

## Aromatic Musks derived from 1,2,3,4-Tetrahydro-1,1,4,4,6,7-hexamethylnaphthalene

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Bromination of the title hydrocarbon gave the 6,7-bis(bromomethyl) compound (2), base-catalysed condensation of which with active methylene compounds gave a series of musks having the 2,3,5,6,7,8-hexahydro-5,5,8,8-tetramethylbenz[*f*]indene skeleton (3) with various functional groups at C-2. Treatment of the dibromide (2) with sodium hydroxide or with sodium sulphide formed the cyclic ether (5a) and sulphide (5b), respectively, the latter being oxidised to the sulphoxide and sulphone. Further bromination produced the tetrabromide (8) which was hydrolysed to the dialdehyde (9), the starting point for a further series of musks. The two strongest musks were the methyl ester (3g) and the naphthofuran (5a).

THE natural macrocyclic musks have been prized in perfumery for many centuries. The first synthetic substitutes were introduced by Baur,<sup>1</sup> who in 1888 made the surprising discovery that certain dinitro-*t*-butylbenzenes smelt of musk. A report of the first aromatic musks not containing nitro-groups appeared in 1948,<sup>2</sup> and since then many such compounds have been described:<sup>3</sup> examples in current use include Celestolide (I), Phantolid (II), Tonalid (III), Versalide (IV), and Galaxolide (V). The characteristic feature of these molecules is a bulky, hydrophobic group, containing at least one quaternary carbon centre, on one side of a benzene ring, and a polar group on the other.

We decided to make a series of such compounds, containing a variety of functional groups, from a common

intermediate, for which we chose the hydrocarbon (1), easily made by condensation of *o*-xylene with 2,5-dichloro-2,5-dimethylhexane.<sup>4</sup> Bromination then gave the dibromide (2). The cyclised derivatives (3a—e) were produced by base-catalysed condensation of the dibromide with the appropriate active methylene compounds. The esters (3f and g) were formed by mild hydrolysis of the acetoacetate derivatives and similarly the monoacetyl compound (3i) from the acetylacetone derivative (3e). More vigorous hydrolysis of (3d) gave the carboxylic acid (3h). The intensities of musk odour of the various substances are indicated next to the formulae. Although weak, the musk odour of the methyl ketone (3i) is distinct, whereas the unsaturated ketone (4) made from it by bromination and dehydrobromination is odourless.

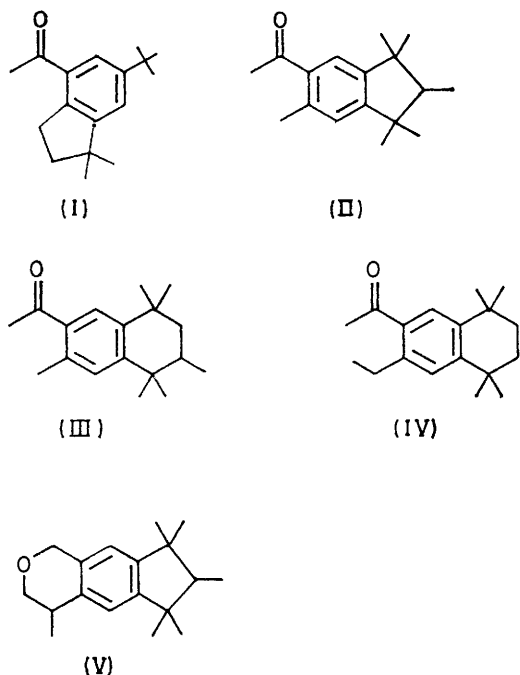
<sup>1</sup> A. Baur, Ger. P., 47599/1888; 62362/1891; *Ber.*, 1891, **24**, 2836.

<sup>2</sup> M. S. Carpenter and W. M. Easter, U.S.P., 2450879/1948.

<sup>3</sup> Reviewed by T. F. Wood, *Givaudanian*, 1968—1970.

<sup>4</sup> H. A. Bruson and J. W. Kroeger, *J. Amer. Chem. Soc.*, 1940, **62**, 36; T. F. Wood, W. M. Easter, M. S. Carpenter, and J. Angiolini, *J. Org. Chem.*, 1962, **28**, 2248.

The dibromide (2) was converted into the naphthofuran (5a), a very powerful musk, when heated with sodium hydroxide in wet bis-(2-methoxyethyl) ether. The derived lactone (6) was a weaker musk. The methyl sulphoxide and methyl sulphone corresponding to the



methyl ketone Versalide (IV) are reported to be musks;<sup>5</sup> it was therefore surprising to find the sulphide (5b) made by reaction of the dibromide (2) with sodium sulphide, and the derived sulphoxide (5c) and sulphone (5d), odourless.

Treatment of the hydrocarbon (1) with 4 mol. equiv. of bromine in carbon tetrachloride under illumination resulted in precipitation of the insoluble tetrabromide (8). It was hydrolysed to the dialdehyde (9) with sodium formate<sup>6</sup> in 95% ethanol. The n.m.r. spectra of the acetals (10) of the dialdehyde showed that they were mixtures of *cis*- and *trans*-isomers. Reduction of the dialdehyde with borohydride led to the diol (11) and thence to the acetals (12a—d) and carbonate (13). The dialdehyde was oxidised to the diacid (14a), the dimethyl and diethyl esters of which had a pleasant fruity smell (but no hint of musk), rather unexpected since the phthalic esters are odourless. Methylmagnesium iodide converted the dialdehyde into the dimethyl diol, which was dehydrated to the odourless dimethyl derivative of the naphthofuran (5a). Both compounds were mixtures of *cis*- and *trans*-isomers.

In molecular dimensions<sup>7</sup> the musks reported here fall fairly closely within the limits previously laid down,<sup>3,8</sup> but so do several of the non-musks.

#### EXPERIMENTAL

I.r. spectra were recorded with a Unicam SP 200 G grating spectrophotometer for Nujol mulls unless otherwise

<sup>5</sup> U.S.P., 3,320,323.

