Ring Transformation of Isoxazoles into Furan and Pyran Derivatives[1]

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A ring transformation of isoxazole into 3,5-dicyano-4*H*-pyran-2-amines (**4**) and *N*-arylidenefuran-2-amines (**7**) is reported. It involves a ring opening of the isoxazole ring in the presence of an aromatic aldehyde, leading to 2-arylidene-3-oxopropanenitrile (**2**), followed by nucleophilic attack by either cyanide or propanedinitrile and then heterocyclization. The reaction can also be applied to 5-substituted isoxazoles.

The facile cleavage of isoxazoles has been used to bring about their transformation into different kinds of heterocycles, such as isothiazoles,[2] pyridines,[3] pyrazoles,[4,5] oxazoles,[6] azirines,[7] triazoles,[8] and oxadiazoles.[8]

In addition, base-promoted ring opening of 5-substituted isoxazoles leads to β-keto nitriles[9] or their condensation products with an aldehyde.[10] In a recent paper, we studied this reaction from which we also isolated a 2,6-dimethyl-4*H*-pyran derivative.[11] We now report on the ring transformation of isoxazole derivatives into pyranamines and furanamines using the above reaction. This represents a useful ring transformation of heterocycles from easily available starting isoxazoles[12] into less easily accessible heterocyclic compounds.

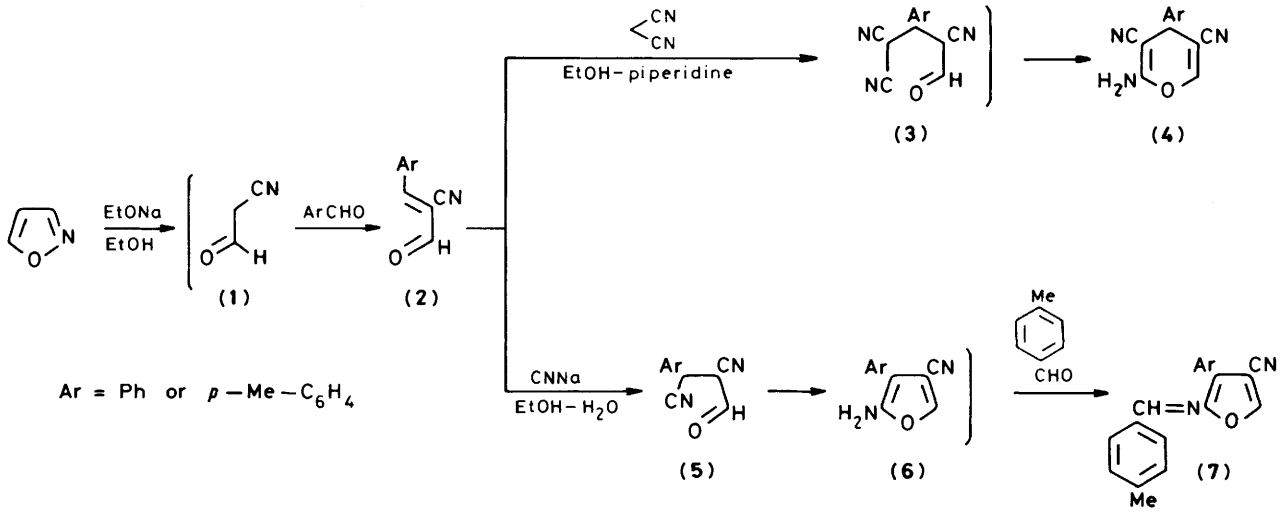
Results and Discussion

The ring transformation reported here involves a two-step process, starting with the ring cleavage of isoxazole upon treatment with a base. The resulting, unisolated, 3-oxopropanenitrile (**1**) reacts *in situ* with an aromatic aldehyde leading to the corresponding 2-arylidene-3-oxopropanenitrile (**2**). Reaction of (**2**) with propanedinitrile affords 3,5-dicyano-4*H*-pyran-2-amine (**4**) *via* a Michael addition and spontaneous cyclization. Compounds (**4**) are isolated as stable, crystalline solids (Scheme 1).

affords its Schiff base. *N*-Arylidenefuran-2-amine (**7**) is thus easily isolated as a crystalline solid. It should be noted that an alternative route to the Michael addition, involving nucleophilic attack of either malononitrile or cyanide at the aldehyde carbonyl group in (**2**), is not observed with malononitrile. In the second reaction, 1,2-addition is observed to some extent and a small amount of the cyanohydrin of (**2**) can be isolated after the reaction mixture is poured into dilute hydrochloric acid. However, the main reaction is always the conjugate addition, followed by heterocyclization, as depicted in Scheme 1.

