallized from ethyl acetate); ir (potassium bromide): 3200, 2500, 2225, 1650, 1600, 1585, 1550, 1530, 1490, 1380, 1330, 1240, 1130, 1080, 1030 cm^{-1} ; nmr (DMSO- d_6): δ 7.30-7.70 (m, 10H, arom), ms: m/e = 297 (M^+ , 100), 296 (95), 278 (30), 268 (29), 242 (13), 241 (19), 121 (22).

Anal. Calcd. for $\text{C}_{19}\text{H}_{11}\text{N}_3\text{O}$: C, 76.77; H, 3.70; N, 14.14. Found: C, 76.30; H, 3.88; N, 13.88.

3,5-Dicyano-4-(*p*-methylphenyl)-6-phenyl-2-pyridone (VIb).

This compound was obtained in 100% yield by method a), 57% yield by method b) and 17% yield by method c), m.p. 308-310° (recrystallized from acetone); ir (potassium bromide): 3200-2500, 2225, 1650, 1620, 1580, 1550, 1530, 1490, 1470, 1440, 1380, 1330, 1240, 1190, 1140, 1130, 1080, 1040, 1020, 1000 cm^{-1} ; nmr (DMSO- d_6): δ 7.20-7.60 (m, 9H, arom), 2.40 (s, 3H, CH_3); ms: m/e 311 (M^+ , 70), 310 (90), 292 (34), 282 (27), 267 (21), 255 (16), 240 (9), 141 (11), 128 (18).

Anal. Calcd. for $\text{C}_{20}\text{H}_{13}\text{N}_3\text{O}$: C, 77.17; H, 4.18; N, 13.50. Found: C, 76.97; H, 4.17; N, 13.54.

3,5-Dicyano-4-(*p*-methoxyphenyl)-6-phenyl-2-pyridone (VIc).

This compound was obtained in 100% yield by method a) and 82% yield by method b), m.p. 325-326° (recrystallized from ethyl acetate); ir (potassium bromide): 3200-2500, 2230, 1655, 1605, 1580, 1550, 1520,

1490, 1470, 1440, 1380, 1310, 1270, 1240, 1190, 1030 cm^{-1} ; nmr (DMSO- d_6): δ 6.86-7.70 (m, 9H, arom), 3.73 (s, 3H, CH_3O).

Anal. Calcd. for $\text{C}_{20}\text{H}_{13}\text{N}_3\text{O}_2$: C, 73.39; H, 3.97; N, 12.84. Found: C, 73.42; H, 4.28; N, 13.19.

3,5-Dicyano-4-(*p*-chlorophenyl)-6-phenyl-2-pyridone (VI_d).

This compound was obtained in 90% yield by method a) and 83% yield by method b), m.p. 337-338° (recrystallized from methanol); ir (potassium bromide): 3200-2500, 2215, 2210, 1700, 1590, 1550, 1490, 1470, 1440, 1380, 1325, 1230, 1130, 1100, 1015 cm^{-1} ; nmr (DMSO- d_6): δ 7.30-7.70 (m, 9H, arom).

Anal. Calcd. for $\text{C}_{19}\text{H}_{10}\text{ClN}_3\text{O}$: C, 68.80; H, 3.03; Cl, 10.70; N, 12.67. Found: C, 68.62; H, 3.15; Cl, 10.89; N, 12.54.

3,5-Dicyano-6-(*p*-methylphenyl)-4-phenyl-2-pyridone (VI_e).

This compound was obtained in 100% yield by method a) and in 17% yield by method c), m.p. 289-291° (recrystallized from benzene); ir (potassium bromide): 3200-2500, 2225, 1650, 1620, 1580, 1570, 1530, 1500, 1470, 1435, 1410, 1380, 1330, 1280, 1240, 1195, 1180, 1160, 1130, 1080, 1035, 1020, 1000 cm^{-1} ; nmr (DMSO- d_6): δ 7.10-7.60 (m, 9H, arom), 2.40 (s, 3H, CH_3).

Anal. Calcd. for $\text{C}_{20}\text{H}_{13}\text{N}_3\text{O}$: C, 77.15; H, 4.20; N, 13.49. Found: C, 76.87; H, 4.26; N, 13.19.

