Tetrahedron Vol 37, No 21, pp 3653 to 3660, 1981
Printed in Great Britain.

0040-4020/81/213653-08$02.00/0
Pergamon Press Ltd.

EFFICIENT SYNTHESES OF SOME 1-NAPHTHYLALKYL KETONES AND STUDIES ON THEIR AUTOOXIDATION IN BASIC MEDIUM[1]

A. CHATTERJEE*, S. R. RAYCHAUDHURI and S. K. CHATTERJEE
Department of Chemistry, Jadavpur University, Calcutta-700032, India

(*Received UK 2 April 1981*)

Abstract—Birch reductions of 4,6-dimethoxy-1-naphthylalkyl ketones **1** provided in fair to good yields the demethoxylated products, 6-methoxy-1-naphthylalkyl ketones **2(a–g)**, not easily accessible by other procedures. Autooxidation of these ketones in basic medium afforded the diketones **6(a–c)**, the acid **2h**, and interestingly the phenol **5**. Extension of this reduction to the related tricyclic ketone **8** afforded **9a**, the phenolic ketone **9b**; and significantly the dihydrocoumarin derivative **10** as a result of autooxidation of **9a**. The mechanisms for demethoxylation and autooxidation have been discussed.

IN CONNECTION with other problems, we were interested in a practical method for demethoxylation of easily accessible 4,6-dimethoxy-1-naphthylalkyl ketones **1** to more useful 6-methoxy-1-naphthylalkyl ketones **2(a–g)**, not easily available by other procedures. It has been reported[2] that during metal–ammonia reduction, a *p*-acyl group labilises a *p*-OMe group to hydrogenolysis, but this aspect of the problem has not been thoroughly investigated for useful preparative purposes.

We now report the results of our study on metal–ammonia reduction of the above naphthyl ketones **1** for the preparation of the demethoxylated ketones **2(a–g)**. The autooxidation of **2(a–g)** in basic medium gave interesting results, and this will also be discussed. Similar reduction (see later) of the related monocyclic and tricyclic ketones are also the subject matter of the present paper.

Preparation of 4,6-dimethoxy-1-naphthylalkyl ketones **1**. Compounds **1f**[3] and **1a**[4] were prepared according to the literature from 1,7-dimethoxynaphthalene **3**. Friedel–Crafts acetylation of **3** following the reported[4] procedure but using slight excess of acetyl chloride afforded, besides the normal product **1a**, a diacetyl compound in low yield, and this has been assigned as **4** from its ^{1}H-NMR spectrum. The C-5 aromatic hydrogen doublet at τ2.4–2.5 (J = 3 Hz), shown by all dimethoxy ketones **1**, is missing in the diacetyl derivative **4**. Furthermore this assignment **4** is supported by the observation that 4,6-dimethoxy-1-methylnaphthalene undergoes formylation[3] at C-5; and bromination of **3** is reported[5] to give 4,8-dibromo-derivative. All other naphthylalkyl ketones **1(b–e)** and **1g** were prepared in excellent yields through Friedel–Crafts acylation of **3** with the appropriate acid chlorides or acid anhydride (Experimental).

Sodium-liquid ammonia reduction of 1-naphthylalkyl ketones **1**. *Results and Discussions.* An efficiently stirred solution of each ketone in tetrahydrofuran and undistilled liquid ammonia was reduced with sodium metal using ethanol as the proton source. After the disappearance of the blue colour, some ammonium chloride, not sufficient to destroy amide ion completely, was added. Evaporation of ammonia and removal of tetrahydrofuran gave a residue which was treated with water. Usual processing (see Experimental) of the resulting alkaline mixture (pH 10–12) afforded the desired demethoxylated ketones **2(a–g)**, and the autooxidation products such as **2h**[6], **6(a–c)** and interestingly the phenol **5**.[7] The results under different experimental conditions are summarised in Table 1.

Examination of Table 1 reveals that the formation of autooxidation products in alkaline solution is favoured by using excess sodium metal, and by long exposure of the homogeneous alkaline solution (when THF is used as the co-solvent) to atmospheric oxygen. In the two phase system (when Et_2O is used as the co-solvent), the desired reduction product, being in ether solution is probably protected from atmospheric oxidation; and this accounts for the high yield of the desired ketone **1c** (compare entries 4 and 7). The formation of the carbanion, an intermediate for autooxidation of the isopropyl ketone **2d**, is not favoured due to its tertiary character, and this probably rationalises the excellent yield of the desired ketone **2d** even under conditions (entry 8) favourable for oxidative degradation. In the case of the benzyl ketone **2e**, the ease of formation of the benzyl carbanion explains the isolation of all sorts of autooxidation products even when ether is used as the co-solvent (entries 9 and 13). The presence of diketones **6(a–b)** in the neutral fractions obtained from the reductions of **1b** and **1c** was revealed in the ir spectra of the crude neutral materials. In one case, the diketone **6b** was isolated in the pure state through laborious column and preparative tlc. The neutral material obtained through reduction of **1e** was directly oxidised with alkaline hydrogen peroxide to furnish, besides the ketone **2e** a *ca.* 1:1 mixture of the acid **2h** and benzoic acid. The isolation of the acid amide **2i** in trace amount from the neutral parts after reductions of **1b** and **1e** probably reflects the nucleophilic addition of $NH_2^{\ominus}$ to α-hydroperoxy ketones (Scheme-3). Careful chromatography of the phenolic fractions obtained through reductions of **1b** and **1c** (entries 3 and 7 of Table 1) provided, besides the phenol **5**, two crystalline phenolic ketones of higher polarity in small amounts, and these have been tentatively assigned as **2J** and **2k** from their ir, ^{1}H-NMR and mass spectra. The position of the signal for C-6 OMe group at τ6.1, as observed for all the dimethoxy ketones **1**, remains unaltered in these phenolic ketones; and this tempted us to assign the phenolic ketones as **2J** and **2k**. Demethylation of phenolic ethers by metal in liquid ammonia or by amide ion is well-

