TABLE I

3-Bromo-4-alkyl- and 3-Iodo-4-alkyl-benzoic Acids

Compound	Solvent	M.P.,°	Yield, %	Formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Bromine, % Calcd.	Bromine, % Found
IIa	C_2H_5OH	204	100	$C_8H_7O_2Br$[4]	44.65	44.25	3.20	3.10	37.20	36.80
IIb	C_2H_5OH	165	100	$C_9H_9O_2Br$	47.16	46.89	3.93	3.75	34.93	34.87
IIc	Benzene-ligroin	89–90	95	$C_{10}H_{11}O_2Br$	49.38	48.97	4.52	4.41	32.92	32.50
									Iodine, % Calcd.	Iodine, % Found
IIIa	C_2H_5OH	205–206	100	$C_8H_7O_2I$[5]	36.64	36.85	2.67	2.50	48.47	48.15
IIIb	C_6H_6	191–192	100	$C_9H_9O_2I$	39.13	38.86	3.26	3.38	46.08	45.42
IIIc	C_2H_5OH	232–233	100	$C_{10}H_{11}O_2I$	41.37	41.0	3.79	3.58	43.79	43.40

hydrobromic acid (100 ml.; 48%) or with an aqueous solution of potassium iodide (18 g.; 0.11 mole). The reaction mixture was stirred for 1 hr. at room temperature, a little sodium bisulfite added, the precipitated acids collected after acidification and crystallized. Mixed melting point determination was carried out between the bromo- acids and IIa–c, and between the iodo- acids and IIIa–c, respectively, and in each case no depression was observed.

An authentic specimen of IIa was also prepared by a series of already known reactions starting with *p*-nitrotoluene (*cf.*[5,6]) which was brominated according to procedure (a) to give 2-bromo-4-nitrotoluene in 100% yield (*cf.*[6]). The latter was converted to the corresponding nitrile which on hydrolysis gave 3-bromo-4-methylbenzoic acid (2-bromo-*p*-toluic acid), m.p. 204°, undepressed when mixed with IIa. The 3-bromo-4-alkyl- and 3-iodo-4-alkyl-benzoic acids are listed in Table I.

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[Contribution from the Department of Chemistry, University of Notre Dame]

Reactions of Furan Compounds. XVIII. Nuclear Acetoxylation[1]

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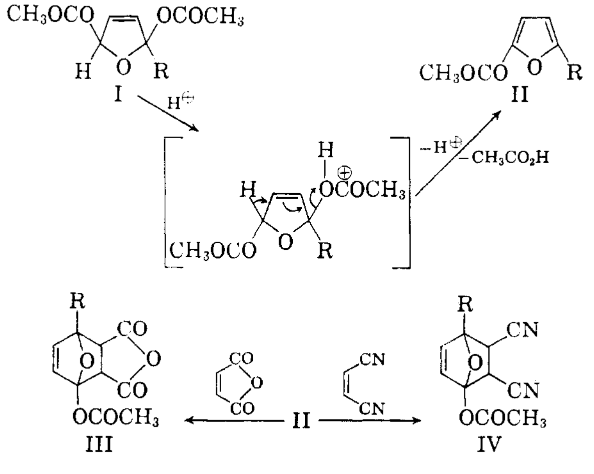
The acid-catalyzed pyrolysis of 2,5-diacetoxy-2,5-dihydrofuran resulting in the elimination of acetic acid and the formation of 2-acetoxyfuran and γ-crotonolactone has been studied further. Lactone formation is believed to involve further pyrolysis of 2-acetoxyfuran in the presence of acetic acid to give the lactone and acetic anhydride. The syntheses of diacetoxylated α-substituted furans by the action of bromine and potassium acetate in acetic acid acetic anhydride on α-substituted furans did not yield the expected products. However, their unstable formation is suspected because of the isolation of 2-acetoxy-5-methylfuran, anemonin, 2-oxo-5-acetoxymethylene-2,5-dihydrofuran, and 2-oxo-5-methoxymethylene-2,5-dihydrofuran from 2-methylfuran, furfuryl acetate, furfural diacetate, and furfuryl methyl ether, respectively.

