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CARBON–CARBON CYANOETHYLATION OF ANISOLE AND ITS DERIVATIVES[1]

SYNTHESIS OF A POTENTIAL INTERMEDIATE FOR RING-C AROMATIC STEROID

AMARESHWAR CHATTERJEE* and B. G. HAZRA
Department of Chemistry, Jadavpur University, Calcutta-700032, India

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Abstract—Cyanoethylations of *o*-cresyl methyl ether, anisole, α-naphthyl methyl ether, resorcinol dimethyl ether, and 1,7-dimethoxynaphthalene provided the desired products in reasonably good yields; synthetic applications are indicated.

Carbon–carbon cyanoethylation of the more reactive phenols such as resorcinol, is known[2] to provide dihydrocoumarin derivatives in the presence of anhydrous zinc chloride and dry hydrogen chloride. Simple phenol in the presence of more active catalyst, such as anhydrous aluminium chloride affords[3] β-(*p*-hydroxyphenyl)-propionitrile in good yield.

In connection with some synthetic problems, we required an efficient direct route for introducing a propionic acid chain *para* to a methoxyl group in an aromatic ring. Cyanoethylations of anisole and its derivatives have therefore been investigated in detail, and we wish to report here the synthetic utility of this reaction.

Cyanoethylation of *o*-cresyl methyl ether **1a** was first investigated under different experimental conditions and the results are summarised in Table 1.

As shown in Table 1, *sym*-tetrachloroethane is the solvent of choice for successful cyanoethylation of *o*-cresyl methyl ether **1a**. The nitrile **1c** on alkaline hydrolysis afforded the known propionic acid derivative **1d** in excellent yield. It may be mentioned that the present method obviates the need for multistep synthesis of the nitrile **1c**[4] and the acid **1d**.[4,5]

Cyanoethylation of anisole **1b** according to the standardised procedure (Table 1, entry 4) provided the desired product **1e** in good yield, and this was hydrolysed in the usual manner to give the known acid **1f** in excellent yield. The present method appears to be more convenient than the methods previously reported[6,7] for the preparation of the acid **1f**.

Similar cyanoethylation of α-naphthyl methyl ether† gave the desired nitrile **2a**[8] in respectable yield. Alkaline hydrolysis of **2a** finally provided the known acid **2b**,[9] and this on demethylation afforded the phenolic acid **2c**.[9] PPA cyclisation of the acid **2b** gave in low yield a crystalline ketone, m.p. 160° identical with that reported[10] for 6-methoxyperinaphthenone **3**. Final proof for the assignment of the ketone as **3** was provided from its mass spectrum which showed the expected molecular ion peak at *m/e* 210.

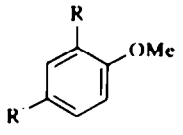
Cyanoethylation of methyl γ-(*m*-methoxyphenyl) butyrate **4** gave an oily nitrile in very low yield. Besides this higher boiling product, 6-methoxy-1-tetralone and the starting ester **4** were isolated in 28 and 33% yields respectively. The above oily nitrile on alkaline hydrolysis furnished a crystalline dibasic acid **5**. As the oxidation of this acid gave no crystalline product for characterisation, the position of the propionic acid chain in **5** remains uncertain. Friedel–Crafts succinoylation of the ester **4**, however, gave a non-crystalline keto-acid, which on subsequent esterification furnished in excellent yield a homogeneous (TLC) keto-diester characterised as **6** through its oxidation to 2-methoxyterephthalic acid.[11]

†After the completion of our work, cyanoethylation of this ether was reported by Dasgupta *et al.* (see Ref. 8) following our reported[1] procedure with slight modification.

Table 1. Carbon–carbon cyanoethylation of *o*-cresylmethyl ether **1a**

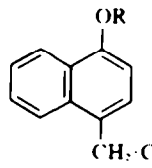
No.	Compound **1a**	Acrylonitrile	$AlCl_3$	Solvent	Reaction period* and temperature	Product (%)
1.	24.4 g (0.2 mole)	10.6 g (0.2 mole)	13.35 g (0.1 mole)	—	1.5 h at 15° and 1.5 h at 80°	**1c** (48%)*
2.	6.1 g (0.05 mole)	5.3 g (0.1 mole)	6.68 g (0.05 mole)	Light petroleum (60–80°)	1.5 h at 15° and 1.5 h at 80°	Recovered **1a** only
3.	6.1 g (0.05 mole)	5.3 g (0.1 mole)	6.68 g (0.05 mole)	Methylene chloride	1.5 h at 15° and 1.5 h at 40°	Recovered **1a** only
4.	6.1 g (0.05 mole)	5.3 g (0.1 mole)	6.68 g (0.05 mole)	*sym.* Tetrachloroethanol	1.5 h at 15° and 1.5 h at 90°	**1c** (70%)
5.	6.1 g (0.05 mole)	5.3 g (0.1 mole)	6.68 g (0.05 mole)	*sym.* Tetrachloroethanol	1.5 h at 15° and 2.5 h at 90°	**1c** (63%)

*Based on the recovered starting material
†Dry HCl gas was continuously passed throughout this period.



