A new region of absorption with $\lambda_{max}$ at *ca.* 308 mμ is present in the spectra of 3-cyano- and 3-acetyl-4-keto - 4H - pyrido[1,2-a]pyrimidines. Ethyl 4 - keto - 4H - pyrido[1,2-a]pyrimidine - 3 - carboxylate displays a similar band. This is corresponding with the region of absorption of the β-amino-α,β-unsaturated ketone chromophore[10] whereas the corresponding carboxylic esters absorb in an essentially similar region.[11,12]

## Experimental

**3-Cyano-4-keto-6,7-benzo-4H-pyrido(1,2-a)pyrimidine.**—2-Aminoquinoline (1.5 g., 1 mol.) and ethyl ethoxymethylene cyanoacetate (1.7 g., 1 mol.) were heated in an oil-bath at 100° for 15 minutes. The solid reaction mass was crystallized after cooling from benzene–petroleum ether to yield white needles, m.p. 171° (Calcd. for $C_{15}H_{13}O_2N_3$: C, 67.4; H, 4.8; N, 15.7. Found: C, 68.0; H, 4.7; N, 15.5). The ester was distilled under reduced pressure (water-pump) and the distillate crystallized from the same solvent as yellow needles, m.p. 215° (Calcd. for $C_{13}H_{17}ON_3$: C, 70.5; H, 3.1; N, 19.0. Found: C, 69.9; H, 3.2; N, 19.2).

**Ethyl 4-Imino-8-methyl-4H-pyrido(1,2-a)pyrimidine-3-carboxylate.**—Ethyl 4-methylpyridyl-2-aminomethylene-cyanoacetate prepared as above from 4-methyl-2-aminopyridine and ethyl ethoxymethylenecyanoacetate separated in white platelets from alcohol, m.p. 134° (Calcd. for $C_{12}H_{13}O_2N_3$: C, 62.6; H, 5.2; N, 18.2. Found: C, 62.4; H, 5.0; N, 18.3). The ester was refluxed in alcoholic solution for 30 minutes on the water-bath. After removal of the solvent the residue was fractionally crystallized from benzene–petroleum ether. In addition to unchanged ester, ethyl 4-imino-8-methyl-4H-pyrido(1,2-a)pyrimidine-3-carboxylate was obtained as yellow needles, m.p. 152° (Calcd. for $C_{12}H_{13}O_2N_3$: C, 62.3; H, 5.6; N, 18.1. Found: C, 61.9; H, 5.1; N, 17.8).

**Ethyl N-(4-methyl-2-imino-1,2-dihydropyridyl)-methylenecyanoacetate** was prepared by heating equimolecular amounts of 4-methyl-2-aminopyridine and ethyl ethoxymethylene cyanoacetate at 150° for 2 hr. or by rearranging the isomeric ester at 150° for 2 hr. **Ethyl N-(4-methyl-2-imino-1,2-dihydropyridyl)-methylenecyanoacetate** crystallized from benzene–petroleum ether in pink plates, m.p. 154° (Calcd. for $C_{12}H_{13}O_2N_3$: C, 62.3; H, 5.6; N, 18.1. Found: C, 62.5; H, 5.5; N, 17.9). The ester was boiled for a few minutes with aqueous 1:1 hydrochloric acid, the solution cooled and neutralized with ammonia. Ethyl 2-keto-8-methyl-2H-pyrido[1,2-a]pyrimidine-3-carboxylate crystallized in yellow plates, m.p. 164° from alcohol (Calcd. for $C_{12}H_{12}O_3N_2$: C, 62.0; H, 5.1; N, 12.0. Found: C, 61.8; H, 4.9; N, 11.8). Distillation of the ester under reduced pressure gave 3-cyano-2-keto-8-methyl-2H-pyrido(1,2-a)-pyrimidine in brown plates, m.p. 274° from alcohol (Calcd. for $C_{10}H_7ON_3$: C, 64.8; H, 3.8; N, 22.7. Found: C, 64.5; H, 3.8; N, 22.5).

CAIRO, EGYPT

(10) N. Cromwell, F. Miller, A. Johnson, R. Frank, and D. Wallace, THIS JOURNAL, **71**, 3337 (1949).
(11) S. Glickman and A. Cope, *ibid.*, **67**, 1017 (1945).
(12) V. Boekelheide and E. Agnello, *ibid.*, **72**, 5005 (1950).

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[CONTRIBUTION FROM THE DEVELOPMENT DEPARTMENT, UNION CARBIDE CHEMICALS CO., DIVISION OF UNION CARBIDE CORP.]