The synthesis of 2-acetoxyfuran has been previously described; vapor-phase pyrolysis of 2,5-diacetoxy-2,5-dihydrofuran (I. R = $-$H) at 400–450° gave 7–40% 2-acetoxyfuran (II. R = $-$H) and varying amounts of a by-product, γ-crotonolactone (V).[3] Milder acid-catalyzed liquid-phase pyrolysis (100°) in the presence of a high-boiling diluent was subsequently reported to give much-improved yields (80%) of 2-acetoxyfuran.[4] The pyrolysis failed in the presence of a basic substance such as sodium acetate, and it was reasoned that the production of 2-acetoxyfuran was an acid-catalyzed elimination of acetic acid. Pyrolysis in the absence of acid was attributed to traces of residual acid and/or by-products of the pyrolysis itself (*e.g.*, acetic



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[1] Abstracted from a portion of the Ph.D. dissertation of C. J. Williams, University of Notre Dame, 1958. Part XVII, *J. Am. Chem. Soc.*, 81, 2440 (1959).

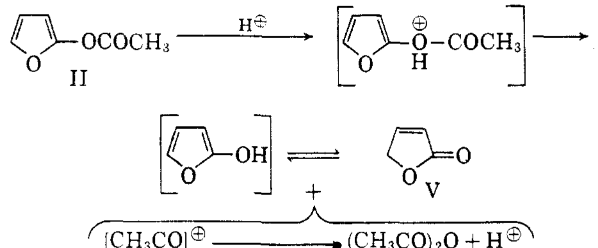
[2] Present address: Research Laboratories, Eastman Kodak Co.

[3] N. Clauson-Kaas and N. Elming, *Acta Chem. Scand.*, 6, 560 (1952).

[4] C. L. Wilson, M. P. Cava, and C. J. Williams, Jr., *J. Am. Chem. Soc.*, 78, 2306 (1956).

acid, acetic anhydride). Such a reaction scheme may be denoted by the equation I→II,

It has now been shown that liquid-phase pyrolysis in the absence of a high-boiling diluent gives only γ-crotonolactone in poor yield because of extensive resinification. It seemed reasonable that this product might arise from further acid-catalyzed acetic acid elimination from 2-acetoxyfuran as shown by the equation



The truth of this proposal was established by subjecting an equimolar mixture of 2-acetoxyfuran and acetic acid to the conditions of pyrolysis. Acetic anhydride (68%) and γ-crotonolactone (V. 48%) were obtained, while the 2-acetoxyfuran was consumed in the reaction. Analogous results were reported when 2-acetoxyfuran was treated with bromine in carbon tetrachloride at a low temperature; the products were 2-bromo-5-oxo-2,5-dihydrofuran and acetyl bromide.[5] Further, the action of the oxidizing reagents (bromine and potassium acetate in acetic acid and acetic anhydride) on 2-acetoxyfuran has now been shown to give 2-oxo-5-acetoxy-2,5-dihydrofuran, the same lactone as that resulting from the action of lead tetraacetate on 2-acetoxyfuran.[5]

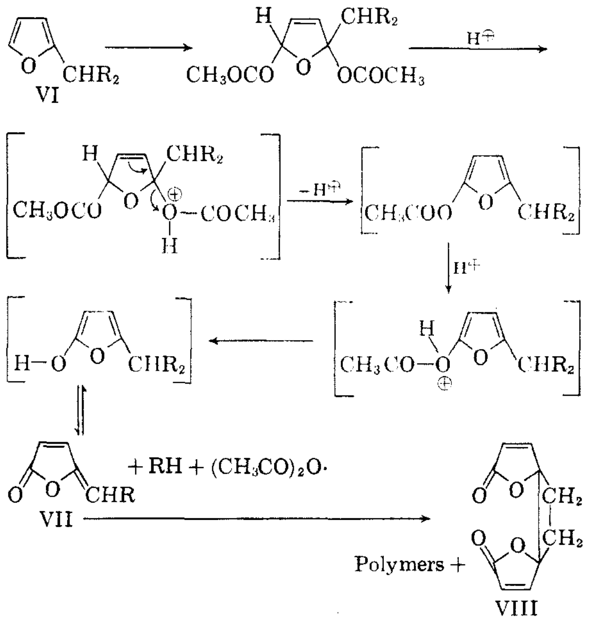
The action of the oxidizing reagents on α-substituted furans such as 2-methylfuran, furfuryl acetate, furfuryl diacetate, furoic acid, and ethyl furoate has not in the past given the predicted nuclear oxidation.[6,7] Among the possible causes of failure are resinification promoted by acidic impurities and by-products, deactivation of the substituted furan nucleus to bromine addition, and oxidation of side-chain substituents.