3,5-Dicyano-4-(*p*-nitrophenyl)-6-phenyl-2-pyridone (VI_f).

This compound was obtained in 18% yield by method c), m.p. 302-303° (recrystallized from methylene chloride); ir (potassium bromide): 3200-2500, 2225, 1660, 1600, 1550, 1510, 1490, 1470, 1440, 1360, 1320, 1290, 1235, 1130, 1000 cm^{-1} ; nmr (DMSO- d_6): δ 7.40-7.80 (m, 9H, arom).

Anal. Calcd. for $\text{C}_{19}\text{H}_{13}\text{N}_4\text{O}_3$: C, 66.66; H, 2.92; N, 16.37. Found: C, 66.77; H, 3.08; N, 16.32.

4,6-Diaryl-5-carbethoxy-3-cyano-3,4-dihydro-2-pyridones (V). General Procedure.

Sulfuric acid (70 ml., 80%) are added dropwise and under stirring to a cooled (ice bath) suspension of 0.003 mole of the corresponding 2-amino-4,6-diaryl-3-carbethoxy-5-cyano-4*H*-pyran (II) in ca. 8 ml. of acetic acid. After 2 hours stirring, the clear solution that results was poured into ice water and the solid collected was purified by recrystallization.

5-Carbethoxy-3-cyano-4,6-diphenyl-3,4-dihydro-2-pyridone (Va).

This compound was obtained in 90% yield, m.p. 151-153° (recrystallized from benzene); ir (potassium bromide): 3400, 3250, 3160, 2990, 2930, 2900, 2860, 2230, 1710, 1650, 1630, 1600, 1580, 1490, 1450, 1370, 1320, 1230 cm^{-1} ; nmr (DMSO- d_6): δ 9.90 (broad 1H, NH), 7.00-7.37 (broad singlet, 10H, arom), 5.27 (d, 1H), 4.33 (d, 1H), 3.60 (q, 2H, CH_2), 0.70 (t, 3H, CH_3).

Anal. Calcd. for $\text{C}_{21}\text{H}_{18}\text{N}_3\text{O}_2$: C, 72.83; H, 5.20; N, 8.10. Found: C, 72.65; H, 5.32; N, 8.27.

5-Carbethoxy-3-cyano-4-(*p*-methylphenyl)-6-phenyl-3,4-dihydro-2-pyridone (Vb).

This compound was obtained in 95% yield, m.p. 179-181° (recrystallized from benzene); ir (potassium bromide): 3400, 3220, 3140, 2920, 2880, 2250, 1710, 1685, 1640, 1600, 1580, 1470, 1445, 1410, 1370, 1320, 1230, 1095 cm^{-1} ; nmr (DMSO- d_6): δ 10.35 (broad 1H, NH), 7.00-7.30 (m, 9H, arom), 5.00 (d, 1H), 4.35 (d, 1H), 3.65 (q, 2H, CH_2), 2.30 (s, 3H, CH_3), 0.75 (t, 3H, CH_3).

Anal. Calcd. for $\text{C}_{22}\text{H}_{20}\text{N}_3\text{O}_2$: C, 73.33; H, 5.55; N, 7.77. Found: C, 73.32; H, 5.66; N, 7.84.

5-Carbethoxy-3-cyano-4-(*p*-chlorophenyl)-6-phenyl-3,4-dihydro-2-pyridone (Vd).

This compound was obtained in 91% yield, m.p. 164-165° (recrystallized from ethanol); ir (potassium bromide): 3420, 3260, 3205, 3160, 2980, 2910, 2225, 1710, 1670, 1630, 1600, 1570, 1490, 1460, 1370, 1320, 1230 cm^{-1} ; nmr (DMSO- d_6): δ 10.10 (broad, 1H, NH), 7.00-7.46 (m, 9H, arom),

5.15 (d, 1H), 4.42 (d, 1H), 3.67 (q, 2H, CH_2), 0.70 (t, 3H, CH_3).

Anal. Calcd. for $\text{C}_{21}\text{H}_{17}\text{ClN}_3\text{O}_2$: C, 66.23; H, 4.47; Cl, 9.33; N, 7.36. Found: C, 66.01; H, 4.47; Cl, 9.17; N, 7.35.

