organic acids composed only of carbon, hydrogen and oxygen, while casein which reversed this selectivity is amphoteric and a protein.

In conclusion, I wish to express my grateful thanks to Professor Grinnell Jones of Harvard University. As his private assistant, space and equipment were afforded me for the carrying out of this work. Also, I am indebted to him for many helpful suggestions and criticisms.

Summary

Diaphragms have been described which exhibited a selective osmotic action with respect to the various ions or molecules present in the solution.

When either *sodium alginate* or *soap* was used in constructing the diaphragm, the selective action favored potassium and retarded sodium ions, or their corresponding salt molecules. The alginate diaphragms also favored bromide at the expense of chloride ions and to a much smaller extent favored sulfate over chloride ions and calcium over magnesium and sodium ions.

When *casein* was used as the diaphragm material, the selective action was *reversed* with respect to sodium and potassium compounds, *i. e.*, sodium was favored and potassium retarded. Calcium also appeared to be greatly retarded.

All materials which were found to exhibit a selective osmotic action were *colloidal* in their behavior and properties.

It has been suggested that this phenomenon may be explained as being due to *adsorption* of the various ions or molecules at the surface of the diaphragm.

RECEIVED JULY 15, 1933

[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORY OF THE UNITED COLLEGE OF ST. SALVATOR AND ST. LEONARD, UNIVERSITY OF ST. ANDREWS]

The Constitution of Inulin. Synthesis of 3,4,6- and 1,4,6-Trimethyl-γ-fructose

BY T. N. MONTGOMERY

It is well known that inulin on methylation and subsequent hydrolysis yields 3,4,6-trimethylfructose, together with a small amount of tetramethyl-γ-fructose.[1] In view of the liquid nature of the products, and of the fact that no satisfactory evidence is available that the trimethyl sugar consists solely of 3,4,6-trimethylfructose, it is not only desirable to confirm by synthesis the structure of this key substance to the constitution of inulin, but of even greater importance to establish in this way the homogeneity of the trimethylfructose obtained from the polysaccharide.

In a recent communication from this Laboratory[1d] proof was given that the sirupy trimethylfructose is a single chemical individual. This rested on the fact that (a) when the sugar was treated with acetone containing hydrogen chloride and specimens of the product isolated at various stages as the reaction proceeded, and (b) when the monoacetone derivative of the sugar thereby produced was subjected to graded hydrolysis, no evidence of separation of the trimethylfructose into different fractions could be detected. Different specimens of trimethylfructose monoacetone isolated in this way, however, showed considerable variation in specific rotation, but this was attributed to α- and β-isomerism. Further work has been devoted to the subject, and it is now possible to confirm by positive results the homogeneity of the trimethyl sugar, and to establish beyond doubt the isomerism of the monoacetone derivative, by a synthesis of 3,4,6-trimethylfructose. The outline of the scheme of synthesis is as follows

Fructose ⟶ β-diacetonefructose ⟶ 1-benzoyl-β-diacetone-fructose ⟶ 1-benzoylfructose ⟶ 1-benzoyl-γ-methylfructoside ⟶ 1-benzoyl-3,4,6-trimethyl-γ-methylfructoside ⟶ 3,4,6-trimethyl-γ-methylfructoside ⟶ 3,4,6-trimethylfructose.

Despite the fact that 3,4,6-trimethylfructose is a liquid and difficult to purify, the synthetic sugar shows good agreement in properties with that derived from methylated inulin. Both yield the same crystalline phenylosazone, and the similarity in the polarimetric curves of the reaction of condensation of the sugar with acetone (A and B, Fig. 1), and of the hydrolysis of the resulting product (D, Fig. 1) leave little doubt as to the identity of the two sugars.

(1) (a) Irvine and Steele, *J. Chem. Soc.*, 1474 (1920); (b) Haworth and Learner, *ibid.*, 619 (1928); (c) Haworth, Hirst and Percival, *ibid.*, 2384 (1932); (d) Irvine and Montgomery, THIS JOURNAL, **55**, 1988 (1933).

The remote possibility still remained that 1,4,6-trimethylfructose, which should also be capable of yielding a monoacetone derivative, is present along with 3,4,6-trimethylfructose in the hydrolysis product of methylated inulin, and that it escapes detection on account of being closely similar in properties to the latter sugar. The synthesis of 1,4,6-trimethylfructose from α-diacetonefructose by a method similar to that used in the synthesis of the 3,4,6-compound showed, however, that this could not be the case.