1

a: R = Me; R' = H
b: R = R' = H
c: R = Me; R' = CH_2CH_2CN
d: R = Me; R' = $CH_2CH_2CO_2H$
e: R = H, R' = CH_2CH_2CN
f: R = H; R' = $CH_2CH_2CO_2H$



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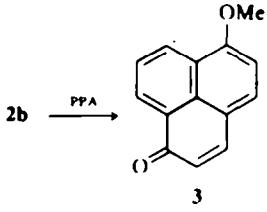
a: R = Me; R' = CN
b: R = Me; R' = CO_2H
c: R = H; R' = CO_2H



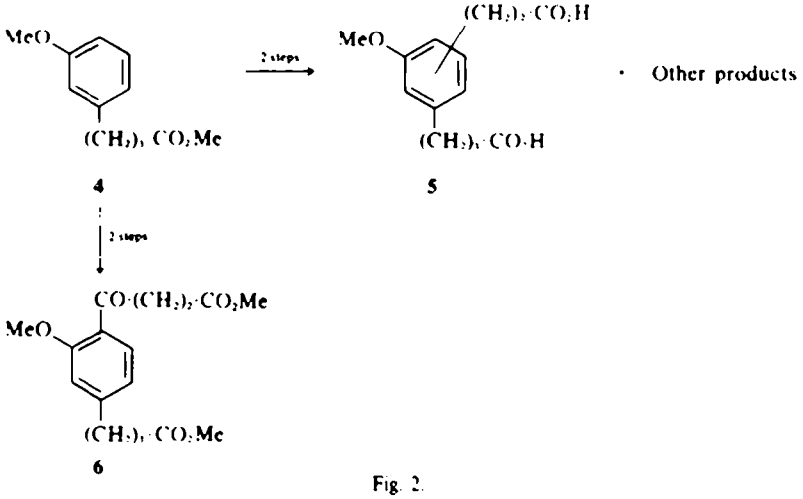
3

Fig. 1.

Cyanoethylation of the tetralin derivative **8b** was also briefly investigated. 8-Methoxy-1-methyl-2-tetralone[13] was reduced with sodium borohydride to give a crystalline alcohol **8a** which on acetylation provided the crystalline acetate **8b** of undefined stereochemistry. Cyanoethylation of **8b** following the usual procedure (Table 1, entry 4) was not at all encouraging.

In 1,7-dimethoxynaphthalene **9a**, the site of Friedel–Crafts substitution would be at the 3 or 4-position, the carbon atom 8 probably being too strongly hindered. It has indeed been observed[14] that 1,7-dimethoxynaphthalene undergoes both formylation and acylation at position 4. Cyanoethylation of **9a** by the procedure mentioned before (Table 1, entry 4) gave the crystalline nitrile **9b** in poor yield. However, controlled reaction conditions (see Experimental) provided the nitrile **9b** in excellent yield, and this on hydrolysis furnished the crystalline acid **9c** in high yield. The structural assignment for the nitrile **9b** and the acid **9c** were finally secured through an unambiguous synthesis of the acid **9c** as shown below.

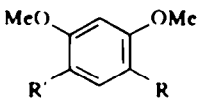
Knoevenagel condensation of the known[14] aldehyde **9d**



4 5 6

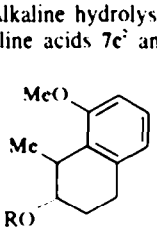
Fig. 2.

More reactive resorcinol dimethyl ether† was cyanoethylated using anhydrous zinc chloride as the catalyst in ether solution. Low temperature and shorter reaction period favoured the formation of *mono*-cyanoethylated product **7a**. Longer reaction period and higher temperature afforded both the *mono*- and *bis*-cyanoethylated products **7a** and **7b**. Alkaline hydrolysis of **7a** and **7b** gave the known crystalline acids **7c**[2] and **7d**[12] respectively.



7

a: R = CH_2CH_2CN; R' = H
b: R = R' = CH_2CH_2CN
c: R = $CH_2CH_2CO_2H$; R' = H
d: R = R' = $CH_2CH_2CO_2H$



8

a: R = H
b: R = Ac

Fig. 3.

