Malic acid (by fractionation of esters)	0.056%
Malic acid (by polarization)	.064%
Citric acid (by fractionation of esters)	.016%
Citric acid (by pentabromoacetone)	.019%
Oxalic acid	Trace
Oxalic acid in residue, dry basis	0.11%
Oxalic acid in residue, fresh basis	.02%

Aconitic acid has been identified previously in two species of the *Gramineae* (sugar cane and sorghum).

Malonic acid has not been found in any of the investigations on the organic acids of fruits, but was reported present in alfalfa by Turner and Hartman.[8]

Summary

In this investigation of the organic acids in growing wheat plants the water extract was found to contain aconitic, citric, malic and malonic acids with a trace of oxalic acid. The residue after water extraction was found to contain oxalic acid.

WASHINGTON, D. C.

THE RELATION OF THE STRUCTURE OF KETONES TO THEIR REACTIVITY AND AFFINITY IN ACETAL FORMATION. II

BY GEORGE J. PFEIFFER AND HOMER ADKINS

The reaction of orthoformic ester and ketones to form acetals and ethyl formate (Equation I) is a reversible reaction suited to the study of the relationship of the structure of compounds to the strength of oxygen to carbon linkages.

$$R_2CO + HC(OC_2H_5)_3 \longleftrightarrow R_2C(OC_2H_5)_2 + HCO_2C_2H_5 \qquad (I)$$
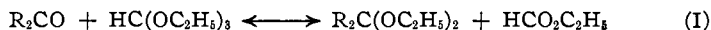
Recently the extent of acetal formation for eight ketones was reported.[1] In extending the study of this reaction it became apparent that the previous evaluation of the analytical data was in error in the case of one ketone, so the method of analysis was subjected to a more thorough study.

The analytical method used by Carswell for the determination of the extent of the acetal reaction was based upon the observation of Geuther that ethyl formate in the presence of sodium ethoxide decomposed into carbon monoxide and alcohol. Geuther formulated the reaction as in Equation II.
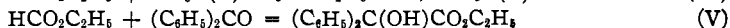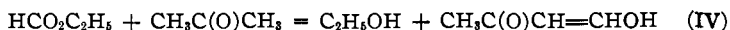
$$HCO_2C_2H_5 = CO + C_2H_5OH \qquad (II)$$

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[8] Turner and Hartman, THIS JOURNAL, **47**, 2044 (1925).

[1] Carswell and Adkins, *ibid.*, **50**, 235 (1928).

Geuther did not obtain the theoretical yield of carbon monoxide but accounted for the discrepancy by the assumption that the reaction is reversible. This assumption was based upon the finding that ethanol inhibited the decomposition of the ester. In order to avoid this effect of ethanol upon the decomposition, Carswell carried out the decomposition in the presence of metallic sodium, thus perhaps changing the course of the reaction. Under these conditions he found that the amount of carbon monoxide was 64.4 $\pm$ 1.5% of that required by Geuther's equation. More recently in a series of eight consecutive decompositions of ethyl formate the amount of carbon monoxide was found to be 66.1, 66.4, 65.7, 69.4, 63.6, 66.1, 66.6, 62.7, or an average of 65.8% of the amount required by Geuther's equation. That is to say, three moles of ethyl formate gave two moles of carbon monoxide. Moreover, methanol was shown by Trillat's test to be in the residue from the decomposition.[2] Mr. Ralph Dunbar in this Laboratory has recently obtained a mixture of alcohols consisting of 9.5% methanol and 90.5% ethanol as a result of the hydrolysis of the residue from the decomposition of ethyl formate with sodium and an excess of sodium ethoxide. The decomposition of ethyl formate under these conditions may then be formulated as in Equation III. The mechanism will be discussed in a later paper.

