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REACTION OF 2,6-DIMETHYL-4-METHOXYBENZALDEHYDE WITH METHYLMAGNESIUM IODIDE AND SOME PROPERTIES OF THE REACTION PRODUCTS

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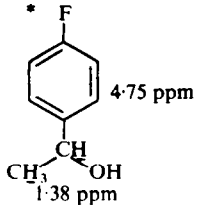
Abstract—Treatment of 2,6-dimethyl-4-methoxybenzaldehyde with MeMgI afforded two isomeric ethers, (1A and 1B), instead of the desired 1-(2,6-dimethyl-4-methoxyphenyl)ethanol. The NMR spectra of the high-melting isomer (1B) showed the presence of hindered rotation of aromatic Me groups. The reactions and properties of these ethers and other related ethers were examined.

IN CONNECTION with the structural elucidation of sclerin,[1] a mould metabolite, it was of interest for us to prepare 1-(2,6-dimethyl-4-methoxyphenyl)ethanol (**2**), as a model compound, which would be obtained by the reaction of 2,6-dimethyl-4-methoxybenzaldehyde with MeMgI. In the course of this work we have found some interesting phenomena on this reaction and some interesting properties of its products.

Treatment of 2,6-dimethyl-4-methoxybenzaldehyde with MeMgI yielded a mixture of products, which on careful chromatography afforded two isomeric crystalline ethers, A; m.p. 71–72° and B; m.p. 105–106°, instead of the desired 1-(2,6-dimethyl-4-methoxyphenyl)ethanol (**2**).

The elemental analysis of the low-melting isomer A indicated an empirical formula $C_{22}H_{30}O_3$, and the mol wt (342) required for this formula was confirmed by a mass spectrometry. Since the IR spectrum of the ether A (Fig. 1a) shows no OH and CO absorption bands, the three oxygen atoms are probably present as ether groups (ν_{max} 1150, 1070 cm^{-1}). The NMR spectrum of the ether A (Fig. 2a) shows the presence of two Me groups attached to secondary carbon atoms bearing an ether oxygen and a Ph group* (δ 1·39 ppm, 6H, d, J = 7 c/s, CH_3CH—; 4·72 ppm, 2H, q, J = 7 c/s, $CH_3\underset{|}{C}H$—). The presence of four atomatic Me groups and four aromatic protons is indicated by a slightly diffused singlet at 2·18 ppm ($W_{\frac{1}{2}}$ = 3 c/s), and a rather broad singlet at 6·26 ppm ($W_{\frac{1}{2}}$ = 3 c/s), respectively. A sharp singlet at 3·64 ppm (6H) is characteristic of the OMe group. These findings require that the low-melting isomer is represented by the structure **1**.

The IR and mass spectra of the high-melting isomer B (Fig. 1b) are quite similar to those of the isomer A. The NMR spectrum of the isomer B (Fig. 2b), although similar to that of the isomer A in several respects, differs noticeably in the region



* N. S. Bhacca, L. F. Johnson and J. N. Shoolery, *NMR Spectra Catalog* Vol. 1; No. 200. Varian Associates.

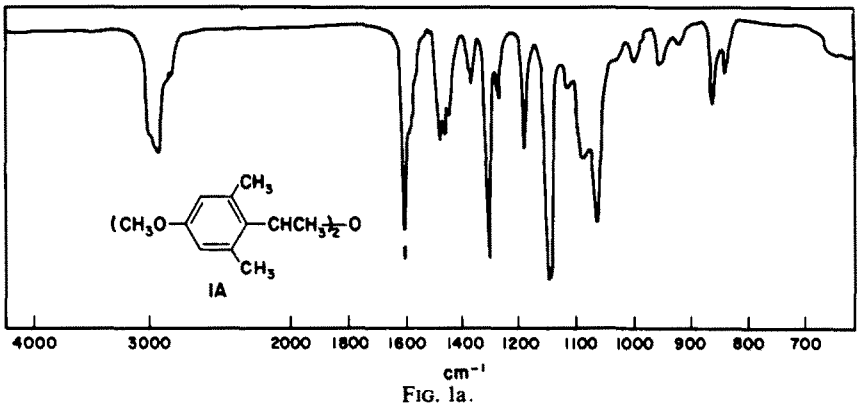


FIG. 1a.

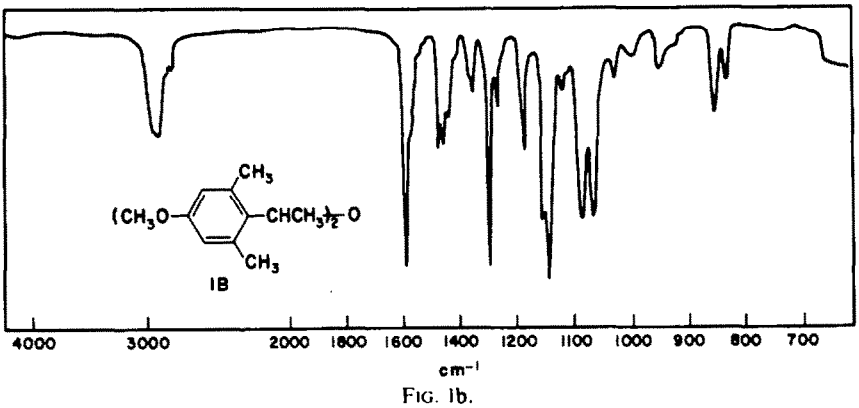


FIG. 1b.

