Synthesis of Heterocyclic Compounds. Part 46.[1] The Reactions of Malonamide and 2-Cyanoacetamide with Substituted Propenones

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The synthesis of substituted 2-pyridone derivatives from malonamide (**1**) and 2-cyanoacetamide (**2**) is reported. Conjugate addition of these compounds to substituted propenones (**3**) and (**4**) leads to 6-hydroxy-2-piperidones, which can be dehydrated and aromatized to 2-pyridones (**7**), (**11**), and (**14**). The intermediate 3,4-dihydro derivatives were also obtained and some chemical transformations of the products prepared are also described.

In a previous communication,[2] we described a modification of the Guareschi pyridone synthesis,[3,4] involving the conjugate addition of 2-cyanoacetamide to α-benzoylcinnamonitriles, and leading to some cyanopyridones which were also obtained by ring transformations of aminopyran derivatives.[5] We now report the extension of this synthesis to different α,β-unsaturated ketones and to the use of malonamide, as well as some chemical transformations of the resulting 2-pyridones.

In contrast to the Guareschi synthesis, conjugate addition to an unsaturated ketone leads to a saturated intermediate (see Scheme), which does not provide an aromatic ring upon dehydration. Thus, addition of malonamide (**1**) to α-benzoylcinnamonitriles (**3**), which takes place in a similar way to the reaction with 2-cyanoacetamide, is followed only by a cyclization to a piperidine ring. The reaction is very easy to perform in basic medium and affords 6-hydroxy-2-piperidones (**5**) in good yields with a variety of substituents on the aryl groups. Dehydration of hydroxy derivatives (**5**) must be carried out in a separate step by using dilute sulphuric acid and leads to 3,4-dihydro-2-pyridones (**6**), which result also from treatment of compounds (**9**) with concentrated sulphuric acid. Transformation of compounds (**6**) into dicarbonitriles (**10**) can be achieved by reaction with phosphoryl trichloride in dimethylformamide (DMF), and the reverse transformation takes place upon acid treatment. It must be pointed out that only the cyano group located at position 3 of compounds (**10**) is hydrolysed, whereas the nitrile at position 5 does not react. This is in agreement with the known facility of hydrolysis of a cyano group contiguous to the carbonyl group in a pyridone ring.[6,7]

Aromatic 2-pyridones (**7**) result from oxidation of their 3,4-dihydro derivatives (**6**) with nitrosylsulphuric acid. Alternatively, this reagent can be employed to bring about the direct transformation of 6-hydroxy-2-piperidones (**5**) into 2-pyridones (**7**). In both cases, the reaction is very easy to perform and the yields obtained are high. On the other hand, the carbamoyl group of 2-pyridones (**7**) can be removed through hydrolysis to a carboxyl group and decarboxylation. In fact, treatment of compounds of (**7**) with concentrated hydrochloric acid in dioxane brings about their transformation into 2-pyridones (**8**), unsubstituted at position 3. Isolation of the intermediate 2-oxopyridine-3-carboxylic acid was not possible. Compounds (**8**) were also obtained from 3,5-dicyano-2-pyridones (**11**) by treatment with hydrochloric acid in ethylene glycol. In both reactions, despite the long reaction time (several days), the cyano group located at position 5 is unaffected.

The reactions of malonamide (**1**) and 2-cyanoacetamide (**2**) with α-benzoylcinnamates (**4**) were of interest because, in this case, cyclization could take place by attack of the amide nitrogen either at the carbonyl group or at the ethoxy carbonyl group. We found that, with 2-cyanoacetamide, the cyclization involves attack at the carbonyl group, leading to 2-piperidones (**12**), whereas no reaction took place between malonamide and ethyl α-benzoylcinnamates (**4**) under a variety of conditions. This is probably due to the lower acidity of the methylene group of malonamide and the lower susceptibility of ethyl α-benzoylcinnamates to Michael attack in comparison with α-benzoylcinnamonitriles. Preparation of piperidones (**12**) requires a longer reaction time than that for piperidones (**9**), but they are obtained in good yield. They are rather unstable compounds and decompose easily on heating. Furthermore, the reaction fails when a methoxy group is present on the starting material [ethyl α-benzoylcinnamate (**4d**)], because the electron-donating effect of the methoxy group makes conjugate addition more difficult.