$$3HCO_2C_2H_5 + 4Na = 2CO + CH_3ONa + 3C_2H_5ONa \qquad (III)$$
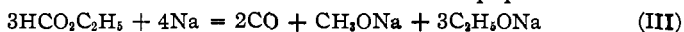
The ratio of carbon monoxide to ethyl formate was found to be independent of the amount of orthoformic ester or of ketone acetal which may be present in the mixture subjected to analysis. However, the ratio of carbon monoxide to ethyl formate was dependent upon the amount of ethanol and the amount and kind of ketone present in the mixture subjected to analysis. Since the ethanol present before the decomposition of the ethyl formate and formed during the decomposition would be in the form of sodium ethoxide, it may perhaps be better to state that the amount of ethyl formate converted to carbon monoxide was a function of the amount of sodium ethoxide and of the amount and kind of ketone in the reaction mixture. Sodium ethoxide no doubt decreased the amount of ethyl formate converted to carbon monoxide because it facilitated the reaction of ethyl formate with the ketone. These reactions are of at least two types as indicated in Equations IV and V. Reaction IV is the Claisen reaction, while reaction V is, so far as the authors are aware, a hitherto unknown reaction which will be described in detail in a later publication.

$$HCO_2C_2H_5 + CH_3C(O)CH_3 = C_2H_5OH + CH_3C(O)CH=CHOH \qquad (IV)$$
$$HCO_2C_2H_5 + (C_6H_5)_2CO = (C_6H_5)_2C(OH)CO_2C_2H_5 \qquad (V)$$

The amount of ethyl formate equivalent to a given volume of carbon monoxide under the conditions of analysis was determined by experi-

[2] Trillat, *Analyst*, **24**, 13, 211 (1899).

ment. Various mixtures containing known amounts of ethyl formate and ethanol, and various kinds and amounts of ketones were therefore subjected to the action of sodium and sodium ethoxide and the amount of carbon monoxide so formed was measured. The sum of the amounts of ester and of ketone in a mixture submitted to analysis was always 0.1 of a mole since that ratio would exist in the reaction mixtures which were to be analyzed. These prepared mixtures were made up to a volume of 50 ml. with dry toluene. A 5-ml. aliquot was taken from each and treated with 0.5 g. of sodium ethoxide and an excess of sodium, and subjected to decomposition at 110 to 115°. There are given in Table I the data obtained in a group of such analyses.

TABLE I

CARBON MONOXIDE (IN MOLES $\times 10^3$) FROM ETHYL FORMATE IN THE PRESENCE OF VARIOUS AMOUNTS OF ETHANOL AND KETONES

‎Ketones		Ester,	Ethanol, ml.			
Name	Moles	moles	8	16	24	32
Dimethyl	0.02	0.08	19.40	19.30	18.30	17.80
	.005	.095	46.70	44.50	42.40	41.60
Methyl ethyl	.09	.01	1.50	1.24	1.17	0.95
	.07	.03	3.30	3.34	3.00	2.90
	.05	.05	4.84	4.28	4.35	4.27
	.03	.07	8.75	8.65	7.60	7.38
	.01	.09	41.50	39.70	38.00	35.00
	.005	.095	47.30	47.00	44.00	41.00
Methyl β-phenyl ethyl	.03	.07	8.15	8.15	7.15	6.55
	.01	.09	41.30	40.30	37.50	36.60
Methyl phenyl	.09	.01	1.59	1.46	1.13	0.53
	.07	.03	3.12	2.70	2.13	1.46
	.05	.05	6.76	5.61	4.67	3.06
	.03	.07	12.70	8.48	6.31	5.30
	.02	.08	26.00	23.10	19.10	14.50
	.01	.09	43.50	39.00	36.30	32.00
Methyl neopentyl	.03	.07	14.30	10.40	9.75	8.30
	.01	.09	36.00	31.60	28.60	26.80
Di-isopropyl	.05	.05	11.20	11.10	9.70	9.20
	.03	.07	21.00	19.60	17.90	17.50
Methyl tert.-butyl	.09	.01	4.20	4.90	4.07	2.93
	.07	.03	7.80	6.75	6.52	6.06
	.05	.05	8.60	7.73	7.42	6.48
	.03	.07	30.40	25.90	22.10	18.20
	.01	.09	43.50	38.40	38.50	32.70
Ethyl tert.-butyl	.08	.02	4.95	4.23	3.82	3.44
	.06	.04	12.90	12.40	12.40	10.70
Diphenyl	.08	.02	4.70	3.80	2.70	2.90
	.05	.05	11.60	10.95	9.28	9.28
Isopropyl tert.-butyl	.09	.01	1.95	1.85	1.75	1.19
	.07	.03	8.73	8.10	7.05	6.80

