THE SYNTHESIS OF ALPHA,BETA-UNSATURATED ETHERS

BY WALTER M. LAUER AND MARVIN A. SPIELMAN

The recent work of Swallen and Boord[1] and Dykstra, Lewis and Boord[2] has drawn attention to the possibilities of halogenated ethers in organic synthesis. The present paper deals with a synthesis of α,β-unsaturated ethers by the use of halogenated ethers in a series of four reactions as shown in the equations

$$RCH_2CHO + R'OH + HCl \longrightarrow RCH_2CH(OR')Cl + H_2O \qquad (1)$$
$$RCH_2CH(OR')Cl + Br_2 \longrightarrow RCHBrCH(OR')Br + HCl \qquad (2)$$
$$RCHBrCH(OR')Br + R''MgBr \longrightarrow RCHBrCH(OR')R'' + MgBr_2 \qquad (3)$$
$$RCHBrCH(OR')R'' + KOH \longrightarrow RCH{=}C(OR')R'' + KCl + H_2O \qquad (4)$$
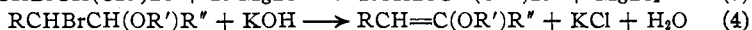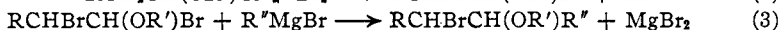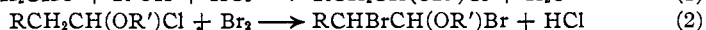
The first three steps in the synthesis were developed by Boord and his co-workers, and in the present work they were carried out in substantially the manner described by these investigators. The last step represents the removal of the elements of hydrobromic acid from a β-bromo ether.

Boord comments on the unusual stability of β-bromo ethers to sodium hydroxide and states that they may be distilled from solid caustic soda without appreciable decomposition. This has been our experience, but we have found finely powdered potassium hydroxide to be an effective reagent for the elimination of hydrobromic acid. In many cases two or three distillations of a β-bromo ether from this substance are sufficient to complete the reaction. Several other reagents were tried, among which were alcoholic potash, quinoline, dimethylaniline, sodium acetate, sodium oxide, potassium carbonate, barium hydroxide, etc. The first two were partially effective, but the yields were small, due to complicating side reactions; the others were almost entirely inert.

It is interesting to note that Hibbert[3] found the same reagent, solid potassium hydroxide, to be the most suitable in the preparation of divinyl ether from β,β'-dichloroethyl ether.

Four vinyl ethers, III, V, VIII and XI, were synthesized as shown below. The α,β-dibromo ethers I, VI and IX given as starting materials were prepared as indicated in equations (1) and (2) above. The proper aldehyde, with an alcohol and gaseous hydrogen chloride, is converted to an α-chloro ether, and this on bromination yields the desired α,β-dibromo ether. By treatment with the Grignard reagent, β-bromo ethers II, IV, VII and X are obtained, and these are distilled from potassium hydroxide to produce the vinyl ethers.

[1] Swallen and Boord, THIS JOURNAL, 52, 651 (1930).
[2] Dykstra, Lewis and Boord, ibid., 52, 3396 (1930).
[3] Hibbert, Perry and Taylor, ibid., 51, 1551 (1929).

$$CH_2BrCH(OC_2H_5)Br \xrightarrow{C_2H_5MgBr} CH_2BrCH(OC_2H_5)C_2H_5 \xrightarrow{KOH} CH_2=C(OC_2H_5)C_2H_5$$

$$I \qquad\qquad\qquad\qquad II \qquad\qquad\qquad\qquad III$$

$$\downarrow C_6H_5MgBr$$

$$\longrightarrow CH_2BrCH(OC_2H_5)C_6H_5 \xrightarrow{KOH} CH_2=C(OC_2H_5)C_6H_5$$

$$IV \qquad\qquad\qquad\qquad V$$

$$CH_3CHBrCH(OCH_3)Br \xrightarrow{C_6H_5MgBr} CH_3CHBrCH(OCH_3)C_6H_5 \xrightarrow{KOH}$$

$$VI \qquad\qquad\qquad\qquad\qquad VII$$

$$CH_3CH=C(OCH_3)C_6H_5$$

$$VIII$$

$$C_2H_5CHBrCH(OCH_3)Br \xrightarrow{C_2H_5MgBr} C_2H_5CHBrCH(OCH_3)C_2H_5 \xrightarrow{KOH}$$

$$IX \qquad\qquad\qquad\qquad\qquad X$$

$$C_2H_5CH=C(OCH_3)C_2H_5$$

$$XI$$

The substituted vinyl ethers are ethereal liquids, miscible with the usual organic solvents and easily distilled without decomposition. In the presence of a trace of acid, or even semicarbazide hydrochloride, they hydrolyze to the corresponding ketones.

$$RCH=C(OR')R'' + H_2O \longrightarrow RCH_2COR'' + R'OH$$

This property was used as a constitution proof for those not described in the literature. The ketones were characterized as semicarbazones.