# The Chemistry of α,β-Unsaturated Ethers. II. Condensation with Aldehydes

BY R. I. HOAGLIN, D. G. KUBLER AND R. E. LEECH[1]

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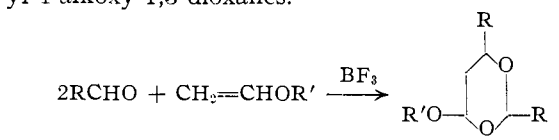
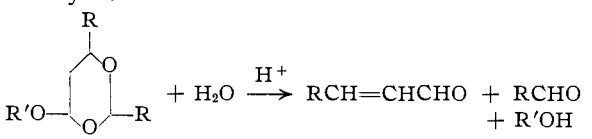
A new reaction of aldehydes and α,β-unsaturated ethers, which is catalyzed by acids to form β-alkoxyaldehydes and β-alkoxyketones, is reported. These products are readily de-alcoholated to conjugated, unsaturated, carbonyl compounds. This method is of particular value for the production of pure conjugated, unsaturated aldehydes containing one, two, three or more unsaturated groups by the proper selection of the aldehyde and the α,β-unsaturated ether. A mechanism for the reaction is proposed.

A previous paper[2] from this Laboratory discussed the scope and utility of the reaction of acetals and α,β-unsaturated ethers to form 1,1,3-trialkoxyalkanes. More recently it has been found that saturated aliphatic aldehydes and vinyl ethers combine in a Prins-type reaction to form 2,6-dialkyl-4-alkoxy-1,3-dioxanes.[3]



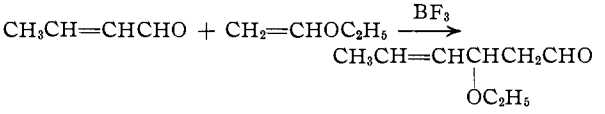
Acid-catalyzed hydrolysis of these products provides α,β-unsaturated aldehydes containing two more carbon atoms in the chain than the starting aldehyde.



(1) Presented in part before the Division of Organic Chemistry at the 132nd Meeting of the American Chemical Society at New York, N. Y., September, 1957.
(2) R. I. Hoaglin and D. H. Hirsh, THIS JOURNAL, **71**, 3468 (1949).
(3) R. I. Hoaglin and D. H. Hirsh, U. S. Patent 2,628,257 (February 10, 1953).

Copenhaver[4] has reported that aldehydes such as benzaldehyde or 2-ethylbutyraldehyde react with vinyl ethers to provide resinous acetals containing the reactants in a 1-to-1 ratio. These resinous acetals were not separated and identified, but acid-catalyzed hydrolysis of these materials provided α,β-unsaturated aldehydes containing two more carbon atoms in the chain than the starting aldehyde. For example, Copenhaver obtained cinnamaldehyde in 60% yield from the hydrolysis of the reaction product of benzaldehyde and vinyl methyl ether.

Our study of this reaction, utilizing crotonaldehyde and vinyl ethyl ether, demonstrates that aldehydes can react with α,β-unsaturated ethers in a 1-to-1 molar ratio. When catalyzed by boron trifluoride, the product was 3-ethoxy-4-hexenal instead of a resinous acetal.



The present investigation shows that the course of the reaction of aldehydes and vinyl ethers will vary depending upon the nature of the reactants

(4) J. W. Copenhaver, U. S. Patent 2,543,312 (February 27, 1951).

and the catalyst. Butyraldehyde and 1-butenyl methyl ether were allowed to react in the presence of boron trifluoride to provide a 63% yield of 2,6-dipropyl-5-ethyl-4-methoxy-1,3-dioxane and only trace amounts, if any, of 3-methoxy-2-ethylhexanal. From butyraldehyde and 1-butenyl ethyl ether, in the presence of a milder catalyst, such as a 1-to-1 molar ratio mixture of boric acid and oxalic acid, 3-ethoxy-2-ethylhexanal was isolated in a 51% yield. Butyraldehyde and vinyl methyl ether reacted in the presence of boron trifluoride-etherate to provide 2,6-dipropyl-4-methoxy-1,3-dioxane in 60–70% yield and no other readily isolable products were formed. When the reaction of butyraldehyde and vinyl ethyl ether[5] was catalyzed by boric acid–oxalic acid, the yield of 2,6-dipropyl-4-ethoxy-1,3-dioxane was considerably diminished (27% yield) and in addition, a 16% yield of 3-ethoxyhexanal was isolated. In marked contrast to the butyraldehyde-vinyl ethyl ether reaction, crotonaldehyde and vinyl ethyl ether reacted to form 3-ethoxy-4-hexenal as the only pure isolable product when either boron trifluoride or other catalysts were used. The yields of 3-ethoxy-4-hexenal obtained with several catalysts are shown in Table I.

TABLE I

THE EFFECT OF CATALYST TYPE ON THE YIELD OF 3-ETHOXY-4-HEXENAL[a]

| Catalyst | Weight, g. | Yield, % |
|---|---|---|
| Zinc chloride[b] | 4.2 | 42 |
| Boric–oxalic acids | 0.42 | 46 |
| Boric–salicylic acids[c] | 0.85 | 33 |
| Boric–tartaric acids[c] | 0.85 | 35 |
| Ferric chloride | 1.0 | 35 |
| Mercuric chloride | 1.7 | 4 |
| Cupric bromide | 1.4 | 29 |
| Boron trifluoride | 0.42 | 26 |
| Sulfuric acid | 0.61 | 12 |

[a] These experiments were conducted with 9 moles of crotonaldehyde and 3 moles of vinyl ethyl ether at a reaction temperature of 60°. [b] Polymerization of the vinyl ethyl ether was the only reaction obtained at 60°. This experiment was conducted at 100°. [c] This experiment was conducted at 80°.