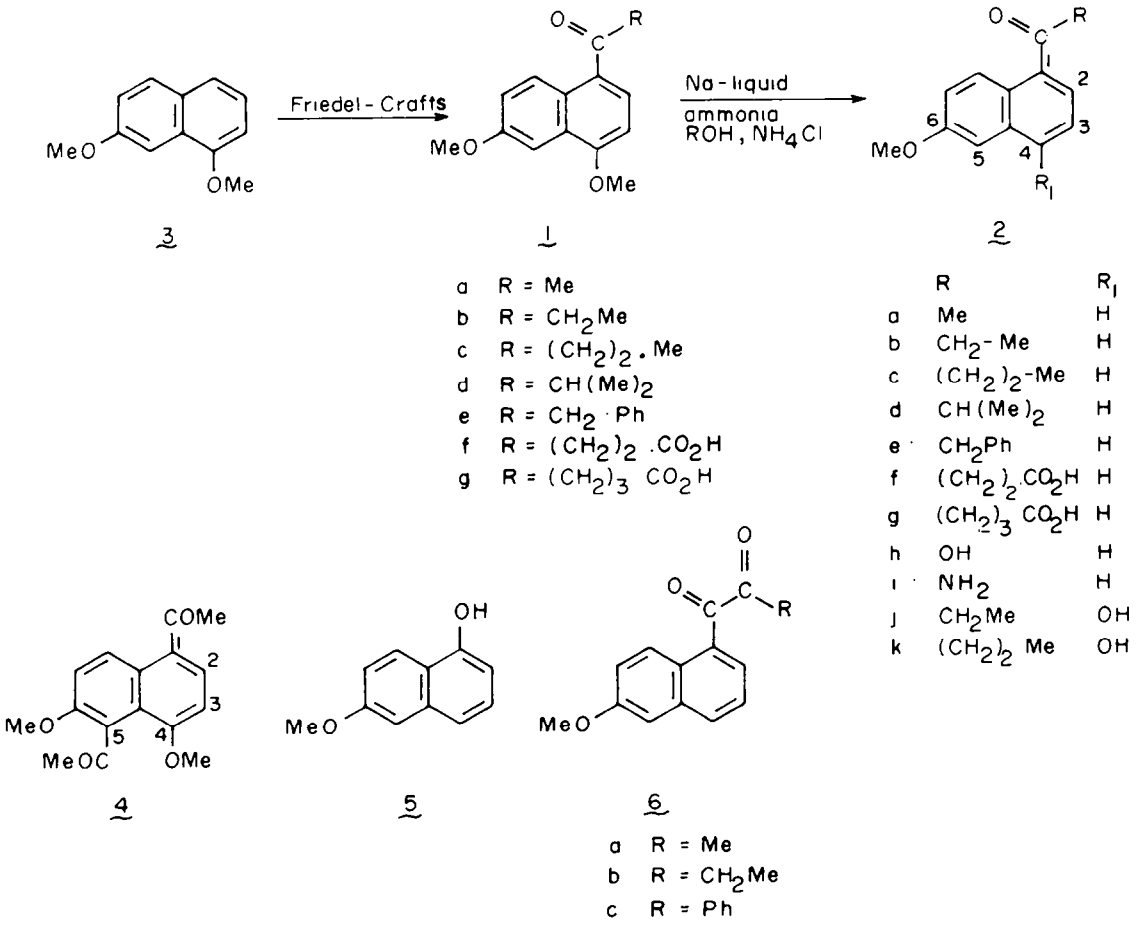


Fig. 1.

known,[8] but it is difficult at this stage to suggest whether the formation of the above phenols occurs by an elimination or a reduction process.

It is interesting to note that 2,4-dimethoxyacetophenone on reduction by the typical procedure (Experimental) behaved like simple acylbenzenes,[9] as the major product isolated, among other unidentified products,[10]† was 2,4-dimethoxyethylbenzene as a result of hydrogenolysis of the CO group.

In order to study the behaviour of the related tricyclic ketone **8** in metal-ammonia reduction, **8** was synthesised in 35% overall yield starting from naphthylmethyl ketone **1a** as shown in Fig. 2. Refluxing a mixture of N-methylanilinium trifluoroacetate[11] (TAMA), paraformaldehyde and the ketone **1a** in anhydrous dioxan afforded a product which was purified by passing its benzene solution through alumina. The vinyl ketone **7**, thus obtained as a waxy-solid, showed characteristic ^{1}H-NMR spectrum. Acid-catalysed cyclisation[12] of **7** provided a homogeneous product, and this was characterised as the benzindanone derivative **8** through its spectral characteristics. The special features of its ^{1}H-NMR spectrum are the singlet at τ3.34 and a doublet at τ0.93 assignable for C-4 and C-4′ aromatic proton respectively. The nonformation of the perinaphthanone, a possibility through cyclisation of **7**, may be ascribed[13] to the presence of the 6-OMe group which will have little influence on the 8-position but will slightly activate the 2-position in **7**.

Sodium-liquid ammonia reduction of **8** by the typical procedure reported earlier for **1c** (Experimental), furnished in respectable yield the demethoxylated product **9a**, previously prepared[14] through an unambiguous route. Processing of the alkaline solution afforded a crystalline phenol and a lactonic product. This phenol has been tentatively assigned as **9b**, and this is supported from the position of the ^{1}H-NMR signal at τ6.14 for the C-2′ OMe, and this is identical with that of the same OMe group in **8** or **9a**. The IR and mass spectra of the phenol are also in agreement with the proposed structure **9b**. The crystalline lactonic product, isolated in small amount, has been assigned as the coumarin derivative **10** from its spectral behaviour (Experimental). No carboxylic acid could be isolated in the pure state in this reaction. The formation of the products **9(a–b)** and **10** through reduction of **8** may be rationalised by the general mechanism suggested below.

Extension of sodium-liquid ammonia reductions to 4-methoxy-1-naphthylbenzyl ketone **11** under two different solvent conditions gave somewhat different results. Use of THF as the co-solvent afforded mainly the oxidation products (Experimental), whereas use of ether permitted us to isolate for the first time in moderate yield a dihydronaphthalene derivative characterised as **12** from its mass and ^{1}H-NMR spectra.

†Under selected conditions, metal–ammonia–alcohol reduction of acetophenone proceeds also by nuclear reduction (see Ref. 10).

TABLE - 1

Entry	Ketone	g.atom of Na per mole	Co-solvent	Time for removal of ammonia	Products[a](%) 2	5	6[b]
1	1a	10	THF	4 hr.	2a(53), 2h(2)	(13)	-
2[f]	1b	10	THF	4 hr.	2b(14), 2h(44.7)	(6)	6a(3.4)
3	1b	10	THF	1.5 hr.	2b(55), 2h(3.4), 2j(6)	(6)	
4	1c	10	THF	4 hr.	2c(12), 2h(29)	trace[c]	6b[e](7)
5	1c	5	THF	0.5 hr.	2c(60), 2k(6.3)	1.5	-
6	1c	10	THF	1.5 hr.	2c(7), 2h(25)	trace[c]	6b[e](18)
7	1c	10	Et_2O	4 hr.	2c(68), 2h(4.5), 2k(4.5)	(9.6)	-
8	1d	10	THF	4 hr.	2d(70), 2h(6.4)	trace[c]	-
9[f]	1e	10	THF	4 hr.	2e(13), 2h(24) $PhCO_2H$(24)	(13.1)	6c[d](12)
10	1f	10	THF	4 hr.	2f(25), 2h(21)	-	-
11	1g	10	THF	4 hr.	2h(52)	(3)	
12	1g	10	THF	1.5 hr.	2g(38), 2h(31)	(3)	-
13[f]	1e	10	Et_2O	4 hr.	2e(5), 2h(28), $PhCO_2H$(28)	(12)	6c[d](11)

[a]Products so far isolated and characterised. [b]The percentages of the diketones 6 were determined from the acid 2h obtained through alkaline H_2O_2 oxidation of the total neutral product. [c]Trace amount was characterised through comparative tlc. [d]Oxidation of this diketone with alkaline H_2O_2 gave 2h and benzoic acid (1:1). [e]This diketone was isolated in pure form. [f]This experiment afforded the amide 2i in small amount.

