A Convenient Preparation of [1,2,4]Triazolo[1,5-*a*]pyridines from Acetohydrazide Derivatives. Synthetic and Mechanistic Aspects

Maria J. Callejo, Pilar Lafuente, Nazario Martín-León, Margarita Quinteiro, Carlos Seoane,* and José L. Soto
Departamento de Química Orgánica, Facultad de Química, Universidad Complutense, 28040-Madrid, Spain

A novel synthesis of triazolo[1,5-*a*]pyridines (**4**) from 2′-acetyl-2-cyanoacetohydrazide (**2**) and arylidenemalononitriles (**3**) is described. The synthesis can be carried out either in one step or *via* 1-acetamidopyridones (**5**). Alternatively, acetylation of 1-aminopyridones (**7**) also gives triazolo[1,5-*a*]pyridines (**4**). Reaction of (**2**) with (**3**) in the presence of piperidine leads to the piperidinium salt of the triazolo[1,5-*a*]pyridine (**6**), which can be neutralized to give (**4**).

We have recently reported the synthesis of *N*-aminopyridones from acetohydrazide derivatives.[1] We now report that 2′-acetyl-2-cyanoacetohydrazide (**2**) can be successfully used to synthesize complex [1,2,4]triazolo[1,5-*a*]pyridones in one or two steps, depending upon the reaction conditions.

Triazolo[1,5-*a*]pyridine systems are reported to be useful compounds as pharmaceuticals,[2] fluorescent brighteners,[3] and complexing agents.[4] They are, however, not easy to obtain. Their synthesis usually involves several steps, and either the pyridine ring[5-10] or the triazole ring[11] can be constructed first. Triazolo[1,5-*a*]pyridines have also been prepared by ring transformation of triazolo[4,3-*a*]pyridines[12] and from 2-thioxopyrones.[13]

In contrast, the synthesis described here allows the direct synthesis of the bicyclic system from acyclic reactants: 2′-acetyl-2-cyanoacetohydrazide (**2**), generated by careful acetylation of 2-cyanoacetohydrazide (**1**), and arylidenemalononitriles (**3**) (Scheme 1). The reaction is performed in refluxing ethanol and the products are easily isolated.

Formation of (**4**) can be rationalized as depicted in Scheme 2. Michael addition of the acidic methylene group in (**2**) to the unsaturated nitrile (**3**) forms an open-chain intermediate, which cyclizes and aromatizes to give the 1-acetamido-2-pyridone (**5**). The presence in (**5**) of adjacent amino and acetamido groups results in the attack by the amino group on the amide group. This intermediate (**5**) undergoes nucleophilic addition at the amide carbonyl group, rather than nucleophilic acyl substitution. Dehydration then leads to the triazolo-[1,5-*a*]pyridine (**4**), for which several tautomeric forms are possible.

In agreement with this interpretation, triazolo[1,5-*a*]pyridines (**4**) can also be obtained in two steps. Reaction of the acetohydrazide (**2**) with arylidenemalononitrile (**3**) at lower temperatures and for shorter times affords 1-acetamido-2-pyridones (**5**) (Scheme 1). When the pyridones (**5**) are heated in ethanol, they cyclize to give the fused system (**4**). The reaction is rather general and works for a number of aryl groups (Scheme 1), but fails with strongly electron-donating or electron-withdrawing groups on the benzene ring. Thus, *p*-dimethylaminobenzylidenemalononitrile (**3f**) fails to react with (**2**), owing to the increased electron density on the olefinic carbon atom undergoing Michael attack. *p*-Nitrobenzylidenemalononitrile (**3e**) reacts with (**2**), but gives only a complex mixture of decomposition products.

Both the direct and the two-step route affords the completely unsaturated triazolo[1,5-*a*]pyridines (**4**) *via* the aromatized 1-acetamidopyridone (**5**). However, the earlier intermediate, the dihydropyridone (**9a**), instead of (**5a**), could be isolated for the parent compound (**4a**) (Scheme 3). Cyclization of this intermediate gives the triazolo[1,5-*a*]pyridine (**4a**) directly.

