[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

# The Haloform Reaction. XIV. An Improved Iodoform Test

BY REYNOLD C. FUSON AND CHARLES W. TULLOCK

The iodoform test of Lieben[1] is one of our most useful tools in the identification of alcohols and ketones which are soluble in water. For water-insoluble compounds, however, this test is uncertain and likely to be misleading. In the hope of making the test more generally applicable we have tried a number of organic solvents, such as pyridine and dioxane, which are water-soluble and, at the same time, have a high solvent power with respect to organic compounds. Dioxane has proved to be very satisfactory, and by its use we have developed an iodoform test which appears to be more reliable and more general than that now in use.

**Procedure.**—Four drops (or 0.1 cc.) of the liquid (0.1 g. of the solid) to be tested are placed in a test-tube (150 mm. wide). Five cubic centimeters of dioxane is added, and the mixture thoroughly shaken. One cubic centimeter of 10% sodium hydroxide solution is introduced, and then iodine–potassium iodide solution[2] is added, with shaking; the addition of iodine is continued until a *slight excess* yields a *definite dark color* of iodine which does not disappear upon standing, with slight shaking now and then, for five minutes.[3]

The test-tube is now placed in a water-bath maintained at a temperature of 60°.[4] If the slight excess of iodine already present is decolorized, the addition of iodine solution is continued (the dioxane solution being maintained at a temperature of 60°), with shaking, until a slight excess of iodine solution again yields a definite dark color. The addition of iodine is continued until a dark color is not discharged by shaking; but warming at 60° should not last over two minutes. This excess of iodine is removed by the addition of a few drops of 10% sodium hydroxide solution and shaking. The test-tube is now filled with water and allowed to stand for fifteen minutes. It is advisable to collect the iodoform on a filter and determine its melting point which should be 119–121°. If the iodoform does not have a lemon-yellow color,[5] it is removed by filtration and suspended in 2–3 cc. of dioxane; 1 cc. of 10% sodium hydroxide solution is then added and the mixture is shaken until only a light lemon color remains. The mixture is diluted with water and filtered.

(1) Lieben, *Ann.*, Suppl. binding, **7**, 218 (1870).

(2) The iodine–potassium iodide solution is made by adding 200 g. of the iodide and 100 g. of iodine to 800 cc. of distilled water and stirring until solution is complete.

(3) The iodine–potassium iodide solution must be added until a slight excess yields a dark color because a few compounds give a yellow color on treatment with hypoiodite. If dilution with water takes place here, no iodoform is obtained.

(4) In the case of methyl ketones heating is usually not necessary; alcohols react more slowly.

## Results

The foregoing procedure has been tried with a large number of compounds with results as indicated below. In a majority of these cases, the behavior toward hypoiodite has not been previously reported.[6]

### Alcohols

**Positive.**—(1) Isopropyl alcohol, (2) methyl-*n*-amylcarbinol, (3) octanol-2, (4) methylisopropylcarbinol, (5) 2,3-butanediol, (6) methylbenzylcarbinol.

**Negative.**—(7) Methyl alcohol, (8) allyl alcohol, (9) trimethylene glycol, (10) mannitol, (11) isobutyl alcohol.

### Aliphatic Ketones

**Positive.**—(12) Acetone, (13) methyl ethyl ketone, (14) methyl propyl ketone, (15) hexanone-2, (16) methyl isobutyl ketone, (17) heptanone-2, (18) octanone-2, (19) methyl isohexyl ketone, (20) 4-methylheptanone-2, (21) methyl cyclohexyl ketone, (22) methyl γ-phenoxypropyl ketone, (23) benzyl acetone, (24) benzohydrylacetone, (25) pinacolone.*[7]

### Mixed Ketones

**Positive.**—(26) Acetophenone, (27) methyl *p*-tolyl ketone, (28) *p*-chloroacetophenone, (29) *p*-bromoacetophenone, (30) methyl *p*-anisyl ketone, (31) 2,4-dimethoxyacetophenone, (32) 2-methyl-4-methoxyacetophenone, (33) 5-methyl-2-methoxyacetophenone, (34) acetocymene, (35) 2,4,5-trimethylacetophenone, (36) *o*-hydroxyacetophenone, (37) *m*-hydroxyacetophenone, (38) *p*-hydroxyacetophenone, (39) 3-methoxy-4-hydroxyacetophenone, (40) *o*-nitroacetophenone, (41) *m*-nitroacetophenone, (42) *p*-nitroacetophenone, (43) *o*-aminoacetophenone, (44) *m*-aminoacetophenone, (45) *p*-aminoacetophenone, (46) 2-aceto-1-naphthoxyacetic acid, (47) 2-aceto-4-bromo-1-naphthoxyacetic acid.

