about 9% by volume of a saturated gas which burnt with a luminous flame, this may have been cyclopropane. At 540° the amount was only 2.8%.

Cyclopropanealdehyde.—The bisulfite extract of the product from the pyrolysis of dihydrofuran at 480° was neutralized (phenolphthalein) with sodium hydroxide (33%). The upper layer was separated and the aqueous layer extracted seven times with ether. The extract was dried over anhydrous magnesium sulfate, the ether separated under a column and the residue distilled. The aldehyde, b. p. 99.3-99.5° (771 mm.), did not solidify at −78°.

Anal. Calcd. for C_4H_6O: C, 68.5; H, 8.6. Found: C, 68.4; H, 8.8.

The yield was 24% calculated on dihydrofuran consumed. Recovery of the aldehyde was 75% of that estimated in the bisulfite. The dinitrophenylhydrazone formed orange red prisms, m. p. 186-187.5°, after recrystallization from ethyl acetate.

Pyrolysis of Cyclopropanealdehyde.—The aldehyde (10 g.) was dripped into the furnace tube at 500° during thirty minutes together with carbon dioxide (2 liters/hour). An upper layer remained after the liquid product had been shaken with bisulfite. This was separated by evacuation through a cooled trap and proved to be 2,3-dihydrofuran (0.7 g.) identified as γ-hydroxybutaldehyde 2,4-dinitrophenylhydrazone. The aldehydes (4.8 g.) in the bisulfite consisted of 4% crotonaldehyde and the rest cyclopropanealdehyde. Gaseous products after removing carbon dioxide measured 700 cc. (770 mm., 20°) and consisted of carbon monoxide and propylene in a ratio 1.08:1.

Pyrolysis of Crotonaldehyde.—Redistilled crotonaldehyde (4.22 g.) was passed with 2 liter/hour of hydrogen into the glass furnace tube at 550°. Consumption was 86% and the yield of propylene 52%. Using carbon dioxide instead of hydrogen gave a CO/C_3H_6 ratio of 1.74 (500°) and 1.68 (550°), these gases accounting for 96% of the total gaseous product.

Summary

1. 2,3-Dihydrofuran has been shown to rearrange on heating to above 375° reversibly to cyclopropane aldehyde.

2. Crotonaldehyde, propylene and carbon monoxide are also present in the reaction product and the formation of these is discussed.

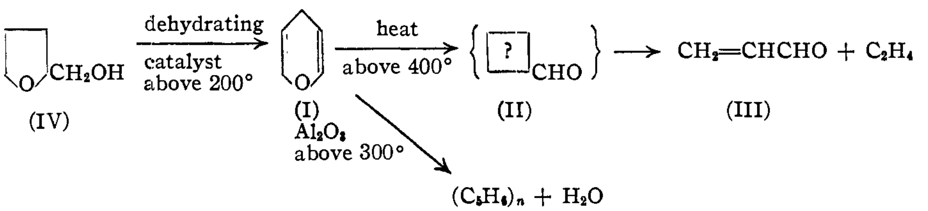
NOTRE DAME, INDIANA RECEIVED JULY 9, 1947

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

Reactions of Furan Compounds. VIII. Dehydration of Tetrahydrofurfuryl Alcohol to 2,3-Dihydropyran and Subsequent Formation of Acrolein and Ethylene[1]

BY CHRISTOPHER L. WILSON

After 2,3-dihydrofuran had been shown to rearrange on heating into cyclopropane aldehyde,[2] it became of interest to study the behavior of the homolog, 2,3-dihydropyran (I) which by an analogous reaction should give cyclobutanealdehyde (II). Dihydropyran on heating above 400°, however, gave no cyclobutanealdehyde (II) but acrolein (III) and ethylene instead. Whilst it is still possible that cyclobutanealdehyde (II) intervened and proved to be very unstable, the process could proceed in other ways. For example, the fission is analogous to a reverse diene addition like the splitting of cyclohexene into butadiene and ethylene and there is no evidence that cyclobutane compounds intervene here.



