

Summary

1. A study of the effects of variations in temperature, time and molar ratios of reactants upon the conversion of methylene-*bis-p*-toluidine or trimeric methylene-*p*-toluidine to N-(5-methyl-2-aminobenzyl)-*p*-toluidine, in the presence of *p*-toluidine and *p*-toluidine hydrochloride, showed: (a) at 80–100° the reaction is rapid and does not proceed beyond the aminobenzylarylamine stage. The conditions previously specified, *viz.*, a temperature of 20° and a reaction time of forty-eight hours, were based on a misconception. (b) The extent of the conversion increases with increase in the molar ratio of free amine to diimine or Schiff base. Highest yields require an inconveniently large ex-

cess of free amine. Satisfactory practical ratios, which give good yields and do not too greatly prolong the isolation procedure, are diimine : amine : amine hydrochloride = 1:10:0.5, or trimeric Schiff base : amine : amine hydrochloride = 1:33:1.5.

2. The procedure based upon the above conditions has been used for the preparation of the aminobenzylarylamines obtainable from *p*-toluidine, *p*-chloroaniline and *p*-bromoaniline. It failed in the cases of *p*-anisidine and *p*-phenetidine and its usefulness apparently is impaired by the limitations of the isolation method now available.

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The Structure of Beta and Gamma Tocopherols

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To date there have been described in the literature three tocopherols, which we designated provisionally as alpha, beta and gamma.^{1,2} Alpha was obtained from wheat germ oil, cottonseed oil, palm oil, and lettuce leaves. Beta was first obtained by us from wheat germ oil, and later by Todd, Bergel, Waldmann and Work, who obtained it in addition from rice bran oil.^{3,4} It was obtained subsequently from wheat germ oil by Drummond and Hoover,⁵ John,⁶ who suggested the name cumo-tocopherol for it, and Karrer, Salomon and Fritsche,⁷ who proposed the name neo-tocopherol. Dr. John⁸ kindly compared a sample of our β -tocopherol allophanate with his cumo-tocopherol allophanate and found them identical. It is interesting that the European workers found that in their preparations of wheat germ oil, β -tocopherol predominated to such an extent that the suggestion was put forward that alpha might be an artifact,⁹ whereas from the Californian wheat germ oil we have regularly

obtained at least twice as much alpha as beta. γ -Tocopherol has been obtained from cottonseed oil and palm oil. In our experience at the University of California and in the Research Laboratories of Merck & Co., Inc., where several hundred pounds of cottonseed oil have been worked up, the ratio of alpha to gamma varies within wide limits. Sometimes there is as much gamma as alpha but usually much less. Other oils beside wheat germ and cotton seed, notably grape seed oil, are known to vary greatly in their chemical constituents, depending not only on the locality, but also on the year of the crop.

On pyrolysis Fernholz¹⁰ showed that α -tocopherol yields durohydroquinone. Under similar conditions, from β -tocopherol John⁶ obtained trimethylhydroquinone, and Bergel, Todd and Work⁹ reported a mixture of trimethylhydroquinone and durohydroquinone.

Fernholz's original view that α -tocopherol is a simple mono-ether of durohydroquinone was modified by the results of the chromic acid oxidation,¹¹ whereby he obtained dimethylmaleic anhydride; a lactone $C_{21}H_{40}O_2$, the hydroxy acid of which forms a characteristic benzylthiuronium salt; and an acid $C_{16}H_{32}O_2$ which on vigorous oxidation yielded two moles of acetic acid. From this evidence Fernholz proposed formula I for α -tocopherol

(1) H. M. Evans, O. H. Emerson and G. A. Emerson, *J. Biol. Chem.*, **113**, 319 (1936).

(2) O. H. Emerson, G. A. Emerson, A. Mohammad and H. M. Evans, *ibid.*, **122**, 99 (1937).

(3) A. R. Todd, F. Bergel, H. Waldmann and T. S. Work, *Nature*, **140**, 361–2 (1937).

(4) A. R. Todd, F. Bergel and T. S. Work, *Biochem. J.*, **31**, 2257 (1937).

(5) J. C. Drummond and A. A. Hoover, *ibid.*, **31**, 1852 (1937).

(6) W. John, *Z. physiol. Chem.*, **250**, 11 (1937).

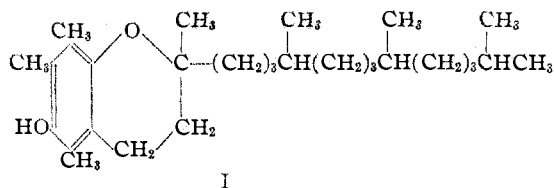
(7) P. Karrer, H. Salomon and H. Fritsche, *Helv. Chim. Acta*, **20**, 1422 (1937).