This transformation of an isoxazole ring into furans and pyrans proved to be general and can be successfully applied to 5-substituted isoxazoles. Thus, the ring cleavage of 5-methyl-or 5-phenyl-isoxazole in the presence of an aromatic or aliphatic aldehyde in a basic medium yields a substituted 3-oxopropanenitrile (**8**) (Scheme 2). The reaction of (**8**) with potassium cyanide to give pyrrol-2(5*H*)-one (**9**), probably arises from photo-oxidation or hydrolysis of the unstable furan-2-amine, according to proposed interpretations of related reactions.[13–16] Reaction of (**8**) with cyanide and an aromatic aldehyde allows the isolation of the furanamine as its stable Schiff base (**10**). The behaviour of (**8**) towards propanedinitrile follows the expected course, leading to 6-substituted pyranamines (**11**).

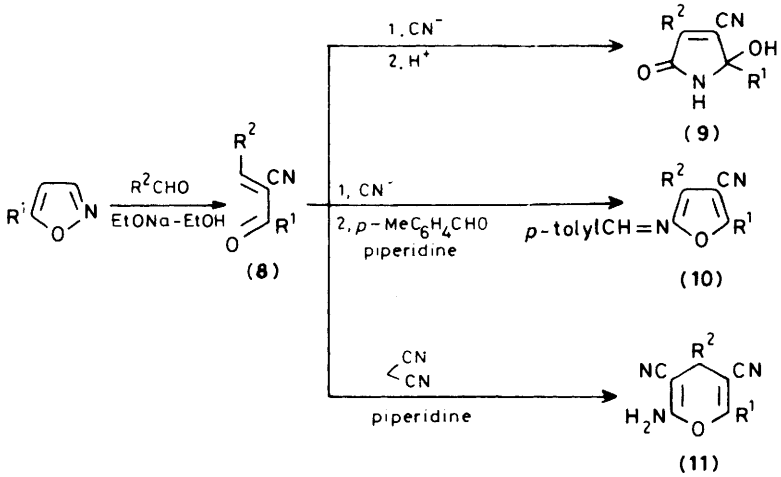
Other conjugate additions of cyanide or malononitrile to



Scheme 1.

Although substitution of cyanide for propanedinitrile should follow a similar course and afford a five-membered ring, the expected furan-2-amine (**6**) cannot be isolated as a stable compound; reaction *in situ* with an aromatic aldehyde however

enones have been reported in the literature, and different results have been described; the Michael addition, the Knoevenagel condensation, or both can take place.[17–19] In other cases, the adduct undergoes a homocyclization to a cyclohexane ring,[19]



(9)—(11): **a**, R^1 = Me, R^2 = Ph; **b**, R^1 = Me, R^2 = *p*-MeC_6H_4; **c**, R^1 = Me, R^2 = *p*-$MeOC_6H_4$; **d**, R^1 = Me, R^2 = Pr^i; **e**, R^1 = Me, R^2 = Bu^s; **f**, R^1 = Ph, R^2 = Pr^i; **g**, R^1 = Ph, R^2 = Bu^s; **h**, R^1 = Ph, R^2 = Et_2CH

Scheme 2.

or a heterocyclization.[20-22] The cyano group in the enone is important to the course of the cyclization. Thus, addition of malononitrile or cyanide to benzylideneacetophenone leads to the open-chain Michael adducts.[18,23]

As their most important spectral features, the n.m.r. spectra of the pyrans (**4**) and (**11a—c**) show a characteristic singlet due to the 4*H*-proton at *ca.* 4 p.p.m., and a doublet or broad peak at *ca.* 3 p.p.m. in (**11d—h**). The hydrogen at position 6 of compounds (**4**) appears as a singlet at *ca.* 7.6 p.p.m. The azomethine proton in furans (**7**) and (**9**) gives rise to a singlet at 8.5 p.p.m. The NH group of pyrroline (**9**) is observed as a broad singlet at 9.3 p.p.m., together with the hydroxy group at 6.6 p.p.m., which disappears on addition of TFA.

