tetrahydropyran-4-ol, b. p. 84–89° (18 mm.) gave 20 g. (88% yield) of product of b. p. 129.0–136.6° (763 mm.), approximately 90%, of which, on redistillation, boiled at 133.0–136.2° (763 mm.) and had n^{20}_{D} 1.4410 and d^{20}_{4} 0.8622.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 75.86; H, 11.20.

The infrared absorption spectrum of this material was almost exactly identical with that of the pyran mixture obtained on dehydration of 2-methyl-2,4-pentanediol and showed the presence of both of the isomeric pyrans in approximately the same relative proportions as in material from the latter source.

Summary

Among the by-products of the dehydration of 2-methyl-2,4-pentanediol have been found acetaldehyde, isobutylene and a mixture of pyrans consisting of 3,6-dihydro-2,4,6-trimethyl-2H-pyran along with a minor amount of 2,6-dimethyl-4-methylenetetrahydropyran.

EMERYVILLE 8, CALIFORNIA RECEIVED MAY 8, 1950

[A CONTRIBUTION FROM THE LABORATORIES OF THE SHELL DEVELOPMENT COMPANY]

A Synthesis of Substituted Pyrans

BY PAUL H. WILLIAMS, GEORGE G. ECKE AND SEAVER A. BALLARD

In the preceding paper[1] it was reported that the dehydration of 2-methyl-2,4-pentanediol gives as one of its products 3,6-dihydro-2,4,6-trimethyl-2H-pyran (I) along with a minor amount of a substance believed to be 2,6-dimethyl-4-methylenetetrahydropyran (II). Further investigation has indicated a mechanism for the formation of these compounds and has shown that the reactions involved can be generalized for the production of a variety of pyrans.[2]

Mechanism of Formation of the Pyrans.—The dehydration of 2-methyl-2,4-pentanediol gives under the conditions employed in the work described in the preceding paper largely 2-methyl- and 4-methyl-1,3-pentadienes along with 4-methyl-4-penten-2-ol, acetaldehyde, isobutylene and the aforementioned pyrans. Inasmuch as the pyrans contain eight carbon atoms, it was suspected that they are formed by reaction of acetaldehyde with either the diol, the methylpentadienes, or 4-methyl-4-penten-2-ol, and a number of experiments were performed in order to ascertain which of these combinations was their most likely source.

Acetaldehyde and 2-methyl-2,4-pentanediol were found to combine readily at about room temperature in the presence of acidic catalysts to give high yields of the cyclic acetal, 2,4,4,6-tetramethyl-*m*-dioxane. This compound decomposes slowly when heated at its boiling point with a trace of hydriodic acid and more rapidly with several volumes of very dilute hydrochloric acid[3] with formation of methylpentadiene, acetaldehyde and water.

Acetaldehyde and methylpentadiene, along with a trace of hydriodic acid, did not combine at room temperature, but interaction did occur slowly when the mixture was heated at 130–135° (under pressure) for five hours. From this reaction was obtained a fraction, representing a 10–15% conversion of the reactants, which appeared from its elemental composition, properties and infrared spectrum to be an impure mixture of the two pyrans and/or their isomers; a small amount of very high boiling condensation product was also obtained. Acetaldehyde and the diene at 185° (under pressure) in the absence of an acid catalyst formed only very high boiling condensation products.

The interaction of acetaldehyde and 4-methyl-4-penten-2-ol on the other hand took place very readily at below room temperature in the presence of acid with formation of 3,6-dihydro-2,4,6-trimethyl-2H-pyran (I) and 2,6-dimethyl-4-methylenetetrahydropyran (II), as well as 2,4,6-trimethyltetrahydropyran-4-ol (III)[4] and a substance of composition $C_{14}H_{26}O_2$ which may be the 4-methyl-4-penten-2-yl ether of III or possibly of 4-methyl-3-heptene-2,6-diol (see footnote 9); formation of higher condensates was negligible.

It thus appears that formation of the pyrans I and II during the dehydration of 2-methyl-2,4-pentanediol takes place by the interaction of acetaldehyde and either methylpentadiene or 4-methyl-4-penten-2-ol or both. However, in view of the ease with which the alcohol reacts, it is believed that this substance is the chief source of the pyrans formed during the diol dehydration.

Both the dehydration of the diol and the condensation between acetaldehyde and 4-methyl-4-penten-2-ol were found to be promoted by a variety of acid-acting substances. Suitable catalysts for the condensation were sulfuric and hydrochloric acids and anhydrous ferric chloride, all resulting in formation of the two pyrans (I and II) and 2,4,6-trimethyltetrahydropyran-4-ol (III); the use of anhydrous calcium chloride, however, yielded only the acetal of 4-methyl-4-penten-2-ol.

The initial step in the reaction between acetaldehyde and the unsaturated alcohol could be postulated to occur either at the olefinic linkage or at the hydroxyl group of the alcohol. In considering the first of these alternatives, the literature on the extensive studies of the reaction of aldehydes, particularly formaldehyde (and its polymeric forms),

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(1) Ballard, Holm, and Williams THIS JOURNAL, **72**, 5734 (1950).

