A Study of 2-Aminofurans

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Catalytic reduction of 2-nitrofurans **2** gives low yields of 2-aminofurans **1** which are not isolated but are trapped using ethyl ethoxymethylenecyanoacetate (**6**) or ethoxymethylenemalononitrile (**7**). In these reactions 2-aminofuran (**1a**) behaves like a dieneamine with substitution occurring at position 5 of the ring. When the 5-position is substituted reaction takes place at position 3 and thermal cyclisation of the product gives furo-[2,3-*b*]pyridine derivatives **16**. An AM1 calculation of the properties of 2-aminofuran (**1a**) is reported and the results are consistent with observed properties.

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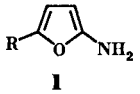
We have described the preparation and reactions of simple 4- and 5-aminoimidazoles [1-3] and now report the results of a similar investigation of 2-aminofurans **1**. 2-Aminofurans have been identified as metabolites of antibacterial 2-nitrofurans (**2**) [4-6] and a number of derivatives in which the furan ring is associated with an electron withdrawing substituent have been isolated and characterized [7]. In the absence of an electron withdrawing group 2-aminofurans are much less stable and although the synthesis of the parent system (**1a**) has been explored using several routes its isolation and characterisation has never been achieved [8-11]. The lack of information on these fundamental systems **1** prompted us to investigate their preparation and properties using methods which we have found useful for the synthesis of aminoimidazoles [1,2].



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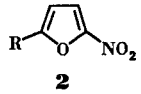

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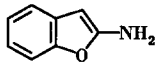

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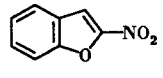

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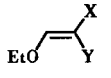
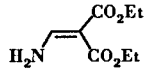
In formulae 1 and 2: a R = H, b R = Me, c R = CHO.



5, X = Y = CO_2Et
6, X = CO_2Et, Y = CN
7, X = Y = CN



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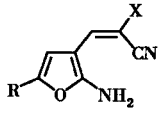
In contrast to the reduction of nitro-imidazoles, when solutions of the 2-nitrofurans **2a,b** or 2-nitrobenzo[*b*]furan (**4**) were reduced in 1,4-dioxane solution under an atmosphere of hydrogen using 40% w/w of 5% Pd/C, the reaction did not cease after three molecular equivalents of hydrogen had been used. The reductions were therefore assumed to be complete after consumption of the theoretical volume of hydrogen and examination of the reduced solutions by tlc showing that very little starting material remained. Filtration of the freshly reduced solutions and rapid evaporation of the solvent gave pale yellow oils which in deuteriochloroform solution were shown by ^1H nmr spectroscopy to be very complex mixtures and assignment of any signals to aminofurans was not possible. These observations confirmed the view that simple 2-aminofurans **1** are extremely unstable and it was clear that any use of these species in synthesis would depend on the rapid reaction of freshly prepared solutions of the amines with appropriate reagents. This is an approach which we successfully applied to 4-aminoimidazoles [2,3].

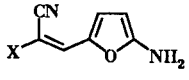
When diethyl ethoxymethylenemalonate (**5**) was added to a freshly reduced 2-nitrofuran solution no reaction was observed to occur, even after several hours (tlc). However, when the flask was stoppered and allowed to stand at ambient temperature for several weeks, diethyl aminomethylenemalonate (**8**) was isolated in 15% yield by evaporation and chromatographic purification of the resulting oil. We presume that this product **8** was formed by reaction of diethyl ethoxymethylenemalonate (**5**) with ammonia which is generated by decomposition or over-reduction of 2-aminofuran (**1a**). This result encouraged us to explore the use of more reactive reagents, namely ethyl ethoxymethylenecyanoacetate (**6**) and ethoxymethylenemalononitrile (**7**).