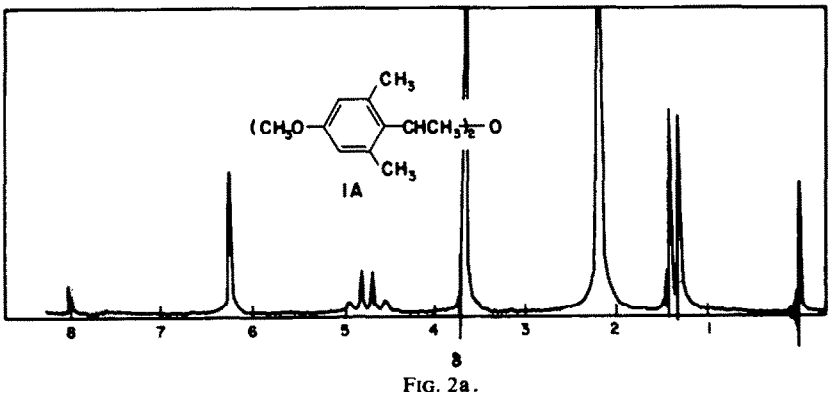


FIG. 2a.

of the aromatic Me group signals. The shape of signals are clearly temperature dependent. In the spectrum measured at 16° two very broad signals are observed and this indicates that the aromatic Me groups become non-equivalent probably due to a hindered rotation. At 20° these two peaks coalesce (1·3–3·0 ppm). The spectrum measured at 45° shows a somewhat broad singlet ($W_{\frac{1}{2}}$ = 5·8 c/s) and this is indicative of rather faster rotation at this temperature. From these findings the isomer B also should be represented by the structure 1.

These ethers were synthesized unambiguously by the acid- or base-catalyzed dehydration of 1-(2,6-dimethyl-4-methoxyphenyl)ethanol (2) obtained from 2,6-

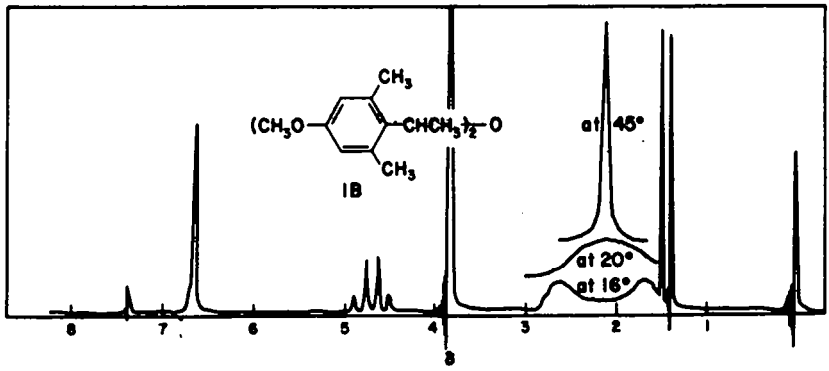


FIG. 2b.

dimethyl-4-methoxybenzaldehyde using methyllithium. When the reaction was conducted in the presence of catalytic amount of *p*-toluenesulphonic acid, in addition to 2,6-dimethyl-4-methoxystyrene, which resulted from intramolecular dehydration, a mixture of the ethers, **1A** and **1B**, was obtained.

When the complex obtained by the Grignard reaction of 2,6-dimethyl-4-methoxybenzaldehyde with MeMgI, was decomposed with hydrochloric acid, the initially formed alcohol **2** suffered an easy intermolecular dehydration to give the esters **1A** and **1B**. On the other hand, when the complex was decomposed with ammonium chloride, only the alcohol **2** was obtained. Furthermore, when the alcohol **2** was treated in boiling benzene without a catalyst, the starting material was recovered unchanged. From these results we concluded that the ethers are formed by the action of a Lewis acid, such as MgClI, on the alcohol **2** during working up. This conclusion is also supported by the fact that the formation of ethers was not observed on a thin-layer chromatogram immediately after decomposition of the magnesium complex. However, after extracting the reaction mixture with ether followed by concentrating the extract, the alcohol **2** was almost completely changed to a mixture of ethers, **1A** and **1B**.

Bromination of the high-melting isomer **1B** with bromine water in acetic acid gave a dibromide, $C_{22}H_{28}O_3Br_2$. The NMR spectrum of the dibromide shows a doublet at 1·43 ppm (6H, J = 7·5 c/s), two very broad signals centered at 2·16 ppm (12H), a sharp singlet at 3·90 ppm (6H), a quartet at 4·58 ppm (2H, J = 7·5 c/s) and a singlet at 6·50 ppm (2H). These results suggest the constitution **3** for the dibromide. However, when bromination was carried out at higher temperature (60°) with bromine water in acetic acid, with dioxan–bromine complex or with bromine in methanol, 2,4-dibromo-3,5-dimethyl-1-methoxybenzene (**4**) was obtained in good yield. This was identified by a direct comparison with an authentic specimen.* 2,4-Dibromo-3,5-dimethyl-1-methoxybenzene was also obtained by treatment of the dibromide **3** with bromine water in acetic acid at 60°. Therefore, the dibromide **3** must be an intermediate in the transformation of **1B** into **4**.

On the other hand, the bromination of the low-melting isomer **1A** with bromine water in acetic acid gave **4**, and with bromine in methanol gave **4**, 3,5-dimethyl-1-methoxy-2,4,6-tribromobenzene (**5**) and **6** (Experimental).† Acetaldehyde was also

* 2,4-Dibromo-3,5-dimethyl-1-methoxybenzene was synthesized by treating 3,5-dimethyl-1-methoxybenzene with bromine water in acetic acid.

† From the available data we could not distinguish between the two formulae, **6A** and **6B**.

isolated as a volatile reaction product. However, a dibromide correspond to **3** was not detected in the reaction products.

