

IV.—*Synthesis of Camphoric Acid.*

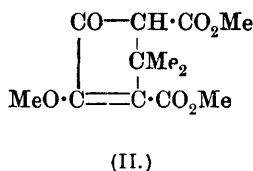
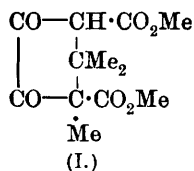
By GUSTAV KOMPPA.

A RECENT paper published simultaneously by G. L. Blanc and J. F. Thorpe in France (*Bull. Soc. chim.*, 1910, [iv], 7, 740) and England (*Trans.*, 1910, 97, 836), throwing doubt on my synthesis of camphoric acid, suggests that I could never have obtained that substance by the process described, and that my conclusions are based on an error. Although in a position to reply immediately to these critics, I thought it desirable first to make some complementary experiments, and at the same time possibly to show that Blanc and Thorpe are themselves mistaken in drawing somewhat hasty conclusions from their incomplete treatment of the subject. In this I have now succeeded, and the present communication is my reply to their arguments.

In the first place, the above-mentioned investigators declare that the basis of my synthesis, methyl diketo $\alpha$ pocamphorate, cannot be produced in sufficient quantities (J. F. Thorpe, *Proc.*, 1909, 25, 94; G. L. Blanc, *Bull. Soc. chim.*, 1909, [iv], 5, xvi). Blanc even goes so far as to say in his address, "Le Camphre," delivered before the Société Chimique, "qu'il lui a été personnellement impossible de reproduire" this substance, and that the reaction according to which it was obtained "sur le papier ne présente pas grande chance de réussite." When I published a complete account of my researches, including the method of preparing the substance, they were able

to make use of the latter for their own experiments; they found it had the properties which I had previously described, although the yield which they obtained was not so good as it might have been according to my prescription. It is unnecessary to dispute this point, however, because it is not easy for a worker unfamiliar with this reaction to arrive at satisfactory results, towards the attainment of which I have been compelled to persevere for years. Nevertheless, my assistants, on becoming accustomed to the task, have usually been successful. For example, Mr. A. Lampén's yield varies from 45 to 70·5 per cent., Mr. B. Ingman's from 49 to 67 per cent., and Mr. W. Salvén's from 45 to 70 per cent., all being calculated as described in my paper. With the best intentions, it is not always possible to give a sufficiently detailed description of such a difficult and complicated method of preparation, and the yield may be affected by some condition as yet unknown; but I have had in my possession several hundred grams of methyl diketo-*apocamphorate*.

The product obtained by Blanc and Thorpe on methylating this diketo-ester by my process was identical with mine, the melting point being 85—88°. In their last paper, these chemists argue that the methyl derivative is not, as I supposed, the *C*-methyl derivative (I), but the *O*-methyl ether (II):



This they claim to have proved by treating the methyl derivative melting at 85—88° with potassium hydroxide, obtaining an amount of potassium derivative corresponding with 50 per cent. of methyl diketo-*apocamphorate*, and isolating from the mother liquor 40 per cent. of  $\beta\beta$ -dimethylglutaric acid without detecting  $\alpha\beta\beta$ -trimethylglutaric acid; according to this result, the methyl group in the diketo-ester melting at 85—88° is eliminated by alkali. On the supposition that the methyl group is not attached to carbon, they argue that I could not have obtained camphoric acid from the ester melting at 85—88°, and that my report is based on "an error." They have made this statement without having even tried to reduce the substance according to my directions. They do not even seek to explain what kind of error underlies my conclusions.

In considering whether a mistake has possibly been made, it is necessary to point out that if the methyl group were attached to oxygen instead of to carbon, reduction would lead to *apocamphoric*

acid as the final product. This melts at about the same temperature as *r*-camphoric acid, and although the appearance of the two substances under a microscope is not exactly similar, yet confusion is possible. But mixing together *apocamphoric* and *r*-camphoric acids causes a depression of 15—16° in the melting point, whereas the saturated acid which I obtained from the ester melting at 85—88° does not in the least depress the melting point of natural *r*-camphoric acid. Moreover, there is a difference of 45° in the melting points of the anhydrides of *apocamphoric* and camphoric acids. This fact, taken in conjunction with the dissimilar appearance, renders it impossible for any chemist to make such a mistake. Furthermore, I have not only synthesised *r*-camphoric acid and its anhydride, but also *r-isocamphoric* acid and *r*-dehydrocamphoric acid, which synthetical acids I have compared directly with the corresponding acids prepared from natural sources, demonstrating that these, when mixed together, do not effect a depression in the melting point, and that they are also in other respects identical. I attach a special significance to the identity of synthetic dehydrocamphoric acid with *r*-dehydrocamphoric acid prepared from *r*-camphoric acid. In 1903 I described the properties of dehydrocamphoric acid (*Ber.*, 1903, **36**, 4334), obtained synthetically from the ester melting at 85—88°, whilst only two years ago I procured this acid from natural *r*-camphoric acid, and showed that they were identical (*Annalen*, 1909, **370**, 212). That this synthetical dehydroacid cannot be the corresponding dehydro*apocamphoric* acid is clear also from the fact that the two acids, although having the same melting point, cause a depression of 14° when mixed together.