†Cyanoethylation of this ether was studied by S. Saha of our Laboratory

with diethyl malonate gave in excellent yield the desired unsaturated ester **10**. Catalytic hydrogenation of **10** gave a reduced product which on alkaline hydrolysis provided the malonic acid derivative **11**. Decarboxylation of **11** afforded an acid identical in all respects with the acid **9c** mentioned above. Of the two pathways for the preparation of the acid **9c**, the cyanoethylation procedure is clearly superior. It may be mentioned here that the acid **9c** has been successfully utilised for the total synthesis[15] of Ring-C aromatic steroid.

Polyphosphoric acid (PPA) cyclisation of the acid **9c** gave in good yield a ketonic material which on recrystallisation provided a product, m.p. 156–157° $\nu_{max}^{CHCl_3}$ 1685 cm^{-1}. The IR spectrum and the elemental analysis indicated the product to be the dihydrophenalenone derivative **12**. It may be mentioned here that the mixed m.p. of this product with an authentic sample[16] of **13**, m.p. 156°, remained undepressed. That our ketonic product was actually a mixture of **12** and **13** was finally established from its IR absorptions at 1712 and 1685 cm^{-1} in KBr pellet. It may be mentioned here that the known indanone derivative **13** showed an IR band at 1712 cm^{-1} both in chloroform solution and in KBr pellet. Repeated recrystallisations of the above ketonic mixture finally

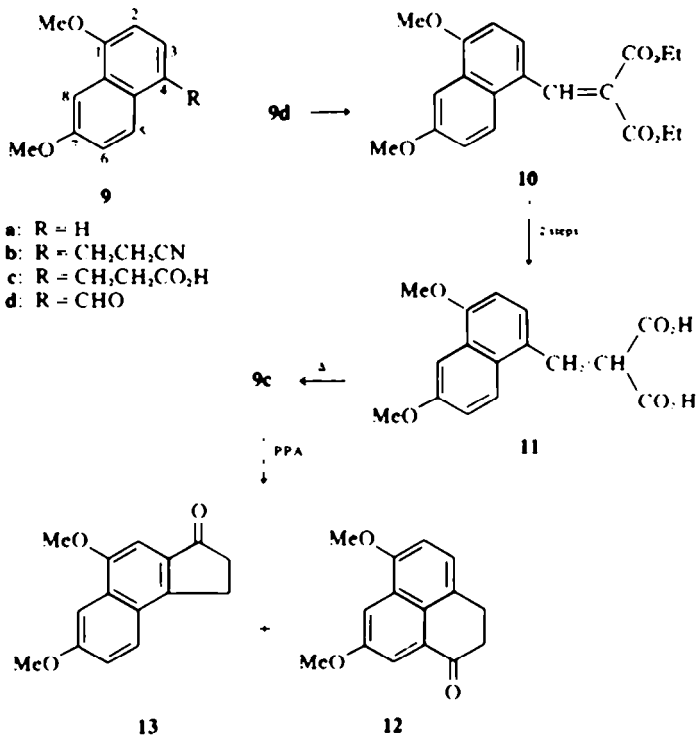


Fig. 4.

provided a pure sample of **12**, ν_{max} (KBr) 1685 cm^{-1}. Gas chomatographic analysis of this sample showed a single peak on SE 30 or OV 17 columns.†

EXPERIMENTAL

M.ps were determined on a H_2SO_4 bath and are uncorrected. UV spectra were measured for solutions in ethanol with a Unicam SP 500 spectrophotometer, IR spectra for solutions in chloroform (until otherwise stated) with a Perkin–Elmer 337-instrument, and NMR spectra for solutions in $CDCl_3$ with a Varian A60-D spectrometer (tetramethylsilane as internal standard). Light petroleum refers to the fraction, b.p. 60–80°. TLC plates were coated with silica gel G (acc. to Stahl) having a thickness of about 0.2 mm and the spots were located by exposing the dried plates in iodine vapour. Gas chromatographic analysis were performed on a Varian Aerograph (single channel) equipped with a flame ionisation detector. Extracts were dried over Na_2SO_4.

β-(3-Methyl-4-methoxyphenyl)propionitrile **1c**. A typical procedure is described for cyanoethylation of *o*-cresyl methyl ether **1a**.