<sup>6</sup> E. L. Eliel and K. W. Nelson, *J. Chem. Soc.*, 1955, 1628.

stated. N.m.r. spectra were obtained with a Perkin-Elmer R12 60 MHz spectrometer, with Me<sub>4</sub>Si as internal standard. All peaks are singlets unless otherwise stated. Mass spectra were recorded with an A.E.I. MS12 spectrometer. Silica gel used was 100—200 mesh as supplied by W. R. Grace Ltd. Organic solutions were dried by shaking with saturated sodium chloride solution and stirring with dried magnesium sulphate.

**6,7,8,9-Tetrahydro-4,6,6,9,9-pentamethylnaphtho[2,3-b]-pyran-2-one (16).**—To a solution of 1,1,4,4-tetramethyltetralin-6-ol<sup>4</sup> (1 g) and freshly distilled ethyl acetoacetate (0.7 g) in dried redistilled nitrobenzene (10 ml) at room temperature was added a solution of aluminium chloride (1.4 g) in nitrobenzene. The mixture was stirred at 100—120 °C for 6 h, then allowed to cool to room temperature. Concentrated hydrochloric acid (3 ml) was added and the solution was washed with water and dried. The nitrobenzene was distilled off to leave a black tar which was chromatographed over silica gel. Diethyl ether—petroleum (b.p. 40—60°) (40 : 60 v/v) eluted the crystalline product (0.6 g), m.p. 119—121°, having a coumarin and musk odour,  $\nu_{\max}$  1 710 cm<sup>-1</sup> (C=O),  $\delta$  (CCl<sub>4</sub>) 1.03 (12 H, CH<sub>3</sub>), 1.07 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 2.41 (3 H, 4-CH<sub>3</sub>), 6.17 (1 H, 3-H), and 7.25 and 7.51 (1 H, 5- and 10-H); *m/e* 270 (M<sup>+</sup>).

**6,7-Bisbromomethyl-1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalene (2).**—A solution of 1,1,4,4,6,7-hexamethyltetralin<sup>4</sup> (1) (21 g) in carbon tetrachloride (400 ml) was boiled gently in a flask fitted with stirrer and condenser. A solution of bromine (32 g) in carbon tetrachloride (100 ml) was added to the boiling solution over 3.5 h. The mixture was then boiled for a further 15 min, cooled, washed with water, and evaporated. The residue was dissolved in petroleum (b.p. 40—60°) (75 ml) and chilled; the dibromide separated as a crystalline solid, m.p. 60—61°, having a faint musk odour (Found: C, 51.1; H, 5.8. C<sub>16</sub>H<sub>22</sub>Br<sub>2</sub> requires C, 51.3; H, 5.9%),  $\delta$  (CCl<sub>4</sub>) 1.27 (12 H, CH<sub>3</sub>), 1.66 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 4.57 (4 H, CH<sub>2</sub>Br), and 8.65 (2 H, aromatic).

**2,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethylbenz[f]indene-2,2-dicarbonitrile (3a).**—To a stirred mixture of sodium hydride (480 mg) and the dibromide (2) (1.87 g) in 1,2-dimethoxyethane (25 ml) was added dropwise a solution of malononitrile (330 mg) in 1,2-dimethoxyethane (10 ml) at 10—15 °C. Stirring was continued for 30 min in the cold, and then at 40 °C for 20 min. The mixture was poured into water and extracted with diethyl ether. The extract was washed with water, dried, and evaporated. The residual oil was chromatographed through silica gel. Diethyl ether—petroleum (b.p. 60—80°) (15 : 85 v/v) eluted the crystalline dicyanide, m.p. 128—130°, raised to 134—135° by recrystallisation from methanol (yield 1 g), having a weak musk odour (Found: C, 82.1; H, 7.8. C<sub>19</sub>H<sub>22</sub>N<sub>2</sub> requires C, 82.0; H, 8.0%),  $\nu_{\max}$  2 270 cm<sup>-1</sup> (CN),  $\delta$  (CCl<sub>4</sub>) 1.31 (12 H, CH<sub>3</sub>), 1.74 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 3.76 [4 H, CH<sub>2</sub>-C(CN)<sub>2</sub>-CH<sub>2</sub>], and 7.47 (2 H, aromatic).

