Reaction of 4-(*N*,*N*-Dimethylamino)-2-phenyl-2-(2-pyridyl)butanenitrile and Related Compounds with Ethyl Chloroformate; Formation of Indolizinium and Quinolizinium Chlorides

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4-(*N*,*N*-Dialkylamino)-2-phenyl-2-(2-pyridyl)butanenitriles (10, 11 and 12) and 5-(*N*,*N*-dimethylamino)-2-phenyl-2-(2-pyridyl)pentanenitrile (13) react with ethyl chloroformate, *via* a cyclization–*N*-dealkylation process, to give indolizinium and quinolizinium salts (1 and 2). Compounds 1 and 2 are also obtained by reaction of the alcohol derivatives 14 and 15 with thionyl chloride. Reaction of 2-phenyl-2-(2-pyridyl)ethanenitrile (9) in the presence of potassium hydroxide in dimethyl sulfoxide, leading to [2-hydroxy-2-phenyl-2-(2-pyridyl)ethyl]methylsulfoxide (21), is also described.

Keywords 1-cyano-2,3-dihydro-1-phenyl-1*H*-indolizinium chloride; 1-cyano-1-phenyl-1,2,3,4-tetrahydroquinolizinium chloride; *N*-dealkylation; cyclization

As part of an extensive research program on the preparation of anticholinergic and antihistaminergic agents, we needed relatively large quantities of 4-(*N*-methylamino)-2-phenyl-2-(2-pyridyl)butanenitrile. Reaction of chloroformate with tertiary aliphatic and alicyclic bases often provides a convenient method for promoting dealkylation.[1] When 4-(*N*,*N*-dimethylamino)-2-phenyl-2-(2-pyridyl)butanenitrile (**10**)[2] was allowed to react with ethyl chloroformate in refluxing CH_2Cl_2, an unexpected cyclization–*N*-dealkylation product, 1-cyano-2,3-dihydro-1-phenyl-1*H*-indolizinium chloride (**1**) was obtained along with the normal *N*-demethylation product (**3**). In this paper we would like to report the reaction of **10** and related compounds with ethyl chloroformate, leading to indolizinium (**1**) and quinolizinium (**2**) salts. The reaction of 2-phenyl-2-(2-pyridyl)ethanenitrile (**9**)[3] in the presence of potassium hydroxide (KOH) in dimethyl sulfoxide (DMSO), leading to [2-hydroxy-2-phenyl-2-(2-pyridyl)ethyl]methylsulfoxide (**21**),[4] is also described.

Results and Discussion

Reaction of **10** with ethyl chloroformate in CH_2Cl_2 was complete after 7 h under reflux to give the normal *N*-demethylation product **3** in 13% yield and the indolizinium chloride **1** as a viscous oil in 51% yield. The 90 MHz proton nuclear magnetic resonance (^{1}H-NMR) spectrum of **1** in a mixed solvent of $CDCl_3$ and D_2O is shown in Fig. 1. Signals between δ 7.2 and 9.1 were allocated to nine aromatic protons, among which four protons at δ 7.80, 8.10, 8.53 and 9.02 ppm were assigned to the pyridine ring. One of the CH_2 moieties in the CH_2CH_2 entity of **1** gave rise to an AA'XX' type spectum. A good resolved multiplet centered at δ 3.14 was assigned to the CH_2 adjacent to the carbon atom at the 1-position. A triplet centered at δ 5.08 (J=7.2 Hz) was assigned to the CH_2 connected to nitrogen. Thus, the structure of **1** was determined as 1-cyano-2,3-dihydro-1-phenyl-1*H*-indolizinium chloride. As can be seen in Table I, similar treatment of *N*,*N*-diethylamino (**11**) and piperidino (**12**) derivatives with ethyl chloroformate gave **1** in high yields. Reaction of 5-(*N*,*N*-dimethylamino)-2-phenyl-2-(2-pyridyl)pentanenitrile (**13**) with ethyl chloroformate yielded quinolizinium chloride **2** in a poor yield of 4% along with the normal *N*-demethylation product (**5**). Reaction of the alcohol **14** with thionyl chloride ($SOCl_2$) yielded **1**. Reaction of **15** with $SOCl_2$ gave **2** along with the chloro derivative **7**. Compound **7** was converted into **2** on standing at room temperature for 48 h in benzene. When **15** was treated with $SOCl_2$ in refluxing benzene, **2** was obtained in 85% yield without giving the chloro derivative **7**.