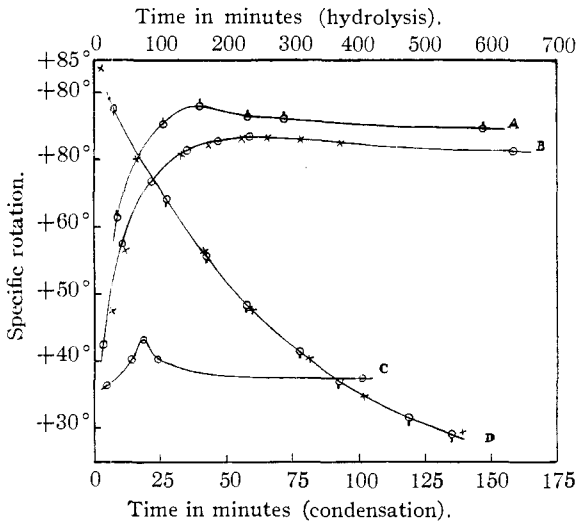

Fig. 1.—Condensation of trimethylfructose with acetone: *A*, ♁ 3,4,6-trimethylfructose; *B*, ⊙ trimethylfructose from methylated inulin; × trimethylfructose regenerated from monoacetone derivative with $[\alpha]_D$ +31.9°; *C*, ⊙ 1,4,6-trimethylfructose. Hydrolysis of trimethylfructose monoacetone: *D*, ♀ monoacetone derivative of 3,4,6-trimethylfructose; × monoacetone derivative of trimethylfructose from methylated inulin.

The new sugar shows a specific rotation different from that of the 3,4,6-isomer, exhibits upward mutarotation in chloroform solution, in contrast to the downward mutarotation of the latter, and gives a distinct polarimetric curve (C, Fig. 1) on treatment with acetone. Moreover, the monoacetone derivatives of the two sugars prepared under the same conditions differ widely in specific rotation.

	3,4,6-Trimethylfructose	Trimethylfructose derived from inulin	1,4,6-trimethylfructose
n_D	1.4658	1.4664	1.4637
$[\alpha]_D$ in chloroform (final value)	+20.4°	+21.4°	+29.7°
$[\alpha]_D$ of monoacetone deriv., in acetone	+70.3°	+74.0°	+17.8°

The fact that methylated inulin on hydrolysis yields only one trimethylfructose, namely, the 3,4,6-derivative, can therefore be taken as proved.

The variation in properties of the monoacetone derivative of 3,4,6-trimethylfructose according to the conditions of preparation is interesting. Specimens isolated at various intermediate stages as the reaction proceeds range in specific rotation from +80 to +58°, and when hydrolysis of the compound is arrested when about 80% complete the recovered unhydrolyzed monoacetone compound shows a specific rotation +32°. The trimethylfructose regenerated from each specimen, however, is identical with the initial sugar, and condenses with acetone to give the same characteristic polarimetric curve (B, Fig. 1).

From these results, and others quoted in the experimental part, it is clear that the condensation product of 3,4,6-trimethylfructose with acetone is not a single substance, but consists of a mixture of isomers. The explanation would appear to lie in the fact that the configuration of the fructose molecule is such that derivatives in which the No. 1 and No. 2 hydroxyl groups are unsubstituted can theoretically form two isopropylidene compounds related to α- and β-fructose.

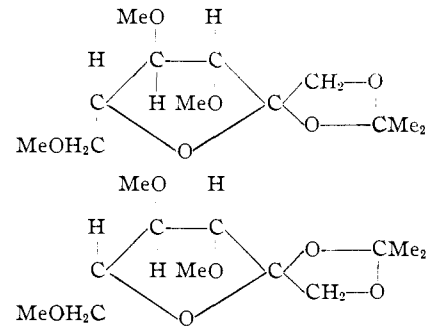

Fig. 2.—Isomeric forms of 3,4,6-trimethylfructose monoacetone.

By analogy with the α- and β-glycosides, isomers of this type would be expected to differ in rates of formation and hydrolysis.

Experimental

Note.—The terms acid methyl alcohol and acid acetone are used throughout to denote methyl alcohol containing 1% and acetone containing 0.5% of dissolved hydrogen chloride.