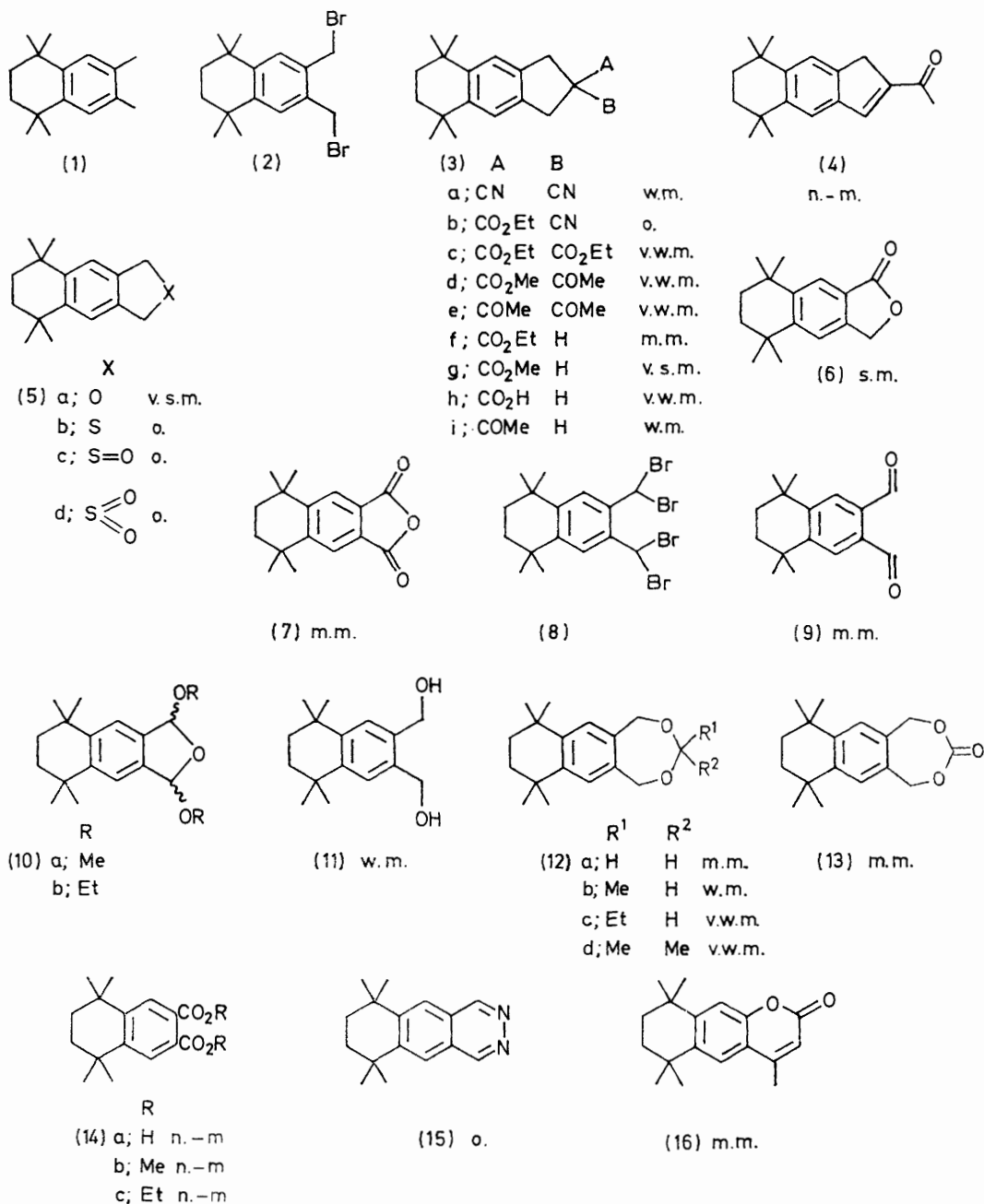
**Diethyl 2,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethylbenz[f]indene-2,2-dicarboxylate (3c).**—To a stirred mixture of sodium hydride (460 mg) and the dibromide (2) (1.9 g) in 1,2-dimethoxyethane (20 ml) was added dropwise a solution of diethyl malonate (800 mg) in 1,2-dimethoxyethane (10 ml) at 10—15 °C. The mixture was then stirred at room temperature for 2 h, warmed to 50—60 °C for 30 min, cooled,

<sup>7</sup> R. J. Wilkinson, Ph.D. Thesis, Southampton, 1973.

<sup>8</sup> J. T. Davies, *J. Theor. Biol.*, 1965, **8**, 1; J. E. Amore, Cold Spring Harbor Symposium on Quantitative Biology, 1965, vol. 30, p. 623.

poured into ice-water, and extracted with diethyl ether. The extract was washed with water, dried, and evaporated. The residue slowly crystallised from petroleum (b.p. 60–80°) to give the *diester* (1.5 g), m.p. 105–106°, having a weak musk odour (Found: C, 74.0; H, 8.6. C<sub>23</sub>H<sub>32</sub>O<sub>4</sub>

*benz[f]indene-2-carboxylate* (3d).—To a stirred mixture of sodium hydride (300 mg) and the dibromide (2) (1 g) in anhydrous dioxan (20 ml) was added dropwise a solution of freshly distilled methyl acetoacetate (350 mg) in anhydrous dioxan (10 ml) at 10–15 °C. The mixture was allowed to



o, odourless at room temp.; n.-m., non-musk; v.w.m., very weak musk; w.m., weak musk; m.m., medium musk; s.m., strong musk; v.s.m., very strong musk

requires C, 74.2; H, 8.7%),  $\nu_{\max}$  1720 (C=O) and 1247  $\text{cm}^{-1}$  (–O–C),  $\delta$  (CDCl<sub>3</sub>) 1.26 (18 H, singlet overlapping triplet, *J* 7 Hz), 1.67 (4 H, CH<sub>2</sub>–CH<sub>2</sub>), 3.57 (4 H, CH<sub>2</sub>·C·CH<sub>2</sub>), 4.22 (4 H, q, *J* 7 Hz, O·CH<sub>2</sub>), and 7.15 (2 H, aromatic).

*Methyl 2-Acetyl-2,3,5,6,7,8-hexahydro-5,5,8,8-tetramethyl-*

reach room temperature, then heated to 60 °C for 1 h, poured into water, and extracted with diethyl ether. The extract was washed with water, dried, and evaporated. The residue was crystallised from methanol; m.p. 106–107°, very weak musk odour (yield 350 mg),  $\nu_{\max}$  1700  $\text{cm}^{-1}$

(C=O),  $\delta$  (CDCl<sub>3</sub>) 1.25 (12 H, CH<sub>3</sub>), 1.65 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 2.14 (3 H, Ac), 3.50 (4 H, ArCH<sub>2</sub>), 3.72 (3 H, OCH<sub>3</sub>), and 7.18 (2 H, aromatic), *m/e* 328 (*M*<sup>+</sup>).

**Methyl 2,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethylbenz[f]indene-2-carboxylate (3g).**—To a stirred mixture of sodium hydride (240 mg) and the dibromide (950 mg) in 1,2-dimethoxyethane (10 ml) was added dropwise a solution of freshly distilled methyl acetoacetate (300 mg) in 1,2-dimethoxyethane (10 ml) at 10–15 °C. The mixture was then stirred at room temperature for 2 h, and for 1 h at 50–60 °C, poured into water, and extracted with diethyl ether. The extract was washed with water, dried, and evaporated. The residue crystallised from petroleum (b.p. 60–80°) to give the *methyl ester*, m.p. 105–106° (300 mg), having a strong and persistent musk odour (hydrolysis of the acetyl group must have been caused by traces of water in the solvent) (Found: C, 79.9; H, 8.9. C<sub>18</sub>H<sub>26</sub>O<sub>2</sub> requires C, 79.7; H, 9.1%),  $\nu_{\max}$  1700 cm<sup>-1</sup> (C=O),  $\delta$  (CDCl<sub>3</sub>) 1.30 (12 H, CH<sub>3</sub>), 1.70 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 3.23 (5 H, CH<sub>2</sub>-CH-CH<sub>2</sub>), 3.73 (3 H, OCH<sub>3</sub>), and 7.18 (2 H, aromatic). Refluxing the ester with 10% sodium hydroxide in aqueous ethanol afforded the acid, m.p. and mixed m.p. with (3h) 238–240°.

