

694. *peri-Hydroxycarbonyl Compounds. Part II.* The Effect of Ring Size on Hydrogen Bonding.*

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Hydrogen bonding in *peri*-hydroxy-indanones, -tetralones, and -benzocycloheptenones and related compounds has been studied spectroscopically and by reactions with diazomethane and phenyl isocyanate. It is shown that chelation in the five-membered is much weaker than in the six- and seven-membered ring ketones, but there is no sharp distinction between the two larger ring systems.

Two major anomalies are reported : (a) quinol ketones of type (I) are not methylated by diazomethane; (b) all the *peri*-hydroxylated five-membered ring ketones examined failed to react with phenyl isocyanate.

PHENOLIC hydroxyl groups *ortho* or *peri* to a carbonyl group frequently exhibit abnormal behaviour which is ascribed to intramolecular hydrogen bonding. Failure to react with diazomethane under normal conditions is a well-known example. This is of diagnostic value in establishing the structure of hydroxy-anthraquinones, -flavones, -xanthenes, etc., although it is true that such *peri*-hydroxyl groups can sometimes be methylated by prolonged treatment with a large excess of the reagent, e.g., 3 : 7 : 3' : 4'-tetra-acetylquercetin¹ and mellein.² There are also a few cases in which *peri*-hydroxyl groups react normally with diazomethane; these include 3-hydroxyphthalic anhydride,³ 7-hydroxy-3-methylphthalide,⁴ and 4-hydroxycoumaranones.⁵ In 4 : 6-dihydroxycoumaranone, the 4-hydroxyl group is preferentially methylated.⁶ In all these normal examples the carbonyl group is located in a five-membered ring.

We have now examined a wider range of compounds of this type (see Experimental section) including a number of *peri*-hydroxyindanones which have been compared with the ring-homologous tetralones and benzocycloheptenones. Some *peri*-hydroxyl derivatives of the latter do not react with diazomethane, e.g., 1' : 4'-dihydroxy-1 : 2-benzocycloheptene-3 : 7-dione⁷ and 1'-hydroxy-2' : 3'-dimethoxy-1 : 2-benzocyclohepten-3-one.⁸ 1' : 2' : 3' : 4-Tetrahydroxy-1 : 2-benzocyclohepten-3-one can be converted into the 1' : 2' : 3'-trimethyl ether with some difficulty but it is not possible to methylate the *peri*-hydroxyl group in the case of the 2' : 3' : 4-triacetate and the 2' : 3' : 4-trimethyl ether.⁹ Our findings agree with the earlier work and it is broadly true that a hydroxyl group behaves normally towards diazomethane when *peri* to a carbonyl group in a five-membered ring but is inert if the carbonyl group is part of a six- or seven-membered ring. On the other hand all the hydroxyl groups were readily methylated with methyl sulphate except in the 8-hydroxy-tetralone group. There is, however, a curious, and as yet inexplicable, exception to the regularities of diazomethane methylations. We find that the 4 : 7-dihydroxyindanones (I; $n = 1$) and the corresponding tetralones and benzocycloheptenones (I; $n = 2$ and 3 respectively) do not react with diazomethane. Even after prolonged contact, at a low temperature, in various solvents, no methylation occurred. It was noted previously¹⁰ that 5 : 8-dihydroxytetralone was not methylated by diazomethane although some reaction, probably with the carbonyl group, could be effected by prolonged treatment. 2 : 5-Dihydroxyacetophenone is also unaffected by this reagent. The failure of the hydroxyl

* Part I, *J.*, 1956, 1585.

¹ Kubota and Perkin, *J.*, 1925, 127, 1889.

² Blair and Newbold, *J.*, 1955, 2871.

³ Corbellini and Rossi, *Gazzetta*, 1931, 61, 281.

⁴ Hochstein and Patternack, *J. Amer. Chem. Soc.*, 1951, 73, 5008; Horii, Okumura, and Tamura, *J. Pharm. Soc. Japan*, 1953, 73, 526.

⁵ Gruber and Hoyos, *Monatsh.*, 1949, 80, 303; Gruber and Horváth, *ibid.*, 1950, 81, 819.

⁶ Geissman and Hinreiner, *J. Amer. Chem. Soc.*, 1951, 73, 782.

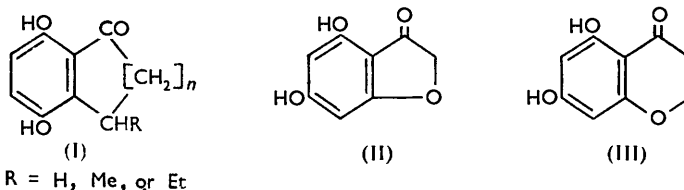
⁷ Bruce, Sorrie, and Thomson, *J.*, 1953, 2403.