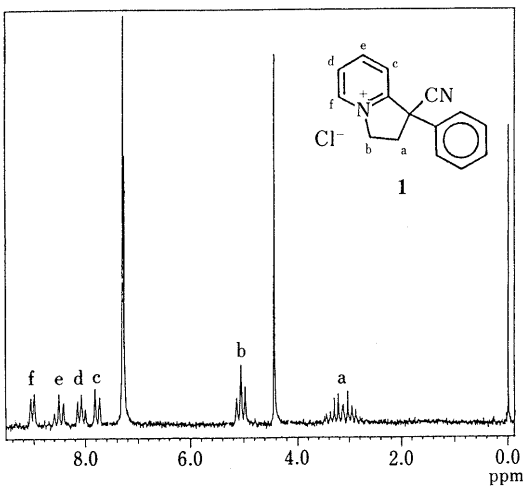

Fig. 1. ^{1}H-NMR Spectrum of **1**
$CDCl_3 + D_2O$, 90 MHz.

The cyclization–*N*-dealkylation observed in this series is depicted in Chart 2. First, a quaternary ammonium chloride intermediate (A) is formed. Then, the intermediate A is converted into the carbamate ester **3** (path iii) or has no net effect on the amine (path iv). Concerning the formation of **1** (or **2**), the reaction appears to proceed through

TABLE I. Preparation of Indolizinium and Quinolizinium Chlorides (**1** and **2**)

Starting material	Conditions[a]				Product (% isolated yield)
	Reagent	Solvent	Temperature	Time (h)	
10	A	CH_2Cl_2	ref	7	**1** (51), **3** (13)
11	A	CH_2Cl_2	ref	2	**1** (81), **4** (9)
12	A	CH_2Cl_2	ref	2	**1** (93)
13	A	CH_2Cl_2	ref	5	**2** (4), **5** (62)
14	B	CH_2Cl_2	rt	2	**1** (78)
15	B	C_6H_6	rt	2	**2** (54), **7** (36)
15	B	C_6H_6	ref	1	**2** (85)

a) A, ethyl chloroformate; B, thionyl chloride; ref, refluxing solvent; rt, room temperature.

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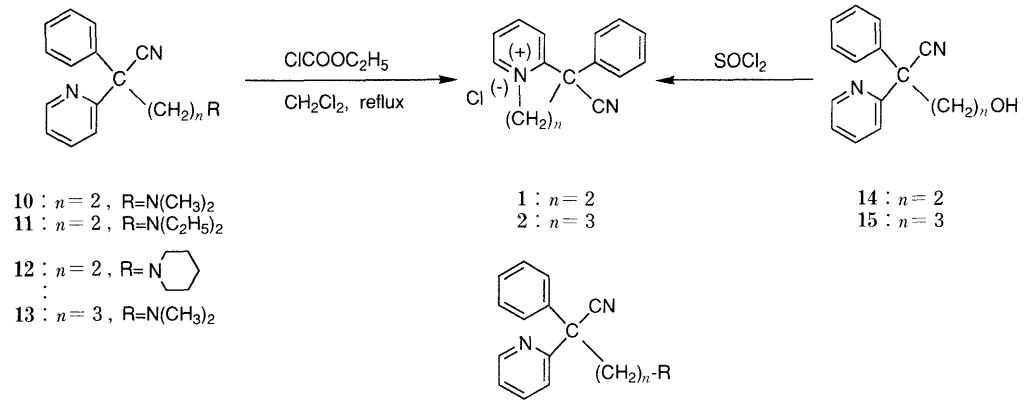