**Ethyl 2,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethylbenz[f]indene-2-carboxylate (3f).**—To a stirred mixture of sodium hydride (460 mg) and the dibromide (2) (1.9 g) in 1,2-dimethoxyethane (20 ml) was added dropwise a solution of ethyl acetoacetate (650 mg) in anhydrous diethyl ether (5 ml) at 10–15 °C. The mixture was then stirred for 10 min in the cold and 3 h at room temperature, poured into cold water, and extracted with diethyl ether. The extract was washed with water, dried, and evaporated. The residue crystallised from propan-2-ol to give the *ethyl ester*, m.p. 108–109° (yield 1 g), having a weak musk odour (Found: C, 79.9; H, 9.15. C<sub>20</sub>H<sub>28</sub>O<sub>2</sub> requires C, 80.0; H, 9.4%),  $\nu_{\max}$  1720 (C=O) and 1200 cm<sup>-1</sup> (C-O),  $\delta$  (CDCl<sub>3</sub>) 1.27 (15 H, singlet overlapping triplet, *J* 7 Hz), 1.68 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 3.20 (5 H, CH<sub>2</sub>-CH-CH<sub>2</sub>), 4.20 (2 H, q, *J* 7 Hz, OCH<sub>2</sub>), and 7.18 (2 H, aromatic).

**Ethyl 2-Cyano-2,3,5,6,7,8-hexahydro-5,5,8,8-tetramethylbenz[f]indene-2-carboxylate (3b).**—To a stirred mixture of sodium hydride (500 mg) and the dibromide (2) (1.9 g) in 1,2-dimethoxyethane (20 ml) was added dropwise a solution of ethyl cyanoacetate (565 mg) in 1,2-dimethoxyethane (10 ml) at 10–15 °C. The mixture was then stirred for 30 min in the cold and for 30 min at 40 °C. The solution was poured into cold water, and the ethereal extract was washed with water, dried, and evaporated. The residue was chromatographed through silica gel, and diethyl ether-petroleum (b.p. 40–60°) (15 : 85 v/v) eluted the crystalline product, m.p. 120–122° (yield 560 mg), odourless,  $\nu_{\max}$  1720 (C=O) and 2270 cm<sup>-1</sup> (CN),  $\delta$  (CDCl<sub>3</sub>) 1.26 (15 H, singlet overlapping triplet, *J* 7 Hz, CH<sub>3</sub>), 1.67 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 3.64 (4 CH<sub>2</sub>-C-CH<sub>2</sub>), 4.22 (2 H, q, *J* 7 Hz, O-CH<sub>2</sub>), and 7.18 (2 H, aromatic).

**2,2-Diacetyl-2,3,5,6,7,8-hexahydro-5,5,8,8-tetramethylbenz[f]indene (3e).**—A solution of the dibromide (2) (3.70 g) and acetylacetone (1.2 g) in anhydrous acetone (25 ml) containing freshly dried potassium carbonate (5 g) was heated for 24 h under reflux. The solution was cooled and filtered and acetone was evaporated off under reduced pressure. The residue was taken up in diethyl ether and the solution washed with water, dried, and evaporated. The residue crystallised from petroleum (b.p. 60–80°). After recrystallisation from diethyl ether-petroleum (b.p. 60–80°) the

*diketone* had m.p. 107–108° (yield 1.5 g), weak musk odour (Found: C, 80.5; H, 8.9. C<sub>21</sub>H<sub>28</sub>O<sub>2</sub> requires C, 80.7; H, 9.0%),  $\nu_{\max}$  1700 cm<sup>-1</sup>,  $\delta$  (CDCl<sub>3</sub>) 1.26 (12 H, CH<sub>3</sub>), 1.66 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 2.16 (6 H, CO-CH<sub>3</sub>), 3.48 (4 H, CH<sub>2</sub>-C-CH<sub>2</sub>), and 7.15 (2 H, aromatic).

**2,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethylbenz[f]indene-2-carboxylic Acid (3h).**—A solution of the ester (3f) (630 mg) in aqueous ethanol (10 ml) was heated under reflux for 2 h with sodium hydroxide (250 mg). Ethanol was partially evaporated off under reduced pressure and the mixture acidified with dilute hydrochloric acid. The solid residue was filtered off, washed with water, and crystallised from propan-2-ol to give the *acid*, m.p. 238–240° (yield 200 mg), having a very weak musk odour (Found: C, 79.5; H, 9.0. C<sub>18</sub>H<sub>24</sub>O<sub>2</sub> requires C, 79.4; H, 8.8%),  $\nu_{\max}$  1700 (C=O) and 3100br cm<sup>-1</sup> (OH),  $\delta$  (CDCl<sub>3</sub>) 1.27 (12 H, CH<sub>3</sub>), 1.68 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 3.24 (5 H, CH<sub>2</sub>-CH-CH<sub>2</sub>), and 7.17 (2 H, aromatic).

Similarly with the diester (3c), the product, after recrystallisation from propan-2-ol, had m.p. 238–240°, alone or mixed with the product described above.

