[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ANTIOCH COLLEGE, AND THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Determination of Double-bond Character in Cyclic Systems. III. Indan and *o*-Xylene

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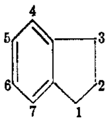
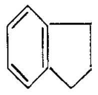
The presence of the alicyclic ring in indan has been shown by a physical method to cause no significant bond fixation of the type proposed by Mills and Nixon. This conclusion results from infrared observations of the reduction in the C=O vibrational frequency arising from conjugated chelation of adjacent hydroxyl and carbonyl-containing groups. These frequency shifts, $\Delta\nu$(C=O), were found previously to be directly proportional to the double-bond character of the bond between the carbon atoms holding the substituents. In this research $\Delta\nu$(C=O) values were observed for the different aromatic bonds in indan and *o*-xylene. A comparison of the $\Delta\nu$(C=O) values for the 4,5- and 5,6-bonds in indan with the values for the analogous bonds in *o*-xylene and for benzene reveals that the small, "normal" substituent effects of the methyl groups in *o*-xylene are nearly identical with the effects observed in indan. These small effects are in the opposite direction from the Mills–Nixon prediction. The synthesis, properties, and proof of structure for the large number of new derivatives of indan and *o*-xylene which were required in this investigation are described. It is shown that N-methylformanilide reacts with 3,4-dimethylanisole and with 5-methoxyindan to give the symmetrical methoxyaldehyde in each case. "Unavailable" 3,4-disubstituted *o*-xylenes and 4,5-disubstituted indans were prepared from the symmetrical hydroxyacids by using the carboxyl group as a blocking substituent and then removing the carboxyl group after substitution had been forced to occur at the "unfavorable" position vicinal to both the hydroxyl and the alkyl or alicyclic substituent.

Introduction

The fertile postulation of Mills and Nixon[2] that indan has the fixed bond structure I, rather than II, has not been substantiated by the large amount of experimental work which the postulate stimulated. Excellent reviews[3,4] of most of this work have been published.



I



II

A modern resolution of the problem would require determination of the relative contribution of structures I and II to the resonance of indan, *i.e.*, determination of the degree of double-bond character of the aromatic bonds in indan. Most of the earlier attacks on the problem involved measuring differences in chemical reactivity of appropriately selected indan derivatives and hence suffered from certain inherent and well-known disadvantages. The relatively small amount of physical evidence, which much more directly indicates the nature of the hybrid, suggests that I and II do not make significantly different contributions to the indan electronic structure. For example, the large resonance energy[5] of indan and the equal acid strengths[6] of 6-nitro-5-indanol and 6-nitro-3,4-xylenol both indicate that the aromatic bonds of indan are of virtually the same nature as in benzene.

Baker's[7] wet melting point method was interpreted as showing that methyl 6-hydroxy-5-indanyl ketone and methyl 5-hydroxy-4-indanyl ketone are both highly chelated but that the former is somewhat more highly chelated than the latter. In a previous paper,[8] there were mentioned the limitations of Baker's method in connection with work on naphthalene derivatives. The large difference in the dipole moments of 5,6-dibromoindan and 4,5-dibromo-*o*-xylene first was interpreted[9] in terms of considerable "bond fixation" in the former. However, when the Br-to-Br distance was found to be the same in each compound, the dipole moment data, and also Baker's data, were rationalized in terms of preferential stabilization of certain *o*-quinonoid excited structures.[10,11] Recently, it has been shown[12] that the 5-position of 4-indanol behaves as a "normal *o*-position."

Several authors[4,13] have emphasized that the excellent work of Arnold[14] and his students, which has established the relative distortion of the bonds connecting the aromatic ring with the saturated part of the indan and *o*-xylene molecules, offers very little, if any, evidence concerning the double-bond character of the aromatic bonds in these molecules. It appears that a bond distortion of the type postulated by Mills and Nixon can exist without a preferential stabilization of either structure I or II.

Earlier papers from our laboratories were devoted to studies of the bond structure of benzene,[8] naphthalene[8] and phenanthrene.[15] A method was developed in which the C=O infrared stretching frequency of a compound with an aldehyde, ketone or ester substituent is compared with the C=O frequency of the compound containing an hydroxyl group *ortho* to the carbonyl. It was demonstrated conclusively[15] that conjugated chelation of the adjacent carbonyl and hydroxyl groups lowers the

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(1) Department of Chemistry, Antioch College, Yellow Springs, Ohio.

(2) W. G. Mills and I. G. Nixon, *J. Chem. Soc.*, 2510 (1930).

(3) L. F. Fieser in Gilman's "Organic Chemistry—An Advanced Treatise," Vol. I, Second Edition, John Wiley and Sons, Inc., New York, N. Y., 1943, pp. 136–140.

(4) G. M. Badger, *Quart. Revs.* (*London*), **5**, 147 (1951).

(5) M. A. Dolliver, T. L. Gresham, G. B. Kistiakowsky and W. E. Vaughan, THIS JOURNAL, **59**, 831 (1937).

(6) R. T. Arnold and R. L. Evans, *ibid.*, **62**, 556 (1940).

(7) W. Baker, *J. Chem. Soc.*, 476 (1937).

(8) I. M. Hunsberger, THIS JOURNAL, **72**, 5626 (1950).

(9) N. V. Sidgwick and H. D. Springall, *J. Chem. Soc.*, 1532 (1936).

(10) A. Kossiakoff and H. D. Springall, THIS JOURNAL, **63**, 2223 (1941).

(11) H. D. Springall, G. C. Hampson, C. G. May and H. Spedding, *J. Chem. Soc.*, 1524 (1949).

(12) W. Baker, J. F. W. McOmie and T. L. V. Ulbricht, *ibid.*, 1825 (1952).

(13) E. E. Royals, "Advanced Organic Chemistry," Prentice–Hall, Inc., New York, N. Y., 1954, p. 512.

(14) R. T. Arnold, V. J. Webers and R. M. Dodson, THIS JOURNAL, **74**, 368 (1952), and preceding papers in this series.

(15) I. M. Hunsberger, R. Ketcham and H. S. Gutowsky, *ibid.*, **74**, 4839 (1952).

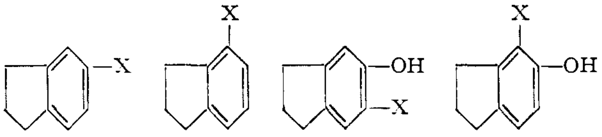
C=O frequency by an amount, $\Delta\nu$(C=O), which is directly proportional to the degree of double-bond character of the bond between the carbon atoms holding the substituents. In the present research, this method was applied to indan with the hope of providing additional direct physical evidence concerning any fixation of the double bonds in the molecule.

The situation is complicated somewhat by the possibility of the alicyclic ring exerting an "ordinary" substituent effect[16] on the aromatic bond structure of indan as well as producing any Mills–Nixon bond fixation. An approximate evaluation of such substituents effects was made by applying the method to *o*-xylene and comparing the two sets of results.

Syntheses of the considerable number of new derivatives of indan and *o*-xylene, which were required for the spectral investigation, also are presented and described.

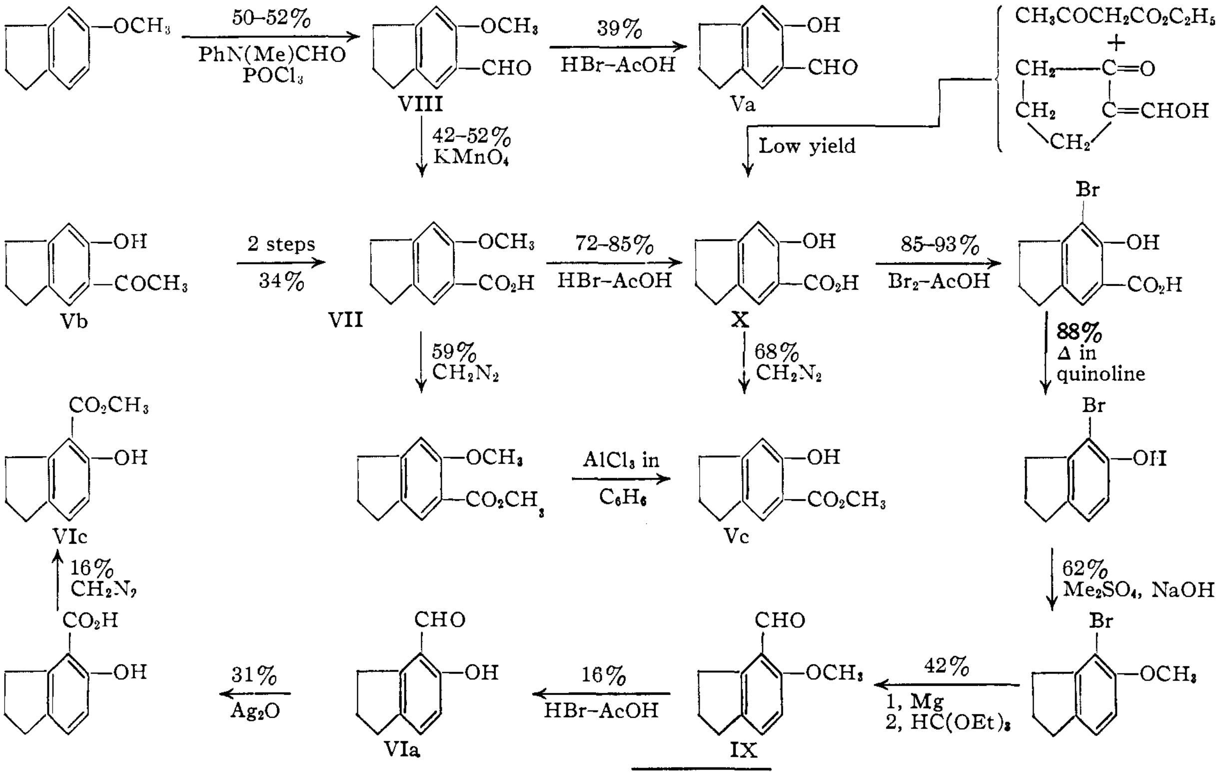
Discussion

Synthetic Work in the Indan Series.—Of the indan derivatives III–VI required in this work, only 5-indancarboxaldehyde (IIIa), methyl 5-indanyl ketone (IIIb) and the two hydroxy ketones (Vb and VIb) have been reported previously in the literature.