4,6-Diaryl-5-carbethoxy-3-cyano-2-pyridones (VII). General Procedure.

A suspension of 0.003 mole of the appropriate 4*H*-pyran (II) in ca 10 ml. of acetic acid was treated at 0° with a solution of nitrosylsulfuric acid prepared from 0.0035 mole of sodium nitrite, 64 g. of sulfuric acid and 10 ml. of water. The mixture was stirred until total solution occurs (about 3-5 hours) and was poured into crushed ice. The solid obtained was filtered off and recrystallized.

5-Carbethoxy-3-cyano-4,6-diphenyl-2-pyridone (VII_a).

This compound was obtained in 26% yield, m.p. 256-257° (recrystallized from benzene); ir (potassium bromide): 3200-2500, 2240, 1720, 1650, 1570, 1500, 1470, 1450, 1400, 1365, 1340, 1290, 1235, 1195, 1170, 1140, 1100, 1080, 1010, 1000 cm^{-1} ; nmr (DMSO- d_6): δ 7.00-7.40 (m, 10H, arom), 3.58 (q, 2H, CH_2), 0.60 (t, 3H, CH_3).

Anal. Calcd. for $\text{C}_{21}\text{H}_{16}\text{N}_2\text{O}_3$: C, 73.25; H, 4.65; N, 8.13. Found: C, 73.40; H, 4.63; N, 7.88.

5-Carbethoxy-3-cyano-4-(*p*-methylphenyl)-6-phenyl-2-pyridone (VII_b).

This compound was obtained in 17% yield, m.p. 300-302° (recrystallized from ethyl acetate); ir (potassium bromide): 3200-2500, 2230, 1720, 1640, 1610, 1570, 1530, 1510, 1490, 1470, 1450, 1400, 1360, 1335, 1275, 1215, 1190, 1140, 1040, 1015 cm^{-1} ; nmr (DMSO- d_6): δ 7.10-7.40 (m, 9H, arom), 3.55 (q, 2H, CH_2), 2.30 (s, 3H, CH_3), 0.60 (t, 3H, CH_3).

Anal. Calcd. for $\text{C}_{22}\text{H}_{18}\text{N}_2\text{O}_3$: C, 73.74; H, 5.02; N, 7.82. Found: C, 73.72; H, 5.22; N, 8.03.

5-Carbethoxy-3-cyano-4-(*p*-nitrophenyl)-6-phenyl-2-pyridone (VII_f).

This compound was obtained in 46% yield, m.p. 270-271° (recrystallized from ethanol); ir (potassium bromide): 3200-2500, 2240, 1730, 1650, 1600, 1590, 1560, 1520, 1490, 1470, 1450, 1350, 1290, 1280, 1230, 1190, 1180, 1160, 1020 cm^{-1} ; nmr (DMSO- d_6): δ 7.30-8.40 (m, 9H, arom), 3.60 (q, 2H, CH_2), 0.60 (t, 3H, CH_3).

Anal. Calcd. for $\text{C}_{21}\text{H}_{15}\text{N}_3\text{O}_5$: C, 64.78; H, 3.86; N, 10.80. Found: C, 64.65; H, 3.99; N, 10.74.

2-Amino-4,6-diaryl-5-carbethoxy-3-cyanopyridines (XII). General Procedure.

A solution of 0.003 mole of the appropriate 2-amino-4,6-diaryl-5-carbethoxy-3-cyano-4*H*-pyran (II) and 0.012 mole of ammonium acetate in ca. 15 ml. of glacial acetic acid was refluxed for 2-3 hours. The solid precipitates after a few hours standing at room temperature was collected by filtration. An additional amount of substance was obtained by pouring the mother liquors into water. The combined fractions of solid are recrystallized in a suitable solvent.

2-Amino-5-carbethoxy-3-cyano-4,6-diphenylpyridine (XII_a).

This compound was obtained in 41% yield, m.p. 184-186° (recrystallized from ethanol); ir (potassium bromide): 3460, 3320, 3200, 3040, 2980, 2800, 2205, 1700, 1620, 1580, 1550, 1530, 1490, 1460, 1440, 1420, 1370, 1360, 1290, 1200, 1150 cm^{-1} ; nmr (DMSO- d_6): δ 7.25 (broad, 2H, NH_2), 7.10-7.50 (m, 10H, arom), 3.70 (q, 2H, CH_2), 0.70 (t, 3H, CH_3).

