A similar study with a series of open-chain amides indicates likewise that the production of alkyl halide decreases with increasing hindrance to rearward attack at the α_N-carbon.

The action of phosphorus pentabromide on N-benzoyl-(+)*s*-butylamine has been shown to give (−)*s*-butyl bromide. The extent of inversion of optical rotation corresponds to preponderant inversion of configuration with some racemization.

The mechanism of the von Braun reaction has been discussed in the light of the new observations.

URBANA, ILLINOIS RECEIVED JANUARY 24, 1949

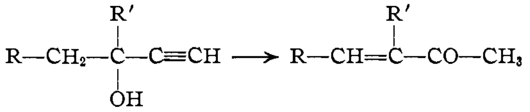
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

The Mechanism of the Rupe Reaction[1]

BY G. F. HENNION, R. B. DAVIS AND D. E. MALONEY

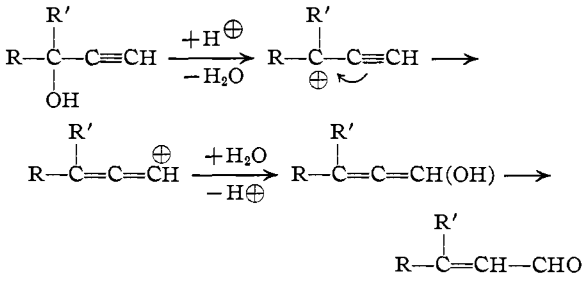
Introduction

The conversion of dialkylethynylcarbinols (I) to the corresponding α,β-unsaturated ketones (II) by heating with strong formic acid is known in this Laboratory as the Rupe reaction.[2] Rupe thought the products to be α,β-unsaturated aldehydes, R—CH₂—C(R′)=CH—CHO, but this notion has been corrected repeatedly.[3] Aldehydes of this type would be expected if the reaction followed the course of the Meyer–Schuster rearrangement,[4] which involves an anionotropic migration similar to the allylic rearrangement.[5]



$$R{-}CH_2{-}\underset{OH}{\overset{R'}{C}}{-}C{\equiv}CH \longrightarrow R{-}CH{=}\overset{R'}{C}{-}CO{-}CH_3$$

(I) (II)



$$R{-}\underset{OH}{\overset{R'}{C}}{-}C{\equiv}CH \xrightarrow[-H_2O]{+H^{\oplus}} R{-}\underset{\oplus}{\overset{R'}{C}}{-}C{\equiv}CH \longrightarrow$$

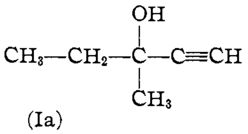
$$R{-}\overset{R'}{C}{=}C{=}\overset{\oplus}{CH} \xrightarrow[-H^{\oplus}]{+H_2O} R{-}\overset{R'}{C}{=}C{=}CH(OH) \longrightarrow$$

$$R{-}\overset{R'}{C}{=}CH{-}CHO$$

The Rupe reaction is thus an apparent 1,2-shift of the hydroxyl group while the Meyer–Schuster rearrangement is a 1,3- or allylic shift. There are a few cases in which these reactions occur in competition.[6] Actually formic acid is not the only reagent for such transformations since they are reported in a wide assortment of acetylenic alcohol reactions with numerous acidic reagents. While there seems to be little doubt about the mechanism of the Meyer–Schuster rearrangement, the mechanism of the Rupe reaction has not been established.

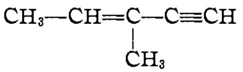
One of the simplest cases in which this reaction proceeds well is that of methylethylethynylcarbinol (Ia).[7] The product, however, is not "*s*-butylidine-acetaldehyde"[7] but rather 3-methyl-3-penten-2-one (IIa). We have proved that the latter is formed by dehydration of the carbinol (Ia) to 3-methyl-3-penten-1-yne (III) and subsequent hydration of the triple bond. This conclusion emerges from the following facts.

The carbinol (Ia) and the corresponding vinylacetylene (III), chloride (IV), and acetate ester (V) yielded the same product (IIa) by treatment with hot formic acid.



