

The Isomeric *m*-Methoxytrimethylphenols and Related Compounds

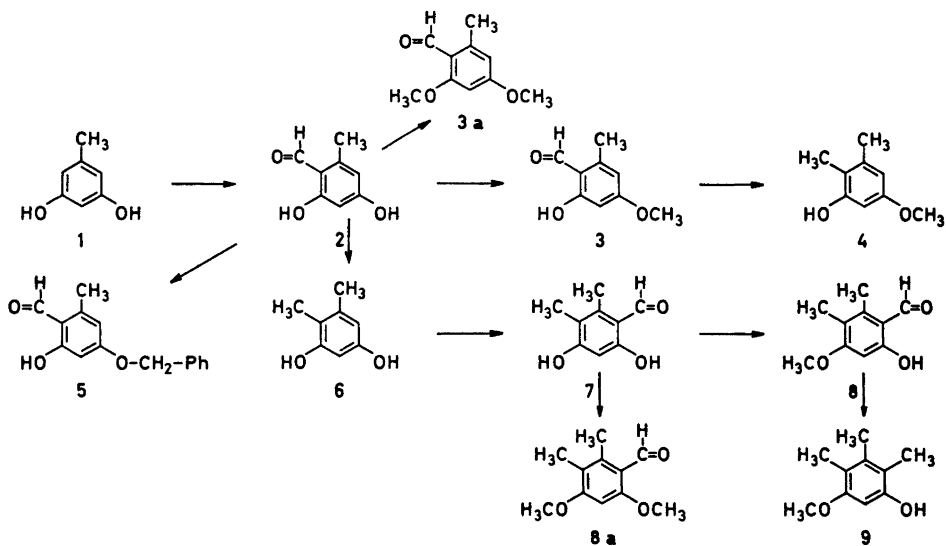
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The isomeric *m*-methoxytrimethylphenols have been synthesised by conventional routes together with some carboxylic derivatives. Physical data of the substances and intermediates are recorded.

In connection with work on the structure of depsides from *Nephroma arcticum*¹ several model compounds were synthesised.

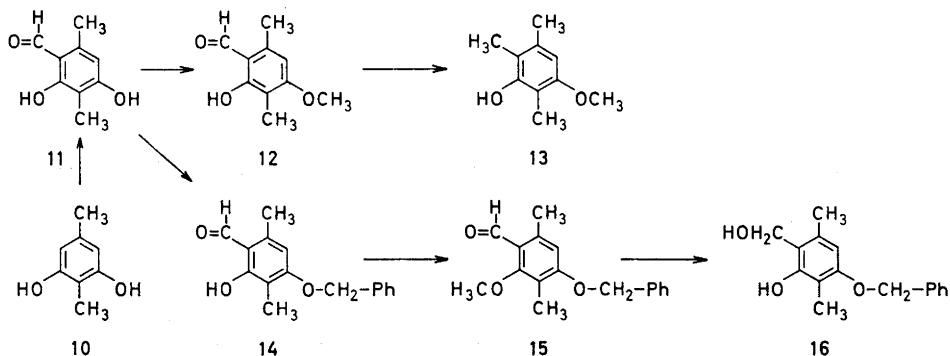
It was originally planned to prepare three of the four *m*-methoxytrimethylphenols from orcin aldehyde (2) via the ethers 3 and 5, but 3-methoxy-5,6-dimethylphenol (4) was not readily formylated by method A.



Scheme 1.

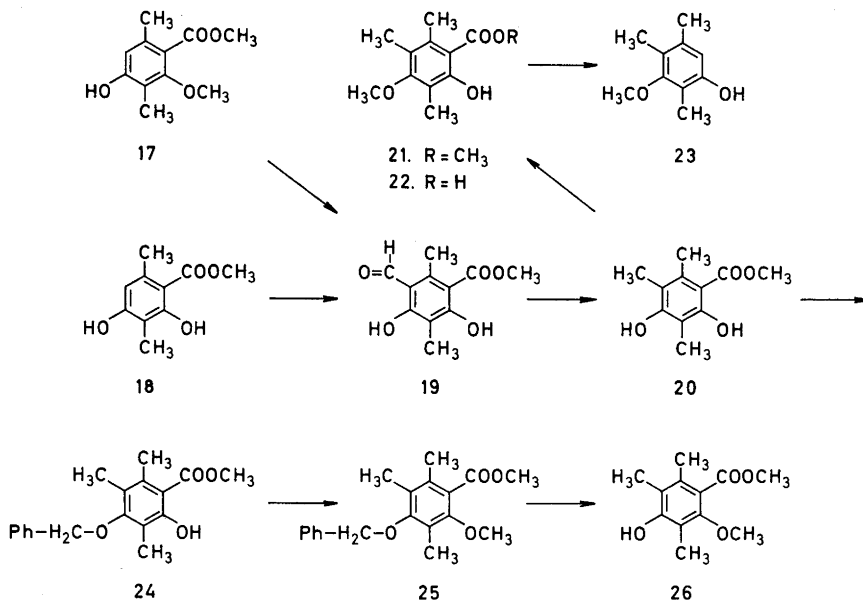
Robertson and Whalley² had prepared 2-hydroxy-4-methoxy-5,6-dimethylbenzaldehyde (8). Clemmensen reduction of this afforded 3-methoxy-4,5,6-trimethylphenol (9) (Scheme 1).