When a freshly reduced solution of 2-nitrofuran (**2a**) was treated with ethyl ethoxymethylenecyanoacetate (**6**) and the mixture was allowed to stand (15 hours) a multicomponent mixture was formed (tlc). Two major components were isolated using mplc. The most polar product, which was obtained in 7% yield as a pink solid (mp 166-168°), had the empirical formula $C_{10}H_{10}N_2O_3$ and showed a molecular ion at m/z 206. The ^1H nmr spectrum (DMSO-d_6) included a broad exchangeable singlet at δ 8.21 which was clearly attributable to a primary amino group (NH_2). This information led us to consider the alternative struc-

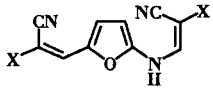
tures **9** and **10** for this product. Structure **9** might be expected to undergo thermal cyclisation and since the isolated product was thermally stable we were encouraged to favour the isomeric structure **10**. An authentic sample of compound **10** was unambiguously synthesized from 5-nitro-2-furfuraldehyde (**2c**) by treatment with sodium azide and ethyl cyanoacetate using the method of Kovac and co-workers [12]. This material **10** was shown to be identical to the isolated reaction product. 2-Aminofuran (**1a**) must, therefore, be present after reduction of 2-nitrofuran (**2a**) and it reacts as a dienamine during its condensation with ethyl ethoxymethylenecyanoacetate (**6**). The second product was obtained in 7% yield as orange needles, mp 206-208°. Elemental analysis ($C_{16}H_{15}N_3O_5$) and spectroscopic analysis showed that this product had structure **11**. An identical sample of this product **11** was obtained by heating the amine **10** with excess ethyl ethoxymethylenecyanoacetate **6**.



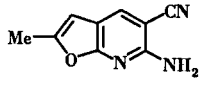
9, X = CO_2Et, R = H
12, X = CN, R = H
15, X = CN, R = Me



10, X = CO_2Et
13, X = CN



11, X = CO_2Et
14, X = CN



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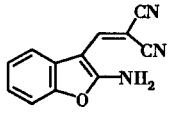

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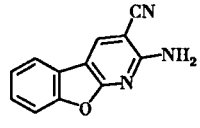

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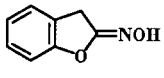

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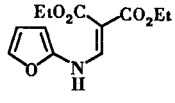

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In an analogous reaction, a freshly prepared solution of 2-aminofuran (**1a**) upon treatment with ethoxymethylenemalononitrile (**7**) gave the amine **13** (15%) and the secondary product **14** (7%). An authentic sample of compound **13** was prepared from 5-nitro-2-furaldehyde (**2c**) using the procedure described by Kovac [12].

Having demonstrated that 2-aminofuran (**1a**) reacts with alkoxymethylenemalonic acid derivatives **6** and **7** at position 5 of the furan ring, we then investigated the blocking of this position using 5-methyl-2-nitrofuran (**2b**) and 2-nitrobenzo[*b*]furan (**4**) as precursors. Treatment of a freshly reduced solution of compound **2b** with ethoxymethylenemalononitrile (**7**) gave a single product in low yield (6%). This was isolated as yellow needles, mp 214-216° and identified as compound **15**, which is formed by condensation at position 3 of the furan ring. The ^1H nmr spectrum fully supported this structural assignment and eliminated the alternative possibility that reaction had occurred on the amino group. Thus, in addition to signals due to the amino protons (δ 8.66) and the methyl substituent (δ 2.15), singlets at δ 6.44 and δ 7.78 were observed and assigned to the furan 4-H and olefinic proton respectively. Further support for the structure (**15**) was provided by the observation that when compound **15** was heated at 200°, cyclisation occurred giving the novel furano[2,3-*b*]pyridine **16** in 71% yield.