Chart 1

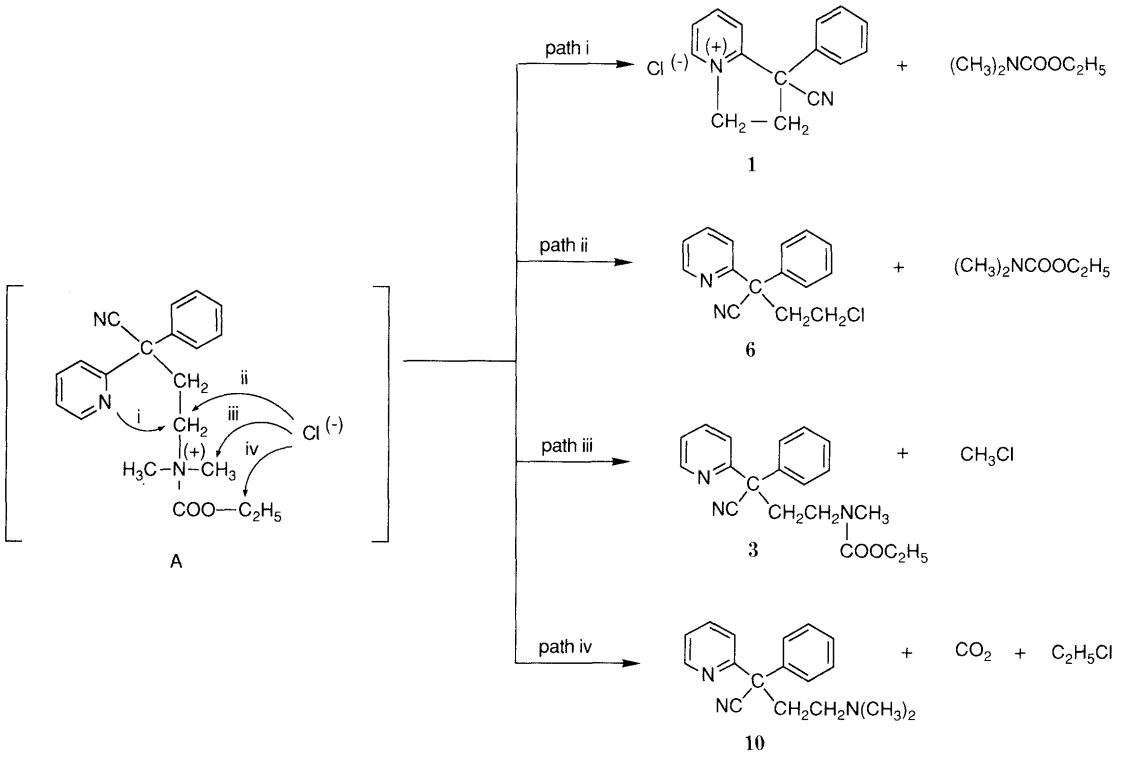

Chart 2

cyclization–*N*-dealkylation involving intramolecular nucleophilic attack by nitrogen of the pyridine ring (path i), giving the indolizinium chloride **1** (or quinolizinium chloride **2**) along with *N*-ethoxycarbonyl-*N*,*N*-dimethylamine. However, we can not rule out completely the possibility that the chloro derivative **6** (or **7**) is converted into **1** (or **2**).

Synthesis of Intermediates Intermediates employed in this study are listed in Chart 3. Alkylation of 2-phenylethanenitrile (**8**) and 2-phenyl-2-(2-pyridyl)ethanenitrile (**9**) was effected in the presence of KOH in DMSO. A key intermediate **9** was prepared by the reaction of **8** with 2-bromopyridine in 70% yield. Compounds **10**, **11**, **12**, **13**, **15** and **16** were prepared in good yields by the reaction of **9** with corresponding alkyl chlorides. Compound **14** was prepared in 75% yield by lithium borohydride ($LiBH_4$) reduction of **16** in refluxing toluene.

