

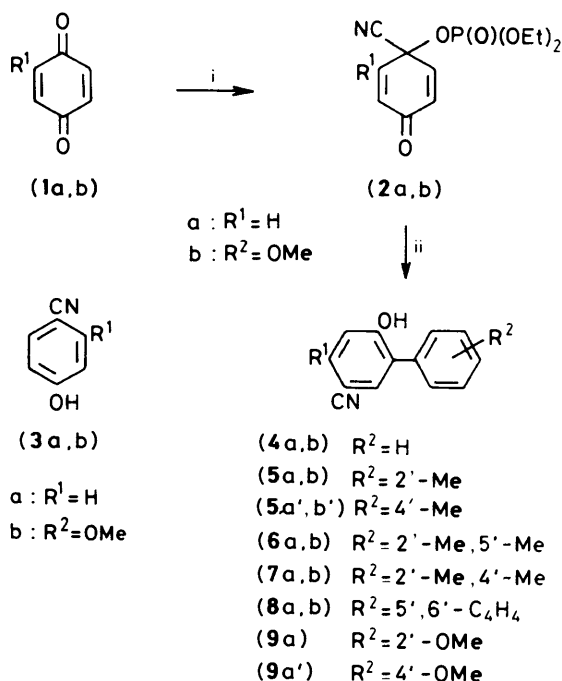
## Regiospecific Arylation of 1,4-Benzoquinone Cyanohydrin Phosphate: Synthesis of 3-Aryl-4-hydroxybenzonitriles

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Reaction of 1,4-benzoquinones (**1a,b**) with diethyl phosphorocyanidate and lithium cyanide was found to give the monocyanophosphates (**2a,b**). When catalysed by  $\text{BF}_3 \cdot \text{OEt}_2$ , the cyanophosphates (**2a,b**) reacted with aromatic and heteroaromatic compounds (indole, thiophene, and furan derivatives) to give 3-aryl-4-hydroxybenzonitriles. Under the same conditions ethyl 1-methylindole-2-carboxylate and 2,5-dimethylfuran were converted into 6-oxobenzopyrano[3,4-*b*]indole-2-carbonitriles (**15a,b**) and benzofuran-5-carbonitriles (**22a,b**) by reaction with the cyanophosphates (**2a,b**), respectively.

In a previous paper,<sup>1</sup> we reported the development of a new and high yield synthesis of  $\alpha,\beta$ -unsaturated nitriles from aromatic ketones *via* a reaction sequence involving cyanophosphorylation using diethyl phosphorocyanidate [DEPC,  $(\text{EtO})_2\text{P}(\text{O})\text{CN}$ ] in the presence of lithium cyanide (LiCN) followed by dephosphorylation with  $\text{BF}_3 \cdot \text{OEt}_2$ . Previously Evans and his co-workers reported a general method for the reverse protection of a 1,4-benzoquinone carbonyl group using trimethylsilylcyanide (TMSCN).<sup>2</sup> With this in mind we have examined the reaction of 1,4-benzoquinones (**1a**) and (**1b**) with DEPC and LiCN, since the 1,4-benzoquinone-TMSCN adduct is closely related to 1,4-benzoquinone cyanohydrin phosphate.<sup>3</sup> We now report the cyanophosphorylation of (**1a,b**), and use of the products (**2a,b**) in the synthesis of biaryls (3-aryl-4-hydroxybenzonitriles), a process related to the Meerwein arylation of quinones.<sup>4</sup>



Scheme 1. Reagents: i DEPC/LiCN; ii  $\text{ArR}^2/\text{BF}_3 \cdot \text{OEt}_2$

† The mechanism for the formation of (**3a**) is not yet clear.

Treatment of compound (**1a**) with DEPC (1.2 equiv.) and LiCN (0.3 equiv.) in THF at room temperature gave the monocyanophosphate (**2a**) (56%), accompanied by 4-hydroxybenzonitrile (**3a**)† (5%). The structure of (**2a**) was confirmed by i.r.,  $^1\text{H}$  n.m.r. and mass spectroscopic evidence (see Experimental section). When the cyanophosphate (**2a**) was boiled under reflux in dry benzene in the presence of  $\text{BF}_3 \cdot \text{OEt}_2$  (3 equiv.) for 1 h, 4-hydroxy-3-phenylbenzonitrile (**4a**) (78%) was obtained as a sole product (Scheme 1). The reaction did not proceed without a catalyst even with a longer reaction time. The structure of (**4a**) was confirmed on the basis of the spectral evidence and by comparison of its melting point with that of an authentic material.<sup>5</sup> The noteworthy regioselective introduction of the benzene ring may be explained by an  $\text{S}_{\text{N}}2'$  process whereby  $\text{BF}_3$  co-ordinates with the phosphate oxygen,<sup>6</sup> and thus precedes nucleophilic attack of the benzene on the allylic position; this is followed by aromatisation. Table 1 summarises the results with other aromatic compounds as well as the results of the reaction of the 2-methoxy analogue (**2b**) with aromatic compounds. Heteroaromatic compounds can also function as the nucleophilic species, 1-substituted and 1,2-disubstituted indoles reacting with compounds (**2a**) and (**2b**) in the presence of  $\text{BF}_3 \cdot \text{OEt}_2$  in acetonitrile to give 3-phenylindoles (**10a,b**), (**11a**), (**12a**), and (**13a**); 1,3-dimethylindole afforded the 2-phenylindole derivative (**14**) on reaction with (**2a,b**) (see Table 2). Ethyl 1-methylindole-2-carboxylate was found to react with (**2a,b**) in the presence of  $\text{BF}_3 \cdot \text{OEt}_2$  in acetonitrile to give 6-oxobenzopyrano[3,4-*b*]indole-2-carbonitrile (**15a,b**) in 30% and 15% yields, respectively, *via* an intermediate (**16a,b**) (Scheme 2). Thiophenes and furans similarly treated with (**2a,b**) gave the 2-furyl and 2-thienyl substituted derivatives of benzonitrile (**17a**), (**18a**), (**19a,b**) and (**20a,b**) (see Table 2) while 2,5-dimethylthiophene afforded 3-(2,5-dimethyl-3-thienyl)-4-hydroxybenzonitrile (**21**) in low yield. In contrast to the reaction of 2,5-dimethylthiophene, treatment of 2,5-dimethylfuran with (**2a**) provided the unexpected product of 2-methyl-3-(2-oxopropyl)benzofuran-5-carbonitrile (**22a**) (34%). The structure of (**22a**) was supported by its analytical and spectral data (see Experimental section). Similarly, 6-methoxybenzofuran-5-carbonitrile (**22b**) was obtained from (**2b**) in 49% yield (Scheme 3). The conversion of 2,5-dimethylfuran into the benzofuran-5-carbonitriles (**22a,b**) can be explained by the following reaction mechanism: initial arylation of 2,5-dimethylfuran gave the intermediate species 3-arylfurans (**23a,b**), which upon a subsequent ring-cyclisation ring-opening sequence gave the benzofurans (**22a,b**), as depicted in Scheme 4. The unsymmetrical 2,5-