Finely powdered anhydrous $AlCl_3$ (6.68 g, 0.05 mole) was added slowly to a vigorously stirred cold soln (10°) of *o*-cresyl methyl ether (6.1 g, 0.05 mole) and acrylonitrile (5.3 g, 0.1 mole) in dry *sym*-tetrachloroethane (30 ml). Dry HCl gas was passed through the resulting mixture maintained at 10–15° for 1.5 h. The resulting homogeneous reaction mixture was then heated in an oil bath maintained at 90–95° for 1.5 h with continuous passing of dry HCl. Dark red reaction mixture was then decomposed with cold water and the product was extracted with ether (3 × 75 ml). The solvent was successively washed with water, NaOH soln (5%) and finally with water. Evaporation of the dry solvent afforded **1c** (6.08 g, 70%) as colourless oil, b.p. 118°/0.2 mm Hg (reported[4] b.p. 145°/8 mm Hg), λ_{max} 276 nm (ε2,455), ν_{max} (film) 2248 cm^{-1} (C≡N). Thin layer chromatography showed a bright single spot using MeOH–benzene (15:85) as the eluting solvent and iodine vapour as the developing agent. (Found: C, 75.19; H, 7.52. Calc. for $C_{11}H_{11}ON$: C, 75.40; H, 7.48%).

†These columns, however, were not capable of separating the mixture of the two ketones **12** and **13**.

β-(3-Methyl-4-methoxyphenyl)propionic acid **1d**. A soln of the above nitrile **1c** (1 g) was hydrolysed by refluxing for 31 h with a soln of KOH (1.6 g) in MeOH (15 ml) and water (1 ml). Solvent was removed under reduced pressure and the residue was dissolved in water. The resulting alkaline soln was extracted with ether (1 × 50 ml) to remove any neutral material if any. The alkaline soln was then acidified and the liberated acid was extracted with ether (3 × 50 ml). Usual processing of the solvent gave the crystalline acid **1d** (0.85 g, 77%), as beautiful plates, m.p. 99° (reported[4] m.p. 100°). Mixture m.p. with an authentic sample[17] remained undepressed.

β-(4-Methoxyphenyl)propionitrile **1e**. Cyanoethylation of anisole following the typical procedure described above gave the cyano-compound (**1e**, 65%), b.p. 127°/0.8 mm Hg (reported[18] b.p. 150–155°/8 mm Hg), λ_{max} 277 nm (ε2138), ν_{max} (film) 2246 cm^{-1} (C≡N). TLC of this product as before gave a single spot. (Found: C, 74.60; H, 6.84. Calc. for $C_{10}H_{11}ON$: C, 74.51; H, 6.88%).

β-(4-Methoxyphenyl)propionic acid **1f**. Alkaline hydrolysis of the above nitrile **1e** as before furnsihed in 75% yield the crystalline acid **1f**, m.p. 103–104° (reported[4] m.p. 103.5–104°). (Found: C, 66.48; H, 6.73. Calc. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71%).

β-(4-Methoxy-1-naphthyl)propionitrile **2a**. Cyanoethylation of α-naphthyl methyl ether (4.74 g) as before provided the desired nitrile **2a** (3.35 g, 53%), b.p. 170–175°/0.4 mm Hg, and m.p. 75–77°. Recrystallisation of this material gave an analytical sample, m.p. 79° (ether–light petroleum, b.p. 40–60°), λ_{max} 234 and 299 nm (ε99,770 and 7379), ν_{max} 2246 cm^{-1} (C≡N). (Found: C, 79.28; H, 6.48. $C_{14}H_{13}NO$ requires C, 79.59; H, 6.20%).

β-(4-Methoxy-1-naphthyl)propionic acid **2b**. The above nitrile **2a** (1.5 g) on alkaline hydrolysis as before furnished the acid **2b** (1.5 g, 91%) as white needles, m.p. 169–170° (reported[9] m.p. 164–167°), λ_{max} 235 and 300 nm (ε35,400 and 7762), ν_{max} 1711 cm^{-1} (acid C=O). (Found: C, 72.91; H, 6.36. Calc. for $C_{14}H_{14}O_3$: C, 73.03; H, 6.13%).

β-(4-Hydroxy-1-naphthyl)propionic acid **2c**. A mixture of the acid **2b** (0.5 g), glacial AcOH (10 ml) and HBr (16 ml, 48%) was heated under reflux for 3 h. Usual work up to the reaction mixture provided the phenolic acid **2c** (0.25 g, 53%), m.p. 128° (reported[9] m.p. 125–126°). (Found: C, 71.91; H, 5.86; Calc. for $C_{13}H_{12}O_3$: C, 72.21; H, 5.59%).