(2) Williams and Ballard (to Shell Development Co.), U. S. Patents 2,422,648 (June 17, 1947) and 2,452,977 (Nov. 2, 1948).

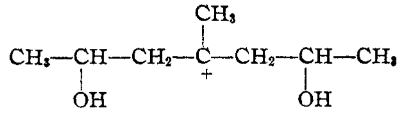
(3) Mikeska and Arundale (to Jasco, Inc.), U. S. Patent 2,350,517 (June 6, 1944).

(4) The steps leading to this product are apparently very stereoselective since but one of the three theoretically possible geometrical isomers was isolated from the reaction mixture.

with olefins was reviewed. The Prins reaction,[5] as the formaldehyde–olefins reactions have generally been known, is postulated as essentially an acid-catalyzed addition of formaldehyde (presumably in form of a protonated intermediate, $^+CH_2OH$) to the double bond of an olefin; although it is also considered that α-methylenic reactivity may contribute under certain conditions to the course of the reaction and the nature of its products.[6] The Prins reaction has been applied to a variety of unsaturated hydrocarbons,[7] giving chiefly *m*-dioxanes and primary unsaturated alcohols; mono- and diacetates of 1,3-diols have resulted when the condensations have been effected in acetic–sulfuric acid medium. The formation of primary unsaturated alcohols seems to be especially favored by the use of tertiary olefins under anhydrous conditions.[7e]

The Prins reaction has been extended by Emerson[8] to the condensation of higher aliphatic aldehydes with styrene giving 1,3-dienes as well as products analogous to those obtained with formaldehyde; and phenylglyoxal has been condensed with methylenecyclohexane with formation of a substance regarded as β-(Δ¹-cyclohexenyl)-α-hydroxypropiophenone.[7c]

Should the reaction of acetaldehyde with 4-methyl-4-penten-2-ol proceed by addition of the carbonyl group to the unsaturated linkage, there would presumably be formed



$$CH_3-\underset{OH}{\underset{|}{CH}}-CH_2-\overset{CH_3}{\overset{|}{\underset{+}{C}}}-CH_2-\underset{OH}{\underset{|}{CH}}-CH_3$$

which might lead in turn to the pyran derivatives and/or to intermediates analogous to those which have been obtained as products in the aldehyde–olefin reactions. Under the mild conditions of the present reaction, the more stable of these possible intermediates, *e. g.*, a *m*-dioxane, would be expected among the final products; however, no such substances have been isolated.

If, alternatively, the reaction involves condensation of the carbonyl group with the hydroxyl of the unsaturated alcohol, hemiacetal formation would obviously be the first step. The hemiacetal (or the acetal) would be susceptible to electrophilic attack by the catalyst, thus forming a carbonium ion (possibly through an intermediate oxonium ion) which could then cyclize to the pyran ring by intramolecular coupling of the carbonium ion with a pair of electrons of the multiple carbon–carbon linkage[9]; the ltater step is superficially very similar to the initial step of the previously postulated mechanism, *i. e.*, addition of the protonated carbonyl group to the olefinic linkage, and would be facilitated by the ease of six-membered ring formation. This course may be illustrated as shown (p. 5740).

This mechanism is somewhat analogous to that proposed for the acid-catalyzed cyclization of citral and citronellal which may be considered an internal Prins reaction[10]; the formation of a 3-ethoxy-*p*-menthadiene in the attempted acetalization of citral[11] may proceed in a like manner.

Either or both of the two postulated mechanisms would appear to be applicable to the present reaction. However, the mechanism involving direct addition of aldehyde to the olefinic linkage seems the less likely one since, with few exceptions, aldehydes other than formaldehyde are not reported to have been combined with olefins in the Prins and related reactions; whereas not only a number of aldehydes, but also several ketones have been shown in this study to combine with the unsaturated alcohol to give substances of the pyran structure. For this reason, as well as the fact that it seems more consistent with the known products of the reaction, the authors favor the second mechanism as a representation of the reaction's course.

As to the reaction between methylpentadiene and acetaldehyde, Gresham and Steadman[12] have reported an ostensibly comparable reaction in the formation of 2,4-dimethyl-3,6-dihydro-2H-pyran from α-polyoxymethylene and methylpentadiene at 185° under pressure (in the absence of an acidic catalyst). They have postulated the latter to be a Diels–Alder reaction in which formaldehyde participates as a dienophile and have suggested that a similar mechanism would account for the formation of pyrans I and II by the reaction of acetaldehyde and the diene. As previously noted, *acetaldehyde* and methylpentadiene combined at elevated temperature, in the presence of an acid catalyst, but gave only a low yield of material which may have been pyrans I and II along with isomeric pyrans.

Reaction of Other Aldehydes and Ketones with 4-Methyl-4-penten-2-ol.—Crotonaldehyde and benzaldehyde reacted with 4-methyl-4-penten-2-ol in a manner similar to acetaldehyde. Crotonaldehyde yielded three products which apparently have structures analogous to those obtained with acetaldehyde. With benzaldehyde, only one product was isolated and its composition corresponded to the expected pyrans.