In three cases (boron trifluoride, boric acid–oxalic acid and zinc chloride), irrespective of the yield of 3-ethoxy-4-hexenal, the residual material obtained after removal of the unreacted crotonaldehyde and prior to isolation of the product, contained a 1-to-1 molar ratio of aldehyde to ether on a weight basis. Hydrolytic de-ethanolation of these residues provided 2,4-hexadienal in greater yields than that to be expected from the amount of contained 3-ethoxy-4-hexenal.

$$CH_3CH{=}CHCHCH_2CHO \xrightarrow{H^+} \underset{\displaystyle OC_2H_5}{\overset{|}{\phantom{O}}}$$

$$CH_3CH{=}CHCH{=}CHCHO + C_2H_5OH$$

The use of boron trifluoride-etherate provided a 26% yield of 3-ethoxy-4-hexenal, but hydrolysis of a reaction mixture after removal of the unreacted crotonaldehyde gave a 57% yield of 2,4-hexadienal. The yields of 3-ethoxy-4-hexenal were 42 and 46% when the reaction was conducted in the presence of

(5) We have observed no significant differences in yields of products when using vinyl ethyl ether or vinyl methyl ether.

TABLE II: CONDENSATIONS OF ALDEHYDES AND $\alpha,\beta$-UNSATURATED ETHERS[a]

| Expt. | Reactants: Aldehyde | Reactants: Ether | Product | Yield, % | B.p. °C. | B.p. Mm. | $n^{20}D$ | Sp.gr. $^{20}_{15.6}$ | Carbon, % Calcd. | Carbon, % Found | Hydrogen, % Calcd. | Hydrogen, % Found | 2,4-Dinitrophenylhydrazone, m.p., °C. | Nitrogen, % Calcd. | Nitrogen, % Found |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | $CH_3CH{=}CHCHO$ | $CH_2{=}CHOC_2H_5$ | 3-Ethoxy-4-hexenal | 46 | 65 | 10 | 1.4318 | 0.907 | 67.57 | 67.21 | 9.92 | 10.08 | 103.5–104[c] | 17.38 | 17.34 |
| 2 | $CH_3CH{=}CHCHO$ | $CH_2{=}CHOC_4H_9$ | 3-Butoxy-4-hexenal | 39 | 92 | 10 | 1.4371 | .896 | 70.55 | 70.60 | 10.65 | 10.80 | 72.5–73.5 | 15.99 | 16.05 |
| 3 | $CH_3CH{=}CHCHO$ | $C_2H_5CH{=}CHOC_2H_5$ | 3-Ethoxy-2-ethyl-4-hexenal | 61 | 83 | 10 | 1.4375 | .895 | 70.55 | 70.70 | 10.65 | 11.20 | 105–105.5 | 15.99 | 16.24 |
| 4 | $CH_3CH{=}CHCHO$ | $(CH_3)_2C{=}CHOCH_3$ | 2,2-Dimethyl-3-methoxy-4-hexenal | 33 | 67 | 10 | 1.4387 | .905 | 69.19 | 69.40 | 10.33 | 10.40 | 105–106.5 | 16.66 | 16.72 |
| 5 | $CH_3CH{=}CHCHO$ | $CH_2{=}CCH_3OC_2H_5$ | 4-Ethoxy-5-heptene-2-one | 30 | 74 | 10 | 1.4332 | .893 | 69.19 | 69.07 | 10.33 | 10.58 | ..... | ... | ... |
| 6 | $n$-$C_3H_7CHO$ | $CH_2{=}CHOC_2H_5$ | 3-Ethoxyhexanal | 16 | 64 | 10 | 1.4167 | .886 | ... | ... | ... | ... | 76–77[d] | 17.28 | 17.05 |
| 7 | $n$-$C_3H_7CHO$ | $C_2H_5CH{=}CHOC_2H_5$ | 3-Ethoxy-2-ethylhexanal | 51 | 83 | 10 | 1.4246 | .879 | 69.72 | 68.75 | 11.70 | 11.87 | 85–86 | 15.90 | 16.15 |
| 8 | $C_3H_7CH{=}CHCHO$ | $C_2H_5CH{=}CHOC_2H_5$ | 3-Ethoxy-2-ethyl-4-octenal | 67 | 109 | 10 | 1.4450 | .882 | 72.68 | 72.89 | 11.18 | 11.43 | 111.5–112 | 14.81 | 14.41 |
| 9 | $C_6H_5CHO$ | $C_2H_5CH{=}CHOC_2H_5$ | 3-Ethoxy-2-ethyl-3-phenylpropanal | 78 | 128 | 10 | 1.5132 | .997 | 75.69 | 75.90 | 8.79 | 8.60 | 128–129 | 14.97 | 14.43 |
| 10 | $CH_3CH{=}CHCH{=}CHCHO$ | $C_2H_5CH{=}CHOC_2H_5$ | 3-Ethoxy-2-ethyl-4,6-octadienal | 49 | 112 | 5 | 1.4815 | .909 | 73.42 | 73.30 | 10.27 | 10.50 | ..... | ... | ... |
| 11 | $C_4H_4OCHO$ | $C_2H_5CH{=}CHOC_2H_5$ | 3-Ethoxy-2-ethyl-3-furylpropanal | 24 | 83 | 1 | 1.4640 | 1.022 | 67.32 | 66.56 | 8.22 | 8.01 | ..... | ... | ... |