Experimental

Melting points were determined in capillary tubes in a Büchi apparatus and are uncorrected. The i.r. spectra were measured with a Perkin-Elmer 257 spectrophotometer in potassium bromide pellets. The ^1H n.m.r. spectra were obtained at 60 MHz with a Varian T-60A spectrometer and chemical shifts are given as δ values relative to TMS as internal standard. Analytical t.l.c. was performed on silica gel plates (Merck 60) using toluene–ethyl acetate as the eluant. Microanalyses were performed by the Centro Nacional de Quimica Orgânica de Madrid.

Isoxazole, 5-methylisoxazole and aromatic aldehydes were commercially available and were used without further purification. Aliphatic aldehydes were distilled just before use. Ether refers to diethyl ether.

4-Cyano-3-phenyl-N-(p-methylbenzylidene)furan-2-amine (**7a**).—A solution of isoxazole (0.1 mol) and benzaldehyde (0.1 mol) in absolute ethanol (40 ml) was added dropwise with stirring to a solution of sodium (0.1 mol) in absolute ethanol (100 ml). After cooling, the mixture was acidified with 50% aqueous sulphuric acid and the sodium sulphate precipitate was filtered off. The filtrate was kept overnight at room temperature, when the yellow crystalline precipitate was filtered off.[24] This solid (1.57 g) was suspended in ethanol (15 ml), and potassium cyanide (0.65 g) in water (3 ml) was added. The mixture was stirred at room temperature for 60 min and then added to 5% aqueous hydrochloric acid (150 ml). The mixture was extracted twice with ether, and the combined extracts washed with water and dried ($MgSO_4$). After evaporation of the solvent, a solution of *p*-methylbenzaldehyde (1.2 g, 10 mmol) in absolute ethanol (15 ml), and a few drops of piperidine, were added to the resulting oil. The mixture was refluxed for 2 h, cooled, and the resulting precipitate [20% from (**2**)] was filtered off, m.p. 116—117 °C (ethanol) (Found: C, 79.35; H, 5.2; N, 9.5. $C_{19}H_{14}N_2O$ requires C, 79.70; H, 4.93; N, 9.79%); $\nu_{max.}$(KBr) 2 240, 1 580, 1 555, 1 440, 1 300, 1 170, 1 140, 960, 810, 770, and 695 cm^{-1}; δ($CDCl_3$) 8.6 (s, 1 H, CH=N), 7.0—8.0 (m, 10 H, ArH), and 2.4 (s, 3 H, Me).

Synthesis of 4-Aryl-3,5-dicyano-4H-pyran-2-amines (**4**): *General Procedure.*—A solution of an isoxazole (10 mmol) and the corresponding aromatic aldehyde (10 mmol) in absolute ethanol (10 ml) was added dropwise with stirring to a solution of sodium (10 mmol) in absolute ethanol (15 ml). After cooling, the mixture was acidified with 50% aqueous sulphuric acid and the sodium sulphate precipitate filtered off. The filtrate was kept overnight at room temperature, after which the solvent was evaporated off under reduced pressure. The resulting compound (oil or solid)[24] was dissolved in absolute ethanol (20 ml) and propanedinitrile (10 mmol) and a few drops of piperidine were added. The reaction mixture was stirred at room temperature for a few minutes until a solid precipitated; this solid was filtered off and recrystallized from ethanol.

3,5-Dicyano-4-phenyl-4H-pyran-2-amine (**4a**). This compound was obtained in 61% yield [from intermediate (**2**)], m.p. 224—226 °C (ethanol) (Found: C, 69.6; H, 4.0; N, 19.0. $C_{13}H_9N_3O$ requires C, 69.94; H, 4.03; N, 18.83%); $\nu_{max.}$(KBr) 3 380, 3 320, 2 220, 2 190, 1 660, 1 630, 1 590, 1 440, 1 395, and 1 205 cm^{-1}; δ[$(CD_3)_2SO$] 7.47 (s, 1 H, =CH–O), 7.13 (s, 5 H, ArH), 6.91 (s, 2 H, NH_2), and 4.20 (s, 1 H, CH); *m/z* 223 (M^+, 44), 222 (23), 157 (12), 146 (100), and 91 (14).