III IV V VI

a, X = CHO; b, X = COCH$_3$; C, X = CO$_2$CH$_3$



The four new monosubstituted indans (IIIc, IVa, IVb, IVc) were prepared by standard methods (*cf.* Experimental part). All of the new disubstituted indans were prepared from 5-indanol, which recently has become available commercially in experimental quantities, by the reaction scheme summarized below. Preparation of the methoxyacid VII from the hydroxyketone Vb of known structure[7] proves that Va and Vc both have the orientation shown. The infrared spectra of VIa and VIc definitely prove that these compounds contain *ortho* substituents, and hence they also must have the structure shown. Furthermore, although the two methoxyaldehydes (VIII and IX) melted at nearly the same temperature, a mixture m.p. exhibited a large depression.

This work apparently represents the first unambiguous proof of structure for the hydroxyacid X. An *o*-hydroxyacid (m.p. 198°), presumably X, has been reported in the patent literature[17] to be the product of the high-pressure carbonation of the sodium salt of 5-indanol.

In our laboratories this carbonation was attempted many times but failed to yield a pure product, so a direct comparison of the two acids was impossible. Also, the General Aniline and Film Corporation had none of this acid available (private communication from P. G. Stevens). However, the m.p. and color with ferric chloride indicate that the two acids are identical. Our work also confirms the 5,6-orientation assigned by Prelog[18] to the acid obtained by

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[16] M. St. C. Flett, *Trans. Faraday Soc.*, **44**, 767 (1948); more detailed recent work has been reported by N. Fuson, M.-L. Josien and E. M. Shelton, THIS JOURNAL, **76**, 2526 (1954).

[17] (a) I. G. Farbenind. A.-G., British Patent 449,045 (June 19, 1936); *C. A.*, **30**, 7871 (1936); (b) I. G. Farbenind. A.-G., French Patent 794,607 (Feb. 21, 1936); *C. A.*, **30**, 5238 (1936); (c) I. G. Farbenind. A.-G., German Patent 638,374 (Nov. 14, 1936); *C. A.*, **31**, 1223 (1937); (d) W. Zerweck, E. Korten and M. Schubert, U. S. Patent 2,078,625 (April 27, 1937); *C. A.*, **31**, 4345 (1937).

[18] V. Prelog, O. Metzler and O. Jeger, *Helv. Chim. Acta*, **30**, 675 (1947).

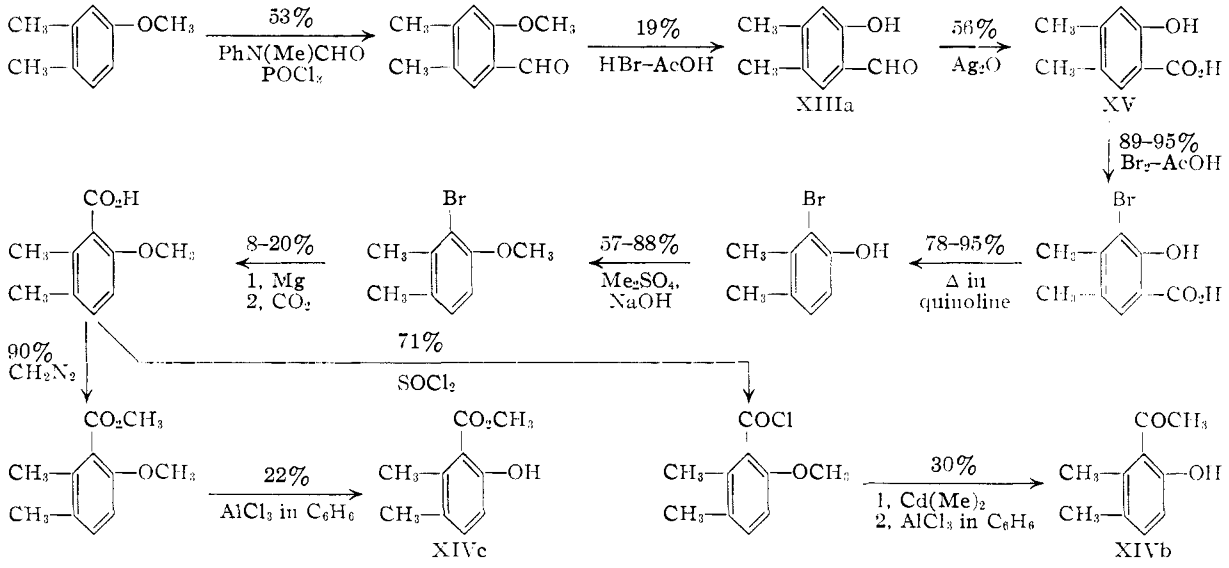
condensation of ethyl acetoacetate and 2-hydroxymethylenecyclopentanone, a synthesis which gave only a very low yield in our hands.

Our inability to prepare X directly from 5-indanol by high-pressure carbonation rendered necessary the longer synthesis *via* the methoxyaldehyde (VIII). Formylation of 5-methoxyindan proceeds preferentially in the 6-position, and this may be correlated with the earlier-reported[2] susceptibility of 5-substituted indans toward substitution at the 6-position.

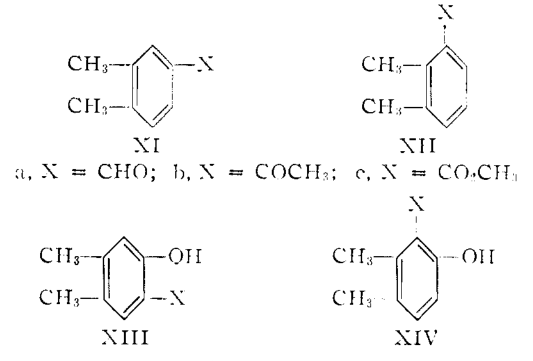
Bromination of 5-indanol occurs at the 6-position,[2] so the 4-bromo-5-indanol was prepared by brominating 6-hydroxy-5-indancarboxylic acid (X) followed by decarboxylating the bromoacid by heating in quinoline. Since both reactions proceeded in high yield, this method constitutes an excellent synthetic route to this otherwise difficultly accessible material. When 5-methoxy-4-indancarboxaldehyde (IX) was heated with hydrobromic and acetic acids, charring soon occurred, thus rendering the demethylation very tedious and causing a low over-all yield of 5-hydroxy-4-indancarboxaldehyde (VIa). The same trouble, but to a lesser extent, was encountered in a similar demethylation of 6-methoxy-5-indancarboxaldehyde (VIII). An attempted demethylation of VIII by heating in benzene with aluminum chloride was unsuccessful, no identifiable product being isolated.

Both hydroxyesters Vc and VIc were prepared by the selective methylation of the corresponding hydroxyacids. The very small amount of 5-hydroxy-4-indancarboxylic acid rendered uncertain the observation of the "end point" in the addition of diazomethane; this undoubtedly was responsible for the much lower yield of the 5,4-isomer VIc.

The very small quantity of VIc that was obtained prevented complete purification. However, its identity appears certain, and carbonyl-containing impurities seem unlikely; hence, the position of the ester carbonyl band in its infrared spectrum is considered to be valid, particularly because the conclusions based on this spectrum agree with those from the other 5,4-disubstituted indans studied.



Synthetic Work in the *o*-Xylene Series.—Of the *o*-xylene derivatives XI–XIV required for this work the two esters XIc and XIIc and the two 3,4-disubstituted *o*-xylenes XIVb and XIVc have not been characterized previously in the literature.



a, X = CHO; b, X = COCH₃; c, X = CO₂CH₃

The two previously uncharacterized esters XIc and XIIc were prepared by standard methods (*cf.* Experimental part). All of the new disubstituted *o*-xylenes were prepared according to the scheme below from 3,4-xylenol *via* the known 6-hydroxy-3,4-xylic acid (XV) which could be produced directly and in excellent yield by high-pressure carbonation of the phenol.

The known hydroxyaldehyde XIIIa was prepared in this work by demethylation of the methoxyaldehyde obtained by reaction of 3,4-dimethylanisole with N-methylformanilide and phosphorus oxychloride. Proof of structure was necessary because the isomeric hydroxyaldehyde XIVa, prepared[19] by the Reimer–Tiemann reaction, had virtually the same m.p. That the two hydroxyaldehydes are different was proved by mixture m.p. and also by examination of their infrared spectra. In dilute solution in carbon tetrachloride their spectra differed markedly, proving that the two samples are not merely different crystal modifications of the same hydroxyaldehyde. The 1,2,4,5-orientation of XIIIa was proved by oxidation to the known 6-hydroxy-3,4-

(19) A. Clayton, *J. Chem. Soc.*, **97**, 1388 (1910).

xylic acid (XV). The structure of the 3,4-disubstituted xylenes above then follows from the same reasoning used in the indan series.