**2-Acetyl-2,3,5,6,7,8-hexahydro-5,5,8,8-tetramethylbenz[f]indene (3i).**—A solution of the diketone (3e) (1 g) in methanol (30 ml) containing sodium hydroxide (500 mg) and water (2 ml) was heated under reflux for 1 h. Most of the methanol was evaporated off under reduced pressure, and the mixture was diluted with water and extracted with diethyl ether. The extract was washed with water, dried, and evaporated. The solid *ketone* had m.p. 94–95° (from methanol) (yield 900 mg), and a very weak musk odour (Found: C, 84.3; H, 9.5. C<sub>19</sub>H<sub>26</sub>O requires C, 84.4; H, 9.7%),  $\nu_{\max}$  1700 cm<sup>-1</sup> (C=O),  $\delta$  (CDCl<sub>3</sub>) 1.27 (12 H, CH<sub>3</sub>), 1.68 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 2.21 (3 H, CO-CH<sub>3</sub>), 3.18 (5 H, m, CH<sub>2</sub>-CH-CH<sub>2</sub>), and 7.17 (2 H, aromatic).

**2-Acetyl-5,6,7,8-tetrahydro-5,5,8,8-tetramethylbenz[f]indene (4).**—A solution of the dihydro-derivative (3i) (300 mg) in carbon tetrachloride (15 ml) was heated on a steam-bath with *N*-bromosuccinimide (200 mg) under reflux for 3 h. The light yellow solution was cooled, washed with water, dried (MgSO<sub>4</sub>), and evaporated. The residual dark green oily bromo-compound was dissolved in *NN*-dimethylacetamide (10 ml) and heated to boiling. Powdered calcium carbonate (400 mg) was added in portions to the boiling solution, which was then left for 5 min, cooled, poured into water, and extracted with diethyl ether. The calcium carbonate was filtered off and washed with diethyl ether. The combined ethereal solutions were washed with water, dried, and evaporated. The residue was passed through a column of alumina and the yellow crystalline product was eluted with diethyl ether-petroleum (b.p. 40–60°) (10 : 90 v/v) to give the *unsaturated ketone* (150 mg), m.p. 125–126° (from diethyl ether and methanol), odourless (Found: C, 85.0; H, 8.9. C<sub>19</sub>H<sub>24</sub>O requires C, 85.0; H, 9.0%),  $\nu_{\max}$  1645 (C=O) and 1620sh cm<sup>-1</sup>,  $\delta$  (CDCl<sub>3</sub>) 1.33 (12 H, CH<sub>3</sub>), 1.73 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 2.48 (3 H, COCH<sub>3</sub>), 3.64 (2 H, CH<sub>2</sub>), and 7.5 (3 H, m, aromatic and olefinic), *m/e* 268 (*M*<sup>+</sup>).

**1,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethylnaphtho[2,3-c]-furan (5a).**—A mixture of the dibromide (2) (12.0 g) and sodium hydroxide (9.0 g) in water (10 ml) was heated to reflux in 1,2-dimethoxyethane (200 ml) for 20 h. The mixture was cooled, poured into water and extracted with diethyl ether. The ethereal solution was washed with water, dried, and evaporated. The semi-solid residue crystallised from methanol to give the *ether*, m.p. 138–139° (yield 6 g), having a strong and persistent musk odour

(Found: C, 83.3; H, 9.6.  $C_{16}H_{22}O$  requires C, 83.4; H, 9.6%),  $\nu_{\max}$  1 047  $cm^{-1}$  (dihydrofuran),  $\delta$  ( $CCl_4$ ) 1.25 (12 H,  $CH_3$ ), 1.66 (4 H,  $CH_2 \cdot CH_2$ ), 4.92 (4 H,  $CH_2O$ ), and 7.08 (2 H, aromatic).

**5,6,7,8-Tetrahydro-5,5,8,8-tetramethylnaphtho[2,3-c]furan-1(3H)-one (6).**—To an ice-cold solution of the dihydrofuran (5a) (1.15 g) in glacial acetic acid (10 ml) was added a solution of chromium trioxide (1 g) in water (0.5 ml) and acetic acid (10 ml). The mixture was kept for 1 h in the cold, before being poured into water and extracted with dichloromethane. The organic extract was washed with water, dried ( $MgSO_4$ ), and evaporated. The residue crystallised in diethyl ether–petroleum (b.p. 60–80°) to give the *lactone* (1 g), m.p. 130–131°, having a moderately strong musk smell (Found: C, 78.6; H, 8.1.  $C_{16}H_{20}O_2$  requires C, 78.65; H, 8.25%),  $\nu_{\max}$  1 760  $cm^{-1}$  (C=O),  $\delta$  ( $CDCl_3$ ) 1.32 (12 H,  $CH_3$ ), 1.73 (4 H,  $CH_2 \cdot CH_2$ ), 5.25 (2 H,  $CH_2 \cdot O$ ), and 7.41 and 7.87 (1 H, each, aromatic).

**5,6,7,8-Tetrahydro-5,5,8,8-tetramethylnaphthalene-2,3-dicarboxylic Anhydride (7).**—Concentrated sulphuric acid (8 ml) was added to a solution of 1,1,4,4,6,7-hexamethyltetralin (4 g) in acetic anhydride (45 ml) at 0 °C. A solution of chromium trioxide (12 g) in acetic anhydride (90 ml) and glacial acetic acid (10 ml) was added dropwise with stirring and the temperature kept below 10 °C. The mixture was stirred at 5–10 °C for 1 h, then at room temperature for 4 h, poured into iced water, and extracted with diethyl ether. The extracts were washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated, and the residual solid was dissolved in ethanol and stirred with dilute hydrochloric acid. The hydrolysed product was extracted with diethyl ether and the extract was washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated. The crude product was chromatographed through alumina, the anhydride being eluted with diethyl ether–petroleum (b.p. 40–60°) (50 : 50 v/v). Recrystallisation from diethyl ether gave crystals (1.8 g), m.p. 156–157°, having a faint musk odour,  $\nu_{\max}$  1 780 and 1 830  $cm^{-1}$  (anhydride),  $\delta$  ( $CCl_4$ ) 1.38 (12 H,  $CH_3$ ), 1.75 (4 H,  $CH_2 \cdot CH_2$ ), and 7.85 (2 H, aromatic), *m/e* 258 ( $M^+$ , 30%), 244 (20), 243 (100), 214 (10), 202 (10), 201 (90), 199 (8), and 187 (30).