[a] These experiments were conducted at 40°, except for expt. 4 (80°), expt. 5 (100°) and expt. 8 (80°). [b] All of the 2,4-dinitrophenylhydrazones were yellow to orange-yellow in color. See the Experimental section for the method of preparation. [c] The semicarbazone of 3-ethoxy-4-hexenal was made and recrystallized three times from water, m.p. 142–143.5°. *Anal.* Calcd. for $C_9H_{17}N_3O_2$: C, 54.25; H, 8.60; N, 21.09. Found: C, 54.42; H, 8.72; N, 21.01. [d] The 2,4-dinitrophenylhydrazone of an authentic sample of 3-ethoxyhexanal (prepared by the reaction of diethyl butyral and vinyl ethyl ether[2] followed by mild hydrolysis) melted at 76–77° and a mixture of the two derivatives melted at 76–77°.

TABLE III

DE-ALCOHOLATION OF β-ALKOXYCARBONYL COMPOUNDS

| Compound | Product | Yield, % | B.p. °C. | Mm. | $n^{20}D$ | Derivative Type | M.p., °C. |
|---|---|---|---|---|---|---|---|
| 3-Ethoxy-4-hexenal | 2,4-Hexadienal[a] | 87 | 53–56 | 10 | 1.5378 | Oxime | 152–154[b] |
| 3-Ethoxy-2-ethyl-4-octenal | 2-Ethyl-2,4-octadienal[c] | 87 | 82–84 | 4 | 1.4970 | Semicarbazone | 167–167.5[d] |
| 4-Ethoxy-5-heptene-2-one | 3,5-Heptadiene-2-one[e] | 72 | 66–67 | 10 | 1.5204 | Semicarbazone | 163–164 |
| 3-Ethoxy-2-ethyl-3-phenyl-propanal | 2-Ethyl-3-phenyl-2-propenal[f] | 90 | 99–102 | 4 | 1.5854 | Semicarbazone | 196–196.5 |
| 3-Ethoxy-2-ethylhexanal | 2-Ethyl-2-hexenal | 78 | 56 | 10 | 1.4520 | 2,4-Dinitrophenylhydrazone | 125.5–126[g] |

[a] The literature values for 2,4-hexadienal are: b.p. 76° (30 mm.),[6] 43° (5 mm.),[2] $n^{20}D$ 1.5384,[2] oxime m.p. 160°.[7] [b] This value was obtained in a sealed tube. [c] This product was hydrogenated to 2-ethyloctanol, b.p. 104° (10 mm.), $n^{20}D$ 1.4380. *Anal.* Calcd. for $C_{10}H_{22}O$: C, 75.88; H, 14.01. Found: C, 75.40; H, 14.00. [d] *Anal.* Calcd. for $C_{11}H_{19}N_3O$: C, 63.12; H, 9.15; N, 20.08. Found: C, 63.56; H, 9.35; N, 19.84. [e] The literature values are[8]: b.p. 74–75° (15 mm.), $n^{20}D$ 1.5210, semicarbazone m.p. 164–166°. [f] The literature values for this compound are[9]: b.p. 126–128° (10 mm.), $n^{16}D$ 1.5847, semicarbazone m.p. 199–200°. [g] The literature value for this derivative is m.p. 124–125° (see ref. 15). The melting point of a mixture of this material and an authentic sample was not depressed.

zinc chloride and boric acid–oxalic acid, respectively, but the yields of 2,4-hexadienal obtained by the hydrolysis of crotonaldehyde-free residues were the same as those obtained from the corresponding hydrolysate of the boron trifluoride-catalyzed reaction. Thus, in the cases studied, while the nature of the catalyst affected the yield of 3-ethoxy-4-hexenal, it had no effect on the yield of total materials which could be converted to 2,4-hexadienal. The other precursors of hexadienal could not be isolated as pure products and hence were not identified.

The products of this reaction are aldehydes (except for the products of enol ethers of ketones which provide ketone products) and therefore compete to a certain extent with the starting aldehyde for reaction with the α,β-unsaturated ether. This was demonstrated in one instance to occur during the reaction of crotonaldehyde and vinyl ethyl ether. Hydrolysis of the residue product after removing the unreacted crotonaldehyde and distillation of the hydrolysate, produced a normal yield of 2,4-hexadienal and a low yield (2%) of 2,4,6-octatrienal.

The crotonaldehyde–vinyl ethyl ether reaction was extended to include other aldehydes and α,β-unsaturated ethers. The reactants used and the products obtained are shown in Table II. From these results the following tentative generalizations can be drawn about the 1-to-1 combination of aldehydes and α,β-unsaturated ethers: (1) the reactivities of the aldehydes increase in the order of saturated aliphatic aldehydes, conjugated unsaturated aliphatic aldehydes, aromatic aldehydes; and (2) alkyl substitution of hydrogen on the β-position of the ether promotes the reaction while substitution on the α-position hinders the reaction.