3,5-Dicyano-4-(p-tolyl)-4H-pyran-2-amine (**4b**). This compound was obtained in 18% overall yield, m.p. 197—199 C (ethanol) (Found: C, 70.3; H, 4.65; N, 17.4. $C_{14}H_{11}N_3O$ requires C, 70.83; H, 4.64; N, 17.72%); $\nu_{max.}$(KBr) 3 380, 3 320, 3 300, 3 260, 3 200, 2 215, 2 210, 1 665, 1 635, 1 595, 1 500, 1 390, 1 200, and 1 170 cm^{-1}; δ[$(CD_3)_2SO$] 7.7 (s, 1 H, =CH–O), 7.21 (s, 5 H, ArH), 7.08 (s, 2 H, NH_2), 4.15 (s, 1 H, CH), and 2.33 (s, 3 H, Me).

4-Cyano-5-hydroxy-5-methyl-3-phenylpyrrol-2(5H)-one (**9a**). To a solution of sodium (0.58 g, 25 mmol) in absolute ethanol (20 ml), 5-methylisoxazole (2.09 g, 25 mmol) was added dropwise with stirring. The sodium salt of cyanoacetone precipitated in a few minutes, when benzaldehyde (2.7 g, 25 mmol) was added. The mixture was stirred at room temperature for 48 h and then acidified with 50% aqueous sulphuric acid. The resulting sodium sulphate was filtered off and the filtrate evaporated under reduced pressure. The resulting oil was dissolved in ether and washed with 10% sodium hydrogen sulphite (×2), water (×1), 10% sodium hydrogen carbonate (×2), and finally with water. The ether was evaporated off under reduced pressure and the resulting oil was dissolved in *ca.* 20 ml of methanol. A solution of potassium cyanide (1.6 g, 25 mmol) in water (4 ml) was added and the reaction mixture was allowed to stand at room temperature for 2 days. The solution was then poured into hydrochloric acid (300 ml). An oil separated and this was extracted with ether, dried ($MgSO_4$), and evaporated under reduced pressure. The pyrrolone (**9**) was isolated as a pure compound by means of column chromatography of the resulting red oil; yield 10%, m.p. 173 °C (decomp.) (from benzene) (Found: C, 67.35; H, 4.85; N, 13.0. $C_{12}H_{10}N_2O_2$ requires C, 67.28; H, 4.70; N, 13.08%); $\nu_{max.}$(KBr) 3 400, 3 220, 2 220, 1 700, 1 490, 1 420, 1 365, 1 295, 1 280, 1 145, 1 070, 950, and 795 cm^{-1}; δ[$(CD_3)_2SO$] 9.3 (s, 1 H, NH), 8.0—7.6 (m, 5 H, ArH), 6.6 (s, 1 H, OH, disappears on addition of TFA), and 1.62 (s, 3 H, Me); *m/z* (relative intensity) 214 (M^+, 74), 199 (100), 197 (87), 196 (52), 195 (14), 187 (14), 181 (14), 171 (15), 170 (5), 169 (9), 168 (19), 154 (8), 153 (14), 141 (13), 140 (10), 129 (10), 128 (78), 127 (48), and 77 (30).

Synthesis of 3-Alkyl or -Aryl Substituted 4-Cyano-5-methyl-N-(p-methylbenzylidene)furan-2-amines (**10a—e**): *General Procedure.*—A mixture of 5-methylisoxazole (10 mmol) and the corresponding aldehyde (10 mmol) in absolute ethanol (40 ml) was added dropwise to a solution of sodium (10 mmol) in absolute ethanol (*ca.* 20 ml). After the reaction mixture had been stirred at room temperature for 24 h, 50% aqueous sulphuric acid was added until acid pH. The precipitated sodium sulphate was filtered off, and the solvent evaporated under reduced pressure. The resulting compound[24] was dissolved in ethanol (*ca.* 20 ml) and a solution of potassium cyanide (10 mmol) in the minimum amount of water was added. The mixture was stirred for a variable time (until t.l.c. showed that the starting compound was exhausted, usually 60 min) and then poured with stirring into *ca.* 100 ml of 5% aqueous hydrochloric acid. After a few minutes an oil separated. The mixture was then extracted with ether, and the extracts dried ($MgSO_4$) and evaporated under reduced pressure; a solution of *p*-methylbenzaldehyde (10 mmol) in absolute ethanol (20 ml), and a few drops of piperidine, were then added to the resulting oil. The mixture was refluxed for 1—2 h and, on cooling, the precipitated furanamine was filtered off and recrystallized from ethanol.