Renewed interest has been directed to the diacetoxylation of 2-methylfuran; rapid bromine decoloration on addition of the 2-methylfuran to the diacetoxylation mixture at −20° indicated that addition had occurred. Subsequent vacuum distillation of the reaction residues, however, resulted in virtually complete resinification. In one instance, however, a small yield (6.1%) of 2-acetoxy-5-methylfuran (II. R = CH_3) was isolated; thus the instability of the diacetoxylated intermediate was again evidenced. The new ester readily formed Diels-Alder adducts with maleic anhydride and fumaronitrile, their melting points being quite apart from the corresponding adducts with the isomeric furfuryl acetate.

Subjection of a series of α-substituted furans to the diacetoxylation reagents furnished additional evidence for the instability of the diacetoxylated intermediates, the products being analogous to γ-crotonolactone. Furfuryl acetate (VI. R_2 = H, $OCOCH_3$) gave furfural diacetate (VI. R_2 = $(OCOCH_3)_2$, 1.6%) and protoanemonin (VII. R = H), an unstable monomeric lactone which rapidly polymerized to anemonin (VIII, 4.9%) and amorphous polymer.

Furfural diacetate with the oxidation reagents yielded, on attempted vacuum distillation of the residues with or without acid-catalysis, a clear, colorless liquid which solidified on cooling. From analytical and experimental data, this compound was identified as 2-oxo-5-acetoxymethylene-2,5-dihydrofuran (VII. R = $OCOCH_3$). The only analytically pure compound isolated from the action of the oxidizing reagents on furfuryl methyl ether satisfied the elemental requirements for the analogous 2-oxo-5-methoxymethylene-2,5-dihydrofuran (VII. R = OCH_3). The production of these lactones possibly resulted from concurrent substitution and addition followed by elimination; such a reaction would be analogous to that by which furfural diacetate was obtained from furfurylacetate.

The initial reaction in the sequences described above probably involved addition to the furan ring with varying amounts of side-chain substitution. The instability of the diacetoxydihydrofuran intermediates and substituted acetoxyfurans in the presence of traces of hydrogen bromide and acidic by-products facilitated elimination to give the various lactones. Such reaction paths may be denoted by the general equation VI→VII,



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(5) N. Elming and N. Clauson-Kaas, *Acta Chem. Scand.*, **6**, 565 (1952).

(6) N. Clauson-Kaas, F. Limborg, and J. Fakstorp, *Acta. Chem. Scand.* **2**, 109–116 (1948).

(7) N. Clauson-Kaas, F. Limborg, and J. Fakstorp, *Acta. Chem. Scand.*, **6**, 569 (1952).

The various reaction paths proposed above again exemplify the multiplicity of furan reactivity. It is possible that addition, substitution, elimination, and ring-cleavage reactions all occurred to some extent, as the substituted furans exhibited the behavior of a resonance-stabilized conjugated diene and vinyl ether.

EXPERIMENTAL

γ-Crotonolactone (V). A mixture of 2,5-diacetoxy-2,5-dihydrofuran (92 g., 0.49 mole) and β-naphthalenesulfonic acid (0.200 g.) was immersed in an oil bath preheated to 105°. Instantaneous pyrolysis gave 36.5 g. of clear colorless distillate and 52.7 g. of solid black residue (representing 57.3% of the starting material). Distillation of the clear product gave γ-crotonolactone (3.7 g., 0.044 mole, 9%, boiling range 85–95°/12 mm., n_D^{25} = 1.4666) (lit.[3], b.p. 88–89°/mm., n_D^{25} = 1.4662, 19%).

Origin of γ-crotonolactone. A mixture of 2-acetoxyfuran (12.6 g., 0.1 mole), acetic acid (6.0 g., 0.1 mole), and β-naphthalenesulfonic acid (0.01 g.) was heated at 100° for 30 min., the color of the mixture turning dark amber. Distillation yielded a 10.6-g. fore-run of acidic material, boiling-range 31–53°/20 mm., γ-crotonolactone (4.0 g., 0.048 mole, 48%, boiling-range 56–70°/4 mm., n_D^{20} = 1.4680), and 3.2 g. of black solid residue. Fractional distillation of the acidic fore-run gave acetic acid (2.2 g., 0.03 mole, boiling range 49–62°/70 mm., n_D^{20} = 1.3732) and acetic anhydride (6.9 g., 0.068 mole, boiling-range 62°/70 mm. −30°/10 mm., n_D^{20} = 1.3892). No 2-acetoxyfuran (b.p. 59–60°/15 mm., n_D^{20} = 1.4467) was recovered.