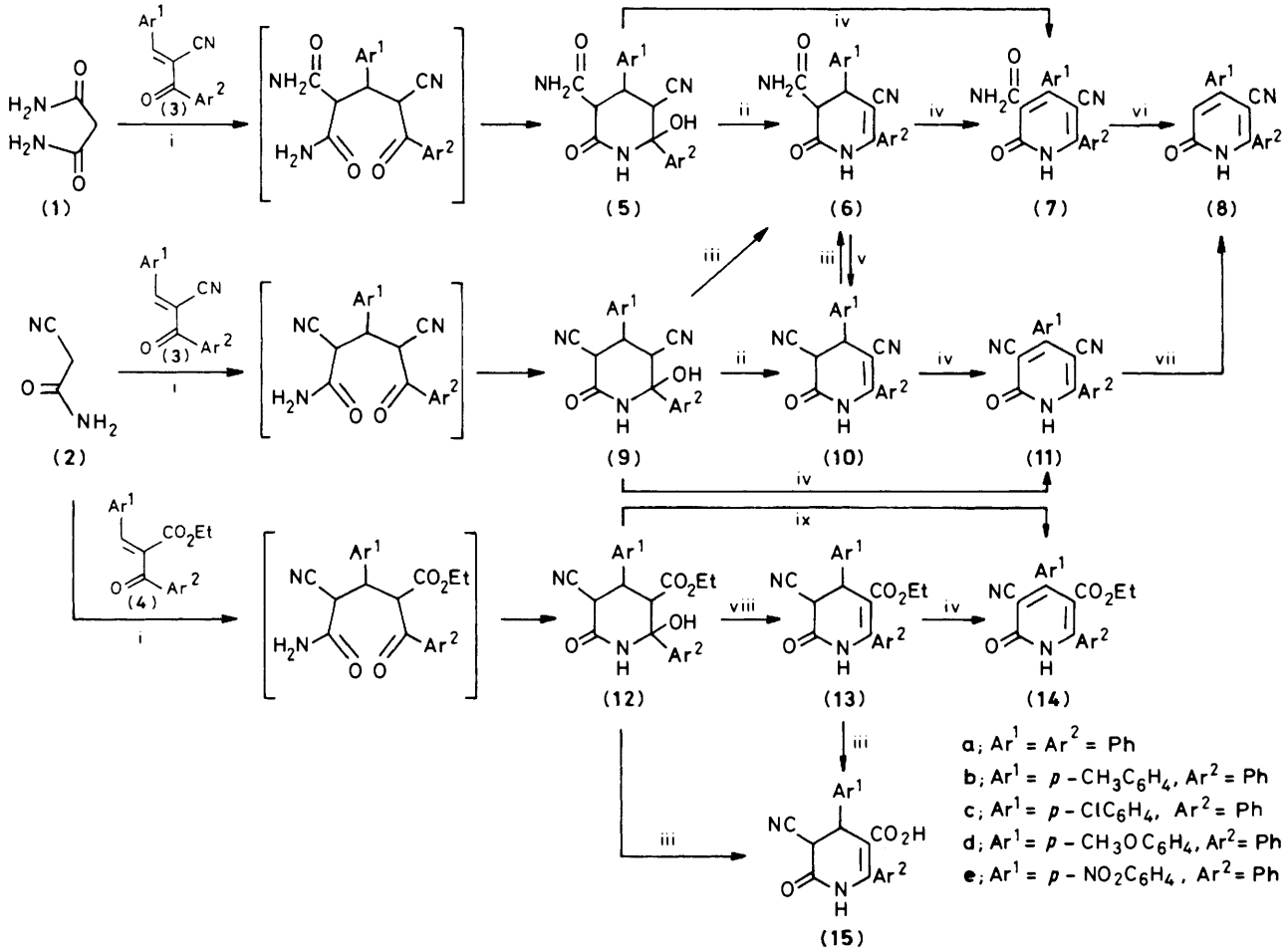
Compounds (**12**) can be dehydrated to 3,4-dihydropyridone derivative (**13**) by treatment with 75% sulphuric acid at room temperature. The reaction gives good yields, but the acid concentration is critical. If 50% sulphuric acid is used no reaction occurs, and with 98% sulphuric acid dehydration is accompanied by hydrolysis of the ethoxycarbonyl group thus leading to carboxylic acids (**15**), which can also be obtained by similar treatment applied to the 3,4-dihydro-2-pyridones (**13**). On the other hand, 6-hydroxy-2-piperidones (**12**) can be transformed into 2-pyridones (**14**) by treatment with thionyl chloride in pyridine at −10 °C. According to the known behaviour of this reagent with other heterocyclic systems,[8,9] it effects dehydration and dehydrogenation, in one single step, of the aromatic system (**14**), which can also be prepared from 3,4-dihydro derivatives (**13**) by reaction with nitrosylsulphuric acid.

Spectral data of the new compounds prepared (see Experimental section) are in agreement with reported values for other 2-pyridones.[10–12]

Finally, in the n.m.r. spectra of the 3,4-dihydro-2-pyridones obtained, the hydrogens located at positions 3 and 4 of the ring appear as two doublets at δ_H 4.2 and 3.6 in compounds (**6**) and at δ_H 5.0 and 4.4 in compounds (**13**). The coupling constant measured for compounds (**6**) is 7 Hz and whereas that for compounds (**13**) is 6 Hz. When the Haasnoot–Leeuw–Altona equation[13] is applied to both compounds, taking into account the correction for the Huggins[14] electronegativities of the groups attached to carbons 3 and 4 of the ring, a dihedral angle of about 40° is obtained. This result indicates an axial–equatorial geometry for the coupled protons.