⁸ Gardner and Horton, *J. Org. Chem.*, 1954, 19, 213.

⁹ Walker, *J. Amer. Chem. Soc.*, 1955, 77, 6699.

¹⁰ Thomson, *J.*, 1952, 1822.

groups, not involved in intramolecular hydrogen bonding, to react, suggested that intermolecular hydrogen bonds might be the cause but this was discounted when molecular-weight determinations (ebullioscopic) on representative compounds (I; $n = 1$, $R = \text{Me}$; $n = 2$, $R = \text{Me}$; and $n = 3$, $R = \text{H}$) showed that they were not associated in solution.



Examination of the infrared spectra of these substances revealed no abnormalities. As the compounds concerned are all quinols, an oxidation-reduction could conceivably be responsible for their non-methylation and a few oxidations by diazomethane have been recorded. Arndt and Schlatter¹¹ found that anthrone and anthranol gave 10:10'-dianthranyl when treated with diazomethane in benzene (similar observations were made earlier by Perkin and Storey¹²), and it has been shown that 1:4-naphthaquinol¹³ and 1:4:5-trihydroxynaphthalene¹⁴ react with ethereal diazomethane to form naphthaquinopyrazoles, indicating that the quinols are first oxidised to quinones and subsequently add a molecule of the diazo-compound. However, 2:3-dichloronaphthaquinol¹⁵ appears to react normally and we find that quinol itself gives a moderate yield of the dimethyl ether, and that 3:6-dihydroxyphthalic anhydride and 3:6-dihydroxyphthalimide are methylated smoothly. In any case, when methylation failed, the starting material was usually recovered in high yield so that oxidation alone is not an adequate explanation.

The preferential methylation of the 4-hydroxyl group in 4:6-dihydroxycoumaranone (II) was attributed by Geissman and Hinreiner⁶ to its greater acidity. The same argument applied to the dihydroxychromanone (III) would imply preferential methylation of the 5-hydroxyl group; as only a monomethyl ether is formed, this must be the 7-methoxy-compound and the difference between the two homologues is evidently due to a stronger hydrogen bond in the chromanone, which is confirmed by the infrared spectra.

Further anomalous behaviour is the failure of almost all the five-membered ring hydroxy-ketones to react with phenyl isocyanate (this includes both hydroxyl groups of II). Phenylurethane formation was attempted by heating the hydroxy-ketone and isocyanate alone, or in a boiling solvent (light petroleum, xylene, anisole) with triethylamine as catalyst, and also in pyridine solution at room temperature.¹⁶ In a single trial, 7-hydroxyindanone did not react with *p*-nitrophenyl isocyanate. The 4:7-dihydroxyindanones are again exceptional in forming mono(4)-phenylurethanes. In this respect they are similar to the dihydroxytetralones which form mono(5)-derivatives whereas the dihydroxybenzocycloheptenones yield bisphenylurethanes. In the latter case, the non-planarity of the seven-membered ring may facilitate the reaction but it is difficult to account for the behaviour of the hydroxyindanones.

Whilst it appears from the foregoing that hydrogen bonding is weakest in the *peri*-hydroxyindanones and strongest in the *peri*-hydroxytetralones, there are many anomalies, and obviously diazomethane and phenyl isocyanate are not reliable reagents for the detection of hydrogen-bonded phenolic groups.

To obtain a better estimate of the degree of hydrogen bonding in the hydroxy-ketones of different ring sizes we then examined their spectroscopic properties. In such compounds, methylation of the hydroxyl group generally results in a shift of the ultraviolet absorption maxima to shorter wavelengths. We find that such shifts are absent (or very small) in

¹¹ Arndt and Schlatter, *Chem. Ber.*, 1954, **87**, 1336.

¹² Perkin and Storey, *J.*, 1929, 1399.

¹³ Moore and Waters, *J.*, 1953, 3405.

¹⁴ Hayes and Thomson, *J.*, 1955, 904.

¹⁵ Bryde and Woodcock, *Ann. Appl. Biol.*, 1953, **40**, 675.