3-Methoxy-2,5,6-trimethylphenol (13) was prepared by Clemmensen reduction of 2-hydroxy-4-methoxy-3,6-dimethylbenzaldehyde^{3,4} (12) (Scheme



Scheme 2.

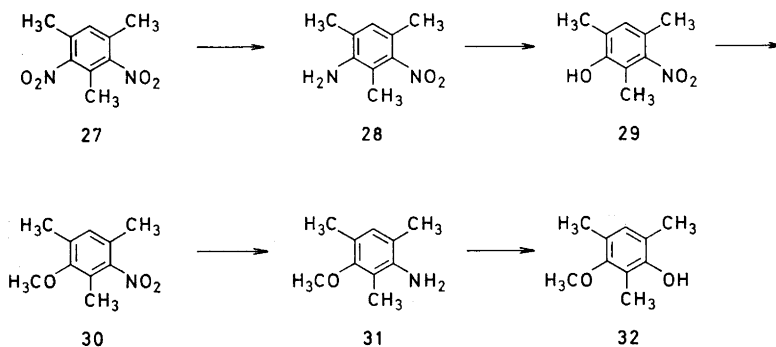
2). Attempts to prepare the isomeric 3-methoxy-2,4,5-trimethylphenol (23) by lithium aluminium hydride reduction of 4-benzyloxy-2-methoxy-3,6-dimethylbenzaldehyde (15), resulted in formation of 4-benzyloxy-2-hydroxy-



Scheme 3.

3,6-dimethylbenzyl alcohol (16) (Scheme 2). Finally, 23 was prepared by decarboxylation of 2-hydroxy-4-methoxy-3,5,6-trimethylbenzoic acid (22) (Scheme 3).

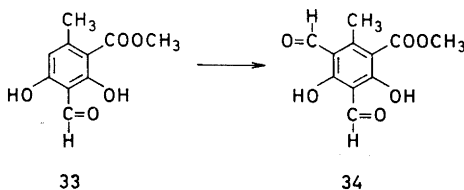
Formylation by method B of methyl 4-hydroxy-2-methoxy-3,6-dimethylbenzoate (17) and of methyl 2,4-dihydroxy-3,6-dimethylbenzoate (18) (Scheme 3) furnished methyl 5-formyl-2,4-dihydroxy-3,6-dimethylbenzoate (19), which was reduced by the Clemmensen method to methyl 2,4-dihydroxy-3,5,6-trimethylbenzoate (20). This ester was converted as shown in Scheme 3 to the compounds methyl 2-hydroxy-4-methoxy-3,5,6-trimethylbenzoate (21), methyl 4-hydroxy-2-methoxy-3,5,6-trimethylbenzoate (26) and 3-methoxy-2,4,5-trimethylphenol (23).



Scheme 4.

3-Methoxy-2,4,6-trimethylphenol (32) was prepared (Scheme 4) from dinitromesitylene (27) as starting material.⁵

Formylation of methyl 3-formyl-2,4-dihydroxy-6-methylbenzoate (methyl haematommate) (33) afforded methyl 3,5-diformyl-2,4-dihydroxy-6-methylbenzoate (34) (Scheme 5).



Scheme 5.

The UV maxima and minima of diphenols and methoxyphenols are collected in Table 1, those of the aldehydic intermediates, together with their carbonyl frequencies, are found in Table 2, the corresponding values for the benzoic acid derivatives are presented in Table 3, whilst the data for the intermediates leading to 3-methoxy-2,4,6-trimethylphenol (32) are shown in Table 4.

The NMR data of the compounds are seen in Tables 5–8. The values appear unexceptional.

Table 1. UV spectra of phenols and phenol ethers.

Subst.	λ_{\max}	λ_{\min}	$\lambda_{\text{infl.}}$	ϵ
6	2815	2510		2000
	2820			250
				2150 ^a
4	2810	2500		2300
				210
9	2860	2530		2800
				250
13	2920 2785 2740	2910 2755 2500		908
				900
				930
				880
				894
				235
23	2815	2490		1580
				135
32	2800	2370		2400
				200
16	2740	2560		2820
				2780
				1230
				1260
				1300
				915
				810
				590

^a Ref. 8, in methanol.

Some mass spectral data of the compounds are presented in Tables 9–13. Only the spectra of the benzyloxy derivatives (Table 13) appear to call for some comment. Whilst they are all overwhelmingly dominated by the m/e 91 fragment, only the esters 24 and 25 appear to offer serious competition from other modes of fragmentation. In the *o*-hydroxyaldehydes 5 and 14 loss of the benzyl group and the aldehydic carbonyl group is a little more favoured than loss of the benzyl group alone (1 % against 0.6 or 0.8 %, respectively), whilst in the *o*-methoxyaldehyde 15 the opposite is true (1 % against 0.7 % for loss of benzyl). In the benzyl alcohol 16 loss of the benzyl group together with the hydroxyl of the alcohol group replaces loss of the benzyl and carbonyl groups in the aldehydes, whilst loss of benzyl alone is insignificant (< 0.1 %).