(5) The red color which the precipitate sometimes has is probably due to the formation of carbon tetraiodide.

(6) In all cases the iodoform was obtained in amounts which preclude the possibility that its formation might be due to traces of impurities, and has been identified by a melting point determination.

(7) Compounds marked with an asterisk give iodoform but require a longer period of heating than that specified in the procedure given

**Negative.**—(48) α-Chloroacetophenone, (49) propiophenone, (50) acetomesitylene, (51) 3,5-dinitroacetomesitylene, (52) 2,4,6-tribromoacetophenone, (53) 3-amino-2,4,6-tribromoacetophenone, (54) 1-aceto-2-naphthoxyacetic acid, (55) 2-methoxy-1-acetonaphthone.

#### Unsaturated Ketones

**Positive.**—(56) Mesityl oxide, (57) benzalacetone, (58) 2-methyl-1-phenyl-1-buten-3-one, (59) furfuralacetone.

#### Diketones

**Positive.**—(60) Acetylacetone, (61) acetonylacetone, (62) benzoylacetone,[8] (63) *p*-bromobenzoylacetone, (64) dibenzoylmethane, (65) 1,3-diketohydrindene, (66) 2,6-dimethyl-4-acetylacetophenone.

**Negative.**—(67) ω-Acetylacetomesitylene, (68) ω-benzoylacetomesitylene, (69) di-(β-isoduryloyl)-methane.

#### Acids and Acid Derivatives

**Positive.**—(70) Ethyl lactate, (71) α-aminoisobutyric acid, (72) levulinic acid, (73) ethyl levulinate, (74) γ-acetylbutyric acid, (75) diethyl acetylsuccinate, (76) diethyl α,α′-diacetylsuccinate.

**Negative.**—(77) Alanine,* (78) *s*-butyl acetate,* (79) *s*-amyl acetate,* (80) diethyl phthalate,* (81) diethyl adipate.*

#### Miscellaneous

**Positive.**—(82) Acetoxime, (83) diacetyl monoxime, (84) α-phenylethylamine.

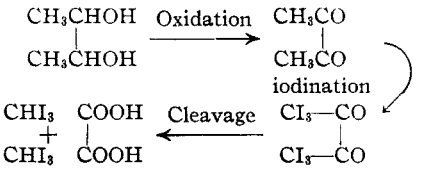
**Negative.**—(85) Pentene-2, (86) 2-methylbutene-2, (87) 1,1-diphenylpropene-1, (88) 1-chloro-2,3-dihydroxypropane, (89) propionitrile, (90) isoeugenol, (91) phenylacetylene, (92) rhamnose, (93) acetophenone oxime,* (94) anethole, (95) resorcinol, (96) phloroglucinol.

### Generalization

The foregoing results may be summarized in the following rule. *The test is positive for compounds which contain the grouping $CH_3CO$—, $CH_2ICO$— or $CHI_2CO$—*[9] *when joined to a hydrogen atom or to a carbon atom which does not carry highly activated hydrogen atoms or groups which provide an excessive amount of steric hindrance. The test will, of course, be positive also for any compound which reacts with the reagent to give a derivative containing one of the requisite groupings. Conversely, compounds which contain one of the requisite groupings will give a negative test in case this grouping is destroyed by the hydrolytic action of the reagent before iodination is complete.*

### Discussion of Results

A theoretical basis for the foregoing generalization is to be found in the fact that the reagent produces three fundamentally different types of effects. It is capable of oxidizing alcohols and amines, of replacing active hydrogen atoms by iodine atoms, and of cleaving certain types of carbon chains. For example, these three types of processes undoubtedly take place in the order mentioned when 2,3-butanediol is converted to iodoform




It is especially important to note that the iodination will occur, not necessarily on an active methyl group, but rather at the point in the molecule where the most active hydrogen atoms are found. Thus β-diketones having the grouping —$COCH_2CO$— are iodinated first at the methylene group. Apparently in these cases chain cleavage then occurs. The soundness of this explanation is attested by the fact that dibenzoylmethane and 1,3-diketohydrindene give a positive test; here the iodoform obviously derives from the methylene group, and diiodomethyl ketones—compounds containing one of the requisite groupings—must be postulated as intermediates. Similarly, although compounds 62 and 63, like acetylacetone, contain an acetyl group, the iodoform comes rather from the methylene group. This conclusion is, in turn, supported by the fact that ω-acetylacetomesitylene ($CH_3COCH_2CO$-$C_9H_{11}$) gives a negative test, which is to be expected since diiodoacetomesitylene, on account of the hindrance involved, would not yield iodoform.[10]

Numerous compounds which do not contain one of the requisite groupings give a positive test presumably because under the influence of the reagent they give rise to products which do contain such groupings. Many alcohols (1, 2, 3, 4, 5, 6) are oxidized to the corresponding carbonyl compounds and so lead to the formation of iodoform. Amines of similar structures (72, 78, 84) apparently undergo analogous transformations. In the case of certain esters (78, 79, 80, 81) and oximes (82, 93) the iodoform must be traced to hydrolysis products.