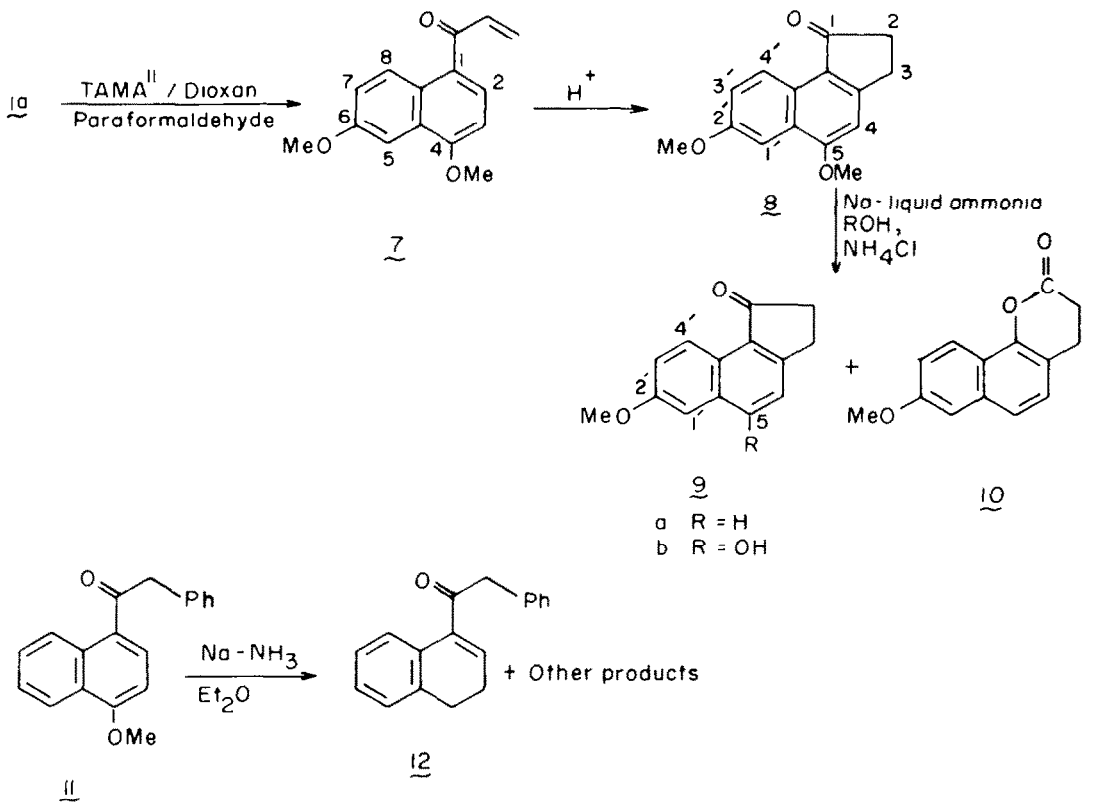
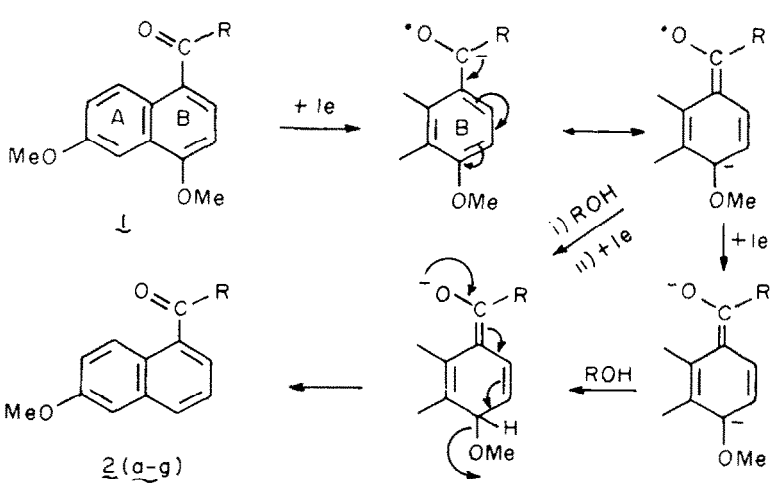


Fig. 2.

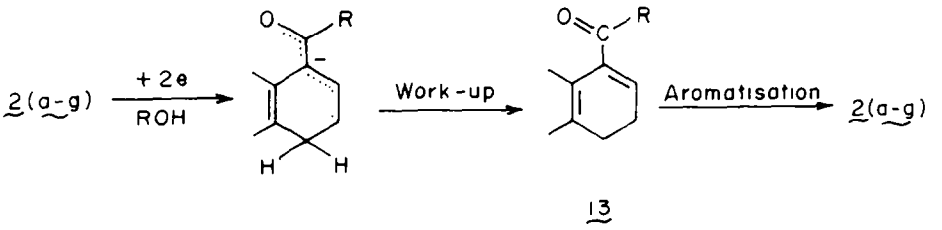
In one experiment, use of excess ammonium chloride (3.3 g in place of usual 0.5 g) in the reduction of **1b** afforded mainly a neutral material, and the phenolic ketone **2J** in very low yield. The non-homogeneous character of the above neutral product (Experimental) discouraged us from further investigations.

Mechanism for demethoxylation of **1** *and autooxidation of* **2**. The reductive removal of C-4 OMe group in ketones **1** leading to the desired products **2(a–g)** probably proceeds through the pathways depicted in Scheme-1. 11-Oxoequilenin derivatives are reduced[15] to α,β-unsaturated carbonyl compounds under the present conditions. Though we could not isolate or detect any α,β-unsaturated ketone of the type **13**, the possibility of its formation and subsequent aromatisation during work-up (Scheme-2) to the desired products **2(a–g)** cannot be ruled out. The isolation of **12** through reduction of **11** possibly supports this pathway.

Autooxidation of ketones in basic media rapidly forms α-hydroperoxy ketones[16] **14** which were sometimes isolated and identified. The α-fission of **14** to form acid has been rationalised by some authors[17] through

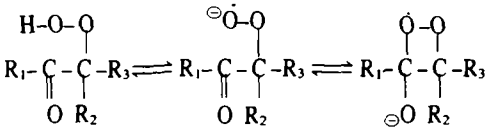


Scheme 1.

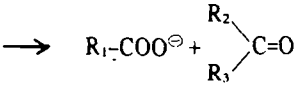


Scheme 2.