Preparation of α- and β-Diacetonefructose.—Fructose (100 g.) was shaken for three hours with acetone (1800 cc.) containing in the case of the α-compound 0.2% hydrogen chloride, and in the case of the β-derivative 72 cc. of concentrated sulfuric acid. After neutralization of the solu-

tion with concentrated ammonium hydroxide, most of the acetone was distilled off, and an aqueous solution of the residue extracted thrice with chloroform. The product obtained was recrystallized from a mixture of petroleum ether and ether: yield of α-diacetonefructose: variable, average 25.0 g.; m. p. 118–119°; yield of β-diacetonefructose: 64.0 g.; m. p. 96°.

Synthesis of 3,4,6-Trimethylfructose

Preparation of 1-Benzoyl-β-diacetonefructose.— β-Diacetonefructose (50 g.) on treatment with benzoyl chloride and pyridine at room temperature yielded 1-benzoyl-β-diacetonefructose (44.7 g.); m. p. 82°.

Hydrolysis of 1-Benzoyl-β-diacetonefructose to 1-Benzoylfructose.—1 - Benzoyl - β - diacetonefructose (106 g.) was boiled under reflux for sixty-five minutes with 50% ethyl alcohol (1970 cc.) containing 2% of oxalic acid. After the addition of 1310 cc. of 2% aqueous oxalic acid, reflux was continued for a further seven hours. The solution was then neutralized with calcium carbonate, taken to dryness under reduced pressure, and the glassy residue dried for twelve hours *in vacuo* at 40°.

Treatment of 1-Benzoylfructose with Acid Methyl Alcohol, and Methylation of the Product.—A solution of the crude 1-benzoylfructose (104 g.) in acid methyl alcohol (990 cc.) was allowed to stand for three hours at room temperature, in order to bring about partial conversion of 1-benzoylfructose to the corresponding γ-methylfructoside.

Time in minutes	8	110	170
$[\alpha]_D$ of solution	−27.9°	−23.1°	−22.2°

After neutralization of the solution with lead carbonate, filtration, and concentration to smaller bulk, ether was added, resulting in the precipitation of part of the unchanged 1-benzoylfructose as a viscous sirup (37.1 g.). The clear solution was decanted and most of the solvent distilled off, a certain amount being left in order that the material should be soluble in methyl iodide. Methylation with methyl iodide and silver oxide then followed; yield, 47.4 g.

Debenzoylation and Hydrolysis.—The methylated material (47.4 g.), containing 1-benzoyl-3,4,6-trimethyl-γ-methylfructoside, was boiled for twenty-five minutes with 0.25 *N* aqueous-alcoholic sodium hydroxide, the solution diluted, and extracted with chloroform. The impure 3,4,6-trimethyl-γ-methylfructoside obtained (20.9 g.) was hydrolyzed for thirty minutes with boiling 0.01 *N* hydrochloric acid to eliminate the γ-fructosidic methyl group, the solution neutralized, and extracted with chloroform to remove impurites. As trimethylfructose was to some extent extracted, the chloroform solution was washed with water and the aqueous washings extracted with chloroform. This procedure was adopted throughout the work to separate trimethylfructose from the corresponding methylfructoside or monoacetone derivative. In addition, these derivatives were in every case distilled. From the bulked aqueous solutions 3,4,6-trimethylfructose (13.1 g.) was obtained in an impure state.

3,4,6-Trimethylfructose.—Purification of the synthetic trimethyl sugar was accomplished as follows. (a) The compound was converted to the corresponding methylfructoside by treatment for two and one-quarter hours at room temperature with acid methyl alcohol, and the product fractionally extracted from aqueous solution with chloroform as described above, impurities more soluble in water remaining in the aqueous solution. Thereafter the fructoside was distilled, and the trimethyl sugar regenerated from it by hydrolysis with 0.01 *N* hydrochloric acid. Fractional extraction of the neutralized solution with chloroform then removed impurities more readily extractable than trimethylfructose.

Method (b) consisted in converting the sugar to the monoacetone derivative in a similar manner, by treatment with acid acetone. In the subsequent hydrolysis 0.02 *N* hydrochloric acid was used.

The crude 3,4,6-trimethylfructose (13.1 g.) after treatment once by methods (a) and (b) yielded 8.21 g. of purified product.