Experimental

M.p.s were determined with a Büchi apparatus for samples in capillary tubes and are uncorrected. I.r. spectra were recorded with a Perkin-Elmer 257 spectrophotometer for samples in potassium bromide pellets and ^{1}H n.m.r. spectra were measured at 60 MHz on a Varian T-60A spectrometer for $(CD_3)_2SO$ solutions; chemical shifts are given in δ values against $SiMe_4$ as



Scheme. *Reagents:* i, piperidine–dry MeOH; ii, 50% H_2SO_4; iii, 98% H_2SO_4; iv, $HOSO_2ONO$–aq. AcOH; v, $POCl_3$–DMF; vi, aq. HCl–dioxane; vii, aq. HCl–$HOCH_2CH_2OH$; viii, 75% H_2SO_4; ix, Cl_2SO–pyridine

internal standard. A Varian MAT 711 spectrometer was used for recording mass spectra. Microanalyses were performed by Centro Nacional de Química Orgánica de Madrid. The reactions and purity of compounds were monitored by t.l.c., performed on silica gel plates (Merck) and using toluene–ethyl acetate as developer.

Malonamide, 2-cyanoacetamide, and ethyl benzoylacetate were commercially obtained and were used without further purification. α-Benzoylcinnamonitriles (**3**)[15,16] and ethyl α-benzoylcinnamates (**4**)[17–20] were prepared according to known methods as was ω-cyanoacetophenone.[21]

4,6-Diaryl-3-carbamoyl-5-cyano-6-hydroxypiperidin-2-ones (**5**). *General Procedure.*—To a suspension of the appropriate α-benzoylcinnamonitrile (**3**) (5 mmol) in dry methanol (5 ml) was added a solution of malonamide (1) (6 mmol) in dry methanol (12 ml), together with a few drops of piperidine. The reaction mixture was stirred at room temperature for 14—16 h. After that time, no starting material remained (t.l.c.) and the solid that precipitated was collected by filtration, washed with cold methanol and purified by recrystallization in methanol.

3-Carbamoyl-5-cyano-6-hydroxy-4,6-diphenylpiperidin-2-one (**5a**). This compound was obtained in 86% yield. M.p. 206—207 °C (Found: C, 68.2; H, 5.1; N, 12.2. $C_{19}H_{17}N_3O_3$ requires C, 68.04; H, 5.10; N, 12.53%); $\nu_{max.}$ 3 480, 3 360, 3 210, 3 100, 2 910, 2 230, 1 660, 1 590, and 1 480 cm^{-1}; δ_H 8.30 (1 H, s, NH), 6.50—7.53 (13 H, m, ArH, OH, and NH_2), and 3.43—4.03 (3 H, m).

3-Carbamoyl-5-cyano-6-hydroxy-6-phenyl-4-(p-tolyl)-piperidin-2-one (**5b**). 82% yield, m.p. 159—160 °C (Found: C, 68.9; H, 5.55; N, 11.8. $C_{20}H_{19}N_3O_3$ requires C, 68.75; H, 5.48; N, 12.02%); $\nu_{max.}$ 3 400, 3 280, 3 220, 3 120, 2 250, 1 670, 1 620, 1 515, and 1 455 cm^{-1}; δ_H 8.36 (1 H, s, NH), 6.50—7.60 (12 H, m, ArH, OH, and NH_2), 3.30—4.10 (3 H, m), and 2.20 (3 H, s, CH_3).

3-Carbamoyl-4-(p-chlorophenyl)-5-cyano-6-hydroxy-6-phenylpiperidin-2-one (**5c**). 80% yield, m.p. 169—170 °C (Found: C, 61.4; H, 4.5; N, 11.3; Cl, 10.1. $C_{19}H_{16}ClN_2O_3$ requires C, 61.70; H, 4.36; N, 11.36; Cl, 9.58%), $\nu_{max.}$ 3 420, 3 360, 3 260, 3 200, 3 090, 2 260, 1 675, 1 660, 1 610, 1 490, and 1 440 cm^{-1}; δ_H 8.43 (1 H, s, NH), 6.60—7.60 (12 H, m, ArH, OH, and NH_2), and 3.30—3.40 (3 H, m).

3-Carbamoyl-5-cyano-6-hydroxy-4-(p-methoxyphenyl)-6-phenylpiperidin-2-one (**5d**). 87% yield, m.p. 155—156 °C (Found: C, 65.3; H, 5.6; N, 11.75. $C_{20}H_{19}N_3O_4$ requires C, 65.74; H, 5.24; N, 11.50%); $\nu_{max.}$ 3 400, 3 300, 3 210, 3 130, 2 240, 1 670, 1 620, 1 580, 1 510, and 1 460 cm^{-1}; δ_H 8.50 (1 H, s, NH), 6.70—7.80 12 H, m, ArH, OH, and NH_2), 3.80—4.60 (3 H, m), and 3.70 (3 H, s, CH_3O).