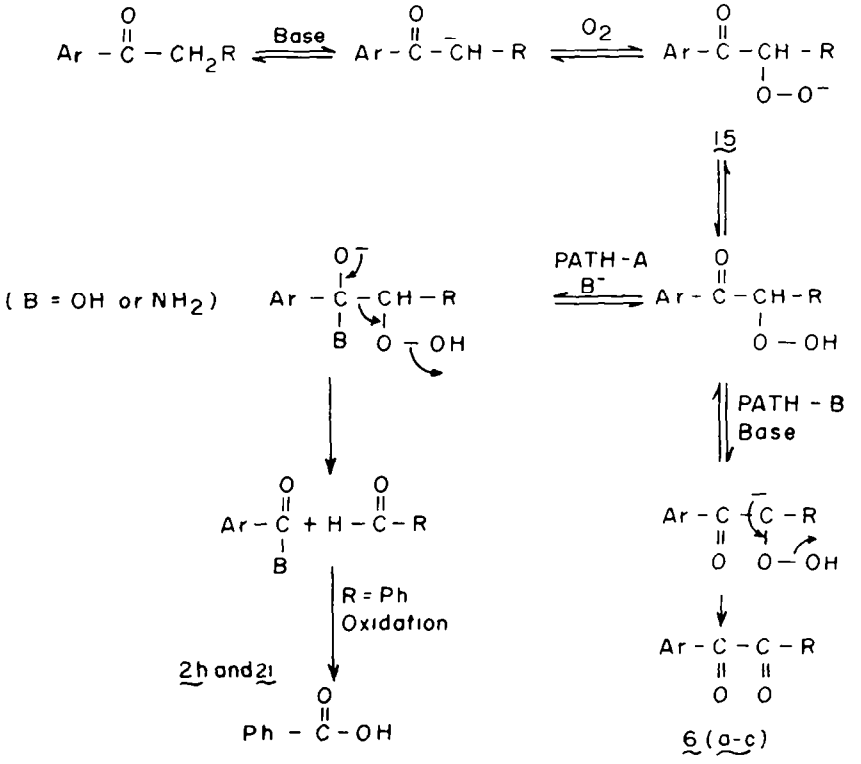
dioxetane mechanism as shown below. The high strain energy[18] (~ 26 Kcal/mole) of 1,2-dioxetane,



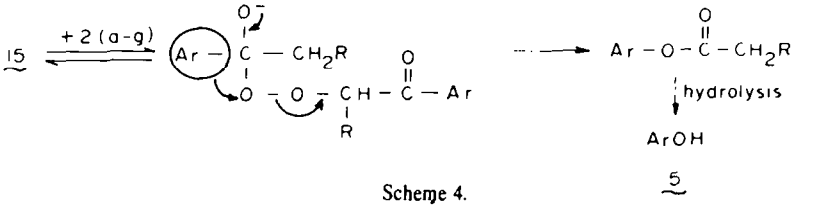
14



and especially the formation of the amide **2i** in two cases mentioned reduces the importance of dioxetane mechanism in the present case. Recent studies[18] on alkoxide-catalysed decomposition of several α-hydroperoxy ketones proved that the α-cleavage reaction proceeds predominantly via an acyclic carbonyl addition intermediate. There are other instances also where acyclic mechanism was shown[19] to be the main pathway for the α-cleavage reaction. It is also known that if the α-hydroperoxy ketone **14** bears an α-H atom, base-catalysed elimination may lead to α-diketone[20] which in some cases has been isolated. The formation of autooxidation products such as **2h**, **2i** and **6(a–c)** in the present case may therefore be best rationalised by the pathways A and B shown in Scheme-3.



Scheme 3.



Scheme 4.

The isolation of phenol **5** in low yield in most of the cases (Table 1) probably reflects an intermolecular pathway involving the anion of α-hydroperoxy ketones **15** and ketones **2** as shown in Scheme-4. It may be mentioned that this is probably the first report of phenol formation through autooxidation of arylalkyl ketones.

EXPERIMENTAL

M.ps were determined on a H_2SO_4 bath. UV spectra were measured for solns in EtOH with a Unicam SP500 spectrophotometer, IR spectra for solns in $CHCl_3$ with a Perkin–Elmer 337 instrument, and NMR spectra for solns in $CDCl_3$ (until otherwise stated) with a Varian T-60 spectrometer (TMS as internal standard). For glc, a Hewlett–Packard 5730 gas chromatograph, with flame ionisation detector was used. Extracts were dried over Na_2SO_4, and light petroleum refers to the fraction of b.p. 60–80°.

Preparation of dimethoxynaphthyl ketones **1(a–g)**

Friedel–Crafts reaction of 1,7-*dimethoxynaphthalene* **3** *with acetyl chloride; formation of* 4,6-*dimethoxy*-1-*naphthylmethyl ketone* **1a**, *and* 5-*acetyl*-4,6-*dimethoxy*-1-*naphthylmethyl ketone* **4**. To an ice-cooled and stirred soln of **3** (8 g) and AcCl (5 g) in $PhNO_2$ (50 ml) was added anhyd $AlCl_3$ (6.5 g) in small portions during 30 min. The mixture was left at r.t. for 16 hr, then poured on ice; the $PhNO_2$ was removed by steam distillation, and the product was taken up in benzene (500 ml). The solvent was washed with 4% NaOH aq. and then with water. Evaporation of the dry solvent gave a residue which was distilled to furnish two fractions: (i) b.p. 178–184°/0.1 mm (7.4 g, 75%) and (ii) b.p. 190–220° (2 g, 17%), m.p. 140–142°. The first fraction on keeping solidified to give **1a**, m.p. 86–88° (MeOH) (lit.[4] m.p. 88°); ν_{max} 1659 cm^{-1} (C=O); λ_{max} 249 (ε15.850), 312 (4677) and 341 nm (3715); τ1.1(1H, d, J = 9 Hz), 2.22(1H, d, J = 9 Hz), 2.48(1H, d, J = 3 Hz), 2.82(1H, m), 3.33(1H, d, J = 9 Hz), 6.00(3H, s), 6.10(3H, s) and 7.33(3H, s); 2,4-*dinitrophenyl-hydrazone* had m.p. 235–237° ($CHCl_3$–MeOH) (Found: C, 58.17; H, 4.29; N, 13.52. $C_{20}H_{18}N_4O_6$ requires: C, 58.54; H, 4.42; N, 13.65%).

The above higher boiling fraction (ii) on crystallisation afforded an analytical sample of **4** (1.7 g, 15%), m.p. 143–144° (MeOH); ν_{max} 1706 (C=O) and 1665 cm^{-1} (C=O); τ1.03(1H, d, J = 9 Hz), 2.17(1H, d, J = 8 Hz), 2.67(1H, d, J = 9 Hz), 3.30(1H, d, J = 8 Hz), 6.10(6H, s), 7.33(3H, s) and 7.47(3H, s) (Found: C, 70.48; H, 6.02. $C_{16}H_{16}O_4$ requires: C, 70.58; H, 5.92%). *Mono*-2,4-*dinitrophenylhydrazone* had m.p. 217–218° ($CHCl_3$–MeOH) (Found: C, 58.28; H, 4.22. $C_{22}H_{20}N_4O_7$ requires: C, 58.41; H, 4.42%).

4,6-*Dimethoxy*-1-*naphthylethyl ketone* **1b**. Friedel–Crafts reaction of **3** (8 g) with propionyl chloride (5.5 g) as above afforded initially **1b** as yellow oil (7.8 g, 75%), b.p. 190–195°/0.4 mm, m.p. 120–125°. An analytical sample of **1b** had m.p. 126–127° (MeOH): ν_{max} 1667 cm^{-1} (C=O); τ1.27(1H, d, J = 9 Hz), 2.28(1H, d, J = 9 Hz), 2.48(1H, d, J = 3 Hz), 2.70–2.90(1H, m), 3.32(1H, d, J = 8 Hz), 6.00(3H, s), 6.12(3H, s), 7.01(2H, q, J = 7 Hz) and 8.77(3H, t, J = 7 Hz) (Found: C, 73.51; H, 6.52. $C_{15}H_{16}O_3$ requires: C, 73.75; H, 6.60%). 2,4-*Dinitrophenylhydrazone* of **1b** had m.p. 149–50° ($CHCl_3$–MeOH) (Found: C, 59.01; H, 5.03. $C_{21}H_{20}N_4O_6$ requires: C, 59.43; H, 7.75%).