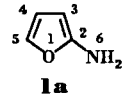
In a similar manner 2-nitrobenzo[*b*]furan (**4**) was transformed into the amine **17** (11%) which underwent thermal cyclisation to compound **18** (50%). It should be noted that a previous attempt to reduce 2-nitrobenzo[*b*]furan (**4**) to the amine **3** gave only the hydrolysis product, benzo[*b*]-furan-2(3*H*)-one. We obtained a second product from the reduction of compound **4** which was identified as 2-benzofuroxime (**19**) (23%). This was unexpected in that three molecular equivalents of hydrogen had been consumed during the reaction. This result provides further evidence that the reduction of 2-nitrofurans is complex and that over-reduction readily occurs, possibly giving ring-opened products.

Although we have been able to generate and trap 2-aminofuran (**1a**), 5-methyl-2-aminofuran (**1b**) and 2-aminobenzo[*b*]furan (**3**), the yields of the isolated products (5-15%) are low, and it is clear that this approach is of limited synthetic value until improved reaction conditions can be found.

In earlier publications [2,3] we rationalised the regioselectivity of electrophilic substitution reactions of 5-aminoimidazoles in terms of a frontier molecular orbital (FMO) model. Like 5-aminoimidazoles, 2-aminofuran (**1a**) can be regarded as an *N,C*-ambident nucleophile which can in principle react at nitrogen (NH_2) or at one of the ring carbon atoms. The results of an AM1 calculation [13] of the

Table 1

AM1 Calculated Charge Distribution (e) and Frontier Orbital Energies (E) and Coefficients for 2-Aminofuran (1a)



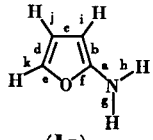
1a

	e/au	HOMO	LUMO
E/eV	-	-8.47	0.78
O^1	-0.14	0.04	0.34
C^2	0.05	0.46	-0.58
C^3	-0.24	0.49	0.32
C^4	-0.17	-0.26	0.33
C^5	-0.11	-0.52	-0.53
N^6	-0.28	-0.39	0.12

μ calcd 1.44 Debye

Table 2

The AM1 Calculated Geometry of 2-Aminofuran (**1a**)



(**1a**)

Bond lengths (A)

a	b	c	d	e	f	g	h	i	j	k
1.360	1.400	1.400	1.400	1.410	1.410	1.010	1.010	1.080	1.080	1.080

Bond angles (deg)

af	ag	ah	bi	cd	cj	de	dk	ef
126.0	120.0	120.0	125.9	108.2	125.9	107.9	126.0	107.7

properties of 2-aminofuran (**1a**) are summarised in Tables 1 and 2. The calculated HOMO energy of compound **1a** (-8.47 eV) is similar to that of 4- and 5-aminoimidazole (-8.38 eV). According to FMO theory, we might therefore expect 2-aminofuran (**1a**) to react with soft electrophiles, such as ethyl ethoxymethylenecyanoacetate (**6**) and ethoxymethylenemalononitrile (**7**), at the position in the molecule where the HOMO coefficient is largest. Inspection of Table 1 reveals that the HOMO coefficient is largest at position 5 of 2-aminofuran (**1a**), and this is clearly consistent with the formation of the observed products **10** and **13** from the reaction of the amine (**1a**) with the reagents **6** and **7**. The coefficient at position 3 is only slightly smaller than at position 5 and so it is not surprising that when position 5 is blocked (*e.g.* **1b**) reaction occurs at position 3. The HOMO coefficient on nitrogen is much smaller than on the carbon atoms and this may explain why products resulting from reaction on nitrogen are not observed as primary products using the reagents **6** and **7**.

Diethyl ethoxymethylenemalonate (**5**) is a harder electrophile than its close analogues **6** and **7** and in its reactions with 5-aminoimidazoles reacts on the exocyclic nitrogen atom [3], which is the harder reaction centre. It is interesting to note, therefore, that unlike reagents **6** and **7**, diethyl ethoxymethylenemalonate (**5**) did not give *C*-substitution products with 2-aminofuran (**1a**). Furthermore, it did not appear to give a *N*-substitution product, indicating that as an amine, 2-aminofuran (**1a**) is less reactive than 4- and 5-aminoimidazoles and aniline. We consider that the 2-[2′,2′-di(ethoxycarbonyl)ethyleneamine]furan (**20**) would be stable if formed and that the diethyl aminomethylenemalonate (**8**) isolated from the reaction between **1a** and **5** is not a decomposition product of compound **20**.