The utility of the reaction of aldehydes and α,β-unsaturated ethers is quite similar to that previously discussed for the reaction of acetals and α,β-unsaturated ethers.[2] It represents an extension of the previous method for controlling crossed aldol reactions in that in many cases the aldehydes are more readily available than the acetals and it has greater utility for the preparation of pure conjugated, polyunsaturated aldehydes and ketones.

The structure of 3-ethoxy-4-hexenal follows from its conversion to the known 2,4-hexadienal in 87% yield by de-ethanolation and to the known 3-ethoxy-1-hexanol in 76% yield by hydrogenation. The infrared spectrum demonstrated the presence of aldehyde and ether groups and of internal unsaturation. The carbonyl group was reduced with lithium aluminum hydride to form 3-ethoxy-4-hexene-1-ol in 80% yield.

An interesting carbon–carbon cleavage occurred when 2,2-dimethyl-3-methoxy-4-hexenal (from the reaction of crotonaldehyde and isobutenyl methyl ether) was subjected to hydrolytic de-alcoholation. The products obtained were crotonaldehyde, isobutyraldehyde and methanol. It is not possible for de-alcoholation to occur with this compound to provide unsaturation conjugated with the carbonyl group. The products could have been obtained by the reversal of the reaction to crotonaldehyde and isobutenyl methyl ether followed by hydrolysis of the ether.

For most of the aldehydes and ethers used, the reaction proceeded at a rapid rate in the temperature range of 40 to 60°. In cases of more hindered reactants such as isopropenyl ethyl ether or isobutenyl methyl ether with crotonaldehyde, higher reaction temperatures (80–100°) were needed.

The mechanism of the reaction has not been elucidated. A distinct feature is the transfer of the carbonyl function to the vinyl ether portion of the product and of the ether function to the former carbonyl position. Whether the transfer requires ionization, a concerted intramolecular displacement of oxygen or a concerted intramolecular alkyl group transfer from the ether to the carbonyl oxygen of the aldehyde is speculative, but we suggest the latter. This could occur as shown.

If the alkyl group is transferred as a carbonium ion, one should expect evidence of rearrangement of the alkyl group because of the known tendency of primary carbonium ions to rearrange to secondary or tertiary carbonium ions.[10] If this occurs, the

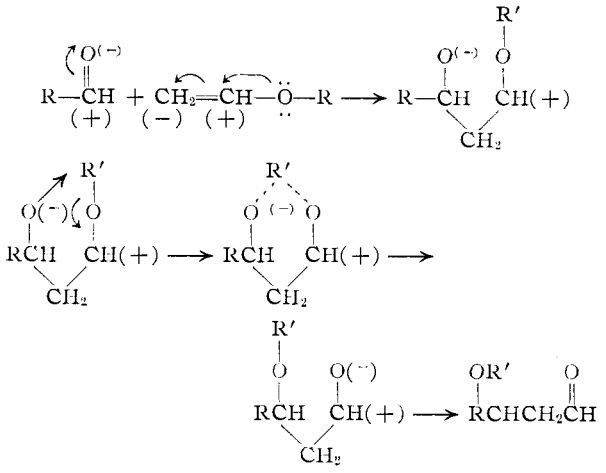
(6) P. Baumgarten and G. Glatzel, *Ber.*, **59B**, 2658 (1926).

(7) R. Kuhn and M. Hoffer, *ibid.*, **64B**, 1977 (1931).

(8) W. S. Rapson and R. G. Shutterworth, *J. Chem. Soc.*, 636 (1940).

(9) P. Sorulgin, *et al.*, *J. Russ. Phys.-Chem. Soc.*, **62**, 2033 (1930); J. V. Braun and G. Manz, *Ber.*, **67B**, 1696 (1934).

(10) A. E. Remick, "Electronic Interpretations of Organic Chemistry," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1949, p. 444.



reaction of crotonaldehyde and vinyl *n*-butyl ether should yield 3-(2′-butoxy)-4-hexenal instead of 3-(1′-butoxy)-4-hexenal, at least in part. Hydrolysis of this reaction product, however, provided only 1-butanol so that the group must transfer intramolecularly.

## Experimental[11]

**Preparation of Starting Materials.**—The aldehydes used in this work are commercially available or may be prepared by methods published in the literature. In all cases the aldehydes were carefully purified prior to their use which was particularly necessary for benzaldehyde and furfural. The unsaturated ethers were prepared by the catalytic, vapor-phase decomposition of the corresponding acetals, but several of these ethers are commercially available.

The boric acid–oxalic acid catalyst was prepared by dissolving 186 g. (3 moles) of orthoboric acid and 270 g. (3 moles) of oxalic acid in 1,100 ml. of water by stirring and warming to 50°. The water was removed by heating the solution under reduced pressure, below 75°. The white crystalline solid was air-dried overnight and then heated at 50° for 3 hours under 2 mm. pressure.