4,6-*Dimethoxy*-1-*naphthyl*-n-*propyl ketone* **1c**. Reaction of **3** (8 g) with *n*-butyryl chloride (7 g) afforded **1c** (7.4 g, 68%), b.p. 187°/0.1 mm; m.p. 85–87°. Analytical sample of **1c**, obtained as needles, had m.p. 86–87° (acetone); ν_{max} 1662 cm^{-1} (C=O); τ1.27(1H, d, J = 9 Hz), 2.24(1H, d, J = 8 Hz), 2.45(1H, d, J = 3 Hz), 2.70–2.90(1H, m), 3.30(1H, d, J = 8 Hz), 5.99(3H, s), 6.10(3H, s), 7.05(2H, t, J = 7 Hz), 8.18(2H, m) and 9.00(3H, t, J = 7 Hz) (Found: C, 74.14; H, 6.91. $C_{16}H_{18}O_3$ requires: C, 74.40; H, 7.02%). 2,4-Dinitrophenylhydrazone of **1c** had m.p. 165–166° (ethyl acetate) (Found: C, 60.56; H, 4.96; N, 12.76. $C_{22}H_{22}N_4O_6$ requires: C, 60.27; H, 5.06; N, 12.78%).

*This amount was insufficient to destroy NH_2^- completely.

4,6-*Dimethoxy*-1-*naphthyl-isopropyl ketone* **1d**. Reaction of **3** (8 g) with isobutyryl chloride (6.4 g) as before, and extraction of the product with ether (3 × 100 ml) afforded **1d** (8.9 g, 81%), b.p. 180°/0.1 mm; m.p. 73–74° (Et_2O-light petroleum, b.p. 40–60°); ν_{max} 1664 cm^{-1} (C=O); τ1.41 (1h, d, J = 9 Hz), 2.28(1H, d, J = 8 Hz), 2.40(1H, d, J = 3 Hz), 2.66–2.88(1H, m), 3.26(1H, d, J = 8 Hz), 5.98(3H, s), 6.08(3H, s), 6.23–6.68(1H, m) and 8.77(6H, d, J = 7 Hz) (Found: C, 74.12; H, 6.81. $C_{16}H_{18}O_3$ requires: C, 74.40; H, 7.02%).

4,6-*Dimethoxy*-1-*naphthylbenzyl ketone* **1e**. Freidel–Crafts reaction of **3** (9 g) with phenyl acetyl chloride (10 g) furnished directly **1e** (12 g, 82%), m.p. 111–112° (MeOH); ν_{max} 1664 cm^{-1}; τ1.23(1H, d, J = 9 Hz), 2.15(1H, d, J = 8 Hz), 2.52(1H, d, J = 3 Hz), 2.72–2.8 (5H, m), 2.95(1H, m), 3.33(1H, d, J = 8 Hz), 5.72(2H, s), 6.00(3H, s) and 6.12(3H, s) (Found: C, 78.46; H, 6.12. $C_{20}H_{18}O_3$ requires: C, 78.41; H, 5.92%). 2,4-*Dinitrophenylhydrazone* of **1e** had m.p. 205–206° ($CHCl_3$–MeOH) (Found: C, 64.31; H, 4.71. $C_{26}H_{22}N_4O_6$ requires: C, 64.19; H, 4.56%).

γ-(4,6-*Dimethoxy*-1-*naphthoyl*)*butyric acid* **1g**. To an ice-cooled and stirred mixture of **3** (17.8 g) and glutaric anhydride (12.2 g) in *sym*-tetrachloroethane (106 ml) was added anhyd $AlCl_3$ (28 g) in small portions during 30 min. After stirring for 5–6 hr in an ice-bath, the mixture was left in the refrigerator for 16 hr. Decomposition of the mixture with ice and HCl (60 ml) and subsequent steam distillation provided an acid. This acid was purified by dissolving in aq Na_2CO_3 and then treating the soln with animal charcoal. Usual work-up then afforded the acid **1g** (26 g, 90%) m.p. 188–192°. A part was recrystallised to give an analytical sample of **1g**, m.p. 194–195° (acetone–light petroleum); ν_{max} 1688 and 1662 cm^{-1}; τ(DMSO-d_6) 1.25(1H, d, J = 9.5 Hz), 2.00(1H, d, J = 8 Hz), 2.44(1H, d, J = 2.5 Hz), 2.73(1H, dd, J = 3 and 9.5 Hz), 3.02(1H, d, J = 8 Hz), 5.93(3H, s), 6.10(3H, s), 6.91(2H, t, J = 6.8 Hz) and 7.65–8.21(4H, m) (Found: C, 67.06; H, 5.91. $C_{17}H_{18}O_5$ requires: C, 67.54; H, 6.00%).

General reduction procedure, and isolation of the products. To an efficiently stirred mixture of undistilled liquid ammonia (500 ml), and a soln of **1c** (1 g) in THF (50 ml) and abs EtOH (11.6 ml), was added Na metal (1 g) in small pieces within 2–3 min. After the disappearance of the blue colour (1 min), ammonium chloride (0.5 g)* was added all at a time. Ammonia was then evaporated during 4 hr, and THF was removed under reduced pressure. The residue was treated with water, and the resulting alkaline mixture (pH 10–12) was extracted with ether (3 × 100 ml). The combined solvent was extracted with 5% NaOH aq (2 × 25 ml), washed with water, dried, and evaporated to furnish a neutral fraction which was separated by chromatography over silica gel to furnish **2c** and **6b**. The combined alkaline soln was acidified and the liberated acidic materials were extracted with ether (3 × 50 ml). Usual separation with $NaHCO_3$ aq provided an acid and a phenolic fraction. Chromatography of each fraction over silica gel afforded the acid **2h** and the phenol **5** (trace amount).

Properties of the reduction and autooxidation products

β-(6-*Methoxy*-1-*naphthoyl*) *propionic acid* **2f**. This acid was crystallised to afford an analytical sample of **2f**, m.p. 151–152° (acetone–light petroleum); ν_{max} 1714 and 1683 cm^{-1}; τ(DMSO-d_6) 1.65(1H, d, J = 9.6 Hz), 1.95–2.89(5H, m), 6.12(3H, s), 6.70(2H, t, J = 6 Hz), 7.34(2H, t, J = 6Hz) (Found: C, 69.64; H, 5.41. $C_{15}H_{14}O_4$ requires: C, 69.76; H, 5.46%).

γ-(6-*Methoxy*-1-*naphthoyl*)*butyric acid* **2g**. An analytical sample of **2g** had m.p. 117–118° (Et_2O-light petroleum); ν_{max} 1710 and 1686 cm^{-1}; τ1.33–1.73(2H, m), 2.03–3.00(4H, m), 6.10(3H, s), 6.90(2H, t, J = 7 Hz) and 7.33–8.23(4H, m) (Found: C, 70.67; H, 6.10. $C_{16}H_{16}O_4$ requires: C, 70.58; H, 5.92%).