2-Oxo-5-acetoxy-2,5-dihydrofuran. To a well-stirred slurry of bromine (40 g., 0.25 mole) and potassium acetate (51 g., 0.51 mole) in acetic acid (100 ml.) and acetic anhydride (150 ml.) at −20°, 2-acetoxyfuran (II. R = H) (40 g., 0.32 mole) was added. A momentary temperature rise to 10° was noted, but the bromine color persisted after stirring 1 hr. at 0°. On heating to 80°, the mixture turned white within 3 min., and potassium bromide was precipitated during 10 min. stirring at 80°. Salt removal (filtration) and solvent removal (at 70°/10–15 mm.) left a black viscous residue to which 100 ml. of ether was added. Salt and solvent removal gave a dark purple solution which, when distilled from a flask coated with potassium acetate, gave 2-oxo-5-acetoxy-2,5-dihydrofuran (23.0 g., 0.16 mole, 64%, b.p. 92–96°/3 mm., n_D^{20} = 1.4596) (lit.,[5] n_D^{25} = 1.4593).

2-Acetoxy-5-methylfuran (II. R = CH_3). The addition of 2-methylfuran (82 g., 1 mole) to a well-stirred slurry of bromine (160 g., 1 mole), potassium acetate (205 g., 2.09 moles) in acetic acid (400 ml.), and acetic anhydride (600 ml.) at −20° gave a colorless mixture in seconds. Subsequent stirring at 0°, 80°, and salt and solvent removal, all as described above, gave a black viscous residue to which 200 ml. of ether was added. Following the removal of precipitated salts, the ether filtrate was divided into four equal parts, each one being distilled from a flask coated with potassium acetate (attempted distillation in bulk resulted in complete resinification). The high-boiling fractions were diluted with 100 ml. of ether and washed successively with water, aqueous bicarbonate, and water. Fractional distillation of the dried ether solution gave 2-acetoxy-5-methylfuran (8.5 g., 0.061 mole, 6.1%, b.p. 72–73°/10 mm.).

Anal. Calcd. for $C_7H_8O_3$: C, 59.99; H, 5.75. Found:[8] C, 59.78; 59.85; H, 5.98, 6.07.

3-Acetoxy-6-methyl-3,6-epoxy-Δ⁴-tetrahydrophthalic anhydride (III). To 2-acetoxy-5-methylfuran (0.648 g., 0.0046 mole) was added maleic anhydride (0.450 g., 0.0046 mole). The addition of benzene-petroleum ether (9:1) produced in 5 min. fine white needles of 3-acetoxy-6-methyl-3,6-epoxy-Δ⁴-tetrahydrophthalic anhydride, m.p. 149.8–150°.

Anal. Calcd. for $C_{11}H_8O_6$: C, 55.46; H, 4.23. Found: C, 56.06, 56.04; H, 4.24, 4.11.

3-Acetoxy-6-methyl-3,6-epoxy-Δ⁴-tetrahydrophthalonitrile (IV). To 2-acetoxy-5-methylfuran (0.54 g., 0.0039 mole) was added fumaronitrile (0.3 g., 0.0038 mole). Gentle heating followed by the addition of 1 ml. of benzene-petroleum ether (9:1) induced the precipitation of fine white needles, m.p. 130.0–130.4°.

Anal. Calcd. for $C_{11}H_8N_2O_3$: C, 61.11, H, 3.73. Found, C, 60.81, H, 3.36.

Anemonin (VIII). The addition of furfuryl acetate (VI. R_2 = H, $OCOCH_3$) (114 g., 1.02 moles) to a well-stirred slurry of bromine (160 g., 1 mole), potassium acetate (205 g., 2.09 moles) in acetic acid (400 ml.), and acetic anhydride (600 ml.) at −20° produced instant decolorization. Subsequent stirring at 0° and 80° and salt and solvent removal, all as described above, gave a black vicous residue to which was added 200 ml. of ether. Following the removal of precipitated salts and ether, the black viscous residue was fractionally distilled from a 1-l. flask coated with potassium acetate. These fractions on refrigeration slowly deposited solid material from which furfural diacetate (VI. R = $OCOCH_3$) (3.2 g., 1.6%, m.p. 48.0–48.4) and anemonin (VIII) (4.7 g., m.p. 142.–142.5°, 4.9%) were isolated and identified; 16.7 g. of insoluble and infusible amorphous polymer was also obtained. Neither the anemonin[9] nor the furfural diacetate depressed the melting point of authentic samples, and the furfural diacetate readily formed a maleic anhydride adduct, m.p. 127–130° (lit.[10] m.p. 126.5–27° C.).