3-Carbamoyl-5-cyano-6-hydroxy-4-(p-nitrophenyl)-6-phenylpiperidin-2-one (**5e**). 63% yield, m.p. 155—156 °C (Found: C, 59.6; H, 4.1; N, 14.7. $C_{19}H_{16}N_4O_5$ requires C, 59.99; H, 4.24;

N, 14.63%); $\nu_{max.}$ 3 400, 3 260, 3 200, 3 100, 2 930, 2 240, 1 665, 1 615, 1 590, 1 515, and 1 490 cm^{-1}; δ_H 8.70 (1 H, s, NH), 6.70—8.30 (12 H, m, ArH, OH, and NH_2), and 3.50—4.50 (3 H, m).

4,6-*Diaryl*-3-*carbamoyl*-5-*cyano*-3,4-*dihydropyridin*-2(1H)-*ones* (**6**). *General Procedure.*—A suspension of the corresponding 6-hydroxypiperidin-2-one (**5**) (2 mmol) in 50% sulphuric acid (20 ml) was stirred at room temperature for 3—6 h. The reaction mixture was then poured into crushed ice and the resulting solid was collected by filtration and washed with plenty of water, to remove any remaining acid, until neutral pH was obtained. Compounds (**6**) thus obtained were recrystallized in methanol.

3-*Carbamoyl*-5-*cyano*-4,6-*diphenyl*-3,4-*dihydropyridin*-2-(1H)-*one* (**6a**). 84% yield, m.p. 225—226 °C (Found: C, 72.3; H, 4.7; N, 13.1. $C_{19}H_{15}N_3O_2$ requires C, 71.90; H, 4.76; N, 13.24%), $\nu_{max.}$ 3 450, 3 340, 3 220, 3 130, 2 220, 1 700, 1 680, 1 635, 1 600, 1 575, and 1 490 cm^{-1}; δ_H 10.43 (1 H, s, NH), 6.90—7.50 (12 H, m, NH_2), 4.13—4.33 (1 H, d, and 3.50—3.70 (1 H, d).

This compound was also obtained by using concentrated sulphuric acid, but the yield was only 75%.

3-*Carbamoyl*-5-*cyano*-6-*phenyl*-4-(p-*tolyl*)-3,4-*dihydropyridin*-2(1H)-*one* (**6b**). 65% yield, m.p. 180—181 °C (Found: C, 72.0; H, 5.6; N, 12.4. $C_{20}H_{17}N_3O_2$ requires C, 72.48; H, 5.17; N, 12.68%); $\nu_{max.}$ 3 660, 3 480, 3 400, 3 320, 2 220, 2 200, 1 700, 1 670, 1 620, 1 510, and 1 480 cm^{-1}; δ_H 10.43 (1 H, s, NH), 6.90—7.60 (11 H, m, ArH and NH_2), 4.10—4.30 (1 H, d), 3.50—3.70 (1 H, d), and 2.26 (3 H, s, CH_3).

3-*Carbamoyl*-4-(p-*chlorophenyl*)-5-*cyano*-6-*phenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**6c**). 84% yield, m.p. 173—174 °C (Found: C, 64.6; H, 4.2; N, 11.7; Cl, 10.0. $C_{19}H_{14}ClN_3O_2$ requires C, 64.86; H, 3.98; N, 11.94; Cl, 10.09%); 3 630, 3 390, 3 320, 3 180, 2 220, 2 200, 1 695, 1 665, 1 615, 1 590, and 1 490 cm^{-1}; δ_H 10.46 (1 H, s, NH), 6.80—7.60 (11 H, m, ArH, and NH_2), 4.13—4.36 (1 H, d), and 3.50—3.74 (1 H, d).

3-*Carbamoyl*-5-*cyano*-4-(p-*methoxyphenyl*)-6-*phenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**6d**). 68% yield, m.p. 197—198 °C (Found: C, 69.0; H, 5.0; N, 12.3. $C_{20}H_{17}N_3O_3$ requires C, 69.15; H, 4.93; N, 12.09%); $\nu_{max.}$ 3 640, 3 400, 3 320, 3 200, 3 140, 2 220, 2 200, 1 685, 1 665, 1 665, 1 610, 1 590, 1 510, 1 490, 1 470, and 1 440 cm^{-1}; δ_H 8.60 (1 H, s, NH), 6.40—7.20 (9 H, m, ArH, and NH_2), 4.00—4.20 (1 H, d, CH_3), 3.40—3.70 (1 H, d), and 3.40 (3 H, s, CH_3O).

3-*Carbamoyl*-5-*cyano*-4-(p-*nitrophenyl*)-6-*phenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**6e**). 62% yield, m.p. 274—275 °C (Found: C, 63.1; H, 4.1; N, 15.5. $C_{19}H_{14}N_4O_4$ requires C, 62.98; H, 3.86; N, 15.46%); $\nu_{max.}$ 3 410, 3 300, 3 200, 3 100, 2 200, 1 690, 1 665, 1 600, 1 570, 1 505, and 1 490 cm^{-1}; δ_H 10.53 (1 H, s, NH), 7.00—8.20 (11 H, m, ArH, and NH_2), 4.40—4.60 (1 H, d), and 3.63—3.83 (1 H, d).