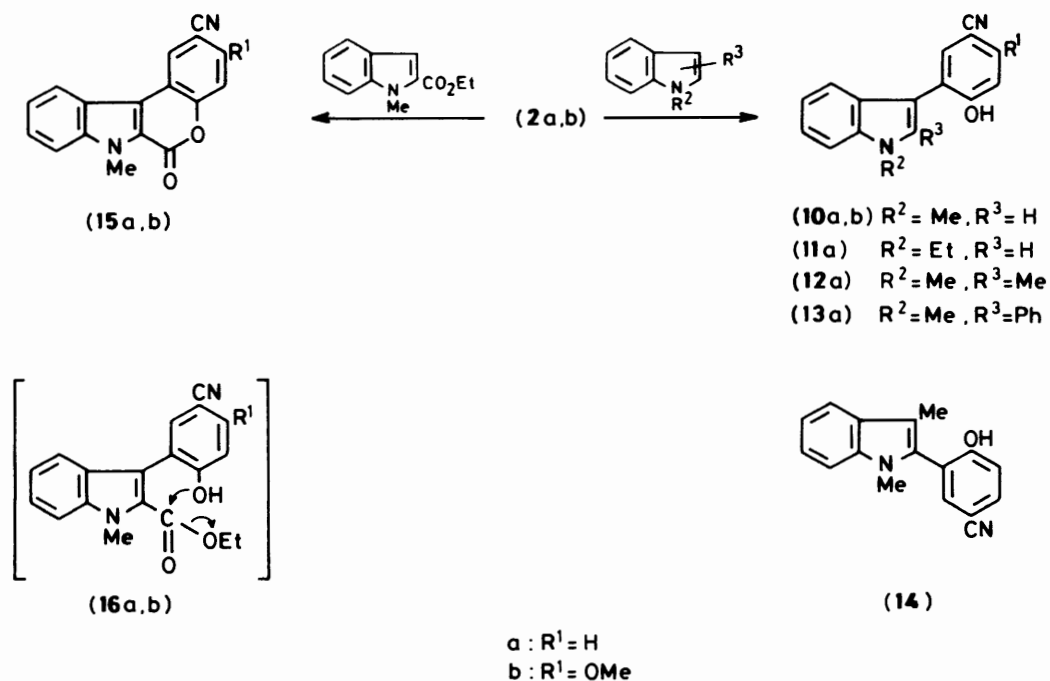
**Table 1.** Physical properties and analytical data for the 3-aryl-4-hydroxybenzonnitriles

Compound (Formula)	Yield (%)	Solvent	M.p. (°C)	Found (%) (Required)		
				C	H	N
(4a) <sup>a</sup> (C <sub>13</sub> H <sub>9</sub> NO)	78	Benzene-Hexane	125-127	79.9 (79.98)	4.6 (4.65)	7.15 (7.17)
(5a') <sup>a</sup> (C <sub>14</sub> H <sub>11</sub> NO)	83 <sup>c</sup>	Benzene-Hexane	146-148	80.35 (80.36)	5.0 (5.30)	6.4 (6.69)
(6a) <sup>a</sup> (C <sub>15</sub> H <sub>13</sub> NO)	82	Benzene	150-152	80.75 (80.69)	5.9 (5.87)	6.35 (6.27)
(7a) <sup>a</sup> (C <sub>15</sub> H <sub>13</sub> NO)	96	Benzene	124-126	80.9 (80.69)	6.1 (5.87)	6.35 (6.27)
(8a) <sup>b</sup> (C <sub>17</sub> H <sub>11</sub> NO)	75	Benzene-Hexane	172-174	83.5 (83.24)	4.3 (4.52)	5.95 (5.71)
(9a) <sup>b</sup> (C <sub>14</sub> H <sub>11</sub> NO <sub>2</sub> · <sup>1</sup> / <sub>3</sub> C <sub>6</sub> H <sub>6</sub> )	72 <sup>c</sup>	Benzene-Hexane	170-172	76.3 (76.47)	5.25 (5.22)	5.65 (5.57)
(4b) <sup>a</sup> (C <sub>14</sub> H <sub>11</sub> NO <sub>2</sub> )	18	Benzene	214-215	74.95 (74.65)	4.85 (4.92)	6.25 (6.22)
(5b) and (5b') <sup>a</sup> (C <sub>15</sub> H <sub>13</sub> NO <sub>2</sub> )	28 <sup>d</sup>	Benzene		75.1 (75.30)	5.6 (5.48)	5.65 (5.85)
(6b) <sup>a</sup> (C <sub>16</sub> H <sub>15</sub> NO <sub>2</sub> )	52	Benzene	158-160	76.15 (75.87)	6.0 (5.97)	5.40 (5.53)
(7b) <sup>a</sup> (C <sub>16</sub> H <sub>15</sub> NO <sub>2</sub> )	46	Benzene	124-126	76.0 (75.87)	5.8 (5.97)	5.50 (5.53)
(8b) <sup>b</sup> (C <sub>18</sub> H <sub>13</sub> NO <sub>2</sub> )	39	Benzene	192-193	78.8 (78.53)	4.7 (4.76)	5.0 (5.09)