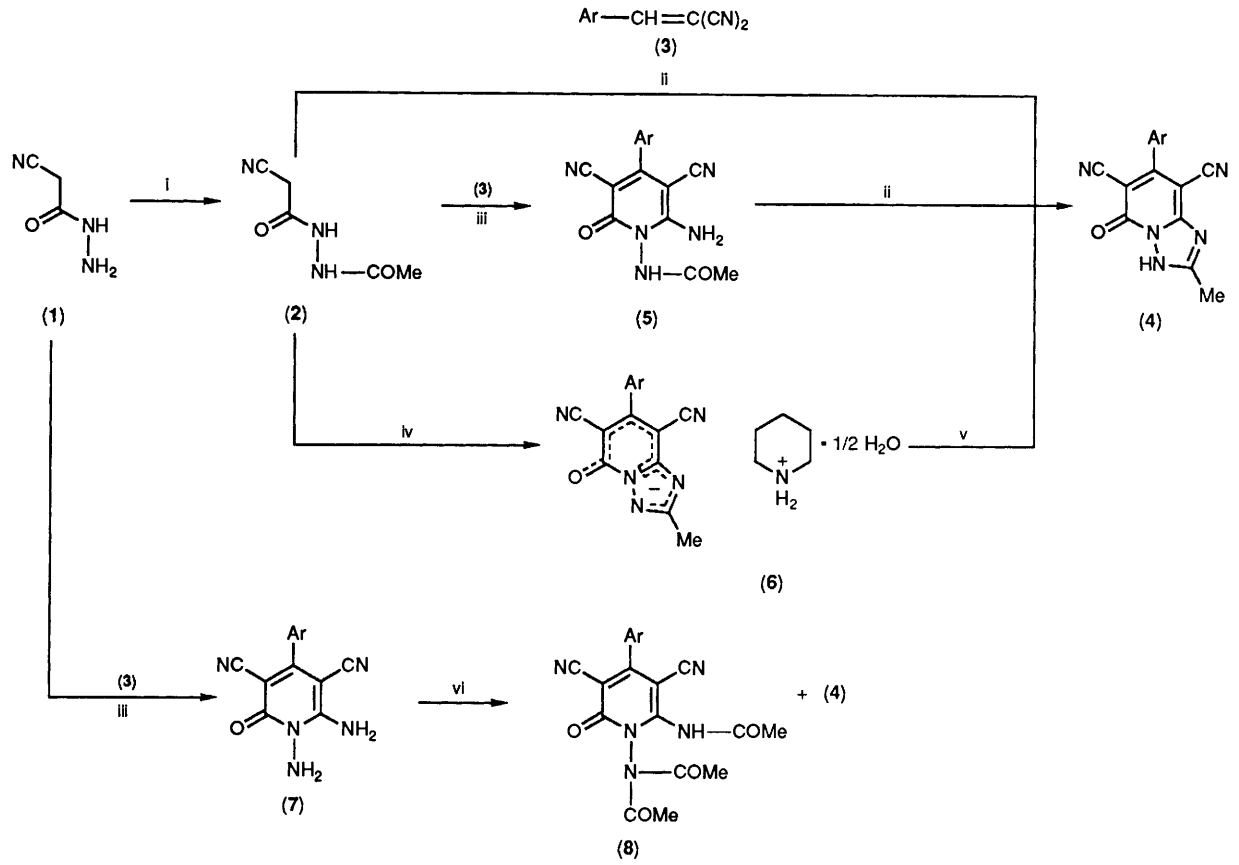
In an attempt to accelerate the synthesis of (**4**) from (**2**) and (**3**) using piperidine as basic catalyst, an unexpected compound was obtained (Scheme 1): the piperidinium salt (**6**) the crystal structure of which, to be published elsewhere,[14] is unusual. The positive charge on the piperidinium cation is balanced by the negative charge on the heterocyclic system, which exists as a stable anion owing to its high acidity, resulting from charge delocalization involving two triazole nitrogens. The pyridone oxygen extends delocalization to the six-membered ring. Treating the salt (**6**) with acid resulted in the neutralization of this heterocyclic anion and the formation of the triazolo-[1,5-*a*]pyridine (**4**).

The triazolo[1,5-*a*]pyridines (**4**) could also be synthesized by an alternative route, involving acetylation of *N*-aminopyridones. Reaction of benzylidenemalononitriles (**3**) with 2-cyanoacetohydrazide (**1**) gives 1,6-diamino-2-pyridones (**7**). Treatment of (**7**) with acetic anhydride led, in a one-step process, to the bicyclic system (**4**), *via* an initial acetylation at the more basic *N*-amino group, followed by cyclization to give the five-membered ring. However, acetylation at the enamino group is also possible, as proved by the isolation of the triacetyl derivative (**8**) as a by-product.