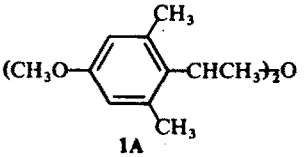
Furthermore, treatment of 1-(2,6-dimethyl-4-methoxyphenyl)ethanol (**2**) with bromine in acetic acid also gave the dibromide **4** and acetaldehyde.

Although there may be several mechanisms by which the formation of these products can be explained, the simplest would be that the nucleophilic displacement by the dibromide **3** on bromine gives the oxonium intermediate **7**, which is in turn cleaved at the C—C bond to give the compound **4** and the cation **8**. Decomposition of the latter would afford acetaldehyde and the compound **4**, as shown in Scheme 1.

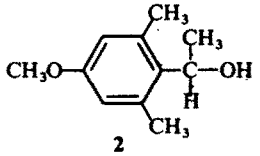
In order to examine the reactivity of *p*-substituted 2,6-dimethylbenzaldehydes, we have also investigated the reactions of 2,4,6-trimethylbenzaldehyde and 2,6-dimethylbenzaldehyde with MeMgI.

In the case of 2,4,6-trimethylbenzaldehyde, similar results to those obtained with 2,6-dimethyl-4-methoxybenzaldehyde was observed; that is besides the normal reaction product, the alcohol **9**,[4] two isomeric ethers, (**10A**), $C_{22}H_{30}O$, m.p. 98·5–99·5°, and (**10B**), $C_{22}H_{30}O$, m.p. 119–120°, which were found to be the ethers of the alcohol **9**. Fuson *et al.*[2] treated mesitylmagnesium bromide with acetaldehyde and obtained a small yield of the corresponding carbinol, but the major product was a compound which, from the analysis, they assumed to be the ether of the carbinol. Although they did not notice that the ether was indeed a mixture, this product must be the same as ours. The IR spectra of these ethers are almost superimposable and differ only in bands near 1080 cm^{-1}. However, the NMR spectra are different from each other. The high-melting isomer **10B** shows similar NMR spectrum to that of the ether **1B** with respect to the signals of the Me groups at 2-, 6-, 2′- and 6′-positions. This indicates that there may be hindered rotation of the Me groups. Bromination of the high-melting isomer **10B** with bromine water in acetic acid at 60° gave a dibromide **11**. In this case resonance effect of *p*-substituent is so weak that there occurs no cleavage reaction but only the bromination of aromatic nuclei.

In contrast with the foregoing cases, treatment of 2,6-dimethylbenzaldehyde with MeMgI gave only a normal reaction product, 1-(2,6-dimethylphenyl)ethyl alcohol. Schwartzman and Corson[3] treated 2,6-dimethylphenylmagnesium iodide with



1A
1B



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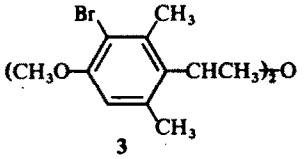

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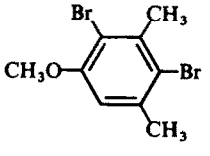

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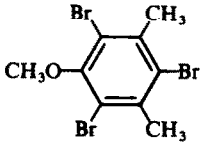

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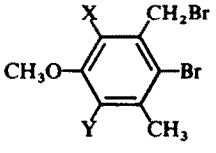
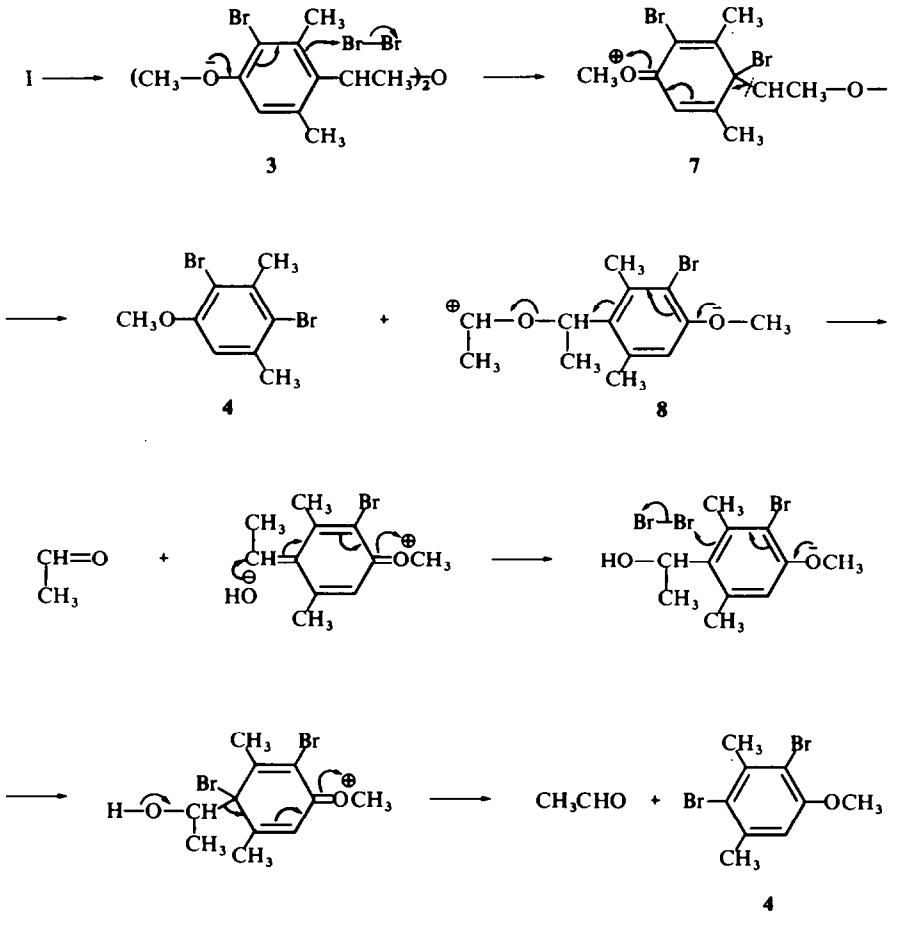