It should be noted that formylation of 3,4-dimethylanisole occurs in the less hindered *ortho* position, as was the case in the indan series. The low yield in the demethylation of 6-methoxy-3,4-xylaldehyde again undoubtedly resulted from the charring which occurred prior to complete demethylation. Demethylation with aluminum chloride in benzene was unsuccessful.

Carbonation of the Grignard reagent from 2-bromo-3,4-dimethylanisole proceeded in low yield and produced some unidentified, lower-melting acid (which was not susceptible to purification) along with the desired 6-methoxyhemellitic acid. In one preparation a violent exothermic reaction occurred on decomposing the carbonation product with aqueous acid. Whether decarboxylation occurred during this violent reaction was not determined, but the assumption of decarboxylation would explain the low yield, particularly since 3,4-dimethylanisole was obtained from this reaction in 34% yield.

The preparation of 2-bromo-3,4-xylenol outlined above constitutes an excellent synthetic route. However, in one methylation of this compound a considerable amount of 3,4-dimethylanisole unexpectedly was obtained along with the expected 2-bromo-3,4-dimethylanisole. No explanation for the formation of the former product can be given. However, in another preparation an 88% yield of the expected bromoether was obtained.

The use of the difference between dry and wet m.p.'s of *ortho* disubstituted aromatic compounds as a measure of chelating *vs.* associating power is well known[20] and has been used by Baker[7] as a method of detecting "bond fixation" in aromatic rings. That this procedure must be used with caution is emphasized by the large wet m.p. depression (18°) exhibited by 6-hydroxy-2,3-dimethylacetophenone (XIVb) as compared to the small (4.5°) depression shown by the isomeric 2-hydroxy-4,5-dimethylacetophenone (XIIIb).

The absence of chelation in the solid 6-hydroxy-2,3-dimethylacetophenone (XIVb) is confirmed by the infrared spectrum of the mull, which has broad strong carbonyl absorption at 1690 cm.$^{-1}$, the same as that observed in 2,3-dimethylacetophenone (XIIb). However, in solution the carbonyl band of XIVb is shifted to 1642 cm.$^{-1}$, proving strong chelation. Apparently, chelation in the solid is prevented by the crystal structure. The chelation in solution is comparable to that in the isomeric 2-hydroxy-4,5-dimethylacetophenone (XIIIb), as indicated by the carbonyl frequency of 1649 cm.$^{-1}$ in the latter. Thus, had only the wet m.p. data been determined, an erroneous conclusion would have been made as to the chelating ability of the two compounds.

This wet m.p. behavior is not general in the disubstituted *o*-xylenes, for 6-hydroxy-3,4-xylaldehyde (XIIIa) and 6-hydroxyhemellitaldehyde (XIVa) show nearly identical wet m.p. depressions (3° and 2°, respectively).

Infrared Results.—The frequencies of the carbonyl absorption bands and the resulting $\Delta\nu(C{=}O)$ values[21] for the indan and *o*-xylene derivatives are given in Table I for the 0.02 molal carbon tetrachloride solutions. Several intercomparisons can be made of these data. First of all, in the sets of monosubstituted compounds for which only the carbonyl containing substituent is different, the C=O frequencies fall over a 36 to 38 cm.$^{-1}$ range about 1700 cm.$^{-1}$ with characteristic values for aldehydes, ketones and esters. It is generally accepted that these well-known characteristic frequencies arise from the different electronic effects (inductive and resonance) of the H, CH_3 and CH_3O groups attached to the C=O.

There is also a related but smaller and somewhat obscure effect. The $\Delta\nu(C{=}O)$ values fall over a 3 to 12 cm.$^{-1}$ range about 47 cm.$^{-1}$, depending on the nature of the substituent containing the C=O group and on the class of compound. These differences arise at least in part from variations in the effect of the H, CH_3 and CH_3O groups (attached to the C=O) upon the strength of the conjugated chelation which produces the frequency shift. Such differences were more systematic[15] for benzene, naphthalene and phenanthrene derivatives and gave a slightly different proportionality constant between double-bond character and $\Delta\nu(C{=}O)$ for aldehydes compared to ketones and esters. The less systematic values for the indans and *o*-xylenes make it advisable to use $\Delta\nu(C{=}O)$ values which are the average for the aldehyde, ketone and ester of a given class. Such average values are included in Table I.

With this introduction, let us turn to the basic question, the double-bond character of the 4,5-bond in indan compared to the 5,6-bond. The average $\Delta\nu(C{=}O)$ value for the 4,5-indan bond is 50 cm.$^{-1}$, while for the 5,6-bond it is 44 cm.$^{-1}$. These values can be compared with an average $\Delta\nu(C{=}O)$ in benzene[8,15] of 43.3 cm.$^{-1}$. The latter value corresponds to 50% double bond character, so at first one might say that the 4,5-bond in indan has (50/43.3) × 50% or 58% double-bond character while the 5,6-bond has about 51%. This result is actually in the opposite direction from the Mills–Nixon prediction. However, it is likely that replacement of hydrogen in benzene by the carbon atoms on the alicyclic ring produces "normal" substituent effects on the double-bond character of the various bonds in the aromatic ring. Such an effect might obscure the Mills–Nixon bond fixation.

The electronic effects of two *o*-methyl groups on benzene will perhaps differ from the "normal" effects of the alicyclic ring, but the $\Delta\nu(C{=}O)$ values for the *o*-xylenes should provide at least an approximate separation of the substituent effects from any Mills–Nixon effect. The average $\Delta\nu(C{=}O)$ value for the 3,4-bond in *o*-xylene is 51 cm.$^{-1}$ which is to be compared with 50 cm.$^{-1}$ for the 4,5-indan bond. The 42.3 cm.$^{-1}$ value for the 4,5-bond in *o*-xylene is to be compared with 44 cm.$^{-1}$ for the 5,6-indan bond. If we accept the *o*-xylene $\Delta\nu(C{=}O)$ values as normal, the 4,5-indan bond has a de-

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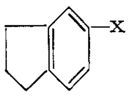
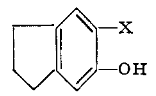
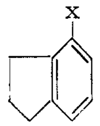
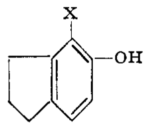
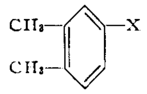
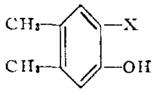
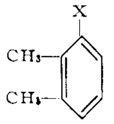
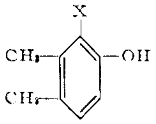
[20] For the significance of the wet m.p. consult E. D. Amstutz, J. J. Chessick and I. M. Hunsberger, *Science*, 111, 305 (1950).

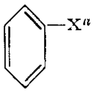
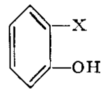
[21] For a detailed discussion of the significance of this parameter, see ref. 15.

TABLE I

FREQUENCIES (IN CM.$^{-1}$) OF THE CARBONYL ABSORPTION BANDS AND $\Delta\nu$(C=O) VALUES (IN CM.$^{-1}$) FOR THE INDAN AND *o*-XYLENE DERIVATIVES IN 0.02 *m* CARBON TETRACHLORIDE SOLUTION

X			$\Delta\nu$(C=O)			$\Delta\nu$(C=O)
CHO	1700	1657	43	1703	1655	48
$COCH_3$	1686	1646	40	1686	1635	51
CO_2CH_3	1723	1674	49	1724	1673	51
		Average	44		Average	50

						
CHO	1699	1622	37	1700	1650	50
$COCH_3$	1690	1649	41	1691	1642	49
CO_2CH_3	1726	1677	49	1728	1674	54
		Average	42.3		Average	51

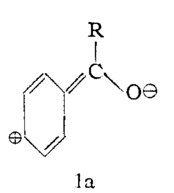
			
CHO	1708	1670	38
$COCH_3$	1693	1648	45
CO_2CH_3	1730	1683	47
		Average	43.3

[a] The data on the benzene compounds were given originally in ref. 8; they are repeated here to simplify the comparison and discussion.

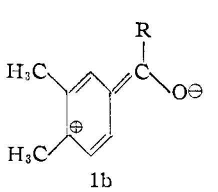
ficiency of about 1% double bond character while the 5,6-indan bond has a surplus of about 2%.

These results are compatible with a very small Mills–Nixon effect. However, the probable errors of the individual $\Delta\nu$(C=O) values are of the order of ±1 to ±2 cm.$^{-1}$, which are of the same size as the effects observed. The uncertainties in allowing for the "normal" substitutent effects on double-bond character also must be considered, so any Mills–Nixon bond fixation is such that the 4,5- and 5,6-bonds in indan would have about 49 ± 3% and 52 ± 3% double-bond character, respectively, if no other effects were present.

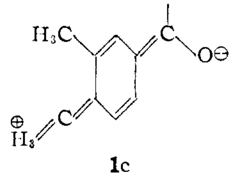
Several aspects of the data merit further comment. The C=O frequencies of the monosubstituted benzenes, which are included in Table I, are consistently higher by an average of 6 cm.$^{-1}$ than in the corresponding indan and *o*-xylene derivatives. This probably occurs because a combination of inductive and resonance substituent effects tends to stabilize the C–O$^-$ structure and hence lower the stretching frequency of the carbonyl groups[16] in the indans and *o*-xylenes as compared to the benzenes. This is suggested for the *o*-xylenes by electronic structures 1a, 1b and 1c.



