vomipyrine and β-collidine. There is sufficient overlap to fix the positions of fusion of the rings.

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[1] Wieland, H., and Horner, L., *Annalen*, **528**, 73 (1937).
[2] Horner, L., *Annalen*, **540**, 73 (1939); cf. ref. 9.
[3] Robinson, R., *Experientia*, **2**, 28 (1946). Openshaw, H. T., and Robinson, R., *Nature*, **157**, 438 (1946). Chakravarti, R. N., and Robinson, R., *Nature*, **160**, 18 (1947).
[4] Pausacker, K. H., and Robinson, R., *J. Chem. Soc.* (in the press, 1948).
[5] Perkin, W. H., Robinson, R., and Smith, J. C., *J. Chem. Soc.*, 1239 (1932).
[6] Bailey, A. S., and Robinson, R., *Nature*, **161**, 433 (1948).
[7] Bradford, L., Elliott, T. J., and Rowe, F. M., *J. Chem. Soc.*, 437 (1947).
[8] Kyker, G. C., and Bost, R. W., *J. Amer. Chem. Soc.*, **61**, 2469 (1939)
[9] Wieland, H., and Horner, L., *Annalen*, **536**, 89 (1938); cf. ref. 2.

## Structure of Dunnione

THE investigation of dunnione and its transformation products by Price and Robinson[1] did not completely establish the structures of these compounds. The work was interrupted by the War; but Dr. Price has recently suggested that the further examination of these substances be included in a programme of research on quinones which is proceeding in this Laboratory. As closely related work is being done in the United States, it seems desirable to give a brief preliminary report of the scope of the present investigations, and of the results already obtained.

The structures previously assigned to dunnione and the *iso*-dunniones have been confirmed by the synthesis of *dl*-dunnione and β-*iso*-dunnione. Claisen rearrangement of 2-γγ-dimethylallyloxy-1 : 4-naphthaquinone gives rise to two products: the normal rearrangement product, 2-hydroxy-3-αα-dimethylallyl-1 : 4-naphthaquinone (m.p. 70–71°), and the abnormal product, 2-hydroxy-3-αβ-dimethylallyl-1 : 4-naphthaquinone. The latter compound proved to be identical with the *iso*-dunniol of Price and Robinson (*loc. cit.*), and by ring closure with sulphuric acid it is converted to αββ-trimethyldihydrofurano-1 : 2-naphthaquinone identical with the β-*iso*-dunnione derived from natural dunnione. Similarly, ring closure of the normal rearrangement product gives ααβ-trimethyldihydrofurano-1 : 2-naphthaquinone (m.p. 93–94°), which is evidently the racemic modification of dunnione. Its melting point is not depressed by mixing with the natural dextrorotatory pigment (m.p. 98–99°), and on treatment with cold alkali it is gradually converted to two products, which are evidently *dl*-α-dunnione (m.p. 110–111°) and *dl*-*allo*-dunnione (m.p. 141–142°). The first of these gives β-*iso*-dunnione on heating with sulphuric acid, and the second shows the characteristic absorption spectrum previously recorded[2] for the dextrorotatory *allo*-dunnione derived from natural dunnione.

It is noteworthy that the normal Claisen rearrangement of the γγ-disubstituted allyl ether was accomplished simply by boiling an alcoholic solution under reflux for a few hours. The yield was 93 per cent. When the ether was heated for a few minutes, without solvent, at a temperature slightly above its melting point, the main product was that resulting from abnormal rearrangement.

The structure of β-*iso*-dunnione has also been proved by an independent synthesis starting from 2-hydroxy-3-βγγ-trimethylallyl-1 : 4-naphthaquinone (m.p. 169–170°).

With the structures of these compounds thus established, it seems evident that the change from the dunnione to the *iso*-dunnione structure is simply a somewhat unusual example of the Wagner–Meerwein type of rearrangement.

Furthermore, it seems probable that the rearrangement of dunnione to *allo*-dunnione involves a reaction characteristic of 2-hydroxynaphthaquinones having a tertiary alkyl group in the quinone ring. This hypothesis is supported by the observation that 2-hydroxy-3-αα-dimethylallyl-1 : 4-naphthaquinone undergoes a similar reaction when heated with aqueous alkali, giving a product (m.p. 148–149°) which dissolves in aqueous sodium bicarbonate to give a *yellow* solution. An analogous product is obtained by the action of alkali on 2-hydroxy-3-ααβ-trimethylallyl-1 : 4-naphthaquinone (m.p. 81–82°).

Full details of this work will be published elsewhere.

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[1] Price and Robinson, *J. Chem. Soc.*, 1522 (1939); 1493 (1940).
[2] Cooke, Macbeth and Winzor, *J. Chem. Soc.*, 878 (1939).

## A Natural Precursor of the Folic Acid Complex

RECENTLY Elvehjem and his co-workers[1] have demonstrated the presence, in rat liver homogenates, of a natural precursor capable of conversion by enzymes also present in liver to material having folic acid activity. They base the use of the term 'folic acid' on the fact that there is no evidence that the material produced is identical with pteroylglutamic acid. The same considerations apply to its use in the present communication.

Following observations made some time ago[2] that similar activity can be produced chemically by the interaction of histidine with certain components of an acid hydrolysate of casein, I have indicated[3] that this amino-acid may also act as a biological precursor of some member of the folic acid complex, and it now appears that in all probability it is identical with the precursor described by Elvehjem.

An enzyme capable of converting histidine into material having growth-stimulatory activity for *Streptococcus fæcalis* R. has been shown to be widely distributed in Nature. It occurs in relatively high concentration in mouse skin tissue, mouse and cat liver, hog spleen and duodenum and in horse heart. Certain of these tissues contain preformed growth factor, as is shown by the fact that samples heated to destroy enzyme activity induce marked growth and acid production in cultures of *S. fæcalis* R. (cf. Table 1). Also apparently they contain appreciable amounts of the precursor postulated by Elvehjem, since incubation of fresh samples causes an increase in activity.

Table 1. The activity of cat liver extract in producing folic acid from histidine at *p*H 7·4, estimated in terms of ml. *N*/20 acid produced in 10 ml. cultures of *S. fæcalis* in 18 hr. after the addition of 1 ml. of the mixture

| Mixture incubated for 18 hr. | Acid production (ml. *N*/20) |
|---|---|
| 0·5 ml. liver + 5·5 ml. phosphate buffer | 4·45 |
| 0·5 ml. liver (boiled) + 5·5 ml. phosphate buffer | 4·10 |
| 0·5 ml. liver + 5·0 ml. phosphate buffer + 0·5 ml. 0·1 per cent histidine | 5·45 |
| 0·5 ml. liver (boiled) + 5·0 ml. phosphate buffer (solution + 0·5 ml. 0·1 per cent histidine solution) | 4·15 |