Experimental Part

A. **Preparation of the Chloro Ethers. Equation (1).**—The procedure followed was essentially that described by Boord. In working with propionaldehyde or butyraldehyde, however, greater care was necessary. When the aldehyde and alcohol were mixed, considerable heat was evolved, and if thorough cooling with an ice–salt bath was not effected before the influx of the hydrogen chloride, unmanageable colored liquids were obtained from which none of the desired product could be isolated.

B. **Preparation of the α,β-Dibromo Ethers. Equation (2).**—The α-chloro ethers were brominated without purification and without a solvent in an ice–salt bath at 0–5°. Bromine was added in small portions as fast as it was taken up. After the last had been added, the mixture was allowed to stand overnight and then distilled under diminished pressure. The average yields based on the aldehyde taken for the first reaction were about 70%.

C. **Preparation of the β-Bromo Ethers. Equation (3).**—The Grignard reactions were carried out by the improved procedure described by Boord in his second paper.[2]

β-**Ethoxybutyl Bromide (II).**—Yield, 80%; n_D^{25} 1.4427; b. p. 154–156° (Boord reports 166°).

α-**Phenyl-β-bromoethyl Ethyl Ether (IV).**—Yield, 66%; b. p. 129–133° at 18 mm.; n_D^{25} 1.5317.

Anal. Calcd. for $C_{10}H_{13}OBr$: Br, 34.93. Found: Br, 35.38, 35.51.

α-**Phenyl-β-bromopropyl Methyl Ether (VII).**—Yield, 71%; b. p. 122–124° at 14 mm.; n_D^{25} 1.5316. This compound has been synthesized by Späth and Göhring[4] by the same Grignard reaction. The violet color observed by these workers was apparent for a time, but soon faded out.

3-Bromo-4-methoxy-hexane (X).—Yield, 56%; b. p. 74–78° at 20 mm.; n_D^{25} 1.4495.

4 Späth and Göhring, *Monatsh.*, 41, 319 (1920).

Anal. Calcd. for $C_7H_{15}OBr$: Br, 41.03. Found: Br, 40.23, 40.20.

D. Preparation of the α,β-Unsaturated Ethers, Equation (4).—In a distilling flask connected to a condenser was placed 40–60 g. of the β-bromo ether with an equal weight of finely powdered technical grade flake potassium hydroxide. A large sandbath was placed under the flask and the temperature was raised very slowly to incipient boiling and maintained at that level for half an hour or longer. More heat was then applied and distillation was allowed to take place over a period of two hours. Suction was advantageously employed in distilling off the last of the material from the potash, which generally fused toward the end of the reaction. In the case of compounds (V) and (VIII) most of the distillation was conducted under diminished pressure to delay the fusion of the alkali and subsequent "layering out" of materials. In three of the four compounds studied, three such distillations were sufficient to remove the last of the bromine, as indicated by the Beilstein test. The products were then purified by distillation.

2-Ethoxy-butene-1 (III).—Yield, 65%; some unchanged halide was recovered, bringing the yield up to 75.6%; b. p. 85–87°; $n_D^{24.5}$ 1.4011.

Anal. Calcd. for $C_6H_{12}O$: OC_2H_5, 45.0. Found: OC_2H_5, 44.9, 44.4.

One-half cc. was hydrolyzed with 5 cc. of water, 0.5 g. of semicarbazide hydrochloride and enough alcohol to effect solution. The hydrolysis proceeded spontaneously. Sodium acetate was added and after half an hour of heating in a beaker of water the test-tube was cooled and the methyl ethyl ketone semicarbazone separated out. After crystallization from hot water it melted at 143–144.5°. Pickard and Kenyon[5] give 135–136°, Robinson[6] gives 148° and Michael[7] gives 139°. A sample prepared from authentic methyl ethyl ketone melted at 143–144° and a mixed melting point showed no depression.