1a



1b



1c

The average $\Delta\nu$(C=O) values for the 4,5-indan (50 cm.$^{-1}$) and the 3,4-*o*-xylene (51 cm.$^{-1}$) bonds are significantly larger than the $\Delta\nu$(C=O) values for the 5,6-indan (44 cm.$^{-1}$) and the 4,5-*o*-xylene (42.3 cm.$^{-1}$) bonds. The detailed mechanism for this difference is not entirely clear to us. It might result from a combination of inductive and resonance substituent effects which actually increases the double-bond character of the first-mentioned set of bonds. It also seems possible that the deformation of the bond angles in the aromatic system by the substituents[14] could promote the conjugated chelation of one type of aromatic bond but not the other. This problem is a rather subtle one and will stand further analysis.

As a matter of general interest, the infrared spectrum of 6-methoxy-5-indancarboxylic acid (VII) was examined. Apparently this acid exists predominantly as a dimer in the solid state and predominantly as a chelated monomer in carbon tetrachloride solution. In the solid mull a broad carbonyl band was found at about 1680 cm.$^{-1}$, while in solution it was displaced to a much *higher* frequency, 1744 cm.$^{-1}$. Moreover, in the solution there was a band at 3360 cm.$^{-1}$ for which no counterpart occurred in the solid. *o*-Methoxybenzoic acid in carbon tetrachloride has been reported[22] to have an absorption band at 3362 cm.$^{-1}$ similar to that in VII, both of which are attributable to intramolecular bonding as shown below in 2a.

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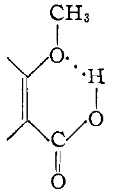
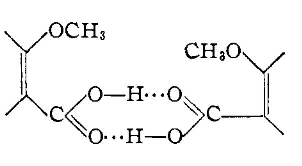
(22) J. J. Fox and A. E. Martin, *Nature*, **143**, 199 (1939).



2a



2b

Furthermore, Flett[16] reported that the monomer of *p*-methoxybenzoic acid shows C=O absorption at 1737 cm.$^{-1}$ and the dimer at 1691 cm.$^{-1}$ (both in 0.05% carbon tetrachloride). These values correspond very closely with those found for VII, particularly when allowance is made for the usual 5 to 15 cm.$^{-1}$ lower C=O frequency in solids compared to solutions. Therefore, it is concluded that VII has essentially structure 2a in solution and 2b in the solid.

Experimental[23]

Indan Series

Part of the large amount of 5-indanol[24] required in this work was prepared from indan,[25] which in turn was obtained from hydrocinnamic acid *via* the acid chloride[26] and 1-indanone.[27] The distilled 5-indanol was recrystallized twice from petroleum ether[28] to yield white needles,[29] m.p. 53.1–53.9°[30]; lit. m.p.'s 53.5°[7], 54–55°.[34] **5-Indancarboxaldehyde (IIIa)** was prepared from 5-chloromethylindan[31] by a modified Sommelet reaction.[32] Purification through the bisulfite adduct followed by two distillations[33] yielded a fragrant oil,[29] b.p. 146–147.5° (29 mm.), lit.[31] b.p. 135–138° (23 mm.). **Methyl 5-indanyl ketone**[34] **(IIIb)** was distilled three times to yield a water-white oil[29] with mint-like odor, b.p. 129.5° (8 mm.), lit.[34] b.p. 134–135° (11 mm.).

Methyl 5-Indancarboxylate (IIIc).—5-Indancarboxylic acid (5.32 g., 0.0328 mole), prepared in 77% yield by hypochlorite oxidation[35] of the corresponding methyl ketone[34] was esterified with methanol and sulfuric acid to yield 4.15 g. (71.8%) of methyl ester, b.p. 114–115° (5 mm.). Two additional distillations afforded a water-white oil[29] with a fruity odor, b.p. 106° (4 mm.). Solidification to white crystals, m.p. 27.2–27.6°,[30] soon occurred.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.82. Found: C, 75.11; H, 6.99.

4-Indancarboxaldehyde (IVa).—4-Indancarboxylic acid (12.2 g., 0.0752 mole), prepared from *o*-chlorobenzaldehyde,[36] was heated for two hours with 20 ml. of purified thionyl chloride. Distillation then produced 11.9 g. (87.5%) of water-white **acid chloride**, b.p. 152–153° (24 mm.). The acid chloride (11.8 g., 0.0656 mole) was reduced by the Rosenmund method,[37] 1.4 g. of 5% palladium-barium sulfate being used with 3 drops of "poison" in 45 ml. of purified, dry decahydronaphthalene. In two hours 93% of the theoretical amount of hydrogen chloride was evolved. The reaction, which started at 140°, was stopped at 196°, most of the reduction having occurred at 180–190°. From the sodium bisulfite adduct, prepared by shaking for 13 hours, 5.05 g. (52.7%) of 4-indancarboxaldehyde, b.p. 136.5–137° (25 mm.), was obtained. Redistillation[33] produced a colorless oil,[29] b.p. 136° (24 mm.), with an odor resembling benzaldehyde.

Anal. Calcd. for $C_{10}H_{10}O$: C, 82.16; H, 6.89. Found: C, 82.17, 82.34; H, 6.52, 6.74.

The 2,4-dinitrophenylhydrazone, recrystallized twice from ethyl acetate, formed orange crystals, m.p. 241–243° dec.

Anal. Calcd. for $C_{16}H_{14}O_4N_4$: N, 17.18. Found: N, 17.40.

Methyl 4-Indanyl Ketone (IVb).—The directions[38] for preparing methyl 9-phenanthryl ketone were followed, a nitrogen atmosphere being used throughout. Thus, a Grignard reagent was prepared from 15.2 g. (0.107 mole) of freshly distilled methyl iodide and 2.60 g. (0.107 g. atom) of magnesium. The ether was replaced by dry benzene and 7.63 g. (0.0534 mole) of 4-indancarbonitrile[36] gradually added (stirring) at a rate which kept the violent reaction under control. The reddish-brown solution was refluxed for three hours, cooled, and cautiously acidified with 55 ml. of 6 *N* hydrochloric acid. The resulting tan suspension was refluxed (stirring) for seven hours, but little solid remained after two hours. The red-orange benzene layer was washed with water and aqueous sodium bicarbonate and dried over magnesium sulfate. Removal of the benzene (foaming) left a dark reddish oil, which was distilled. After a forerun of about 1 ml. of red oil (presumably the nitrile), 4.19 g. (49.1%) of ketone distilled as a pale-yellow oil, b.p. 103–103.5° (4 mm.), having an odor like acetophenone. On redistillation a few drops of yellow oil preceded the colorless main fraction, b.p. 123.5–124° (9 mm.). A final distillation afforded a nitrogen-free, colorless oil,[29] b.p. 103.5° (4 mm.).

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.24; H, 7.27.

The 2,4-dinitrophenylhydrazone, recrystallized twice from ethyl acetate, formed red crystals, m.p. 221–223°.

Anal. Calcd. for $C_{17}H_{16}N_4O_4$: N, 16.47. Found: N, 16.73.

Methyl 4-Indancarboxylate (IVc).—4-Indancarboxylic acid[36] (4.00 g., 0.0246 mole) was esterified with diazomethane. An ether extract of the product was washed with sodium carbonate, dried, and distilled to yield 2.55 g. of ester, b.p. 125–126° (6 mm.). An additional 0.75 g. was collected at 121.5–125°; total yield 3.30 g. (76.2%). A final distillation of the larger fraction produced a colorless oil, b.p. 130–131° (7 mm.), with an odor of mint.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.82. Found: C, 74.90; H, 6.84.

6-Methoxy-5-indancarboxaldehyde (VIII).—Using essentially the procedure for methylation of carbazole,[39] 5-indanol was converted in 90% yield to 5-methoxyindan, b.p. 116.5–118° (17 mm.).

N-Methylformanilide (8.5 g., 0.063 mole) and 10.5 g. (0.069 mole) of phosphorus oxychloride were allowed to stand one-half hour. 5-Methoxyindan (5.0 g., 0.034 mole) was added (heat evolved), and the flask was heated two hours in a bath at 85°. The resulting brown sirupy mass was poured into 180 ml. of ice-water with vigorous stirring. Subsequent stirring and scratching caused the original tar to change into a flocculent tan solid. After standing overnight, the solid was filtered, thoroughly washed with water, pressed free of adhering oil, and recrystallized from aqueous ethanol to yield 3.0 g. (50%) of methoxyaldehyde as tan crystals, m.p. 70–73°. Two additional re-

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(23) All m.p.'s and b.p.'s are uncorrected unless specified otherwise. Nearly all of the distillations reported were performed in a modified Claisen flask with a short vacuum-jacketed column. All combustion analyses were performed by the Clark Microanalytical Laboratory, Urbana, Ill.

(24) A. H. Cook and R. P. Linstead, *J. Chem. Soc.*, 946 (1934).

(25) E. Clemmensen, *Ber.*, **47**, 681 (1914).

(26) C. K. Ingold and J. F. Thorpe, *J. Chem. Soc.*, **115**, 143 (1919).

(27) C. K. Ingold and H. A. Piggott, *ibid.*, **123**, 1469 (1923); N. Levin, B. E. Graham and H. G. Kolloff, *J. Org. Chem.*, **9**, 380 (1944).

(28) B.p. 35–60°.