Experimental

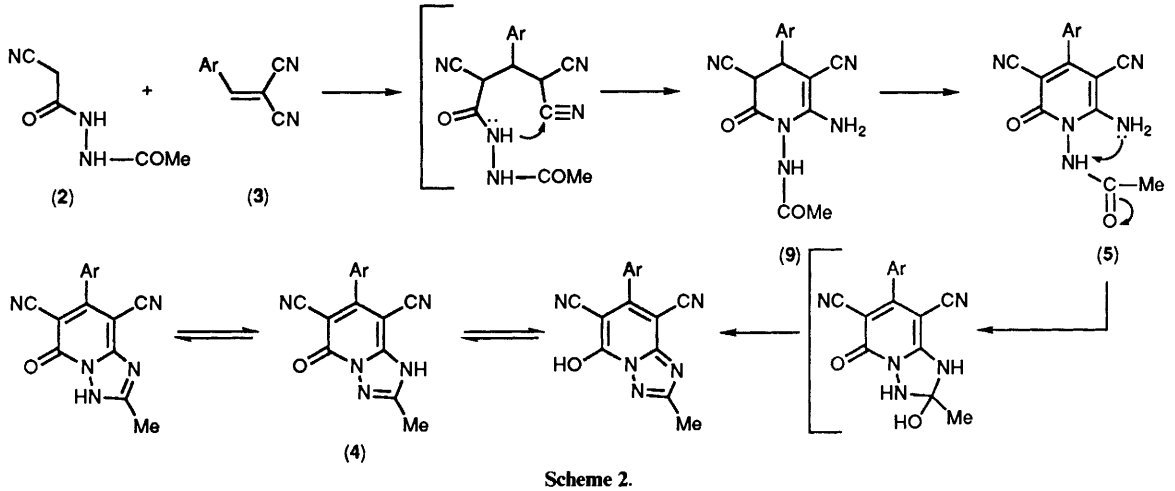
M.p.s were determined in capillary tubes in a Gallenkamp apparatus and are uncorrected. ^{1}H NMR spectra were recorded at 60, 300, and 400 MHz, on a Varian T-60A, a Varian VXR 300S, and a Bruker WM 400 spectrometer. ^{13}C NMR spectra were recorded on the last two spectrometers. All NMR spectra were recorded for $(CD_3)_2SO$ solutions, chemical shifts being given as δ values with respect to $SiMe_4$ as the internal standard. IR spectra were measured with a Perkin-Elmer 781 instrument for KBr pellets. Mass spectra were obtained with a Varian MAT 711 machine. Microanalyses were performed by C.S.I.C. of Madrid and Barcelona. The reactions and the purity of compounds were monitored by TLC performed on silica gel plates (Merck 60-F) and using chloroform–ethanol or methanol as the eluant.

Cyanoacetohydrazide, malononitrile, and piperidine were obtained from commercial sources (Aldrich and Merck) and were used without further purification. Aromatic aldehydes were distilled before use. Benzylidenemalononitrile was also a commercial product, but the remaining arylidenemalononitriles were prepared from aromatic aldehydes and malononitrile as described.[15]

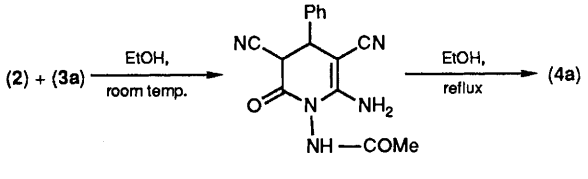


a; Ar = Ph
b; Ar = p-MeC_6H_4
c; Ar = p-$MeOC_6H_4$
d; Ar = p-ClC_6H_4
e; Ar = p-$Me_2(NC_6H_4)$
f; Ar = p-$O_2(NC_6H_4)$

Scheme 1. *Reagents:* i, Ac_2O, 60 °C; ii, EtOH, reflux; iii, EtOH, room temp.; iv, EtOH, piperidine, reflux; v, CF_3CO_2H, Me_2SO; vi, Ac_2O, reflux.



Scheme 2.



Scheme 3.

