[Contribution from the School of Chemistry, University of Minnesota]

The Preparation of Cyclic Vinyl Ethers

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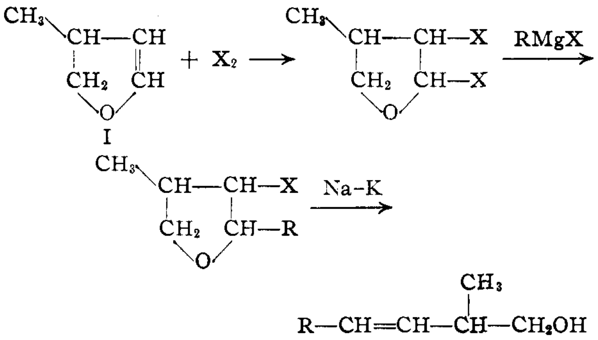
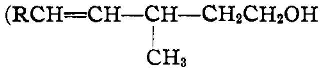
A convenient synthesis of 3-methyl-2,3-dihydrofuran and 4-methyl-3,4-dihydro-2H-pyran from readily available starting materials has been achieved. The application of these cyclic ethers to the synthesis of compounds containing isoprene units as part of their structure is discussed.

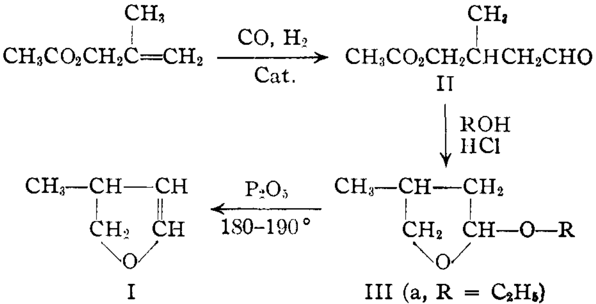
The hydroformylation of methallyl acetate results in the formation of γ-acetoxy-β-methylbutyraldehyde. The structure of this compound was established by oxidation and by its conversion to 2-alkoxy-4-methyltetrahydrofuran. The pyrolysis of 2-alkoxy-4-methyltetrahydrofuran results in the formation of 3-methyl-2,3-dihydrofuran.

The condensation of crotonaldehyde with vinyl *n*-butyl ether results in the formation of 2-*n*-butoxy-4-methyl-3,4-dihydro-2H-pyran, which yields 4-methyl-3,4-dihydro-2H-pyran upon reduction and dealkoxylation.



The present work was initiated with the object of developing an expedient synthesis for the hitherto unknown 3-alkyl-2,3-dihydrofurans and 4-alkyl-3,4-dihydro-2H-pyrans. Our interest in these cyclic vinyl ethers stems from their possible application as intermediates for the synthesis of compounds which contain one or more isoprene units as part of their structure. As shown in the accompanying flow sheet, an extension of the olefin synthesis previously described starting with dihydropyran[2] to 3-methyl-2,3-dihydrofuran (I) should offer a convenient method for the stepwise introduction of an isoprene unit into organic compounds which form Grignard reagents. Similarly, the extension of the reaction to 4-methyl-3,4-dihydro-2H-pyran (VI) should result in the formation of compounds  $(RCH{=}CH\text{—}\underset{CH_3}{CH}\text{—}CH_2CH_2OH$ structurally related to certain natural products (vitamin A, phytol, etc.). A convenient synthesis for 3-methyl-2,3-dihydrofuran (I) and 4-methyl-3,4-dihydro-2H-pyran (VI) from readily available starting materials has now been achieved and is the subject of this report.