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[5] Prins, *Chem. Weekblad*, **14**, 932 (1917); **16**, 1072, 1510 (1919); *Proc. Acad. Sci., Amsterdam*, **22**, 51 (1919); Baker, *J. Chem. Soc.*, 296 (1944); 89 (1948).

[6] Baker, ref. 5, suggests that in the Prins reaction with propylene and acetic–sulfuric acid, the unsaturated linkage and an α-methylenic hydrogen of the olefin are both reactive and he employs a mechanism involving direct reaction of formaldehyde with an α-methylenic hydrogen to account for the formation of the acetate of tetrahydropyran-4-ol. The latter step of this mechanism, as postulated by Baker, appears to hold some similarity to the one later herein advanced involving a hemiacetal intermediate.

[7] (a) Bain, THIS JOURNAL, **68**, 638 (1946); (b) Shortridge, *ibid.*, **70**, 873 (1948); (c) Arnold and Dowdall, *ibid.*, **70**, 2590 (1948); (d) Price, Benton and Schmidle, *ibid.*, **71**, 2860 (1949); (e) Mikeska and Arundale (to Standard Oil Development Co.), U. S. Patent 2,308,192 (Jan. 12, 1943).

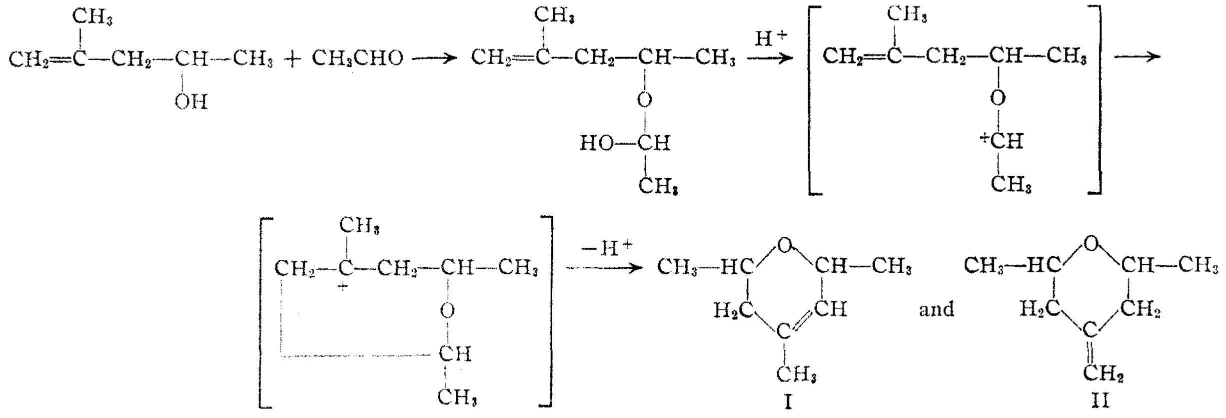
[8] Emerson, *J. Org. Chem.*, **10**, 464 (1945).

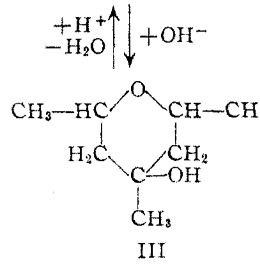
[9] Intermolecular reaction between the carbonium ion and the unsaturated linkage of the methylpentenol or its hemiacetal might also occur, leading to the 4-methyl-4-penten-2-yl monoether of 4-methyl-3-heptene-2,6-diol.

[10] Price and Dickman, *Ind. Eng. Chem.*, **40**, 257 (1948); Price and Pappalardo, THIS JOURNAL, **72**, 2613 (1950).

[11] Sigmund and Herschdörfer, *Monatsh.*, **58**, 268 (1931).

[12] Gresham and Steadman, THIS JOURNAL, **71**, 737 (1949).



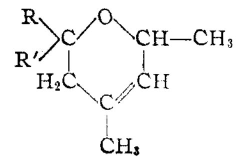


Reaction of ketones with 4-methyl-4-penten-2-ol was not observed at room temperature, but it did occur at temperatures of 90 to 100°. Acetone, acetophenone, cyclohexanone, mesityl oxide, methyl ethyl ketone, methyl isobutyl ketone and 3,3,5-trimethylcyclohexanone gave good yields of products which corresponded in elemental composition to substituted pyrans analogous to those obtained with acetaldehyde and the alcohol; pyranols and other intermediate by-products were not obtained, presumably due to their easy decomposition to the pyrans under the conditions of the reactions.

Identification of the Reaction Products.—The mixture of pyrans (I and II) from the reaction of acetaldehyde and the unsaturated alcohol corresponded in physical properties and infrared absorption spectrum to an independently synthesized mixture of I and II. 2,4,6-Trimethyltetrahydropyran-4-ol (III) was identified by its elemental composition and physical properties, and by mixed melting point taken with an independently synthesized sample. The structure of a fourth product was not determined, but it is believed from its elemental composition, which corresponds to the empirical formula $C_{14}H_{26}O_2$, to be derived from two molecules of 4-methyl-4-penten-2-ol and one of acetaldehyde; it did not, however, behave chemically as an acetal.