It is surprising, in view of the fission reaction, that acrolein has not been detected before in the products of catalytic dehydration of tetrahydrofurfuryl alcohol (IV) to dihydropyran[3] when the temperature is 400° or higher. Kline and Turkevich[4] using a thoria catalyst at 550° referred to the formation of low-boiling material which "polymerized on standing and had a sharp odor" but they failed to identify acrolein. Paul's experience was similar.[5]

The reason for the anomaly has now become apparent. If the catalyst used for dehydrating tetrahydrofurfuryl alcohol to dihydropyran is too active, as is alumina, the dihydropyran molecule first produced is further dehydrated to hydrocarbon material (given as $(C_5H_6)_n$ in Table I) before it has a chance to split into acrolein and ethylene. It is possible using a less active catalyst to get high yields of acrolein in one step from tetrahydrofurfuryl alcohol. Such a catalyst has been found to be an alumina–silica combination in the mole ratio 1:2 employed at 450–500° at which temperature dihydropyran splits rapidly.

Data illustrating the behavior of alumina and alumina–silica are given in Tables I and II. The

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(1) A preliminary announcement of this work has already been made (Wilson, *Nature*, **157**, 846 (1946)). Subsequently an independent publication appeared describing the thermal fission of dihydropyran (Bremner, Jones and Beaumont, *J. Chem. Soc.*, 1018 (1946)).

(2) Wilson, THIS JOURNAL, **69**, 3002 (1947).

(3) "Organic Syntheses," **23**, 25 (1943); Paul, *Compt. rend.*, **96**, 1409 (1933); *Bull. Soc. Chim.*, **53**, 1489 (1933).

(4) Kline and Turkevich, THIS JOURNAL, **67**, 498 (1945).

(5) R. Paul, private communication. *Bull. Soc. Chim.*, **14**, 167 (1947).

first catalyst gave no acrolein at any temperature whereas the second gave good yields if the temperature of operation was 450°. At still higher temperatures the yield fell off due partly to the decomposition of acrolein into ethylene and carbon monoxide, and partly to the formation of hydrocarbon material by further dehydration of dihydropyran.

Other catalysts were also tried. Titanium dioxide and a basic aluminum phosphate prepared by a precipitation method[6] both gave some acrolein at 500°.

The activity of these catalysts would place them between alumina and aluminum silicate.

TABLE I

DEHYDRATION OF TETRAHYDROFURFURYL ALCOHOL BY ACTIVATED ALUMINA

Input: Alcohol, 0.5 mole/hour. Hydrogen, 5 liters/hour. The experiments were consecutive without reactivation of the catalyst.

Temp., °C.	Alcohol Input, moles	Alcohol Consumed, %	Yield of products (%)[a] Dihydropyran	$(C_5H_6)_n$
200	1	41	. .	. .
250	9	84	56	25
300	8	87	62	34
350	4	99	19	72
400	2	100	2	85
480	2	100	0	88

[a] Of theory, calculated on alcohol consumed,

TABLE II

DEHYDRATION OF TETRAHYDROFURFURYL ALCOHOL BY ALUMINA–SILICA CATALYST

Input: Alcohol, 0.5 mole/hour. Hydrogen, 5 liters/hour. Catalyst activated between experiments,

Temp., °C.	Alcohol Input, moles	Alcohol Consumed, %	Yield of products Dihydropyran	Acrolein
275	1	25	. .	0
325	18	67	59	0
350	8	74	72	0
400	3	73	48	Trace
450	5	73	7	62
490	4	74	5	47
520	4	73	0	34

It is of interest that the same basic aluminum phosphate material was used[6] for dehydrating tetrahydrofurfuryl alcohol to dihydropyran and no mention was made of the formation of acrolein although temperatures as high as 500° were recorded. Our experiments showed that at this temperature without added carrier gas acrolein was the major product although the amount decreased relative to dihydropyran if the contact time was shortened. This is in agreement with the view that the fission reaction is homogeneous whereas the dehydration is surface catalyzed.

Using the aluminum silicate catalyst the reaction (see Table II) is a convenient preparative method for acrolein. The catalyst life is short but reactivation is easy. Alternatively dihydropyran may be cracked at 450–490°[7,8] to give acrolein in good yields (60–70%)[8].

Experimental

Isolation and Estimation of Products.—The products from the catalyst chamber were distilled using a 5-plate fractionating column. The product, b. p. below 160°, was shaken with sodium bisulfite solution to remove acrolein, dried and redistilled to give dihydropyran, b. p. 86–88°. It was also possible satisfactorily to separate acrolein (b. p. 51.5–53.0°) from dihydropyran b. p. 74–76° when wet) and water using a 12-plate column.