Anal. Calcd. for $\text{C}_{21}\text{H}_{17}\text{N}_3\text{O}_2$: C, 73.46; H, 4.95; N, 12.24. Found: C, 73.44; H, 5.07; N, 12.19.

2-Amino-5-carbethoxy-3-cyano-4-(*p*-methylphenyl)-6-phenylpyridine (XII_b).

This compound was obtained in 59% yield, m.p. 190-191° (recrystallized from ethanol); ir (potassium bromide): 3480, 3450, 3280, 3200, 3100, 2980, 2930, 2800, 2700, 2210, 1720, 1600, 1540, 1510, 1490, 1460, 1440, 1420, 1400, 1390, 1380, 1360, 1240, 1200 cm^{-1} ; nmr (acetone- d_6): δ 7.30-7.60 (m, 9H, arom), 6.50 (broad, 2H, NH_2), 3.73 (q, 2H, CH_2), 0.83 (t, 3H, CH_3).

Anal. Calcd. for $C_{22}H_{19}N_3O_2$: C, 73.92; H, 5.35; N, 11.75. Found: C, 73.83; H, 5.54; N, 11.97.

2-Amino-5-carbethoxy-3-cyano-4(*p*-chlorophenyl)-6-phenylpyridine (XIIId).

This compound was obtained in 60% yield, m.p. 194-196° (recrystallized from ethanol); *ir* (potassium bromide): 3470, 3280, 3120, 2980, 2220, 1720, 1625, 1610, 1590, 1570, 1545, 1490, 1450, 1440, 1420, 1390, 1360, 1290, 1250, 1200 cm^{-1} ; *nmr* (DMSO- d_6): δ 7.10-7.65 (m, 11H, arom, NH_2), 3.32 (q, 2H, CH_2), 0.70 (t, 3H, CH_3).

Anal. Calcd. for $C_{21}H_{16}ClN_3O_2$: C, 66.77; H, 4.26; N, 11.12; Cl, 9.35. Found: C, 66.29; H, 4.06; N, 10.90; Cl, 9.56.

2-Amino-5-carbethoxy-3-cyano-4(*p*-nitrophenyl)-6-phenylpyridine (XIIIf).

This compound was obtained in 44% yield, m.p. 198-200° (recrystallized from ethanol); *ir* (potassium bromide): 3460, 3280, 3180, 2980, 2205, 1720, 1620, 1550, 1510, 1490, 1440, 1360, 1340, 1270, 1250, 1200 cm^{-1} ; *nmr* (deuteriochloroform): δ 7.00-8.30 (m, 9H, arom), 5.50 (broad, 2H, NH_2), 3.80 (q, 2H, CH_2), 0.85 (t, 3H, CH_3).

Anal. Calcd. for $C_{21}H_{16}N_4O_4$: C, 64.95; H, 4.12; N, 14.43. Found: C, 64.82; H, 4.22; N, 14.47.

2,4,6-Triaryl-3,5-dicyano-1,4-dihydropyridines (XV). General Procedure.

The appropriate pyran I (0.003 mole) was refluxed for 3 hours with 0.012 mole of ammonium acetate in 15 ml. of glacial acetic acid. After cooling the solution at room temperature, the product either precipitates from the reaction mixture or was isolated by pouring into water. The solid collected was purified by recrystallization.

3,5-Dicyano-2,4,6-triphenyl-1,4-dihydropyridine (XVa).

This compound was obtained in 40% yield from pyran Ia and in 80% yield from pyran XVI m.p. 279-280°C (lit. 280°) (18).

3,5-Dicyano-4(*p*-methylphenyl)-2,6-diphenyl-1,4-dihydropyridine (XVb).

This compound was obtained from pyran Ib in 45% yield and in 41% yield from α -benzoyl-*p*-methylcinnomonitrile (IXb), m.p. 259-260° (lit. 259°) (18).

3,5-Dicyano-4(*p*-nitrophenyl)-2,6-diphenyl-1,4-dihydropyridine (XVc).

This compound was obtained from pyran If in 50% yield, m.p. 270-271° (lit. 272°) (18).

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