6-*Methoxy*-1-*acetylnaphthalene* **2a**. An analytical sample of **2a** had m.p. 63–64° (Et_2O-light petroleum) (lit.[21] m.p. 64–65°); ν_{max} 1678 cm^{-1} (C=O); λ_{max} 241(ε 22,910) and 304 nm (5012), τ1.30(1H, d, J = 9.2 Hz), 1.99–2.84(5H, m), 6.08(3H, s) and 7.32(3H, s) (Found: C, 77.83; H, 6.21. $C_{13}H_{12}O_2$ requires: C, 77.98; H, 6.04%); 2,4-*dinitrophenylhydrazone* had m.p. 248° (CH_2Cl_2) (Found: C, 59.92; H, 4.26; N, 14.81. $C_{19}H_{16}N_4O_5$ requires: C, 60.00; H, 4.24; N, 14.73%)

6-*Methoxy*-1-*naphthol* **5**. An analytical sample of **5** had m.p. and mixed m.p. 83–85°(Et_2O–light petroleum) (lit.[7] m.p. 85°); ν_{max} 3575 cm^{-1}; λ_{max} 243 (ε 26,300) and 205 nm (3162); λ_{max}^{NaOH} 259(ε 31,620), 321(8913) and 344 nm (9550); τ1.90(1H, d, J = 10 Hz), 2.70–2.90(5H, m), 3.23–3.37(1H, m) and 6.07(3H, s); *m/e* 174(M^+).

6-*Methoxy*-1-*naphthoic acid* **2h**. The analytical sample had m.p. and m.m.p. 178–180° (Et_2O–light petroleum) (lit.[6] m.p. 180°); ν_{max} (KBr) 1699 cm^{-1} (acid C=O); λ_{max} 227 (ε 52,480) and 278 nm (5248); τ(DMSO-d_6), 1.24(1H, d, J = 9.6 Hz), 1.95–2.88(5H, m) and 6.12(3H, s); *m/e* 202(M^+) (Found: C, 70.80; H, 5.30. $C_{12}H_{10}O_3$ requires: C, 71.28; H, 4.98%).

6-*Methoxy*-1-*naphthylethyl ketone* **2b**. This ketone was isolated as pale yellow oil, b.p. 80°/0.1 mm; ν_{max} 1675 cm^{-1} (C=O); τ1.58(1H, d, J = 9 Hz), 2.20–2.97(5H, m), 6.15(3H, s), 7.00(2H, q, J = 7 Hz) and 8.77 (3 H, t, J = 7 Hz) (Found: C, 78.21; H, 6.30. $C_{14}H_{14}O_2$ requires: C, 78.48; H, 6.59%). 2,4-*Dinitrophenylhydrazone* of **2b** had m.p. 174–175° ($CHCl_3$–MeOH) (Found: C, 60.62; H, 4.74. $C_{20}H_{18}N_4O_5$ requires: C. 60.91; H, 4.60%).

4-*Hydroxy*-6-*methoxy*-1-*naphthylethyl ketone* **2J**. This phenol was isolated in very poor yield (entry 3, Table 1) from the phenolic fraction after chromatography over silica gel (70 times) and elution of the chromatogram with Et_2O–light petroleum (20:30). It had m.p. 128–132° (Et_2O–light petroleum; ν_{max} 3592 (OH) and 1682 cm^{-1} (C=O); *m/e* 230(M^+), 201(M^+–Et, base peak) and 173(M^+–COEt).

6-*Methoxy*-1-*naphthyl-isopropyl ketone* **2d**. The crude neutral product was distilled to afford pure **2d**, b.p. 140° (bath)/0.1 mm; ν_{max} 1680 (C=O) cm^{-1}; τ(CCl_4) 1.75(1H, d, J = 9 Hz), 2.24–2.99(5H, m), 6.18(3H, s), 6.58(1H, m) and 8.92(6H, d, J = 7 Hz) (Found: C, 78.92; H, 7.06. $C_{15}H_{16}O_2$ requires: C, 78.90; H, 7.34%).

6-*Methoxy*-1-*naphthylbenzyl ketone* **2e**. The neutral material (0.56 g), ν_{max} 1711 (m) and 1678 cm^{-1} (s), obtained from reduction of the dimethoxy ketone **1e** (1.3 g) was oxidised in methanolic soln with 15% H_2O_2 and 5% aq NaOH. The neutral product (0.37 g) isolated from this oxidation was chromatographed over silica gel (12 g), and elution with Et_2O–light petroleum (5:95) afforded the desired ketone **2e** (0.15 g), m.p. 117° (Et_2O–light petroleum); ν_{max} 1673 cm^{-1}; τ1.51(1H, d, J = 9 Hz); 2.12–2.90(10H, complex m), 5.69(2H, s) and 6.13(3H, s) (Found: C, 82.59; H, 6.03. $C_{19}H_{16}O_2$ requires: C, 82.58; H, 5.84%).

Elution with ether gave a small amount of solid, characterised as 6-*methoxy*-1-*naphthylamide* **2i**, m.p. 198° (Et_2O–light petroleum); ν_{max} 3530, 3415 and 1670 cm^{-1} (C=O); τ1.81(1H, d, J = 10 Hz), 2.07–2.60(3H, m), 2.67(1H, d, J = 3 Hz), 2.81(1H, dd, J = 3 and 10 Hz), 6.11(3H, s) and 6.48(2H, s); *m/e* 201(M^+, base peak), 185(M^+–NH_2) and 157(M^+–$CONH_2$).

6-*Methoxy*-1-*naphthyl*-n-*propyl ketone* **2c**, *and* 4-*hydroxy*-6-*methoxy*-1-*naphthyl*-n-*propyl ketone* **2k**. Na–liquid ammonia reduction of **1c** (entry 5, Table 1) afforded **2c**, b.p. 160°/0.1 mm; ν_{max} 1678 cm^{-1}; τ1.58(1H, d, J = 8 Hz), 2.20–2.70(5H, m), 6.15(3H, s), 7.07(2H, t, J = 7 Hz), 8.23(2H, m) and 9.02(3H, t, J = 7 Hz) (Found: C, 78.88; H, 7.04. $C_{15}H_{16}O_2$ requires: C, 78.92; H, 7.06%); 2,4-*dinitrophenylhydrazone of* **2c** separated from MeOH and had m.p. 138° (Found: C, 61.63; H, 5.03. $C_{21}H_{20}N_4O_5$ requires: C, 61.76; H, 4.94%).

The phenolic part was chromatographed over silica gel (30 times). Elution of the chromatogram with Et_2O–light petroleum (2:98) gave **5**, and further elution with the same solvent mixture (10:90); provided **2k**, m.p. 110° (Et_2O–light petroleum); ν_{max} 3598 and 1680 cm^{-1}; τ1.85(1H, d, J = 9 Hz), 2.70–3.12(5H, m), 6.15(3H, s), 7.08(2H, t, J = 7 Hz), 8.23(2H, m) and 9.02(3H, t, J = 7 Hz); *m/e* 244(M^+), 201(M^+–C_3H_7, base peak) and 173(M^+–COC_3H_7) (Found: C, 73.61; H, 6.30. $C_{15}H_{16}O_3$ requires: C, 73.75; H, 6.60%).