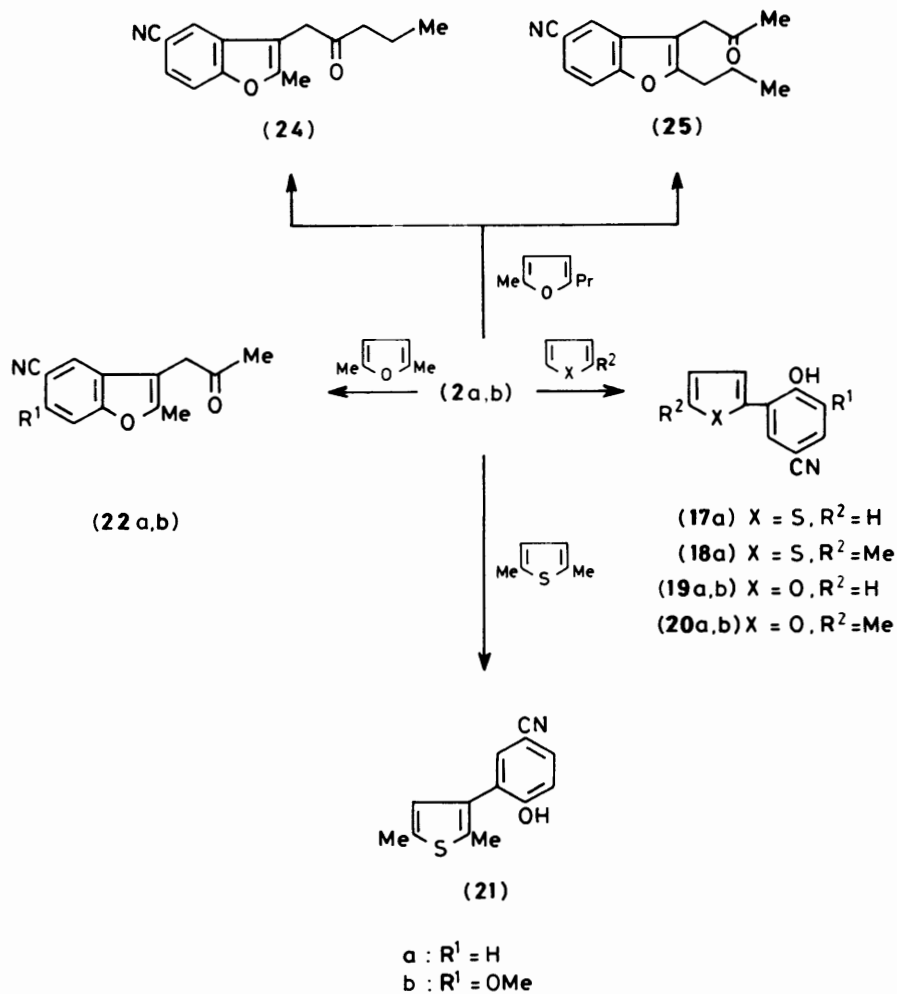
<sup>a</sup> This reaction was carried out in a substrate as solvent. <sup>b</sup> This reaction was carried out in refluxing acetonitrile. <sup>c</sup> This represents a combined yield of 2'- and 4'-substituted derivatives [(5a)/(5a') = 3:7 and (9a)/(9a') = 2:8, analysed by <sup>1</sup>H n.m.r.], but only (5a') and (9a') were isolated in a pure form. <sup>d</sup> This represents a combined yield of (5b) and (5b') (ca. 6:4, analysed by <sup>1</sup>H n.m.r.), but these were not separated in a pure form.

**Table 2.** Physical properties and analytical data for the 3-indolyl-, 3-thienyl-, and 3-furyl-4-hydroxybenzonnitriles

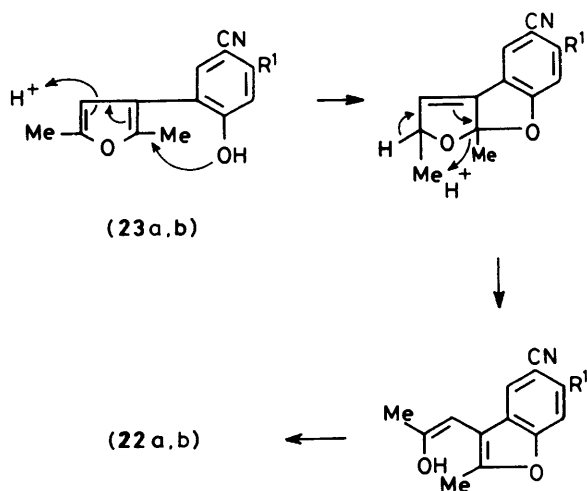
Compound (Formula)	Yield (%)	Solvent	M.p. (°C)	Found (%) (Required)		
				C	H	N
(10a) (C <sub>16</sub> H <sub>12</sub> N <sub>2</sub> O)	41	MeOH-Hexane	229-231	77.25 (77.49)	4.85 (4.87)	11.05 (11.28)
(11a) (C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O)	41	Benzene	170-172	77.75 (77.84)	5.35 (5.38)	10.8 (10.68)
(12a) (C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O)	60	Pr <sup>i</sup> OH	227-229	78.0 (77.84)	5.65 (5.38)	10.7 (10.68)
(13a) (C <sub>22</sub> H <sub>16</sub> N <sub>2</sub> O)	36	EtOH	265-266	81.6 (81.46)	5.2 (4.97)	8.4 (8.64)
(10b) (C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub> )	51	AcOEt-Benzene	240-242	73.3 (73.36)	5.03 (5.07)	10.05 (10.07)
(14) (C <sub>17</sub> H <sub>14</sub> N <sub>2</sub> O)	38	Benzene	192-194	77.9 (77.84)	5.4 (5.38)	10.45 (10.68)
(17a) (C <sub>11</sub> H <sub>7</sub> NOS)	20	Benzene-Ligroin	110-112	65.85 (65.65)	3.5 (3.51)	7.0 (6.96)
(18a) (C <sub>12</sub> H <sub>9</sub> NOS)	49	Benzene-Hexane	108-109	67.0 (66.95)	4.2 (4.21)	6.55 (6.51)
(19a) (C <sub>11</sub> H <sub>7</sub> NO <sub>2</sub> )	41	Benzene	158-160	70.85 (70.96)	4.05 (4.33)	7.5 (7.52)
(20a) (C <sub>12</sub> H <sub>9</sub> NO <sub>2</sub> )	55	Benzene-Hexane	156-158	72.4 (72.35)	4.55 (4.55)	7.05 (7.03)
(19b) (C <sub>12</sub> H <sub>9</sub> NO <sub>3</sub> )	31	AcEOt	234-235	66.85 (66.97)	4.2 (4.22)	6.4 (6.51)
(20b) (C <sub>13</sub> H <sub>11</sub> NO <sub>3</sub> )	44	Benzene	180-183	68.1 (68.11)	4.8 (4.84)	6.15 (6.11)
(21) (C <sub>13</sub> H <sub>11</sub> NOS)	8	Benzene-Ligroin	142-144	68.35 (68.09)	4.9 (4.84)	6.05 (6.11)



Scheme 2.