¹⁶ Illari, Marengi, and Stuani, *Ann. Chim. (Italy)*, 1953, **43**, 744.

the five-membered ring ketones but are larger in the six- and seven-membered ring compounds. Typical curves are shown in Fig. 1 and the shifts ($\Delta m\mu$) of the long-wavelength maxima are recorded in Table 1. The ultraviolet absorption of the five-membered ring compounds is in line with their chemical properties (anomalies being ignored), indicating no appreciable intramolecular hydrogen bonding. The striking similarity* of the absorption of corresponding hydroxy- and methoxy-compounds is in contrast even to *o*-hydroxyacetophenone where methylation produces a shift of 22 $m\mu$ (in alcohol).¹⁷ This indicates that the oxygen atoms in the bicyclic hydroxy-ketones are further apart than in *o*-hydroxyacetophenone and measurement of a scale diagram of 7-hydroxyindanone gives a separation of 3 Å which corresponds to a very weak hydrogen bond.

We have not examined many six- and seven-membered ring compounds as the position here is complicated by steric factors, but at least it is clear that these two groups can be easily distinguished from the five-membered ring compounds. The anomalous 1'-hydroxy-2' : 3'-dimethoxybenzocycloheptenone also differs from other members of the same group in that it does not react with phenyl *isocyanate*. Hydrogen bonding is slightly stronger (see the infrared data), but a steric factor may be important for Gardner and Horton⁸

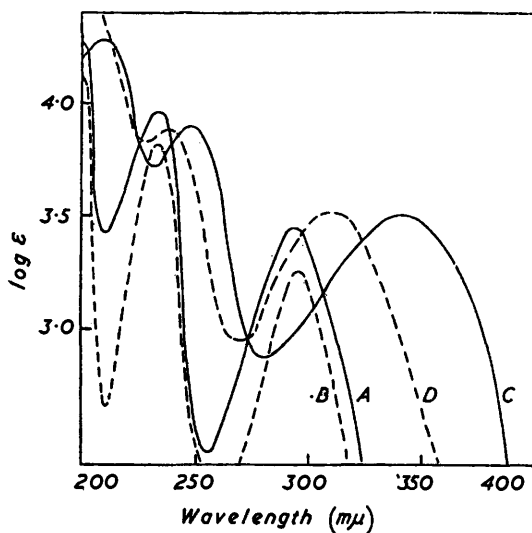


FIG. 1. A, 7-Hydroxyindanone; B, 7-methoxyindanone; C, 5-chloro-8-hydroxy-7-methoxytetralone; D, 5-chloro-7 : 8-dimethoxytetralone (in EtOH).

found that this compound can be obtained from the trimethyl ether with remarkable ease and further work¹⁸ has shown that this occurs when a second methoxyl group is placed next to the one in the *peri*-position. Swain¹⁹ and Harborne²⁰ have reported that the spectral changes which occur on addition of aluminium chloride or sodium ethoxide to alcoholic solutions of hydroxycarbonyl compounds enable hydrogen-bonded structures to be detected. We investigated this phenomenon briefly but the results were somewhat divergent and did not assist the determination of ring size.

The stretching frequencies of both hydroxyl and carbonyl groups are lowered when these groups form a hydrogen bond, and the displacement from the normal frequencies is a function of the degree of interaction between the groups.²¹ Accordingly, these infrared absorption frequencies were determined for the *peri*-hydroxycarbonyl compounds in chloroform solution: the results are summarised in Table 1. The differences between the

* Since this paper was submitted a similar observation has been made by Geissman and Harborne (*J. Amer. Chem. Soc.*, 1956, **78**, 832) in the hydroxyaurone series.

¹⁷ Morton and Stubbs, *J.*, 1940, 1347.

¹⁸ Horton and Spence, *J. Amer. Chem. Soc.*, 1955, **77**, 2894.

¹⁹ Swain, *Nature*, 1953, **172**, 23; *Chem. and Ind.*, 1954, 1480.

²⁰ Harborne, *ibid.*, p. 1142.

²¹ Bellamy, "The Infra-red Spectra of Complex Molecules," Methuen, London, 1954.

carbonyl frequencies of the *peri*-hydroxyl compounds and those of the corresponding *peri*-methoxyl compounds ($\Delta\nu\text{CO}$) are also given.