Anal. Calcd. for $C_9H_{18}O_6$: OCH_3, 41.9. Found: OCH_3, 40.5. n_D 1.4665; $[\alpha]_D$ in chloroform +18.9° (final value), for c = 2.93. Two further stages of purification by method (a) gave a product (A) showing: n_D 1.4658; $[\alpha]_D$ +20.4° for c = 2.88. Trimethylfructose (B) derived from methylated inulin showed: $[\alpha]_D$ in chloroform +21.4° (final value) for c = 3.48.

The phenylosazone when crystallized from aqueous alcohol melted at 81–82°, and showed no depression of melting point when mixed with the phenylosazone of trimethylfructose (B).

Condensation of 3,4,6-Trimethylfructose with Acetone.—Below are tabulated the changes in the specific rotation of the solution observed when trimethylfructose (A) was treated at room temperature with acid acetone. The corresponding figures for sugar (B) are given for comparison.

Trimethylfructose (A)		Trimethylfructose (B)	
Time in minutes	$[\alpha]_D$	Time in minutes	$[\alpha]_D$
9	+61.3°	11	+57.6°
26	+75.3°	22	+66.9°
40	+78.1°	35	+71.5°
58	+76.7°	47	+72.9°
72	+76.2°	59	+73.6°
147	+74.8°	158	+71.5°

After two and one-half hours the product was isolated by pouring the solution into excess aqueous potassium bicarbonate and extracting with chloroform. From 5.30 g. of initial sugar there was obtained on distillation 5.44 g. of mobile sirup, b. p. 110° (0.2 mm.) (bath temperature).

Anal. Calcd. for $C_{12}H_{22}O_6$: OCH_3, 35.5. Found: OCH_3, 33.7. n_D 1.4450; $[\alpha]_D$ in acetone +70.3° for c = 3.03. The monoacetone derivative of trimethylfructose (B), isolated under approximately similar conditions, showed: n_D = 1.4483; $[\alpha]_D$ +74.0° in acetone for c = 3.22.

Interrupted Condensation with Acetone.—When the condensation was arrested at various stages and the products isolated, specimens of trimethylfructose monoacetone showing the constants tabulated below were obtained:

$[\alpha]_D$ of soln. when product isolated	Trimethylfructose monoacetone Yield, %	n_D	$[\alpha]_D$ in acetone
+54.0°	35	1.4468	+80.7°
+80.6°	83	1.4482	+76.2°
+72.4°	86	1.4492	+65.5°
+63.4°	84	1.4507	+57.7°

Equilibrium is reached when approximately 85% of the sugar has reacted, but the recovered uncondensed sugar is identical with the initial substance.

Graded Hydrolysis of 3,4,6-Trimethylfructose Monoacetone.—A solution of 0.2 *N* hydrochloric acid (73.5 cc.) containing 5.20 g. of trimethylfructose monoacetone and 3.7 cc. of acetone was maintained at 30°, and a polarimetric record of the reaction kept by withdrawing a small amount of the solution at intervals, cooling it to room temperature, and determining the specific rotation.

Monoacetone derivative of sugar (A)		Monoacetone derivative of sugar (B)	
Time in minutes	$[\alpha]_D$	Time in minutes	$[\alpha]_D$
30	+77.8°	10	+83.7°
110	+64.2°	65	+70.2°
170	+55.8°	91	+66.0°
230	+48.4°	168	+56.3°
310	+41.3°	238	+47.8°
370	+37.0°	323	+40.4°
475	+31.5°	407	+34.9°
540	+29.0°	558	+29.3°

The reaction was arrested before completion by pouring the acetone solution into excess bicarbonate solution, and unhydrolyzed monoacetone derivative separated by fractional extraction with chloroform. Owing to the large proportion of trimethylfructose present, a sharp separation was not achieved in this case, and even after distillation the recovered trimethylfructose monoacetone contained 10–15% of trimethylfructose. This may be removed by boiling the material for fifteen minutes with 0.2 *N* sodium hydroxide, and extracting the solution with chloroform.

		Unhydrolyzed trimethylfructose monoacetone			Regenerated trimethylfructose		
	% hydrolysis	n_D	$[\alpha]_D$ in acetone	OCH_3 %	n_D	$[\alpha]_D$ in chloroform	OCH_3 %
(A)	77.3	1.4495	+31.9°	34.9	1.4665	+19.5°	40.5
(B)	78.0	1.4518	+36.7°	35.0	1.4662	+21.2°	40.3

The regenerated trimethylfructose condensed again with acid acetone giving the same characteristic polarimetric curve as the initial sugar. The figures below refer to the trimethyl sugar regenerated from the monoacetone derivative with $[\alpha]_D$ +31.9°.