The hydroformylation of methallyl acetate with carbon monoxide and hydrogen, effected by the general procedure developed by Adkins and Krsek[3] for the preparation of aldehydes from olefins, resulted in the formation of γ-acetoxy-β-methylbutyraldehyde (II) in 64% yield. When II was treated with excess ethyl or *n*-butyl alcohol and a trace of hydrogen chloride, ester interchange and acetal formation took place[4] resulting in the formation of 2-alkoxy-4-methyltetrahydrofuran (III) (yield of IIIb 69%). Proof that the hydroformylation of methylallyl acetate introduced the aldehyde group on the terminal carbon atom was afforded by the oxidation of II to methylsuccinic acid, identified by mixed melting point determination of the acid with an authentic sample, and by the conversion of II to the cyclic acetal III. The other possible product from the hydroformylation, β-acetoxy - α,α - dimethylpropionaldehyde, could cyclize only to a four-membered ring. The possibility of intermolecular acetal formation was eliminated by molecular weight determinations on IIIb. The pyrolysis of IIIb in the presence of catalytic amounts of phosphoric anhydride[5] resulted in the formation of *n*-butyl alcohol and 3-methyl-2,3-dihydrofuran (I) in 42–55% yield. 3-Methyl-2,3-dihydrofuran was observed to decolorize bromine rapidly and had the composition calculated for C_5H_8O. Additional evidence for the structure of I was its conversion into the 2,4-dinitrophenylhydrazone of γ-hydroxy-β-methylbutyraldehyde. The 2,4-dinitrophenylhydrazone of γ-hydroxy-β-methylbutyraldehyde was also obtained from II and IIIb.



4-Methyl-3,4-dihydro-2H-pyran (VI) was prepared from crotonaldehyde and vinyl *n*-butyl ether as outlined by the equations below.

The condensation of crotonaldehyde and vinyl *n*-butyl ether was effected in a manner similar to that reported[6] for the condensation of crotonaldehyde and vinyl methyl ether. Catalytic reduction of IV resulted in the formation (93% yield) of 2-*n*-butoxy-4-methyltetrahydropyran (V) which was dealkoxylated by pyrolysis in the presence of phosphoric anhydride to give a 75% yield of 4-methyl-3,4-dihydro-2H-pyran (VI). The mix-

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[1] Abstracted from the thesis of H. E. Holmquist presented in partial fulfillment for the Degree of Doctor of Philosophy in Chemistry.

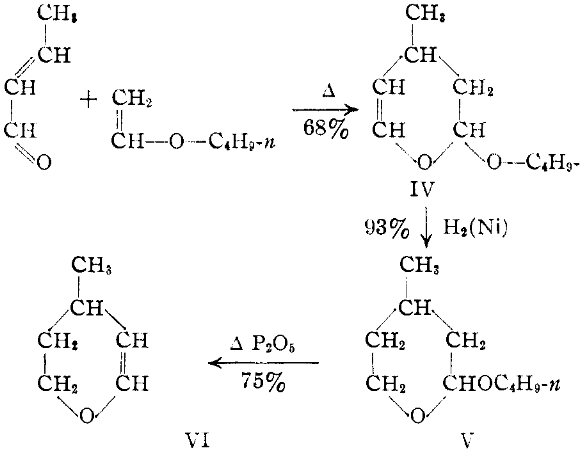
[2] (a) Paul and Riobe, *Compt. rend.*, **224**, 474 (1947); (b) Riobe, *Ann. Chim.*, [12] **4**, 593 (1949); (c) Jacobson, This Journal, **72**, 1489 (1950); (d) Brandon, Derfer and Boord, *ibid.*, **72**, 2120 (1950).

[3] Adkins and Krsek, *ibid.*, **70**, 383 (1948); **71**, 3051 (1949).

[4] *Cf.* Parham, *ibid.*, **69**, 2449 (1947); Paul, *Compt. rend.*, **215**, 303 (1942), for the cyclization of hydroxy acetals and hydroxy aldehydes.

[5] *Cf.* Claisen, *Ber.*, **29**, 2931 (1896); **31**, 1019 (1898), for the dealkoxylation of other acetals.