4-Cyano-5-methyl-3-phenyl-N-(p-methylbenzylidene)furan-2-amine (**10a**). This compound was obtained in 57% yield [from intermediate (**8**)], m.p. 144—146 °C (ethanol) (Found: C, 79.8; H, 5.3; N, 9.25. $C_{20}H_{16}N_2O$ requires C, 79.97; H, 5.37; N, 9.33%); $\nu_{max.}$(KBr) 2 230, 1 585, 1 550, 1 445, 1 265, 1 170, 1 150, 1 100, 970, 955, 910, 810, and 760 cm^{-1}; δ($CDCl_3$) 8.55 (s, 1 H, CH=N), 7.0—8.0 (m, 9 H, ArH), 2.53 (s, 3 H, MeC–O), and 2.4 (s, 3 H, MeC_6H_4).

4-Cyano-5-methyl-3-(p-tolyl)-N-(p-methylbenzylidene)furan-2-amine (**10b**). This compound was obtained in 75% yield [from intermediate (**8**)], m.p. 174—176 °C (ethanol) (Found: C, 80.1; H, 6.0; N, 8.9. $C_{21}H_{18}N_2O$ requires C, 80.23; H, 5.77; N, 8.91%); $\nu_{max.}$(KBr) 2 230, 1 590, 1 550, 1 500, 1 420, 1 270, 1 170, 1 145, 1 100, 1 000, 965, and 955 cm^{-1}; δ($CDCl_3$) 8.51 (s, 1 H, CH=N), 7.0—8.0 (m, 8 H, ArH), 2.48 (s, 3 H, MeC–O), and 2.36 (s, 6 H, 2 *p*-MeC_6H_4).

4-Cyano-3-isopropyl-5-methyl-N-(p-methylbenzylidene)furan-2-amine (**10d**). This compound was obtained in 19% overall yield, m.p. 116—117 °C (ethanol) (Found: C, 76.85; H, 6.65; N, 10.45. $C_{17}H_{18}N_2O$ requires C, 76.66; H, 6.81; N, 10.52%); $\nu_{max.}$(KBr) 2 970, 2 240, 1 600, 1 565, 1 470, 1 410, 1 310, 1 210, 1 175, 1 150, 1 110, 1 040, 990, 965, 820, and 700 cm^{-1}; δ($CDCl_3$) 8.36 (s, 1 H, CH=N), 7.0—8.0 (m, 4 H, ArH), 2.96—3.6 (m, 1 H, CH), 2.43 (s, 3 H, MeC_6H_4), and 1.35 (d, 6 H, $CHMe_2$, *J* 6 Hz).

Synthesis of 4-Alkyl or -Aryl Substituted 3,5-Dicyano-6-methyl-4H-pyran-2-amines (**11a—e**): *General Procedure.*—A mixture of 5-methylisoxazole (10 mmol) and the corresponding aldehyde (10 mmol) in absolute ethanol (40 ml) was added dropwise to a solution of sodium (10 mmol) in absolute ethanol (*ca.* 20 ml). The reaction mixture was stirred at room temperature for 24 h and then acidified with 50% aqueous sulphuric acid. The precipitated sodium sulphate was filtered off and the solvent was evaporated under reduced pressure. The resulting oil[24] was dissolved in absolute ethanol (20 ml), and propanedinitrile (10 mmol) and a few drops of piperidine were added. The reaction was stirred at room temperature for a few minutes, and the resulting precipitate was filtered off, washed with ethanol, and recrystallized from the appropiate solvent.

3,5-Dicyano-6-methyl-4-phenyl-4H-pyran-2-amine (**11a**). This compound was obtained in 19% overall yield, m.p. 215—217 °C (ethanol) (Found: C, 70.5; H, 4.9; N, 17.9. $C_{14}H_{11}N_3O$ requires C, 70.88; H, 4.64; N, 17.72%); $\nu_{max.}$(KBr) 3 400, 3 310, 3 200, 2 230, 2 215, 1 685, 1 645, 1 610, 1 250, and 1 065 cm^{-1}; δ[$(CD_3)_2SO$] 7.2 (s, 5 H, ArH), 6.95 (s, 2 H, NH_2), 4.2 (s, 1 H, CH), and 2.2 (s, 3 H, Me); *m/z* (relative intensity) 237 (M^+, 26), 236 (10), 194 (5), 171 (40), 160 (100), 156 (14), 129 (18), 128 (17), 102 (17), 77 (15), 66 (44), and 43 (97).