6A X = H Y = Br
6B X = Br Y = H

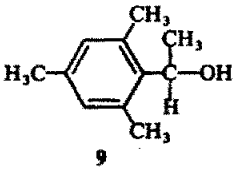
SCHEME 1



acetaldehyde. In one experiment they obtained a poor yield of 2,6-dimethylphenylmethylcarbinol and 2,6-dimethylstyrene. In another experiment, they obtained the ether of 2,6-dimethylphenylmethylcarbinol, although in poor yield. In our case the formation of the ether was not observed.*

These observations strongly suggest that the electron donating *p*-substituents assist the ether formation under the action of Lewis acid. Each pair of these ethers must be DL- and meso-type of isomers. It appears to be the first example that these types of isomers show the presence of hindered rotation of aromatic Me groups. But we can not draw any conclusion on the stereochemical assignment of these ethers from our experimental results. An unambiguous proof on this problem is now in progress.

* When 1-(2,6-dimethylphenyl)ethyl alcohol was treated with a catalytic amount of *p*-toluenesulphonic acid in benzene, two isomeric ethers were obtained. See Experimental.



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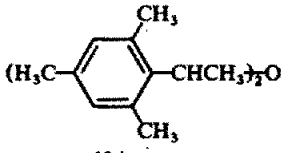
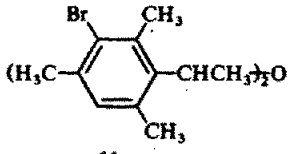


10A
10B



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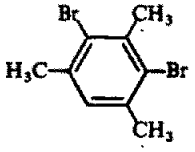

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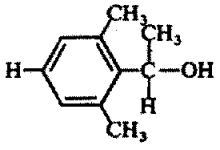

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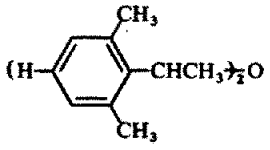
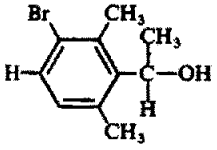


14A
14B



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EXPERIMENTAL

M.ps are uncorrected. $CHCl_3$ was purified by shaking with conc H_2SO_4 and NaOH aq, dried over solid NaOH and distilled prior to use. IR absorption spectra were recorded on Japan Spectroscopic IRS spectrometer. NMR spectra were measured on Japan Electron Optics C-60 spectrometer operating at 60 Mc/s with TMS as internal standard. Chemical shifts and coupling constants are expressed in ppm from TMS and in c/s, respectively. Mass spectra were measured by Dr. Tatematsu of Nagoya University. Thin-layer chromatoplates were prepared from Merck's Kieselgel G.

Grignard reaction of 2,6-dimethyl-4-methoxybenzaldehyde

(a) A soln of MeI (4·3 g; 0·03 mole) in dry ether (25 ml) was added during 30 min at room temp to a stirred mixture of Mg (590 mg; 0·024 mole) and dry ether (5 ml). After refluxing for an additional hr, the mixture was cooled in an ice bath, and a soln of 2,6-dimethyl-4-methoxybenzaldehyde (3·3 g; 0·02 mole) in dry ether (20 ml) was added with stirring during 20 min. After refluxing for a ½ hr, the resulting complex was decomposed with cold dil HCl. The ether layer was separated, washed with dil $Na_2S_2O_3$ aq, $NaHCO_3$ aq and water, and dried. The crude product, obtained following removal of the solvent, was chromatographed over silica gel. Elution with $CHCl_3$ gave **1A** (539 mg) as plates from EtOH, m.p. 71–72°. (Found: C, 77·21; H, 8·92. $C_{22}H_{30}O_3$ requires: C, 77·15; H, 8·83%): MS *m/e* 342, 206, 191, 162 (base peak): ν_{max} (CCl_4) 1600, 1150, 1090, 1070, 860 cm^{-1}: λ_{max}^{EtOH} 225 mμ (ε, 16,170): NMR (CCl_4) δ 1·39 d (6H, J = 7 c/s), 2·81 s (12H, $W_{\frac{1}{2}}$ = 3 c/s), 3·64 s (6H), 4·72 q (2H, J = 7 c/s), 6·26 s (4H, $W_{\frac{1}{2}}$ = 3 c/s) ppm. Further elution with the same solvent gave the second isomer (**1B**; 636 mg) as plates from EtOH, m.p. 105–106°. (Found: C, 77·25; H, 9·12. $C_{22}H_{30}O_3$ requires: C, 77·15; H, 8·83%): MS *m/e* 342, 206, 191, 162 (base peak): ν_{max} (CCl_4) 1600, 1150, 1090, 1070, 860 cm^{-1}: λ_{max}^{EtOH} 225 mμ (ε 15,570): NMR (CCl_4) δ 1·37 d (6H, J = 7 c/s), 1·3–3·0 m (12H), 3·81 s (6H), 4·59 q (2H, J = 7 c/s), 6·53 s (4H) ppm. Elution with $CHCl_3$ containing MeOH (0·5% v/v) gave unchanged 2,6-dimethyl-4-methoxybenzaldehyde (1·13 g). Further elution with $CHCl_3$ containing MeOH (5% v/v) gave a mixture (270 mg) of **1A** and **1B** and **2** (by TLC and IR spectrum).