4-(6-*Methoxy*-1-*naphthyl*)-3,4-*dioxobutane* **6b**. The neutral fraction, ν_{max} 1711 and 1667 cm^{-1}, obtained from the reduction of **1c**, (entry 6, Table 1) on twice chromatography over silica gel afforded a mixture of two products (tlc). Gas chromatography of this mixture (3% SE 52 column, temp. 195°) indicated the product to be a 27:73 mixture (retention times 27.13 and 34 min) of the monoketone **2c**, and the diketone **6b** respectively. Separation of this mixture by chromatography on thick layer plate (coated with silica gel of thickness 2 mm, and using a ½:1 mixture of cyclohexane-ethylacetate as the eluting solvent) furnished **6b** as glass, τ1.14(1H, d, J = 9 Hz), 2.1–2.9(5H, complex m), 6.15(3H, s), 7.06(2H, q, J = 7.5 Hz) and 8.78(3H, t, J = 7 Hz); *m/e* 242(M^+), 185(M^+–COEt, base peak) and 157(M^+–COCOEt).

Sodium–liquid ammonia reduction of 2,4-*dimethoxyacetophenone; formation of* 2,4-*dimethoxy ethylbenzene*. Reduction of 2,4-dimethoxyacetophenone (0.5 g) by the general procedure afforded a neutral fraction characterised as 2,4-*dimethoxyethylbenzene* (0.25 g), b.p. 95° (bath)/0.2 mm; ν_{max} 1610 cm^{-1}; τ(CCl_4) 3.13(1H, d, J = 8 Hz), 3.70–3.86(2H, m), 6.23(3H, s), 6.30(3H, s), 7.51(2H, q, J = 7.5 Hz) and 8.90(3H, t, J = 7.5 Hz) (Found: C, 71.90; H, 8.67. $C_{10}H_{12}O_3$ requires: C, 72.26; H, 8.49%).

2′,5-*Dimethoxy*-6:7-*benzindan*-1-*one* **8**. A magnetically stirred mixture of **1a** (6 g), paraformaldehyde (3.6 g) and N-methylanilinium trifluoroacetate[11] (TAMA) (7.5 g) in dry dioxan (20 ml) was refluxed under N_2 for 6 hr. The mixture was cooled and paraformaldehyde (1.8 g), TAMA (3.8 g) and dioxan (10 ml) were again added. The resulting mixture was further refluxed for 4 hr, then diluted with water (500 ml), and the product was extracted with ether (2 × 100 ml). The aq layer was then treated with AcONa, and the resulting soln was further extracted with ether (2 × 100 ml). Usual processing of the combined extract gave a gummy material. A benzene soln of this material was passed through a column of alumina (80 g) to furnish **7** as waxy solid (3.8 g, 60%), m.p. 57–59°; ν_{max} 1661 and 1623 cm^{-1}. τ 1.42(1H, d, J = 10 Hz), 2.18(1H, d, J = 9.5 Hz), 2.43(1H, d, J = 3 Hz), 2.67–3.01(2H, m), 3.26(1H, d, J = 8.5 Hz), 3.72(1H, dd, J = 2.5 and 17.5 Hz), 4.08(1H, dd, J = 2.5 and 10 Hz), 5.98(3H, s) and 6.08(3H, s).

The ketone **7** (2 g) was cyclised according to the reported procedure[12] to furnish the desired indanone derivative **8** (1.35 g), m.p. 165–166°. Recrystallisation provided an analytical sample of **8**(1.15 g, 57%), m.p. 171° (Et_2O-light petroleum); ν_{max} 1675 cm^{-1}; τ0.93(1H, d, J = 9 Hz), 2.51(1H, d, J = 3 Hz), 2.73(1H, dd, J = 3 and 9 Hz), 3.34(1H, s), 5.97(3H, s), 6.08 (3h, s), 6.80–7.02(2H, m) and 7.20–7.41(2H, m) (Found: C, 74.35; H, 5.85. $C_{15}H_{14}O_3$ requires: C, 74.36; H, 5.82%).

Sodium–liquid ammonia reduction of the indanone derivative **8**; *formation of the demethoxylated ketone* **9a**, *the phenol* **9b**, *and the coumarin derivative* **10**. Na–liquid ammonia reduction of **8** (1.12 g) (*cf* entry 4, Table 1) afforded a neutral product (0.6 g) Chromatography over silica gel (25 g), and elution with ether–light petroleum (1:1) furnished 2′-*methoxy*-6:7-*benzindan*-1-*one* **9a** (0.47 g, 47%), m.p. 149–150° (Et_2O–light petroleum) (lit.[14] m.p. 154–155°), ν_{max} 1682 cm^{-1}; τ0.93(1H, d, J = 9 Hz), 2.15(1H, d, J = 8.5 Hz), 2.67–2.83(3H, m), 6.10(3H, s), 6.80–7.02(2H, m) and 7.20–7.41(2H, m) (Found: C, 79.12; H, 5.78. $C_{14}H_{12}O_2$ requires: C, 79.23; H, 5.70%). 2,4-*Dinitrophenylhydrazone* of **9a** separated from MeOH and had m.p. 286° (d) ($CHCl_3$–benzene) (lit.[14] m.p. 286–288°) (Found: C, 61.06; H, 4.36. $C_{20}H_{16}N_4O_5$ requires: C, 61.22; H, 4.11%).

The phenolic part (270 mg) was directly crystallised to afford 2′-*methoxy*-5-*hydroxy*-6:7-*benzindan*-1-*one* **9b** (165 mg, 16%), m.p. 229° (acetone–light petroleum); ν_{max} 3580, 1695 and 1630 cm^{-1}; special features of ^1H NMR are τ(DMSO-d_6) – 0.95(broad s, OH), 0.88(d, J = 9 Hz, C_4–H) and 6.14(s, OMe); *m/e* 228(M^+, base peak), 200(M^+ – 28), 185(M^+ – 43) and 157(M^+ – 71) (Found: C, 73.74; H, 5.36. $C_{14}H_{12}O_3$ requires: C, 73.67; H, 5.30%).

The bicarbonate soluble portion was a gummy product (0.25 g). Chromatography of this material over silica gel (10 g), and elution with Et_2O–light petroleum (1:9) gave a crystalline material which was recrystallised to furnish 2′-*methoxy*-3,4-*dihydro*-7:8-*benzcoumarine* **10** (15 mg); m.p. 97–98°; ν_{max} 1762 and 1630 cm^{-1}; τ1.906(1H, d, J = 9 Hz), 2.55(1H, d, J = 8 Hz), 2.90–2.76(3H, m), 6.10(3H, s) and 7.22–6.67(4H, complex m); *m/e* 228(M^+, base peak), 200(M^+–CO), 186(M^+–CH_2CO) and 158(M^+ – 70).

Sodium–liquid ammonia reduction of 4-*methoxy*-1-*naphthylbenzyl ketone* **11** *under two solvent conditions*. Compound **11** was prepared in 60% yield through Friedel–Crafts reaction, and had m.p. 83–84° (MeOH) (lit.[22] m.p. 84°).

(a) Na–liquid ammonia reduction of **11** (1.2 g) using THF as

co-solvent (see entry 2, Table 1) afforded a neutral (0.3 g), phenolic (0.27 g) and an acidic fraction (0.60 g).