3,5-Dicyano-4-(p-methoxyphenyl)-6-methyl-4H-pyran-2-amine (**11c**). This compound was obtained in 55% yield [from intermediate (**8**)], m.p. 144—146 °C (ethanol) [Found: C, 67.05; H, 4.7; N, 15.75. $C_{15}H_{13}N_3O_2$ requires C, 67.41; H, 4.86; N, 15.73%); $\nu_{max.}$(KBr) 3 420, 3 330, 3 220, 2 220, 2 205, 1 685, 1 645, 1 605, and 1 240 cm^{-1}; δ[$(CD_3)_2SO$] 7.2—6.6 (m, 6 H, ArH, NH_2), 4.2 (s, 1 H, CH), 3.7 (s, 3 H, MeO), and 2.2 (s, 3 H, Me).

3,5-Dicyano-4-isopropyl-6-methyl-4H-pyran-2-amine (**11d**). This compound was obtained in 30% overall yield, m.p. 198—200 °C (ethanol) (Found: C, 65.25; H, 6.45; N, 20.35. $C_{11}H_{13}N_3O$ requires C, 65.02; H, 6.40; N, 20.68%). $\nu_{max.}$(KBr) 3 410, 3 330, 3 220, 2 220, 2 195, 1 675, 1 645, 1 600, 1 410, 1 240, and 1 045 cm^{-1}; δ[$(CD_3)_2SO$] 6.8 (s, 2 H, NH_2), 2.95 (br, 1 H, CH), 2.1 (s, 3 H, Me), 1.4—2.1 (m, 1 H, C*H*Me_2), 0.83 (d, 3 H, Me, *J* 6 Hz), and 0.91 (d, 3 H, Me, *J* 6 Hz); *m/z* (relative intensity) 203 (M^+, 1), 161 (11), 160 (100), 122 (14), 118 (31), 94 (18), 66 (20), and 43 (80).

3,5-Dicyano-6-methyl-4-s-butyl-4H-pyran-2-amine (**11e**). This compound was obtained in 19% overall yield, m.p. 164—166 °C (ethanol) (Found: C, 66.0; H, 6.75; N, 19.25. $C_{12}H_{15}N_3O$ requires C, 66.35; H, 6.91; N, 19.35%); $\nu_{max.}$(KBr) 3 410, 3 320, 2 230, 2 190, 1 675, 1 635, 1 600, 1 405, 1 385, 1 230, and 1 095 cm^{-1}; δ[$(CD_3)_2SO$] 6.95 (s, 2 H, NH_2), 3.15 (br, 1 H, CH), 2.2 (s, 3 H, Me), and 1.7—0.7 (m, 9 H, Bu^s).

Synthesis of 3-Alkyl-4-cyano-N-(p-methylbenzylidene)-5-phenyl-2-furanamines (**10f—h**): *General Procedure.*—A mixture of α-benzoylacetonitrile (10 mmol; obtained from 5-phenylisoxazole[12] or by acylation of acetonitrile[13]), the corresponding aliphatic aldehyde (10 mmol), hexanoic acid (0.25 ml) and piperidine (0.1 ml) in benzene (40 ml) was refluxed

for 2 h in a Dean-Stark apparatus. After cooling, the solvent was evaporated under reduced pressure. The resulting oil[24] was dissolved in ethanol (30 ml) and a solution of potassium cyanide (10 mmol) in water (4 ml) was added at room temperature and the mixture stirred for 60 min. It was then poured into hydrochloric acid (150 ml), and the resulting oil was extracted with ether and the extracts dried ($MgSO_4$) and evaporated under reduced pressure. The oil obtained in this way was dissolved in absolute ethanol (30 ml), and *p*-methylbenzaldehyde (10 mmol) and a few drops of piperidine were added. The mixture was refluxed for 2 h, and, on cooling, the furanamine precipitated, and was filtered off and recrystallized from ethanol.