The reaction of the various ketones with orthoformic ester was carried out by mixing 0.1 mole of the ketone and 0.1 mole of orthoformic ester in enough dry ethanol to give a total volume of 49 ml., and then after the mixture was at 25°, adding 1 ml. of an ethanol solution containing 0.0136 g. of hydrogen chloride. After fifty to sixty hours 5-ml. aliquots were removed and decomposed with sodium and sodium ethoxide as previously described. The evolved gas was collected and analyzed and the amount of carbon monoxide calculated. The amounts of carbon monoxide formed from the various reaction mixtures are recorded in Column 3 of Table II. Duplicate syntheses of acetal and duplicate analyses of the reaction mixture were made and the variation in the amount of carbon monoxide found is indicated in the table. The amount of ethyl formate required to produce the amount of carbon monoxide actually obtained in the decomposition of an aliquot from an acetal reaction mixture, in the concentration of ethanol given in Column 2 of Table II, may then be determined from the data given in Table I. In order to facilitate this determination the relationship of ethanol and ethyl formate to the amount of carbon monoxide produced in the presence of the various concentrations of each ketone was plotted and the amount of ethyl formate equivalent to a given amount of carbon monoxide read off directly, usually without extensive interpolation from the experimental values. The amount of ethyl formate so calculated is given in Column 4 of Table II. From this value the percentage conversion of the ketone to the acetal and the equilibrium constant are readily calculated.

TABLE II

EXTENT OF ACETAL FORMATION IN REACTION OF 0.1 MOLE OF ORTHOFORMIC ESTER WITH 0.1 MOLE OF VARIOUS KETONES IN A SOLUTION MADE UP TO 50 ML. WITH ETHANOL

Ketone	Ethanol, ml.	CO, mole	HCOOEt, mole	% Acetal, calcd.	$K_E \times 10^2$
Dimethyl	24.5	0.0426 ≒ 4	0.0948	94.8	3.34
Methyl ethyl	25.3	.0375 ≒ 5	.0901	90.1	0.83
Methyl β-phenylethyl	19.2	.0377 ≒ 10	.0891	89.1 (88.9)	.66
Methyl phenyl	22.0	.0302 ≒ 5	.0862	86.2 (85.1)	.39
Methyl neopentyl	18.0	.0257 ≒ 7	.0840	84.0	.28
Di-isopropyl	19.5	.0173 ≒ 3	.0654	65.4	.034
Methyl tert.-butyl	17.5	.0081 ≒ 2	.0501	50.1 (52.9)	.0101
Ethyl tert.-butyl	20.8	.0106 ≒ 2	.0362	36.2	.0033
Diphenyl	19.0	.0052 ≒ 1	.0337	33.7	.0026
Tert.-butyl isopropyl	18.2	.0067 ≒ 2	.0258	25.8	.0012
Di-tert.-butyl	17.0	.0036 ≒ 2	.0172	17.2	.0004

The equilibrium point in the acetal reaction was also arrived at from the reaction of ethyl formate with an acetal of three of the ketones. One tenth mole each of the acetal and of the ethyl formate was made up to a volume of 49 ml. with dry ethanol and 1 ml. of ethanol containing 0.0136 g.

of hydrogen chloride was added. After the reaction had proceeded for several days, the ethyl formate in an aliquot was decomposed and the amount of carbon monoxide, ethyl formate and percentage conversion to the acetal calculated as in the synthesis of the acetal. The results are given in parentheses in Table II, for the three ketones involved.