TABLE I. *Infrared absorption frequencies of the hydroxyl (νOH) and carbonyl (νCO) vibrations of peri-hydroxy-ketones, and the shifts in carbonyl frequency ($\Delta\nu\text{CO}$) and ultraviolet maximum ($\Delta m\mu$) following methylation.*

Compound	νOH (cm.^{-1})	νCO (cm.^{-1})	$\Delta\nu\text{CO}$ (cm.^{-1})	$\Delta m\mu$
Indanones				
7-Hydroxy	3369	1681	19	0
7-Hydroxy-4-methyl	3369	1678	22	—
7-Hydroxy-3 : 4-dimethyl	3369	1679	22	0
4 : 7-Dihydroxy	3606, 3378	1684	19 †	10
4 : 7-Dihydroxy-3-methyl	3600, 3375	1684	21 †	10
4-Chloro-7-hydroxy-3-methyl	3372	1686	23	0
4-Chloro-7-hydroxy	3371	1686	25	—
Tetralones				
5 : 8-Dihydroxy	3603, B	1643	38 †	30
8-Hydroxy-5-methoxy	B	1644	37	—
8-Hydroxy-5 : 7-dimethoxy-2-methyl	B	1642	46	40
5-Chloro-8-hydroxy-7-methoxy	B	1641	54	30
Benzo[cyclo]heptenones				
1' : 4'-Dihydroxy	3605, B	1637	54 †	45
1'-Hydroxy-2' : 3'-dimethoxy	B	1616	67	18 ^B
1' : 4'-Dihydroxybenzo[cyclo]heptene-3 : 7-dione	B	1638	64 †	75
Related Compounds				
4-Hydroxycoumaranone	3455	1697*	—	0
		1689		
4 : 6-Dihydroxycoumaranone ‡	—	1679	21 †	0 †
4-Hydroxy-6-methoxycoumaranone ‡	—	1682	18	—
3 : 6-Dihydroxyphthalic anhydride	3520	1762	13 †	0
		1833	14	
5-Hydroxyflavanone	B	1648	35	19
5-Hydroxy-7-methoxyflavanone	B	1639	33	—
5 : 7-Dihydroxychromanone	3584, B	1643	28 †	—
1 : 2 : 3 : 4-Tetrahydro-5 : 8-dihydroxy-1 : 4-dioxo-naphthalene	B	1643	—	—
1 : 2 : 3 : 4-Tetrahydro-5 : 8-dihydroxy-6-methyl-1 : 4-dioxonaphthalene	B	1639	—	—

B, Broad band extending from 3500 cm.^{-1} to beyond 2500 cm.^{-1} .

— Not determined.

† Compared with the dimethoxy-derivatives.

* Two bands of equal intensity.

‡ Determined by Dr. L. A. Duncanson.

As the variation in the frequency of a free phenolic hydroxyl group ($3602 \pm 14 \text{ cm.}^{-1}$)²² is small compared with the frequency shifts associated with hydrogen bonding, these shifts should be a good measure of the strength of that bond. By this criterion, the indanones, where the hydroxyl band occurs at $3373 \pm 5 \text{ cm.}^{-1}$, are clearly distinguished from compounds with six- or seven-membered rings, where the strongly bonded hydroxyl groups give weak broad bands, similar to that of *o*-hydroxyacetophenone,²³ whose maxima are obscured by C-H absorption bands near 2900 cm.^{-1} . Typical spectra are shown in Fig. 2. The weakness of the hydrogen bond in the indanones has been ascribed (above) to the greater separation of the carbonyl and the hydroxyl groups in these compounds. This separation is further increased in 4-hydroxycoumaranone and 3 : 6-dihydroxyphthalic anhydride by the presence of the shorter C-O bonds in their five-membered rings. This is reflected in their hydroxyl bands which are displaced only to 3520 cm.^{-1} in the anhydride, and to 3455 cm.^{-1} in the coumaranone. The weakness of the intramolecular bond in the anhydride is also revealed in the spectrum of the solid, where a strong broad band extending from 3450 to beyond 2500 cm.^{-1} indicates that at least one of the hydroxyl groups forms

²² Goulden, *Spectrochim. Acta*, 1954, **6**, 129; Ingraham, Corse, Bailey, and Stitt, *J. Amer. Chem. Soc.*, 1952, **74**, 2297.

²³ Martin, *Nature*, 1950, **166**, 474.

an intermolecular bond. In the solid indanones, and in the coumaranone, the weak but sharp peak of the chelated hydroxyl group persists. This band is, of course, largely obscured in compounds containing an additional unchelated hydroxyl group, which gives rise to a strong broad band in the solid state.²¹

Those six- and seven-membered ring compounds, which were sufficiently soluble (*i.e.*, contain only chelated hydroxyl groups), were examined in carbon tetrachloride solution, as chloroform obscures part of their broad hydroxyl absorption. That this band arises from the *peri*-hydroxyl group is clearly seen by comparing 8-hydroxy-5-methoxytetralone (Fig. 2, curve B) with 5:8-dimethoxytetralone (curve C). These diffuse bands are easily overlooked, and their presence in the spectra of these compounds does not appear to have been previously reported.²⁴ In general, the hydroxyl bands of the tetralones, flavanones, tetrahydrodioxonaphthalenes, and 1':4'-dihydroxybenzocycloheptenedione were found to form a closely spaced group, of which curve B (Fig. 2) is typical, apart from variations in C-H absorption. That of 1'-hydroxy-2':3'-dimethoxybenzocycloheptenone (curve D) is, however, clearly displaced to lower frequencies, approached only by