EXPERIMENTAL

The ^{1}H nmr spectra were recorded on Varian CFT-20 (80 MHz) and XL-200 (200 MHz) spectrometers; ir spectra on a Pye-Unicam SP3-200 spectrometer, mass spectra on a VG Micromass 6F or VG 7070E spectrometer, and microanalyses on a Carlo-Erba 1106. Unless otherwise stated, ir spectra were measured using potassium bromide discs and 80 and 200 MHz nmr spectra in hexadeuteriodimethylsulphoxide (tetramethylsilane as internal standard). Only significant bands from the ir spectra are quoted.

Thin layer chromatography (tlc) was carried out on Merck silica gel (layer thickness 0.2 mm) pre-coated plastic plates and visualised under ultra violet light (254 and 366 nm).

Separations by medium pressure liquid chromatography (mplc) were carried out using Merck Kieselgel 60 (230-400 mesh). Evaporation refers to the removal of volatile materials under reduced pressure. Substances stated to be identical were so with respect to melting points, mixed melting points, and ir spectra. Melting points are uncorrected.

Ethyl 3-Amino-2-ethoxycarbonylpropenoate (Diethyl Aminomethylenemalonate) (**8**).

A mixture of 2-nitrofuran (**2a**) [14] (3.4 g, 30 mmoles) and diethyl ethoxymethylenemalonate (**5**) [15] (6.5 g, 30 mmoles) in 1,4-dioxane (200 ml) was shaken with 5% palladium on charcoal (1.7 g) under an atmosphere of hydrogen until three molecular equivalents of hydrogen had been consumed. The catalyst was then removed by filtration and the pale yellow filtrate allowed to stand at ambient temperature (16 hours). The solution was then evaporated and the resulting yellow-brown oil was kept at ambient temperature in a stoppered flask (4 months). The oil was then subjected to mplc (19:1 dichloromethane:methanol as eluent). The eluent was evaporated from the major fraction giving ethyl 3-amino-2-ethoxycarbonylpropenoate (**8**) (0.85 g, 15%) as a pale orange solid, mp 57-60° (lit [16] mp 65.5-66.5°); ir: 3400, 3320, 2980, 1690, 1660, 1630, 1410, 1380, 1280, 1220 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 1.3 (t, J = 7 Hz, C*H*$_3$), 1.36 (t, J = 7 Hz, C*H*$_3$), 4.2 (q, J = 7 Hz, C*H*$_2$), 4.28 (q, J = 7 Hz, C*H*$_2$), 6.24 (br s, N*H*), 8.04-8.18 (m, olefinic *H*), 8.66 (br s, N*H*).

Anal. Calcd. for $C_8H_{13}NO_4$: C, 51.3; H, 7.0; N, 7.5. Found: C, 51.5; H, 7.2; N, 7.2.

The Reaction of 2-Aminofuran (**1a**) with Ethyl Ethoxymethylenecyanoacetate (**6**).

Ethyl 2-Cyano-3-[5-(2-cyano-2-ethoxycarbonyl)vinylfuran-2-yl]-aminopropenoate (**11**) and Ethyl 2-Cyano-3-(2-aminofuran-5-yl)-propenoate (**10**) (Method 1).