(b) The reaction was repeated as described above except that 2,6-dimethyl-4-methoxybenzaldehyde (500 mg; 0·03 mole) was added to MeMgI (from 1·5 g MeI), and the resulting complex was decomposed with cold NH_4Cl aq. The crude product was chromatographed over silica gel. Elution with benzene–pet. ether (1:1) gave unchanged 2,6-dimethyl-4-methoxybenzaldehyde (152 mg). Further elution with $CHCl_3$

gave **2** (306 mg) as prisms from pet. ether, m.p. 51–52°. (Found: C, 73·56; H, 9·12. $C_{11}H_{16}O_2$ requires: C, 73·30; H, 8·95%): ν_{max} (CCl_4) 3800, 3400–3200, 1620, 1320, 1200, 1100, 1070 cm^{-1}: NMR ($CDCl_3$) δ 1·50 d (3H, J = 7 c/s), 1·94 s (1H), 2·40 s (6H), 3·75 s (3H), 5·31 q (1H, J = 7 c/s), 6·53 s (2H) ppm.

(c) To a stirred mixture of Li (200 mg; 0·029 mole) and dry ether (20 ml) a soln of MeI (5 g; 0·035 mole) in dry ether (40 ml) was added during 30 min cooling in an ice bath. After refluxing for 1·5 hr, the mixture was cooled. To this mixture a soln of 2,6-dimethyl-4-methoxybenzaldehyde (0·81 g; 0·005 mole) in dry ether (15 ml) was added with stirring during 30 min. After refluxing for an additional hr, the complex was decomposed with the cold mixture of $Na_2S_2O_3$ aq and Na_2SO_4 aq with stirring. The ether layer was separated, washed with water, dried over Na_2SO_4, concentrated, and the residue was chromatographed over silica gel. Elution with $CHCl_3$ containing MeOH (5% v/v) gave **2** (0·76 g) as plates from pet. ether, m.p. 51–52°; this alcohol was identical (m.p., mixed m.p., and R spectrum) with **2** obtained above.

Treatment of 1-(2,6-*dimethyl-4-methoxyphenyl*)*ethanol* (**2**) *with magnesium iodide*

The alcohol **2** (100 mg) was dissolved in an ether soln of MgI_2 and the soln allowed to stand for 24 hr at room temp. Removal of the solvent afforded a gum which was chromatographed over silica gel. Elution with $CHCl_3$ gave **1A** as plates, m.p. 71–72° (9 mg). Further elution with the same solvent gave **1B** as plates, m.p. 105–106° (51 mg). These ethers were identical (m.p., mixed m.p., IR and NMR spectrum) respectively with **1A** and **1B** obtained previously.

Treatment of 1-(2,6-*dimethyl-4-methoxyphenyl*)*ethanol* (**2**) *with* p-*toluenesulphonic acid*

The alcohol **2** (200 mg) was boiled with a catalytic amount of *p*-toluenesulphonic acid in pet. ether for 20 min. The crude product was chromatographed over silica gel. Elution with pet. ether afforded 2,6-dimethyl-4-methoxystyrene (25 mg) as needles from EtOH, m.p. 65–66°. (Found: C, 81·17; H, 8·53. $C_{11}H_{14}O$ requires: C, 81·44; H, 8·70%): ν_{max} (CCl_4) 1610, 1590 (sh), 1200, 1150, 1070, 865, 842 cm^{-1}. Elution with benzene gave **1A** (49 mg), and further elution with the same solvent gave **1B** (48 mg).

Treatment of 1-(2,6-*dimethyl-4-methoxyphenyl*)*ethanol* (**2**) *with basic alumina*

The alcohol **2** (100 mg) was heated under reflux with basic alumina (20 mg) in pet. ether for 3·5 hr. The catalyst was filtered off, the solvent was removed, and the crude product was chromatographed over silica gel. Elution with benzene gave **1A** (16 mg). Further elution with the same solvent gave **1B** (12 mg).

Bromination of bis[1-(2,6-*dimethyl-4-methoxyphenyl*)*ethyl*] *ether* (**1B**) *with bromine water in acetic acid*

(a) *At room temperature.* To a soln of **1B** (80 mg) in AcOH (10 ml) Br_2 in water containing KBr was added with shaking at room temp until a red colour persisted. On standing at room temp, a white gum separated, which was crystallized from EtOH to give **3** (27 mg) as plates, Beilstein test (+), m.p. 126–127°. (Found: C, 52·78; H, 5·75. $C_{22}H_{28}O_3Br_2$ requires: C, 52·82; H, 5·64%): ν_{max} (CCl_4) 1584, 1312, 1192, 1163, 1102, 1090, 838 cm^{-1}: NMR (CCl_4) δ 1·43 d (6H, J = 7·0 c/s), 1·4–3·0 m (12H), 3·90 s (6H), 4·58 q(2H, J = 7·0 c/s), 6·50 s (2H, $W_{\frac{1}{2}}$ = 4·9 c/s) ppm.

(b) *At* 60°. To a soln of **1B** (130 mg) in AcOH (20 ml), Br_2 in water containing KBr was added with shaking at 60° until a red colour persisted. On standing at room temp, white crystals separated, which was recrystallized from EtOH to give **4** (170 mg) as plates, Beilstein test (+), m.p. 109·5–110°. (Found: C, 36·95; H, 3·66; Br, 54·51. $C_9H_{10}OBr_2$ requires: C, 36·77; H, 3·43; Br, 54·33%): ν_{max} (CCl_4) 1570, 1327, 1214, 1102, 1047, 936, 835 cm^{-1}: NMR (CCl_4) δ 2·38 s (3H), 2·60 s (3H), 3·86 s (3H), 6·66 s (1H, $W_{\frac{1}{2}}$ = 3·4 c/s) ppm. This was identified by a direct comparison with an authentic sample which was obtained by treatment of 3,5-dimethyl-1-methoxybenzene with Br_2 water in AcOH (m.p., mixed m.p., IR and NMR spectrum).