The proposed structures for the substances obtained by reaction of the other aldehydes and the ketones are based on the elemental compositions of these substances and on analogy between the reactions by which they were formed and the reaction of acetaldehyde with the alcohol. The formation and structures of these pyrans are illustrated by the general equation

$$R{-}CO{-}R' + CH_2{=}C(CH_3)CH_2CHOHCH_3 \xrightarrow{-H_2O}$$



where R–CO–R′ represents the aldehyde or ketone employed. Each reaction product may actually be a mixture of isomeric pyrans which differ in respect to the position of the unsaturation about the position 4 carbon atom; where R or R′ represents an alkenyl group, the double linkage of the latter may have migrated, perhaps even into the ring.

Acknowledgment.—The authors thank Drs. R. R. Brattain and the late R. S. Rasmussen of Shell Development Company for determining and interpreting the infrared spectra discussed in this paper and Mr. R. T. Holm for assistance in carrying out some of the reactions.

Experimental[13]

Materials.—Acetaldehyde, benzaldehyde, crotonaldehyde, acetophenone and cyclohexanone were obtained from the Eastman Kodak Company. Acetone, mesityl oxide, methyl ethyl ketone, methyl isobutyl ketone, and 2-methyl-2,4-pentanediol were obtained from the Shell Chemical Corporation.

3,3,5-Trimethylcyclohexanone was prepared by hydrogenation of isophorone over Raney nickel. 3,3,5-Trimethylcyclohexanol, present as impurity, was removed by refluxing in the presence of sodium bisulfate. Distillation yielded substantially pure 3,3,5-trimethylcyclohexanone boiling at 189–190° (759 mm.).

Methylpentadiene (a mixture composed of about 85% 2-methyl-1,3-pentadiene and 15% 4-methyl-1,3-pentadiene) was prepared by dehydration of 2-methyl-2,4-pentanediol. It distilled at 75–77° (760 mm.) and was redistilled just prior to use. 4-Methyl-4-penten-2-ol was obtained as a crude material (containing 70 to 80% alcohol) as a coproduct of the dehydration of 2-methyl-2,4-pentanediol over copper sulfate. This material was repeatedly steam distilled through an efficient fractionating column over a temperature range of 92 to 94.4°. The fraction boiling at 94.4° after removal of water distilled at 130.5 to 130.8° and was shown to be 99% alcohol on reaction with acetyl chloride-pyridine reagent.[14]

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(13) See footnote 12, preceding paper.

(14) Smith and Bryant, This Journal, 57, 61 (1935).

TABLE I

PRODUCTS OF THE REACTION OF 4-METHYL-4-PENTEN-2-OL WITH ALDEHYDES AND KETONES

Aldehyde or ketone reacted	Product (or isomers), pyran	Boiling point °C.	Mm.	n^{20}_D	d^{20}_4	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
Acetaldehyde	3,6-Dihydro-2,4,6-trimethyl-2H-	132–139	760	1.4403	0.8638	$C_8H_{14}O$	76.14	76.50	11.18	10.90
Benzaldehyde	3,6-Dihydro-2,4-dimethyl-6-phenyl-2H-	107.2	5	1.5269	.9869	$C_{13}H_{16}O$	82.92	83.02	8.58	8.57
Crotonaldehyde	3,6-Dihydro-2,4-dimethyl-6-(1-propenyl)-2H-	182.0–184.2	766	1.4643	.8854	$C_{10}H_{16}O$	78.89	78.39	10.59	10.61
Acetophenone	3,6-Dihydro-2,4,6-trimethyl-6-phenyl-2H-	60.4–60.8	1	1.5225	.9825	$C_{14}H_{18}O$	83.12	82.83	8.97	9.05
Cyclohexanone	3,6-Dihydro-2,4-dimethyl-6,6-pentamethylene-2H-	87.4	10	1.4770	.9308	$C_{12}H_{20}O$	79.94	79.86	11.18	11.26
Mesityl oxide	3,6-Dihydro-2-isocrotyl-2,4,6-trimethyl-2H-	60.0	5	1.4667	.8757	$C_{12}H_{20}O$	79.94	80.42	11.18	11.26
Methyl ethyl ketone	3,6-Dihydro-2-ethyl-2,4,6-trimethyl-2H-	164.5–165.0	759	1.4441	.8619	$C_{10}H_{18}O$	77.86	77.37	11.76	11.70
Methyl isobutyl ketone	3,6-Dihydro-2-isobutyl-2,4,6-trimethyl-2H-	103.3–104.6	40	1.4492	.8564	$C_{12}H_{22}O$	79.06	79.11	12.16	12.18
3,3,5-Trimethylcyclohexanone	3,6-Dihydro-2,4-dimethyl-6,6-(2,2,4-trimethylpentamethylene)-2H-	94.7	5	1.4720	.9018	$C_{15}H_{26}O$	81.02	81.09	11.79	11.81