6-Methoxyperinaphthenone **3**. To PPA (prepared from H_3PO_4

(9 ml, 89%) and P_2O_5 (15 g)] was added the acid **2b** (1 g). The acid was thoroughly mixed with PPA by heating the mixture on a free flame. The reaction mixture was further heated on the steam bath for 40 min with stirring. Usual processing of the reaction mixture afforded crude solid material (0.25 g, 27%), m.p. 150–155°. Recrystallisations provided an analytical sample of **3** as yellow needles, m.p. 160° (ether–light petroleum) (reported[10] m.p. 160–161°), *m/e* 210 (M^+), 195, 167 and 139; ν_{max} 1650 cm^{-1}. 2,4-Dinitrophenylhydrazone had m.p. 279–280° (d) (CH_2Cl_2–MeOH). (Found: N, 14.36. $C_{20}H_{14}N_4O_7$ requires: N, 14.35%).

Cyanoethylation of methyl γ-(m-methoxyphenyl)butyrate **4**. *Formation of the dibasic acid* **5**, *6-methoxy-1-tetralone, and the recovered ester* **4**. Cyanoethylation of **4** (4.168 g) was performed as in the case of **1a** reported earlier to give an oily product which was fractionated to give the following fractions: (i) (2.65 g), b.p. 115–120°/0.4 mm, and (ii) (1.22 g), b.p. 150–170°/0.4 mm Hg. Fraction (i) (free from N_2) was hydrolysed by methanolic KOH as before to furnish *6-methoxy-1-tetralone* (1 g, 28.5%), and γ-(methoxyphenyl)butyric acid (1.35 g, 33%) m.p. 48–49°. Fraction (ii) was redistilled to give a nitrile (0.75 g, 14%), b.p. 165–170° (bath)/0.2 mm Hg, ν_{max} 2246 (C≡N) and 1730 cm^{-1} (ester C=O). This product (0.75 g) was hydrolysed by heating under reflux for 31 h with methanolic KOH (10%) as before to provide an acid (0.68 g), m.p. 115–120°. Recrystallisation afforded an analyitcal sample of the dibasic acid **5** as colourless needles, m.p. 123–124° (ether–light petroleum). (Found: C, 63.25; H, 6.90; N.E., 134. $C_{14}H_{18}O_4$ requires: C, 63.15; H, 6.81%; N.E. 133.15).

Oxidation of the above acid (0.15 g) by heating for 2.5 h with aqueous alkaline $KMnO_4$ (10%) provided an oily acidic material (0.04 g) which could not be characterised.

Friedel–Crafts succinoylation of γ-(m-methoxyphenyl)butyrate **4**-*formation of methyl β-4-(3-methoxycarbonylpropyl)-2-methoxybenzoylpropionate* **6**. To an ice-cold stirred soln of anhydrous $AlCl_3$ (6.55 g) in dry nitrobenzene (10 ml) was added powdered succinic anhydride (1.88 g, 0.018 mole) all at once. The butyric ester **4** (3 g, 0.014 mole) was then added dropwise over a period of 15 min., the temperature of the reaction mixture being maintained at 10°. After stirring for 5 h at 10°, the reaction mixtures was left for 36 h at 5°. The reaction mixture was decomposed with ice and HCl, nitrobenzene was removed by steam distillation, and the product was extracted with ether (3 × 75 ml). The acidic product was purified by extraction with aq Na_2CO_3. Acidification and subsequent ether extraction furnished a keto-acid (3.5 g) as viscous oil, ν_{max} (film) 1672 (conj. C=O), 1707 (acid C=O) and 1730 cm^{-1} (ester C=O). This acid (3.5 g) was directly esterified by heating under reflux for 13 h with MeOH (30 ml) and conc. H_2SO_4 (3 ml) to give the keto-diester **6** as colourless oil (3.5 g, 70%), b.p. 205–210°/4 mm Hg. A middle fraction was collected which was again distilled under vacuum to afford an analytical sample of **6**, b.p. 190° (bath)/0.2 mm Hg, λ_{max} 261 nm (ε1,072), ν_{max} 1672 (conj. C=O) and 1730 cm^{-1} (ester C=O). The homogenous nature was followed from t.l.c. using two solvent system, ethyl acetate–light petroleum (40:60), and MeOH–benzene (15:85). (Found: C, 63.25; H, 6.79. $C_{17}H_{22}O_6$ requires: C, 63.34; H, 6.88%).