An inspection of the values given in Table II for the percentage conversion of various ketones to their acetals makes it clear that any substitution in the methyl groups in acetone results in a lowering of the extent of the reaction. The extent of conversion is decreased only slightly by the substitution of a benzyl group for one of the hydrogens of acetone. The effect of the replacement of a methyl group in acetone by a phenyl group is marked but much less so than might be expected from the differences between methyl and phenyl in most reactions. In contrast with this observation is the fact that two phenyl groups reduce the percentage conversion to acetal to about one-third of the value for acetone. The replacement of a methyl group in acetone by the tertiary butyl group results in a decrease in conversion to the acetal from 94.8 to 50.1%. If the tertiary butyl group is separated from the carbonyl group by one carbon atom it is much less effective in decreasing the extent of the acetal reaction.

The replacement of both methyl groups in acetone by isopropyl groups is also very effective in reducing the percentage conversion to an acetal although not so effective as is one tertiary butyl group. This is further evident from a comparison of the symmetrical and unsymmetrical tetramethyl acetone as the former shows 65.4% conversion to the acetal while the latter is but 36.2%. A further substitution of methyl groups in acetone results in marked lowerings of the percentage conversion to the acetal. The percentage conversion of the ketone to the acetal decreased by about 30% of the former value each time one of the hydrogens in methyl tertiary butyl ketone was replaced by a methyl group. It should be noted that in the case of acetophenone and pinacolone the extent of conversion to the acetal is considerably higher than that previously reported.

Preparation and Purity of Reagents.—Benzyl acetone was prepared in 96% yield by the hydrogenation of benzal acetone at 65° under a pressure of 135 atmospheres of hydrogen over a nickel catalyst. Di-isopropyl ketone was obtained in 10 to 11% yield by the decomposition of calcium isobutyrate at 500°. Some of it was also purchased from Poulenc-Frères (Paris). Methyl neopentyl ketone was prepared as previously described.[3] The two tetramethyl, the pentamethyl and the hexamethyl acetones were prepared by the Haller and Bauer[4] method involving the use of sodamide, methyl iodide and the appropriate ketone. Their directions were followed except that in the prepara-

　　　[3] McCubbin and Adkins, THIS JOURNAL, 52, 2547 (1930).
　　　[4] Haller and Bauer, Vog'l Erd. Acad. Sciences, 149, 5 (1909); Chem. Centr., 1910, 1589.

tion of hexamethyl acetone it was found necessary to carry out the methylation at 115° in a sealed tube rather than under a reflux. The acetal of acetophenone was prepared by allowing 60 g. of acetophenone to react for twenty-four hours at 25° with 100 g. of orthoformic ester in the presence of 50 g. of ethanol and 0.0136 g. of hydrogen chloride. The mixture was then made alkaline by the addition of a few drops of an anhydrous ethanol solution of sodium ethoxide and fractionated. The yield was 73% of the theoretical. The other acetals were prepared in a similar manner. The other reagents used were prepared or purified by the standard methods. The reagents had the physical constants noted in Table III.

<div align="center">

TABLE III

PHYSICAL CONSTANTS OF REAGENTS

</div>

Name of compound	Boiling point, °C.	d^{25}_{25}
Acetone	56.2–56.7	0.7973
Acetophenone	200–202 (m. p. 20°)	1.029
Benzophenone	156–158 (15 mm.) (m. p. 48°)	....
Benzyl acetone	130–133	1.0079
Di-isopropyl ketone	123–126	0.8021
Methyl ethyl ketone	79–81	.8065
Methyl neopentyl ketone	123–126	.8036
Orthoformic ester	144–146	.9278
Pinacolone	104–107	.8067
Ethyl tert.-butyl ketone	123–126	.8017
Tert.-butyl isopropyl ketone	133–134	.8067
Di-tert.-butyl ketone	149–151	.8107
Dimethyl acetal of acetophenone	110–112 (16 mm.)	1.0097
Diethyl acetal of pinacolone	52–55 (30 mm.)	0.8446
Diethyl acetal of benzyl acetone	128–132 (8 mm.)	1.0242
Diethyl acetal methyl neopentyl ketone	55–58 (30 mm.)	0.8297
Ethyl formate	54–54.5	.9250

Summary

The extent of conversion of eleven ketones to their acetals through their reaction with orthoformic ester has been determined. This has necessitated a rather extensive experimental investigation of the extent of reaction of various amounts of ten ketones with ethyl formate in the presence of various amounts of sodium ethoxide.

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