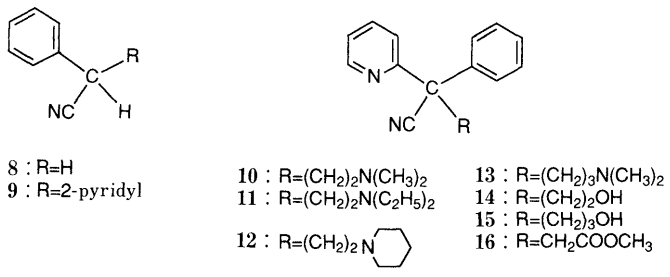

Chart 3

When reaction of **9** with 2-chloroethanol was carried out

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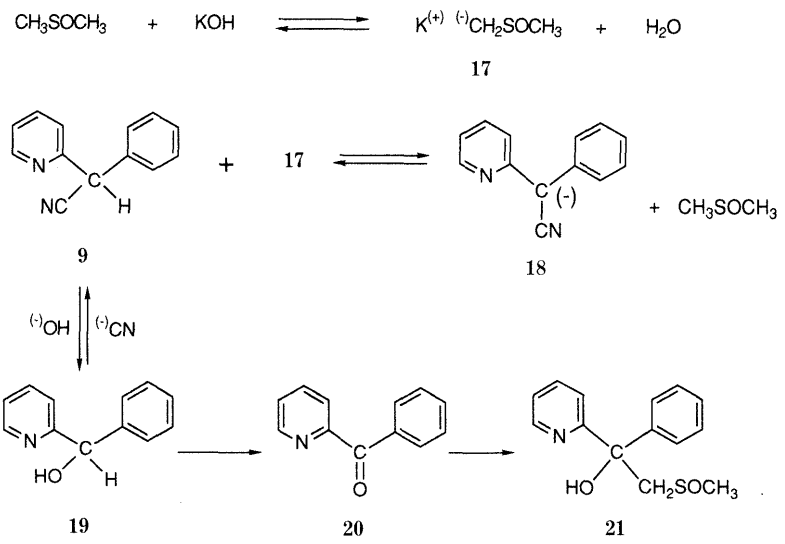

Chart 4

in the presence of KOH in DMSO, 2-benzoylpyridine (**20**)[5] and [2-hydroxy-2-phenyl-2-(2-pyridyl)ethyl]methylsulfoxide[4] (**21**) were obtained in 11% and 67% yields, respectively, without formation of the desired alcohol **14**. In order to estimate conversion of **9** into **20** and **21** several reaction runs were conducted (Chart 4). When **9** was heated at 50 °C for 24 h in the presence of KOH in dimethylformamide (DMF), **20** was obtained in a quantitative yield. However, **9** was recovered unchanged after heating in the absence of KOH in DMSO and DMF at 50 °C for 24 h. Treatment of the alcohol **19**[6] with KOH in DMSO at 70 °C for 16 h gave **20** and **21** in 21% and 74% yields, respectively. When the alcohol **19** was treated with KOH in DMF, the ketone **20** was obtained in a quatitative yield. When **20** was treated with KOH in DMSO, **21** was obtained in 82% yield. From these findings, a plausible mechanism for the formation of **20** and **21** may be as follows (Chart 4). First, the methylsulfinyl carbanion[7] (**17**) is formed by the reaction of DMSO with KOH, with release of water. Anion exchange between **9** and the anion **17** gives the carbanion **18** and DMSO. The anion **18** reacts with alkyl halide to give the desired C-alkyl derivative. On the other hand, the cyano group of **9** is replaced with hydroxy anion to give the alcohol **19**, which is oxidized in the presence of KOH and gives the ketone **20**. Compound **20** reacts with **17** to yield **21**.

Similar treatment of 3- and 4-benzoylpyridines gave [2-hydroxy-2-phenyl-2-(3-pyridyl)ethyl]- and [2-hydroxy-2-phenyl-2-(4-pyridyl)ethyl]methylsulfoxides[4] in 13% and 38% yield, respectively. Reaction of benzhydrol with KOH in DMSO also gave benzophenone, which was not converted into [2-hydroxy-2,2-diphenylethyl]methylsulfoxide[7] under the conditions used in this series. It is an interesting observation that the methylsulfinyl carbanion (**17**) was produced by the reaction of DMSO with KOH, compared with the reaction of DMSO with such strong bases as sodium hydride and sodium amide,[7] although the reaction was limited to a series of benzoylpyridines.