Treatment of bis[1-(2,6-*dimethyl-4-methoxyphenyl*)*ethyl*] *ether* (**1A**) *with bromine water in acetic acid*

To a soln of **1A** (60 mg) in AcOH (10 ml), Br_2 in water containing KBr was added with shaking in an ice bath until a red colour persisted. On standing at room temp, white crystals separated. Recrystallization from EtOH gave **4** as plates, m.p. 109·5–110° (32 mg), which was identical (m.p., mixed m.p. and IR spectrum) with **4** described above.

Bromination of the high-melting ether (**1B**) *with dioxan–bromine complex*

To a soln of **1B** (60 mg) in dry ether (50 ml) dioxan–bromine complex (140 mg) was added at room temp with shaking. The solvent was removed and the residue was crystallized from EtOH to give **4** as plates (50 mg).

Bromination of the low-melting ether (**1A**) *with bromine in methanol*

The low-melting ether **1A** (53 mg) was dissolved in MeOH containing Br_2. After standing for 10 min, the solvent was removed under a stream of N_2. The effluent vapour was bubbled through a soln of 2,4-dinitrophenylhydrazine in HCl aq. The ppt was collected by filtration and recrystallized from EtOH to give needles, m.p. 146–147° (62 mg). This was identified with 2,4-dinitrophenylhydrazone of acetaldehyde by a direct comparison with an authentic sample (m.p. and IR spectrum). The residue was chromatographed over silica gel. Elution with pet. ether gave **5** (18 mg) as needles from EtOH, Beilstein test (+), m.p. 116·5°. (Found: C, 29·34; H, 2·64. $C_9H_9OBr_3$ requires: C, 28·99; H, 2·46%): ν_{max} (CCl_4) 1365, 1320, 1083, 983, 944 cm^{-1}: NMR ($CDCl_3$) δ 2·61 s (6H), 3·88 s (3H) ppm. Further elution with the same solvent gave **4**, m.p. 110° (18 mg). Furthermore, elution with pet. ether containing benzene (10% v/v) gave **6A** or **6B** (16 mg) as needles from EtOH, Beilstein test (+), m.p. 140–141°. (Found: C, 29·13; H, 2·76. $C_9H_9OBr_3$ requires: C, 28·99; H, 2·46%): ν_{max}($CHCl_3$) 1580, 1335, 1103, 1056, 990, 950, 880, 848 cm^{-1}: NMR ($CDCl_3$) δ 2·62 s (3H), 3·88 s (3H), 4·61 s (2H), 6·90 s (1H) ppm.

Bromination of the high-melting ether (**1B**) *with bromine in methanol*

Working-up in a manner similar to the one described for **1A**, the high-melting ether **1B** (90 mg) gave **4** (125 mg), **5** (23 mg), m.p. 116°, and acetaldehyde as a volatile reaction product.

Treatment of the dibromide (**3**) *with bromine water in acetic acid*

To a soln of **3** (35 mg) in AcOH (5 ml) Br_2 in water containing KBr was added with shaking at 60° until a red colour persisted. On standing at room temp, white crystals separated and were recrystallized from EtOH to give **4** (25 mg), m.p. 109·5–110°.

Bromination of 1-(2,6-*dimethyl*-4-*methoxyphenyl*)*ethanol* (**2**) *with bromine water in acetic acid*

Working-up in a manner similar to the one described for **1A**, compound **2** gave **4** and acetaldehyde as a volatile reaction product (identified as 2,4-dimitrophenylhydrazone).

Treatment of the high-melting ether (**1B**) *with aluminium chloride*

The ether **1B** (400 mg) was heated with $AlCl_3$ (1·2 g) in benzene (20 ml) at 70° for 22 hr. The reaction mixture was poured into ice water (10 g) and the benzene layer was separated. The aqueous layer was acidified with HCl, extracted with benzene, and the combined benzene extracts washed with 1% NaOH aq. The resulting alkaline soln was acidified with HCl and extracted with ether. Removal of the solvent gave 3,5-dimethylphenol as needles, m.p. 62–64° (70 mg); identical with an authentic sample (m.p. and IR spectrum).

Treatment of the dibromide (**4**) *with hydroiodic acid*

The dibromide **4** (550 mg) was heated under reflux in a soln of AcOH (13 ml), Ac_2O (6·5 ml) and HI (*d*, 1·7: 32 ml) for 2 hr. The reaction mixture was poured into ice water (200 g) and extracted with ether. The ether layer was washed with $Na_2S_2O_3$ aq, $NaHCO_3$ aq and water, and dried. Removal of the solvent gave 3,5-dimethylphenol (204 mg) as needles from pet. ether, m.p. 62–64°.