α-Ethoxystyrene (V).—Yield, 62%; b. p. 109–112° at 30 mm.; $n_D^{25.5}$ 1.5287. This compound has been prepared by Hoering,[8] Claisen,[9] Moureu[10] and Tiffeneau.[11] It was hydrolyzed to acetophenone, which was identified as the semicarbazone; m. p. and mixed m. p. 198–199°. Shriner[12] gives the same figure.

α-Methoxy-β-methylstyrene (VIII).—Yield, 42%; b. p. 96–98° at 19 mm.; n_D^{26} 1.5271.

Anal. Calcd. for $C_9H_{12}O$: OCH_3, 20.9. Found: OCH_3, 20.9, 21.3.

This compound was collected by Späth and Göhring[4] as a by-product in their synthesis of ephedrine, but not in a form sufficiently pure for analysis. One cc. was hydrolyzed by warming with 50% alcohol and a drop of hydrochloric acid. The propiophenone which settled out on dilution was converted to the semicarbazone: m. p. and mixed m. p. 172–174°. Shriner[12] gives 173–174°.

3-Methoxyhexene-3 (XI).—Yield, 79%; b. p. 114–115°; n_D^{25} 1.4130.

Anal. Calcd. for $C_7H_{14}O$: OCH_3, 27.2. Found: OCH_3, 27.3, 27.7.

This was hydrolyzed to ethyl propyl ketone and converted to the semicarbazone: m. p. 110–110.5°. Michael[7] gives 111°. Blaise[13] gives 110°.

[5] Pickard and Kenyon, *J. Chem. Soc.*, **103**, 1936 (1913).

[6] Robinson, *ibid.*, **109**, 1044 (1916).

[7] Michael, THIS JOURNAL, **41**, 416 (1919).

[8] Hoering, *Ber.*, **41**, 1889 (1908).

[9] Claisen, *ibid.*, **29**, 2931 (1896); **31**, 1020 (1898).

[10] Moureu, *Bull. soc. chim.*, [3] **31**, 493 (1904).

[11] Tiffeneau, *Compt. rend.*, **145**, 813 (1907).

[12] Shriner and Turner, THIS JOURNAL, **52**, 1269 (1930).

[13] Blaise, *Compt. rend.*, **133**, 1218 (1901).

Summary

A method for the synthesis of α,β-unsaturated ethers is described and examples are given. This method appears to be quite general in its application.

MINNEAPOLIS, MINNESOTA

MIXED BENZOINS.
III. THE STRUCTURE OF SOME UNSYMMETRICALLY SUBSTITUTED DESOXYBENZOINS

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In general, the structure of a mixed benzoin, when produced in the usual manner from two aldehydes, cannot be assigned with any degree of probability. The same remark applies to the desoxy compound derived from it by the usual methods of reduction, for even were the structure of the mixed benzoin known, the desoxy compound might be derived from it via the hydrobenzoin or the isohydrobenzoin, from which compounds water can be eliminated in several ways. Thus RCOCHOHR' could give RCHOH-CHOHR' which, by elimination of a molecule of water, could give either RCOCH₂R' or RCH₂COR' by the "vinyl-dehydration" of Tiffeneau. Other compounds, for example, diphenylacetaldehydes, produced by the "pinacoline-dehydration" of Tiffeneau, might also be expected to occur. The authors therefore sought for an unambiguous reaction to prove the structure of desoxy compounds and selected for this purpose the Beckmann transformation. A given mixed benzoin, on reduction, can give two desoxy compounds, each of which can, in turn, give two oximes. With a suitable reagent these oximes are converted into amides, the amide being different in each case. The amides are readily identified, either by hydrolysis or by synthesis, so that it is possible to assign a structure to both the oxime and to the parent desoxy compound. Usually a mixed benzoin gives but one desoxy compound, but this is not general.[1] In turn a given desoxy compound yields usually only one oxime, but again this is not general, the authors having in one case obtained both oximes in sufficient amounts to carry out Beckmann transformations on them.

There appears to be only one instance recorded of the application of the Beckmann transformation to a desoxy type of compound,[2] in this case produced by a Friedel-Crafts reaction and of known structure. The present authors have applied the transformation to seven desoxy compounds

[1] Jenkins, Buck and Bigelow, THIS JOURNAL, 52, 4495 (1930).

[2] Cain, Simonsen and Smith, J. Chem. Soc., 103, 1035 (1913).