2'-Acetyl-2-cyanoacetohydrazide (**2**).—A suspension of 2-cyanoacetohydrazide (**1**) (2.0 g, 20 mmol) in acetic anhydride (50 ml) was kept at 60–70 °C for 10 h, and then set aside overnight. The white precipitate was then filtered off and washed well with water to give the hydrazide (**2**) (1.2 g, 40% yield), m.p. 176–178 °C (from ethyl acetate) (Found: C, 42.7; H, 5.1; N, 29.8. $C_5H_7N_3O_2$ requires C, 42.55; H, 5.0; N, 29.8%); ν_{max} 3 270 (NH), 3 200 (NH), 2 250 (CN), and 1 620 (CO) cm^{-1}; δ_H 1.83 (3 H, s, CH_3), 3.67 (2 H, s, CH_2), 9.77 (1 H, br s, NH), and

9.97 (1 H, br s, NH); δ_C 20.5 (CH_3), 23.9 (CH_2), 115.8 (CN), 161.5 (CO), and 168.3 (CO); *m/z* (relative intensity) 141 (M^+, 9), 102 (4), 101 (17), 100 (12), 99 (51), and 70 (7).

7-Aryl-2-methyl-5-oxo-3,5-dihydro-[1,2,4]triazolo[1,5-a]pyridine-6,8-dicarbonitriles (**4**). General Procedure.—2′-Acetyl-2-cyanoacetohydrazide (**2**) (20 mmol) and the appropriate arylidenemalononitrile (**3**) (20 mmol) were suspended in dry ethanol (*ca.* 25 ml). The mixture was heated at reflux temperature for 100–300 h. During the reaction, TLC showed that (**5**) was formed first as an intermediate; some compound (**5**) was precipitated, but redissolved. Refluxing was continued until TLC showed the absence of (**3**) or (**5**). The solution was then concentrated *in vacuo* to about half bulk, and set aside either at room temperature or in a refrigerator. The precipitate was filtered off, the mother liquors were evaporated to dryness, and ethyl acetate was added to the resulting oil. A second crop of crystalline solid was thus obtained. The combined solids were dissolved in dimethyl sulphoxide (*ca.* 30 ml) and a few drops of trifluoroacetic acid added. The solution was then poured into cold water (*ca.* 40 ml). Compounds (**4**) precipitated and were then isolated by filtration under reduced pressure. Alternatively, the initial reaction mixture can be evaporated to dryness, trifluoroacetic acid added to the oil, and the solution poured into cold water. This procedure, however, afforded a crude product which was much more difficult to purify.

2-Methyl-5-oxo-7-phenyl-3,5-dihydro-[1,2,4]triazolo[1,5a]-pyridine-6,8-dicarbonitrile (**4a**) was obtained in 25% yield by the general procedure just described, m.p. > 300 °C (decomp.) (from acetonitrile) (Found: C, 65.8; H, 3.3; N, 25.7. $C_{15}H_9N_5O$ requires C, 65.45; H, 3.3; N, 25.45%); ν_{max} 3 120, 2 220, 1 690, 1 650, 1 590, 1 510, 1 490, 1 450, 1 440, 1 420, 1 410, 1 385, 1 360, 1 300, 1 290, 1 280, 1 260, 1 230, 1 200, 1 160, and 1 050 cm^{-1}; δ_H 2.50 (3 H, s, CH_3), 7.50 (5 H, s, ArH), and 9.85 (1 H, s, NH); *m/z* (relative intensity) 275 (M^+, 34), 274 (15), 150 (4), 127 (7), 105 (7), and 71 (27).

2-Methyl-5-oxo-7-p-tolyl-3,5-dihydro-[1,2,4]triazolo[1,5-a]-pyridine-6,8-dicarbonitrile (**4b**) was obtained in 20% yield, m.p. > 300 °C (from acetonitrile) (Found: C, 66.15; H, 3.75; N, 24.3. $C_{16}H_{11}N_5O$ requires C, 66.4; H, 3.8; N, 24.2%); ν_{max} 3 100, 2 230, 1 700, 1 660, 1 610, 1 520, 1 420, 1 390, 1 330, 1 280, 1 240, 1 220, 1 190, 1 180, 1 120, and 1 050 cm^{-1}; δ_H (300 MHz) 2.41 (3 H, s, CH_3), 2.46 (3 H, s, CH_3), 6.05 (1 H, s, NH), and 7.36–7.44 (4 H, m, ArH); δ_C 12.5 (CH_3-Het.), 21.1 (CH_3-C_6H_4), 74.5 (8-C), 86.7 (6-C), 115.7, 117.3 (2 × CN), 128.2, 128.5 (2′-C, 3′-C), 132.5, 139.9 (1′-C, 4′-C), 149.8, 154.8, 156.7, and 156.9 (7-C, 8a-C, 2-C, 5-C) (prime denotes phenyl ring).