A solution of 2-nitrofuran (**2a**) (6.8 g, 60 mmoles) in 1,4-dioxane (200 ml) containing 5% palladium on carbon (2.72 g) was shaken under an atmosphere of hydrogen until three molecular equivalents of hydrogen had been consumed. The catalyst was then removed by filtration and ethyl ethoxymethylenecyanoacetate (**6**) [17] (10.14 g, 60 mmoles) was added to the filtrate with stirring. After keeping at ambient temperature (15 hours), the orange solution was evaporated and the residue subjected to mplc (chloroform as eluent). The first major fraction (Rf 0.1) was collected, the eluent concentrated and the resulting solid collected giving compound **11**, (1.4 g, 7%), as fine orange needles, mp 206-208°; ir: 3180, 2990, 2220, 1715, 1650, 1605, 1575, 1450, 1385, 1240 cm^{-1}; ^1H nmr: δ 1.24 (t, J = 7 Hz, C*H*$_3$), 1.28 (t, J = 7 Hz, C*H*$_3$), 4.19 (q, J = 7 Hz, C*H*$_2$), 4.28 (q, J = 7 Hz, C*H*$_2$), 6.24 (d, J = 4 Hz, 4-*H*), 7.58 (d, J = 4 Hz, 3-*H*), 7.96 (s, olefinic *H*), 8.38 (s, olefinic *H*), 12.3 (br s, N*H*); ms: m/z 329 ($M^{+\cdot}$).

Anal. Calcd. for $C_{16}H_{15}N_3O_5$: C, 58.4; H, 4.59; N, 12.8. Found: C, 58.3; H, 4.59; N, 12.8.

The second major fraction (Rf 0.05) was collected, the eluent evaporated and the residue recrystallized (1:1 diethyl ether:40-60° petroleum) giving compound **10**, (0.8 g, 6.5%), as an orange-pink solid, mp 166-168°; ir: 3320, 3170, 2220, 1670, 1610, 1535, 1485, 1425, 1350, 1250 cm^{-1}; ^1H nmr: δ 1.24 (t, J = 7 Hz, C*H*$_3$), 4.18 (q, J = 7 Hz, C*H*$_2$), 5.61 (d, J = 4 Hz, 4-*H*), 7.40 (s, olefinic *H*), 7.54 (d, J = 4 Hz, 3-*H*), 8.21 (br s, N*H*$_2$); ms: m/z 206 ($M^{+\cdot}$).

Anal. Calcd. for $C_{10}H_{10}N_2O_3$: C, 58.2; H, 4.89; N, 13.6. Found: C, 57.8; H, 4.97; N, 13.5.

Ethyl 2-Cyano-3-(2-aminofuran-5-yl)propenoate (**10**) (Method 2).

A solution of 5-nitro-2-furaldehyde (**2c**) [12] (2.12 g, 15 mmoles) in dimethylformamide (5 ml) was added to a stirred mixture of sodium azide (1.95 g, 30 mmoles) and ethyl cyanoacetate (3.39 g, 30 mmoles) in dimethylformamide (10 ml) at 5° maintaining the temperature of the addition below 12°. The mixture was then warmed to maintain the temperature at 45° ± 5° (0.25 hour) and then poured into water (100 ml). The resulting mixture was extracted with ethyl acetate (2 x 100 ml) and the combined extract dried (magnesium sulfate), evaporated, and the residue subjected to mplc (ethyl acetate as eluent). The major fraction was collected, the solution concentrated (to *ca* 5 ml) and the remaining solution then diluted with diethyl ether. The resulting solid which crystallized was collected, washed with a little ether and dried giving the title compound **10** (1.0 g, 32%), as a pink solid, mp 167-169°; ir: 3320, 3170, 2220, 1670, 1610, 1535, 1485, 1425, 1350, 1250 cm^{-1}; ^1H nmr: δ 1.24 (t, J = 7 Hz, C*H*$_3$), 4.18 (q, J = 7 Hz, C*H*$_2$), 5.61 (d, J = 4 Hz, 4-*H*), 7.40 (s, olefinic *H*), 7.54 (d, J = 4 Hz, 3-*H*), 8.21 (br s, N*H*$_2$); ms: m/z 206 ($M^{+\cdot}$).