Experimental

Melting points were measured in a Gallenkamp melting point apparatus and are reported uncorrected. Infrared (IR) spectra were recorded on a Hitachi 260-10 IR spectrophotometer and ^{1}H-NMR spectra were measured on Hitachi R-90H (90 MHz) and Bruker AM360 (360 MHz) spectrometers with tetramethylsilane as an internal standard. Chemical shifts are reported in ppm (δ) and signals are described as s (singlet), br s (broad singlet), d (doublet), t (triplet), m (multiplet) or br (broad). All spectra were consistent with the assigned structures. Mass spectra (MS) and high resolution mass spectra (HRMS) were obtained on a JMS-DX300 spectrometer operating at an ionization potential of 70 eV. Combustion analyses were performed on a Perkin-Elmer Model 240C elemental analyzer.

Solvents were dried over Molecular Sieves 4A. 2-Bromopyridine, 2-, 3- and 4-benzoylpyridines, benzhydrol and benzophenone were commercial products.

Reaction of Dialkylamino Derivatives 10, 11, 12 and 13 with Ethyl Chloroformate General Procedure: A mixture of **10** (2.2 g, 8.3 mmol) and ethyl chloroformate (1.5 g, 13.8 mmol) in CH_2Cl_2 (15 ml) was refluxed for 7 h. The CH_2Cl_2 layer was extracted with 1 N HCl and the aqueous layer was washed with CH_2Cl_2 and evaporated to dryness in high vacuum to give an oil, which was dried over concentrated H_2SO_4 to give 1-cyano-2,3-dihydro-1-phenyl-1*H*-indolizinium chloride (**1**) as a viscous oil.

The CH_2Cl_2 layer was washed with H_2O and brine, successively, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel with a mixture of $CHCl_3$ and MeOH (60 : 1) to give 4-(ethoxycarbonylmethylamino)-2-phenyl-2-(2-pyridyl)butanenitrile (**3**) as a colorless oil.

Reaction of **11**, **12** and **13** with ethyl chloroformate was carried out according to a procedure similar to that used for **10**. The results are given in Table I. The structures of **1**, **2**, **3**, **4** and **5** were determined on the basis of IR and ^{1}H NMR spectral data.

1: A viscous oil, IR (neat): 2250, 1630 cm^{-1}. ^{1}H-NMR ($CDCl_3$–D_2O) δ: 2.8—3.5 (2H, m, 2-CH_2), 5.08 (2H, t, J=7.2 Hz, 3-CH_2), 7.25 (5H, s, Ph), 7.80 (1H, d, J=7.9 Hz, 8-CH), 8.10 (1H, t, J=7.2 Hz, 6-CH), 8.53 (1H, t, J=7.9 Hz, 7-CH), 9.02 (1H, d, J=5.4 Hz, 5-CH).

2: A viscous oil, IR (neat): 2240, 1640 cm^{-1}. ^{1}H-NMR (CD_3OD) δ: 2.15—2.58 (2H, m), 2.61—2.90 (2H, m), 4.95 (2H, t, J=7.2 Hz), 7.51 (5H, br s, Ph), 8.09 (2H, m), 8.58 (1H, td, J=7.9, 1.7 Hz), 9.06 (1H, m).

3: A colorless oil, IR (neat): 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.28 (3H, t, J=7.0 Hz, CH_3), 2.93 (3H, s, NCH_3), 2.8—3.0 (2H, m, $\underline{CH_2}CH_2N$), 3.2—3.7 (2H, m, $CH_2\underline{CH_2}N$), 4.42 (2H, q, J=7.0 Hz, $\underline{CH_2}CH_3$), 7.2—7.8 (8H, m, Ph, Py-3, 4, 5), 8.6—8.8 (1H, m, Py-6).

4: A colorless oil, IR (neat): 2240, 1710 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.08 (3H, t, J=7.1 Hz), 1.24 (3H, t, J=7.1 Hz), 2.68—3.44 (6H, m, $CH_2CH_2NCH_2$), 4.18 (2H, q, J=7.1 Hz), 7.16—7.77 (8H, m, Ph, Py-3, 4, 5), 8.59—8.67 (1H, m, Py-6).

5: An oil, IR (neat): 2240, 1705 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.21 (3H, t, J=7.0 Hz, CH_3), 1.54—1.81 (2H, m), 2.38—2.90 (2H, m), 2.82 (3H, s, NCH_3), 3.32 (2H, t, J=6.9 Hz, CH_2), 4.09 (2H, q, J=7.0 Hz, $\underline{CH_2}CH_3$), 7.12—7.67 (8H, m, Ph, Py-3, 4, 5), 8.57—8.64 (1H, m, Py-6).