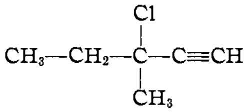
$$CH_3{-}CH_2{-}\underset{CH_3}{\overset{OH}{C}}{-}C{\equiv}CH$$

(Ia)



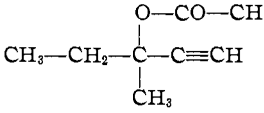
$$CH_3{-}CH{=}\underset{CH_3}{C}{-}C{\equiv}CH$$

(III)



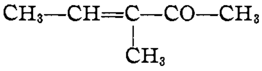
$$CH_3{-}CH_2{-}\underset{CH_3}{\overset{Cl}{C}}{-}C{\equiv}CH$$

(IV)



$$CH_3{-}CH_2{-}\underset{CH_3}{\overset{O-CO-CH_3}{C}}{-}C{\equiv}CH$$

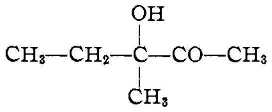
(V)



$$CH_3{-}CH{=}\underset{CH_3}{C}{-}CO{-}CH_3$$

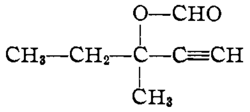
(IIa)

That hydration of the triple bond did not precede the dehydration was evident from the fact that the acyloin (VI) did not react with boiling formic acid. An alternative explanation involving thermal decomposition of the formate ester (VII) was considered untenable because



$$CH_3{-}CH_2{-}\underset{CH_3}{\overset{OH}{C}}{-}CO{-}CH_3$$

(VI)



$$CH_3{-}CH_2{-}\underset{CH_3}{\overset{O-CHO}{C}}{-}C{\equiv}CH$$

(VII)

---

[1] Paper LIII on the chemistry of substituted acetylenes; previous paper, THIS JOURNAL, **71**, 1964 (1949).

[2] Rupe, *et al.*, *Helv. Chim. Acta*, **9**, 672 (1926), and subsequent papers.

[3] (a) Fischer and Lowenburg, *Ann.*, **475**, 183 (1929); (b) Hurd, *et al.*, THIS JOURNAL, **56**, 1924 (1934); **59**, 118 (1937); **71**, 398 (1949); (c) Price and Meisel, *ibid.*, **69**, 1497 (1947).

[4] Meyer and Schuster, *Ber.*, **55B**, 819 (1922).

[5] MacGregor, THIS JOURNAL, **70**, 3953 (1948).

[6] Chanley, *ibid.*, **70**, 244 (1948).

[7] Rupe and Kambli, *Helv. Chim. Acta*, **9**, 672 (1926); Rupe U. S. Patent 1,670,825 (1928).

(VII) was not decomposed by heating above its boiling point. By way of further evidence, it should be mentioned that when the carbinol (Ia) was added dropwise to 80–90% formic acid during distillation, all three substances, (Ia), (IIa) and (III), were found in the distillate.

Since (III) is obviously an intermediate in the Rupe reaction, its hydration was examined in some detail. It dissolved slowly when refluxed with 80% formic acid and produced less tarry material than did the others (Ia, IV, V). When heated with 80% acetic acid containing a little sulfuric acid, its behavior was similar and (IIa) was obtained in 50% yield. The acetic–sulfuric acid reagent was not so effective with (Ia) however, and gave the ketone only in poor yield.

There remained to prove the structure of the ketone (IIa). This was accomplished by an independent synthesis from acetaldehyde and methyl ethyl ketone *via* the aldol condensation.[8] The two samples had substantially the same physical properties (b. p., $n^{25}\text{D}$ and d^{25}), and their hydroxylamine, semicarbazide and 2,4-dinitrophenylhydrazine derivatives had the same melting points and mixed melting points. Furthermore, the ultraviolet spectrum of (IIa) corresponded excellently with the spectra given by Price and Meisel[3c] for similar compounds.

Experimental

Methylethylethynylcarbinol and **methylethylethynylcarbinyl chloride** were prepared by the methods of Campbell, Campbell and Eby.[9]

3-Methyl-3-penten-1-yne was made from the carbinol by dehydration with acetic anhydride.[10]

Methylethylethynylcarbinyl Acetate.—Acetic anhydride (1.2 moles, 122 g.) containing 10 drops of sulfuric acid was added dropwise to the carbinol (1 mole, 98 g.) to maintain a temperature of 50–55°. The mixture was allowed to stand overnight. It was then washed twice with cold water and the washings extracted with ether. The ester and the ether layers were combined, washed with 10% sodium carbonate solution, ice water, and dried over calcium chloride. Distillation gave 92 g. (66% yield) of ester, b. p. 75–77° at 50 mm., $n^{25}\text{D}$ 1.4240, d^{25} 0.9265.

Anal. Calcd. for $C_8H_{12}O_2$: C, 68.53; H, 8.63; *MR*, 38.80. Found: C, 68.50; H, 8.71; *MR*, 38.62.