Even yet the facts are not all disclosed, but the foregoing is sufficient evidence that an earnest chemist could not possibly commit an error such as Blanc and Thorpe would suggest, and that the experimental results, as I have stated them to be, can be established.

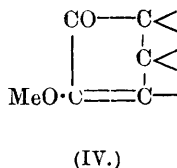
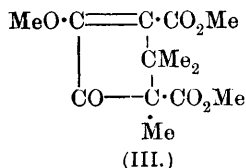
In his quoted paper, Thorpe lays special stress on the passage: "It was from the pure crystalline material that Komppa prepared camphoric acid." As it appears from my laboratory notes that the methyl diketocamphorate used for my synthesis had been crystallised once only, I deemed it important to show that the camphoric acid I obtained could not have arisen from any possible impurities in the diketo-ester. Accordingly, with the assistance of Dr. O. Routala, I have again prepared a thoroughly purified ester melting at 85—88°, and reduced it, first with sodium amalgam and then with hydrogen iodide, precisely as was stated in my complete report (*Annalen*, 1909, **370**, 209), obtaining once more the same yield of the same dehydro-acid, melting at 223—224° (normal thermometer);

the product, when mixed with *r*-dehydrocamphoric acid, again failed to cause depression of the melting point. This is the fifth occasion on which, with the aid of three different assistants, I have completely synthesised the acid; as it is identical with *r*-dehydrocamphoric acid prepared from *r*-camphor, and as I have also three times, with two different assistants, changed this synthetical dehydroacid into *r*-camphoric acid and also into *isocamphoric acid*, it seems to me wholly impossible that other chemists should fail to prepare camphoric acid from the same substance.

But how is it to be explained that Blanc and Thorpe have not even tried to reduce the substance melting at 85—88°, in order to ascertain whether they could obtain camphoric acid or dehydrocamphoric acid according to my method? It is evident from the discussion following Thorpe's paper that the reason for this neglect was the supposition that, because the methyl group is removed by alkali from the ester melting at 85—88°, it is also removed by reducing, according to my prescription, with sodium amalgam followed by hydriodic acid. Here they have made the serious mistake of not taking into account the fact that I do not reduce in caustic alkali solution, but in alkali carbonate, or rather in alkali bicarbonate, a rapid stream of carbon dioxide being led, during the whole operation, through the reducing solution. That sodium carbonate does not eliminate the methyl group from the substance melting at 85—88° must be known to them, because in preparing the latter according to my method they separated it from the neutral product of methylation by extracting it several times with sodium carbonate solution, and isolating the ester by acidifying this liquid. It would surely have been worth while to reduce the ester in question by my process, even if the methyl group is eliminated by caustic alkali, a point which I have not yet had time to verify.

I do not, however, admit that the ester melting at 85—88° is the *O*-methyl derivative (II), as claimed by Blanc and Thorpe on account of its behaviour towards alkali, because camphoric and dehydrocamphoric acids can be synthesised from it. That this ester is, as I have supposed from the outset, the *C*-methyl derivative is demonstrated in the following manner. The ester in question produces, in common with all  $\alpha$ -diketones, a yellowish-brown colouring matter (quinoxaline), which has a strong green fluorescence when dissolved in ether and in alcohol, developing with mineral acids a dark red coloration destroyed by water, properties which characterise quinoxalines. I have not succeeded in crystallising this colouring matter, or the one from *o*-tolylenediamine, and have therefore not been able to analyse it. When one takes into account the fact that the neutral ether, obtained by methylating diketo-

*apocamphoric* ester, and to which I have ascribed the following constitution (III):



does not give the above-mentioned fluorescence, although it contains the same grouping of elements (IV) which Blanc and Thorpe suppose to exist in the ester melting at 85—88°, the coloration observed is not to be ignored. The difference in constitution between the ester melting at 85—88° and the neutral ester (III) is indicated more plainly when phenylenediamine hydrochloride is used instead of the free base. With this agent, the ester melting at 85—88° develops a red coloration at the ordinary temperature, and slight heating produces the effect very easily, this intense red solution not being given by the neutral ester (III). Attempts to produce osazones from the ester melting at 85—88° have led to oils, which have not been investigated further.

The constitutional formulæ which I have ascribed to these substances are confirmed by the following determinations of the methoxy-group according to Zeisel's method:

0·2500 (ester m. p. 85—88°) gave 0·4495 AgI. MeO = 23·74.

0·2000 " " " 0·3620 AgI. MeO = 23·89.

Formula I requires 24·22; formula II requires 36·33 per cent.

0·2106 (neutral ether) gave 0·5223 AgI. MeO = 32·76.

Formula III requires 34·44 per cent.

As the methyl group in the ester melting at 85—88° is not removed by boiling hydriodic acid, it is certainly not attached to oxygen, as suggested by Blanc and Thorpe, thus indicating the constitution (formula I) which I have already advocated, namely, that of diketocamphoric ester.

From all these facts, it is evident that the criticisms of my camphoric acid synthesis put forward by Blanc and Thorpe are completely baseless.

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