7-(p-Methoxyphenyl)-2-methyl-5-oxo-3,5-dihydro-[1,2,4]triazolo[1,5-a]pyridine-6,8-dicarbonitrile (**4c**) was obtained in 26% yield, m.p. > 300 °C (decomp.) (from acetonitrile) (Found: C, 62.85; H, 3.55; N, 22.75. $C_{16}H_{11}N_5O_2$ requires C, 63.0; H, 3.6; N, 23.0%); ν_{max} 3 450, 3 000, 2 200, 1 700, 1 610, 1 580, 1 505, 1 470, 1 450, 1 430, 1 410, 1 390, 1 340, 1 320, 1 300, 1 270, 1 210, 1 190, 1 180, 1 170, 1 130, 1 080, and 1 050 cm^{-1}; δ_H 2.4 (3 H, s, CH_3), 3.73 (3 H, s, CH_3O), 6.83–7.43 (4 H, m, ArH), and 7.7 (1 H, s, NH).

7-(p-Chlorophenyl)-2-methyl-5-oxo-3,5-dihydro-[1,2,4]triazolo[1,5-a]pyridine-6,8-dicarbonitrile (**4d**) was obtained in 36% yield, m.p. > 300 °C (decomp.) (from acetonitrile) (Found: C, 58.0; H, 2.4; Cl, 11.55; N, 22.7. $C_{15}H_8ClN_5O$ requires C, 58.2; H, 2.6; Cl, 11.5; N, 22.6%); ν_{max} 3 100, 2 240, 1 665, 1 600, 1 520, 1 510, 1 400, 1 340, 1 280, 1 240, 1 230, 1 190, 1 100, and 1 060 cm^{-1}; δ_H 2.4 (3 H, s, CH_3), 7.3 (4 H, s, ArH), and 9.7 (1 H, s, NH).

1-Acetamido-6-amino-4-aryl-2-oxo-1,2-dihydropyridine-3,5-dicarbonitriles (**5**). *General Procedure.*—2′-Acetyl-2-cyanoacetohydrazide (**2**) (7 mmol) and the appropriate arylidenemalononitrile (**3**) (7 mmol) were suspended in *ca.* 10 ml of dry ethanol. The mixture was stirred at 50 °C for 3–20 h until the starting materials had reacted completely (TLC). The mixture was set aside, and the precipitate that separated during the reaction filtered off. From the concentrated mother liquors, a second crop was recovered. The combined solids were recrystallized from the appropriate solvent.

1-Acetamido-6-amino-2-oxo-4-p-tolyl-1,2-dihydropyridine-3,5-dicarbonitrile (**5b**) was obtained in 22% yield by the foregoing general procedure; m.p. > 300 °C (decomp.) (from ethanol) (Found: C, 62.4; H, 4.0; N, 22.5. $C_{16}H_{13}N_5O_2$ requires C, 62.5; H, 4.2; N, 22.8%); ν_{max} 3 260, 3 180, 2 200, 1 720, 1 630, 1 570, 1 530, 1 490, 1 450, 1 365, 1 295, 1 185, 1 115, and 1 020 cm^{-1}; δ_H 2.0 (3 H, s, CH_3CO), 2.3 (3 H, s, CH_3Ph), 7.2 (4 H, br s, ArH), 8.5 (2 H, br s, NH_2), and 10.5 (1 H, br, NH).

1-Acetamido-6-amino-4-(p-methoxyphenyl)-2-oxo(1,2-dihydropyridine-3,5-dicarbonitrile (**5c**) was obtained in 26% yield, m.p. > 300 °C (decomp.) (from ethanol) (Found: C, 59.35; H, 4.2; N, 21.55. $C_{16}H_{13}N_5O_3$ requires C, 59.4; H, 4.0; N, 21.7%); ν_{max} 3 280, 3 200, 2 930, 2 220, 1 725, 1 660, 1 630, 1 610, 1 580, 1 530, 1 515, 1 450, 1 410, 1 370, 1 300, 1 260, and 1 180 cm^{-1}; δ_H 2.1 (3 H, s, CH_3CO), 3.8 (3 H, s, CH_3O), 6.9–7.5 (4 H, m, ArH), 8.6 (2 H, s, NH_2), and 10.7 (1 H, s, NH); δ_C 21.0 (CH_3), 55.4 (CH_3O), 74.2 (5-C), 86.8 (3-C), 114.1 (3′-C), 115.5, 116.2 (2 × CN), 126.4, 129.9 (1′-C, 2′-C), 157.4, 157.7, 160.9, 161.1 (4-C, 4′-C, 6-C, 2-C), and 169.9 ($COCH_3$).[16]

