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Anomalous Hofmann Elimination Reactions

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It is shown that the product from the Hofmann elimination of 3-phenylpropyltrimethylammonium hydroxide is 1-phenylpropene accompanied by varying amounts of 3-phenylpropene. It is concluded that 3-phenylpropene is the primary product, and that under the conditions necessary for the elimination it rearranges to 1-phenylpropene. It is suggested that while a similar explanation probably is valid in explaining the source of other abnormal Hofmann products, other routes are also open to give abnormal products. Thus, evidence is presented to indicate that the product obtained by Rogers and Ingold in the decarbethoxylation and Hofmann elimination of 3,3-dicarbethoxy-4-phenylbutyltrimethylammonium hydroxide is ethyl 1-benzylcyclopropanecarboxylate.

Recently we have presented evidence indicating the occurrence of a *cis* elimination in the formation of 1-phenylcyclohexene by a Hofmann elimination from trimethyl-*trans*-2-phenylcyclohexylammonium hydroxide.[1] In this work we showed that 3-phenylcyclohexene, the intermediate which would arise if a normal *trans* elimination occurred,[2] does not rearrange to 1-phenylcyclohexene, the observed product,[3] under the conditions of the reaction. In view of this it seemed of interest to investigate some other examples of the Hofmann elimination in which the observed product arises by means of a rearrangement.

There are several examples of abnormal Hofmann elimination products in the literature. Thus the final Hofmann elimination in the exhaustive methylation of piperidine gave 1,3-pentadiene (rather than the expected 1,4-pentadiene)[4] and the Hofmann elimination of 3-phenylpropyltrimethylammonium hydroxide gave 1-phenylpropene rather than the expected 3-phenylpropene.[5,6] Also, the Hofmann elimination and decarbethoxylation of 3,3-dicarbethoxy-4-phenylbutyltrimethylammonium hydroxide was reported to give ethyl *iso*-α-benzylcrotonate rather than the expected ethyl-α-benzylvinylacetate.[7] We decided to study one of these reactions in order to establish its course.

Reinvestigation of the Hofmann elimination of 3-phenylpropyltrimethylammonium hydroxide has confirmed the observation that the major product is 1-phenylpropene. However, under the normal conditions for this reaction (almost anhydrous quaternary ammonium hydroxide heated at 120–130°) about 9% of 3-phenylpropene is also found. Under the same conditions exogenous 3-phenylpropene isomerizes to the same mixture of phenylpropenes. Reducing the contact time of the product with unreacted quaternary ammonium hydroxide raised the 3-phenylpropene content of the product to 13% and in the presence of some water as much as 36% of the product was 3-phenylpropene. This indicates that 3-phenylpropene is the original product and that this is rearranged under the reaction conditions to 1-phenylpropene.

$$\phi CH_2CH_2CH_2\overset{+}{N}(CH_3)_3OH^- \longrightarrow \phi CH_2CH{=}CH_2 \rightleftharpoons \phi CH{=}CHCH_3$$

In order to determine the facility with which 3-phenylpropene isomerizes under basic conditions, a brief kinetic study was carried out. It was found that in 0.1 *normal* ethanolic potassium hydroxide at 100° the isomerization has a half-life of about 25 hours. The very much more rapid isomerization under ordinary Hofmann conditions indicates that an almost anhydrous quaternary ammonium hydroxide melt has a greater basicity than would be expected from its concentration of hydroxide ion (in the case of 3-phenylpropyltrimethylammonium hydroxide the hydroxide ion is about five *molar*). The decrease of base strength of hydroxide ion on solvation has been attributed to hydrogen bonding.[8] The possible leveling effect of water on base strength in general has also been discussed.[9]

No reaction was observed when 3-phenylpropyltrimethylammonium hydroxide was refluxed in aqueous solution for 32 hours. Arnold and Richardson[3] found that both *cis* and *trans*-trimethyl-2-phenylcyclohexylammonium hydroxide react in about one hour in refluxing water to give a 70% yield of 1-phenylcyclohexene. Since a *trans* elimination from trimethyl-*trans*-2-phenylcyclohexylammonium hydroxide to give 3-phenylcyclohexene would have to go by loss of an unactivated hydrogen, this reaction would be expected to proceed at about the same rate as the elimination reaction of 3-phenylpropyltrimethylammonium hydroxide. Actually it goes under much less vigorous conditions,

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[1] Weinstock and Bordwell, *J. Am. Chem. Soc.*, **77**, 6706 (1955).

[2] Ingold, *Structure and Mechanism in Organic Chemistry*, Cornell University Press, Ithaca, New York, 1953, p. 464.

[3] Arnold and Richardson, *J. Am. Chem. Soc.*, **76**, 3649 (1954).

[4] Hofmann, *Ber.*, **14**, 659 (1881).

[5] Senfters and Tafel, *Ber.*, **27**, 2309 (1894).