4-*Cyano*-3-*isopropyl*-N-(p-*methylbenzylidene*)-5-*phenylfuran*-2-*amine* (**10f**). This compound was obtained in 60% yield [from the intermediate (**8**)], m.p. 153—154 °C (ethanol) (Found: C, 80.3; H, 6.1; N, 8.3. $C_{22}H_{20}N_2O$ requires C, 80.46; H, 6.14; N, 8.53%); $\nu_{max.}$(KBr) 2 220, 1 590, 1 580, 1 530, 1 480, 1 140, 1 305, 1 170, 1 140, 1 045, 960, 810, and 770 cm^{-1}; $\delta(CDCl_3)$ 8.55 (s, 1 H, CH=N), 6.8—8.2 (m, 9 H, ArH), 3.05—3.66 (m, 1 H, CH), 2.40 (s, 3 H, MeC_6H_4), and 1.47 (d, 6 H, $CHMe_2$, *J* 6 Hz).

4-*Cyano*-N-(p-*methylbenzylidene*)-3-*pentan*-3-*yl*-5-*phenylfuran*-2-*amine* (**10h**). This compound was obtained in 66% overall yield, m.p. 140—141 °C (ethanol) (Found: C, 81.0; H, 7.0; N, 8.1. $C_{24}H_{24}N_2O$ requires C, 80.86; H, 6.79; N, 7.86%); $\nu_{max.}$(KBr) 2 230, 1 540, 1 450, 1 180, 1 150, 970, 815, 770, and 690 cm^{-1}; $\delta(CDCl_3)$ 8.58 (s, 1 H, CH=N), 7.0—8.1 (m, 9 H, ArH), 2.58—3.25 (m, 1 H, CH), 2.4 (s, 3 H, MeC_6H_4), 1.9 (m, 4 H, 2 CH_2), and 0.93 (t, 6 H, 2 $MeCH_2$, *J* 7 Hz).

Synthesis of 4-*Alkyl*-3,5-*dicyano*-6-*phenyl*-4H-*pyran*-2-*amines* (**11f—h**): *General Procedure*.—A mixture of α-benzoylacetonitrile (10 mmol; obtained from 5-phenylisoxazole[25] or by acylation of acetonitrile[26]), the corresponding aliphatic aldehyde (10 mmol), hexanoic acid (0.25 ml), and piperidine (0.1 ml) in benzene (40 ml) was refluxed for 2 h in a Dean-Stark apparatus. After cooling, the solvent was evaporated under reduced pressure. To the resulting oil[24] a solution of propanedinitrile (10 mmol) and a few drops of piperidine were added. The reaction mixture was stirred at room temperature for a few minutes and the resulting precipitate was filtered off, washed with ethanol, and recrystallized from ethanol.

3,5-*Dicyano*-4-*isopropyl*-6-*phenyl*-4H-*pyran*-2-*amine* (**11f**). This compound was obtained in 58% overall yield, m.p. 165—167 °C (ethanol) (Found: C, 72.65; H, 5.95; N, 15.75. $C_{16}H_{15}N_3O$ requires C, 72.45; H, 5.66; N, 15.85%); $\nu_{max.}$(KBr) 3 430, 3 310, 2 210, 2 190, 1 650, 1 585, 1 400, and 1 255 cm^{-1}; $\delta[(CD_3)_2SO]$ 7.3—7.7 (m, 5 H, ArH), 7.0 (s, 2 H, NH_2), 3.1 (d, 1 H, CH, *J* 4 Hz), 1.4—2.15 (m, 1 H, $CHMe_2$), 1.0 (d, 3 H, Me, *J* 6 Hz), and 0.95 (d, 3 H, Me, *J* 6 Hz).

3,5-*Dicyano*-6-*phenyl*-4-*s*-*butyl*-4H-*pyran*-2-*amine* (**11g**). This compound was obtained in 76% overall yield, m.p. 152—154 °C (ethanol) (Found: C, 72.9; H, 6.45; N, 15.4. $C_{17}H_{17}N_3O$ requires C, 73.12; H, 6.09; N, 15.05%); $\nu_{max.}$(KBr) 3 430, 3 310, 2 210, 2 190, 1 650, 1 615, 1 585, 1 400, 1 255, and 1 130 cm^{-1}; $\delta[(CD_3)_2SO]$ 7.3—7.7 (m, 5 H, ArH), 7.0 (s, 2 H, NH_2), 3.2 (d, 1 H, CH, *J* 4 Hz), and 0.7—1.8 (m, 9 H, Bu^s).