Anal. Calcd. for $C_{10}H_{10}N_2O_3$: C, 58.2; H, 4.89; N, 13.6. Found: C, 57.9; H, 4.77; N, 13.4.

Ethyl 2-Cyano-3-[5-(2-cyano-2-ethoxycarbonyl)vinylfuran-2-yl]-aminopropenoate (**11**) (Method 2).

A mixture of ethyl 2-cyano-3-(2-aminofuran-5-yl)propenoate (0.25 g, 1.2 mmoles) (**10**) and ethyl ethoxymethylenecyanoacetate (**6**) [17] (5.07 g, 30 mmoles) was heated at 140° (4 hours). The mixture was allowed to cool and was then purified by mplc (ethyl acetate as eluent). The major fraction (Rf 0.6) was collected, the eluent evaporated, and the residue recrystallised (ethyl acetate) giving the title compound **11** (0.14 g, 35%), as tiny orange brown needles, mp 203-205°; ir: 3180, 2990, 2220, 1715, 1650, 1605, 1575, 1450, 1385, 1240 cm^{-1}; ^1H nmr: δ 1.24 (t, J = 7 Hz, C*H*$_3$), 1.28 (t, J = 7 Hz, C*H*$_3$), 4.19 (q, J = 7 Hz, C*H*$_2$), 4.28 (q, J = 7 Hz, C*H*$_2$), 6.24 (d, J = 4 Hz, 4-*H*), 7.58 (d, J = 4 Hz, 3-*H*), 7.96 (s, olefinic *H*), 8.38 (s, olefinic *H*), 12.3 (br s, N*H*).

Anal. Calcd. for $C_{16}H_{15}N_3O_5$: C, 58.4; H, 4.59; N, 12.8. Found: C, 58.6; H, 4.93; N, 12.3.

The Reaction of 2-Aminofuran (**1a**) with Ethoxymethylenemalononitrile (**7**).

2-Cyano-3-(2-aminofuran-5-yl)propenitrile (**13**) and 2-Cyano-3-[5-(2,2-dicyano)vinylfuran-2-yl]aminopropenenitrile (**14**) (Method 1).

A solution of 2-nitrofuran (**1a**) [14] (13.6 g, 120 mmoles) in 1,4-dioxane (200 ml) containing 5% palladium on carbon (5.44 g) was shaken under an atmosphere of hydrogen until three molecular equivalents of hydrogen had been consumed. The catalyst was then removed by filtration and ethoxymethylenemalononitrile (**7**) [18,19] (14.8 g, 120 mmoles) was added to the filtrate with stirring. After keeping at ambient temperature (24 hours), the deep red solution was evaporated and the residue subjected to mplc (9:1, chloroform:methanol as eluent). The first major fraction (Rf 0.3) was collected, the eluent concentrated and the residue triturated with diethyl ether. The solid which crystallised was collected, washed with ether and dried giving compound **13**, (2.8 g, 15%), as fine orange brown needles, mp 204-206°; ir: 2220, 2200, 1620, 1530, 1325, 1300, 1140 cm^{-1}; ^1H nmr: δ 5.71 (d, J = 4 Hz, 4-*H*), 7.16 (s, olefinic *H*), 7.44 (d, J = 4 Hz, 3-*H*), 8.57 (br s, N*H*$_2$); ms: m/z 159 ($M^{+\cdot}$).

Anal. Calcd. for $C_8H_5N_3O$: C, 60.4; H, 3.17; N, 26.4. Found: C, 60.4; H, 3.07; N, 26.3.

The second major fraction (Rf 0.05) was collected, and the eluent concentrated giving compound (**14**), (2.1 g, 7.4%), as a purple black solid, mp indistinct, (dec >200°); ir: 2220, 2205, 1610, 1500, 1465, 1395 cm^{-1}; ^1H nmr: δ 6.15 (d, J = 4 Hz, 4-*H*), 7.38 (s, olefinic *H*), 7.40 (d, J = 4 Hz, 3-*H*), 8.2 (s, olefinic *H*), N*H* not visible.