Table 2. UV absorption and carbonyl frequencies of benzaldehyde derivatives.

Subst.	λ_{\max}	λ_{\min}	$\lambda_{\text{infl.}}$	ϵ	$\nu_{\text{CO}} \text{ cm}^{-1}$
2	2910	2550	3200	7 500	1625
				16 500	
	2330			680 8 500	
3	2870	2480	3180	6 000	1627
				15 500	
	2310			575	
				9 500 8 500	
3a	3120	2450		8 000	1672
				6 500	
	2770			15 500	
	2320			1 100 13 000	
5	2880	2480	3180	7 500	1603
				8 500	
				800	
7	3380	2550		6 500	1624 ^a
				6 000	
	2930			15 000	
				800	
	2380			8 500 7 000	
8	3380	2520	2390	5 500	1615
				4 000	
	2890			14 000	
				775	
	2350			9 500 10 000 8 000	
8a	3240	2990		7 500	1665
				4 000	
	2770			13 000	
	2350			1 800 15 000	
11	2985	2515		16 000	1624 ^a
				310	
12	2960	2490		20 000	1625
				345	
14	2970	2490		21 500	1630
				555	
15	2840	2465		19 500	1670
				1 700	

^a Shoulder.

In the ester 24 loss of toluene (3 %) is more important than loss of benzyl (< 0.1 %). However, loss of benzyl and methoxycarbonyl (3 %) is about as favoured as loss of toluene and methoxycarbonyl (4 %). In the ester 25

Table 3. UV absorption and carbonyl frequencies of benzoic acid derivatives.

Subst.	λ_{\max}	λ_{\min}	$\lambda_{\text{infl.}}$	ϵ	$\nu_{\text{CO}} \text{ cm}^{-1}$
17	2520	2380		5 400	1688
				4 700	
19	2930	2715		11 000	1660 ^a
	2575			10 000	1640
				30 000	
34	3440	3095	2710	6 000	1707
	2570			4 000	
		16 000		1627	
		19 000		7 000	
20	3130	2940		4 500	1643
	2710			3 000	
		12 500		2 500	
		2430			
21	3180	2830		3 000	1722 ^b
	2570			1 000	
				2375	
22	3160	2800		3 500	1624
	2550			620	
		8 000		4 500	
		2370			
24	3185	2845		3 500	1653 ^b
	2680			1 400	
				2385	
25	3165	3025		250	1722 ^b
				225	
26			2450	3 500	1720 ^b

^a Shoulder.

^b In chloroform.

the former losses occur equally (2 %), whilst loss of toluene and methoxycarbonyl (8 %) dominate over loss of benzyl and methoxycarbonyl (1 %). Metastable peaks in the spectrum of (25) suggest the alternative sequences

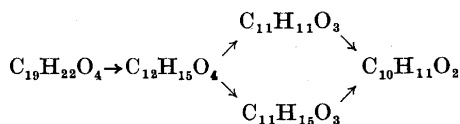


Table 4. UV absorption of mesitylenic intermediates.

Subst.	λ_{\max}	λ_{\min}	$\lambda_{\text{infl.}}$	ϵ
27	3330	3130		560
				505
			2430	3 400
			2380	3 990 ^a
28	3530	3190		805
	2370			600
				10 000
29	3280	3040		1 800
				1 600
	2565		2680	3 900
		2390		4 500
				2 900
30	2500		2640	1 600
				1 650
		2370		1 500
31	2800	2630		2 000
				550
	2330			6 850

^a Canbäck, T. *Farm. Rev.* **48** (1949) 217, in pentane.

Table 5. NMR values (δ ppm) for m-alkoxyphenols. Figures in parentheses give the number of methyl groups if more than one.

Subst.	Ar-CH ₃	O-CH ₃	O-CH ₂ -	OH	Ar-H
4	2.08	2.23	3.75	6.58	6.25 ^b 6.36 ^b
9	2.12 (2)	2.16	3.72	4.75	6.26
13	2.10 (2)	2.25	3.78	4.66	6.35
23	2.12	2.16 (2)	3.68	4.74	6.41
32	2.18 (3)		3.70	4.25 ^a	6.78
16	2.15	2.20	4.84 5.04	7.55	6.31 7.38 ^c

^a Approximate value, detected by integration before and after exchange with deuterium oxide.

^b Doublet, J=2 Hz.

^c Benzylic phenyl group.

Table 6. NMR values (δ ppm) for benzaldehyde derivatives. When in doubt, the number of hydrogens are given in parentheses.