[6] Smith, Norton and Ballard (to Shell Development Company), U. S. Patent 2,514,168 (July 4, 1950); Langley and Emerson, This Journal, **72**, 3079 (1950).



ture of alcohol and VI obtained from the pyrolysis of V could not be separated satisfactorily by fractionation alone; however, the alcohol was easily removed by heating with phenyl isocyanate or sodium. Evidence for the structure of VI was afforded by its unsaturation, composition, and conversion into a 2,4-dinitrophenylhydrazone identical to that obtained from V, and regarded as that of δ-hydroxy-β-methylvaleraldehyde.

The application of these unsaturated ethers to the synthesis of compounds related to phytol and vitamin A is being investigated.

Experimental

γ - Acetoxy - β - methylbutyraldehyde (II).—The hydroformylation of methallyl acetate was carried out in a 270-ml. steel bomb. In each run, 50 to 53 g. of methallyl acetate,[7] 5 to 10 ml. of a 10–13% solution of dicobalt octacarbonyl in ether,[3] and 50 ml. of anhydrous ether were used. The initial pressure of carbon monoxide and hydrogen (1:1 ratio) varied from 3500 to 3600 p.s.i. and the final pressure in the cooled bomb from 1450 to 1650 p.s.i. The reaction started at 135–140°. The product from seven runs (364 g., 3.19 moles of methallyl acetate) was distilled to give 294 g. (64%) of the aldehyde, boiling at 78–83° (8 mm.). Oxidation of I first with cold acidic potassium permanganate and then with hot alkaline potassium permanganate gave methylsuccinic acid, which showed no depression in melting point when mixed with a sample prepared according to the directions in "Organic Syntheses."[8]

γ-Acetoxy-β-methylbutyraldehyde-2,4-dinitrophenylhydrazone.—This hydrazone was prepared in the usual way[9] from γ-acetoxy-β-methylbutyraldehyde. The hydrazone was recrystallized from petroleum ether, m.p. 56°.

Anal. Calcd. for $C_{13}H_{16}O_6N_4$: C, 48.14; H, 4.97. Found: C, 48.33; H, 5.16.

2-Ethoxy-4-methyltetrahydrofuran (IIIa).—A mixture of 35 ml. of anhydrous ethanol, through which dry hydrogen chloride had been passed for a few seconds, and 14.0 g. (0.097 mole) of II was heated under reflux for 5 hours. Anhydrous potassium carbonate and magnesium sulfate were added to the cooled solution, which was filtered and fractionated through a six-inch glass helix-packed column. The yield of IIa, boiling at 135–139°, was 7.0 g. (55%). A redistilled sample, b.p. 139°, n^{21}D 1.4130, was submitted for analysis.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.57; H, 10.84. Found: C, 64.38; H, 11.16.

2-*n*-Butoxy-4-methyltetrahydrofuran (IIIb).—Dry hydrogen chloride was passed through 250 ml. of freshly distilled *n*-butyl alcohol for a few seconds. After the addition of 65.9 g. (0.46 mole) of II, the solution was heated under reflux for 6 hours. The mixture was cooled and dried over anhydrous potassium carbonate and magnesium sulfate. The product was fractionated through a metal-packed column to yield 50.5 g. (69%) of IIIb, b.p. 180–186°. A redistilled sample, b.p. 185°, n^{19}D 1.4230, was submitted for analysis.

Anal. Calcd. for $C_9H_{18}O_2$: C, 68.31; H, 11.47; mol. wt., 158. Found: C, 68.10; H, 11.42; mol. wt., 154, 160 (f.p. benzene).

3-Methyl-2,3-dihydrofuran (I).—A trace of phosphoric anhydride was added to 87.0 g. (0.55 mole) of IIIb which was heated in an oil-bath at 180–190°. The mixture of I and *n*-butyl alcohol was distilled as formed (4 to 5 hours) into anhydrous sodium carbonate. The combined distillate was redistilled. The fractions boiling below 115° were refluxed with sodium for one-half hour and then fractionated through a small Vigreux-type column to give 19.6 g. (42%) of I, b.p. 69–74°. The fractions boiling above 115° were refractionated to give 19.0 g. (13%) of unchanged IIIb. A sample of I was redistilled for analysis, b.p. 69.5–70°, n^{25}D 1.4161.