Analytical figures indicated this product to have a purity of *ca* 90%. All attempts to purify the compound failed.

2-Cyano-3-(2-aminofuran-5-yl)propenitrile (**13**) (Method 2).

A solution of 5-nitro-2-furaldehyde (**2c**) [12] (2.82 g, 20 mmoles) in dimethylformamide (5 ml) was added to a stirred mixture of sodium azide (2.6 g, 40 mmoles) and malononitrile (2.64 g, 40 mmoles) in dimethylformamide (10 ml) at 5°. The rate of the addition was controlled to keep the temperature of the mixture at 33 ± 3°. The mixture was then warmed to maintain the temperature at 42 ± 5° (0.25 hour) and then poured into water (100 ml). The resulting mixture was extracted with ethyl acetate (3 x 100 ml) and the combined extract dried (sodium sulfate), evaporated, and the residue subjected to mplc (9:1, chloroform:methanol as eluent). The major fraction (Rf 0.2) was collected, the solution concentrated (to *ca* 5 ml) and the remaining solution then triturated with diethyl ether. The solid which crystallised was col-

lected, washed with a little ether and dried giving the title compound **13**, (1.7 g, 54%), as a brown solid, mp 204-206° (lit [12] mp 198-200°); ir: 2220, 2200, 1620, 1530, 1325, 1300, 1140 cm^{-1}; ^1H nmr: δ 5.71 (d, J = 4 Hz, 4-*H*), 7.16 (s, olefinic *H*), 7.44 (d, J = 4 Hz, 3-*H*), 8.57 (br s, NH_2); ms: m/z 159 ($M^{+\cdot}$).

Anal. Calcd. for $C_8H_5N_3O$: C, 60.4; H, 3.17; N, 26.4. Found: C, 60.2; H, 3.02; N, 26.5.

2-Cyano-3-(2-amino-5-methylfuran-3-yl)propenitrile (**15**).

A solution of 5-methyl-2-nitrofuran (**2b**) [20] (3.81 g, 30 mmoles) in 1,4-dioxane (120 ml) containing 5% palladium on carbon (1.9 g) was shaken under an atmosphere of hydrogen until three molecular equivalents of hydrogen had been consumed. The catalyst was then removed by filtration and ethoxymethylenemalononitrile (**7**) (3.7 g, 30 mmoles) was added to the filtrate with stirring. After keeping at ambient temperature (3 hours), the mixture was evaporated to a brown oil. The oil on standing partially solidified and this solid was collected and recrystallised (ethyl acetate) giving the title compound **15** (0.33 g, 6.4%) as yellow needles, mp 214-216°; ir: 3350, 3200, 2210, 2205, 1680, 1600, 1560, 1375, 1340 cm^{-1}; ^1H nmr: δ 2.15 (s, CH_3), 6.44 (s, 4-*H*), 7.78 (s, olefinic *H*), 8.66 (br s, NH_2); ms: m/z 173 ($M^{+\cdot}$).

Anal. Calcd. for $C_9H_7N_3O$: C, 62.4; H, 3.99; N, 24.3. Found: C, 62.7; H, 4.07; N, 24.3.

Reduction of 2-Nitrobenzofuran (**4**) in the Presence of Ethoxymethylenemalononitrile (**7**). 2-Benzofuroxime (**19**) and 2-Cyano-3-(2-aminobenzofuran-3-yl)propenenitrile (**17**).