Subst.	Ar-CH ₃	O-CH ₃	O-CH ₂ -	Ar-H	H -C=O	OH
2	2.52			6.22 ^b	10.12	1.57 11.87 ^a
3	2.50	3.84		6.26	10.13	12.47
3a	2.58	3.85	3.88	6.34	10.50	
5	2.50			5.07	6.33(2) 7.36(5)	10.08
8	2.05	2.43	3.85	6.26	10.16	12.65
8a	2.08	2.54	3.90	6.33	10.53	
11	2.08	2.50		6.23	10.12	5.78 12.68
12	2.03	2.55	3.90	6.28	10.15	12.42
14	2.12	2.52		5.14	6.33(1) 7.40(5)	10.08
15	2.18	2.58	3.82	5.14	6.58(1) 7.41(5)	10.38

^a Saturated solution. ^b Broad.Table 7. NMR values (δ ppm) for benzoic acid derivatives.

Subst.	Ar-CH ₃	O-CH ₃	O-CH ₂ -	Ar-H	H C=O	OH
17	2.12	2.20	3.78	3.92	6.38	5.89
18	2.10	2.45	3.90	6.18		5.18 11.93
19	2.06	2.76	3.98			10.31 12.14 13.16
33		2.50	3.95	6.23		10.29 12.32 13.75
34		2.56	3.95		10.19	10.33 13.15 13.75
20	2.14 ^a	2.42	3.94			5.20 11.45
21	2.16 ^a	2.42	3.70	3.95		11.00
24	2.18 ^a	2.44	3.96	4.80	7.45 ^c	11.10
25	2.20 ^b		3.76	3.95	4.78	7.47 ^c
26	2.12	2.15 ^a	3.73	3.95		5.04

^a Two methyl groups. ^b Three methyl groups. ^c Five hydrogens.Table 8. NMR values (δ ppm) for mesitylenic intermediates.

Subst.	Ar-CH ₃	NH ₂	OCH ₃	OH	Ar-H
27	2.23	2.33 ^a			7.12
28	2.05	2.15 ^a			3.55 6.84
29	2.16	2.18	2.23		6.51 6.90
30	2.23	2.28 ^a			3.73 6.95
31	2.12 ^a	2.18			3.35 3.68 6.75

^a Two methyl groups.

Table 9. Some mass spectral data of phenols and methoxyphenols.

Subst.	Found	RI (%)	Calc.	Formula	
4	152.0838	(100)	152.0837	C ₉ H ₁₂ O ₂	152 →* 137
	151	(33)			
	137.0601	(53)	137.0602	C ₈ H ₈ O ₂	
6	138.0682	(100)	138.0681	C ₈ H ₁₀ O ₂	138 →* 123
	137	(50)			
	123.0449	(91)	123.0446	C ₇ H ₇ O ₂	
9	166.0992	(100)	166.0994	C ₁₀ H ₁₄ O ₂	166 →* 151
	165	(21)			
	151.0762	(75)	151.0759	C ₉ H ₁₁ O ₂	
13	166.0992	(100)	166.0994	C ₁₀ H ₁₄ O ₂	166 →* 151
	165	(19)			
	151.0764	(67)	151.0759	C ₉ H ₁₁ O ₂	
23	166.0997	(100)	166.0994	C ₁₀ H ₁₄ O ₂	166 →* 151
	165	(8)			
	151.0760	(56)	151.0759	C ₉ H ₁₁ O ₂	166 →* 135
	135.0808	(27)	135.0810	C ₉ H ₁₁ O	
32	166.0998	(100)	166.0994	C ₁₀ H ₁₄ O ₂	166 →* 151
	165	(9)			
	151.0759	(64)	151.0759	C ₉ H ₁₁ O ₂	

EXPERIMENTAL

M.p.'s are uncorrected. Mixed m.p. determinations were made by observing the m.p.'s of the two substances and their admixture at the same time. Petroleum ether refers to a fraction of b.r. 40–50°, whilst petroleum refers to a fraction of b.r. 60–70°. IR spectra were recorded on a Perkin-Elmer Model 257 spectrometer in potassium bromide, unless specified. UV spectra were measured in ethanolic solutions with a Coleman-Hitachi Model 124 spectrometer. NMR spectra were run on a Varian A-60A instrument in deuteriochloroform solutions. Signals stated to be due to OH or NH₂ were shown to disappear on exchange with deuterium oxide. Mass spectra were obtained with an AEI MS 902 instrument.

Methoxylations and benzoxylations were made with methyl iodide and benzyl bromide, respectively, in refluxing acetone solution, usually for 1 h, with addition of freshly ignited potassium carbonate. The reaction mixture was filtered, the potassium carbonate washed with a little acetone, and then the acetone distilled off.

Clemmensen reductions were performed with the reagents in proportion: zinc wool (25 g) was treated with mercuric chloride (2 g) and water (30 ml) for 5 min. The aqueous solution was decanted, and a mixture of conc. hydrochloric acid (75 ml) and water (60 ml) was added. The mixture was heated, and at reflux the aldehyde (10 g) in hot ethanol (60 ml) was added at such a rate that the aldehyde did not crystallise in the funnel. The ensuing mixture was refluxed for 40 min, water added, and the organic material isolated with ether.

Formylations were made by the Gattermann procedure employing zinc cyanide (Method A) as described by Adams and Levine⁶ or with addition of aluminium trichloride (Method B) as described by Grundmann and Richter⁷ for the preparation of 2,4-diformyl-5-methyl resorcinol.