Scheme 3.



Scheme 4.

disubstituted furan 2-methyl-5-propylfuran gave a *ca.* 1:1 (by  $^1\text{H}$  n.m.r. analysis) mixture of the benzofurans (**24**) and (**25**) in 42% combined yield. The structures of (**24**) and (**25**), partially separated by chromatography on  $\text{SiO}_2$ , were established from their spectral data, especially from mass spectroscopy (see Experimental section).

## Experimental

$^1\text{H}$  N.m.r. spectra were determined with a Varian XL-300 spectrometer (tetramethylsilane as an internal standard), mass spectra with a Hitachi M-80 instrument, and i.r. spectra with a Shimadzu IR-435 spectrometer. Extracts from the reaction mixture were dried over anhydrous sodium sulphate.

**Diethyl 1-Cyano-4-oxocyclohexa-2,5-dienyl Phosphate (2a).**—A mixture of 1,4-benzoquinone (**1a**) (1.08 g, 10 mmol), DEPC (1.95 g, 12 mmol), and  $\text{LiCN}$  (0.1 g, 3 mmol) in THF (50 ml) was stirred at room temperature for 2 h. The solvent was removed under reduced pressure and the residue was dissolved in water (10 ml) and EtOAc (30 ml). The organic layer was separated, washed, dried, and evaporated and the residue was chromatographed on silica gel ( $\text{SiO}_2$ ). The first fraction eluted with benzene–EtOAc (5:1) gave starting material (**1a**) (378 mg, 35%). The second fraction eluted with benzene–EtOAc (5:1) gave 4-hydroxybenzonitrile (**3a**) (52 mg, 5%), whose i.r. spectrum was identical with that of an authentic sample.<sup>7</sup> The third fraction eluted with benzene–EtOAc (3:1) afforded the cyanophosphate (**2a**) (1.49 g, 55%) as a pale brown oil;  $\nu_{\text{max}}$  (liquid) 2 220 (CN), 1 675 (CO), 1 625 (C=C), 1 280 (P=O), and 1 140–900  $\text{cm}^{-1}$  (P–O–C);  $\delta(\text{CDCl}_3)$  1.35 (6 H, t,  $J$  8 Hz,  $\text{OCH}_2\text{Me}$ ), 4.15 (4 H, quint,  $J$  8 Hz,  $\text{OCH}_2\text{Me}$ ), 6.40 and 7.10 (4 H, ABq,  $J$  10 Hz,  $\text{CH}=\text{CH}$ ). (Found:  $M^+$ , 271.0609.  $\text{C}_{11}\text{H}_{14}\text{NO}_6\text{P}$  requires  $M$ , 271.0610).

**Diethyl 1-Cyano-2-methoxy-4-oxocyclohexa-2,5-dienyl Phosphate (2b).**—A mixture of (**1b**)<sup>8</sup> (1.38 g, 10 mmol), DEPC (1.95 g, 12 mmol), and  $\text{LiCN}$  (0.1 g, 3 mmol) in THF (50 ml) was treated as described for the preparation of the cyanophosphate (**2a**) to give a brown oil, which was chromatographed on  $\text{SiO}_2$ . The first fraction eluted with benzene–EtOAc (10:1) gave starting material (**1b**) (193 mg, 14%). The second fraction eluted with benzene–EtOAc (5:1) gave 4-hydroxy-2-methoxybenzonitrile (**3b**) (30 mg, 2%), m.p. 147–149 °C, recrystallised from benzene–ligroin (lit.,<sup>9</sup> 156–157 °C);  $\nu_{\text{max}}$  (Nujol) 3 250 (OH) and 2 220  $\text{cm}^{-1}$  (CN);  $\delta([\text{C}_2\text{H}_6]-\text{DMSO})$  3.84 (3 H, s, OMe), 6.47 (1 H, dd,  $J$  1.9 and 8 Hz, 5-H), 6.53 (1 H, d,  $J$  1.9 Hz, 3-H), 7.49 (1

H, d,  $J$  8 Hz, 6-H), and 10.65 (1 H, s, OH);  $m/z$  149 ( $M^+$ ). The third fraction eluted with benzene–EtOAc (3:1) afforded the cyanophosphate (**2b**) (2.17 g, 71%) as a pale brown oil;  $\nu_{\text{max}}$  (liquid) 2 220 (CN), 1 670 (CO), 1 630 (C=C), 1 280 (P=O), and 1 140–900  $\text{cm}^{-1}$  (P–O–C);  $\delta(\text{CDCl}_3)$  1.39 (6 H, m,  $\text{OCH}_2\text{Me}$ ), 3.92 (3 H, s, OMe), 4.20 (4 H, m,  $\text{OCH}_2\text{Me}$ ), 5.69 (1 H, d,  $J$  1.9 Hz, 3-H), 6.42 (1 H, dd,  $J$  1.9 and 9.9 Hz, 5-H), and 7.03 (1 H, d,  $J$  9.9 Hz, 6-H) (Found:  $M^+$ , 301.0714.  $\text{C}_{12}\text{H}_{16}\text{NO}_6\text{P}$  requires  $M^+$ , 301.0716).

**General Procedure for the Preparation of Biaryls (4a,b), (5a,b)(5a',b'), (6a,b), (7a,b) (8a,b), and (9a)(9a').**—A mixture of compounds (**2a,b**) (1 mmol) and  $\text{BF}_3 \cdot \text{OEt}_2$  (3 mmol) in substrates [benzene, toluene, *p*- and *m*-xylenes (3 mmol)] as solvent (10 ml) or MeCN (for anisole and naphthalene) (10 ml) was heated at 80–90 °C. After dilution with EtOAc (50 ml), the solution was washed, dried, and evaporated. The resultant biaryls were purified by chromatography on  $\text{SiO}_2$  using benzene–EtOAc (20:1) as eluant to give colourless crystals.