**A. Condensation Reactions.**—Excess aldehyde (3 moles of aldehyde to one mole of unsaturated ether) was treated with the catalyst, usually in an amount of 0.05% of the total weight of the reactants, and the solution was heated to the desired reaction temperature (in the case of the reaction of 2-hexenal and 1-butenyl ethyl ether, 0.1% catalyst by weight was required). The reaction was conducted at 40°, except for the following examples: crotonaldehyde and isobutenyl methyl ether (80°), crotonaldehyde and isopropenyl ethyl ether (100°) and 2-hexenal and 1-butenyl ethyl ether (80°). The unsaturated ether was added at a rate such that the reaction temperature could be maintained conveniently by external cooling or slight heating. The mixture was allowed to cool and the catalyst was neutralized by the addition of aqueous sodium bicarbonate or sodium carbonate. After removing the aqueous layer, the organic portion was distilled to recover unreacted aldehyde and the product aldehyde.

**3-Ethoxy-4-hexenal.**—To 630 g. (9 moles) of crotonaldehyde and 0.42 g. of boric acid–oxalic acid there was added 216 g. (3 moles) of vinyl ethyl ether over a period of 26 minutes while maintaining a reaction temperature of 40° by periodic cooling. The red solution was stirred an additional 15 minutes followed by neutralization of the catalyst with 5 g. of sodium carbonate in 200 ml. of water. Neutralization of the catalyst caused a color change from red to pale yellow. The organic layer was distilled to provide 469 g. of wet crotonaldehyde and 195 g. (46% yield) of 3-ethoxy-4-hexenal which distilled at 60–65° (10 mm.).

**3-Ethoxy-2-ethyl-3-phenylpropanal.**—Freshly refined benzaldehyde (954 g., 9.0 moles) and 0.63 g. of boric acid–oxalic acid were mixed. To this solution at 40°, there was added 300 g. (3.0 moles) of 1-butenyl ethyl ether over a period of 24 minutes. After standing for 15 minutes, the catalyst was neutralized with 10 g. of sodium bicarbonate in 200 ml. of water. Distillation of the organic layer provided 485 g. (78% yield) of 3-ethoxy-2-ethyl-3-phenylpropanal distilling at 121–129° (10 mm.).

**2,6-Dipropyl-5-ethyl-4-methoxy-1,3-dioxane.**—A mixture of 1,875 g. (26 moles) of butyraldehyde and 1,120 g. (13 moles) of 1-butenyl methyl ether was added to a stirred solution of 50 g. of diethyl ether and 6 g. of 33% boron trifluoride in diethyl ether. The addition required 1.2 hours and during this time the temperature was maintained at 42 to 46° by means of brine-cooled bath. The mixture was stirred for 25 minutes at room temperature and 20 g. of anhydrous sodium carbonate was added and the mixture was stirred for 4 hours. Distillation of a portion (2,727 g.) of the filtered reaction mixture provided 1,676 g. (63% yield) of 2,6-dipropyl-5-ethyl-4-methoxy-1,3-dioxane which distilled at 112 to 117° at 10 mm. Other physical properties of this material are: $n^{20}D$ 1.4425, sp. gr. 20/15.6, 0.932.

*Anal.* Calcd. for $C_{13}H_{26}O_3$: C, 67.78; H, 11.38. Found: C, 67.5; H, 10.7.

B. **Hydrolytic De-alcoholations.**—The de-alcoholations were effected, in general, by heating the alkoxycarbonyl compound with an equal weight of aqueous acetic acid, using a column equipped with a liquid–liquid separating head. In all experiments, solutions of 50 to 75% acetic acid in water provided complete solubility of the aldehyde after heating the mixture to the reflux temperature. If the de-alcoholation did not proceed in the acetic acid solution, addition of 0.5 to 1.0 ml. of concentrated sulfuric acid to the mixture for each mole of aldehyde effected a rapid de-alcoholation. The alcohol was removed as fast as possible by distillation until the vapor temperature could no longer be maintained at the boiling point of the alcohol. The unsaturated aldehyde or ketone product was co-distilled with water and separated in the column head. In the isolation of 2-ethylcinnamaldehyde, 2-ethyl-2,4-octadienal and 2-ethyl-2,4,6-octatrienal, the products were not separated by co-distillation with water but by dilution of the aqueous acid solution with water to separate the organic layer with subsequent distillation of the organic layer under reduced pressure.

**2,4-Hexadienal.**—A mixture of 284 g. (2.0 moles) of 3-ethoxy-4-hexenal and 300 g. of 50% aqueous acetic acid was heated vigorously at the reflux temperature and the ethanol removed as rapidly as possible through an efficient distillation column. When the vapor temperature could no longer be maintained below 80° (after about 9 hours), the product was steam distilled and removed from the separating head as the upper layer. There was obtained 190 g. of wet 2,4-hexadienal which was 88% pure (87% yield). Redistillation of the crude material provided 148 g. (77% yield) of refined material. This material readily yielded a 2,4-dinitrophenylhydrazone which was difficult to purify. The semicarbazone of 2,4-hexadienal was prepared as white plates (m.p. 196–197°, lit.[6] m.p. 203°), but it rapidly decomposed in air to a gummy yellow solid. The oxime was prepared, m.p. 152–154° (sealed tube). The infrared spectrum of the oxime was determined to distinguish it as an authentic derivative and not hydroxylamine hydrochloride which melts at 151°.