The above neutral fraction (0.3 g) on oxidation with alkaline H_2O_2 in MeOH gave benzoic acid (40 mg), and a gummy neutral material (0.15 g) which on chromatography over silica gel (6 g) and elution with ether–light petroleum (3:1) afforded α-naphthylamide (12 mg), m.p. 200° (reported m.p. 201°), ν_{max} 3525, 3405 and 1675 cm^{-1} ($CONH_2$).

Phenolic part was distilled to furnish *α-naphthol* (88 mg, 13%), m.p. and m.m.p. 95–96°.

The acidic fraction (0.6 g) on distillation afforded *benzoic acid* (0.25 g, 47%), b.p. 60°(bath)/1 mm.

(b) Similar reduction of **11** (1.2 g) in Et_2O by the condition mentioned in entry 7 (Table 1) furnished mostly a neutral product as foamy solid (1.06 g). Alkaline H_2O_2 oxidation of this material provided *benzoic acid* (6%) and a neutral fraction (1 g). Careful distillation of this material gave 3,4-dihydro-1-naphthylbenzyl ketone **12** (0.4 g, 37%), b.p. 140°(bath)/0.005 mm, m.p. 76° (Et_2O–light petroleum); ν_{max} 1660 cm^{-1}; τ2.90–2.48(9H, complex m), 3.05(1H, t, J = 5 Hz), 5.96(2H, s) and 7.75–7.20(4H, m); *m/e* 248(M^+) and 157(M^+–CH_2Ph) (Found: C, 87.14; H, 6.42. $C_{18}H_{16}O$ requires: C, 87.06; H, 6.49%); and a higher boiling material which could not be characterised.

Sodium–liquid ammonia reduction of 4,6-dimethoxy-1-naphthylethyl ketone **1b** *in presence of excess ammonium chloride.* Reduction of **1b** (1 g), but using excess NH_4Cl (3.3 g in place of 0.5 g), afforded a neutral material (0.86 g); ν_{max} 1710 and 1675 cm^{-1}, a phenolic product (72 mg), and an acid (10 mg). Oxidation of the neutral product (0.86 g) with alkaline H_2O_2 as before furnished a neutral fraction (0.3 g), b.p. 100°(bath)/0.2 mm, ν_{max} 1680 cm^{-1}; and an acidic material (0.4 g). Attempted preparation of DNP derivative of the above neutral fraction gave a gummy derivative. Repeated crystallisations of this derivative finally provided a small amount of pure *2,4-DNP*, m.p. 174–175° of the ketone **2b**.

The above crude acidic material (0.4 g), obtained after H_2O_2 oxidation, was chromatographed over silica gel (50 times) and elution with ether–light petroleum (1:1) furnished a solid acid (0.28 g, 33%), m.p. 170–190°, ν_{max} 1705 cm^{-1} probably as a mixture of **2h**, and the corresponding 3,4-dihydroderivative. Separation of this mixture so far failed.

Chromatography of the above phenolic fraction (72 mg) over silica gel afforded *4-hydroxy-6-methoxy-1-naphthylethyl ketone* **2j** (45 mg, 4.8%), m.p. 130–132°; ν_{max} 3590 and 1680 cm^{-1}.

Acknowledgements—We thank U.G.C. (Government of India), and the East India Pharmaceutical Works Ltd. for financial assistance.

REFERENCES

[1]For a preliminary communication of part of this work, see A. Chatterjee, S. R. Raychaudhuri and S. K. Chatterjee, *Tetrahedron Letters* 3487 (1978).

[2]A. J. Birch, J. A. K. Quartey and H. Smith, *J. Chem. Soc.* 1768 (1962).

[3]R. A. Barnes and W. M. Bush, *J. Am. Chem. Soc.* **80**, 4714 (1958).

[4]NG. Ph. Buu Hoi and D. Lavit, *J. Org. Chem.* **21**, 1257 (1956).

[5]F. Bell and K. R. Buck, *J. Chem. Soc.* 4626 (1963).

[6]C. C. Price, E. C. Chaplin, A. Goldman, E. Krebs and H. M. Shaper, *J. Am. Chem. Soc.* **63**, 1857 (1941).

7. T. R. Kasturi and T. Arunachalam, *Can. J. Chem.* **46**, 3625 (1968); R. J. W. Byrde, D. F. Downing and D. Woodcock, *Biochem. J.* **72**, 344 (1959).

[8]A. J. Birch and G. S. R. Subba Rao, *Advances in Organic Chemistry, Methods and Results*, Vol. 8, pp. 32–33. Wiley Interscience, New York (1972).

[9]A. R. Pinder and H. Smith, *J. Chem. Soc.* 113 (1954).

[10]S. M. Narisada and F. Watanabe, *J. Org. Chem.* **38**, 3887 (1973).

[11]Jean-Louis Gras. *Tetrahedron Letters* 2111 (1978); *Ibid*, 2955 (1978).

[12]See, E. D. Thorsett and F. R. Stermitz, *Synthetic Communications* 375 (1972).

[13]See, A. L. Green and D. H. Hey, *J. Chem. Soc.* 4306 (1954).

[14]P. McCloskey, *Ibid.* 3811 (1965).

[15]S. Mejer and S. Respondek, *Chem. Abstr.* **66**, 105088[a] (1967); D. K. Banerjee, E. J. Jacob and N. Mahishi, *Steroid* **16**, 733 (1970); A. J. Birch and G. S. R. Subba Rao, *Aust. J. Chem.* **23**, 547 (1970).

[16]H. O. House, *Modern Synthetic Reactions* 2nd Edn. p. 349. Benjamin, California (1972); C. Fuson and H. L. Jackson, **72**, 1637 (1950); W. H. Richardson and R. F. Steed, *J. Org. Chem.* **32**, 771 (1967).

[17]W. E. Doering and R. M. Haines, *J. Am. Chem. Soc.* **76**, 482 (1954); P. Aeberli and W. J. Houlihan, *J. Org. Chem.* **33**, 1640 (1968); W. Cocker, K. J. Crowley and K. Srinivasan, *J. Chem. Soc.* Perkin I, 1971 (1972); and W. H. Richardson, V. F. Hodge, D. L. Stiggal, M. B. Yelvington and F. C. Montgomery, *J. Am. Chem. Soc.* **96**, 6652 (1974).

[18]Y. Sawaki and Y. Ogata, *Ibid.* **97**, 6983 (1975).

[19]F. G. Bordwell, R. G. Scamehorn and A. C. Knipe, *Ibid.* **92**, 2172 (1970); F. G. Bordwell and A. C. Knipe, *Ibid.* **93**, 3416 (1971); M. F. Ansell, I. S. Shephard and B. C. L. Weedon, *J. Chem. Soc.* (C), 1857 (1971).

[20]E. J. Bailey, D. H. R. Barton, J. Elbs and J. F. Templeton, *Ibid.* 1578 (1962); D. H. R. Barton, S. K. Pradhan, S. Sternhell and J. F. Templeton, *Ibid.* 255 (1961).

[21]I. N. Nazarov, G. P. Verkholetova, S. N. Ananchenko, I. V. Torgov and G. V. Aleksandrova, *Chem. Abstr.* **50**, 14683[h] (1956).

[22]S. I. Burmistrov and E. A. Shilov, *Ibid.* **42**, 2595[f] (1948).