**4-Hydroxy-3-phenylbenzonitrile (4a).** The reaction time was 1 h;  $\nu_{\text{max}}$  (Nujol) 3 340 (OH), 2 210 (CN), and 1 600  $\text{cm}^{-1}$  (C=C);  $\delta(\text{CDCl}_3)$  5.80 (1 H, br s, OH), 7.07 (1 H, d,  $J$  9 Hz, 5-H), and 7.4–7.65 (7 H, m, ArH);  $m/z$  195 ( $M^+$ ).

**4-Hydroxy-3-(*p*-tolyl)benzonitrile (5a').** The crude product obtained by the general procedure (reaction time 1 h) from the cyanophosphate (**2a**) was purified by  $\text{SiO}_2$  column chromatography with benzene–EtOAc (20:1) as eluant to give a colourless solid, which showed the presence of two components (**5a**) and (**5a'**) in a ratio of *ca.* 3:7 in its  $^1\text{H}$  n.m.r. spectrum [ $\delta$  2.10 and 2.40 (each s, Me)]. The mixture was again chromatographed on  $\text{SiO}_2$  using benzene as an eluant to afford pure (**5a'**) (45 mg);  $\nu_{\text{max}}$  (Nujol) 3 340 (OH), 2 220 (CN), and 1 595  $\text{cm}^{-1}$  (C=C);  $\delta(\text{CDCl}_3)$  2.40 (3 H, s, 4'-Me), 6.10 (1 H, s, OH), 7.0 (1 H, d,  $J$  8 Hz, 5-H), 7.35–7.4 (5 H, m, ArH), and 7.45 (1 H, dd,  $J$  8 and 2.5 Hz, 6-H).

**3-(2,5-Dimethylphenyl)-4-hydroxybenzonitrile (6a).** The reaction time was 0.5 h;  $\nu_{\text{max}}$  (Nujol) 3 320 (OH), 2 210 (CN), and 1 600  $\text{cm}^{-1}$  (C=C);  $\delta(\text{CDCl}_3)$  2.09 (3 H, s, 2'-Me), 2.36 (3 H, s, 5'-Me), 4.05 (1 H, br s, OH), 7.0 (1 H, s, 6'-H), 7.05 (1 H, d,  $J$  8.4 Hz, 5-H), 7.25 (2 H, m, 3'- and 4'-H), 7.40 (1 H, d,  $J$  2 Hz, 2-H), and 7.60 (1 H, d,  $J$  8.4 Hz, 6-H).

**3-(2,4-Dimethylphenyl)-4-hydroxybenzonitrile (7a).** The reaction time was 0.5 h;  $\nu_{\text{max}}$  (Nujol) 3 330 (OH), 2 210 (CN), and 1 595  $\text{cm}^{-1}$  (C=C);  $\delta(\text{CDCl}_3)$  2.10 (3 H, s, 2'-Me), 2.38 (3 H, s, 4'-Me), 7.05–7.20 (4 H, m, ArH), 7.42 (1 H, d,  $J$  2 Hz, 2-H), and 7.58 (1 H, d,  $J$  8.4 Hz, 6-H).

**4-Hydroxy-3-(1-naphthyl)benzonitrile (8a).** The reaction time was 1 h;  $\nu_{\text{max}}$  (Nujol) 3 260 (OH), 2 210 (CN), and 1 610  $\text{cm}^{-1}$  (C=C);  $\delta(\text{CDCl}_3)$  5.40 (1 H, s, OH), 7.18 (1 H, d,  $J$  8.5 Hz, 5-H), 7.45–7.70 (6 H, m, ArH), and 8.0 (2 H, t,  $J$  8.5 Hz, 2'- and 8'-H).

**4-Hydroxy-3-(4-methoxyphenyl)benzonitrile (9a').** The crude product obtained by the general procedure (reaction time 10 min) from the cyanophosphate (**2a**) was purified by  $\text{SiO}_2$  column chromatography with benzene–EtOAc (20:1) as eluant to give a colourless solid, which showed the presence of two components (**9a**) and (**9a'**) in a ratio of 2:8 in its  $^1\text{H}$  n.m.r. spectrum [ $\delta$  3.75 and 3.85 (each s, OMe)]. The mixture was again chromatographed on  $\text{SiO}_2$  using benzene as an eluant to give pure (**9a'**) (210 mg);  $\nu_{\text{max}}$  (Nujol) 3 320 (OH), 2 210 (CN), and 1 600  $\text{cm}^{-1}$  (C=C);  $\delta(\text{CDCl}_3)$  3.85 (3 H, s, OMe), 6.05 (1 H, s, OH), 6.95 (1 H, d,  $J$  8 Hz, 5-H), 7.10 (4 H, ABq,  $J$  8.5 Hz, ArH), 7.15 (1 H, d,  $J$  2 Hz, 2-H), and 7.45 (1 H, dd,  $J$  2 and 8 Hz, 6-H);  $m/z$  225 ( $M^+$ ).

**4-Hydroxy-2-methoxy-5-phenylbenzonitrile (4b).** The reaction time was 0.5 h;  $\nu_{\text{max}}$  (Nujol) 3 300 (OH), 2 205 (CN), and 1 608  $\text{cm}^{-1}$  (C=C);  $\delta([\text{C}_2\text{H}_6]-\text{DMSO})$  3.88 (3 H, s, OMe), 6.71 (1 H, s, 3-H), 7.28–7.58 (6 H, m, ArH), and 10.89 (1 H, s, OH);  $m/z$  225 ( $M^+$ ).

4-Hydroxy-2-methoxy-5-(*o*- or *p*-tolyl)benzonitrile (**5b**) and (**5b'**). The products (**5b**) and (**5b'**) obtained by the general procedure (reaction time 0.5 h) from the cyanophosphate (**2b**) were not separated in a pure form;  $\nu_{\max}$ . (Nujol) 3 250 (OH), 2 210 (CN), and 1 605  $\text{cm}^{-1}$  (C=C);  $\delta(\text{CDCl}_3)$  2.15 and 2.41 (s, Me) 3.93 and 3.95 (s, OMe), 6.59 and 6.65 (s, 3-H), and 7.20—7.50 (m, ArH).