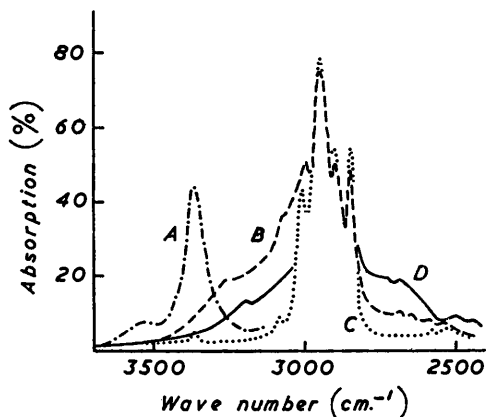


FIG. 2. Infrared absorption curves given by 0.1M-solutions in 0.4 mm. cells :

A, 7-Hydroxy-4-methylindanone (CHCl_3 and CCl_4 solution); B, 8-hydroxy-5-methoxytetralone (CCl_4); C, 5:8-dimethoxytetralone (CCl_4); D, 1'-hydroxy 2':3'-dimethoxybenzocycloheptenone (CCl_4).

5-chloro-8-hydroxy-7-methoxytetralone. Stronger intramolecular bonds are therefore indicated in these compounds. The above distinctions are clear, but finer distinctions are difficult to make, as the absorption in this region probably includes overtone bands. For example, the overtone of the strong carbonyl absorption could always be detected between 3200 and 3300 cm^{-1} .

Hunsberg and his co-workers²⁵ have used the drop in frequency in carbonyl groups involved in intramolecular bonds as a measure of the strength of these bonds, comparing, for example, *o*-hydroxyacetophenone with acetophenone. A similar comparison was not, in general, possible with the compounds studied here; instead, the difference between the carbonyl frequencies of the *peri*-hydroxyl and the corresponding *peri*-methoxyl compounds ($\Delta\nu$) has been measured. These differences are rather unsatisfactory, although the indanones ($\Delta\nu 22 \pm 3 \text{ cm}^{-1}$) are again distinguished both from 3:6-dihydroxyphthalic anhydride ($\Delta\nu 14 \text{ cm}^{-1}$) and from the six- and seven-membered ring compounds ($\Delta\nu 28\text{--}67 \text{ cm}^{-1}$). The differences between the flavanones ($\Delta\nu 33$ and 35 cm^{-1}), tetralones ($37\text{--}54 \text{ cm}^{-1}$), and benzocycloheptenones ($54\text{--}67 \text{ cm}^{-1}$) are not, however, matched by any systematic difference in their hydroxyl bands, which indicates that no general distinction can be made between the six- and seven-membered ring ketones.

The high $\Delta\nu$ values for two of the benzocycloheptenones, indeed, seem to be partly due to the abnormally high values of the carbonyl frequencies of the methylated compounds.

²⁴ Brockman and Frank, *Naturwiss.*, 1955, **42**, 45; Shaw and Simpson, *J.*, 1955, 655; Gardner and Horton, *ref.* 8.

²⁵ Hunsberg, *J. Amer. Chem. Soc.*, 1950, **72**, 5626; Hunsberg, Ketcham, and Gutowsky, *ibid.*, 1952, **74**, 4839.

This effect is shown in Table 2 where the 1': 4'-dimethoxybenzocycloheptenones and the similarly substituted indanone and tetralone are compared with their parent compounds :

TABLE 2. Carbonyl frequencies (cm.⁻¹) in chloroform solution.

	ν_{CO}	Substituents	ν_{CO}	$\Delta\nu$
Benzocycloheptenone	1672	1': 4'-dimethoxy-	1691	+19
Benzocycloheptene-3 : 7-dione	1689	1': 4'-dimethoxy-	1702	+13
Tetralone	1680	5 : 8-dimethoxy-	1680	0
Indanone	1708	4 : 7-dimethoxy-	1703	-5

The infrared data of Schubert and Sweeney²⁶ suggest that the carbonyl group in benzocycloheptenone is at least partially conjugated with the aromatic ring, its frequency being 33 cm.⁻¹ lower than that of cycloheptanone. The shift to higher frequencies in the *peri*-methoxy-substituted benzocycloheptenones is then consistent with a steric effect, similar to that of *o*-methyl groups in the acetophenones,²⁶ forcing the carbonyl group out of the plane of the ring. That this effect does not occur with the corresponding tetralone and indanone is consistent with the greater rigidity of their five- and six-membered ketone rings.²⁷

