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THE KOMPPA SYNTHESIS OF CAMPHORIC ACID

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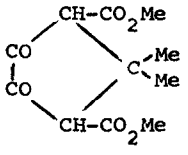
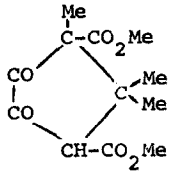
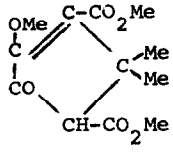
During the period 1909-1912 certain aspects of Komppa's synthesis of camphoric acid were discussed, with the implication that the work was not above criticism (1-5). The bone of contention was a crystalline substance melting at 85-88° which is the all-important intermediate in the synthesis. It was obtained from methyl diketo<u>apo</u>camphorate (I) by methylation with methyl iodide in the presence of sodium methoxide and Komppa assigned to it the structure of a <u>C</u>-methyl derivative (II) (1). Thorpe and Blanc (2), however, asserted that it must be the <u>O</u>-methyl derivative (III) since they observed that cold aqueous alkali slowly hydrolysed it to the extent of 90%, to give (I) in an amount corresponding to 50% and ββ-dimethylglutaric acid corresponding to a further 40%, without yielding any αββ-trimethylglutaric acid. Since Komppa prepared camphoric acid from the substance melting at 85-88°, the yields claimed for the synthesis were considered to be open to doubt.



I



II



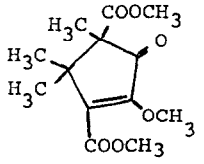
III

In reply (3) Komppa pointed out that his critics had not attempted to reduce the ester melting at 85-88° according to his directions. The controversy ended with an admission by Thorpe and Blanc (4) that "under the experimental conditions used by Komppa for the reduction of methyl diketo-camphorate, the methyl group remains attached to the carbon. Our criticism of his synthetical formation of camphoric acid is therefore baseless". Nothing more was said about the supposed O-methyl compound (III) and no explanation was given for the results of their hydrolysis experiments.

In view of this unsatisfactory state of affairs and since it cannot be

ruled out that the O-methylation had indeed occurred in the first instance, but that the methyl group had migrated from oxygen to carbon under the influence of hydriodic acid used in the subsequent reduction, as suggested by Pickles (5), it was considered desirable to re-examine the ester, m.p. 85-88°, with the aid of NMR.

Methyl diketoapocamphorate (I) and methyl diketocamphorate (II) were prepared as described by Komppa. According to the NMR spectrum, compound (II) has the structure assigned to it by Komppa. Both compounds (I and II) are entirely in the enolic form. Komppa also isolated a neutral compound from the methylation of methyl diketoapocamphorate and this he considered to be methyl 5-methoxy-4-ketodehydrocamphorate (IV). Though he was unable to obtain a good analysis (C, H) of this compound, his structural assignment has now also been shown by NMR to be correct.



IV

The chemical shifts (τ) in the NMR spectra of compounds (I), (II) and (IV) taken in CCl_4 as solvent with TMS as the internal standard are presented in the Table below. The chemical shifts are accurate to .02 ppm.

TABLE

	Protons	Total No. of Protons	τ
Compound I	enol H	2	.05
	CH_3 (Ester)	6	6.13
	CH_3	6	8.65
Compound II	enol H		0.59
	CH_3 (Ester)	3	6.09
	"	3	6.38
	CH_3	6	8.76
	CH_3	3	8.72
Compound IV	Ester CH_3	3	6.03
	O CH_3	3	6.22
	Ester CH_3	3	6.37
	CH_3	3	8.76
	"	3	8.78
	"	3	8.83

In an attempt to find out how Thorpe and Blanc obtained the hydrolysis product with aqueous alkali, their experiment was repeated. Owing to insufficient experimental details, viz. "the substance melting at 85-88° was dissolved in cold aqueous potassium hydroxide and a large excess of strong alkali was added, etc.", it could not be duplicated exactly. However, treatment of methyl diketocamphorate with a twentyfold excess of a 40% solution of potassium hydroxide at room temperature for 1 hour, caused the deposition of a crystalline solid which was found to be the potassium salt of methyl diketocamphorate (recovery 84%), and methyl diketoapocamphorate could not be detected in the mother liquor.

The authors thank Sir Robert Robinson for drawing their attention to this problem.

References

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2. J. F. Thorpe and G. L. Blanc, J. Chem. Soc., 97, 836 (1910)
3. G. Komppa, J. Chem. Soc., 99, 29 (1912)
4. J. F. Thorpe and G. L. Blanc, ibid., 2010
5. S. Pickles, Discussion in Proc. Chem. Soc., 26, 84 (1910)