Alkaline potassium permanganate oxidation of the dimethyl ester **6**-*formation of 2-methoxyterephthalic acid*. To a suspension of **6** (0.5 g) in aq NaOH (2ml, 10%), heated on the steam bath, was added dropwise during 30 min a soln of $KMnO_4$ in water (50 ml, 10%). Each drop of permanganate soln was added after the pink colour due to previous one was discharged. After complete addition, the reaction mixture was heated for 2 h on the steam bath and 2 h under reflux. The colour of the excess permanganate was discharged by adding a few drops of ethanol. Precipitated MnO_2 was filtered and the alkaline solution was concentrated and acidified with HCl. The liberated acid was extracted with ether repeatedly (4 × 50 ml) to give *2-methoxyterephthalic acid* (0.24 g, 79%), m.p. and m.m.p. with an authentic sample,[11] 285–286°.

Cyanoethylation of resorcinol dimethyl ether–formation of β-(2,4-dimethoxyphenyl)propionitrile **7a** *and 1,3-dimethoxy-4,6-bis(2-cyanoethyl)benzene* **7b** (a). To a soln of resorcinol dimethyl ether (7.6 g, 0.05 mole), acrylonitrile (3.7 ml, 0.05 mole) in dry ether (40 ml) maintained at 5°, was added anhydrous $ZnCl_2$ (4.1 g, 0.06 mole) all at once. Dry HCl gas was passed through the clear homogeneous soln for 1.5 h maintaining the reaction mixture at 5–7°. The reaction mixture was then allowed to attain room temp (25°) and dry HCl gas was passed through the reaction mixture for 0.5 h at 25° when it became turbid. At this stage, the mixture was decomposed with cold water and the product was extracted with ether (3 × 50 ml). The solvent was successively washed with water, aq $NaHCO_3$ and finally with water. Evaporation of dry solvent and distillation of the residue afforded resorcinol dimethyl ether (4.65 g) and the desired nitrile **7a** (2.75 g, 67% based on recovered starting material), b.p. 130–134°/0.2 mm Hg. A middle fraction was collected for analysis, ν_{max} 2248 cm^{-1} (C≡N). (Found: C, 68.82; H, 6.88. $C_{11}H_{13}NO_2$ requires: C, 69.09; H, 6.85%) (b) To a soln of resorcinol dimethyl ether (14.3 g, 0.1 mole), acrylonitrile (7.4 ml, 0.1 mole) in dry ether (70 ml) maintained at 5° was added freshly fused anhydrous $ZnCl_2$ (4.1 g, 0.03 mole). Dry HCl gas was passed through the clear yellow soln for 2.5 h keeping the reaction mixture at 5–7° with constant stirring. The resulting reaction mixture, saturated with HCl gas, was left at room temp (25°) for 18–20 h when two distinct layers were separated. The upper ether layer was separated and the heavy oily layer was once extracted with ether. Usual processing of the either soln afforded the recovered resorcinol dimethyl ether (5.6 g), and the nitrile **7a** (2.5 g), b.p. 130–132°/0.15 mm Hg. The above oily layer was dissolved in chloroform and the solvent was processed as before. Evaporation of the dry solvent gave the dinitrile **7b** (2 g) as viscous oil, b.p. 195°/0.2 mm Hg; m.p. 53–55°. Recrystallisation afforded pure sample of **7b** m.p. 59–60° (ethyl acetate/light petroleum) ν_{max} 2248 cm^{-1} (Found: C, 68.52; H, 6.89; N, 11.66. $C_{14}H_{16}N_2O_2$ requires: C, 68.83; H, 6.60; N, 11.47%).

β-(2,4-Dimethoxyphenyl)propionic acid **7c**. Alkaline hydrolysis of the nitrile **7a** (1 g) with methanolic KOH as before provided the crude acid **7c** (0.9 g), m.p. 90–96°. Recrystallisations provided pure **7c**, m.p. 103° (ether–light petroleum) (reported[2] m.p. 102–103°). (Found: C, 62.56; H, 6.85. Calc. for $C_{11}H_{14}O_4$: C, 62.85; H, 6.71%).

1,3-Dimethoxy-4,6-bis(2-carboxyethyl)benzene **7d**. Alkaline hydrolysis of the dinitrile **7b** (1 g) as before furnished the crude dicarboxylic acid **7d** (0.9 g), m.p. 96–104°. Recrystallisations provided a pure sample of **7d**, m.p. 122° (ethylacetate–light petroleum) (reported[12] m.p. 120–121°) (Found: C, 59.35; H, 6.35. Calc. for $C_{14}H_{18}O_6$: C, 59.57; H, 6.43%).