**1,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethylnaphtho[2,3-c]-thiophen (5b).**—A stirred mixture of the dibromide (2) (3.74 g) and sodium sulphide nonahydrate (2.4 g) in 95% ethanol (50 ml) was heated for 9 h under reflux, poured into water, and extracted with diethyl ether. The extract was washed with water, dried, and evaporated. The residual solid was filtered through a short alumina column, decolourised by boiling with charcoal, and recrystallised from ethanol to give fine plates (2.3 g), m.p. 145–146°, odourless,  $\nu_{\max}$  770 and 800  $cm^{-1}$  (–C–S–),  $\delta$  ( $CCl_4$ ) 1.25 (12 H,  $CH_3$ ), 1.64 (4 H,  $CH_2 \cdot CH_2$ ), 4.11 (4 H,  $CH_2 \cdot S \cdot CH_2$ ), and 7.08 (2 H, aromatic), *m/e* 246 ( $M^+$ , 40%), 232 (20), 231 (100), 201 (20), 189 (20), 185 (30), 175 (20), and 157 (20).

**1,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethylnaphtho[2,3-c]-thiophen S-Oxide (5c).**—The sulphide (5b) (200 mg) was stirred with sodium periodate (180 mg) in 50% aqueous methanol (20 ml) at room temperature for 12 h. The solution was filtered and the product extracted with diethyl ether. The extract was washed with water, dried, and evaporated. Recrystallisation of the yellow residue from diethyl ether–petroleum (b.p. 40–60°) (20 : 80 v/v) gave needles (200 mg), decomp. 125°, odourless,  $\nu_{\max}$  1 040  $cm^{-1}$  (S=O),  $\delta$  ( $CCl_4$ ) 1.27 (12 H,  $CH_3$ ), 1.65 (4 H,  $CH_2 \cdot CH_2$ ), 3.97 (d, 4 H,  $CH_2 \cdot SO \cdot CH_2$ ), and 7.17 (2 H, aromatic), *m/e* 262

( $M^+$ , 21%), 231 (17), 215 (15), 214 (88), 199 (43), 156 (17), 155 (22), and 141 (19).

**1,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethylnaphtho[2,3-c]thiophen SS-Dioxide (5d).**—A stirred mixture of the sulphide (5b) (250 mg) and sodium periodate (500 mg) in 75% aqueous methanol (20 ml) was heated for 24 h under reflux, filtered, and poured into water. The product was extracted with diethyl ether. The extract was washed with water, dried, and evaporated to leave a yellow solid which was recrystallised from diethyl ether–petroleum (b.p. 40–60°) (20 : 80 v/v), m.p. 165–167° (yield 260 mg), odourless,  $\nu_{\max}$  1 150 and 1 320  $cm^{-1}$  ( $SO_2$ ),  $\delta$  ( $CDCl_3$ ) 1.27 (12 H,  $CH_3$ ), 1.69 (4 H,  $CH_2 \cdot CH_2$ ), 4.3 (4 H,  $CH_2 \cdot S \cdot CH_2$ ), and 7.2 (2 H, aromatic), *m/e* 278 ( $M^+$ , 5.5%), 215 (20), 214 (100), 199 (64), 157 (22), 156 (20), 155 (29), and 141 (26).

**1,3,5,6,7,8-Hexahydro-5,5,8,8-tetramethyl-2-p-tolylsulphonylbenz[*f*]isoindole.**—To a stirred mixture of sodium hydride (1 g) in dry dimethylformamide (7 ml) was added a solution of toluene-*p*-sulphonamide (1.8 g) in dimethylformamide (6 ml) dropwise during 1 h. When the froth subsided 1 h after the addition, a solution of the dibromide (2) (3.74 g) in dimethylformamide (18 ml) was added during 2 h at 75–80 °C. The solution was stirred for 3 h at room temperature, poured into cold water, and extracted with methylene chloride. The extract was washed with water, dried, and evaporated. The semisolid residue crystallised from diethyl ether to give the *sulphonamide* (2 g), m.p. 205–206° (Found: C, 72.3; H, 7.45; N, 3.8; S, 8.4.  $C_{23}H_{29}NO_2S$  requires C, 72.0; H, 7.6; N, 3.65; S, 8.35%),  $\nu_{\max}$  1 355  $cm^{-1}$ ,  $\delta$  ( $CDCl_3$ ) 1.25 (12 H,  $CH_3$ ), 1.67 (4 H,  $CH_2 \cdot CH_2$ ), 2.42 (3 H,  $CH_3$ ), 4.63 (4 H,  $CH_2N$ ), 7.22 (2 H, aromatic), and 7.41 (2 H, *ortho*-protons) and 7.85 (2 H, *meta*-protons) (both  $A_2B_2$  patterns).

**6,7-Bisdibromomethyl-1,2,3,4-tetrahydro-1,1,4,4-tetramethylnaphthalene (8).**—A solution of 1,1,4,4,6,7-hexamethyltetralin<sup>4</sup> (21 g) in carbon tetrachloride (100 ml) in a flask fitted with stirrer and condenser was heated to reflux by a 175 W lamp 1 cm from the flask. Bromine (64 g) was added slowly from a dropping funnel. The addition was complete after about 5 h. The product separated as a fine white solid. The solution was filtered and the product was washed with water and dried; m.p. 253–255°, yield 50 g (95%), odourless,  $\delta$  ( $CDCl_3$ ) 1.3 (12 H,  $CH_3$ ), 1.68 (4 H,  $CH_2 \cdot CH_2$ ), 7.1 (2 H,  $CHBr_2$ ), and 7.51 (2 H, aromatic), *m/e* 530/531/532/533/534 ( $M^+$ ).