Table 10. Some mass spectral data of benzaldehyde derivatives. For loss of CO, cf. Ref. 11.

Subst.	Found	RI (%)	Calc.	Formula	
2	152.0472	(72)	152.0473	C ₉ H ₉ O ₃	151 → 123
	151.0400	(100)	151.0395	C ₈ H ₇ O ₃	
	123.0446	(2)	123.0446	C ₇ H ₇ O ₂	
3	166.0629	(69)	166.0629	C ₉ H ₁₀ O ₃	
	165.0550	(100)	165.0551	C ₉ H ₉ O ₃	
3a	180.0780	(100)	180.0786	C ₁₀ H ₁₄ O ₃	163 → 136
	179	(91)			
	163.0759	(52)	163.0759	C ₁₀ H ₁₁ O ₂	
	136.0521	(10)	136.0524	C ₈ H ₈ O ₂	
7	166.0629	(81)	166.0630	C ₉ H ₁₀ O ₃	165 → 137
	165	(100)			
	137.0601	(7)	137.0603	C ₈ H ₉ O ₂	
8	180.0787	(100)	180.0786	C ₁₀ H ₁₂ O ₃	179 → 151
	179	(98)			
	165.0555	(12)	165.0552	C ₉ H ₉ O ₃	
	151.0760	(9)	151.0759	C ₉ H ₁₁ O ₂	
8a	194.0939	(100)	194.0943	C ₁₁ H ₁₄ O ₃	194 → 177
	193	(83)			
	179	(20)			
	177.0913	(46)	177.0915	C ₁₁ H ₁₃ O ₃	
11	166.0628	(76)	166.0629	C ₉ H ₁₀ O ₃	165 → 137
	165	(100)			
	137.0602	(5)	137.0602	C ₈ H ₉ O ₂	
12	180.0781	(100)	180.0786	C ₁₀ H ₁₂ O ₃	179 → 162
	179.0706	(97)	179.0708	C ₁₀ H ₁₁ O ₃	
	162.0678	(11)	162.0680	C ₁₀ H ₁₀ O ₂	

For physical data not given in Experimental, see the tables.

The following compounds were prepared according to literature. Orcin aldehyde (2),⁶ 1,2-dimethyl-3,5-dihydroxybenzene (6),⁹ 2-hydroxy-4-methoxy-6-methylbenzaldehyde (3),¹⁰ the by-product 2,4-dimethoxy-6-methylbenzaldehyde (3a) dimorphous, m.p. 51–52° and 66–67° from petroleum ether, deep depression on admixture with the monomethyl ether, 2,4-dihydroxy-5,6-dimethylbenzaldehyde (7),⁹ 2-hydroxy-4-methoxy-5,6-dimethylbenzaldehyde (8)² (extracted with 0.5 N NaOH instead of 2 N NaOH²), the by-product 2,4-dimethoxy-5,6-dimethylbenzaldehyde (8a),² β-orein aldehyde (11) from 2,5-dimethyl-resorcinol (cf., e.g., Ref. 3), 2-hydroxy-4-methoxy-3,6-dimethylbenzaldehyde (12),³ dinitromesitylene (27),⁵ nitromesidine (28),⁵ nitromesitol (29).⁵ Methyl 4-hydroxy-2-methoxy-3,6-dimethylbenzoate was prepared from atranorine by methylation followed by treatment with sodium methoxylate in methanol.

3-Hydroxy-5-methoxy-1,2-dimethylbenzene (4) (520 mg crude) was prepared by Clemmensen reduction of 2-hydroxy-4-methoxy-6-methyl-benzaldehyde (550 mg), colourless prisms, m.p. 93–94° from carbon tetrachloride.

Table 12. Some mass spectral data of mesitylenic intermediates.

Subst.	Found	RI (%)	Calc.	Formula	
27	210.0638	(73)	210.0641	$C_9H_{10}N_2O_4$	210 \rightarrow 193
	193.0613	(100)	193.0613	$C_9H_8N_2O_3$	193 \rightarrow 148
	148.0632	(4)	148.0636	$C_8H_8N_2O$	
28	180.0896	(100)	180.0898	$C_9H_{12}N_2O_2$	180 \rightarrow 163
	163.0871	(50)	163.0871	$C_9H_{11}N_2O$	
29	181.0746	(100)	181.0739	$C_9H_{11}NO_3$	181 \rightarrow 164
	164.0717	(93)	164.0711	$C_9H_{10}NO_2$	164 \rightarrow 136
	136.0765	(21)	136.0762	$C_8H_{10}NO$	
30	195.0886	(100)	195.0895	$C_{10}H_{13}NO_3$	
	178.0868	(79)	178.0633	$C_{10}H_{12}NO_2$	
31	165.1159	(100)	165.1153	$C_{10}H_{15}NO$	165 \rightarrow 150
	150.0919	(27)	150.0919	$C_9H_{10}NO$	

4-Benzylloxy-2-hydroxy-6-methylbenzaldehyde. Benzylation of orcin aldehyde (3.2 g) afforded 3.6 g of crude product extracted with N NaOH after more acidic material had been removed by extraction with half saturated sodium carbonate solution. Crystallisation from ethanol furnished colourless crystals which soon became blue, m.p. 69–71°. Recrystallisation from ethanol-water 1:1 (v/v) furnished apparently pure *4-benzylloxy-2-hydroxy-6-methylbenzaldehyde* (5), m.p. 71–72°.

