Cyclopropyl methyl ketone was pyrolyzed at 525° at a rate of 45 g./hour. The product contained acetone, an unidentified material, b.p. 69.6–75°, unchanged ketone and methyl propenyl ketone.

Using infrared methods search was made for cyclopentanone, crotonaldehyde and allyl methyl ketone but no trace was found.

COLUMBUS, OHIO

[CONTRIBUTION FROM THE UNIVERSITY OF NOTRE DAME]

Reactions of Furan Compounds. XVII. Pyrolysis of Tetrahydrofurfuryl Esters to Methyl Propenyl Ketone[1]

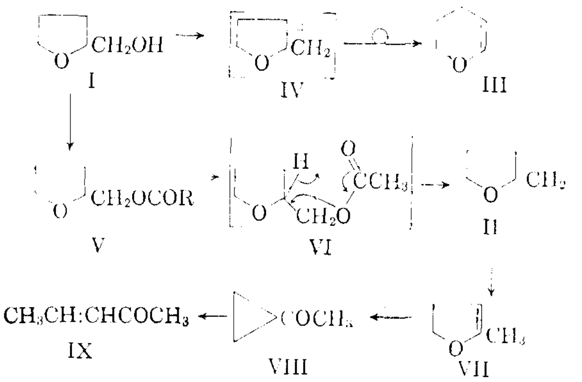
BY GEORGE J. BAUMGARTNER AND CHRISTOPHER L. WILSON

RECEIVED NOVEMBER 10, 1958

Tetrahydrofurfuryl acetate, propionate, formate, benzoate and oxalate have been pyrolyzed at between 450 and 580°. The main product was methyl propenyl ketone in yields as high as 51%. A mechanism for the reaction is proposed.

Dehydration of tetrahydrofurfuryl alcohol (I) in the vapor phase gives not tetrahydromethylenefuran (II) but 2,3-dihydro-1,4-pyran (III) and it is generally believed that the reaction involves the rearrangement of an intermediate (adsorbed) cation (IV).[2] Paul[3] thought that tetrahydromethylenefuran (II) was intermediate in this reaction and attempted to prove his point by passing the compound over alumina at 380°. He did obtain a small amount of the pyran, but it is now clear[4] that what Paul thought was tetrahydromethylenefuran was in fact dihydromethylfuran (VII) and the dihydropyran he obtained was present in his starting material.

The pyrolysis of alcohol esters as a means of making olefins was pioneered by Krafft[5] and has been extensively studied by others.[6,7] In general, the method gives unrearranged olefins although isomerization may result as a secondary reaction catalyzed by carbonaceous deposits.[7] Tetrahydrofurfuryl esters (V) on pyrolysis should, therefore, give tetrahydromethylenefuran (II) as primary product. Since this olefin is very sensitive to heat and acids and rearranges very rapidly to dihydromethylfuran (VII) which in turn isomerizes if the temperature is above about 400°[4] successively to cyclopropyl methyl ketone (VIII) and methyl propenyl ketone (IX), the ultimate product from ester pyrolysis should be the last of this series since the esters mostly decompose only above this temperature. Actually the acetate, propionate, formate, benzoate and oxalate had to be heated to above 450° before splitting and the only important product in all cases was methyl propenyl ketone (IX). The best results were obtained from the acetate and propionate and the yield of ketone rose to 51%. The method can be the basis for a preparative route to the ketone. Propionate is preferred to acetate since it is easier to separate the products of pyrolysis. It has already been shown that better results are obtained the lower the dissociation constant of the eliminated acid.[8] This would explain the inferior results obtained from the benzoate, formate and oxalate.



Unlike the dehydration of an alcohol which seems to go through positively charged intermediates, the pyrolysis of an ester is usually a homogeneous reaction involving neutral or cyclic intermediates such as VI.[9] This accounts for observed *cis* elimination.[9]

In the pyrolysis of esters other minor side reactions have been observed from time to time. Occasionally acyl–oxygen scission to two molecules of carbonyl compound occurs. In the present work small amounts of formaldehyde, acetone, acetaldehyde. butyraldehyde and valeraldehyde were identified in the products from tetrahydrofurfuryl acetate. Each of these substances other than acetone could arise by acyl–oxygen scission followed by further reactions of the primary products. Other known modes of decomposition involve splitting to alcohol and ketene, and decarboxylation. No evidence for these alternative reactions was obtained, but amongst the by-products methylfuran was identified. This compound probably

---

(1) This work is taken from the Ph.D. thesis of G. J. Baumgartner, University of Notre Dame, 1955.