Transformation of 3,4-*Dicyano*-6-*hydroxy*-4,6-*diphenylpiperidin*-2-*one* (**9a**) *into* 3-*Carbamoyl*-5-*cyano*-4,6-*diphenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**6a**).—The piperidinone (**9a**) (0.3 mmol) was dissolved in concentrated sulphuric acid (1 ml) and the solution was kept for 24 h. The mixture was then poured into crushed ice and the precipitate was collected by filtration and washed with water. Compound (**6a**) thus obtained in 24% yield was recrystallized from methanol.

Transformation of 3,5-*Dicyano*-4,6-*diphenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**10a**) *into* 3-*Carbamoyl*-5-*cyano*-4,6-*diphenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**6a**).—A solution of compound (**10a**) (0.7 mmol) in concentrated sulphuric acid (2 ml) was kept at room temperature for 20 h and was then poured into crushed ice. The collected precipitate is washed with water and recrystallized from methanol. Yield of (**6a**) 40%.

Transformation of 3-*Carbamoyl*-5-*cyano*-4,6-*diphenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**6a**) *into* 3,5-*Dicyano*-4,6-*diphenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**10a**).—Compound (**6a**) (0.6 mmol) was dissolved in DMF (10 ml) and phosphoryl trichloride (0.1 ml, 1 mmol) was slowly added to the continuously stirred solution, using the reaction procedure reported by Bailey *et al.*[22] The reaction mixture was then heated at 80 °C in a water-bath for 10 min. The solution was then allowed to cool and was poured into ice. Aqueous ammonium hydroxide was used to neutralize the aqueous solution, and the reaction product which precipitated was collected by filtration, washed with water, and recrystallized from methanol. Yield 86%.

4,6-*Diaryl*-3-*carbamoyl*-5-*cyanopyridin*-2(1H)-*ones* (**7**). *General Procedure.*—*Method* (*a*). To a suspension of the corresponding 3,4-dihydropyridin-2(1*H*)-one (**6**) in acetic acid (*ca.* 10 ml) at 0 °C was added a solution of nitrosylsulphuric acid at 0 °C, prepared from sodium nitrite (5 mmol) in sulphuric acid (50 ml) and water (16 ml).[23,24] The reaction mixture was stirred until total solution occurred and the mixture was then kept at room temperature until no starting material remained (t.l.c.) (about 10—12 h). The solution was poured into crushed ice and the resulting solid was filtered off and recrystallized from methanol.

Method (*b*). The corresponding 6-hydroxypiperidin-2-one (**5**) was subjected to treatment similar to the one described in method (a), but the reaction time was *ca.* 24 h.

3-*Carbamoyl*-5-*cyano*-4,6-*diphenylpyridine*-2(1H)-*one* (**7a**). 82% yield by method (a) and 95% by method (b), m.p. 301—302 °C (Found: C, 72.1; H, 4.3; N, 13.5. $C_{19}H_{13}N_3O_2$ requires C, 72.38; H, 4.12; N, 13.33%); $\nu_{max.}$ 3 430, 3 270, 3 100—2 500, 2 220, 1 660, 1 590, 1 565, 1 540, and 1 490 cm^{-1}; δ_H 7.00—7.60 (12 H, m, ArH and NH_2).

3-*Carbamoyl*-5-*cyano*-6-*phenyl*-4-(p-*tolyl*)*pyridin*-2(1H)-*one* (**7b**). 92% yield by method (a) and 90% yield by method (b), m.p. 272—273 °C (Found: C, 72.7; H, 4.4; N, 12.7. $C_{20}H_{15}N_3O_2$ requires C, 72.94; H, 4.55; N, 12.76%); $\nu_{max.}$ 3 620, 3 430, 3 200—2 500, 2 220, 1 735, 1 640, 1 610, 1 560, 1 540, 1 490, and 1 440 cm^{-1}; δ_H 6.90—7.70 (11 H, m, ArH, and NH_2) and 2.30 (3 H, s) CH_3).

3-*Carbamoyl*-4-(p-*chlorophenyl*)-5-*cyano*-6-*phenylpyridin*-2(1H)-*one* (**7c**). 85% yield by method (a) and 93% yield by method (b), m.p. 280—281 °C (Found: C, 64.9; H, 3.3; N, 11.7; Cl, 9.9. $C_{19}H_{12}ClN_3O_2$ requires C, 65.23; H, 3.43; N, 12.01; Cl, 10.15%); $\nu_{max.}$ 3 440, 3 200—2 500, 2 220, 1 715, 1 630, 1 590, 1 560, 1 485, 1 455, and 1 435 cm^{-1}; δ_H 7.33—7.96 (11 H, m, ArH, and NH_2).