Reaction of Acetaldehyde with 2-Methyl-2,4-pentanediol.—A 455-g. (10.4 moles) quantity of acetaldehyde was slowly added to 1180 g. (10.0 moles) of the diol containing 2.0 g. of *p*-toluenesulfonic acid, maintaining the reaction mixture below 35° by cooling and stirring. After two hours the reaction mixture had separated into two layers, the lower of which (130 cc.) was aqueous. The upper layer was shaken with 10 g. of aqueous sodium carbonate and then distilled, yielding a fraction of b. p. 138.8–141.0° at 763 mm. (almost entirely at 141°, n^{20}_D 1.4205),[15] weight 1102 g. (84.5% conversion), and 186.5 g. of water-soluble residue assumed to be unreacted diol. The condensate reacted with aqueous ethanolic hydroxylamine (100°, 2 hours) to the extent of 96% (calculated as the cyclic acetal).

Refluxing 62 g. (0.43 mole) of this acetal with 0.5 ml. of 48% hydriodic acid for 1.5 hours resulted on distillation in a few ml. of distillate consisting of water, acetaldehyde and methylpentadiene; the major portion of the cyclic acetal was recovered unchanged.

Reaction of Acetaldehyde with Methylpentadiene.—Eighty-two grams (1.0 mole) of methylpentadiene, 44 g. (1.0 mole) of acetaldehyde, 0.4 ml. of 48% hydriodic acid and 1.0 ml. of water were shaken together in a glass bomb for five hours at 130–135°. The product consisted of a water phase (lower), weight 8 g., and a dark brown organic phase, weight 119 g. Distillation of the latter gave 20 g. (0.454 mole) of acetaldehyde, 43 g. (0.53 mole) of methylpentadiene, 27 g. of material of boiling range 123–166°, and 27 g. of a viscous residue. Redistillation of the material of boiling range 123–166° gave 11.6 g. of boiling range 132–140° which was collected in two fractions: Fraction (a), b. p. 132–136.5°, n^{20}_D 1.4448; fraction (b), b. p. 136.5–140°, n^{20}_D 1.4452.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: Fraction (a), C, 76.4; H, 11.2; fraction (b), C, 77.0; H, 11.4.

Each fraction reacted but negligibly with aqueous ethanolic hydroxyamine hydrochloride at 60° for two hours.

These two fractions were similar in odor to the pyran mixture from the diol dehydration; their infrared spectra were similar to those of pyrans I and II, but the presence of substantial amounts of impurities was apparent.

In a second run 82 g. (1.0 mole) of methylpentadiene and 44 g. (1.0 mole) of acetaldehyde were heated together in the absence of acid in a steel bomb at 185° and about 500 p.s.i.g. for six hours. On distillation of the homogeneous product (less 6 g. bomb leakage loss) about 27 g. (0.61 mole) of acetaldehyde and 15 g. (0.18 mole) of methylpentadiene were recovered and 40.5 g. of product (unidentified) distilling at 65–87° (20 mm.) (mainly 85–87°), and 37 g. of viscous residue were obtained. No product was found which distilled in the range of 130–140° (760 mm.).

Reaction of Aldehydes with 4-Methyl-4-penten-2-ol.—The procedure followed was the same for all of the aldehydes. 4-Methyl-4-penten-2-ol, containing 0.5 to 1.0 mole % of concentrated sulfuric acid, was added dropwise to an equal molar quantity of the aldehyde. During the addition the reaction mixture was stirred and maintained at 10 to 15° by external cooling. After standing about fifteen hours at room temperature, it was neutralized by shaking with an excess of saturated aqueous sodium carbonate solution and distilled. The various products obtained are discussed below. Analytical data and physical properties of the pyrans are given in Table I.

With Acetaldehyde.—Distillation of the reaction product of two moles each of alcohol and aldehyde gave three fractions:

Fraction 1, distilled at 119–160°, mainly 130–139°, weight 81 g. The acetyl value indicated the presence of 31% of 4-methyl-4-penten-2-ol. This was removed by dehydration to methylpentadiene in the presence of *p*-toluenesulfonic acid. The remaining material (52 g., 24% yield) distilling at 132–139°, was identified as a mixture of 3,6-dihydro-2,4,6-trimethyl-2H-pyran (I) and 2,6-dimethyl-4-methylenetetrahydropyran (II) by its elemental composition and physical properties (see Table I) and infrared absorption spectrum. The latter is identical with that of an authentic sample of the pyran mixture.[16]

Fraction 2, distilled at 160° (760 mm.) to 101° (18 mm.), (90% at 84–90° at 18 mm.), weight 122 g. (49% yield). This material solidified with the formation of fine white needles. Redistillation gave product boiling at 88–89° at 18 mm. (188–189° at 764 mm.), n^{20}_D 1.4528 and d^{20}_4 0.9667 (III). It solidified on standing.