Time, min.	7	12	22	33	43
$[\alpha]_D$ of soln.	+47.5°	+56.5°	+67.3°	+71.0°	+72.1°
Time, min.	56	66	78	93	500
$[\alpha]_D$ of soln.	+73.2°	+73.5°	+73.0°	+72.7°	+67.5°

When a specimen of the recovered unhydrolyzed trimethylfructose monoacetone (1.459 g.) with $[\alpha]_D$ +48.7° was treated with acid acetone, the specific rotation of the solution altered smoothly in three and one-half hours from +48.4 to +59.9°, and the product (1.385 g.) showed $[\alpha]_D$ +58.1° in acetone.

Anal. Calcd. for $C_{12}H_{22}O_6$: OCH_3, 35.5. Found: OCH_3, 34.0.

Synthesis of 1,4,6-Trimethylfructose.—The method employed was essentially that used in the synthesis of 3,4,6-trimethylfructose, the starting material being in this case α-diacetonefructose, and the nitrate group being used instead of the benzoyl group as a substituent. On account of the low yield of final product, the accuracy of the constants quoted for the sugar cannot be claimed to be above question, but the results show clearly the marked difference in properties between 1,4,6- and 3,4,6-trimethylfructose and their monoacetone derivatives. In connection with the low yield it might be mentioned that unpublished work in this Laboratory has shown that in the glucose series a nitrate group substituting the 3-hydroxyl is labile. It is not improbable, therefore, that in the present case partial elimination of the nitrate group during the hydrolysis of 1,2-monoacetonefructose-3-nitrate, during the treatment with acid methyl alcohol, or the subsequent methylation is responsible for the low yield.

Preparation of α-Diacetonefructose-3-nitrate.—Sixty grams of α-diacetone fructose was dissolved in ice-cold chloroform (300 cc.), and an ice-cold chloroform solution (200 cc.) containing 30.0 g. of nitrogen pentoxide was added. After standing for five minutes the solution was poured onto chipped ice, the chloroform solution washed with dilute bicarbonate solution, and dried. On removing the solvent under reduced pressure, α-diacetonefructose-3-nitrate was obtained as a crystalline solid. This melts at 61–62° when pure. However, on account of the fact that the corresponding monoacetonefructose-3-nitrate is more easily purified, the crude product was generally converted directly to this compound. Acknowledgment is due to Mr. T. B. Clark, B.Sc., of this Laboratory, who first prepared both these compounds.

1,2-Monoacetonefructose-3-nitrate.—The crude α-diacetonefructose-3-nitrate was boiled under reflux for nine and one-half hours with 400 cc. of acetone solution containing 20% of 0.1 *N* hydrochloric acid, the solution neutralized with barium carbonate, filtered, and the acetone distilled off. The 1,2-monoacetonefructose-3-nitrate which came out of solution on cooling was filtered off and recrystallized from water; yield, 47.4 g.; m. p. 151–152°.

The remainder of the synthesis was exactly parallel to that of 3,4,6-trimethylfructose, the nitrate group being eliminated by reduction with sodium amalgam.

Forty grams of 1,2-monoacetonefructose-3-nitrate was hydrolyzed to fructose-3-nitrate by boiling for four hours with 2% aqueous oxalic acid (400 cc.). The crude product (32.6 g.) was treated in the cold with acid methyl alcohol, the specific rotation of the solution changing from −54.8 to −42.5° in one and a half hours. On methylation of the total product there was obtained 24.5 g. of mobile sirup, consisting partly of 1,4,6-trimethyl-γ-methylfructoside-3-nitrate. This was treated in 50% alcohol solution with sodium amalgam until the solution failed to give a positive test for nitrate with diphenylamine, and the product (10 g.), isolated by extraction of the filtered solution with chloroform, was boiled for thirty minutes with 0.01 *N* hydrochloric acid to convert the 1,4,6-trimethyl-γ-methylfructoside to 1,4,6-trimethylfructose. After fractional extraction with chloroform the aqueous solution yielded a moderately mobile sirup (4.10 g.) showing n_D 1.4638; $[\alpha]_D$ in chloroform +18.1° (final value) for c = 2.32.

1,4,6-Trimethylfructose.—The purification of the crude sugar was carried out exactly according to the details of methods (a) and (b) above. (a) 4.10 g. gave finally 2.17 g. of product.