(2) R. Paul, *Compt. rend.*, **96**, 1409 (1933); *Bull. soc. chim.*, [4] **53**, 1489 (1933); L. E. Schniepp and H. H. Geller, THIS JOURNAL, **68**, 1646 (1946); C. L. Wilson, British Patent 569,625 (to Revertex Ltd., June 1, 1945); *Nature*, **157**, 846 (1946); THIS JOURNAL, **69**, 3004 (1947); C. H. Kline and J. Turkevitch, *ibid.*, **67**, 498 (1945); H. P. Thomas and C. L. Wilson, *ibid.*, **73**, 4803 (1951).

(3) R. Paul, *Bull. soc. chim.*, [5] **2**, 745 (1935).

(4) D. M. Aten Armitage and C. L. Wilson, THIS JOURNAL, **81**, 2437 (1959).

(5) F. Krafft, *Ber.*, **16**, 3018 (1883); **19**, 2227 (1886).

(6) J. P. Wibaut and A. J. van Pelt, Jr., *Rec. trav. chim.*, **57**, 1055 (1938); **60**, 55 (1941); P. L. Cramer and M. J. Mulligan, THIS JOURNAL, **58**, 373 (1936); F. C. Whitmore and H. S. Rothrock, *ibid.*, **55**, 1106 (1933).

(7) J. P. W. Houtman, J. van Steenis and P. M. Heertjes, *Rec. trav. chim.*, **65**, 781 (1946); W. J. Bailey and J. Rosenberg, THIS JOURNAL, **77**, 73 (1955).

(8) W. J. Bailey and J. J. Hewitt, *J. Org. Chem.*, **21**, 543 (1956).

(9) W. J. Bailey and R. Barclay, Jr., *ibid.*, **21**, 328 (1956).

arises by dehydrogenation of dihydromethylfuran (VII) over the carbonaceous deposit which always forms during pyrolysis.

It is of interest to observe that another ester of tetrahydrofurfuryl alcohol, the α-acetoxypropionate, on pyrolysis at 475-525° gives, not methyl propenyl ketone, but tetrahydrofurfuryl acrylate in as high as 79% yield.[10] Finally, in view of Brandenberg and Galat's[11] demonstration that boric acid is a useful catalyst for the dehydration of alcohols, the decomposition of both tetrahydrofurfuryl alcohol in the presence of boric acid and tetrahydrofurfuryl borate itself was studied. The only recognizable product was dihydropyran (III) in a yield of 22 and 43%, respectively, by the two variations.

Experimental

Preparation of Esters.—The tetrahydrofurfuryl esters of acetic, propionic, benzoic and oxalic acids were prepared from commercial tetrahydrofurfuryl alcohol (Quaker Oats Co.) which was distilled before use, b.p. 175–180°. The alcohol (5 moles) and the C.P. acid (5 moles) were placed in a 2-l. flask along with the corresponding anhydrous sodium salt (5 g.) and benzene (300 ml.). The flask was fitted with a 40 × 1.3 cm. column packed with glass helices and fitted with a phase separator head. The mixture was gently refluxed and the water automatically removed. When the theoretical amount had formed, refluxing was continued for one hour and the benzene distilled through the head. The ester was then distilled to give the acetate, b.p. 192–196°, or the propionate, b.p. 202–207°, in yields of up to 96%. The formate was made by refluxing anhydrous formic acid (92 g., 2 moles) and the alcohol (510 g., 5 moles, for five hours. Fractionation gave the ester, b.p. 184–186 (743 mm.), 176 g., n^{25}D 1.4393, d^{24} 1.102.

Anal. Calcd. for $C_6H_{10}O_3$: C, 55.4; H, 7.75. Found: C, 55.6; H, 8.0.

TABLE I

PYROLYSIS OF TETRAHYDROFURFURYL ESTERS TO METHYL PROPENYL KETONE

Temp., °C.	Contact time, sec.	Input, mole/hr. Ester	N_2	Ester consumed, %	Ketone yield, %[a]
		A. Acetate			
512	73	0.35	0.0	57	19.4
538	83	.29	.0	76	31.0
562	74	.32	.0	87	14.1
570	43	.54	.0	80	18.3
580	28	.83	.0	83	19.5
		B. Propionate			
450	43	0.43	0.21	15	3.2
470	46	.36	.21	21	11.3
520	49	.48	.09	35	51.2
532	51	.41	.09	53	48.0
545	56	.34	.09	62	47.3
570	13	.38	1.41	76	31.5

[a] Based on consumed ester.