Anal. Calcd. for $C_8H_{16}O_2$: C, 66.63; H, 11.18. Found: C, 66.67; H, 11.19.

On recrystallizing twice from isopentane, this material melted at 50.5–51.0°. It gave no melting point depression when mixed with a sample of the higher boiling, higher melting fraction of independently synthesized 2,4,6-trimethyltetrahydropyran-4-ol.[16] None of the lower boiling, lower melting form of the pyranol was isolated.

Dehydration of III in the presence of *p*-toluenesulfonic acid yielded (82%) the pyran mixture, b. p. 131–137°, n^{20}_D 1.4399 and d^{20}_4 0.8620.

Reaction of III with acetic anhydride gave an 83% yield of the acetate, b. p. 88–90° at 16 mm., saponification equivalent, 180 (calcd. for $C_8H_{15}O(OCOCH_3)$, 186.24).

Fraction 3, distilled at 89–117° at 10 mm. (mainly at 110–113°), weight 45.5 g. (23% yield). Redistillation gave material boiling at 111–112° at 10 mm., n^{20}_D 1.4526 and d^{20}_4 0.9043.

Anal. Calcd. for $C_{14}H_{26}O_2$: C, 74.28; H, 11.58. Found: C, 74.10; H, 11.60.

This material corresponds in composition to the acetal of 4-methyl-4-penten-2-ol and to the 4-methyl-4-penten-2-yl ether of either 2,4,6-trimethyltetrahydropyran-4-ol or 4-

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[15] Hill and Hibbert, THIS JOURNAL, **45**, 3108 (1923), report b. p. 139–140° for the cyclic acetal of 2-methyl-2,4-pentanediol prepared by treating the diol with acetylene, using mercuric sulfate as catalyst.

[16] See preceding paper for its synthesis from 2,6-dimethyltetrahydro-1,4-pyrone and methyl Grignard reagent.

TABLE II

REACTION OF KETONES WITH 4-METHYL-4-PENTEN-2-OL

Ketone reacted	Quantities of reactants,[a] moles Ketone	Quantities of reactants,[a] moles Alcohol	Benzene, g.	Product wt., g.	B. p. of product °C.	Mm.	Yield of product on ketone consumed, %
Acetone	2.0	1.0	None	21.0	139–143	771	80
Acetophenone	1.0	1.0	183	36.0	55–65 (90% at 60–61)	1	95
Cyclohexanone	1.5	1.5	200	191.8	80–90 (90% at 87–88)	10	91
Mesityl oxide	1.0	1.0	150	41.0	54–60 (90% at 58–59)	5	81[b]
Methyl ethyl ketone	2.0	1.0	None	95.2	160–166 (91% at 164–166)	758	75
Methyl isobutyl ketone	1.5	1.5	200	92.4	90–105 (90% at 98–103)	40	98
3,3,5-Trimethylcyclohexanone	1.5	1.5	250	182.3	90–96 (96% at 94–96)	5	94

[a] In addition, 2 g. of *p*-toluenesulfonic acid was added as catalyst. [b] Unreacted mesityl oxide and 4-methyl-4-penten-2-ol could not be separated from each other by distillation; unreacted mesityl oxide was determined quantitatively by reaction of the mixture with hydroxylamine hydrochloride.[14]

methyl-3-heptene-2,6-diol. It does not correspond in physical properties to the acetal (see below), however, and reacted to the extent of only 4.7% with aqueous ethanolic hydroxylamine hydrochloride at 100° for one hour. In the presence of a trace of *p*-toluenesulfonic acid at 140°, it gave an 88% yield of product identified by physical constants as the pyran mixture, as well as methylpentadiene and water, indicating either one of the two suggested ethers.

Reaction between 4-methyl-4-penten-2-ol and acetaldehyde with formation of the aforementioned products occurred also in the presence of hydrogen chloride (0.005 mole per mole of alcohol) and of anhydrous ferric chloride (0.01 mole per mole of alcohol). With anhydrous calcium chloride (Merck, reagent grade; 5 g. per mole each of alcohol and aldehyde) at room temperature for 18 hours, the only product obtained boiled at 101° at 10 mm. and had $n^{20}D$ 1.4391 and d^{20}_4 0.8604; weight 17.4 g. This material was treated with aqueous ethanolic hydroxylamine hydrochloride at 60° for two hours[17] and gave a carbonyl value of 0.426 equivalent per 100 g. (theory, 0.441 eq./100 g.); it is therefore regarded as the acetal of 4-methyl-4-penten-2-ol.

Anal. Calcd. for $C_{14}H_{26}O_2$: C, 74.28; H, 11.58. Found: C, 74.11; H, 11.60.

With Benzaldehyde.—From 3.0 moles each of benzaldehyde and 4-methyl-4-penten-2-ol was obtained 293 g. (62% yield) of product boiling at 100–108° at 5 mm. Analyses of a pure cut of this material showed it to have a composition corresponding to 3,6-dihydro-2,4-dimethyl-6-phenyl-2H-pyran. No other products, with the exception of water and a small amount of methylpentadiene, were isolated from the reaction mixture. Approximately 50 g. of the alcohol and 71.5 g. of benzaldehyde were recovered unchanged.