Hydrocarbon material (b. p. below 160°) was isolated by shaking the dihydropyran fraction after removal of acrolein with 0.5 *N* hydrochloric acid (4 volumes) until all the dihydropyran had been converted into δ-hydroxyvaleraldehyde which dissolved in the water layer. Tetrahydrofurfuryl alcohol was estimated in the residue by acetylation with acetic anhydride in the presence of pyridine as catalyst. It was separated from hydrocarbon material by shaking with water.

Dihydropyran was accurately estimated when necessary by precipitation as hydroxyvaleraldehyde-2,4-dinitrophenylhydrazone from hydrochloric acid solution. Acrolein 2,4-dinitrophenylhydrazone which could be precipitated from the bisulfite solution of the aldehyde had m. p. 165–167° (dec.).

Catalysts. Alumina.—A commercial granulated alumina (4–6 mesh, 850 g.) was heated in air to 500° before use. After experiments at various temperatures, the amount of tetrahydrofurfuryl alcohol present (estimated by acetylation) in the recovered material was as follows: 69.4 (200°), 52.8 (250°), 11.5 (300°), 4.9 (350°), 0.5% (400 and 490°). At 400° the product was insoluble in water and had a green color. It boiled over a very wide range and a fraction, b. p. 200–250°, was shown by analysis to be largely oxygen-free.

Anal. Calcd. for C_5H_6: C, 91.0; H, 9.1. Found: C, 89.7; H, 10.0.

At 350°, 90% of the oxygen present in the original tetrahydrofurfuryl alcohol turned up as water in the product.

Titanium Dioxide.—Granular titanium dioxide (4–16 mesh, 280 g., 99.4% pure) was heated in air to 330° before use. The catalyst occupied 13″ of the reaction tube (1.5″ diam.) and deteriorated rapidly in use. It was readily activated by heating in air at 520°. The nature of the carrier gas (hydrogen, nitrogen or carbon dioxide) did not appear to influence the reaction.

At 420°, 0.5 mole of tetrahydrofurfuryl alcohol with 5 liters/hour of hydrogen gave dihydropyran (15.0 g.) and acrolein (3.5 g.) and unchanged alcohol (20 g.).

Basic Aluminum Phosphate.—This catalyst (450 g.), which behaved like an inferior alumina was prepared as described.[6] Tetrahydrofurfuryl alcohol (1 mole during two hours) gave after passage over the catalyst with 5 liters/hour carbon dioxide at 480°, acrolein (11.3 cc.), dihydropyran (17.5 cc.) and some unchanged alcohol. Increase in input of carrier gas decreased acrolein and increased dihydropyran. With no carrier acrolein (15.1 cc.) and dihydropyran (12.9 cc.) were produced.

The catalyst when fresh was very active giving hydrocarbon material but it deteriorated rapidly. Maximum yield of acrolein resulted after the catalyst had had some use.

Aluminum Silicate.—Granular aluminum silicate (Al_2O_3 : SiO_2 = 1:2 mole; containing 4% other substances, 1083 g., 4–8 mesh) was heated in a stream of air at 500° before use.

At 490° the nature of the carrier gas (water, nitrogen, hydrogen or carbon dioxide) did not appear to affect either

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(6) Bremner and McNeil, British Patent 547,334.

(7) Wilson, British Patent 569,625; *cf.* Bremner and Jones, British Patent 573,507.

(8) Bremner, Jones and Beaumont, ref. 1, give a maximum yield of 84.5%.

consumption or yield of products. Increase in carrier gas (hydrogen) from 5 to 20 liters/hour reduced consumption but not the rate of decay of catalyst activity.

Consumption fell from 73 to 66% at 325° after the passage of 16 moles (1632 g.) of alcohol. At 350° consumption, originally 90%, was halved after the passage of 12 moles. At higher temperatures consumption fell off more rapidly, thus at 520° it fell to 20% after the passage of only 3 moles of alcohol.

Acrolein was detectable at 390° using hydrogen as carrier gas (5 liters/hour). The product, b. p. above 160°, at various temperatures contained the following amounts of tetrahydrofurfuryl alcohol: 67.1 (325°), 66.8 (350°), 66.8 (400°), 64.7 (450°), 65.0 (490°) and 63.0% (520°).

Reduction of pressure lowered consumption. At 8 mm. consumption (input 0.5 mole/hour) was 65% and yield of dihydropyran 61%.