1-Acetamido-6-amino-4-(p-chlorophenyl)-2-oxo-1,2-dihydropyridine-3,5-dicarbonitrile (**5d**) was obtained in 29% yield, m.p. > 300 °C (decomp.) (from ethanol) (Found: C, 54.8; H, 3.15; Cl, 10.85; N, 21.2. $C_{15}H_{10}ClN_5O_2$ requires C, 55.0; H, 3.05; Cl, 10.8; N, 21.4%); ν_{max} 3 290, 3 190, 2 220, 1 720, 1 660, 1 635, 1 595, 1 570, 1 535, 1 490, 1 450, 1 390, 1 370, 1 300, 1 230, 1 100, and 1 020 cm^{-1}; δ_H 2.0 (3 H, s, CH_3), 7.4 (4 H, s, ArH), 8.5 (2 H, s, NH_2), and 10.4 (1 H, s, NH).

Cyclization of the Pyridone (**5d**).—A suspension of the pyridone (**5d**) in *ca.* 25 ml of dry ethanol was heated under reflux for 230 h, then evaporated *in vacuo* to half bulk. The solid obtained was dissolved in dimethyl sulphoxide (*ca.* 2 ml) and a few drops of trifluoroacetic acid were added. Compound (**4d**) was obtained in 39% yield on pouring the solution into *ca.* 4 ml of cold water.

1-Acetamido-6-amino-2-oxo-4-phenyl-2,3,4,5-tetrahydropyridine-3,5-dicarbonitrile (**9a**).—2′-Acetyl-2-cyanoacetohydrazide (**2**) (0.50 g, 3.6 mmol) and benzylidenemalononitrile (**3a**) (0.55 g, 3.6 mmol) were suspended in *ca.* 10 ml of dry ethanol. The mixture was kept either at room temperature for 100 h or at 50–60 °C for 16 h, until TLC showed the absence of starting material. The precipitate that separated was filtered off (0.30 g), and the concentrated mother liquors afforded a second crop (0.20 g). The combined solid was recrystallized from acetonitrile to give the *pyridone* (**9a**) in 47% yield, m.p. 230–232 °C (Found: C, 61.0; H, 4.25; N, 23.4. $C_{15}H_{13}N_5O_2$ requires C, 61.0; H, 4.4; N, 23.7%); ν_{max} 3 420, 3 300, 3 210, 3 000, 2 260, 2 200, 1 735, 1 695, 1 645, 1 590, 1 510, 1 490, 1 450, 1 420, 1 360, 1 340, 1 300, and 1 240 cm^{-1}; δ_H 1.95 (3 H, s, CH_3), 3.83–5.20 (2 H, m, 2 × CH), 6.7–7.3 (5 H, m, ArH), 8.44 (1 H, br, NH), and 10.14 (2 H, br, NH_2); *m/z* (relative intensity) 295 (M^+, 44), 277 (22), 253 (28), 252 (17), 210 (22), 209 (61), 204 (17), 201 (17), 200 (33), 199 (44), 198 (22), 186 (28), 185 (72), 169 (28), 156 (78), 138 (22), and 95 (22).

Transformation of the Pyridone (**9a**) *into the Triazolopyridine* (**4a**).—A solution of compound (**9a**) (9 mmol) in dry ethanol (25 ml) was heated under reflux for 350 h, then evaporated *in vacuo* to half bulk. The precipitate was filtered off and then dissolved in *ca.* 30 ml of dimethyl sulphoxide; a few drops of

trifluoroacetic acid were added. Compound (**4a**) was obtained in 50% yield on pouring the solution into *ca.* 40 ml of cold water.