The iodoform reaction is greatly retarded by

(8) In this and similar cases, as well as with certain nitro and amino compounds, a deep color appears during the addition. This must not be mistaken for the iodine color which appears subsequently on further addition of iodine.

(9) Compounds containing the $CI_3CO$- group would undoubtedly give a positive test also, but as yet no such compound is known in a pure state.

(10) See Woodward and Fuson, THIS JOURNAL, **55**, 3472 (1933).

steric hindrance. The test is negative for all compounds which contain one of the requisite groupings joined to an aryl radical carrying two ortho substituents. As a matter of fact, the reaction is slow, even with pinacolone. The question as to what is actually formed in the case of hindered methyl ketones is under investigation. In no case is the compound recovered unchanged.


## Summary

By the use of dioxane as solvent an iodoform test has been developed which can be used with water-insoluble compounds as well as with those which are soluble in water.

On the basis of results with a large number of compounds a new rule has been formulated concerning the generality of the test.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# NOTES

## Pecan Shells as a Source of *d*-Xylose

BY CLIFFORD J. B. THOR AND C. L. SMITH

It has already been pointed out[1] that the alcohol-insoluble residue from samples of pecan shells yielded more than 20% of its dry weight of reducing sugar when subjected to the official method for determining "starch" by direct acid hydrolysis.[2] More recently we have succeeded in isolating crystalline *d*-xylose from such sirups with yields of 11.2 to 12.8% of the untreated air-dry shells.

Our procedure was to sift with cheesecloth and extract with either hot or cold water, hydrolyzing the extracted shell material with about four times its weight of normal sulfuric acid for periods of six to eight hours. The isolation of xylose from the sirups follows essentially the customary methods, with crystallization from ethyl alcohol. The mother liquors gave strong xylose reactions and also yielded some saccharic acid, indicating the presence of glucose, but the amount probably was not great since baker's yeast produced no visible fermentation at a sugar concentration of about 10%. Tests for the other commonly occurring monosaccharides were negative.

A decided advantage of pecan shells as compared with corn cobs or cottonseed hulls is their relative compactness (bulk density about 0.5) and the fact that they can be easily and quickly washed after acid hydrolysis.

BUREAU OF PLANT INDUSTRY
U. S. PECAN RESEARCH LABORATORY
AUSTIN, TEXAS
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(1) C. J. B. Thor and C. L. Smith, to appear in *J. Agr. Research.*

(2) "Association of Official Agricultural Chemists, Official and Tentative Methods of Analysis," 2d ed., revised to July 1, 1924 (1925), p. 119 (21).

## Some Strychnine Benzoates

BY CHARLES F. POE AND JOHN F. SUCHY

During the course of a series of toxicological and pharmacological experiments, it became necessary to prepare a number of strychnine salts. These were made by the union of strychnine with benzoic acid and the various substituted benzoic acids. Of the salts described in this paper, the benzoate and the salicylate are the only ones mentioned in the literature.

The purest chemicals obtainable were used. Many of these were recrystallized several times, and the melting points were checked in each case. Molecular quantities of strychnine and the various benzoic acids were separately dissolved in alcohol with the aid of heat. After solution the alkaloid and acid were mixed and boiled for about ten minutes. The salt usually crystallized out upon cooling. A number of the benzoic acids, especially those containing two halogen or nitro groups, were rather insoluble in alcohol. In these cases chloroform was used to dissolve the acid, and after mixture with the alcoholic solution of strychnine, the combined solution was allowed to boil until most of the chloroform had volatilized. Each salt was recrystallized until pure. The strychnine content of the salts was determined by the method given in the U. S. Pharmacopoeia,[1] and in cases where the acid radical was not too insoluble, the picrate method of Elmore[2] was also used. The nitrogen was determined by the official Kjeldahl method[3] to include nitrogen of nitrates. The melting points were determined by the usual capillary tube method in conjunction with the Thiele apparatus. Check determinations were made by the "bloc Maquenne" method. With the Thiele apparatus the melting points were very unsatisfactory. Decomposition took place in many cases and no sharp melting point could be obtained. It is well known that the melting point of strychnine varies under different conditions and it is impossible to get a

(1) U. S. Pharmacopoeia, Tenth Revision, 1926.

(2) Elmore, *J. Assoc. Off. Agr. Chem.*, **9**, 224 (1926).

(3) "Official and Tentative Methods of Analysis," Assoc. Official Agric. Chem., 1930, 3d edition, p. 21.