Summary

1. 2,3-Dihydropyran has been shown to split into acrolein and ethylene on heating the vapor to temperatures in the region 400–500°.
2. Tetrahydrofurfuryl alcohol is readily dehydrated at low temperatures over Alumina (250–300°) to give dihydropyran, but acrolein is not formed at high temperatures since the dihydropyran first formed is dehydrated further before it can split.
3. An aluminum silicate catalyst can be used at high temperatures to convert tetrahydrofurfuryl alcohol directly into acrolein.

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[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, UNIVERSITY OF WISCONSIN]

Streptolin, a New Antibiotic from a Species of Streptomyces[1]

BY R. W. RIVETT AND W. H. PETERSON

Actinomycetes have been the source of several antibiotics, among which the most important are streptothricin[1a] and streptomycin.[2] In the course of an extensive survey of actinomycetes isolated from soil, a culture has now been found which is capable of producing in submerged fermentations an antibacterial substance, highly active against both gram-negative and gram-positive bacteria. This culture has been designated *Streptomyces* No. 11 and the antibiotic isolated from its culture filtrates has been named *streptolin*. Some of the factors affecting the production of streptolin by *Streptomyces* No. 11 were investigated and the chemical, physical and biological properties of streptolin studied.

Fermentations were carried out in flasks shaken continuously in order to find a suitable medium for the production of streptolin. A soybean meal–glucose medium (medium B, Table I) allowed the formation of the highest yields of streptolin in shaken flasks. Medium A was used in larger scale production with very good results, but gave only 7500 units[3] per ml. in shaken flasks. A nitrate–glucose synthetic medium, C, produced 10,400 units per ml. (Table I).

TABLE I

PRODUCTION OF STREPTOLIN IN SHAKEN FLASKS

	Media	Max. yield, units/ml.	Age, hr.
A.	1% soybean meal, 1% corn steep (solids), 1% glucose, 0.5% NaCl, 0.1% $CaCO_3$	7,500	70
B.	2% soybean meal, 0.5% Curbay BG, 2% glucose, 1% NaCl, 0.1% $CaCO_3$	35,000	72
C.	0.05% NH_4NO_3, 0.5% $NaNO_3$, 0.05% $MgSO_4 \cdot 7H_2O$, 0.005% $FeSO_4 \cdot 7H_2O$, 1% glucose, 0.1% $CaCO_3$, 0.6% K_2HPO_4[a]	10,400	77

[a] Sterilized phosphate was added to the other ingredients after sterilization bringing the *p*H to 8.

For the production of larger batches of fermented medium suitable for the isolation of streptolin, 30-liter laboratory fermenters were employed. The highest yields, 48,000 units per ml., were obtained on medium A, Table II. Medium D, differing only slightly from medium B, Table I, gave about 75% of the yield obtained in shaken flasks. A synthetic medium, E, gave approximately the same yield as was obtained in flask cultures on medium C.

TABLE II

PRODUCTION OF STREPTOLIN IN 30-LITER FERMENTERS

	Media	Max. yield units/ml.	Age, hr.
A.	1% soybean meal, 1% corn steep (solids), 1% glucose, 0.5% NaCl, 0.1% $CaCO_3$	48,600	70
D.	2% soybean meal, 0.25% Curbay BG, 2% glucose, 1% NaCl, 0.1% $CaCO_3$	27,300	65
E.	0.3% NH_4NO_3, 1% glucose, 0.3% NaCl, 0.05% $MgSO_4 \cdot 7H_2O$, 0.005% $FeSO_4 \cdot 7H_2O$, 0.1% $CaCO_3$ and 0.5% K_2HPO_4[a]	8,900	93

[a] Added after sterilization bringing *p*H to 8.

In an effort to increase the yield of streptolin on Medium B in the fermenters, a series of runs were made in which agitation and aeration were

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(1) Published with the approval of the Director of the Wisconsin Experiment Station. Supported in part by grants from The Upjohn Company and Abbott Laboratories.

(1a) Waksman and Woodruff, *Proc. Soc. Exptl. Biol. Med.*, **49**, 207 (1942).

(2) Schatz, Bugie and Waksman, *ibid.*, **55**, 66 (1944).

(3) A unit of streptolin was defined as that amount which when dissolved in one ml. of 0.75% peptone, 0.25% yeast extract broth at *p*H 7.2 would just inhibit the growth of *Escherichia coli* H52 during an eighteen–twenty hour incubation at 37°, when the inoculum was 0.00005 ml. of a twenty-hour broth culture per ml.