Piperidinium 6,8-*Dicyano*-2-*methyl*-6-*oxo*-7-*phenyl*-[1,2,4]-*triazolo*[1,5-a]*pyridinide Hemihydrate* (**6a**).—2′-Acetyl-2-cyanoacetohydrazide (**2**) (0.5 g, 4 mmol) and α-cyanocinnamonitrile (**3a**) (0.54 g, 4 mmol) were suspended in *ca.* 8 ml of ethanol containing a few drops of piperidine. The mixture was refluxed for 9 h, until TLC showed the absence of starting materials. The precipitate was filtered off to give compound (**6a**) (0.38 g, 37% yield), m.p. 143–145 °C (decomp.) (from ethanol).[14]

Neutralization of Piperidinium 6,8-*Dicyano*-2-*methyl*-5-*oxo*-7-*phenyl*-[1,2,4]*triazolo*[1,5-a]*pyridinide Hemihydrate* (**6a**).—To a solution of the salt (**6a**) (0.15 g, 0.6 mmol) in dimethyl sulphoxide (1.5 ml) a few drops of trifluoroacetic acid were added. The solution was then poured into cold water (*ca.* 1.5 ml). The precipitate was filtered off and washed with water until the pH of the water was neutral. The solid isolated (0.05 g, 30% yield) was identified as the triazolo[1,5-*a*]pyridine (**4a**) by comparison with an authentic sample.

1,6-*Diamino*-4-*aryl*-2-*oxo*-1,2-*dihydropyridine*-3,5-*dicarbonitriles* (**7**).—Compounds (**7**) were prepared by the reaction of 2-cyanoacetohydrazide (**1**) with the arylidenemalononitriles (**3**) according to the previously reported procedure.[17]

Reaction of the Pyridones (**7**) *with Acetic Anhydride. General Procedure.*—A suspension of the appropriate pyridone (**7**) (2 mmol) in freshly distilled acetic anhydride (*ca.* 6 ml), was heated under reflux for about 1 h, until TLC showed the absence of starting material. The precipitate was filtered off and washed with water until the pH of the water was neutral. This precipitate was shown by TLC to contain two compounds, (**4**) and (**8**), which were separated by fractional crystallization.

Reaction of the 4-*phenylpyridine* (**7a**) *with acetic anhydride.* Following the foregoing general procedure, compound (**4a**) was obtained from the second fraction in 7% yield. From the first fraction, 6-*acetamido*-1-*diacetylamino*-2-*oxo*-4-*phenyl*-1,2-*dihydropyridine*-3,5-*dicarbonitrile* (**8a**) was isolated in 29% yield, m.p. 280 °C (decomp.) (from acetonitrile) (Found: C, 60.25; H, 4.05; N, 18.4. $C_{19}H_{15}N_5O_4$ requires C, 60.5; H, 4.0; N, 18.6%); ν_{max} 3 000–2 600br, 2 220, 1 735, 1 725, 1 695, 1 665, 1 590, 1 570, 1 530, 1 500, 1 485, 1 440, 1 435, 1 425, 1 370, 1 305, 1 260, 1 230, 1 200, 1 170, and 1 025 cm^{-1}; δ_H 2.33 (9 H, br s, 3 × CH_3), 7.23 (5 H, br s, ArH), and 12.58 (1 H, br, NH).

Reaction of the 4-p-*tolylpyridone* (**7b**) *with acetic anhydride.* Compound (**4b**) was precipitated first in 18% yield. Upon concentration of the mother liquors, 6-*acetamido*-1-*diacetylamino*-2-*oxo*-4-p-*tolyl*-1,2-*dihydropyridine*-3,5-*dicarbonitrile* (**8b**) was precipitated in 23% yield, m.p. 275 °C (decomp.) (from acetonitrile) (Found: C, 61.5; H, 4.5; N, 18.05. $C_{20}H_{17}N_5O_4$ requires C, 61.4; H, 4.3; N, 17.9%); ν_{max} 3 200–2 600br, 2 230, 1 740, 1 700, 1 665, 1 570, 1 530, and 1 515 cm^{-1}; δ_H 2.35 (12 H, br s, 4 × CH_3), 7.1 (4 H, br s, ArH), and 11.72 (1 H, br, NH).