With Crotonaldehyde.—From 2.0 moles each of crotonaldehyde and 4-methyl-4-penten-2-ol were obtained the following fractions on distillation:

Fraction 1, distilled at 174–203°, weight 24 g. (12% yield). The elemental composition of a heart cut corresponded to that of 3,6-dihydro-2,4-dimethyl-6-(1-propenyl)-2H-pyran.

Fraction 2, distilled at 112–128° at 20 mm., weight 106 g. (47% yield). Redistillation gave material boiling at 122.8–123.0° at 20 mm., $n^{20}D$ 1.4730 and d^{20}_4 0.9690. Its composition corresponded to that of 2,4-dimethyl-6-(1-propenyl)-tetrahydropyran-4-ol.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.56; H, 10.57. Found: C, 70.54; H, 10.65.

Treatment of this product with 1% of *p*-toluenesulfonic acid at about 150° yielded material identical with that of fraction 1.

Fraction 3, distilled at 114–122° at 5 mm., weight 65.5 g. (40% yield). Redistillation gave material boiling at 121–122° at 5 mm., $n^{20}D$ 1.4675, d^{20}_4 0.9341.

Anal. Calcd. for $C_{16}H_{28}O_2$: C, 76.14; H, 11.18. Found: C, 73.53; H, 11.02.

This material may be analogous to the product obtained from acetaldehyde and the alcohol which was tentatively identified as an ether of the methylpentenol. It was investigated no further.

In addition to the above fractions, 70 g. of 4-methyl-4-penten-2-ol and 26 g. of crotonaldehyde were recovered unchanged.

Reaction of Ketones with 4-Methyl-4-penten-2-ol.—In each experiment the ketone and the alcohol were heated together under a column in the presence of *p*-toluenesulfonic acid. In most cases benzene was also added to the reaction mixture in order to maintain a reaction temperature in the neighborhood of 90–100° and to remove water azeotropically as formed. The reaction was generally continued until an approximately molar quantity of water was formed or until the rate of water formation had greatly diminished (5 to 15 hours). The quantity of water formed, however, was not a true measure of the extent of the desired reaction due to the fact that some dehydration of the alcohol also occurred during the period of reflux.

The reaction products were worked up by neutralization followed by distillation.

Data for the reaction of seven ketones with 4-methyl-4-penten-2-ol are summarized in Table II. Analytical and physical data for six of the products are given in Table I. The product of the reaction of acetone with the unsaturated alcohol is believed to be 3,6-dihydro-2,4,6,6-tetramethyl-2H-pyran, but it appeared on the basis of chemical analysis to contain a considerable amount of impurity. For this reason its analytical and physical data are not included in Table I. The purest fraction of this product distilled at 142.2–142.7° and had $n^{20}D$ 1.4400 and d^{20}_4 0.8587.

Summary

1. The reaction of acetaldehyde with 4-methyl-4-penten-2-ol has been found to yield 3,6-dihydro-2,4,6-trimethyl-2H-pyran, 2,6-dimethyl-4-methyl-

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[17] According to the method of Bryant and Smith, THIS JOURNAL, **57**, 57 (1935).

enetetrahydropyran, and 2,4,6-trimethyltetrahydropyran-4-ol. It is suggested that the formation of the two pyrans during the dehydration of 2-methyl-2,4-pentanediol occurs principally by a similar reaction.

2. The reaction of other aldehydes and of ketones with 4-methyl-4-penten-2-ol has given products which are believed to be analogous to those obtained by the similar reaction of acetaldehyde.

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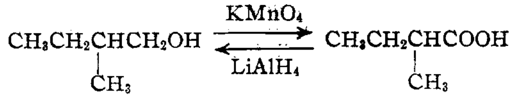
[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF CALIFORNIA]

Steric Effects and Stereochemistry of Lithium Aluminum Hydride Reduction

BY DONALD S. NOYCE AND DONALD B. DENNEY

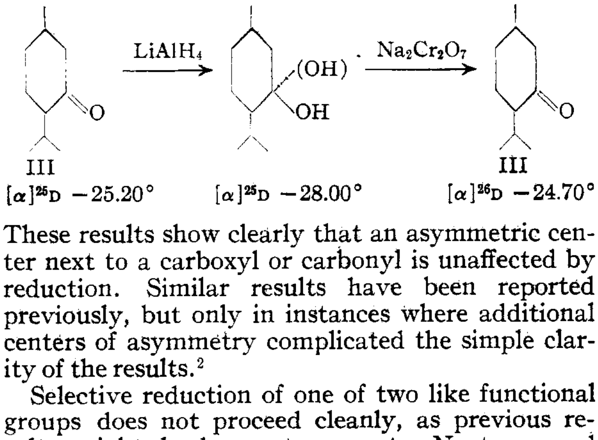
The versatility of reduction with lithium aluminum hydride[1] has prompted a study of the applicability of this reagent to selective reduction. Three different types of reduction have been explored in the present investigation: reduction next to a racemizable asymmetric center, selective reduction of one of two like functional groups, and reduction to introduce a new center of asymmetry, to determine the suitability of this reagent for preparation of one isomer in preponderance over the alternate isomer.