(8) W. John, *Z. physiol. Chem.*, **252**, 201 (1938).

(9) F. Bergel, A. R. Todd and T. S. Work, *J. Chem. Soc.*, 253 (1938).

(10) E. Fernholz, *THIS JOURNAL*, **59**, 1154 (1937).

(11) E. Fernholz, *ibid.*, **60**, 700 (1938).



We have oxidized β - and γ -tocopherol under the conditions described by Fernholz and have obtained from both the same lactone that had been obtained from α -tocopherol. We failed to obtain dimethylmaleic anhydride, but the amount of material used by us was much smaller than that employed by Fernholz so that dimethylmaleic anhydride, if formed, might have escaped our attention.

We have also pyrolyzed γ -tocopherol at 360° , and obtained trimethylhydroquinone. From these facts, it is evident that β - and γ -tocopherol differ from alpha only in the absence of one of the three methyl groups attached to the benzene ring. This had been suspected by John⁶ and Karrer, Salomon and Fritzsche.¹²

Oxidation of β -Tocopherol.—Eight hundred and nine milligrams of β -tocopherol was oxidized as described by Fernholz.¹¹ A lactone was obtained which was purified by distillation in high vacuum (yield 351 mg.). This yielded a benzylthiuronium salt which, after several recrystallizations from acetone, melted at 116 – 117° . A sample of the corresponding benzylthiuronium salt, prepared by Fernholz from α -tocopherol, melted at 116 –

(12) P. Karrer, H. Salomon, and H. Fritzsche, *Helv. Chim. Acta.*, **21**, 302 (1938).

117.5° ; mixed m. p. 116 – 117° . *Anal.* Calcd. for $C_{29}H_{52}O_2N_2S$: C, 68.45; H, 10.30; N, 5.50. Found: C, 68.22, 68.51, 68.15; H, 10.23, 10.44, 10.23; N, 5.42, 5.54.

Oxidation of γ -Tocopherol.—Three hundred and seventy four milligrams of γ -tocopherol, oxidized as above, yielded 90 mg. of lactone after purification by high vacuum distillation. This gave a benzylthiuronium salt melting at 116 – 117° which showed no depression on admixture with a sample of the corresponding benzylthiuronium salt of the same melting point from α -tocopherol. *Anal.* Calcd. for $C_{29}H_{52}O_2N_2S$: C, 68.45; H, 10.30; N, 5.50. Found: C, 68.59, 68.65; H, 10.35, 10.26; N, 5.48.

Pyrolysis of γ -Tocopherol.—Five hundred milligrams of γ -tocopherol was heated at 360° in an atmosphere of carbon dioxide. This gave 30 mg. of a crystalline sublimate, which appeared to be a mixture of trimethylhydroquinone with a little durohydroquinone. By careful recrystallization from benzene there was obtained a fraction melting at 167 – 170° which gave no depression with authentic trimethylhydroquinone. A benzoate was also obtained melting at 175 – 178° which gave no depression when mixed with an authentic sample of trimethylhydroquinone dibenzoate melting at 178 – 180° .

The trimethylhydroquinone and its dibenzoate were supplied by Professor Lee Irvin Smith to whom we wish to express our thanks.

Summary

Oxidation of β - and γ -tocopherols yielded the same $C_{21}H_{40}O_2$ lactone that had been obtained by Fernholz from α -tocopherol.

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Carbamic Esters from Urea

BY RALPH A. JACOBSON

Esters of carbamic acid are usually prepared either by treating an alcohol with phosgene and adding ammonia to the chloroformic ester thus formed, or by treating the alcohol with cyanic acid. The reaction of urea with an alcohol has also been utilized¹ but the method has not been applied widely, probably because the lower alcohols, *e. g.*, methyl and ethyl, require pressure. Butanol, however, reacts with urea at atmospheric pressure² to give butyl carbamate in 75% yield. This suggests wider application of the

method for the preparation of carbamic esters of alcohols having boiling points higher than that of butanol. In the present paper, we have adapted this method to the synthesis of octyl carbamate, *n*-dodecyl carbamate, and several other esters of carbamic acid.

The optimum temperature range for carbamate formation appears to be 175 – 190° . At this temperature, aliphatic monohydric alcohols react smoothly with urea with the evolution of ammonia and the formation of carbamates. While the reaction is usually over within a few hours at this temperature, a reaction period of twelve to twenty-four hours or longer is required for al-

(1) Hoffmann, *Ber.*, **4**, 268 (1871); Bunte, *Ann.*, **181**, 181 (1869); Cahours, *Chem. Zentr.*, **4**, 482 (1873); *Compt. rend.*, **76**, 1387 (1873); Werner, *J. Chem. Soc.*, **118**, 626 (1918).

(2) Davis and Lane, *Org. Syntheses*, **9**, 24 (1920).