3-*Carbamoyl*-5-*cyano*-4-(p-*methoxyphenyl*)-6-*phenylpyridin*-2(1H)-*one* (**7d**). 67% yield by method (a) and 75% yield by method (b), m.p. 246—247 °C (Found: C, 69.3; H, 4.25; N, 11.9. $C_{20}H_{15}N_3O_3$ requires C, 69.56; H, 4.34; N, 12.17%); $\nu_{max.}$ 3 560, 3 410, 3 200—2 500, 2 220, 1 715, 1 635, 1 605, 1 560, 1 540, 1 520, 1 485, 1 470, 1 460, and 1 440 cm^{-1}; δ_H 6.70—7.70 (11 H, m, ArH, and NH_2) and 3.70 (3 H, s, CH_3O).

3-*Carbamoyl*-5-*cyano*-4-(p-*nitrophenyl*)-6-*phenylpyridin*-2(1H)-*one* (**7e**). 67% yield by method (a) and 80% yield by method (b), m.p. 320—321 °C (Found: C, 63.5; H, 3.6; N, 15.6. $C_{19}H_{12}N_4O_4$ requires C, 63.33; H, 3.33; N, 15.55%); $\nu_{max.}$ 3 440, 3 300, 3 180, 3 100—2 500, 2 220, 1 665, 1 640, 1 600, 1 580, 1 560, 1 540, 1 510, and 1 490 cm^{-1}; 7.20—8.30 (11 H, m, ArH, and NH_2).

4,6-*Diaryl*-5-*cyanopyridin*-2(1H)-*ones* (**8**). *General Procedure.*—Concentrated hydrochloric acid (100 ml) was added to a solution of the appropriate 4,6-diaryl-3-carbamoyl-5-cyanopyridin-2(1*H*)-one (**7**) (1.4 mmol) in dioxane (*ca.* 50 ml). The reaction mixture was heated at reflux temperature for a variable reaction time (3—20 days) until t.l.c. showed no

starting material remaining. The solution was then poured into crushed ice and the precipitate was filtered off, washed with water, and recrystallized.

5-*Cyano*-4,6-*diphenylpyridin*-2(1H)-*one* (**8a**). Reaction time 8 days, yield 67%, m.p. 281—282 °C (from methanol) (Found: C, 79.2; H, 4.3; N, 10.0. $C_{18}H_{12}N_2O$ requires C, 79.41; H, 4.41; N, 10.29%); $\nu_{max.}$ 3 200—2 500, 2 220, 1 660, 1 600, 1 590, 1 570, 1 530, 1 490, and 1 450 cm^{-1}; δ_H 7.20—7.80 (10 H, m, ArH) and 6.30 (1 H, s); *m/z* (relative intensity) 272 (M^+, 85%), 271 (100), 254 (10), 253 (31), 244 (6), 243 (8), 242 (8), 127 (10), and 126 (8).

5-*Cyano*-6-*phenyl*-4-(p-*tolyl*)*pyridin*-2(1H)-*one* (**8b**). Reaction time 3 days, yield 81%, m.p. 305—306 °C (from ethanol) (Found: C, 79.7; H, 4.9; N, 9.8. $C_{19}H_{14}N_2O$ requires C, 79.72; H, 4.89; N, 9.79%); $\nu_{max.}$ 3 200—2 500, 2 225, 1 655, 1 605, 1 570, 1 535, 1 515, 1 495, and 1 460 cm^{-1}; δ_H 7.00—7.66 (9 H, m, ArH), 6.30 (1 H, s), and 2.33 (3 H, s, CH_3).

4-(p-*Chlorophenyl*)-5-*cyano*-6-*phenylpyridin*-2(1H)-*one* (**8c**). Reaction time 20 days, yield 74%, m.p. 276—277 °C (from methanol); (Found: C, 69.9; H, 3.3; N, 9.0; Cl, 11.3. $C_{18}H_{11}ClN_2O$ requires C, 70.47; H, 3.59; N, 9.14; Cl, 11.58%); $\nu_{max.}$ 3 200—2 500, 2 225, 1 665, 1 600, 1 560, 1 530, 1 495, and 1 470 cm^{-1}; δ_H 7.40—7.90 (9 H, m, ArH) and 6.50 (1 H, s).

5-*Cyano*-4-(p-*nitrophenyl*)-6-*phenylpyridin*-2(1H)-*one* (**8**). Reaction time 20 days, yield 57%, m.p. 320—321 °C (from methanol) (Found: C, 68.2; H, 3.7; N, 13.0. $C_{18}H_{11}N_3O_3$ requires C, 68.14; H, 3.47; N, 13.25%); $\nu_{max.}$ 2 500—3 200, 2 220, 1 665, 1 610, 1 600, 1 590, 1 570, 1 520, 1 495, and 1 470 cm^{-1}; δ_H 7.40—8.60 (9 H, m, ArH) and 6.60 (1 H, s).