Grignard reaction of mesitaldehyde

(a) To an ether soln of MeMgI (from 8·5 g of MeI) mesitaldehyde (3 g) in ether was added with stirring in an ice bath. After refluxing for 1 hr, the resulting complex was decomposed with cold dil HCl. The ether layer was washed with $Na_2S_2O_3$ aq, $NaHCO_3$ aq and water, and dried. The crude product was chromatographed over silica gel. Elution with $CHCl_3$ gave **10A** (571 mg) as plates from EtOH, m.p. 98·5–99·5. (Found: C, 84·97; H, 9·74 $C_{22}H_{30}O$ requires: C, 85·11; H, 9·74%): ν_{max} (CCl_4) 1615, 1160, 1095, 1075, 945, 855 cm^{-1}: NMR ($CDCl_3$) δ 1·43 d (6H, J = 6·7 c/s), 2·20 s (18H), 4·91 q (2H, J = 6·7 c/s), 6·81 s (4H, $W_{\frac{1}{2}}$ = 2·3 c/s) ppm. Further elution with the same solvent gave **10B** (825 mg) as plates from EtOH, m.p. 119–120°. (Found: C, 85·14; H, 9·80. $C_{22}H_{30}O$ requires: C, 85·11; H, 9·74%): ν_{max} (CCl_4) 1615, 1150, 1095, 940, 855 cm^{-1}: NMR ($CDCl_3$) δ 1·44 d (6H, J = 6·7 c/s), 1·5–2·5 m (12H), 2·25 s (6H), 4·63 q (2H, J = 6·7 c/s), 6·79 s (4H, $W_{\frac{1}{2}}$ = 3·3 c/s) ppm. Further elution with $CHCl_3$ containing MeOH (0·5% v/v) gave **7** (1·1 g) as prisms from pet. ether, m.p. 71·5–72°. (Found: C, 80·47; H, 9·83. $C_{11}H_{16}O$ requires: C, 80·44; H, 9·83%): ν_{max} (CCl_4) 3850, 3400, 1620, 1260, 1150, 1092, 1070, 892, 855 cm^{-1}.

(b) To a soln of MeLi in ether [prepared from MeI (5 g) and Li (200 mg)] an ether soln of mesitaldehyde (1 g) was added with stirring in an ice bath. After refluxing for 1 hr, the complex was decomposed with the cold mixture of $Na_2S_2O_3$ aq and Na_2SO_4 aq. The ether layer was washed with water and dried. The crude product was chromatographed over silica gel. Elution with $CHCl_3$ containing MeOH (3% v/v) gave **7** (825 mg) as plates from pet. ether, m.p. 71·5–72°. This alcohol was identical (m.p., mixed m.p., TLC, and IR spectrum) with **7** described above.

Treatment of 1-(2,4,6-*trimethylphenyl*)*ethanol* (**7**) *with magnesium iodide*

The alcohol **7** (200 mg) was dissolved in an ether soln of MgI_2 and allowed to stand for 48 hr. As the alcohol **7** was unchanged, the ether soln was refluxed for 1·5 hr. After removal of the solvent, the crude product was chromatographed over silica gel. Elution with $CHCl_3$ gave **10A** (8 mg) as plates from EtOH, m.p. 98·5–99·5°. Further elution with the same solvent gave **10B** (129 mg) as plates from EtOH, m.p. 119–120°. These ethers were identical (m.p., mixed m.p., TLC, IR, and NMR spectrum) respectively with **10A** and **10B** obtained previously.

Treatment of 1-(2,4,6-*trimethylphenyl*)*ethanol* (**7**) *with* p-*toluenesulphonic acid*

The alcohol **7** was boiled with a catalytic amount of *p*-toluenesulphonic acid in ether for 5 min. The crude product was chromatographed over silica gel. Elution with $CHCl_3$ gave **10A**, m.p. 99° (40 mg). Further elution with the same solvent gave **10B**, m.p. 119–120° (84 mg).

Treatment of 1-(2,4,6-*trimethylphenyl*)*ethanol* (**7**) *with basic alumina.*

The alcohol **7** (70 mg) was heated under reflux with basic alumina (20 mg) in pet. ether for 22 hr. The catalyst was filtered off, the solvent was removed, and the crude product was chromatographed over silica gel. Elution with $CHCl_3$ gave a mixture (2 mg) of **10A** and **10B**. Further elution with $CHCl_3$ containing MeOH (5% v/v) gave the unchanged **7** (65 mg).

Treatment of the high-melting ether (**10B**) *with dioxan–bromine complex*

To soln of **10B** (100 mg) in dry ether (50 ml) dioxan–bromine complex (200 mg) was added at room temp with stirring. The solvent was removed and the crude product was chromatographed over silica gel. Elution with pet. ether gave **11** (50 mg) as plates from EtOH, m.p. 154–155°. (Found: C, 56·75; H, 6·20. $C_{22}H_{28}OBr_2$ requires: C, 56·42; H, 6·03%): ν_{max} (CCl_4) 1185, 1163, 1093, 979, 947, 865 cm^{-1}: NMR ($CDCl_3$) δ 1·44 d (6H, J = 6·7 c/s), 1·3–3·0 m (12H), 2·36 s (6H), 4·58 q (2H, J = 6·7 c/s), 6·84 s (2H, $W_{\frac{1}{2}}$ = 4·5 c/s) ppm.

Treatment of the low-melting ether (**10A**) *with dioxan–bromine complex*

To a soln of **10A** (30 mg) in dioxan, dioxan–bromine complex (50 mg) was added at room temp with shaking. The solvent was removed and the crude product was chromatographed over silica gel. Elution with pet. ether gave **12** (12 mg) as needles from EtOH, m.p. 57–58°. (Found: C, 38·30; H, 3·88. $C_9H_{10}Br_2$ requires: C, 38·87; H, 3·63%): ν_{max} (CCl_4) 1590, 1170, 980, 895, 865 cm^{-1}: NMR ($CDCl_3$) δ 2·32 s (6H), 2·61 s (3H), 6·99 s (1H, $W_{\frac{1}{2}}$ = 2·4 c/s).