Methylethylethynylcarbinyl Formate.—Acetic anhydride (0.57 mole, 56 g.) was added slowly to 0.55 mole (25 g.) of 99% formic acid with cooling. One-half mole (49 g.) of methylethylethynylcarbinol was added slowly and the solution heated at 50–55° for three hours. It was allowed to stand for three days and then poured over 100 g. of ice. Ether was added to effect separation. The ethereal solution was washed with 10% sodium carbonate, etc., as described above. Distillation gave 28 g. (45% yield) of ester, b. p. 69–72° at 50 mm., 144–146° at atm. press.; $n^{25}\text{D}$ 1.4250; d^{25} 0.9455. It distilled with only slight decomposition when dropped on a little boric oxide preheated to 300°.

Anal. Calcd. for $C_7H_{10}O_2$: C, 66.64; H, 7.99; *MR*, 34.18. Found: C, 66.93; H, 8.26; *MR*, 34.12.

3-Methyl-3-hydroxy-2-pentanone was prepared from methylethylethynylcarbinol by direct hydration. The catalyst was composed of 2.5 g. of mercuric oxide and 5 g. of sulfuric acid in 30 g. of water and 60 g. of methyl alcohol. Seventy-three grams (0.75 mole) of the carbinol was added slowly to this mixture to maintain a temperature of 60–65°. After stirring for three hours, 10 g. of anhydrous potassium carbonate was added and the stirring continued for thirty minutes. The solids were allowed to settle overnight and the supernatant liquid decanted and distilled, yielding 53 g. of product (60% yield), b. p. 70–73° at 50 mm., $n^{25}\text{D}$ 1.4200. The semicarbazone[11] melted at 149–150° in agreement with the literature value.

Rupe Reactions.—One-half mole of methylethylethynylcarbinol (or the corresponding vinylacetylene, chloride, or ester) was refluxed with 288 g. (5 moles) of 80% formic acid for one and one-half hours. The product was diluted with 200 ml. of water and distilled until a test portion of the distillate gave no oily layer on neutralization with 30% sodium hydroxide. The distillate was neutralized with strong sodium hydroxide, extracted with ether, the ether extract washed with water and dried with calcium chloride or potassium carbonate. Distillation gave 3-methyl-3-penten-2-one in 36 to 42% yield; b. p. 63–64° at 50 mm., 138–140° at atm. press., $n^{25}\text{D}$ 1.4465, d^{25} 0.8694. The derivatives had the following melting points: semicarbazone, 190–191°; 2,4-dinitrophenylhydrazone, 193–194°; oxime, 73°. The ketone turned yellow on standing and repeated distillation did not remove the color. An independent synthesis was accomplished as described below.

Reaction of Acetaldehyde with Methyl Ethyl Ketone.—Ten milliliters of 3 *N* alcoholic potassium hydroxide was added to 3.3 moles (240 g.) of methyl ethyl ketone and the mixture cooled with ice. One and one-tenth mole (48 g.) of acetaldehyde was dropped in with good stirring over a period of three hours. The reaction was allowed to proceed for an additional hour and 2 g. of oxalic acid dihydrate added. The potassium oxalate was filtered off and excess methyl ethyl ketone distilled. Two grams of anhydrous oxalic acid was then added and distillation resumed. The material boiling from 100–141° at atm. press. and to 100° at 50 mm. was retained. After drying, redistillation gave 50 g. (46% yield) of 3-methyl-3-penten-2-one, b. p. 62–65° at 50 mm., $n^{25}\text{D}$ 1.4462, d^{25} 0.8677. The semicarbazone, 2,4-dinitrophenylhydrazone, and oxime had the melting points cited above. Mixtures of the derivatives made from the two samples of ketone showed no depressions of the melting points.

Ultraviolet Absorption.—One milliliter of a solution of 0.0490 g. of 3-methyl-3-penten-2-one in 100 ml. of 95% ethyl alcohol was further diluted to 150 ml. of solution. Maximum absorption (ϵ = 12,600) was observed at a wave length of 230 mμ.

Summary

The mechanism of the Rupe reaction is shown to involve dehydration of the acetylenic alcohol to a substituted vinylacetylene followed by hydration of the triple bond. The products are therefore α,β-unsaturated ketones. The evidence for this mechanism was obtained from a study of the reactions of methylethylethynylcarbinol and its derivatives with formic acid.

NOTRE DAME, INDIANA RECEIVED APRIL 2, 1949

---

[8] Colonge, *Bull. soc. chim.*, [4] **49**, 449 (1931).

[9] Campbell, Campbell and Eby, THIS JOURNAL, **60**, 2882 (1938).

[10] Thompson, Milas and Rovno, *ibid.*, **63**, 752 (1941).

[11] Diels and Johlin, *Ber.*, **44**, 406 (1911).