**De-methanolation of 2,2-Dimethyl-3-methoxy-4-hexenal.**—A mixture of 312 g. (2 moles) of 2,2-dimethyl-3-methoxy-4-hexenal, 300 g. of 67% aqueous acetic acid and 5.0 ml. of concentrated sulfuric acid was heated vigorously while slowly (3.5 hours) distilling off 252 g. of a fraction consisting essentially of methanol (2.2%), methyl acetate (48.3%), isobutyraldehyde (36.7%), crotonaldehyde (1.5%) and water (6.5%). The residue was cooled and the sulfuric acid neutralized with a solution of 7.5 g. of sodium hydroxide in 100 ml. of water. The solution was then co-distilled with water until no more organic products distilled and the organic layer was removed by means of the liquid–liquid separating head. A total of 89 g. of organic material was obtained which contained 81.6% crotonaldehyde by unsaturation analysis. From quantitative functional group analyses of the two fractions, there was obtained a total of 1.1 moles (55% yield) of crotonaldehyde, 1.2 moles (60% yield) of isobutyraldehyde and 1.8 moles (90% yield) of methanol as the alcohol and methyl acetate.

(11) All melting points are corrected, boiling points are uncorrected. We wish to thank Mr. H. L. Thornburg and Mr. J. Bodenschatz of this Laboratory for the carbon and hydrogen analyses reported here. Mr. J. H. Ross of this Laboratory kindly measured and interpreted the infrared spectrum of 3-ethoxy-4-hexenal.

Redistillation of a portion (197 g.) of the first fraction provided three fractions: (1) 61 g., b.p. 53–55°; (2) 92 g., b.p. 55–58°; (3) 28 g., b.p. 58–59°. All three fractions had a pronounced odor of isobutyraldehyde. A portion of fraction 2 was characterized as its 2,4-dinitrophenylhydrazone (m.p. 184–184.5°) and its melting point was not depressed when mixed with an authentic sample of the 2,4-dinitrophenylhydrazone of isobutyraldehyde.

A portion (72 g.) of the steam-distilled fraction was redistilled to provide 22 g. of a fore-fraction consisting mainly of the water–crotonaldehyde azeotrope, 38 g. of refined crotonaldehyde boiling at 99–101° and 11 g. of viscous residue. The 2,4-dinitrophenylhydrazone of the refined material melted at 191–192.5° after one recrystallization from a mixture of ethanol and ethyl acetate. The melting point of this material was not depressed when mixed with an authentic sample of the 2,4-dinitrophenylhydrazone of crotonaldehyde.

**De-alcoholation of 3-Butoxy-4-hexenal.**—A mixture of 128 g. (0.75 mole) of 3-butoxy-4-hexenal, 300 ml. of water and 0.34 ml. of concentrated sulfuric acid was heated at the reflux temperature for 2.5 hours. An additional 0.66 ml. of sulfuric acid was added and the mixture heated for 3 hours longer. After cooling the mixture, the water layer was removed, neutralized with sodium bicarbonate and extracted 3 times with 100-ml. portions of diethyl ether. The extracts and the organic layer were combined and distilled. After distilling off the ether, there were obtained 5 fractions: fract. 1, 20 g., b.p. 56–57° (50 mm.); fract. 2, 8 g., b.p. 56 to 52° (50 to 10 mm.); fract. 3, 32 g., 52–53° (10 mm.); fract. 4, 8 g., 53 to 86° (10 mm.); fract. 5, 29 g., 86–88° (10 mm.).

Fraction 1 contained in excess of 95% 1-butanol, little or no secondary butanol and a small amount of an unknown, high-boiling material which may have been 2,4-hexadienal. These values were determined by mass spectroscopy. Fraction 3 was 2,4-hexadienal and fraction 5 was recovered 3-butoxy-4-hexenal.

**2-Ethyl-2,4,6-octatrienal.**—The residue (575 g.) from the reaction of 9 moles of 2,4-hexadienal and 3 moles of 1-butenyl ethyl ether, from which the unreacted hexadienal had been removed, was mixed with 575 g. of 50% aqueous acetic acid containing 1 ml. of concentrated sulfuric acid. The mixture was heated at the reflux temperature on a still and 128 g. of a mixture of ethanol and ethyl acetate was removed by distillation. The residue was cooled and the sulfuric acid neutralized with a solution of 1.5 g. of sodium hydroxide in 100 ml. of water. The organic layer was removed and washed once with 250 ml. of water. Distillation of the organic material provided 209 g. of crude 2-ethyl-2,4,6-octatrienal, b.p. 77–94° (1 to 2 mm.). This product was identified by hydrogenation in 250 ml. of ethanol solvent in the presence of 20 g. of Raney nickel catalyst at 150 p.s.i.g. There was obtained 175 g. (81% yield, assuming 100% pure 2-ethyl-2,4,6-octatrienal starting material) of 2-ethyloctanol, b.p. 104–105° (10 mm.), $n^{20}D$ 1.4379. The allophanate of 2-ethyloctanol was prepared[12] and after three recrystallizations from ethanol–water melted at 111–111.5°.