Reduction of the first type shows clean-cut results. When 2-methylbutanoic acid (I) (prepared by the oxidation of 2-methyl-1-butanol (II)) was reduced, II of unchanged rotation was obtained in 83% yield. Further, when *l*-menthone (III) was reduced, a mixture of menthols was obtained which was reoxidized to *l*-menthone with insignificant change of rotation.



$$\underset{\displaystyle CH_3}{CH_3CH_2\overset{|}{C}HCH_2OH} \underset{LiAlH_4}{\overset{KMnO_4}{\rightleftarrows}} \underset{\displaystyle CH_3}{CH_3CH_2\overset{|}{C}HCOOH}$$

II $[\alpha]^{23}D$ −4.98°, −5.03° I



III $[\alpha]^{25}D$ −25.20° $[\alpha]^{25}D$ −28.00° III $[\alpha]^{26}D$ −24.70°

These results show clearly that an asymmetric center next to a carboxyl or carbonyl is unaffected by reduction. Similar results have been reported previously, but only in instances where additional centers of asymmetry complicated the simple clarity of the results.[2]

Selective reduction of one of two like functional groups does not proceed cleanly, as previous results might lead one to expect. Nystrom and Brown[3] reported failure in selective reduction of sebacic acid. The highly hindered carboxyl group of podocarpic acid has been reduced under conditions somewhat more drastic than usual,[4] and Bachmann and Dreiding[5] have recently reported an unsymmetrically substituted diester to give 53% of crude hydroxy ester. On the other hand, an amido acid has been reported to be reduced only at the free carboxyl group.[6] Two acids were investigated, camphoric acid and α-ethyl-α-butylglutaric acid (IV). Camphoric acid gave poorly defined results, large amounts of diol and recovered acid being the main products of reduction. Inverse addition of one mole of lithium aluminum hydride to IV gave 39% of the theoretical amount of α-ethyl-α-butyl-δ-valerolactone (V), 14% recovered acid and 11% crude 2-ethyl-2-butyl-1,5-pentandiol (VI). This contrasts with the observation that esterification of IV gives only α-ethyl-α-butyl-γ-carbomethoxybutyric acid,[7] with no detectable amounts of its isomer. In these cases there are undoubtedly better ways to accomplish the same results, and hence there appears to be no advantage to lithium aluminum hydride for this type reduction.

More interesting results were obtained in the investigation of the introduction of a new center of asymmetry. The results are summarized in Table I.

TABLE I

Compound reduced	*cis* product, %			Method of analysis, present work
	$LiAlH_4$	$Al(O\text{-}i\text{-}Pr)_3$	$H_2(Pt)$	
4-Methylcyclohexanone	19	33[8]		Density
3-Methylcyclohexanone	8	55[8](30[9])		Density
2-Methylcyclohexanone	36	58(50,[8] 6–14[10])	75[12]	Density
l-Menthone	29	70[11]	"Mainly"[13]	Opt. rot.
d-Camphor	90	70[8]	90[14]	Opt. rot.

Trevoy and Brown[15] have shown that lithium aluminum hydride opens oxide rings by a bimolecular inversion mechanism, and it seemed likely that similar addition of hydrogen to a carbonyl group

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[1] (a) Nystrom and Brown, THIS JOURNAL, **69**, 1197 (1947); (b) Karrer, Portman and Suter, *Helv. Chim. Acta*, **31**, 1617 (1948).

[2] Fieser, Fieser and Chakravarti, THIS JOURNAL, **71**, 2226 (1949); Stoll, Hofman and Schleintz, *Helv. Chim. Acta*, **32**, 1947 (1949).

[3] Nystrom and Brown, THIS JOURNAL, **69**, 2548 (1947).

[4] Zeiss, Slimowicz and Pasternak, *ibid.*, **70**, 1981 (1948).

[5] Bachmann and Dreiding, *ibid.*, **71**, 3222 (1949).

[6] Karrer, Suter and Waser, *Helv. Chim. Acta*, **32**, 1937 (1949).

[7] Cason, *J. Org. Chem.*, **13**, 227 (1948).

[8] Jackman, Macbeth and Mills, *J. Chem. Soc.*, 2641 (1949).

[9] Mousseron, Marszak and Bolle, *Bull. soc. chim.*, **9**, 260 (1942).

[10] Anziani and Cornubert, *ibid.*, **12**, 359 (1945).

[11] Zeitschel and Schmidt, *Ber.*, **59**, 2303 (1926); also ref. 8.

[12] Skita and Faust, *ibid.*, **64**, 2878 (1931).

[13] Vavon and Couderc, *Compt. rend.*, **179**, 405 (1924).

[14] Vavon and Peignier, *ibid.*, **181**, 183 (1925).

[15] Trevoy and Brown, THIS JOURNAL, **71**, 1675 (1949).