(29) Spectral sample.

(30) Corrected.

(31) R. T. Arnold, THIS JOURNAL, **61**, 1405 (1939).

(32) G. M. Badger, *J. Chem. Soc.*, 535 (1941).

(33) Performed under nitrogen.

(34) J. v. Braun, G. Kirschbaum and H. Schuhmann, *Ber.*, **53**, 1155 (1920).

(35) (a) L. F. Fieser and E. B. Hershberg, THIS JOURNAL, **62**, 49 (1940); (b) M. S. Newman and H. L. Holmes, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 428.

(36) L. F. Fieser and E. B. Hershberg, THIS JOURNAL, **59**, 394 (1937).

(37) E. B. Hershberg and J. Cason, *Org. Syntheses*, **21**, 87 (1941); E. Mosettig in "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, p. 369.

(38) J. E. Callen, C. A. Dornfeld and G. H. Coleman, *Org. Syntheses*, **28**, 6 (1948).

(39) T. S. Stevens and S. H. Tucker, *J. Chem. Soc.*, **123**, 2140 (1923); H. Gilman and T. H. Cook, THIS JOURNAL, **62**, 2813 (1940).

crystallizations from aqueous alcohol afforded white crystals, m.p. 72.5–73.5°.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 74.90, 75.11; H, 6.31, 6.34.

In four other preparations using up to 25 g. of methoxyindan the yields were 50–52%. The crude aldehyde also may be recrystallized from petroleum ether[28] containing a little benzene.

6-Hydroxy-5-indancarboxaldehyde (Va).—To 1.0 g. (0.0057 mole) of the methoxyaldehyde in 7.5 ml. of boiling glacial acetic acid 2 ml. of 48% hydrobromic acid was added over 7 minutes. The reaction was stopped after 25 minutes of boiling because the originally green mixture had started to carbonize. On diluting to 100 ml. with water a black tar separated. An ether extract of this mixture was filtered, shaken with 5% sodium hydroxide, and the alkaline layer acidified to yield 0.18 g. of tan hydroxyaldehyde, m.p. 81.5–83°. Evaporation of the ether afforded 0.50 g. of methoxyaldehyde, m.p. 67–72°. The yield of hydroxyaldehyde was 39%, based on methoxyaldehyde not recovered. The above hydroxyaldehyde was recrystallized twice from a very small amount of petroleum ether[28] to yield the analytical sample,[29] m.p. 82–83°.

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.04; H, 6.21. Found: C, 74.30; H, 5.91.

Methyl 6-Hydroxy-5-indanyl Ketone (Vb).—A Fries rearrangement[7] of 6.0 g. (0.0341 mole) of 5-acetoxyindan[7] produced, after steam distillation, an oily solid melting over a wide range. A very tedious fractional crystallization of this product separated 0.48 g. of solid, m.p. 47.5–56.5°, from some higher-melting material. Further purification via the acetyl derivative as directed by Baker[7] finally produced the pure hydroxyketone as fine white needles,[29] m.p. 59.6–60.4°,[30] which in alcohol gave a purple color with ferric chloride. Baker[7] reported m.p. 59.5° and a reddish-blue color with ferric chloride

6-Methoxy-5-indancarboxylic Acid (VII). (a) From the Methoxyaldehyde.—To 15.0 g. (0.0852 mole) of aldehyde in 375 ml. of acetone was added 18.6 g. of potassium permanganate in 500 ml. of water. The temperature rose spontaneously to 50° within 5 minutes and was held there for another 20 minutes. The cooled mixture was treated with sulfur dioxide until the brown precipitate disappeared and then extracted with ether, from which 5% sodium bicarbonate removed 7.76 g. of white acid, m.p. 108–111.5°. The unchanged aldehyde (2.3 g., m.p. 67–72°) recovered from the ether was oxidized as above to yield another 0.66 g. (total yield, 51%) of acid, m.p. 109–112°. Two recrystallizations from benzene produced the analytical sample, m.p. 111–113°.

Anal. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.30. Found: C, 68.98; H, 6.14.

Four other oxidations similar to the above produced yields of 42–52%. Longer heating with the permanganate decreased the yield.

Several attempts to brominate this acid in acetic acid solution were unsuccessful.

(b) From the **Hydroxyketone.**—The pure hydroxyketone (0.18 g., 0.0010 mole), methylated as in the case of 5-indanol, yielded a small amount of nearly colorless methyl ether[40] on evaporation of the dried ether extract of the reaction mixture. This ether was oxidized at 65–70° with a solution containing about 0.01 mole of potassium hypochlorite in general accordance with the method used on methyl 5-indanyl ketone. The odor of chloroform was noticed during the heating period. Pure 6-methoxy-5-indancarboxylic acid (0.064 g., 34% based on hydroxyketone) was obtained, without recrystallization, as a white solid, m.p. 111–113.5°. A mixture m.p. with the sample prepared in (a) showed no depression.

6-Hydroxy-5-indancarboxylic Acid (X). (a) From the Methoxyacid.—To 6.55 g. (0.0341 mole) of methoxyacid in 55 ml. of glacial acetic acid held at 90°, 13 ml. of 48% hydrobromic acid was added over 10 minutes. After refluxing for two hours, water was added to the hot dark red mixture so that the product just remained soluble. Cooling afforded 4.38 g. of hydroxyacid, m.p. 189.5–192° dec., plus 0.78 g., m.p. 183–189°, on further dilution of the mother liquor; total yield 85%. Two recrystallizations of the latter fraction from benzene produced the pure acid, m.p. 189.5–191.5° dec., unchanged by further recrystallization from acetic acid.

Three other demethylations as above but using 0.3, 3.0 and 36 g. of starting material gave yields of 75, 85 and 72%, respectively. The purest fraction melted at 192–193.5° (196.5–197.5°[30]).

In our laboratories carbonation of the sodium salt of 5-indanol was attempted many times,[41] using temperatures of 150–200° and pressures of 600–1500 lb./in.[2] with a reaction time of about 12 hours. However, in no case could a pure product be obtained. Several carbonations also were attempted according to the procedure used on *p*-cresol by Cameron, *et al.*[42] Thus, 5-indanol and dry potassium carbonate were heated for 12 hours at 190–200° with carbon dioxide at 900–1000 lb./in.[2], but again repeated crystallization and sublimation of the product failed to produce a pure hydroxyacid.

(b) From **2-Hydroxymethylenecyclopentanone.**—In our hands Prelog's directions[18] produced the hydroxyacid in extremely low yield from 2-hydroxymethylenecyclopentanone and ethyl acetoacetate. By a combination of distillation and sublimation at high vacuum and recrystallization a minute amount of fairly pure acid was obtained as white crystals, m.p. 191–192.5°[30] dec., mixture m.p. with the hydroxyacid obtained in (a) was 192.5–195.5°[30] dec., lit.[18] m.p. 195–196°.

Methyl 6-Methoxy-5-indancarboxylate.—The methoxyacid (1.0 g., 0.0052 mole) was esterified with diazomethane in the usual manner. Crystallization of the product from petroleum ether[28] yielded 0.36 g. of ester, m.p. 59.5–61.5°, plus an additional 0.25 g., m.p. 58.5–61°, from the concentrated mother liquor; total yield 57%. Three more recrystallizations from the same solvent produced the analytical sample, m.p. 60–61°.

Anal. Calcd. for $C_{12}H_{14}O_3$: C, 69.89; H, 6.84. Found: C, 69.91; H, 6.65.

Methyl 6-Hydroxy-5-indancarboxylate (Vc).—The hydroxyacid (1.0 g., 0.0056 mole) was esterified with diazomethane as in other similar cases[8] to yield 0.64 g. of ester, m.p. 38.5–41°. Since 0.12 g. of unchanged hydroxyacid was recovered, the yield of ester was 68%, based on acid consumed. Three crystallizations of the crude ester from cold methanol[43] produced the analytical sample,[29] m.p. 40.5–42°.

Anal. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.30. Found: C, 68.67; H, 6.18.

The hydroxyester also was prepared in 54% yield by Fischer esterification. An impure sample of the hydroxyester was obtained by preferential demethylation of the methoxyester with aluminum chloride in benzene.

6-Hydroxy-7-bromo-5-indancarboxylic Acid.—To 0.67 g. (0.0038 mole) of the hydroxyacid in 15 ml. of acetic acid was added 0.67 g. of bromine in 7 ml. of acetic acid. This solution was allowed to stand (hydrogen bromide evolved) for 1 hour and then poured into 200 ml. of water to yield 0.90 g. (93%) of brominated acid, m.p. 220–224° dec. The analytical sample was obtained as long tan needles, m.p. 226–229° dec., by four recrystallizations (one with charcoal) from aqueous ethanol.

Anal. Calcd. for $C_{10}H_9O_3Br$: C, 46.71; H, 3.53; Br, 31.09; neut. equiv., 257. Found: C, 46.85; H, 3.52; Br, 31.10; neut. equiv., 262, 257.

The yields in two other similar preparations were 85 and 91%. A bromination permitted to stand overnight produced an 89% yield of product, m.p. 235–236°, from 26 g. of hydroxyacid.

4-Bromo-5-indanol.—A solution of 31.0 g. (0.121 mole) of bromohydroxyacid in 256 ml. of freshly distilled quinoline was heated under nitrogen for 3.5 hours in a bath at 170–180°. At the end of this time the exit gases contained negligible carbon dioxide. The cooled reaction mixture was diluted with ether and benzene, quinoline removed by repeated extraction with dilute hydrochloric acid, and unchanged carboxylic acid (less than 1 g.) removed by extrac-

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(40) This compound has not been reported in the literature, but its small quantity precluded purification and analysis.