2-Oxo-5-acetoxymethylene-2,5-dihydrofuran (VII. R = $OCOCH_3$). The addition of furfural diacetate[11] (VI. R = $OCOCH_3$) (50 g., 0.25 mole, in 50 ml. acetic anhydride) to a well-stirred slurry of bromine (80 g., 0.5 mole), potassium acetate (100 g., 1 mole) in acetic acid (400 ml.), and acetic anhydride (600 ml.) at −17° produced a temperature rise to 0° but no color change. Following a 30 min. stirring period at 0°, the mixture was heated to 80° for 1 hr., during which time progressive decolorization from orange to light tan occurred. Salt and solvent removal as described above gave a black viscous residue to which 100 ml. of ether was added. Precipitated salts were removed, and after alkaline washing and drying, ether removal left a black viscous residue. Fractional distillation (with or without acid catalysis) gave a clear, white acidic distillate which deposited solid material on standing at room temperature. This solid was characterized in the following manner: Attempts to prepare a maleic anhydride adduct, a bromine adduct, or an analytically pure dinitrophenylhydrazone were unsuccessful, although a positive Fehling's test was noted, the compound dissolved slowly in either acidic or basic aqueous media, yielding a dark violet alkaline solution and an amber acidic solution—no isolable solid was obtained from either solution; following Gilman's procedure,[12] the solid (1 g.) was suspended in 40 ml. of acetic acid, and 4 g. of chromic anhydride was added. The exothermic reaction mixture was cooled to room temperature and stirred for 24 hr. The acetic acid was removed by distillation under reduced pressure, and the residues were extracted with two 25-ml. portions of ether. The addition of aniline (0.5 ml.) to this extract produced, on standing, maleic anhydride dianilide (m.p. 186–188°). A mixed melting-point with maleic anhydride dianilide (m.p. 186–188°) showed no depression. The compound which best seems to fit the analytical data and these experimental observations

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(8) Analyses by Midwest Microlab. Inc., Indianapolis, Ind.

(9) C. Grundemann and E. Kober, *J. Am. Chem. Soc.*, **77**, 2333 (1955).

(10) M. G. Van Campen, Jr., and J. R. Johnson, *J. Am. Chem. Soc.*, **55**, 430 (1933).

(11) H. E. Burdick and J. Adkins, *J. Am. Chem. Soc.*, **56**, 438 (1934).

(12) H. Gilman, R. A. Franz, A. P. Hewlett, and G. F. Wright, *J. Am. Chem. Soc.*, **72**, 3 (1950).

is 2-oxo-5-acetoxymethylene-2,5-dihydrofuran; the yields of 8–9.7 g. of sublimed material represented 21–24%.

Anal. Calcd. for $C_7H_6O_4$: C, 54.55; H, 3.92. Found: C, 54.39, 54.65; H, 3.77, 4.07.

2-Oxo-5-methoxymethylene-2,5-dihydrofuran (VII. R = OCH_3). The addition of furfuryl methyl ether (VI. R_2 = H, OCH_3) (28 g., 0.25 mole) to a well stirred slurry of bromine (40 g., 0.25 mole) and potassium acetate (51.5 g., 0.52 mole) in acetic anhydride (150 ml.) at −17° produced instantaneous decolorization and a temperature rise to 4°. Stirring at 0° and 80° followed by salt and solvent removal, all as described above, gave a dark-brown viscous residue. Removal of salts precipitated by the addition of ether (100 ml.) and subsequent ether removal gave a black viscous residue which was distilled from a flask coated with potassium acetate. The high-boiling distillate (12.6 g., boiling-range 60–107°/2–3 mm.) was immediately washed with dilute aqueous cold carbonate and quickly extracted with ether. Fractional distillation of the ether extract yielded 2 g. (0.012 mole, 6.4%) of a colorless liquid, b.p. 51–52°/3 mm., n_D^{20} = 1.4743; microanalysis, the formation of a purple color with phosphoric acid and the immediate hydrolysis with sulfuric acid to a product which gives a dinitrophenylhydrazone derivative support the identification of this material as 2-oxo-5-methoxymethylene-2,5-dihydrofuran.