Acknowledgements

Support of this work by a grant from the Comision Asesora de Investigación Cientifica y Técnica of the Presidencia de Gobierno of Spain is gratefully acknowledged. One of us (J. A. C.) would like to thank the Ministerio de Educación y Ciencia of Spain for a fellowship.

References

1 A previous account of some of the new compounds of this paper was reported as a preliminary communication in *Heterocycles*, 1984, **22**, 1.
2 D. N. McGregor, U. Corbin, J. E. Swigor, and L. C. Cheney, *Tetrahedron*, 1969, **25**, 389.
3 G. Stork, M. Ohashi, H. Kamachi, and H. Kakisawa, *J. Org. Chem.*, 1971, **36**, 2784.
4 N. K. Kochetkov and S. D. Sokolov, *Adv. Het. Chem.*, 1963, **2**, 365.
5 C. Musante and S. Fatutta, *Gazz. Chim. Ital.*, 1958, **88**, 879.
6 A. Padwa and E. Chen, *J. Org. Chem.*, 1974, **39**, 1976.
7 T. Nishiwaki, K. Azechi, and F. Fujiyama, *J. Chem. Soc., Perkin Trans. 1*, 1974, 1867.
8 A. J. Boulton, A. R. Katritzky, and A. M. Hamick, *J. Chem. Soc.*, 1967, 2005.
9 See for instance 'Comprehensive Organic Chemistry,' ed. D. H. R. Barton, vol. 2, p. 533; vol. 4, 999, Pergamon Press, Oxford and New York, 1978; A. I. Meyers in 'Heterocycles in Organic Synthesis,' pp. 243—306, Wiley-Interscience, New York, 1974, and references therein.
10 C. H. Eugster, L. Leichner, and E. Jenny, *Helv. Chim. Acta*, 1963, **46**, 543.
11 J. A. Ciller, C. Seoane, and J. L. Soto, *Heterocycles*, 1984, **22**, 1989.
12 See for instance 'Comprehensive Heterocyclic Chemistry,' eds. A. R. Katritzky and C. W. Rees, Pergamon, Oxford, 1984.
13 R. S. Zimmerman, K. Eger, and H. J. Roth, *Arch. Pharm. (Weinheim)*, 1981, **314**, 127.
14 J. A. Ciller, C. Seoane, and J. L. Soto, *Liebigs Ann. Chem.*, 1985, 51.
15 M. Sánchez and J. M. Guerra, *Opt. Commun.*, 1981, **40**, 144.
16 H. C. Van der Plas, 'Ring Transformations of Heterocycles,' Academic Press, London and New York, 1973, vol. 1, p. 161.
17 S. Ruheman, *J. Chem. Soc.*, 1904, **85**, 1456.
18 A. C. Hann and A. Lapworth, *J. Chem. Soc.*, 1904, **85**, 1358.
19 J. W. ApSimon, J. W. Hooper, and B. A. Laishes, *Can. J. Chem.*, 1970, **48**, 3064.
20 A. Sakurai and H. Midorikawa, *Bull. Chem. Soc. Jpn.*, 1968, **41**, 430.
21 H. H. Otto, *Arch. Pharm. (Weinheim)*, 1974, **307**, 367.
22 I. P. Sword, *J. Chem. Soc. C*, 1970, 1916.
23 J. L. Soto, C. Seoane, and J. A. Ciller, *An. Quim.*, 1980, **76C**, 281.
24 Some of these intermediates have been previously reported in the literature and can be isolated as pure compounds. See, for instance A. Herbert, BASF A-G Ger. Offen. 2 623 170. (*Chem. Abstr.* 62159j, 1978); reference 10, and R. Danion-Bougot and R. Carrie, *Bull. Soc. Chim. Fr.*, 1972, **9**, 3511.
25 L. Clisen and R. Stock, *Chem. Ber.*, 1891, **24**, 130.
26 C. J. Eby and C. R. Hauser, *J. Am. Chem. Soc.*, 1957, **79**, 723.

Received 12*th March* 1985; *Paper* 5/421