Transformation of 3,5-*Dicyano*-4,6-*Dicyano*-4,6-*diphenylpyridin*-2(1H)-*one* (**11a**) *into* 5-*Cyano*-4,6-*diphenylpyridin*-2(1H)-*one* (**8a**).—Compound (**11a**) (0.15 mmol) was dissolved in a mixture of ethylene glycol (5 ml) and concentrated hydrochloric acid (10 ml) and the reaction mixture was refluxed for 60 days. T.l.c. showed clearly the transformation of (**11a**) into the 3-carbamoyl derivative (**7a**) and then into the title compound (**8a**). The solution was poured into crushed ice, and the product was filtered off and recrystallized. Yield 61%.

4,6-*Diaryl*-3-*cyano*-5-*ethoxycarbonyl*-6-*hydroxypiperidin*-2-*ones* (**12**). *General Procedure.*—To a suspension of the appropriate ethyl α-benzoylcinnamate (**4**) (14 mmol) in dry methanol (*ca.* 40 ml) was added a solution of 2-cyanoacetamide (**2**) (14 mmol) in the minimal amount of methanol, together with a few drops of piperidine. The reaction mixture was stirred at room temperature for 2—3 days and the solid which precipitated was then collected by filtration and washed with a small amount of methanol. The resulting compounds were purified by dissolution in methanol at room temperature, followed by cooling the solution at −25 °C, because compounds (**12**) decompose at reflux temperature.

3-*Cyano*-5-*ethoxycarbonyl*-6-*hydroxy*-4,6-*diphenylpiperidin*-2-*one* (**12a**). 50% yield, m.p. 106—108 °C (Found: C, 69.45; H, 5.6; N, 7.3. $C_{21}H_{20}N_2O_4$ requires C, 69.23; H, 5.49; N, 7.69%); 3 650, 3 400, 3 300, 2 250, 1 725, 1 670, 1 595, 1 475, and 1 450 cm^{-1}; δ_H 8.76 (1 H, s, NH), 7.00—7.80 (10 H, m, ArH), 6.60 (1 H, s, OH), 3.00—4.60 (5 H, m, CH_2 and ring Hs), and 0.50 (3 H, t, CH_3).

3-*Cyano*-5-*ethoxycarbonyl*-6-*hydroxy*-6-*phenyl*-4-(p-*tolyl*)-*piperidin*-2-*one* (**12b**). 39% yield, m.p. 108—109 °C (Found: C, 69.3; H, 5.55; N, 7.5. $C_{22}H_{22}N_2O_4$ requires C, 69.84; H, 5.82; N, 7.41%); $\nu_{max.}$ 3 655, 3 400, 3 290, 3 100, 2 250, 1 725, 1 675, 1 590, and 1 515 cm^{-1}; δ_H 8.60 (1 H, s, NH), 6.70—7.50 (9 H, m, ArH), 6.50 (1 H, s, OH), 3.10—4.50 (5 H, m CH_2 and ring Hs), 2.16 (3 H, s, CH_3), and 0.50 (3 H, t, CH_3).

4-(p-*Chlorophenyl*-3-*cyano*-5-*ethoxycarbonyl*-6-*hydroxy*-6-*phenylpiperidin*-2-*one* (**12c**). 31% yield, m.p. 107—108 °C (Found: C, 62.9; H, 4.9; N, 6.85; Cl, 9.2. $C_{21}H_{19}ClN_2O_4$ requires C, 63.23; H, 4.76; N, 7.02; Cl, 8.91%); $\nu_{max.}$ 3 660, 3 400, 3 310, 3 180, 2 250, 1 720, 1 675, 1 595, 1 495, and 1 475 cm^{-1}; δ_H 8.80 (1 H, s, NH), 7.00—7.60 (9 H, m, ArH), 6.70 (1 H, s, OH), 3.20—4.60 (5 H, m, CH_2 and ring Hs), and 0.53 (3 H, t, CH_3).

4,6-*Diaryl*-3-*cyano*-5-*ethoxycarbonyl*-3,4-*dihydropyridin*-2(1H)-*ones* (**13**). *General Procedure.*—A suspension of the appropriate compound (**12**) (2 mmol) in 75% sulphuric acid (*ca.* 10 ml) was stirred at room temperature for 30 min. The reaction mixture was then poured into ice–water and the resulting precipitate was washed with water and recrystallized from aqueous ethanol.

3-*Cyano*-5-*ethoxycarbonyl*-4,6-*diphenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**13a**). 89% yield, m.p. 150—151 °C (lit.,[5] 151—153 °C).

3-*Cyano*-5-*ethoxycarbonyl*-6-*phenyl*-4-(p-*tolyl*)-3,4-*dihydropyridin*-2(1H)-*one* (**13b**). 82% yield, m.p. 180—181 °C (lit.,[5] 179—181 °C).

4-(p-*Chlorophenyl*)-3-*cyano*-5-*ethoxycarbonyl*-6-*phenyl*-3,4-*dihydropyridin*-2(1H)-*one* (**13c**). 65% yield, m.p. 163—164 °C (lit.,[5] 164—165 °C).