Reaction of Alcohol Derivatives 14 and 15 with $SOCl_2$ A solution of **15** (3.0 g, 12 mmol) and $SOCl_2$ (4 ml, 54 mmol) in CH_2Cl_2 (30 ml) was

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stirred for 2 h at room temperature. The CH_2Cl_2 layer was extracted with 1 N HCl solution. The aqueous layer was washed with CH_2Cl_2, evaporated to dryness in high vacuum and dried over concentrated H_2SO_4 to give **2** as a viscous oil.

The CH_2Cl_2 layer was washed with aqueous $NaHCO_3$ and dried over $MgSO_4$. After removal of the solvent, the residue was purified by column chromatography on silica gel with $CHCl_3$ as an eluent to give 5-chloro-2-phenyl-2-(2-pyridyl)pentanenitrile (**7**) as an oil. IR (neat): 2240 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.75—2.05 (2H, m, $CH_2\underline{CH_2}CH_2Cl$). 2.20—2.89 (2H, m, $\underline{CH_2}CH_2CH_2Cl$), 3.57 (2H, t, J=6.2 Hz, $CH_2CH_2\underline{CH_2}Cl$), 7.15—7.78 (8H, m, Ph, Py-3, 4, 5), 8.55—8.60 (1H, m, Py-6). *Anal.* Calcd for $C_{16}H_{15}ClN_2$: C, 70.98; H, 5.58; N, 10.35. Found: C, 71.01; H, 5.40; N, 10.48.

Reaction of **14** with $SOCl_2$ was carried out according to a procedure similar to that used for **15**. The results are given in Table I.

2-Phenyl-2-(2-pyridyl)ethanenitrile (9) This compound was prepared by an improved method: **8** (12 g, 100 mmol) was added to a solution of KOH (16 g, 270 mmol) in DMSO (75 ml). The mixture was stirred for 30 min, then 2-bromopyridine (15 g, 95 mmol) was added dropwise over 30 min at 50—55 °C. The reaction mixture was stirred for 2 h at 70 °C, and then more 2-phenylethanenitrile (3 g, 25 mmol) was added. The mixture was stirred for 2 h at 70 °C, and poured into ice-water (800 ml). The whole was stirred for 15 min, then precipitated crystals were collected by filtration and washed with H_2O. The wet crystals were dissolved in AcOEt, then the AcOEt layer was separated, dried over $MgSO_4$ and evaporated *in vacuo* to give brown crystals, which were recrystallized from isopropyl alcohol to give pure **9**. Yield: 13.5 g (70%); mp 88—89 °C [lit.[3] 88—89 °C].

4-(*N*,*N*-Dimethylamino)-2-phenyl-2-(2-pyridyl)butanenitrile (10) Powdered KOH (10 g, 168 mmol) in DMSO (30 ml) was stirred for 30 min at room temperature, then **9** (10 g, 50 mmol) was added, and the mixture was stirred for 30 min at room temperature. 2-(*N*,*N*-Dimethylamino)ethyl chloride (27 g, 253 mmol) in ether solution was added dropwise to the resulting solution over 40 min at 50 °C and then the mixture was stirred for 3 h at 60 °C, poured into ice-water (250 ml) and extracted with CH_2Cl_2. The CH_2Cl_2 layer was extracted with 6 N HCl. The aqueous solution was made alkaline with 8 N NaOH and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O and dried over $MgSO_4$. After removal of the solvent, the oily material was purified by column chromatography on silica gel with a mixture of $CHCl_3$ and MeOH (25 : 1) as the eluent to give a red-brown oil, which was distilled under reduced pressure to give pure **10** as an oil. Yield: 9.0 g (67%); bp 155—159 °C (2 mmHg) [lit.[2] 162—165 °C (0.5 mmHg)].

4-(*N*,*N*-Diethylamino)-2-phenyl-2-(2-pyridyl)butanenitrile (11) This compound was prepared as an oil from **9** and 2-(*N*,*N*-diethylamino)ethyl chloride by a procedure similar to that used for **10**. Yield: 52%; bp 170—176 °C (0.4 mmHg) [lit.[2] bp 162—164 °C (0.3 mmHg)].