A solution of 2-nitrobenzofuran (**4**) [21] (1.4 g, 8.6 mmoles) and ethoxymethylenemalononitrile (**7**) [18,19] (1.05 g, 8.6 mmoles) in 1,4-dioxane (40 ml) containing 5% palladium on carbon (0.7 g) was shaken under an atmosphere of hydrogen until three molecular equivalents of hydrogen had been consumed. The catalyst was then removed by filtration and the filtrate evaporated to an orange oil which was subjected to mplc (19:1, chloroform:methanol as eluent). The first major fraction (Rf 0.5) was collected, the eluent concentrated and the residue triturated with diethyl ether. The solid which crystallised was collected, washed with ether and dried giving compound **19**, (0.3 g, 23%), as a buff solid, mp 148-150°; ir: 3270-3100, 1706, 1617, 1479, 1463, 1225 cm^{-1}; ^1H nmr: δ 3.94 (s, CH_2), 7.08-7.35 (m, 4 aromatic *H*), 9.99 (br s, O*H*); ms: m/z 149 ($M^{+\cdot}$).

Anal. Calcd. for $C_8H_7NO_2$: C, 64.4; H, 4.77; N, 9.4. Found: C, 63.8; H, 4.61; N, 9.1.

The second component (Rf 0.4) was collected and the solution concentrated. The solid which separated was collected, washed with ether and dried giving compound **17** (0.2 g, 11%) as yellow green needles, mp indistinct (cyclisation); ir: 3330, 3170, 2220, 2205, 1675, 1590, 1550, 1460, 1350 cm^{-1}; ^1H nmr: δ 7.22 (m, 2 aromatic *H*), 7.4 (m, 1 aromatic *H*), 7.98 (s, olefinic *H*), 8.03 (m, 1 aromatic *H*), 9.32 (br s, NH_2); ms: m/z 210 (MH^+).

Anal. Calcd. for $C_{12}H_7N_3O$: C, 68.9; H, 3.37; N, 20.1. Found: C, 68.8; H, 3.28; N, 20.0.

6-Amino-5-cyano-2-methylfuro[2,3-*b*]pyridine (**16**).

2-Cyano-3-(2-amino-5-methylfuran-3-yl)propenitrile (**15**) (0.55 g, 3.2 mmoles) was heated at 200° (2 minutes) and then allowed to cool. The residue was subjected to mplc (19:1, chloroform:methanol as eluent) and the major fraction (Rf 0.45) collected. Concentration of the eluent resulted in crystallisation and the solid was collected, washed with ether, and dried giving the title compound **16** (0.39 g, 71%), as a buff solid, mp 207-209°; ir: 3450, 3320, 3200, 2220, 1635, 1575, 1490, 1420, 1300, 1275 cm^{-1}; ^1H nmr: δ 2.36 (s, CH_3), 6.44 (s, 3-*H*), 6.88 (br s, NH_2), 8.08 (s, 4-*H*); ms: m/z 173 ($M^{+\cdot}$).

Anal. Calcd. for $C_9H_7N_3O$: C, 62.4; H, 3.99; N, 24.3. Found: C, 62.2; H, 3.95; N, 24.2.

2-Amino-3-cyanobenzofuro[2,3-*b*]pyridine (**18**).

A solution of 2-cyano-3-(2-aminobenzofuran-3-yl)propenenitrile (**17**) (0.1 g, 0.48 mmole) in ethoxyethanol (20 ml) was boiled (10 minutes) and then evaporated. The residue was subjected to mplc (19:1, chloroform:methanol as eluent) and the major fraction (Rf 0.5) collected. Concentration of the eluent and trituration with diethyl ether resulted in crystallisation. The solid was collected, washed with ether, and dried giving the title compound **18** (0.05 g, 50%), as a colourless solid, mp 288-290°; ir: 3470, 3370, 2230, 1650, 1570, 1470, 1430, 1285 cm^{-1}; ^1H nmr: δ 7.3-7.46 (m, 2 aromatic *H*, NH_2), 7.55-7.65 (m, 1 aromatic *H*), 7.85-7.95 (m, 1 aromatic *H*), 8.7 (s, 4-*H*).

REFERENCES AND NOTES

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