**5,6,7,8-Tetrahydro-5,5,8,8-tetramethylnaphthalene-2,3-dicarbaldehyde (9).**—The tetrabromide (8) (50 g) and sodium formate (25 g) in ethanol (1 500 ml) and water (500 ml) were heated to reflux in nitrogen. After 4 days the mixture became a clear pale yellow solution. The solution was boiled for one more day and then for 1 h after acidification with concentrated hydrochloric acid (6 ml). Ethanol (1 l) was distilled off. The yellow oil was separated from the aqueous layer, which was then extracted with diethyl ether. The oil and the extracts were washed with sodium hydrogen carbonate solution, dried ( $MgSO_4$ ), and evaporated. The yellow solid was recrystallised from petroleum (b.p. 40–60°); m.p. 114–115° (yield 18 g, 80%), having a musk odour,  $\nu_{\max}$  1 695 (aromatic aldehyde) and 2 700 and 2 910  $cm^{-1}$  (aldehyde CH str.),  $\delta$  ( $CCl_4$ ) 1.37 (12 H,  $CH_3$ ), 1.74 (4 H,  $CH_2 \cdot CH_2$ ), 7.82 (2 H, aromatic), and 10.4 (2 H, CHO), *m/e* 244 ( $M^+$ , 100%), 245 (10), 243 (10), 229 (10), 202 (10), 201 (60), 187 (15), and 159 (30).

**1,2,3,4-Tetrahydro-6,7-bis(hydroxymethyl)-1,1,4,4-tetramethylnaphthalene (11).**—The dialdehyde (9) (10 g) in dry

methanol (100 ml) was stirred at 20 °C with sodium borohydride (1 g) for 3 h. The solution was poured into water and extracted with diethyl ether, and the ethereal solution was washed with water, dried, and evaporated, leaving a white crystalline solid (9.5 g). Recrystallisation from diethyl ether-petroleum (b.p. 40–60°) gave crystals, m.p. 126–128°, having a faint musk odour,  $\nu_{\max}$  1 048 (CH<sub>2</sub>-OH) and 3 250br cm<sup>-1</sup> (OH),  $\delta$  (CCl<sub>4</sub>) 1.26 (12 H, CH<sub>3</sub>), 1.65 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 3.49 (2 H, OH), 4.55 (4 H, ArCH<sub>2</sub>-OH), and 7.21 (2 H, aromatic), *m/e* 248 (*M*<sup>+</sup>, 25%), 249 (5), 234 (15), 233 (100), 230 (20), 229 (10), 215 (30), and 201 (5).

1,5,7,8,9,10-Hexahydro-7,7,10,10-tetramethylnaphtho-[2,3-*e*][1,3]dioxepin (12a).—The diol (11) (1 g), paraformaldehyde (250 mg), and toluene-*p*-sulphonic acid (250 mg) in dry benzene (25 ml) were heated to reflux for 3 h in a Dean-Stark apparatus. The solution was poured into water and the benzene extract washed with sodium hydrogen carbonate solution, dried, and evaporated. The brown solid was recrystallised from ethanol and gave a colourless crystalline solid (1 g), m.p. 74–75°, having a medium musk odour,  $\nu_{\max}$  1 058 cm<sup>-1</sup> (C-O),  $\delta$  (CCl<sub>4</sub>) 1.25 (12 H, CH<sub>3</sub>), 1.65 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 4.73 (4 H, benzylic), 4.9 (2 H, O-CH<sub>2</sub>-O), and 3.5 (2 H, aromatic), *m/e* 260 (*M*<sup>+</sup>, 100%), 261 (10), 245 (60), 244 (20), 215 (10), 214 (10), 186 (10), and 185 (60).

1,5,7,8,9,10-Hexahydro-3,7,7,10,10-pentamethylnaphtho-[2,3-*e*][1,3]dioxepin (12b).—The diol (11) (1 g), acetaldehyde (250 mg), and toluene-*p*-sulphonic acid (50 mg) in dry benzene (40 ml) were stirred at room temperature for 8 h. The solution was worked up as above to give a yellow solid which was recrystallised from ethanol leaving colourless plates (1 g, 80%), m.p. 148–150°, having a faint musk odour,  $\nu_{\max}$  1 065 cm<sup>-1</sup> (C-O),  $\delta$  (CCl<sub>4</sub>) 1.22–1.35 (15 H, s + d, CH<sub>3</sub>), 1.64 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 4.67 (4 H, benzylic), 5.0 (1 H, q, *J* 7 Hz, acetal proton), and 6.91 (2 H, aromatic), *m/e* 274 (*M*<sup>+</sup>) and 260.

3-Ethyl-1,5,7,8,9,10-hexahydro-7,7,10,10-tetramethylnaphtho[2,3-*e*][1,3]dioxepin (12c).—The reaction was carried out as for (12b) with propionaldehyde (280 mg) instead of acetaldehyde. The product was recrystallised from benzene-petroleum (b.p. 40–60°) to give crystals (800 mg), m.p. 113–114°, having a faint musk odour,  $\nu_{\max}$  1 070 cm<sup>-1</sup> (C-O),  $\delta$  (CCl<sub>4</sub>) 0.92 (3 H, t, *J* 8 Hz, CH<sub>3</sub>), 1.25 (12 H, gem-CH<sub>3</sub>), 1.65 (6 H, s + m, CH<sub>2</sub>), 4.7 (3 H, s + t, benzylic + acetal proton), and 6.95 (2 H, aromatic), *m/e* 288 (*M*<sup>+</sup>).

1,5,7,8,9,10-Hexahydro-3,3,7,7,10,10-hexamethylnaphtho-[2,3-*e*][1,3]dioxepin (12d).—The reaction was carried out as for (12b) with acetone (350 mg) instead of acetaldehyde and the mixture was heated to reflux for 0.5 h. The product was purified by chromatography on silica gel and was eluted with diethyl ether-petroleum (b.p. 40–60°) (20 : 80 v/v) giving crystals (450 mg), m.p. 130–132°, having a very faint musk odour,  $\delta$  (CDCl<sub>3</sub>) 1.25 (18 H, CH<sub>3</sub>), 1.65 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 4.71 (4 H, benzylic), and 7.15 (2 H, aromatic), *m/e* 231 (*M* - C<sub>3</sub>H<sub>5</sub>O, 100), 229 (50), 215 (100), 214 (100), and 199 (45).