Anal. Calcd. for C_5H_8O: C, 71.36; H, 9.59. Found: C, 71.56; H, 9.89.

γ - Hydroxy - β - methylbutyraldehyde - 2,4 - dinitrophenylhydrazone.—This hydrazone was obtained in the usual manner[9] from both IIIb and I, m.p. 101.5–102° (recrystallized from ethyl acetate–petroleum ether). The same hydrazone was also obtained by the acid hydrolysis of γ-acetoxy - β - methylbutyraldehyde - 2,4 - dinitrophenylhydrazone. Mixed melting points of the various samples showed no depression.

Anal. Calcd. for $C_{11}H_{14}O_5N_4$: C, 46.80; H, 5.00. Found: C, 46.83; H, 5.00.

2-*n*-Butoxy-4-methyl-3,4-dihydro-2H-pyran (IV).—A mixture of 400 g. (5.72 moles) of crotonaldehyde (tech., Eastman Kodak Co.) and 572 g. (5.72 moles) of vinyl *n*-butyl ether (tech., General Aniline and Film Corp.) was placed in a 1850-ml. steel bomb and heated rapidly at 225°. This temperature was maintained for 1 hour. The temperature was then allowed to drop slowly to 125° over a period of 2 hours and then the heating was stopped. The yield of crude IV, boiling at 76–82° (14–15 mm.) was 663 g. (68%). A redistilled sample, b.p. 75.5° (12 mm.), n^{25}D 1.4383, was submitted for analysis.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.39; H, 10.97.

2-*n*-Butoxy-4-methyltetrahydropyran (V).—To 620 g. (3.65 moles) of IV (b.p. 76–82°) in a 1850-ml. steel bomb were added twelve teaspoons (about 36 g.) of Raney nickel in absolute ethanol. Hydrogen was introduced at a pressure of 2120 p.s.i. and reduction was complete 25 minutes after shaking was begun (the temperature rose to 50° immediately due to the heat of reaction). The crude product boiling at 79–86° (4–5 mm.), weighed 586 g. (93%). A redistilled sample, b.p. 91° (16 mm.), n^{25}D 1.4308, was submitted for analysis.

Anal. Calcd. for $C_{10}H_{20}O_2$: C, 69.72; H, 11.70. Found: C, 69.40; H, 11.61.

4-Methyl-3,4-dihydro-2H-pyran (VI).—The dealkoxylation of 89.2 g. (0.52 mole) of V was carried out in the same manner as described for IIIb. Fractionation of the distillate (collected over anhydrous sodium carbonate) boiling at 107–109° gave *n*-butyl alcohol and an azeotrope (b.p. 100°; n^{25}D 1.4250) containing approximately 28% alcohol. The azeotrope was boiled for 5 minutes with 50 g. of phenyl isocyanate and the product distilled. There was obtained 33.8 g. (66%) of VI distilling at 98–103°. The pure compound, distilled from sodium, boiled at 101.0–101.5°, n^{25}D 1.4350.

Anal. Calcd. for $C_6H_{10}O$: C, 73.42; H, 10.27. Found: C, 73.12; H, 10.47.

In subsequent runs the use of phenyl isocyanate was discontinued in the purification of VI. The butyl alcohol was removed by refluxing crude VI with excess sodium for several hours prior to distillation (yield 75%).

δ-Hydroxy-β-methylvaleraldehyde-2,4-dinitrophenylhydrazone.—This hydrazone was obtained in the usual manner[9] from both V and VI, m.p. 108–109° (recrystallized from chloroform–petroleum ether). A mixed melting point of the two samples showed no depression.

Anal. Calcd. for $C_{12}H_{16}O_5N_4$: C, 48.64; H, 5.44. Found: C, 48.51; H, 5.38.

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RECEIVED JULY 31, 1950

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[7] Ryan and Shaw, THIS JOURNAL, **62**, 3469 (1940).

[8] *Org. Syntheses*, **26**, 54 (1946).

[9] Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1940, p. 143.