5-(2,5-Dimethylphenyl)-4-hydroxy-2-methoxybenzonitrile (**6b**). The reaction time was 0.5 h;  $\nu_{\max}$ . (Nujol) 3 280 (OH), 2 205 (CN), and 1 610  $\text{cm}^{-1}$  (C=C);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  2.04 and 2.27 (3 H, s, 2- and 5-Me), 3.89 (3 H, s, OMe), 6.68 (1 H, s, 3-H), 6.90 (1 H, s, 6'-H), 7.04 and/or 7.11 (1 H, d, *J* 7.9 Hz, 3'- and/or 2'-H), 7.37 (1 H, s, 6-H), and 10.67 (1 H, s, OH); *m/z* 253 ( $M^+$ ).

5-(2,4-Dimethylphenyl)-4-hydroxy-2-methoxybenzonitrile (**7b**). The reaction time was 0.5 h;  $\nu_{\max}$ . (Nujol) 3 200 (OH), 2 205 (CN), and 1 600  $\text{cm}^{-1}$  (C=C);  $\delta(\text{CDCl}_3)$  2.10 and 2.35 (3 H, s, 2- and 5-Me), 3.80 (3 H, s, OMe), 5.55 (1 H, br s, OH), 6.55 (1 H, s, 3-H), and 7.0—7.3 (4 H, m, ArH); *m/z* 253 ( $M^+$ ).

4-Hydroxy-2-methoxy-5-(1-naphthyl)benzonitrile (**8b**). The reaction time was 1 h;  $\nu_{\max}$ . (Nujol) 3 240 (OH), 2 200 (CN), and 1 595  $\text{cm}^{-1}$  (C=C);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  3.93 (3 H, s, OMe), 6.77 (1 H, s, 3-H), 7.39—7.60 (6 H, m, ArH), and 7.95 (2 H, t, *J* 8.6 Hz, 2'- and 8'-H).

*General Procedure for the Preparation of Indol-3-yl-, 3-Thienyl- and 3-Furyl-4-hydroxybenzonitriles [(10a,b), (11a), (12a), (13a), (14), (17a), (18a), (19a,b), (20a,b), and (21)].*—A mixture of the compounds (**2a,b**) (1 mmol) and substrate (2 mmol) containing  $\text{BF}_3 \cdot \text{OEt}_2$  (3 mmol) in MeCN (5 ml) was heated at 50 °C for 0.5 h. After being diluted with EtOAc (30 ml), the solution was washed, dried, and evaporated. The crude product was purified by  $\text{SiO}_2$  column chromatography to give colourless crystals.

4-Hydroxy-3-(1-methylindol-3-yl)benzonitrile (**10a**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and 1-methylindole was purified (benzene-EtOAc, 10:1);  $\nu_{\max}$ . (Nujol) 3 340 (OH) and 2 220  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  3.88 (3 H, s, NMe), 6.83 (1 H, dd, *J* 8.6 and 2 Hz, 6-H), 7.10 (1 H, d, *J* 2 Hz, 2-H), 7.14—7.66 (4 H, m, ArH), 7.71 (1 H, d, *J* 8.6 Hz, 5-H), 7.75 (1 H, s, 2'-H), and 10.62 (1 H, s, OH); *m/z* 248 ( $M^+$ ).

3-(1-Ethylindol-3-yl)-4-hydroxybenzonitrile (**11a**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and 1-ethylindole was purified (benzene-hexane 1:1);  $\nu_{\max}$ . (Nujol) 3 330 (OH) and 2 220  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  1.41 (3 H, t, *J* 7.3 Hz,  $\text{CH}_2\text{Me}$ ), 4.30 (2 H, q, *J* 7.3 Hz,  $\text{CH}_2\text{Me}$ ), 6.83 (1 H, dd, *J* 8.6 and 2.6 Hz, 6-H), 7.11 (1 H, d, *J* 2.6 Hz, 2-H), 7.15—7.65 (4 H, m, ArH), 7.72 (1 H, d, *J* 8.6 Hz, 5-H), 7.81 (1 H, s, 2'-H), and 10.60 (1 H, s, OH).

3-(1,2-Dimethylindol-3-yl)-4-hydroxybenzonitrile (**12a**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and 1,2-dimethylindole was purified (benzene-EtOAc 20:1);  $\nu_{\max}$ . (Nujol) 3 320 (OH) and 2 230  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  2.38 (3 H, s, Me), 3.79 (3 H, s, NMe), 6.88—6.92 (2 H, m, 2- and 6-H), 7.05—7.49 (4 H, m, ArH), 7.74 (1 H, d, *J* 8.2 Hz, 5-H), and 10.60 (1 H, s, OH).

4-Hydroxy-3-(1-methyl-2-phenylindol-3-yl)benzonitrile (**13a**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and 1-methyl-2-phenylindole was purified (benzene);  $\nu_{\max}$ . (Nujol) 3 400 (OH) and 2 210  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  3.72 (3 H, s, NMe), 6.74—7.62 (12 H, m, ArH), and 10.51 (1 H, s, OH).

4-Hydroxy-3-methoxy-5-(1-methylindol-3-yl)benzonitrile (**10b**). The crude product obtained by the general procedure from the cyanophosphate (**2b**) and 1-methylindole was purified (benzene-EtOAc 10:1);  $\nu_{\max}$ . (Nujol) 3 300 (OH) and 2 210  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  3.87 and 3.89 (3 H, s, NMe and/or OMe), 6.49 (1 H, s, 5-H), 6.70 (1 H, s, 2-H), 7.15—7.64 (4 H, m, ArH), 7.72 (1 H, s, 2'-H), and 10.60 (1 H, s, OH).

3-(1,3-Dimethylindol-2-yl)-4-hydroxybenzonitrile (**14**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and 1,3-dimethylindole was purified (benzene-EtOAc 20:1);  $\nu_{\max}$ . (Nujol) 3 270 (OH) and 2 220  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  2.11 (3 H, s, Me), 3.49 (3 H, s, NMe), 7.06—7.53 (5 H, m, ArH), 7.70 (1 H, d, *J* 2 Hz, 2-H), 7.77 (1 H, dd, *J* 8.6 and 2 Hz, 2-H), and 10.97 (1 H, s, OH).