4,6-*Diaryl*-3-*cyano*-5-*ethoxycarbonylpyridin*-2(1H)-*ones* (**14**). *General Procedure.*—*Method* (*a*). The appropriate 4,6-diaryl-3-cyano-5-ethoxycarbonyl-6-hydroxypyridin-2(1*H*)-one (**13**) (2 mmol) was dissolved in the minimal amount of pyridine. The solution was cooled to −10 °C and thionyl chloride (20 ml) was added dropwise to the magnetically stirred solution. The mixture was kept for a further 30 min and was then poured into crushed ice. The resulting precipitate was collected by filtration and purified by recrystallization in ethanol.

Method (*b*). To a magnetically stirred suspension (0.14 mmol) of the corresponding 4,6-diaryl-3-cyano-5-ethoxycarbonyl-3,4-dihydropyridin-2(1*H*)-one (**13**) in acetic acid (0.4 ml) was added a solution of nitrosylsulphuric acid [prepared from sodium nitrite (0.2 mmol), sulphuric acid (2 ml), and water (0.6 ml)] dropwise. After 15 min the reaction mixture was poured into ice–water. The precipitate was filtered off, washed with water, and recrystallized.

3-*Cyano*-5-*ethoxycarbonyl*-4,6-*diphenylpyridin*-2(1H)-*one* (**14a**). 78% yield by method (a) and 80% yield by method (b), m.p. 261—262 °C (lit.,[5] 256—257 °C).

3-*Cyano*-5-*ethoxycarbonyl*-6-*phenyl*-4-(p-*tolyl*)*pyridin*-2(1H)-*one* (**14b**). 94% yield by method (a), m.p. 295—296 °C (lit.,[5] 300 °C).

4-(p-*Chlorophenyl*)-3-*cyano*-5-*ethoxycarbonyl*-6-*phenylpyridin*-2(1H)-*one* (**14c**). 78% yield by method (a), m.p. 282—284 °C (Found: C, 66.4; H, 4.1; N, 7.8; Cl, 9.3. $C_{21}H_{15}ClN_2O_3$ requires C, 66.52; H, 3.94; N, 7.47; Cl, 9.45%); $\nu_{max.}$ 3 450, 3 400—2 700, 2 220, 1 700, 1 640, 1 600, 1 590, and 1 490 cm^{-1}; δ_H 7.20—8.10 (9 H, m, ArH), 3.60 (2 H, q, CH_2), and 0.63 (3 H, t, CH_3).

3-*Cyano*-5-*ethoxycarbonyl*-4-(p-*nitrophenyl*)-6-*phenylpyridin*-2(1H)-*one* (**14e**). 94% yield by method (a), m.p. 270—271 °C (lit.,[5] 270—271 °C).

5-*Cyano*-6-*oxo*-2,4-*diphenyl*-3,4,5,6-*tetrahydropyridine*-3-*carboxylic Acid* (**15a**).—3-Cyano-5-ethoxycarbonyl-6-hydroxy-4,6-diphenylpiperidin-2-one (**12a**) (3 mmol) was suspended in 98% sulphuric acid (10 ml) and the reaction mixture was stirred at room temperature for 5 h. The resulting solution was poured into ice–water and the solid which precipitated was filtered off and washed with cold water. The mother liquors were extracted with chloroform, and the extract was dried (Na_2SO_4) and evaporated. The residue was added to the first crop of solid, and the whole was recrystallized from ethanol. Yield 82%, m.p. 262—264 °C.

The title compound was also obtained by similar treatment of 3-cyano-5-ethoxycarbonyl-4,6-diphenyl-3,4-dihydropyridin-

2(1*H*)-one (**13a**), yield 70% (Found: C, 71.6; H, 4.65; N, 8.8. $C_{19}H_{14}N_2O_3$ requires C, 71.50; H, 4.40; N, 8.80%); $\nu_{max.}$ 3 300—2 550, 1 700, 1 675, 1 625, 1 595, 1 510, and 1 450 cm^{-1}; δ_H 11.2 (1 H, s, NH), 7.1—7.6 (10 H, m, ArH), 4.2 (1 H, d), and 3.5 (1 H, d); *m/z* (rel. int. 318 (M^+, 4%), 276 (6), 275 (35), 274 (100), 273 (7), 272 (6), 257 (5), and 256 (19).

Attempted Reaction of Ethyl α-Benzoylcinnamate (**4a**) *with Malonamide* (1).—To a suspension of ethyl α-benzoylcinnamate (**4a**) (3.6 mmol) in dry ethanol (10 ml) was added a suspension of malonamide (1) (3.6 mmol) in dry methanol (5 ml), together with a few drops of piperidine. The reaction mixture was stirred at room temperature for a long time without any progress. The starting materials were also recovered when the reaction was performed at room temperature or with sodium ethoxide as the basic catalyst. If a molar amount of sodium ethoxide was used, or the reaction was performed without any solvent at 200 °C, only an intractable complex mixture was obtained.

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