(41) The sodium salt of 5-indanol carbonized on drying in an oven unless it was prepared by treating the phenol with sodium methoxide in methanol.

(42) D. Cameron, H. Jeskey and O. Baine, *J. Org. Chem.*, **15**, 233 (1950).

(43) Hot methanol appeared disadvantageous.

tion with 5% sodium bicarbonate. The product was removed by repeated extraction with 5% sodium hydroxide, acidification of which produced 22.8 g. (88.4%) of bromoindanol, m.p. 67.2–69.1°. The analytical sample, m.p. 73–74.5°, was prepared by two recrystallizations from aqueous methanol.

Anal. Calcd. for C_9H_9OBr: Br, 37.50. Found: Br, 36.96.

4-Bromo-5-methoxyindan.—Over 40 minutes a solution of 22.8 g. (0.107 mole) of 4-bromo-5-indanol and 32.1 g. (0.255 mole) of dimethyl sulfate in 50 ml. of acetone was added dropwise with stirring to 23 g. (0.58 mole) of sodium hydroxide dissolved in a minimum of water. After addition of 70 ml. of water the mixture was heated for 1 hour, poured into 500 ml. of water, extracted with ether, and the latter dried and distilled, leaving a greenish oil which crystallized on standing. Recrystallization (Norit) from petroleum ether[28] gave 15.1 g. (62.1%) of methyl ether, m.p. 64.0–66.5°. Two additional recrystallizations produced the analytical sample as white flakes, m.p. 65.8–66.3°.

Anal. Calcd. for $C_{10}H_{11}OBr$: C, 52.88; H, 4.88. Found: C, 53.32; H, 4.84.

5-Methoxy-4-indancarboxaldehyde (IX).—The general procedure of Smith and Nichols[44] was followed. Thus, a Grignard reagent was prepared under nitrogen from 1.83 g. (0.0753 g. atom) of magnesium and 14.7 g. (0.0648 mole) of the methoxybromide, 4 drops of ethyl bromide being used to start the reaction. To the Grignard was added 11.7 g. (0.0791 mole) of ethyl orthoformate[45] in 12.5 ml. of dry ether, and the mixture was refluxed 5 hours. The ether was distilled off without any violent reaction. The acetal was hydrolyzed by adding ice and dilute hydrochloric acid and refluxing 0.5 hour. Ether was added and the organic layer separated and shaken mechanically for 2 days with a saturated sodium bisulfite solution until no more adduct formed. The oil obtained on heating the adduct with 10% sodium carbonate solution was extracted into ether and the dried extract distilled to leave the crude aldehyde as a brown solid. Recrystallization (charcoal) from petroleum ether[28] afforded 4.8 g. (42%) of aldehyde, m.p. 65.2–67.4°. Two more recrystallizations gave the analytical sample as white needles, m.p. 68.3–69.1°; a mixture m.p. with 6-methoxy-5-indancarboxaldehyde showed a large depression.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.86. Found: C, 75.10; H, 6.62.

5-Hydroxy-4-indancarboxaldehyde (VIa).—Demethylation was accomplished according to the procedure described below for preparing 6-hydroxy-3,4-xylaldehyde, the heating in hydrobromic and acetic acids being discontinued as soon as charring started (usually after 15–20 minutes). A total of nine runs was made; the average yield of hydroxyaldehyde melting over about a 2° range near 80° was 16%, and 59% of unchanged starting material was recovered. Two recrystallizations (one with Norit) from petroleum ether[28] and one from ligroin afforded light yellow needles,[29] m.p. 83.8–84.5°.

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.04; H, 6.22. Found: C, 73.88; H, 6.29.

Methyl 5-hydroxy-4-indanyl ketone (VIb), prepared according to Baker,[7] was recrystallized twice from aqueous alcohol and twice from hexane. Two sublimations at 60–70° and 0.3 mm. then produced a pale yellow solid,[29] m.p. 123.8–125.3°,[30] lit.[7] m.p. 124.5°.

5-Hydroxy-4-indancarboxylic Acid.—Using Pearl's procedure[46] 0.61 g. (0.0038 mole) of 5-hydroxy-4-indancarboxaldehyde was oxidized by heating with silver oxide at 55–60°. After acidification, the organic products were extracted into ether and the latter extracted with 5% sodium bicarbonate. Acidification yielded the crude hydroxyacid, which was not purified further. This acid gave a deep blue color with ferric chloride. By evaporation of the above ether solution of the non-acidic product unchanged aldehyde was recovered. Three runs were performed, using recovered aldehyde as starting material for the last two. The heating period was 12–60 minutes. The over-all yield of crude acid, which decomposed without melting in the 160–180° range, was 0.21 g. (31%). In each run about 50% of aldehyde was recovered unchanged.

Methyl 5-Hydroxy-4-indancarboxylate (VIc).—The acid (0.211 g., 0.00119 mole) was esterified with the theoretical amount of a standardized ethereal solution of diazomethane. The bicarbonate-soluble portion of the product was retreated with diazomethane and the combined sodium hydroxide-soluble products recrystallized three times (once with charcoal) from ligroin (b.p. 60–90°) to yield 0.037 g. (16%) of methyl ester as pale yellow, oily, needle-like crystals,[29] m.p. 45.5–48°, which gave a green color with ferric chloride. The small quantity of product prevented further purification.

Anal. Calcd. for $C_{11}H_{12}O_3$: C, 68.73; H, 6.30. Found: C, 70.56; H, 8.39.

o-Xylene Series

Eastman Kodak White Label **3,4-xylenol**, m.p. 65.2–65.8°,[30] was used[29] without purification.

3,4-Xylaldehyde (XIa).—4-Bromo-*o*-xylene[47] was converted *via* the Grignard reagent to 3,4-xylic acid[48] and the latter with thionyl chloride to the acid chloride.[49] The acid chloride (5.8 g., 0.034 mole) was reduced by the Rosenmund method,[37] 0.7 g. of 5% palladium–barium sulfate being used with 2 drops of "poison" in 24 ml. of purified, dry decahydronaphthalene. Evolution of hydrogen chloride began at 183° and virtually ceased 5 hours later at 233°, the bath temperature having been raised gradually until 91% of the theoretical amount of hydrogen chloride was evolved. From the bisulfite adduct, prepared by shaking for 14 hours, 3.0 g. (65%[50]) of aldehyde, b.p. 83–84° (4 mm.), was obtained after two distillations.[33] A middle cut, b.p. 97° (10 mm.), was taken[29] from a third distillation[33]; lit.[50] b.p. 101° (11 mm.).

3,4-Dimethylacetophenone (XIb).—In general accord with literature directions[51] a Grignard reagent (prepared from methyl bromide and 11.7 g. of magnesium) was treated with 76.0 g. (0.415 mole) of anhydrous cadmium chloride and then 13.5 g. (0.0799 mole) of the acid chloride of 3,4-xylic acid. Distillation of the crude product afforded 6.4 g. (54%) of 3,4-dimethylacetophenone, b.p. 129.5–130.5° (28 mm.). A middle cut, b.p. 93.5–94° (2 mm.), was taken[29] from a second distillation; lit.[52] b.p. 132° (19 mm.).

Methyl Ester of 3,4-Xylic Acid (XIc).—The acid (5.9 g., 0.039 mole) was esterified with diazomethane. Distillation of the crude product afforded 3.2 g. (50%) of ester, b.p. 140–145° (74 mm.). Two more distillations yielded the analytical sample,[29,53] b.p. 132° (38 mm.).

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 72.65, 72.34; H, 7.26, 7.27.

Hemellitaldehyde (XIIa).—Hemellitonitrile was prepared *via* the Sandmeyer reaction. Thus, Brunner's procedure[54] was modified to fit the general procedure of Clarke and Read,[55] and the alkali cyanide–cuprous cyanide solution was prepared according to Vogel.[56] From 100 g. (0.633 mole) of 2,3-xylidine hydrochloride (Eastman Kodak Practical) was obtained 29.5 g. (35.6%) of nitrile as a very pale yellow oil, b.p. 118–122.5° (34 mm.), n^{25}_{D} 1.5330. From

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(44) L. I. Smith and J. Nichols, *J. Org. Chem.*, **6**, 489 (1941).

(45) Eastman Kodak White Label orthoformate was fractionated in a Todd Column and the fraction, b.p. 145.4–146°, used.

(46) I. A. Pearl, *Org. Syntheses*, **30**, 101 (1950).

(47) W. A. Wisansky and S. Ansbacher, *ibid.*, **28**, 22 (1948).

(48) H. A. Smith and R. B. Hurley, THIS JOURNAL, **72**, 112 (1950).

(49) G. T. Morgan and E. A. Coulson, *J. Chem. Soc.*, 2323 (1931).

(50) S. Sugasawa and N. Sugimoto [*J. Pharm. Soc. Japan*, **61**, 62 (1941); *C. A.*, **36**, 92 (1942)] list a 33% yield from the Rosenmund reduction; *cf.* ref. 37b, p. 373.

(51) H. Gilman and J. F. Nelson, *Rec. trav. chim.*, **55**, 518 (1936); J. Cason, *Chem. Revs.*, **40**, 15 (1947); M. S. Newman and T. J. O'Leary, THIS JOURNAL, **68**, 258 (1946); J. Cason and F. S. Prout, *ibid.*, **66**, 46 (1944).