8-Methoxy-1-methyl-1,2,3,4-tetrahydronaphthalene-2-ol **8a**. To an ice-cold stirred soln of 8-methoxy-1-methyl-2-tetralone[13] (0.95 g) in a mixture of acetone-free methanol (5 ml) and water (0.5 ml) was added sodium borohydride (0.378 g). The reaction mixture was stirred for 3 h at 5° and then left at room temp. (30°) for 18 h. The reaction mixture was then cooled and decomposed with cold dil. AcOH, and the product was extracted with ether (3 × 50 ml). The solvent was washed successively with water, saturated $NaHCO_3$ soln and finally with water. Evaporation of the dry solvent furnished the crystalline alcohol **8a** (0.8 g, 83%), m.p. 90° (ether–light petroleum), λ_{max} 270 and 277 nm (ε1259 and 1349), ν_{max} 3610 cm^{-1} (OH). (Found: C, 74.75; H, 8.60. $C_{12}H_{16}O_2$ requires: C, 75.01; H, 8.33%).

2-Acetoxy-1-methyl-8-methoxy-1,2,3,4-tetrahydronaphthalene **8b**. To a cold soln of the above alcohol **8a** (1.0 g) in dry pyridine (1 ml) was added acetic anhydride (1.1 ml). The resulting mixture was kept at 5–10° for 4 h and 24 h at 30°. The reaction mixture was then decomposed with water, the resulting crystalline product was filtered, and dried to give the crude acetate **8b** (1.2 g, 98%), m.p. 48–50°. Recrystallisations of this material provided an analytical sample of **8b**, as white needles, m.p. 51–52° (petroleum ether, 40–60°), λ_{max} 270 and 277 nm (ε1452 and 1521), ν_{max} 1724 and 1250 cm^{-1} (acetate C=O). (Found: C, 71.59; H, 7.86. $C_{14}H_{18}O_3$ requires: C, 71.77; H, 7.74%).

Attempted cyanoethylation of 2-acetoxy-1-methyl-8-methoxy-1,2,3,4-tetrahydronaphthalen **8b**. Cyanoethylation of **8b** (1.17 g) was carried out following the procedure described before for *o*-cresyl methyl ether. A higher boiling material (0.21 g), ν_{max} (film) 2240 cm^{-1} thus obtained on alkaline hyrolysis gave no crystalline product which could be characterised.

Cyanoethylation of 1,7-dimethoxynaphthalene **9a**-*formation of*

β-(4,6-*dimethoxy*-1-*naphthyl*)*propionitrile* **9b**. (a) To an ice-cold (5°) stirred soln of **9a** (4 g, 0.02 mole) and acrylonitrile (3 ml, 0.04 mole) in dry *sym*-tetrachloroethane (16 ml) was added finely powdered anhydrous $AlCl_3$ (2.84 g, 0.02 mole) all at once. Dry HCl gas was then bubbled for 3 hr through the resulting homogeneous solution maintained at 5°. The resulting deep green reaction mixture was then allowed to warm up and HCl gas was passed for 30 min keeping the temperature of the reaction mixture at 33°. Usual work-up of the reaction mixture afforded the desired nitrile **9b** (3.8 g, 74%), b.p. 180° (bath)/0.2 mm Hg, m.p. 98–100°. Recrystallisations provided an analytical sample of **9b**, m.p. 104–105° (ether–light petroleum), λ_{max} 242, 248 and 285 nm (ε31,620; 31,620 and 6166), ν_{max} 2248 cm^{-1} (C≡N). (Found: C, 74.29; H, 6.18. $C_{15}H_{15}NO_2$ requires: C, 74.67; H, 6.27%).

When the bubbling of HCl gas at 33° was avoided in the above reaction, the nitrile **9b** was isolated in lower yield (65%). (b) Cyanoethylation of 1,7-dimethoxynaphthalene **9a** according to the procedure described for *o*-cresyl methyl ether furnished the desired nitrile **9b** in poor yiled (18%).

β-(4,6-*Dimethoxy*-1-*naphthyl*)*propionic acid* **9c**. (a) *By hydrolysis of nitrile* **9b**. The above nitrile **9b** (2 g) on alkaline hydrolysis as before provided the crystalline acid **9c** (1.72 g, 79%), m.p. 184–188°. Recrystallisations afforded pure material, m.p. 188° (ethyl acetate–light petroleum), λ_{max} 250 and 285 nm (ε28,840 and 4,898, ν_{max} 1710 cm^{-1} (carboxy C=O). (Found: C, 69.15; H, 6.41, N.E. 259.3. $C_{15}H_{18}O_4$ requires: C, 69.22; H, 6.20%; N.E. 260.3).

(b) *By decarboxylation of the malonic acid derivative* **11**. The malonic acid derivative **11** (2 g) was decarboxylated by heating for 20 min in an oil bath maintained at 190–195°. On cooling, the solid material was dissolved in saturated $NaHCO_3$ soln. The alkaline soln was acidified and the liberated acid was extracted with a mixture of ethyl acetate and ether (3 × 50 ml). The solvent was washed with water, dried, and evaporated to give the above propionic acid derivative **9c** (1.3 g, 76%), m.p. 188°, ν_{max} 1711 cm^{-1}.