1,5,7,8,9,10-Hexahydro-7,7,10,10-tetramethylnaphtho-[2,3-*e*][1,3]dioxepin-3-one (13).—(i) The diol (11) (500 mg), ethyl chloroformate (250 mg), and pyridine (1 ml) were heated to reflux in toluene (25 ml) for 8 h. The mixture was poured into iced dilute hydrochloric acid, and the organic layer was washed with saturated aqueous sodium hydrogen carbonate, dried (MgSO<sub>4</sub>), and evaporated to leave the uncyclised ethyl formate as a yellow oil (540 mg),

$\delta$  (CCl<sub>4</sub>) 1.29 (15 H, s + t, CH<sub>3</sub>), 1.66 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 2.7 (1 H, OH), 4.15 (2 H, q, *J* 7 Hz, O-CO<sub>2</sub>-CH<sub>2</sub>), 4.65 (2 H, d, *J* 6 Hz, CH<sub>2</sub>-O-CO<sub>2</sub>Et), 5.13 (2 H, ArCH<sub>2</sub>-OH), and 7.25 (2 H, aromatic).

(ii) The crude product from (i) was heated under reflux in xylene (20 ml) with diethylamine (2 ml) for 24 h. The mixture was poured into dilute hydrochloric acid and extracted with diethyl ether, and the extracts were washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated. The crystalline product (400 mg) was sublimed to give crystals, m.p. 83°, having a musk odour,  $\nu_{\max}$  1 740 cm<sup>-1</sup>,  $\delta$  (CDCl<sub>3</sub>) 1.29 (12 H, CH<sub>3</sub>), 1.7 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 4.6 (4 H, benzylic), and 7.1 (2 H, aromatic), *m/e* (no *M*<sup>+</sup>) 216 (100%), 202 (40), 201 (100), and 159 (50), *m*<sup>\*</sup> 125 (*M*<sup>+</sup> → 185) and 187 (216 → 201).

6,7,8,9-Tetrahydro-6,6,9,9-tetramethylbenzo[*g*]phthalazine (15).—A mixture of the dialdehyde (9) (1 g) and hydrazine hydrate (215 mg) in 95% ethanol (25 ml) was stirred for 8 h at room temperature. The solution was poured into water and extracted with diethyl ether. The extracts were washed with water, dried, and evaporated. The brown solid was recrystallised from methanol; m.p. 190–192° (yield 900 mg),  $\delta$  (CCl<sub>4</sub>) 1.4 (12 H, CH<sub>3</sub>), 1.78 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 7.87 (2 H, aromatic), and 9.3 (2 H, heteroaromatic), *m/e* 240 (*M*<sup>+</sup>, 100%), 241 (20), 225 (40), 184 (70), and 168 (25), *m*<sup>\*</sup> 211 and 149.

5,6,7,8-Tetrahydro-5,5,8,8-tetramethylnaphthalene-2,3-dicarboxylic Acid (14a).—To a stirred solution of the dialdehyde (9) (5 g) in acetone (100 ml) was added dropwise over 24 h a solution of potassium permanganate (10 g) in 50% aqueous acetone (50 ml). The solution was then heated under reflux for 1 h. Water (50 ml) was added and the acetone evaporated off under reduced pressure. Sulphur dioxide was bubbled through the solution to reduce the precipitated manganese dioxide. The solution and thick white precipitate were neutralised with sodium hydrogen carbonate, filtered, and acidified. The resulting white precipitate was filtered off and dried. The crystals decompose at 180–185° (yield 3.5 g) and have a non-musk, carboxylic acid type odour. A small sample was heated to give the anhydride (7), m.p. and mixed m.p. 156–157°,  $\nu_{\max}$  1 690 cm<sup>-1</sup>, *m/e* 276 (*M*<sup>+</sup>, 10%), 261 (30), 258 (100), 202 (60), 201 (100), and 186 (70).

Dimethyl 5,6,7,8-Tetrahydro-5,5,8,8-tetramethylnaphthalene-2,3-dicarboxylate (14b).—The diacid (14a) (0.5 g) and concentrated sulphuric acid (0.1 ml) in methanol (25 ml) were heated under reflux for 4 h. The solution was poured into water and extracted with diethyl ether, and the extracts were washed with saturated aqueous sodium hydrogen carbonate, dried, and evaporated. The crystals were recrystallised from petroleum (b.p. 40–60°) to give plates (430 mg), m.p. 113–114°, having a pleasant fruity odour,  $\nu_{\max}$  1 720 cm<sup>-1</sup>,  $\delta$  (CCl<sub>4</sub>) 1.3 (12 H, CH<sub>3</sub>), 1.69 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 3.8 (6 H, OCH<sub>3</sub>), and 7.55 (2 H, aromatic), *m/e* 304 (*M*<sup>+</sup>) and 289.

Diethyl 5,6,7,8-Tetrahydro-5,5,8,8-tetramethylnaphthalene-2,3-dicarboxylate (14c).—The reaction was carried out as for the dimethyl ester but with ethanol (25 ml) instead of methanol. Recrystallisation from petroleum (b.p. 40–60°) gave plates (420 mg), m.p. 90–91°, with a pleasant ester-type odour,  $\nu_{\max}$  1 720 cm<sup>-1</sup>,  $\delta$  (CCl<sub>4</sub>) 1.32 (s) and 1.33 (t, *J* 7.1 Hz) (18 H, CH<sub>3</sub>), 1.71 (4 H, CH<sub>2</sub>-CH<sub>2</sub>), 4.27 (4 H, q, *J* 7.1 Hz, OCH<sub>2</sub>), and 7.53 (2 H, aromatic).