3-Methoxy-4,5,6-trimethylphenol. Clemmensen reduction of 2-hydroxy-4-methoxy-5,6-dimethylbenzaldehyde (8) (406 mg) afforded *3-methoxy-4,5,6-trimethylphenol* (9) (400 mg crude), long, colourless, felted needles from carbon tetrachloride, m.p. 122–122.5° (255 mg), no colour with iron(III) chloride. A mixture with the starting material (m.p. 121–122°) melted at 95–115°.

4-Benzylloxy-2-hydroxy-3,6-dimethylbenzaldehyde. β -Orcin aldehyde (1.53 g) by benzylation furnished 1.16 g of crude benzyloxy compound extracted with 2 N NaOH. Sodium carbonate solution extracted 32 mg which were discarded, whilst 0.5 N NaOH solution extracted 132 mg of the title compound. Crystallisation from petroleum afforded pure *4-benzylloxy-2-hydroxy-3,6-dimethylbenzaldehyde* (14), m.p. 89–90°.

4-Benzylloxy-2-methoxy-3,6-dimethylbenzaldehyde. Prepared by methylation of *4-benzylloxy-2-hydroxy-3,6-dimethylbenzaldehyde* (947 mg) *4-benzylloxy-2-methoxy-3,6-dimethylbenzaldehyde* (15) (846 mg crude) remained as neutral towards 4 N NaOH, m.p. 95–96° from carbon tetrachloride-petroleum (546 mg). A mixture with the starting material melted at 72–80°.

3-Methoxy-2,5,6-trimethylphenol. 2-Hydroxy-4-methoxy-3,6-dimethylbenzaldehyde (206 mg) by Clemmensen reduction yielded 178 mg of crude product, which crystallised from petroleum ether to give pure *3-methoxy-2,5,6-trimethylphenol* (13) (111 mg), m.p. 70–71°.

4-Benzylloxy-2-hydroxy-3,6-dimethylbenzyl alcohol. *4-Benzylloxy-2-methoxy-3,6-dimethylbenzaldehyde* (274 mg) was refluxed in dried tetrahydrofuran (50 ml) for 24 h with lithium aluminium hydride (1 g). Excess lithium aluminium hydride was destroyed by careful addition of water, and the reduction product was isolated with ether. 0.5 N NaOH extracted 91 mg, whilst 173 mg remained in the ether solution. The latter material was crystallised from carbon tetrachloride to give 55 mg of *4-benzylloxy-2-hydroxy-3,6-dimethylbenzyl alcohol* (16) as colourless crystals, m.p. 101–102°. The IR spectrum in chloroform showed bands at 3585 and 3350 cm^{-1} (hydrogen bonded OH) and at 1125 cm^{-1} (ether).

Table 11. Some mass spectral data of benzoic acid derivatives.

Subst.	Found	RI (%)	Calc.	Formula	
17	210.0891	(49)	210.0892	$C_{11}H_{14}O_4$	210 → 179
	193.0868	(4)	193.0864	$C_{11}H_{13}O_3$	
	179.0709	(100)	179.0708	$C_{10}H_{11}O_3$	
	163.0393	(11)	163.0395	$C_9H_7O_3$	
18	196.0734	(61)	196.0735	$C_{10}H_{13}O_4$	196 → 164
	182.0577	(2)	182.0579	$C_9H_{10}O_4$	
	164.0474	(100)	164.0473	$C_8H_8O_3$	164 → 136
	136.0528	(71)	136.0524	$C_8H_8O_2$	
19	224.0687	(28)	224.0685	$C_{11}H_{13}O_5$	192 → 164
	192.0425	(44)	192.0423	$C_{11}H_{13}O_4$	192 → 147
	164.0474	(100)	164.0473	$C_9H_9O_3$	164 → 149
	149.0239	(1)	149.0239	$C_8H_5O_3$	164 → 147
	147.0448	(2)	147.0446	$C_8H_7O_2$	
	136.0525	(28)	136.0524	$C_8H_7O_2$	
33	210.0525	(47)	210.0528	$C_{10}H_{10}O_5$	
	182.0577	(17)	182.0579	$C_9H_{10}O_4$	182 → 150
	178.0262	(21)	178.0266	$C_8H_8O_4$	178 → 150
	150.0315	(100)	150.0317	$C_8H_8O_3$	150 → 122
	122.0368	(16)	122.0368	$C_7H_8O_3$	
34	238.0475	(31)	238.0477	$C_{11}H_{10}O_6$	238 → 210
	210.0529	(35)	210.0528	$C_{10}H_{10}O_5$	210 → 179
	207.0295	(35)	207.0293	$C_{10}H_{10}O_5$	
	179.0308	(13)	179.0344	$C_9H_7O_4$	179 → 133
	178.0267	(100)	178.0266	$C_9H_7O_4$	178 → 150
	150.0318	(38)	150.0317	$C_8H_8O_3$	150 → 122
	122.0368	(14)	122.0368	$C_7H_8O_3$	
20	210.0891	(32)	210.0892	$C_{11}H_{14}O_4$	
	178.0628	(86)	178.0630	$C_{10}H_{10}O_3$	178 → 150
	150.0683	(100)	150.0681	$C_9H_{10}O_2$	
21	224.1051	(58)	224.1049	$C_{12}H_{16}O_4$	
	210.0889	(2)	224.0892	$C_{11}H_{14}O_4$	
	192.0784	(100)	192.0786	$C_{11}H_{13}O_3$	192 → 164
	164.0838	(75)	164.0837	$C_{10}H_{12}O_3$	164 → 149
	149.0599	(16)	149.0603	$C_9H_8O_3$	
22	210.0886	(47)	210.0892	$C_{11}H_{14}O_4$	
	192.0791	(71)	192.0786	$C_{11}H_{13}O_3$	192 → 164
	177.0553	(16)	177.0552	$C_{10}H_9O_3$	164 → 149
	164.0840	(100)	164.0837	$C_{10}H_{12}O_3$	164 → 121
	149.0604	(47)	149.0603	$C_9H_8O_3$	149 → 121
	121.0652	(53)	121.0653	C_8H_8O	
26	224.1048	(64)	224.1048	$C_{12}H_{16}O_4$	224 → 207
	207.1019	(4)	207.1021	$C_{12}H_{16}O_3$	224 → 193
	193.0861	(100)	193.0865	$C_{11}H_{13}O_3$	224 → 177
	177.0551	(10)	177.0552	$C_{10}H_9O_3$	