Anal. Calcd. for $C_9H_{18}O_6$: OCH_3, 41.9. Found: OCH_3, 40.0.

(b) An acid acetone solution (72 cc.) containing 1.927 g. of the product from treatment (a) showed the following changes in specific rotation.

Time, min.	5	14	19	24	30	101
$[\alpha]_D$	+36.4°	+40.2°	+43.1°	+40.2°	+39.3°	+37.4°

The 1,4,6-trimethylfructose monoacetone isolated distilled at 100° (0.2 mm.) (bath temperature).

Anal. Calcd. for $C_{12}H_{22}O_6$: OCH_3, 35.5. Found: OCH_3, 34.4. n_D 1.4464; $[\alpha]_D$ in acetone +17.8° for c = 1.85.

The purified specimen of 1,4,6-trimethylfructose (0.790 g.) recovered by the hydrolysis of 1.319 g. of the monoacetone derivative showed: n_D 1.4639; $[\alpha]_D$ in chloroform +29.7° (final value) for c = 2.13.

The author wishes to express his thanks to Principal Sir James C. Irvine, LL.B., F.R.S., for his help and advice, and to acknowledge his indebtedness to the Carnegie Trust for the Universities of Scotland for the award of a Research Fellowship.

Summary

1. Positive and unquestionable evidence has been obtained proving that inulin on methylation and subsequent hydrolysis yields only one trimethylfructose.

2. Two interesting closely related isomeric trimethyl sugars, 3,4,6- and 1,4,6-trimethyl-γ-fructose, have been synthesized.

3. The capability of 3,4,6-trimethylfructose monoacetone of existing in isomeric forms has been demonstrated.

ST. ANDREWS, SCOTLAND RECEIVED JULY 17, 1933

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 99]

The Reactivity of Atoms and Groups in Organic Compounds. XIII. The Influence of Structure on the Pyrolysis of Esters of Triphenylacetic Acid[1]

BY JAMES F. NORRIS AND ARTHUR CRESSWELL

It has been shown in this Laboratory that when the members of a series of homologous compounds are heated under fixed conditions the temperatures at which the several compounds first show signs of decomposition at a particular bond vary with the nature of the radicals present.[2]

When ethers of the type $(C_6H_5)_3C-OR$ were heated[2a] the temperatures at which the bond between the triphenylmethyl radical and the oxygen atom broke indicated the relative labilizing influence toward heat of different alkyl radicals on a carbon–oxygen linkage transmitted through an oxygen atom to which the radical was joined.

In order to gain additional information in regard to the influence of radicals on activating bonds toward heat the temperatures at which the alkyl esters of triphenylacetic acid begin to decompose were studied. In the case of these compounds, $(C_6H_5)_3C-COO-R$, the products of pyrolysis, except with the methyl and benzyl esters, are almost exclusively triphenylmethane, carbon dioxide, and an olefin.[3] In the pyrolysis of these esters the bonds indicated by lines in the above formula are broken.

In determining the cracking temperatures of the ethers the compounds were heated at the rate of one degree per minute in the presence of air. In the study of the esters, reported here, different conditions were used to determine whether the order of activating influence was affected by the conditions. The esters were heated in tubes sealed to a small U-shaped mercury manometer and evacuated to about 3 mm. pressure. The tubes were held at a constant temperature for one hour and any change in pressure noted. The temperature at which the first observable increase in pressure (0.1 mm.) occurred after heating for one hour was taken as the cracking temperature.

In order to determine the effect of pressure on the cracking temperature, the normal butyl and the isopropyl esters were heated at constant temperatures in the presence of air at atmospheric pressure and the temperature of cracking determined by the measurement of a bead of mercury in a tube attached to the apparatus in the way

(1) From a part of the thesis of Arthur Cresswell presented in partial fulfilment of the requirements for the degree of Doctor of Philosophy, 1932.

(2) (a) Norris and Young, THIS JOURNAL, **52**, 753 (1930); (b) *ibid.*, **52**, 5066 (1930); (c) Norris and Thomson, *ibid.*, **53**, 3108 (1931); (d) Norris and Tucker, *ibid.*, **55**, 4697 (1933).

(3) Schmidlin and Hodson, *Ber.*, **41**, 438 (1908), have shown that ethyl triphenylacetate yields, when heated, triphenylmethane, carbon dioxide and ethylene.