4-Hydroxy-3-(2-thienyl)benzonitrile (**17a**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and thiophene was purified (benzene-EtOAc 20:1);  $\nu_{\max}$ . (Nujol) 3 270 (OH) and 2 220  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  6.90 (1 H, dd, *J* 8.6 and 2.2 Hz, 6-H), 7.04 (1 H, d, 2-H), 7.22 (1-H, dd, *J* 5.4 and 3.6 Hz, 4'-H), 7.55 (1 H, dd, *J* 3.6 and 1.5 Hz, 3'-H), 7.73—7.76 (2 H, m, 5- and 5'-H), and 10.83 (1 H, s, OH).

4-Hydroxy-3-(5-methyl-2-thienyl)benzonitrile (**18a**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and 2-methylthiophene was purified (benzene-EtOAc 10:1);  $\nu_{\max}$ . (Nujol) 3 290 (OH) and 2 220  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  2.51 (3 H, s, Me), 6.86 (1 H, dd, *J* 8.6 and 2.3 Hz, 6-H), 6.90 (1 H, d, *J* 3.6 Hz, 4'-H), 6.98 (1 H, d, *J* 2.3 Hz, 2-H), 7.38 (1 H, d, *J* 3.6 Hz, 3'-H), 7.71 (1 H, d, *J* 8.6 Hz, 5-H), and 10.79 (1 H, s, OH).

3-(2-Furyl)-4-hydroxybenzonitrile (**19a**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and furan was purified (benzene-EtOAc 20:1);  $\nu_{\max}$ . (Nujol) 3 320 (OH) and 2 210  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  6.71 (1 H, dd, *J* 3.4 and 2.0 Hz, 4'-H), 6.86 (1 H, dd, *J* 8.6 and 2.6 Hz, 6-H), 7.21 (1 H, dd, *J* 3.4 and 1.0 Hz, 3'-H), 7.25 (1 H, d, *J* 2.6 Hz, 2-H), 7.72 (1 H, d, *J* 8.6 Hz, 5-H), 7.90 (1 H, dd, *J* 2.0 and 1.0 Hz, 5'-H), and 10.80 (1 H, s, OH).

4-Hydroxy-3-(5-methyl-2-furyl)benzonitrile (**20a**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and 2-methylfuran was purified (benzene-EtOAc 10:1);  $\nu_{\max}$ . (Nujol) 3 250 (OH) and 2 220  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  2.37 (3 H, s, Me), 6.32 (1 H, d, *J* 3.6 Hz, 4'-H), 6.80 (1 H, dd, *J* 8.6 and 2.3 Hz, 6-H), 7.11 (1 H, d, *J* 3.6 Hz, 3'-H), 7.21 (1 H, d, *J* 2.3 Hz, 2-H), 7.68 (1 H, d, *J* 8.6 Hz, 5-H), and 10.70 (1 H, s, OH).

5-(2-Furyl)-4-hydroxy-3-methoxybenzonitrile (**19b**). The crude product obtained by the general procedure from the cyanophosphate (**2b**) and furan was purified (benzene-EtOAc, 5:1);  $\nu_{\max}$ . (Nujol) 3 250 (OH) and 2 220  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  3.88 (3 H, s, OMe), 6.52 (1 H, s, 6-H), 6.68—6.70 (1 H, m, 4'-H), 6.89 (1 H, s, 2-H), 7.20 (1 H, d, *J* 3.6 Hz, 3'-H), 7.88 (1 H, d, *J* 2.2 Hz, 5'-H), and 10.83 (1 H, s, OH).

4-Hydroxy-3-methoxy-5-(5-methyl-2-furyl)benzonitrile (**20b**). The crude product obtained by the general procedure from the cyanophosphate (**2b**) and 2-methylfuran was purified (benzene-EtOAc 5:1);  $\nu_{\max}$ . (Nujol) 3 220 (OH) and 2 220  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  2.37 (3 H, s, Me), 3.91 (3 H, s, OMe), 5.64 (1 H, s, OH), 6.13 (1 H, d, *J* 3.6 Hz, 3'-H), 6.33 (1 H, s, 5-H), 6.89 (1 H, s, 2-H), and 7.27 (1 H, d, *J* 3.6 Hz, 4'-H).

3-(2,5-Dimethyl-3-thienyl)-4-hydroxybenzonitrile (**21**). The crude product obtained by the general procedure from the cyanophosphate (**2a**) and 2,5-dimethylthiophene was purified (benzene-EtOAc, 10:1);  $\nu_{\max}$ . (Nujol) 3 270 (OH) and 2 230  $\text{cm}^{-1}$  (CN);  $\delta([\text{H}_6\text{O}]\text{-DMSO})$  2.22 and 2.38 (3 H, s, 2'- and/or 5'-Me), 6.67 (1 H, s, 4'-H), 7.05 (1 H, d, *J* 8.7 Hz, 5-H), 7.52 (1 H, d, *J* 1.8 Hz, 2-H), 7.60 (1 H, dd, *J* 8.7 and 1.8 Hz, 6-H), and 10.68 (1 H, s, OH).

*Reaction of the Cyanophosphates (2a) and (2b) with Ethyl 1-Methylindole-2-carboxylate.*—A mixture of the compounds (**2a,b**) (2 mmol), ethyl 1-methylindole-2-carboxylate (815 mg, 4 mmol), and  $\text{BF}_3 \cdot \text{OEt}_2$  (682 mg, 4.8 mmol) in MeCN (5 ml) was heated at 50 °C for 40 min. After the mixture had been cooled in an ice-bath, the resulting precipitate was collected, washed with cold EtOH, and dried. The residue from the

mother liquor was chromatographed on SiO<sub>2</sub>. The fraction eluted with benzene–EtOAc (10:1) gave a further crop of product which was recrystallised from MeCN.

**7-Methyl-6-oxobenzopyrano[3,4-b]indole-2-carbonitrile (15a).** Yield, 30%; m.p. 270–272 °C;  $\nu_{\max}$ . (KBr) 2 220 (CN) and 1 725 cm<sup>-1</sup> (CO);  $\delta$ ([<sup>2</sup>H<sub>6</sub>]-DMSO) 4.19 (3 H, s, NMe), and 7.41–8.85 (7 H, m, ArH);  $m/z$  274 ( $M^+$ ) (Found: C, 74.35; H, 3.75; N, 10.15. C<sub>17</sub>H<sub>10</sub>N<sub>2</sub>O<sub>2</sub> requires C, 74.44; H, 3.68; N, 10.21%).