Bellamy and Beecher's²⁸ suggestion that the carbonyl frequencies of chelated hydroxy-ketones are themselves a good measure of strength of hydrogen bonding seems to be roughly true, since, apart from 1'-hydroxy-2' : 3'-dimethoxybenzocycloheptenone, all the six- and seven-membered ring compounds absorb between 1637 and 1648 cm.⁻¹. *o*-Hydroxyacetophenone, too, absorbs in this range, *i.e.*, at 1648 cm.⁻¹ in carbon tetrachloride solution,²⁵ in which these carbonyl frequencies have been found to be about 3 cm.⁻¹ higher. The benzocycloheptenone, which absorbs at 1616 cm.⁻¹, is also clearly distinguished by its hydroxyl absorption. A low carbonyl frequency (near 1622 cm.⁻¹) has also been reported for 1'-hydroxy-2' : 3' : 4-trimethoxybenzocyclohepten-3-one;⁹ this implies partial bond fixation in the aromatic rings.

The markedly higher carbonyl frequencies of the indanones (1678—1686 cm.⁻¹) are, of course, partly due to the ring-strain effect,²¹ which cannot be allowed for with any precision.

EXPERIMENTAL

The infrared measurements were made on 0.02M-solutions in chloroform, except where otherwise stated, with a Grubb-Parsons Double-beam spectrometer, type S4, equipped with a sodium chloride prism. The frequency scale was calibrated against phenol in carbon tetrachloride²⁹ and polystyrene film³⁰ in the 3000 cm.⁻¹ region (accuracy ± 10 cm.⁻¹) and by water-vapour bands in the 1600—1850 cm.⁻¹ region (accuracy ± 2 cm.).⁻¹

Methylations with Diazomethane.—General procedure: To a solution of the hydroxy-compound in a suitable solvent, ethereal diazomethane (ten-fold excess) was added. The mixture was kept in ice overnight, the solvent removed, and the residue crystallised from light petroleum.

4 : 7-Dimethoxy-3-methylindanone.—4 : 7-Dihydroxy-3-methylindanone (0.5 g.) was refluxed for 2 hr. with methyl sulphate (3.6 g.), acetone (10 ml.), and anhydrous potassium carbonate (7 g.). After dilution with water the *product* was taken into ether and distilled at 200°/0.05 mm., to give a solid which crystallised from light petroleum (b. p. 50—60°) in rosettes, m. p. 73° (Found: C, 69.7; H, 6.65. C₁₃H₁₄O₃ requires C, 69.9; H, 6.8%).

1' : 4'-Dimethoxybenzocyclohepten-3-one.—Methylation of the 1' : 4'-dihydroxy-compound with methyl sulphate, as above, gave the *dimethyl ether* as needles, m. p. 60° (from light petroleum) (Found: C, 70.8; H, 7.55. C₁₃H₁₆O₃ requires C, 70.9; H, 7.3%).

3 : 4-Diacetoxybenzofuran.—A mixture of 4-hydroxycoumaran-3-one (0.2 g.), acetic anhydride (0.5 ml.), and a trace of sulphuric acid was boiled for 5 min. The *diacetate* formed prisms, m. p. 61° (from light petroleum) (Found: C, 61.7; H, 4.3. C₁₂H₁₀O₅ requires C, 61.6; H, 4.3%).

²⁶ Schubert and Sweeney, *ibid.*, 1955, **77**, 4172.

²⁷ Braude and Sondheimer, *J.*, 1955, 3754.

²⁸ Bellamy and Beecher, *J.*, 1954, 4487.

²⁹ Fox and Martin, *Proc. Roy. Soc.*, 1937, *A*, **162**, 419; also ref. 22.

³⁰ Plyler and Peters, *J. Res. Nat. Bur. Stand.*, 1950, **45**, 462.

5 : 7-Dihydroxychromanone.—5 : 7-Dimethoxychromanone (100 mg.) and 48% hydrobromic acid (5 ml.) were refluxed for 1½ hr. Dilution with water and ether-extraction gave a solid *phenol* which crystallised from water in slender needles, m. p. 230° (Found : C, 59.8; H, 4.7. $C_9H_8O_4$ requires C, 60.0; H, 4.4%). The *diacetate* separated from light petroleum in needles, m. p. 102° (Found : C, 59.0; H, 4.45. $C_{13}H_{12}O_8$ requires C, 59.1; H, 4.55%).