4-(Piperidino)-2-phenyl-2-(2-pyridyl)butanenitrile (12) This compound was prepared as an oil from **9** and *N*-(2-chloroethyl)piperidine by a procedure similar to that used for **10**. Yield: 53%; bp 180—183 °C (1.0 mmHg) [lit.[2] bp 175—180 °C (1.0 mmHg)].

5-(*N*,*N*-Dimethylamino)-2-phenyl-2-(2-pyridyl)pentanenitrile (13) This compound was synthesized as an oil from **9** (5.0 g, 25.5 mmol) and 3-(*N*,*N*-dimethylamino)propyl chloride (15.5 g, 126.5 mmol) in the same way as described for the preparation of **7**. Yield: 6.5 g (88%); bp 160—163 °C (2 mmHg). [lit.[2] bp 168—170 °C (1.0 mmHg)].

4-Hydroxy-2-phenyl-2-(2-pyridyl)butanenitrile (14) A suspension of $LiBH_4$ (90 mg, 4.1 mmol) in tetrahydrofuran (THF) (3 ml) was stirred for 1.5 h and then a solution of **16** (1.98 g, 7.4 mmol) in THF (6 ml) was added dropwise to it over 10 min. Toluene (3 ml) was added to the resulting mixture. After removal of THF at 100 °C, the residue in toluene was heated for an additional 1.5 h, concentrated *in vacuo* and poured into a mixture of ice-water (15 ml) and 3 N HCl (30 ml). The aqueous layer was stirred for 10 min, made alkaline with K_2CO_3 and extracted with Et_2O. The ethereal solution was dried over $MgSO_4$ and evaporated *in vacuo* to give a crude oil, which was purified by column chromatography on silica gel with a mixture of $CHCl_3$ and MeOH (60 : 1) as an eluent to give pure **14** as a colorless oil. Yield: 1.32 g (75%). IR (neat): 3410, 2240 cm^{-1}. ^{1}H-NMR ($CDCl_3$–D_2O) δ: 2.69 (1H, dt, J=14.4, 6.4 Hz, CCH_2), 2.97 (1H, dt, J=14.4, 6.4 Hz, CCH_2), 3.77 (1H, dt, J=11.2, 6.4 Hz, CH_2OH), 3.85 (1H, dt, J=11.2, 6.4 Hz, CH_2OH), 7.25—7.38 (5H, m, Ph), 7.42—7.48 (2H, m, Py-3, 5), 7.95 (1H, dt, J=1.7, 7.7 Hz, Py-4), 8.61—8.63 (1H, m, Py-6). HRMS Calcd for $C_{15}H_{14}N_2O$: 238.1105. Found: 238.1109.

5-Hydroxy-2-phenyl-2-(2-pyridyl)pentanenitrile (15) This compound was prepared from **9** (2.5 g, 12.5 mmol), 3-chloro-propanol (1.3 g, 13 mmol) and KOH (3.5 g, 73 mmol) according to a procedure similar to that used for **10**. The reaction was run at 50 °C for 24 h. The crude material was purified by column chromatography on silica gel with a mixture of $CHCl_3$ and MeOH (25 : 1) as an eluent to give pure **15** (185 mg, 7%) along with **20** (670 mg, 28%) and **21** (1.1 g, 32%).

15: An oil, IR (neat): 3410, 2230 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 1.55—1.84 (3H, m, $CH_2\underline{CH_2}CH_2O\underline{H}$), 2.25—3.00 (2H, m, CCH_2), 3.68 (2H, t, J=6.0 Hz, CH_2OH), 7.12—7.78 (8H, m, Ph, Py-3, 4, 5), 8.59—8.62 (1H, m, Py-6). HRMS Calcd for $C_{16}H_{16}N_2O$: 252.1262. Found: 252.1293. **20**: mp 42—44 °C [lit.[5] 40—43 °C]. **21**: mp 114.5—125 °C [lit.[4] 118.0—120.0 °C].