Treatment of 1-(2,4,6-*trimethylphenyl*)*ethanol* (**9**) *with bromine water*

To a soln of **9** (300 mg) in AcOH (30 ml) Br_2 in water containing KBr was added with shaking at room temp until a red colour persisted. The solvent was removed under reduced press and the residue was washed with water. The crude product was chromatographed over silica gel. Elution with pet. ether gave **12** (310 mg) as needles from EtOH, m.p. 57–58°: this bromide was identical (m.p., mixed m.p., TLC, and IR spectrum) with **12** described above.

Grignard reaction of 2,6-*dimethylbenzaldehyde*

To an ether soln of MeMgI (from 3 g of MeI), 2,6-dimethylbenzaldehyde (1 g) in ether was added with stirring in an ice bath. After refluxing for 1 hr, the resulting complex was decomposed with cold dil HCl. The ether layer was washed with $Na_2S_2O_3$ aq, $NaHCO_3$ aq and water, and dried. The crude product was chromatographed over silica gel. Elution with $CHCl_3$ gave **13** (600 mg) as prisms from pet. ether, m.p. 66–67°. (Found: C, 79·90; H, 9·55. $C_{10}H_{14}O$ requires: C, 79·95; H, 9·39%): ν_{max} (CCl_4) 3800, 3400, 1590, 1105, 1085 (sh), 1070, 910, 892 cm^{-1}: NMR ($CDCl_3$) δ 1·51 d (3H, J = 6·7 c/s), 1·95 s (1H), 2·42 s (6H), 5·37 q (1H, J = 6·7 c/s), 7·03 s (3H) ppm.

Grignard reaction of 2,6-*dimethylbromobenzene*

The reaction was carried out according to Schwartzman's method.[3] To an ether soln of 2,6-dimethylphenylmagnesium bromide (from 1 g of 2,6-dimethylbromobenzene) acetaldehyde (0·7 g) in dry ether was added with stirring in an ice bath. After refluxing for 4 hr, the resulting complex was decomposed with cold dil HCl. The ether layer was washed with $Na_2S_2O_3$ aq, $NaHCO_3$ aq and water, and dried. The

crude product was chromatographed over silica gel. Elution with $CHCl_3$ gave **13** (60 mg) as prisms from pet. ether, m.p. 66–67°: this alcohol was identical (m.p., TLC, and IR spectrum) with **13** described above.

Treatment of 1-(2,6-*dimethylphenyl*)*ethanol* (**13**) *with* p-*toluenesulphonic acid*

(a) The alcohol **13** (300 mg) was boiled with a catalytic amount of *p*-toluenesulphonic acid in ether for 12 hr. Only unchanged **13** was recovered.

(b) The alcohol **13** (300 mg) was refluxed with a catalytic amount of *p*-toluenesulphonic acid in benzene for 12 hr. The crude product was chromatographed over silica gel. Elution with pet. ether gave **14A** (15 mg) as prisms from EtOH, m.p. 81·5–82°. (Found: C, 85·04; H, 9·49. $C_{20}H_{26}O$ requires: C, 85·05; H, 9·28%): ν_{max} (Nujol) 1580, 1095 (sh), 1088, 1093, 945, 792, 790, 750 cm^{-1}: NMR (CCl_4) δ 1·42 d (6H, J = 6·7 c/s), 2·12 s (12H), 4·81 q (2H, J = 6·7 c/s), 6·77 s (6H) ppm. Further elution with the same solvent gave **14B** (106 mg) as plates from EtOH, m.p. 143–144°. (Found: C, 84·78; H, 9·21. $C_{20}H_{26}O$ requires: C, 85·05; H, 9·28%): ν_{max} (Nujol) 1580, 1092, 1076, 940, 780, 750 cm^{-1}: NMR ($CDCl_3$) δ 1·45 d (6H, J = 6·7 c/s), 1·6–2·6 m (12H, broad), 4·62 q (2H, J = 6·7 c/s), 6·96 s (6H, $W_{\frac{1}{2}}$ = 2·4 c/s) ppm.

Treatment of 1-(2,6-*dimethylphenyl*)*ethanol* (**13**) *with bromine water.*

To a soln of **13** (100 mg) in AcOH (20 ml) Br_2 in water containing KBr was added with shaking at 60° until a red colour persisted. The solvent was removed under reduced press and the residue was washed with water. The crude product was chromatographed over silica gel. Elution with $CHCl_3$ gave **15** (89 mg) as plates from pet. ether, m.p. 61–62°. (Found: C, 52·20; H, 5·95. $C_{10}H_{13}OBr$ requires: C, 52·42; H, 5·72%): ν_{max} (oil) 3300, 1180, 1143, 1095, 1085, 1075, 1010, 1000, 900, 810, 760 cm^{-1}: NMR (CCl_4) δ 1·37 d (3H, J = 6·7 c/s), 2·22 s (IH), 2·27 s (3H), 2·45 s (3H), 5·24 q (1H, J = 6·7 c/s), 6·73 d (1H, J = 9 c/s), 7·29 d (J = 9 c/s) ppm.

Treatment of bis[1-(2,6-*dimethylphenyl*)*ethyl*] *ether* (**14A**) *with bromine water*

To a soln of **14A** (30 mg) in AcOH (10 ml) Br_2 in water containing KBr was added at room temp until a red colour persisted. The product was isolated in the usual way and the unchanged **14A** was recovered.

Treatment of bis[1-(2,6-*dimethylphenyl*)*ethyl*] *ether* (**14B**) *with bromine water*

To a soln of **14B** (30 mg) in AcOH (10 ml) Br_2 in water containing KBr was added at room temp until a red colour persisted. The product was isolated in the usual way and the unchanged **14B** was recovered.

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