5 : 7 : 8-Trimethoxy-2-methyl-1-tetralone (with J. F. GARDEN).—Anhydrous aluminium chloride (80 g.) was added, during 75 min., to a mixture of 1 : 2 : 4-trimethoxybenzene (50 g.) and methylsuccinic anhydride (33 g.) in *s*-tetrachlorethane (320 ml.), stirred (Hg seal) at 0–5°.

No.	Hydroxy-carbonyl compound	Solvent	Product	M. p.
1	4-Hydroxycoumaran-3-one	Chloroform	4-Methoxy	151°
2	4 : 6-Dihydroxycoumaran-3-one	Dioxan	4-Methoxy ⁶	290
		Tetrahydrofuran	4 : 6-Dimethoxy	136
3	3 : 6-Dihydroxyphthalic anhydride	Acetone	3 : 6-Dimethoxy	264
4	3 : 6-Dihydroxyphthalimide	Acetone	3 : 6-Dimethoxy- <i>N</i> -methyl	192
5	3-Hydroxyphthalimide	Dioxan	3-Methoxy- <i>N</i> -methyl	144
6	7-Hydroxyphthalide	Ether	7-Methoxy	108*
7	7-Hydroxyindanone	Ether	7-Methoxy	106
8	7-Hydroxy-3-methylindanone	Ether	7-Methoxy	55
9	7-Hydroxy-4-methylindanone	Ether	7-Methoxy	112
10	7-Hydroxy-3 : 4-dimethylindanone	Ether	7-Methoxy	77
11	4-Chloro-7-hydroxyindanone	Ether	7-Methoxy	148
12	4-Chloro-7-hydroxy-3-methylindanone	Ether	7-Methoxy	94
13	5 : 7-Dihydroxychromanone	Ether	7-Methoxy	76

No.	Found (%)			Formula	Required (%)		
	C	H	N or Cl		C	H	N or Cl
1	65.4	4.9	—	$C_9H_8O_3$	65.7	5.0	—
4	59.9	4.85	6.4	$C_{11}H_{11}O_4N$	59.7	5.0	6.3
5	62.5	4.8	7.3	$C_{10}H_8O_3N$	62.8	4.9	7.3
6	65.7	4.85	—	$C_9H_8O_3$	65.8	4.9	—
7	74.2	6.4	—	$C_{10}H_{10}O_2$	74.1	6.5	—
10	76.2	6.9	—	$C_{12}H_{14}O_2$	76.4	6.9	—
11	60.9	4.4	Cl 17.6	$C_{10}H_8O_2Cl$	61.1	4.6	Cl 18.0
12	62.6	5.2	Cl 16.3	$C_{11}H_{11}O_2Cl$	62.8	5.2	Cl 16.7
13	61.6	5.05	—	$C_{10}H_{10}O_4$	61.85	5.15	—

* Duncanson, Grove, and Zealley (*J.*, 1953, 1333) record m. p. 96°. This is probably due to incomplete separation from 4-methoxyphthalide formed simultaneously in their method of preparation.

After a further hour's stirring, the mixture was left at *ca.* 10° for 2 days and then allowed to warm to room temperature. Addition of ice (300 g.) and concentrated hydrochloric acid (200 ml.), followed by removal of the solvent in steam, left an oil which solidified. This was extracted with 10% aqueous sodium carbonate and filtered, the residue was washed with hot water, and the combined alkaline solutions were cooled in ice and acidified. The crude keto-acids were collected, dried, and taken up in the minimum of hot ethanol from which α -methyl- β -(2 : 4 : 5-trimethoxybenzoyl)propionic acid separated in prisms, m. p. 161° (25.5 g.) (Found : C, 60.1; H, 6.7. $C_{14}H_{18}O_8$ requires C, 59.6; H, 6.4%). Oxidation of this with alkaline permanganate gave 2 : 4 : 5-trimethoxybenzoic acid, m. p. and mixed m. p. 144°. The position of the methyl group in the acid of m. p. 161° was not proved.³¹ Evaporation of the ethanol mother-liquor left an oil which crystallised from benzene (charcoal) and then from aqueous ethanol, yielding β -methyl- β -(2 : 4 : 5-trimethoxybenzoyl)propionic acid in needles, m. p. 125–126° (8 g.) (Found : C, 59.8; H, 6.5. $C_{14}H_{18}O_8$ requires C, 59.6; H, 6.4%).