Apparatus.—The pyrolysis chamber consisted of a Pyrex tube 45 mm. outside diameter and about 5 feet in length. It was filled with Pyrex chips for 33 in. over the region of constant temperature. A thermocouple pocket was inserted concentrically down the chamber. The pyrolysis tube was swept out with dry nitrogen before each run. Ester was admitted at a definite rate from a constant head dropping funnel usually along with nitrogen. When all the ester had been introduced the nitrogen flow was increased for half an hour. Products were caught in three traps the first cooled in water and the other two in Dry Ice.

Analysis of Products. Tetrahydrofurfuryl Acetate.—The material in the three traps was combined and distilled through a 40 × 1.3 cm. column packed with glass helices. Five fractions were collected: 1, b.p. below 110°; 2, 110–130°; 3, 130–170°; 4, 170–180°; and 5, 180–197°. A viscous tarry residue remained in the distilling flask. Fraction 1 was small and contained water. Several compounds were identified in this fraction, including formaldehyde, acetaldehyde, acetone, 2-methylfuran, butyraldehyde, valeraldehyde and methyl propenyl ketone. Fraction 2 contained both acetic acid, b.p. 118°, and methyl propenyl ketone, b.p. 120–122°. The acetic acid was neutralized with 6 *N* sodium hydroxide with strong cooling. The organic layer was dried and distilled. The fraction boiling from 118–124° was collected and weighed as methyl propenyl ketone. A 2,4-dinitrophenylhydrazone made from this distillate had m.p. 153–155°, mixed m.p. with authentic material (m.p. 153.5–155°) was 153–155°. Fractions 3 and 4 were small, usually from 1 to 3 ml. Fraction 4 contained some tetrahydrofurfuryl alcohol which was probably formed by hydrolysis of some of the unpyrolyzed ester. Fraction 5 contained the unchanged ester. The residue amounted to approximately 5% of the pyrolysate. It was dark brown in color and had no definite b.p. It was insoluble in water, insoluble in saturated sodium bisulfite solution and gave no 2,4-dinitrophenylhydrazone.

Fraction 1, which should have contained pyrolysis intermediates, was carefully analyzed. This fraction from several pyrolysis runs was combined and refractionated.

Formaldehyde was evolved when the pyrolysate was heated. Some of this condensed as solid paraformaldehyde in the head of the distilling column. Its 2,4-dinitrophenylhydrazone had m.p. 165–167° and showed no depression of m.p. when mixed with authentic material (m.p. 167–168°).

Acetaldehyde was present in the first few drops of distillate. A 2,4-dinitrophenylhydrazone made from them melted at 145–147°. Mixed with authentic material (m.p. 166–167°) it melted at 146–146.5°. Acetaldehyde dinitrophenylhydrazone has been reported[12] to give two melting points of 147 and 166°.

Acetone was present in the fraction b.p. 53–56°. Its dinitrophenylhydrazone had m.p. 118–121°. There was no depression of m.p. when mixed with authentic material.

2-Methylfuran was isolated from the fraction b.p. 56–110° by separating carbonyl compounds by repeated shaking with saturated aqueous sodium bisulfite. The insoluble layer slowly formed a derivative with dinitrophenylhydrazine. This had m.p. 237.5°. The mixed m.p. with the authentic derivative (m.p. 235.5–236.5°) of levulinic aldehyde was 238.5°.

A mixture of dinitrophenylhydrazones was prepared from the sodium bisulfite solution used to separate methylfuran. Its m.p. was 88 to 160°. The material was dissolved in benzene and chromatographed over adsorption alumina (80–200 mesh). Three bands were formed on the column. The lowest band eluted and recrystallized using benzene gave m.p. 110–112°. It was identified as the derivative of **butyraldehyde** by non-depression of m.p.

Anal. Calcd. for $C_{10}H_{12}O_4N_4$: C, 47.7; H, 4.8; N, 22.2. Found: C, 48.3; H, 4.6; N, 22.1.

The middle band was eluted using ethanol (5%) in benzene. The derivative had m.p. 100–105°. Mixed m.p. with authentic **valeraldehyde** dinitrophenylhydrazone (m.p. 106°) was 104–105°.