[6] von Braun, *Ann.*, **382**, 47 (1911).

[7] Ingold and Rogers, *J. Chem. Soc.*, 722 (1935).

[8] Stevens and Richmond, *J. Am. Chem. Soc.*, **63**, 3132 (1941).

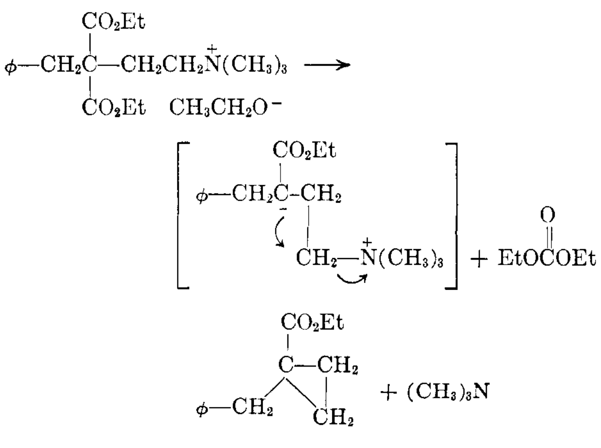
[9] Davis and Metzer, *Natl. Bur. Standards J. Research*, **48**, 381 (1952).

and this can be interpreted as further evidence[1] for the occurrence of a *cis* elimination in this case.

It seems probable that many Hofmann elimination reactions that give abnormal products when carried out under vigorous conditions[4] proceed by formation of a normal primary product followed by a base-catalyzed rearrangement. However, this is not always the case.

Thus Ingold and Rogers[6] reported that they obtained ethyl *iso*-α-benzylcrotonate from an attempted Hofmann elimination of 3,3-dicarbethoxy-4-phenylbutyltrimethylammonium ethoxide. They found that hydrolysis of this ester gave an acid, m.p. 107°, which was isomeric with the α-benzylcrotonic acid obtained by the base-catalyzed isomerization of α-benzylvinylacetic acid. Also, this acid, which gave an amide, m.p. 82–83°, could be prepared by treating ethyl α-benzyl-γ-bromobutyrate with alkali. This preparation is reminiscent of many cyclopropane syntheses; indeed, the decomposition of the quaternary ammonium ethoxide is analogous to the preparation of ethyl 1-acetamidocyclopropanecarboxylate by the decomposition of 3-acetamido-3,3-dicarbethoxypropyltrimethylammonium hydroxide.[10]

1-Benzylcyclopropanecarboxylic acid is reported to be a solid, m.p. 103°[11] and 106.5–108°.[12] The melting point of the amide is 84°.[11] The correspondence of the melting points and consideration of the methods of preparation suggest that the product obtained by Ingold and Rogers was ethyl 1-benzylcyclopropanecarboxylate. This is thus another example[10] of the formation of a cyclopropane ring by a displacement of trimethylamine when a stable anion is formed *gamma* to the nitrogen during a potential Hofmann elimination reaction and illustrates another source of abnormal Hofmann products.



The absence of phenylcyclopropane in the product from the elimination reaction of 3-phenylpropyltrimethylammonium hydroxide indicates that a hydrogen β to a trimethylammonium group is more easily lost to give a double bond than a hydrogen α to a phenyl group and γ to a trimethylammonium group to give a cyclopropane ring.

EXPERIMENTAL

Materials. 3-Phenyl-1-bromopropane, b.p. 108–109° at 10 mm., was prepared by refluxing 3-phenyl-1-propanol with twice its weight of 48% HBr for eight hours.[13] *3-Phenylpropyltrimethylammonium bromide* was prepared by refluxing 3-phenyl-1-bromopropane with trimethylamine in alcohol solution.[14] Recrystallization from an ethanol-ethyl acetate mixture gave colorless crystals, m.p. 148–152°. *3-Phenylpropyltrimethylammonium hydroxide* was prepared by passing an aqueous solution of the bromide over a column of the ion exchange resin *Amberlite IRA-400* (hydroxide form) and eluting the column with water until the eluate was essentially neutral.[15] The water then was evaporated under a vacuum on a steam-bath, the last traces of water being removed by an azeotropic distillation with methanol and benzene. 3-Phenylpropene was prepared by coupling phenylmagnesium bromide and allyl bromide.[16] The product had b.p. 156–157°, n_D^{25} 1.5114.