Clemmensen reduction of the keto-acid, m. p. 161°, gave α -methyl- γ -(2 : 4 : 5-trimethoxyphenyl)butyric acid which separated from light petroleum (b. p. 50–60°) in leaflets, m. p. 62° (Found : C, 62.65; H, 7.3. $C_{14}H_{20}O_5$ requires C, 62.65; H, 7.5%). This acid (3 g.) was stirred into polyphosphoric acid (30 g.) at 60°. After 30 min. the red mixture was poured on ice. The *tetralone* crystallised from light petroleum (b. p. 80–90°) in sheaves, m. p. 118° (95%) (Found : C, 67.0; H, 7.0. $C_{14}H_{18}O_4$ requires C, 67.2; H, 7.25%). The *semicarbazone* formed needles, m. p. 220° (from ethanol) (Found : N, 13.8. $C_{15}H_{21}O_4N_3$ requires N, 13.7%).

Clemmensen reduction and cyclisation of the keto-acid, m. p. 126°, gave 5 : 7 : 8-trimethoxy-3-methyltetralone in needles, m. p. 112–113° (from light petroleum) (Found : C, 66.95; H, 7.0.

³¹ Berliner in "Organic Reactions," Wiley, New York, 1949, Vol. V, p. 242.

$C_{14}H_{18}O_4$ requires C, 67.2; H, 7.25%), which formed a *semicarbazone*, needles, m. p. 236° (from ethanol) (Found: N, 13.9. $C_{15}H_{21}O_4N_3$ requires N, 13.7%).

8-Hydroxy-5 : 7-dimethoxy-2-methyl-1-tetralone.—The trimethoxytetralone (0.5 g.) (above) in glacial acetic acid (5 ml.) was refluxed for 2 hr. with concentrated hydrochloric acid (20 ml.) and poured into water. The *hydroxy-ketone* was collected and crystallised from light petroleum in bright, yellow needles, m. p. 89° (Found: C, 66.15; H, 6.6. $C_{15}H_{16}O_4$ requires C, 66.1; H, 6.8%). The *acetate* formed pale yellow needles, m. p. 141° (from light petroleum) (Found: C, 64.75; H, 6.3. $C_{15}H_{18}O_5$ requires C, 64.8; H, 6.5%).

Reactions with Phenyl isocyanate.—General procedure: A solution of the hydroxy-compound (0.2 g.) in light petroleum (20 ml., b. p. 100–120°) was refluxed for 2 hr. with an equimolecular portion of phenyl *isocyanate* and a few drops of triethylamine. The urethane separated on cooling and was recrystallised from the same solvent or from acetic acid. The results, tabulated, include some miscellaneous compounds which are new.

New urethanes.

No.	Hydroxy-ketone	Urethane	M. p.
1	4 : 7-Dihydroxy-3-methylindanone	4-Mono	158°
2	5 : 8-Dihydroxy-4-methyltetralone	5-Mono	152
3	1' : 4'-Dihydroxy-7-methylbenzocyclohepten-3-one	1' : 4'-Di	220
4	1' : 4'-Dihydroxybenzocycloheptene-3 : 7-dione	1' : 4'-Di	182
5	<i>o</i> -Fluorophenol	—	104
6	2-Hydroxydiphenyl sulphide	—	119
7	2-Hydroxydiphenyl sulphone	—	127
8	1- <i>p</i> -Tolylthio-2-naphthol	—	153
9	1-Toluene- <i>p</i> -sulphonyl-2-naphthol	—	152

No.	Found (%)				Formula	Required (%)			
	C	H	N	S		C	H	N	S
1	67.8	4.9	5.1	—	$C_{17}H_{16}O_4N$	67.6	5.1	4.9	—
2	69.3	5.3	4.3	—	$C_{18}H_{17}O_4N$	69.5	5.5	4.5	—
3	68.9	5.7	6.35	—	$C_{23}H_{24}O_5N_2$	70.25	5.45	6.3	—
4	67.2	4.8	6.3	—	$C_{25}H_{20}O_5N_2$	67.5	4.5	6.3	—
5	67.3	4.5	5.85	—	$C_{13}H_{10}O_3NF$	67.5	4.4	6.05	—
6	71.5	4.7	4.4	9.7	$C_{19}H_{15}O_2NS$	71.6	4.6	4.4	10.0
7	63.3	4.3	3.7	9.7	$C_{19}H_{15}O_4NS$	63.6	4.4	4.1	9.3
8	74.9	4.8	3.5	8.4	$C_{24}H_{19}O_4NS$	74.8	4.9	3.6	8.3
9	68.8	4.5	3.7	7.8	$C_{24}H_{19}O_4NS$	69.1	4.5	3.4	7.7

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