The remaining band was eluted with ethyl acetate (10%) in benzene. The crystals had m.p. 145–148° not depressed by the authentic derivative (m.p. 153.5–155°) of **methyl propenyl ketone.**

Tetrahydrofurfuryl Propionate.—The pyrolysate of this ester was distilled and separated into fractions: 1, b.p. below 110°; 2, 110–125°; 3, 125–145°; 4, 145–170°; 5, 170–180°; and 6, 180–208°. A residue remained. Fraction 2 contained most of the methyl propenyl ketone. Acid present was neutralized with sodium hydroxide (6 *N*) with cooling and the ketone dried. Fraction 3 contained propionic acid (b.p. 141°) and it was neutralized as above and the insoluble layer combined with that from fraction 2. The combined fractions were distilled and the material, b.p. 118–124°, weighed as methyl propenyl ketone.

Gases not caught in the traps were passed through a solution of bromine in carbon tetrachloride. The bromides

---

[10] H. V. Claborn, U. S. Patents 2,222,363 (Nov. 19, 1940) and 2,229,997 (Jan. 28, 1941); M. L. Fein, W. P. Ratchford and C. H. Fisher, THIS JOURNAL, **66**, 1201 (1944).

[11] W. Brandenberg and A. Galat, *ibid.*, **72**, 3275 (1950).

[12] W. M. D. Bryant, *ibid.*, **60**, 2815 (1938).

formed were distilled and seemed to consist of 1,2-dibromopropane, b.p. 139–143° (743 mm.) and 2,3-dibromobutane, b.p. 153–158° along with the tetrabromide from butadiene, m.p. 118–121°.

Tetrahydrofurfuryl Benzoate.—The ester (1.4 moles) was pyrolyzed at a rate of 0.18 mole/hr. with nitrogen carrier at 0.24 mole/hr. at 563°. The contact time was 56 sec. The yield of methyl propenyl ketone was 13.3% and no unchanged ester was recovered.

Tetrahydrofurfuryl Formate.—The ester (0.54 mole) was pyrolyzed at 0.31 mole/hr. at 535° with a contact time of 79 sec. The yield was 31% of ketone.

Tetrahydrofurfuryl Oxalate.—The ester (0.22 mole) was introduced at a rate of 0.04 mole/hr. at 532° with nitrogen carrier (0.21 mole/hr.) corresponding with a contact time of 98 sec. The yield of ketone based on consumed ester was 10.5%.

Pyrolysis of 4,5-Dihydro-2-methylfuran.—The furan (6.3 g.) was passed through a semi-micro pyrolysis furnace at 540°. The product gave a dinitrophenylhydrazone, m.p. 148–154°, depressed by admixture with the derivative from cyclopropyl methyl ketone but not depressed by mixing with methyl propenyl ketone derivative.

Pyrolysis of Cyclopropyl Methyl Ketone.—The ketone (89.5 g.) was pyrolyzed at 500° with a contact time of 47 sec. The product contained methyl propenyl ketone (30.5 g.) corresponding with a 35% yield based on consumed material. A viscous residue (15 g.) remained in the flask. Like the residue obtained in the pyrolysis of tetrahydrofurfuryl esters, it was insoluble in sodium bisulfite solution and gave no dinitrophenylhydrazone.

Dehydration of Tetrahydrofurfuryl Alcohol by Boric acid.[11]—Tetrahydrofurfuryl alcohol (1 mole) and boric acid (1 mole) were placed in a 250-ml. flask fitted with a 40 × 1.3 cm. column packed with glass helices and fitted with a partial take-off head. Heat was applied and the water was removed continuously. After 1 mole of water had been removed, water and 2,3-dihydropyran distilled together. Toward the end of the distillation, tetrahydrofurfuryl alcohol also distilled. Carried along with this was a high boiling, water-insoluble, pale green liquid. Redistillation of the pyrolysate gave 14.7 g. of 2,3-dihydropyran, a 22% yield based upon alcohol consumed. The 2,4-dinitrophenylhydrazone from it had m.p. 113.5–115° and did not depress the melting point of a derivative from authentic 2,3-dihydropyran. The pale green, high boiling, water-insoluble material mentioned above was combined with the same material from other runs and vacuum distilled. A large fraction, b.p. 158–164° (2 mm.) was obtained. This substance was an ester of boric acid; it gave white crystals of boric acid when placed on a watch glass and allowed to stand overnight. A sample, b.p. 159° (2 mm.), was shown to be tetrahydrofurfuryl borate.

Anal. Calcd. for $(C_5H_9O_2)_3B$: C, 57.4; H, 8.6. Found: C, 57.5; H, 8.5.

Pyrolysis of Tristetrahydrofurfuryl Borate.—This ester (60 g.) was pyrolyzed at 500°. 2,3-Dihydropyran (6.5 g.) was obtained, along with unchanged ester (41.1 g.). This is a 43% conversion to 2,3-dihydropyran based upon the ester consumed.