*Anal.* Calcd. for $C_{12}H_{24}N_2O_3$: C, 58.99; H, 9.90; N, 11.47. Found: C, 58.99; H, 9.93; N, 11.40.

**C. Derivatives of 3-Ethoxy-4-hexenal.—3-Ethoxy-4-hexen-1-ol** was prepared by the lithium aluminum hydride reduction of 3-ethoxy-4-hexenal using the procedure of Nystrom and Brown.[13] The reactant quantities were 142 g. (1.0 mole) of 3-ethoxy-4-hexenal, 16 g. (0.42 mole) of lithium aluminum hydride and 700 ml. of diethyl ether. The product (115 g., 80% yield) distilled at 85–86° (10 mm.), $n^{20}D$ 1.4417.

*Anal.* Calcd. for $C_8H_{16}O_2$: C, 66.61; H, 11.17; unsaturation, 13.89 meq./g. (bromination). Found: C, 66.20; H, 11.20; unsaturation, 13.72 meq./g. (bromination).

The allophanate of this alcohol melted at 128.5–129.5° after two recrystallizations from water.

*Anal.* Calcd. for $C_{10}H_{18}O_4N_2$: C, 52.16; H, 7.88; N, 12.17. Found: C, 52.18; H, 7.85; N, 12.25.

**3-Ethoxy-1-hexanol.**—Hydrogenation of 504 g. (3.5 moles) of 3-ethoxy-4-hexenal at 125° and 500 p.s.i.g. over 25 g. of Raney nickel gave 392 g. of 3-ethoxy-1-hexanol (76% yield), b.p. 89–90° (10 mm.), $n^{20}D$ 1.4262. The allophanate of this alcohol melted at 137.5–138° and its melting point was not depressed when mixed with the allophanate of an authentic sample of 3-ethoxy-1-hexanol.[14]

*Anal.* Calcd. for $C_{10}H_{20}O_4N_2$: C, 51.71; H, 8.68; N, 12.06. Found: C, 51.96; H, 8.22; N, 12.28.

**2,4-Dinitrophenylhydrazones.**—The preparation of the 2,4-dinitrophenylhydrazones of the β-alkoxyaldehyde products by standard techniques[15] always resulted in partial and sometimes complete de-alcoholation of the aldehyde. The resulting products proved difficult to purify or were completely converted to the derivative of the α,β-unsaturated aldehyde. The hydrazones were prepared by the procedure which follows for 3-ethoxy-4-hexenal. To a hot solution of 1.6 g. of 2,4-dinitrophenylhydrazine and 300 ml. of methanol was added 2 g. of 3-ethoxy-4-hexenal and 75 ml. of water. The product crystallized on standing to give long, yellow needles which were recrystallized three times from heptane; m.p. 103.5–104°. In some instances the formation of the derivative was facilitated by the addition of a drop or two of concentrated phosphoric acid.

(12) A. Behal, *Bull. soc. chim. France*, [4] **25**, 473 (1919).

(13) R. F. Nystrom and W. G. Brown, THIS JOURNAL, **69**, 1197 (1947).

(14) 3-Ethoxy-1-hexanol was prepared by the reaction of diethyl butyral and vinyl ethyl ether[2] followed by hydrolysis of the 1,1,3-triethoxyhexane to 3-ethoxyhexanal which was catalytically hydrogenated.

(15) R. L. Shriner and R. C. Fuson, "The Systematic Identification of Organic Compounds," 3rd ed., John Wiley and Sons, Inc., New York, N. Y., 1948, p. 171.

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[CONTRIBUTION FROM THE LABORATORIES OF THE ALDRICH CHEMICAL CO. AND THE PITTSBURGH PLATE GLASS CO.]

# Unsaturated Phenols. V. The Reaction of Isoprene with Phenol[1]

BY ALFRED R. BADER AND WILLIAM C. BEAN

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The reaction of isoprene with phenol, catalyzed by phosphoric acid, yields the *o*- and *p*-3-methylcrotylphenols IV and V, the γ-hydroxyisoamylphenols II and VIII, and the two chromans I and IX.

The reactions of isoprene with phenol have been studied briefly by Claisen[2] and by Pines and Vesely.[3] Claisen obtained 2,2-dimethylchroman (I) which proved identical with the ether synthesized by ring closure of the tertiary alcohol II prepared by the action of methylmagnesium iodide on ethyl dihydrocoumarate. Pines and Vesely, who used the alcohol and ether complexes of stannic chloride, and the ether complex of 85% phosphoric acid to prepare pentenylphenols, considered condensation to take place between phenol and the tertiary double bond of isoprene, but beyond that did not elaborate on the structures of the alkenylphenols formed. In the alkylation of phenol by the reso-

(1) For paper IV, see THIS JOURNAL, **79**, 6164 (1957).

(2) L. Claisen, *Ber.*, **54B**, 200 (1921); German Patent 374,142 (Dec., 1920).

(3) H. Pines and J. A. Vesely, U. S. Patents 2,553,470 and 2,578,206 (May and Dec., 1951).