Reaction of the 4-p-*methoxyphenylpyridone* (**7c**) *with acetic anhydride.* Compound (**4c**) was isolated first in 18% yield. Upon concentration of the mother liquors, 6-*acetamido*-1-*diacetylamino*-4-(p-*methoxyphenyl*)-2-*oxo*-1,2-*dihydropyridine*-3,5-*dicarbonitrile* (**8c**) was precipitated in 6% yield, m.p. 278 °C (decomp.) (from acetonitrile) (Found: C, 58.85; H, 4.45; N, 17.5. $C_{20}H_{17}N_5O_5$ requires C, 59.0; H, 4.2; N, 17.2%); ν_{max} 3 000–2 600br, 2 240, 1 770, 1 740, 1 710, 1 680, 1 605, and 1 495 cm^{-1}; δ_H 2.37 (9 H, br s, 3 × CH_3), 3.73 (3 H, s, CH_3O), and 7.23–6.73 (4 H, m, ArH).

Acknowledgements

Support of this work by a grant from the Comisión Interministerial de Ciencia y Tecnología of Spain (PB 86-0570) is gratefully acknowledged.

References

1 C. Aparicio, N. Martín, M. Quinteiro, C. Seoane, J. L. Soto, J. A. Valdés, and S. Velázquez, *J. Chem. Soc., Perkin Trans. 1*, 1989, 1975, and references cited therein.
2 As immune adjuvants, stomach secretion inhibitors, antivirals, and antihypertensives: Kyorin Pharmaceutical Co., Fr. Pat., 2450259, 1980 (*Chem. Abstr.*, 1982, **97**, 72373z); K. Kubo, N. Itoh, I. Sohzu, Y. Isomura, and H. Honma, Jpn. Pat., 7905996, 1979 (*Chem. Abstr.*, 1979, **91**, 57007); F. Busseran, J. C. Chermann, E. De Clercq, and C. Hannoun, *Ann. Virol.*, 1983, **134E**, 127; L. Carey, M. Martin-Smith, B. J. Price, P. Blatcher, J. W. Clitherow, D. E. Bays, and J. Bradshaw, Eur. Pat. Appl., EP 48555, 1982 (*Chem. Abstr.*, 1982, **97**, 55814b).
3 B. G. Buell and R. S. Long, U.S. Pat., 3272831, 1966 (*Chem. Abstr.*, 1967, **66**, 19832g); K. Weber, Eur. Pat. Appl., EP 67792, 1982 (*Chem. Abstr.* 1983, **98**, 127689k).
4 S. B. Sanni, H. Behm, P. T. Beurkens, J. Cornelissen, J. P. Haasnoot, and A. T. Leustra, *J. Cryst. Spect. Res.*, 1987, **17**, 81.
5 P. Molina, A. Tárraga, and C. García, *Heterocycles* 1988, **27**, 733.
6 T. C. Phadke and D. W. Rangnekar, *Synthesis*, 1986, 860.
7 T. Irikura and S. Suzne, Ger. Pat., 2905823, 1980 (*Chem. Abstr.*, 1981, **94**, 121541).
8 K. Gewald, A. Schubert, and G. Martin, *J. Prakt. Chem.*, 1975, **317**, 561.
9 Y. I. Lin and S. A. Lang, *J. Org. Chem.*, 1981, **46**, 3123.
10 K. Suzne, Jpn. Pat., 7939094, 1979 (*Chem. Abstr.*, 1979, **91**, 91646).
11 V. A. Chuiguk and K. V. Fedotov, *Ukr. Khim. Zh.*, 1980, **46**, 1306 (*Chem. Abstr.*, 1981, **94**, 208680).
12 K. Potts and C. R. Surapeni, *J. Heterocycl. Chem.*, 1970, **7**, 1019.
13 P. Molina, M. Alajarin, and A. Soler, *An. Quím.*, 1980, **76C**, 207.
14 Details of X-ray diffraction analysis of this salt: N. Martín, M. Quinteiro, C. Seoane, J. L. Soto, I. Fonseca, F. Florencio, and J. Sanz, *J. Org. Chem.*, in press.
15 B. Corson and R. Stoughton, *J. Am. Chem. Soc.*, 1928, **50**, 2825; A. C. Cope and K. E. Hoyle, *ibid.*, 1941, **63**, 733.
16 Values in agreement with chemical shifts reported for *N*-aminopyridones: N. Martín, C. Seoane, and J. L. Soto, *Heterocycles*, 1985, **23**, 2013.
17 C. Seoane, J. L. Soto, P. Zamorano, and J. Cuadrado, *Synthesis*, 1981, 529.

Paper 9/04299G
Received 6th *October* 1989
Accepted 18th *December* 1989