Analysis of 1- and 3-phenylpropene mixtures. The method of analysis used was that of Berti.[17] He showed that the refractive index is a linear function of composition for mixtures of 1- and 3-phenylpropene. In our opinion the best value for the refractive index of 3-phenylpropene[18] is n_D^{25} 1.5082. The many higher values reported are probably due to contamination with bromobenzene, a starting material which boils quite close to the product. We used n_D^{25} 1.5491 for the refractive index of 1-phenylpropene.[19]

Hofmann degradation of 3-phenylpropyltrimethylammonium hydroxide. (*A*). The quaternary ammonium hydroxide from 13.0 g. (0.05 mole) of 3-phenylpropyltrimethylammonium bromide was decomposed in a molecular still at 120–130° at 10–20 mm.; Pyrex wool was used to control bumping. The crude product was diluted with pentane, and washed successively with dilute HCl, water, and sodium bicarbonate solution. Distillation gave (1) 0.4 g., b.p. to 171°, n_D^{25} 1.5448; (2) 1.3 g., b.p. 171–173°, n_D^{25} 1.5455; (3) 1.0 g., b.p. 173°, n_D^{25} 1.5460. There was a total of 2.7 g. (46%) of product, composite n_D^{25} 1.5455. This corresponds to 9% 3-phenylpropene. The infrared spectrum of (2) appeared to be identical with that of 1-phenylpropene. (American Petroleum Institute Catalog of Infrared Spectra, Spectrum No. 330).

(*B*). The quaternary ammonium hydroxide from 13.0 g. (0.05 mole) of 3-phenylpropyltrimethylammonium bromide was added dropwise to a flask heated to 130–135° and evacuated through a Dry Ice-propanol cooled trap to 0.5–1.0 mm. The rate of addition was such that the previous drop had completely decomposed and distilled before another drop was added. The material in the cold trap was diluted with ligroin and worked up as described above. Distillation

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(10) Rinderknecht and Niemann, *J. Am. Chem. Soc.*, **73**, 4259 (1951).

(11) Haller and Benoist, *Ann. chim.*, **17**, 26 (1922).

(12) Piehl and Brown, *J. Am. Chem. Soc.*, **75**, 5023 (1953).

(13) Aspinall and Baker, *J. Chem. Soc.*, 743 (1950).

(14) Hochstein and Brown, *J. Am. Chem. Soc.*, **70**, 3484 (1948).

(15) Weinstock and Boekelheide, *J. Am. Chem. Soc.*, **75**, 2546 (1953).

(16) Hershberg, *Helv. Chim. Acta*, **17**, 351 (1934).

(17) Berti, *J. Am. Chem. Soc.*, **76**, 1213 (1954).

(18) Levy and Cope, *J. Am. Chem. Soc.*, **66**, 1684 (1944).

(19) Campbell and Young, *J. Am. Chem. Soc.*, **69**, 688 (1947).

gave 4.3 g. (73%) of phenylpropenes, composite n_D^{25} 1.5439 (13% 3-phenylpropene).

(*C*). The quaternary ammonium hydroxide from 13 g. (0.05 mole) of 3-phenylpropyltrimethylammonium hydroxide dissolved in 250 ml. of water when refluxed for 32 hours using a continuous liquid-liquid separator gave no water-insoluble product. This same solution on concentration to about 85 ml. and addition of 48 g. (0.85 mole) of solid potassium hydroxide reacted in three hours. The water-insoluble steam-distillable product on working up in the usual way and distilling gave (1) 1.15 g., b.p. 165–170°, n_D^{25} 1.5381; (2) 2.45 g., b.p. 170–172°, n_D^{25} 1.5434. The total product weighed 3.60 g. (64%) and had a composite n_D^{25} 1.5418 (18% 3-phenylpropene).

(*D*). A solution of 13.0 g. (0.05 mole) of 3-phenylpropyltrimethylammonium bromide and 60 g. (1.07 moles) of potassium hydroxide in 100 ml. of water on decomposition as in *C* gave 1.5 g. (24%) of product in 5 hours, n_D^{25} 1.5343 (36.2% 3-phenylpropene).

Isomerization of 3-phenylpropene. (*A*). A mixture of 3.0 g. of 3-phenylpropene and the quaternary ammonium hydroxide obtained from 6.5 g. (0.025 mole) of 3-phenylpropyltrimethylammonium bromide was heated in a molecular still at 130° for 30 minutes at atmospheric pressure and then at 20 mm. at the same temperature until no more product distilled over. On working up in the usual way, 3.75 g. of product was obtained, n_D^{25} 1.5455, (9% allylbenzene). Assuming a yield similar to that in the Hofmann reaction carried out under similar conditions, this corresponds to an 80% recovery of hydrocarbon from the added 3-phenylpropene.

(*B*). Ten-ml. aliquots of an ethanolic solution 0.1 *N* in potassium hydroxide and 1.0 *N* in 3-phenylpropene were sealed in Pyrex vials, placed in a 100° steam-bath, and removed at appropriate time intervals. The vials then were cooled, opened, diluted with water, acidified with hydrochloric acid, extracted with pentane, and the pentane was washed with bicarbonate solution, dried, and evaporated. The residue then was analyzed by means of refractive index. The results showed that a half-life for approach to equilibrium under these conditions is 25 hours.

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