NOTRE DAME, IND.

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Studies in Purine Chemistry. II. A Facile Synthesis of 2-Substituted Adenines[1,2]

BY EDWARD C. TAYLOR, O. VOGL AND C. C. CHENG

RECEIVED AUGUST 15, 1958

The reaction of the silver salt of isonitrosomalononitrile with amidine hydrohalides yields amidine salts of isonitrosomalononitrile (I), which are quantitatively isomerized by heating in appropriate solvents to 2-substituted 4,6-diamino-5-nitrosopyrimidines (II). Heating the latter with formamide, formic acid and sodium dithionite yields 2-substituted adenines (III) in high yield. Direct conversion of I to III is realized in a mixture of formamide, formic acid and sodium dithionite, and provides what is essentially a one-step synthesis of a variety of hithertofore unavailable adenine derivatives from simple aliphatic precursors. Modifications of these procedures lead to new syntheses of adenine and isoguanine and to the preparation of a novel purine type, illustrated by α,δ-bis-(2-adenyl)-butane (VII, $n = 4$). The direct conversion of an amidine to a purine is realized in the reaction of guanidine carbonate, the potassium salt of isonitrosomalononitrile, formamide, formic acid and sodium dithionate, to give 2,6-diaminopurine in 71% yield.

The conventional synthetic route to adenines involves the condensation of guanidine or thiourea with malononitrile to give a 2-substituted 4,6-diaminopyrimidine, which is then nitrosated, reduced, acylated and subsequently ring-closed under dehydrating conditions.[3] The requisite 4,5,6-triaminopyrimidine intermediates may alternately be prepared by reduction of 5-arylazo derivatives, formed either by coupling of a 4,6-diaminopyrimidine[4] or directly by condensation of arylazomalononitriles with amidines.[4,5] Adenine itself may be prepared by desulfurization of a 2-mercapto or 2-methylmercapto substituent at an appropriate stage of the synthesis.[6–10] Alternate routes to adenines include aminolysis of 6-mercapto-,[11] 6-methylmercapto-,[12–21] 6-carboxymeth-

---

[1] This investigation was supported by a research grant (C-2551 PET) from the National Cancer Institute of the National Institutes of Health, Public Health Service.

[2] Presented in part before the Division of Medicinal Chemistry at the 131st National A.C.S. Meeting in Miami, Fla., April 7–12, 1957.

[3] A. Bendich in "The Nucleic Acids, Chemistry and Biology," ed. by E. Chargaff and J. N. Davidson, Vol. 1, Academic Press, Inc., New York, N. Y., 1955, p. 81.

[4] B. Lythgoe, A. R. Todd and A. Topham, *J. Chem. Soc.*, 315 (1944).

[5] J. Baddiley, B. Lythgoe and A. R. Todd, *ibid.*, 386 (1943).

[6] W. Traube, *Ann.*, **331**, 64 (1904).

[7] M. Hoffer, "Jubilee Volume Dedicated to Emil C. Barell," Basle, 1946, p. 428.

[8] A. Bendich, J. F. Tinker and G. B. Brown, THIS JOURNAL, **70**, 3109 (1948).

[9] G. A. Howard, B. Lythgoe and A. R. Todd, *J. Chem. Soc.*, 556 (1945).

[10] G. W. Kenner, B. Lythgoe, A. R. Todd and A. Topham, *ibid.*, 574 (1943).

[11] G. B. Elion in "The Chemistry and Biology of Purines," ed. by G. E. W. Wolstenholme and C. M. O'Connor, J. and A. Churchill Ltd., London, 1957, p. 39.

[12] G. B. Elion, E. Burgi and G. H. Hitchings, THIS JOURNAL, **74**, 411 (1952).

[13] A. Albert and D. J. Brown, *J. Chem. Soc.*, 2060 (1954).

[14] C. G. Skinner and W. Shive, THIS JOURNAL, **77**, 6692 (1955).

[15] R. G. Ham, R. E. Eakin, C. G. Skinner and W. Shive, *ibid.*, **78**, 2648 (1956).

[16] C. G. Skinner, W. Shive, R. G. Ham, D. C. Fitzgerald, Jr., and R. E. Eakin, *ibid.*, **78**, 5097 (1956).

[17] C. G. Skinner, P. D. Gardner and W. Shive, *ibid.*, **79**, 2843 (1957).

[18] C. O. Miller, F. Skoog, F. S. Okumura, M. H. von Saltza and F. M. Strong, *ibid.*, **78**, 1375 (1956).