Methyl 3-Cyano-3-phenyl-3-(2-pyridyl)propionate (16) Powdered KOH (1.6 g, 23.5 mmol) in DMSO (30 ml) was stirred for 30 min at room temperature, then **9** (3.0 g, 15.4 mmol) was added to it. Methyl bromoacetate (3.5 g, 22.9 mmol) was added dropwise to the resulting mixture over 10 min at 5 °C. The reaction mixture was stirred for 2 h, then poured into ice-water. The precipitate was collected, washed with H_2O, air-dried and recrystallized from isopropyl ether to give **16** as colorless needles. Yield: 3.7 g (93%). IR (KBr): 2220, 1735 cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 3.37 (1H, d, J=6.9 Hz), 3.63 (3H, s), 3.91 (1H, d, J=6.9 Hz), 7.12—7.80 (8H, m, Ph, Py-3, 4, 5), 8.55—8.62 (1H, m, Py-6). *Anal.* Calcd for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 72.43; H, 5.09; N, 10.68.

Phenyl-2-pyridylmethanol (19) This compound was obtained by $NaBH_4$ reduction of 2-benzoylpyridine (**20**) in MeOH. Yield: 92%; mp 75 °C [lit.[6] 74—75 °C].

[2-Hydroxy-2-phenyl-2-(2-pyridyl)ethyl]methylsulfoxide (21) Powdered KOH (0.1 g, 2.7 mmol) in DMSO (5 ml) was stirred for 30 min at room temperature to give a clear solution, then **20** (0.5 g, 2.7 mmol) was added to it. The resulting mixture was stirred for 7 h at 70 °C. More KOH (0.4 mg) was added and then the mixture was stirred for a further 3 h at 70 °C, poured into ice-water (50 ml) and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, crude **29** was purified by column chromatography on silica gel (40 g) with CH_2Cl_2 and AcOEt, successively, as eluents to give pure **21**. Yield: 715 mg (82%); mp 114.5—125 °C [lit.[4] 118.0—120.0 °C].

[2-Hydroxy-2-phenyl-2-(3-pyridyl)ethyl]methylsulfoxide This compound was prepared from 3-benzoylpyridine (0.5 g, 2.7 mmol) and KOH (0.58 g) in DMSO (5 ml) according to a procedure similar to that used for the preparation of **21**. Yield: 475 mg (13%); mp 113.0—114.2 °C [lit.[4] mp 114—118 °C].

[2-Hydroxy-2-phenyl-2-(4-pyridyl)ethyl]methylsulfoxide This compound was prepared from 4-benzoylpyridine (0.5 mg, 2.7 mmol) and KOH (0.58 mg) in DMSO (5 ml) according to a procedure similar to that used for the preparation of **21**. Yield: 578 mg (38%); mp 138.2—140.5 °C [lit.[4] mp 140—142 °C].

Reaction of 19 with KOH in DMSO A solution of **19** (0.2 g, 1.08 mmol) in DMSO was stirred for 2 h at room temperature. Powdered KOH was added to the resulting DMSO solution and the mixture was stirred for 24 h at room temperature and an additional 16 h at 70 °C, then poured into ice-water and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with H_2O, dried over $MgSO_4$ and evaporated *in vacuo* to give a crude material, which was purified by column chromatography on silica gel with a mixture of $CHCl_3$ and MeOH (50 : 1) as an eluent to give **20** and **21** in 21 and 74% yields, respectively.

Reaction of 19 with KOH in DMF Powdered KOH (0.54 g, 8.2 mmol) in DMF (3 ml) was stirred for 30 min at room temperature, then **19** (0.5 g, 2.7 mmol) was added, and the mixture was stirred for 10 h at 70—75 °C, poured into ice-water and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, **20** was obtained in 97% yield.

Reaction of Benzhydrol with KOH in DMSO A solution of benzhydrol (0.2 g, 1.09 mmol) in DMSO (2 ml) was stirred for 2 h at room temperature. Powdered KOH (0.07 g, 1.06 mmol) was added to the resulting DMSO solution and the mixture was stirred for 26 h at room temperature, then poured into ice-water and extracted with $CHCl_3$. The $CHCl_3$ layer was washed with brine, dried over $MgSO_4$ and evaporated *in vacuo* to give crude crystals, which were recrystallized from ligroin to give analytically pure benzophenone. Yield: 98%; mp 50—51 °C.

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