**3-Methoxy-7-methyl-6-oxobenzopyrano[3,4-b]indole-2-carbonitrile (15b).** Yield, 15%; m.p. > 300 °C;  $\nu_{\max}$ . (KBr) 2 220 (CN) and 1 720 cm<sup>-1</sup> (CO);  $\delta$ ([<sup>2</sup>H<sub>6</sub>]-DMSO) 4.02 (3 H, s, OMe), 4.20 (3 H, s, NMe), 7.46 (1 H, s, 4-H), 7.20–8.69 (4 H, m, ArH), and 8.82 (1 H, s, 1-H);  $m/z$  304 ( $M^+$ ) (Found: C, 70.1; H, 3.95; N, 9.10. C<sub>18</sub>H<sub>12</sub>N<sub>2</sub>O<sub>3</sub>· $\frac{1}{3}$ H<sub>2</sub>O requires C, 70.21; H, 4.06; N, 9.10%).

**Reaction of the Cyanophosphates (2a) and (2b) with 2,5-Dimethylfuran.**—A mixture of the compounds (2a,b) (3 mmol), 2,5-dimethylfuran (579 mg, 6 mmol), and BF<sub>3</sub>·OEt<sub>2</sub> (852 mg, 6 mmol) in MeCN (12 ml) was heated at 50 °C for 45 min. The solvent was removed under reduced pressure and the residue was diluted with EtOAc. The organic solution was washed, dried, evaporated and the residue was purified by column chromatography on SiO<sub>2</sub> eluted with benzene–EtOAc (15:1).

**2-Methyl-3-(2-oxopropyl)benzofuran-5-carbonitrile (22a).** Yield, 34%; m.p. 133–135 °C (recrystallised from benzene–ligroin);  $\nu_{\max}$ . (KBr) 2 220 (CN) and 1 710 cm<sup>-1</sup> (CO);  $\delta$ ([<sup>2</sup>H<sub>6</sub>]-DMSO) 2.18 and 2.21 (3 H, s, 2-Me and/or COMe), 4.09 (2 H, s, CH<sub>2</sub>CO), 7.70–8.13 (3 H, m, ArH);  $m/z$  213 ( $M^+$ ) (Found: C, 73.25; H, 5.20; N, 6.65. C<sub>13</sub>H<sub>11</sub>NO<sub>2</sub> requires C, 73.22; H, 5.20; N, 6.57%).

**6-Methoxy-2-methyl-3-(2-oxopropyl)benzofuran-5-carbonitrile (22b).** Yield, 49%; m.p. 154–156 °C (recrystallised from benzene–ligroin);  $\nu_{\max}$ . (KBr) 2 220 (CN) and 1 710 cm<sup>-1</sup> (CO);  $\delta$ ([<sup>2</sup>H<sub>6</sub>]-DMSO) 2.13 and 2.18 (3 H, s, 2-Me and/or COMe), 3.39 (3 H, s, OMe), 4.0 (2 H, s, CH<sub>2</sub>CO), 7.42 (1 H, s, 6-H), and 7.98 (1 H, s, 4-H);  $m/z$  243 ( $M^+$ ) (Found: C, 69.20; H, 5.4; N, 5.75. C<sub>14</sub>H<sub>13</sub>NO<sub>3</sub> requires C, 69.12; H, 5.39; N, 5.76%).

**Reaction of the Cyanophosphate (2a) with 2-Methyl-5-propylfuran.**—A mixture of the cyanophosphate (2a) (4.09 g, 15.08 mmol), 2-methyl-5-propylfuran (3.74 g, 30.16 mmol), and BF<sub>3</sub>·OEt<sub>2</sub> (5.14 g, 36.2 mmol) in MeCN (10 ml) was heated at 50 °C for 2.5 h. The solvent was removed under reduced

pressure and the residue was diluted with EtOAc. The organic solution was washed, dried, evaporated and the residue was purified by column chromatography on SiO<sub>2</sub> eluted with benzene–EtOAc (30:1) to give a viscous oil (1.51 g, 42%), which was found to be a mixture of the benzofurans (24) and (25) in a ratio of ca. 1:1 by <sup>1</sup>H n.m.r. spectroscopy. These were partially separated by chromatography on SiO<sub>2</sub> using benzene as an eluant.

**2-Methyl-3-(4-oxopentyl)benzofuran-5-carbonitrile (24).** Colourless crystals; m.p. 78–80 °C (recrystallised from benzene–ligroin);  $\nu_{\max}$ . (Nujol) 2 220 (CN) and 1 720 cm<sup>-1</sup> (CO);  $\delta$ (CDCl<sub>3</sub>) 0.91 (3 H, t, *J* 7.3 Hz, CH<sub>2</sub>Me), 1.65 (2 H, m, CH<sub>2</sub>Me), 2.21 (3 H, s, CMe), 2.50 (2 H, s, *J* 7.3 Hz, COCH<sub>2</sub>), 3.84 (2 H, s, CH<sub>2</sub>CO), 7.50 (2 H, m, 6- and 7-H), and 7.80 (1 H, s, 4-H);  $m/z$  241 ( $M^+$ , 12%), 170 (20), and 71 (100) (Found: C, 74.9; H, 6.25; N, 5.75. C<sub>15</sub>H<sub>15</sub>NO<sub>2</sub> requires C, 74.66; H, 6.27; N, 5.81%).

**3-(2-Oxopropyl)-2-propylbenzo[b]furan-5-carbonitrile (25).** Colourless oil;  $\nu_{\max}$ . (liquid) 2 220 (CN) and 1 720 cm<sup>-1</sup> (CO);  $\delta$ ([<sup>2</sup>H<sub>6</sub>]-DMSO) 0.96 (3 H, t, *J* 7.5 Hz, CH<sub>2</sub>Me), 1.68 (2 H, m, CH<sub>2</sub>Me), 2.25 (3 H, s, COMe), 2.61 (2 H, t, *J* 7.5 Hz, CH<sub>2</sub>CH<sub>2</sub>Me), 3.86 (2 H, s, CH<sub>2</sub>CO), 7.50 (2 H, m, 6- and 7-H), and 7.84 (1 H, s, 4-H);  $m/z$  241 ( $M^+$ , 35%), 199 (65), and 43 (100) (Found:  $M^+$ , 241.1102. C<sub>15</sub>H<sub>15</sub>NO<sub>2</sub> requires  $M$ , 241.1103).

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