Anal. Calcd. for $C_6H_6O_3$: C, 57.20; H, 4.76. Found: C, 56.72, 56.97; H, 4.96, 4.71.

Repetition of this reaction sequence on a molar scale gave inconclusive results; unstable higher-boiling materials of nonanalytical purity were obtained.

Acknowledgment. We wish to thank the University of Notre Dame and the E. I. du Pont de Nemours and Company for their support of this work.

NOTRE DAME, IND.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF NOTRE DAME]

Reactions of Furan Compounds. XIX. Synthesis of 2-Methoxyfuran and its 5-Methyl- and 5-Methoxymethyl Derivatives[1]

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Modification of the acid-catalyzed pyrolysis of 2,5-dimethoxy-2,5-dihydrofuran has given an improved yield of 2-methoxyfuran. Similar pyrolyses of 2,5-dimethoxy-2,5-dihydro-2-methylfuran and 2,5-dimethoxy-2,5-dihydro-2-furfuryl methyl ether have given 2-methoxy-5-methylfuran and 2-methoxy-5-furfuryl methyl ether, respectively. Diels-Alder adducts of these new substituted methoxyfurans with maleic anhydride are reported, as well as the synthesis of 3-methoxy-6-methyl phthalic anhydride by the aromatization of 3-methoxy-6-methyl-3,6-epoxy-Δ^4-tetrahydrophthalic anhydride.

The synthesis of 2-methoxyfuran (II. R = H) has been previously reported by two different routes: the reaction of 5-bromo-2-furoic ester with sodium methoxide followed by saponification and decarboxylation (10–36%),[3] and the acid-catalyzed pyrolysis of 2,5-dimethoxy-2,5-dihydrofuran (11%).[4]

The pyrolytic technique has been improved by the dropwise introduction of 2,5-dimethoxy-2,5-dihydrofuran (I. R = H) into a preheated (220–250°) mixture of β-naphthalenesulfonic acid and high-boiling diluent. Resinification was minimized by maintaining the rate of intermediate addition, as accurately as possible, equal to that of product distillation. Once this condition was established, the pyrolysis proceeded with relative smoothness, and 51% of 2-methoxyfuran (II. R = H) was obtained.

The general applicability of this acid-catalyzed elimination of methanol has now been demonstrated. The intermediates, 2,5-dimethoxy-2,5-dihydro-2-methylfuran (I. R = $-CH_3$) and 2,5-dimethoxy-2,5-dihydro-2-furfuryl methyl ether (I. R = $-CH_2OCH_3$), were prepared by electrolytic oxidation of 2-methyl furan and furfuryl methyl ether respectively.[5]

The dropwise introduction of 2,5-dimethoxy-2,5-dihydro-2-methylfuran into a mixture of β-naphthalenesulfonic acid and high-boiling diluent gave no elimination; the intermediate was recovered unchanged. The addition of a few drops of glacial acetic acid to the pyrolysis flask provided sufficient acidity for elimination, and 2-methoxy-5-methylfuran (II. R = $-CH_3$, 28%) was obtained. Analytical results indicated a sensitivity of 2-methoxy-5-methylfuran to atmospheric oxygen; redistillation and storage under nitrogen at 5° gave an analytically stable sample. Oxidation of 2-methoxy-5-methylfuran by potassium ferricyanide to recognizable products failed.

The pyrolysis of 2,5-dimethoxy-2,5-dihydro-2-furfuryl methyl ether (I. R = $-CH_2OCH_3$) required even more stringent acidic conditions. The intermediate was recovered in good yield from successive treatments with β-naphthalenesulfonic acid, glacial acetic acid, or *o*-phosphoric acid in the pyrolysis flask at 250°. Partially pyrolysis, induced by mixing *o*-phosphoric acid with the intermediate be-

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(1) Abstracted from a portion of the Ph.D. dissertation of C. J. Williams, University of Notre Dame, 1958.

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(3) E. K. Amstutz and R. J. Petfield, *J. Org. Chem.*, **19**, 1944 (1954).

(4) C. L. Wilson, M. P. Cava, and C. J. Williams, Jr., *Chem. and Ind.*, **1955**, 17.

(5) N. Clauson-Kaas *et al.*, *Acta Chem. Scand.*, **6**, 545, 556 (1952).