Diethyl (4,6-*dimethoxy*-1-*naphthylidene*)*malonate* **10**. A mixture of 4,6-dimethoxy-1-naphthaldehyde[14] **9d** (3.6 g), diethyl malonate (3.5 g), piperidine (0.5 ml), dry benzene (40 ml) and a catalytic amount of benzoic acid was heated under reflux for 16 h in a Dean and Stark water separator. The reaction mixture was then cooled and diluted with water. The benzene layer was separated and the aqueous layer was extracted with ether (2 × 75 ml). The combined solvent was successively washed with cold dil. HCl (3%), water, aq $NaHCO_3$ and finally with water. Evaporation of the dry solvent afforded the crude unsaturated ester **10** (5.05 g, 84.5%), m.p. 84–88°. Recrystallisation of this material provided an analytical sample of **10**, m.p. 89–90° (ether–light petroleum), λ_{max} 222, 238, 264 and 354 nm (ε23,010; 23,010; 19,500 and 13,000); ν_{max} 1718 cm^{-1} (conj. ester C=O). (Found: C, 67.00; H, 6.36. $C_{20}H_{22}O_6$ requires: C, 67.03; H, 6.19%).

α-*Carboxy*-*β*-(4,6-*dimethoxy*-1-*naphthyl*)*propionic acid* **11**. A soln of the above unsaturated ester **10** (2.5 g) in ethanol (40 ml, 95%) was hydrogenated over Pd–C (0.2 g, 10%) at room temp. and atmospherric pressure. Theoretical quantity of hydrogen was absorbed within 1 h. Usually processing of the reaction mixture provided a reduced product as highly viscous oil (2.5 g, quantitative), λ_{max} 249 and 286 nm (ε22,916 and 4786), ν_{max} (film) 1726 cm^{-1}. This product was hydrolysed by heating under reflux for 4 h with a soln of KOH (2 g) in MeOH (40 ml). Usual work-up gave the malonic acid derivative **11** (2.10 g, 97%), m.p. 178–180°. Recrystallisation provided an analytical sample, m.p. 183° (d) (ether–light petroleum), λ_{max} 242 and 289 nm (ε29,510 and 6310). (Found: C, 63.36; H, 5.50. $C_{18}H_{18}O_6$ requires C, 63.15; H, 5.30%).

Polyphosphoric acid cyclisation of *β*-(4,6-*dimethoxy*-1-*naphthyl*)-*propionic acid* **9c**—*formation of a mixture of* 2,3-*dihydro*-6-8-*dimethoxyphenalen*-1-*one* **12** *and the isomeric benzindanone derivative* **13**; *and a pure sample of* **12**. To PPA [prepared from H_3PO_4 (6 ml, 89%) and P_2O_5 (10 g)] was added the acid **9c** (1 g). The acid was thoroughly mixed by heating the mixture on a free flame for a short time. The reaction mixture was heated on the steam bath for a further period of 30 min with constant stirring. Usual processing of the reaction mixture gave a ketonic material (0.7 g, 75%), m.p. 155–157°. Recrystallisations of this product gave a mixture of the isomeric ketones **12** and **13**, m.p. 156–157° (ethylacetate–light petroleum), m.m.p. with an authentic sample[16] of **13** (m.p. 156°) was undepressed. ν_{max}(CHCl$_3$) 1683 cm^{-1}, ν_{max} (KBr) 1712 and 1685 cm^{-1}; λ_{max} 266 and 318 nm (ε45,710 and 10,000); τ 2.45–2.19 (2H, m), 2.00–6.76 (2H, m), 6.10 (3H, s), 6.06 (3H, s), 3.20–2.22 (4H, m). (Found: C, 74.03; H, 5.99. $C_{14}H_{14}O_3$ requires: C, 74.36; H, 5.82%). The 2,4-dinitrophenylhydrazone separated from methanol as red needles, m.p. 284–285° (CH_2Cl_2–MeOH). (Found: C, 60.11; H, 4.59. $C_{20}H_{18}N_4O_6$ requires: C, 59.71; H, 4.30%).

Several recrystallisations of the above ketonic mixture from ethylacetate finally provided a pure sample of **12**, m.p. 156–157°, ν_{max} (KBr) 1712 cm^{-1}. (Found: C, 74.10; H, 5.92). Gas chromatography of this sample showed a single peak on SE 30 or OV 17 columns.

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