Table 13. Some mass spectral data of benzyloxy derivatives.

Subst.	Found	RI (%)	Calc.	Formula	
5	242.0944	(30)	242.0943	C ₁₅ H ₁₄ O ₃	
	123.0449	(1)	123.0446	C ₇ H ₇ O ₄	
	91	(100)			
14	256.1095	(16)	256.1099	C ₁₆ H ₁₆ O ₃	
	137.0602	(1)	137.0603	C ₈ H ₉ O ₂	
	91	(100)			
15	270.1251	(14)	270.1256	C ₁₇ H ₁₈ O ₃	
	179.0718	(1)	179.0708	C ₁₀ H ₁₁ O ₃	
	91	(100)			
16	258.1259	(12)	258.1256	C ₁₆ H ₁₈ O ₃	
	240.1151	(5)	240.1150	C ₁₅ H ₁₆ O ₂	
	150.0683	(2)	150.0681	C ₉ H ₁₀ O ₂	
	91	(100)			
24	300.1362	(14)	300.1362	C ₁₈ H ₂₀ O ₄	
	268.1098	(7)	268.1099	C ₁₇ H ₁₆ O ₃	
	241.1226	(1)	241.1228	C ₁₆ H ₁₇ O ₂	
	208.0737	(3)	208.0735	C ₁₁ H ₁₂ O ₄	
	176.0472	(5)	176.0473	C ₁₀ H ₈ O ₃	
	91	(100)			
25	314.1519	(5)	314.1518	C ₁₉ H ₂₂ O ₄	314 → 121
	283.1328	(2)	283.1334	C ₁₈ H ₁₉ O ₃	
	223.0971	(2)	223.0970	C ₁₂ H ₁₆ O ₄	223 → 191
	195.1016	(1)	195.1021	C ₁₁ H ₁₆ O ₃	195 → 163
	191.0703	(2)	191.0708	C ₁₁ H ₁₁ O ₃	
	163.0757	(8)	163.0759	C ₁₀ H ₁₁ O ₂	163 → 149
	149.0593	(2)	149.0601	C ₉ H ₉ O ₂	
91	(100)				

3-Methoxy-2,4,5-trimethylphenol. 2-Hydroxy-4-methoxy-3,5,6-trimethylbenzoic acid (below) (102 mg) was heated at reflux temperature for 5 min in quinoline (2 ml) with copper powder (0.1 g). The decarboxylation product was isolated with ether, and the ether solution extracted successively with sodium hydrogen carbonate and 0.2 N sodium hydroxide. The former extract (2 mg) was discarded, the latter crystallised from petroleum ether to give *3-methoxy-2,4,5-trimethylphenol* (23) as faintly yellow plates in clusters, m.p. 83–84°.

Methoxynitromesitylene. Methylation of nitromesitol (0.54 g) afforded *methoxynitromesitylene* (30) (0.56 g crude), b.p. 135–137° at 6 torr (0.53 g).

Methoxymesidine. Methoxynitromesitylene (2.06 g) was reduced following the procedure of Stein for reduction of nitromesitol.⁵ The reduction product was poured into water and extracted with ether. The aqueous layer was made alkaline and extracted with ether (0.5 g). The procedure was repeated with the material in the first ether extract to give another 0.8 g of crude methoxymesidine. Crystallisation from petroleum ether at low temperature afforded hard, faintly yellow crystals of *methoxymesidine* (31) (514 mg) m.p. 28–29°. The material in the mother liquor distilled at 130–135° and 7 torr (805 mg) and crystallised on seeding.