(52) S. F. Birch, R. A. Dean, F. A. Fidler and R. A. Lowry [THIS JOURNAL, **71**, 1362 (1949)] prepared this ketone by heating 3,4-xylic and acetic acids over thoria.

(53) Although Smith and Hurley (ref. 48) studied the rate of esterification of this acid with methanol, they gave no physical constants for the ester.

(54) O. Brunner, H. Hofer and R. Stein, *Monatsh.*, **63**, 79 (1933).

(55) H. T. Clarke and R. R. Read, "Organic Syntheses," Coll. Vol. I, Second Edition, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 514.

(56) A. I. Vogel, "A Textbook of Practical Organic Chemistry," Second Edition, Longmans, Green and Co., London, 1951, p. 188.

28.7 g. (0.219 mole) of nitrile was obtained 23.9 g. (72.6%) of hemellitic acid, m.p. 141.5–144°, by Brunner's procedure[54] except that 2 instead of 30 hours of heating was used. The acid chloride (8.0 g., 0.047 mole), prepared by use of thionyl chloride, was reduced by the Rosenmund method,[37] 1.0 g. of 5% palladium–barium sulfate being used with 2 drops of "poison" in 33 ml. of decahydronaphthalene. Most of the reduction occurred in 2 hours at 170–200° (bath temperature), but the reaction was allowed to proceed for an additional hour (bath at 200–235°), the hydrogen chloride evolved being 60% of the theoretical amount.[57] From the bisulfite adduct, prepared by shaking for 22 hours, 2.4 ml. of aldehyde, b.p. 69–85° (11 mm.), was obtained. Redistillation afforded 2.3 g. (37%) of pure aldehyde,[29] b.p. 86–88° (10 mm.),[58] which was characterized through the **oxime**, m.p. 92–94.5° (lit.[54] m.p. 80–82°), and the **semicarbazone**, m.p. 221–223° (lit.[54] m.p. 222°).

2,3-Dimethylacetophenone (XIIb).—The procedure used above to prepare the 3,4-isomer was applied to 7.2 g. (0.043 mole) of hemellitoyl chloride. After the first distillation 4.8 g. (75%) of ketone, b.p. 92–93.5° (6 mm.), was obtained. Two more distillations produced the analytical sample,[29] b.p. 93.5° (6 mm.), lit.[59] b.p. 108° (13 mm.).

Methyl Hemellitate (XIIc).—Esterification of 5.0 g. (0.033 mole) of the acid with diazomethane produced 3.5 g. (65%) of ester, b.p. 104–105° (12 mm.). The middle cut from a second distillation was used as the analytical sample.[29,53]

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.22; H, 7.24.

6-Methoxy-3,4-xylaldehyde.—Using the procedure described above for methylating 5-indanol, 3,4-xylenol was converted in 81% yield to the methyl ether, b.p. 122.5–125° (87 mm.). The latter (37.7 g., 0.277 mole) was converted to the methoxyaldehyde with N-methylformanilide as described above. The crude product was recrystallized twice from ligroin to yield 23.8 g. (53.3%) of pure aldehyde as pale yellow crystals, m.p. 66–67°, lit.[60] m.p. 66°.

6-Hydroxy-3,4-xylaldehyde (XIIIa).—To 10.0 g. (0.0610 mole) of methoxyaldehyde in 75 ml. of refluxing acetic acid 20 ml. of 48% hydrobromic acid was added dropwise over 22 minutes. Refluxing was continued for another 50 minutes, when carbonization started. The crude product, isolated as before, was recrystallized (Norit) from petroleum ether[28] to yield 1.71 g. (18.7%) of hydroxyaldehyde, m.p. 68.5–70.5°, wet m.p. 65.3–67.3°, wet m.p. depression 3°.[20] Two more recrystallizations (one with Norit) afforded light brown crystals,[29] m.p. 69.7–70.0°; lit. m.p.'s, 71°,[19,61] 70°.[62]

A single attempt to demethylate the methoxyaldehyde by heating with aluminum chloride in benzene resulted in a product which formed no adduct on shaking 26 hours with sodium bisulfite solution.

2-Hydroxy-4,5-dimethylacetophenone (XIIIb).—3,4-Xylyl acetate, b.p. 132.5–133°, was converted[63] in 23% yield to the hydroxyketone, m.p. 66–68°. Recrystallization from aqueous methanol left white flakes,[29] m.p. 70.9–71.7°,[30] wet m.p. 65.3–68.3°,[30] wet m.p. depression 4.5°, lit.[63] m.p. 71°.

6-Hydroxy-3,4-xylic Acid (XV).—(a) Carbonation[64] of 3,4-xylenol produced an average yield in the first five runs of only 34% of acid melting between the extremes of 193 and 201°. However, when thoroughly dry xylenol and potassium carbonate were used, the average yield from eight runs was 89%; m.p. between 204–215°. The twice recrystallized acid, m.p. 208–212° (lit.[65] m.p. 199°) exhibited the correct neutral equivalent (calcd. 166, found 168).

(b) Oxidation[46] of 0.50 g. (0.0033 mole) of 6 hydroxy-3,4-xylaldehyde produced 0.31 g. (56%) of acid, which was identical (mixture m.p.) with the acid from (a). Since the structure of the hydroxyaldehyde is known, this constitutes a proof of structure for the methoxyaldehyde and compounds made from it.

Methyl Ester of 6-Hydroxy-3,4-xylic Acid (XIIIc).—The hydroxyacid (3.0 g., 0.018 mole) was treated with diazomethane until there was no appreciable delay[66] in evolution of nitrogen. The crude ester was fractionally crystallized twice from petroleum ether[28] to yield 1.1 g. (34%) of pure ester,[29] m.p. 34.5–35.5°, lit.[67] m.p. 33°.

6-Hydroxyhemellitaldehyde (XIVa).—Application of the Reimer–Tiemann reaction to 3,4-xylenol according to Clayton's directions[19] afforded a mixture of plates and needles which was separated mechanically. Recrystallization of the latter from petroleum ether[28] finally afforded a very small yield of pure 6-hydroxyhemellitaldehyde as pale yellow needles, m.p. 70.0–71.4°, lit.[19] m.p. 72°, mixture m.p. with authentic 6-hydroxy-3,4-xylaldehyde (m.p. 69.7–70°) was 49–68°, wet m.p. 67.5–69.5°, wet m.p. depression 2°. Unlike Clayton,[19] we were unable to obtain pure 6-hydroxy-3,4-xylaldehyde by recrystallization of the plates mentioned above.

5-Bromo-6-hydroxy-3,4-xylic Acid.—To a solution of 73.3 g. (0.442 mole) of hydroxyacid in 1830 ml. of acetic acid was added 79.0 g. of bromine in 860 ml. of acetic acid. The mixture was stirred alternately for 68 hr., after which time no more hydrogen bromide was evolved. The mixture was poured into 10 times its volume of dilute sodium chloride solution. Filtration produced 99.5 g. (92.1%) of bromoacid, m.p. 217–218°. Crystallization from benzene and from aqueous alcohol did not alter the m.p. A mixture m.p. with the starting material showed a very large depression.

Anal. Calcd. for $C_9H_9O_3Br$: Br, 32.60; neut. equiv., 245. Found: Br, 32.36; neut. equiv., 245, 243.

Three other preparations similar to the above produced yields of 89–95%.

2-Bromo-3,4-xylenol.—A solution of 21.5 g. (0.0878 mole) of bromohydroxyacid in 220 ml. of freshly distilled quinoline was refluxed (stirring) overnight in a nitrogen atmosphere. After adding 125 ml. each of ether and benzene to the cooled solution the alkali-soluble material was extracted by shaking repeatedly with small portions of 5% sodium hydroxide. The acidified alkaline solution was extracted with ether and unchanged hydroxyacid (0.3 g., 1.4%) taken into 5% sodium bicarbonate solution. Distillation of the dried ether extract then afforded 16.9 g. (95.5%) of 2-bromo-3,4-xylenol, b.p. 126–129° (26 mm.), n^{23}D 1.5732. Two similar preparations gave yields of 81.0 and 78.0%, but lower yields were obtained (in 5 runs) when the quinoline was removed with acid before isolation of the product. The analytical sample was obtained from a product, b.p. 95–98° (9 mm.), by redistilling twice, a center cut being taken each time.

Anal. Calcd. for C_8H_9OBr: Br, 39.74. Found: Br, 39.58.

2-Bromo-3,4-dimethylanisole.—(a) A solution of 68.7 g. (0.342 mole) of 2-bromo-3,4-xylenol and 96.8 g. (0.768 mole) of dimethyl sulfate in 150 ml. of acetone was added dropwise and with vigorous stirring to 68 g. (1.7 moles) of sodium hydroxide dissolved in a minimum of water. The addition, regulated to permit vigorous refluxing, required 65 minutes, and spontaneous ebullition continued for another 50 minutes. On adding 60 ml. of water, refluxing (applied heat) for another 0.5 hour, and working up the product as before there was obtained 64.4 g. (87.6%) of bromoether as a water-white liquid, b.p. 138–141° (18 mm.), n^{27}D 1.5640, which gave no color with ferric chloride and which partly solidified on standing. Also obtained were two lower-boiling unidentified, non-phenolic fractions: b.p. 41–46° (22 mm.), n^{27}D 1.4412, b.p. 48–56° (18 mm.), n^{27}D 1.4537.

(b) A solution of 10.0 g. of the phenol and 14.2 g. of dimethyl sulfate in 50 ml. of acetone was added dropwise over 25 minutes and with vigorous stirring to 10.0 g. of sodium hydroxide in 8 ml. of water. An ice-bath was used at the start, but the temperature was allowed to rise after 10

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(57) Brunner, Hofer and Stein (ref. 54) required a reaction time of 30 hours in refluxing xylene.

(58) Brunner, Hofer and Stein (ref. 54) gave no physical constants for this aldehyde.

(59) Birch, *et al.* (ref. 52), prepared this ketone by passage of 2,3-xylic and acetic acids over thoria.

(60) E. Späth, M. Pailer and G. Gergely [*Ber.*, **73B**, 795 (1940)] prepared this compound by methylation of the hydroxyaldehyde.

(61) A. Zinke, G. Zigeuner, G. Weiss and W. Leupold-Löwenthal, *Monatsh.*, **81**, 1098 (1950).

(62) L. Gattermann, *Ann.*, **357**, 313 (1907).

(63) K. v. Auwers, H. Bundesmann and F. Wieners, *ibid.*, **447**, 162 (1926).

(64) F. Wessely, K. Benedikt, H. Benger, G. Friedrich and F. Prillinger, *Monatsh.*, **81**, 1071 (1950).

(65) O. Jacobsen, *Ber.*, **12**, 434 (1879).

(66) Since this was rather difficult to determine, considerable acid was not esterified.

(67) L. Birkofer, *Z. physiol. Chem.*, **261**, 87 (1939).

minutes. The mixture was stirred for 2 hours, refluxed for 0.5 hour, and allowed to stand overnight. Another preparation was performed similarly with 22.6 g. of phenol and the crude product from the combined ether extracts of the two reaction mixtures was fractionated. The first fraction consisted of 10.5 g. of crude, halogen-free product, b.p. 85-94.5° (20 mm.), identified by its refractive index (n^{25}_D 1.5140) as 3,4-dimethylanisole. The main fraction consisted of 20.1 g. (56.6%) of 2-bromo-3,4-dimethylanisole, b.p. 133-140° (17 mm.), n^{25}_D 1.5620. A portion of this was redistilled twice to obtain the analytical sample, b.p. 125-128° (25 mm.).

Anal. Calcd. for $C_9H_{11}OBr$: Br, 37.10. Found: Br, 36.77.

6-Methoxyhemellitic Acid.[68]—(a) A Grignard reagent was prepared under nitrogen from 2.19 g. (0.0901 g. atom) of magnesium and 17.7 g. (0.0824 mole) of the methoxybromide, a little ethyl bromide serving as initiator. After treatment at −5 to −10° for 1.5 hours with dry carbon dioxide, the reaction mixture was acidified, extracted with ether, and the ether shaken with 5% sodium bicarbonate solution. Acidification yielded 5.92 g. (40%) of crude product, m.p. 127-155°. This material was heated with ligroin (b.p. 60-90°) and 2.9 g. (20%) of insoluble acid, m.p. 157-165°, removed and recrystallized three times from benzene-ligroin to produce the pure 6-methoxyhemellitic acid, m.p. 162.0-163.0°.[30]

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71; neut. equiv., 180. Found: C, 66.59; H, 6.82; neut. equiv., 181, 184.

From the ligroin-soluble material was obtained 0.95 g. of acid, m.p. 125-166° (neut. equiv. 183), plus a small amount of unidentified, halogen-free acid, m.p. 120-127°.

(b) The procedure used in (a) was repeated on 64.6 g. of methoxybromide, iodine being used as "initiator." The final carbonated ether solution was cooled in an ice-bath and treated dropwise with 100 ml. of dilute sulfuric acid, the temperature rising until the ether boiled. However, after 20 minutes of addition a sudden, violent reaction set in and only gradually subsided. Another 100 ml. of acid was added, the organic layer was drawn off, and the aqueous layer was extracted with ether. The combined ether solutions were extracted with 5% sodium bicarbonate and the latter acidified to yield 4.29 g. (7.94%) of solid, m.p. 147-158°. Fractionation as before gave 2.51 g. (4.65%) of pure methoxyacid, m.p. 161.7-163.1°,[30] which was identical (mixture m.p.) with that from (a). An additional 1.85 g. of product, m.p. 137-153°, was obtained by ether extraction of the acidified bicarbonate solution.

6-Hydroxy-2,3-dimethylacetophenone (XIVb).—Refluxing of 2.50 g. (0.0139 mole) of the methoxyacid and 9.5 ml. of purified thionyl chloride produced 1.96 g. (71.0%) of **acid chloride** as a water-white liquid, b.p. 119-119.5° (7 mm.), which soon solidified to a white solid[69] that gave a strong Beilstein test for halogen.

Following the earlier-mentioned general procedure,[51] 5.94 g. (0.0325 mole) of dry cadmium chloride was added in small portions to a solution of methylmagnesium bromide prepared under nitrogen from 1.60 g. (0.0658 g. atom) of magnesium. After replacing the ether with 50 ml. of dry benzene, 1.96 g. (0.00986 mole) of the above acid chloride in 15 ml. of benzene was added dropwise so that little rise in temperature occurred. After being stirred 15 minutes at room temperature the mixture was refluxed (frothing) for 2 hours. At no time was the mixture excessively pasty or difficult to stir. An ether extract of the acidified reaction mixture was washed with aqueous sodium hydroxide, dried, and evaporated to yield the presumed **methoxyketone** as a light brown oil. Although this was not purified further, a presumably pure sample was recovered from the demethylation (*cf.* below).

A mixture of the unpurified methoxyketone and 4 g. of anhydrous aluminum chloride in 15 ml. of dry, thiophene-free benzene was heated (gas evolved) over 45 minutes to reflux temperature and then held there for 0.5 hour. The cooled mixture was decomposed in the usual manner, extracted with ether, and the latter extracted with 5% sodium hydroxide. The alkaline extract was acidified, extracted with ether, and the latter dried and distilled to yield 0.48 g. (30%, based on acid chloride) of **hydroxyketone**, b.p. about 126°[70] (4.5 mm.), as a viscous oil which soon solidified to a yellowish solid, m.p. 63-69°, having a phenolic odor. Two recrystallizations from petroleum ether[28] gave long, nearly transparent, white needles,[29] m.p. 73.8-75°, which produced a green color in alcohol with ferric chloride; wet m.p. 54-59°, wet m.p. depression 18°; a mixture with authentic 2-hydroxy-4,5-dimethylacetophenone (m.p. 71.5-72.5°) fused completely below 45°.

Anal. Calcd. for $C_{10}H_{12}O_2$: C, 73.14; H, 7.37. Found: C, 73.54, 73.15, 73.25; H, 7.31, 7.27, 7.18.

The above benzene-ether solution (containing the neutral reaction products) was dried and distilled to yield 0.41 g. (23%, based on acid chloride) of water-white oil, b.p. about 108°[70] (4 mm.), which solidified only in the freezing compartment of a refrigerator. Presumably this material was fairly pure **6-methoxy-2,3-dimethylacetophenone.** It gave a weak green color with ferric chloride, presumably because of incomplete removal of the hydroxyketone.

Methyl 6-Methoxyhemellitate.—The methoxyacid was esterified with diazomethane and the crude product crystallized from petroleum ether[28] to yield 1.55 g. (90.1%) of ester, m.p. 61-66°. Three additional recrystallizations afforded the analytical sample, m.p. 62.0-64.5°.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.91; H, 7.39.

Methyl 6-Hydroxyhemellitate (XIVc).—A mixture of 1.0 g. (0.0051 mole) of methoxyester, 4.5 g. of aluminum chloride and 50 ml. of dry benzene was placed in a bath preheated to 50°. The bath temperature was raised slowly, and then the mixture was refluxed for 15 minutes, very little methyl chloride being evolved below 68°. Working up as before produced, after distillation, 0.20 g. (22%) of somewhat impure hydroxyester, b.p. about 101°[70] (3 mm.), n^{28}_D 1.5400, which gave a dark blue color with ferric chloride.

Anal. Calcd. for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 68,17; H, 7.19.

Infrared Work.—The apparatus and procedures used were generally similar to those described previously.[15] However, during the course of the work the model 12B Perkin-Elmer spectrometer was converted to double-pass operation, model 112. The infrared data on most of the xylenes and the 5-hydroxyindans were obtained with the latter arrangement. The frequencies of the C=O absorption bands were observed at room temperature in 0.02 molal solutions in redistilled Baker and Adamson Reagent grade carbon tetrachloride. Sample cells from 0.2 to 1.6 mm. in thickness were employed.

The frequencies of the C=O absorption bands were measured with respect to the internal reference provided by the 6 μ atmospheric water vapor absorption. The sharpness of the absorption bands was the main factor limiting the accuracy of the C=O frequency determinations. In most cases the probable error is ±1 cm.$^{-1}$ and no more than ±2 cm.$^{-1}$.

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[68] In general, the directions of H. Gilman and R. H. Kirby [*Org. Syntheses*, Coll. Vol. I, Second Edition, John Wiley and Sons, Inc., New York, N. Y., 1941, p. 361] were followed.

[69] This product sintered at 52-54° and partly melted at 63-90° while some semi-solid collected on the walls of the capillary. The latter material finally melted at 135-140°, indicating that some hydrolysis may have occurred in the open capillary tube during the m.p. determination.

[70] The small quantity prevented an accurate b.p. determination.