Methoxymesitol. The distilled methoxymesidine (805 mg) (above) was dissolved in water (5 ml) and sulphuric acid (1.1 ml conc.) to which were added ice (11 g) and then sodium nitrite (0.4 g) in water (2 ml) in one portion (cf. Stein ⁵). After standing for 20 min urea (1.5 g) was added. The mixture was left at room temperature for 2 h and then heated on the water bath for 15 min. A strong smell of phenol was discernible. The mixture was extracted with ether. The extracted material was distilled in a vacuum to give 90 mg of residue and 473 mg of distillate, which crystallised from petroleum. *Methoxymesitol* (32) was obtained as colourless crystals (140 mg), m.p. 67–68°.

Methyl 5-formyl-2,4-dihydroxy-3,6-dimethylbenzoate. Formylation by method B of methyl 4-hydroxy-2-methoxy-3,6-dimethylbenzoate (5.3 g) and of methyl 2,4-dihydroxy-3,6-dimethylbenzoate (14 g) furnished 4.8 g and 13.6 g, respectively, of pure *methyl 5-formyl-2,4-dihydroxy-3,6-dimethylbenzoate* (19), long, thin needles from methanol, m.p. 115–116°.

Methyl 2,4-dihydroxy-3,5,6-trimethylbenzoate. Clemmensen reduction of methyl 5-formyl-2,4-dihydroxy-3,6-dimethylbenzoate (5 g) afforded 4.5 g of crude product which crystallised from carbon tetrachloride to give pure *methyl 2,4-dihydroxy-3,5,6-trimethylbenzoate* (20) (3.15 g), m.p. 97–98°.

Methyl 2-hydroxy-4-methoxy-3,5,6-trimethylbenzoate. Methyl 2,4-dihydroxy-3,5,6-trimethylbenzoate (0.7 g) gave a crude methylation product which was extracted first with sodium carbonate solution (9 mg, discarded) and then with 0.1 N sodium hydroxide (8 portions of 25 ml). There remained 0.2 g of neutral material. The extracted product distilled at 85–90° and 0.1 torr. The distilled *methyl 2-hydroxy-4-methoxy-3,5,6-trimethylbenzoate* (21) crystallised from petroleum ether at low temperature as faintly yellow rhombohedra, m.p. 39–40° (82 mg).

2-Hydroxy-4-methoxy-3,5,6-trimethylbenzoic acid. Methyl 2-hydroxy-4-methoxy-3,5,6-trimethylbenzoate (0.4 g) was refluxed for 1 h with KOH (2.5 g) in water (25 ml). The reaction mixture was made acidic with sulphuric acid and extracted with ether. Sodium hydrogen carbonate solution removed the desired acid (217 mg), whilst 36 mg remained in the ether. Crystallisation and recrystallisation from carbon tetrachloride furnished pure *2-hydroxy-4-methoxy-3,5,6-trimethylbenzoic acid* (22) as long, fine, colourless needles, m.p. 150–151°.

Methyl 4-benzyloxy-2-hydroxy-3,5,6-trimethylbenzoate. Benzylation of methyl 2,4-dihydroxy-3,5,6-trimethylbenzoate (1 g) produced a reaction mixture which was purified first by extraction with 0.1 N sodium hydroxide (0.2 g, discarded) and then distilled at 145–150° and 0.1 torr to give 873 mg of distillate and 277 mg of residue. Crystallisation of the distillate from petroleum ether afforded *methyl 4-benzyloxy-2-hydroxy-3,5,6-trimethylbenzoate* (24) as colourless needles, m.p. 59–60°.

Methyl 4-benzyloxy-2-methoxy-3,5,6-trimethylbenzoate. Methyl 4-benzyloxy-2-hydroxy-3,5,6-trimethylbenzoate (0.5 g) was methylated and the product distilled at 148–152° and 0.1 torr. The distilled *methyl 4-benzyloxy-2-methoxy-3,5,6-trimethylbenzoate* (25) weighed 486 mg.

Methyl 4-hydroxy-2-methoxy-3,5,6-trimethylbenzoate. Methyl 4-benzyloxy-2-methoxy-3,5,6-trimethylbenzoate (0.3 g) was hydrogenated in ethyl acetate with a palladium-on-carbon catalyst. The hydrogenation mixture was extracted with sodium hydroxide, which removed 194 mg. Crystallisation from petroleum of the extracted material afforded *methyl 4-hydroxy-2-methoxy-3,5,6-trimethylbenzoate* (26) as short, colourless prisms (116 mg), m.p. 81–82°.

Methyl 3,5-diformyl-2,4-dihydroxy-6-methylbenzoate. Methyl haematommate (0.6 g), obtained by methanolysis of atranorine, was formylated by method B to give 0.5 g of crude product. Crystallisations successively from carbon tetrachloride, chloroform-petroleum and methanol afforded constant melting *methyl 3,5-diformyl-2,4-dihydroxy-6-methylbenzoate* (34) (0.1 g), m.p. 156–157°.

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