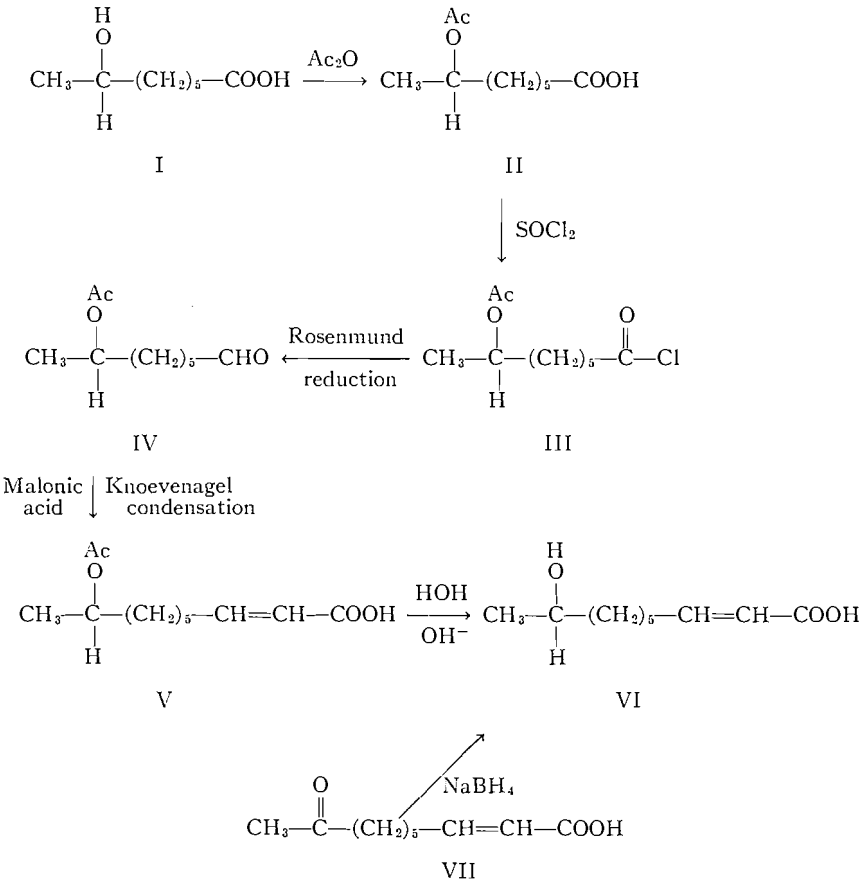
SYNTHESIS AND PHYSIOLOGICAL PROPERTIES OF 9-HYDROXY-2-DECENOIC ACID

Wm. H. Brown,[1] Ethel E. Felauer,[1] and M. V. Smith[2]

It has been recently reported by Brown and Felauer (1) that small amounts of 9-hydroxy-2-decenoic acid (VI) are present in the mixture of carboxylic acids isolated from royal jelly by the procedure described by Brown and Freure (2). It was of interest to synthesize the acid and determine its physiological properties since it is closely related to 9-keto-2-decenoic acid (VII). The latter acid is known as "queen substance" and has interesting effects on the behavior of worker bees (3). Several methods of synthesis for VII have been reported, the most recent by Kennedy *et al.* (4).

Our method of synthesis of (VI) is shown in the following scheme:



The 7-hydroxyoctanoic acid (I) was prepared by the method of Lease and McElvain (5). Since both 9-acetoxy-2-decenoic acid (V) and 9-hydroxy-2-decenoic acid (VI) are liquids which do not crystallize, a solid derivative, the *p*-bromophenacyl ester of VI, was

[1]*Department of Chemistry, Ontario Agricultural College.*
[2]*Department of Apiculture, Ontario Agricultural College.*

prepared. The latter was shown to be identical with the same derivative of authentic VI prepared by sodium borohydride reduction of 9-keto-2-decenoic acid (VII). The iodoform test is given readily by VI, which is contrary to the findings of Barbier and Hügel (6).

EXPERIMENTAL

Melting points are corrected. Infrared data were determined on a Beckman IR5 instrument and ultraviolet data on a Bausch and Lomb Spectronic 505.

9-Hydroxy-2-decenoic Acid (VI) and p-Bromophenacyl Ester

Saponification of 0.3 g of 9-acetoxy-2-decenoic acid (V) with 10% aqueous sodium hydroxide solution gave 0.2 g of crude VI, a liquid which did not crystallize. After chromatography on Whatman seed test paper using propanol-1 – ammonia (70:30) as the developing solvent (R_f 0.73 at 25°) the compound still failed to crystallize. The ultraviolet spectrum showed that the compound is unsaturated. The infrared spectrum showed bands for unsaturation and free hydroxyl group. The iodoform test was positive.

Treatment of VI with *p*-bromophenacyl bromide by the usual procedure gave the ester, white needles from hexane (150 ml/g), m.p. 73–74°. Anal. Calc. for $C_{18}H_{23}BrO_4$ (383.28): C, 56.4; H, 6.05; Br, 20.8. Found: C, 56.4; H, 6.08; Br, 21.0.

Physiological Activity

The bioassay method described by Butler and Gibbons (7) was used. The acid (VI) was supplied to 10 cages of test bees by dissolving 10 mg of the compound in 2 ml of acetone and dipping the dead bodies of worker bees in this solution. Two bee bodies, so treated, were placed in each cage. The 10 control cages all built queen cells but results with the acid were extremely variable, i.e., in some cages queen cells were constructed while in others they were not. Repeated tests and doubling of the amount of acid presented to the bees gave no clear-cut differences.

Presentation of the acid on filter paper to cages of young bees according to the method of Pain (8) gave no indication that it has any attractiveness to the bees.

Results of the evaluation of the antitumor activity of 9-hydroxy-2-decenoic acid (VI) will be reported in the series "Studies on the in vitro antitumor activity of fatty acids", of which the fourth paper appeared recently (9).

ACKNOWLEDGMENTS

The studies herein described were carried out in connection with projects supported by the National Cancer Institute of Canada, whose financial assistance is gratefully acknowledged.

We are indebted to Dr. R. K. Callow of the National Institute for Medical Research, London, England, for providing a sample of authentic 9-keto-2-decenoic acid. DuPont of Canada Limited supplied a generous amount of adipic acid.

1. W. H. Brown and E. E. Felauer. Nature, **190**, 88 (1961).
2. W. H. Brown and R. J. Freure. Can. J. Chem. **37**, 2042 (1959).
3. C. G. Butler. The world of the honeybee. Collins, London. 1954; Bee World, **40**, 269 (1959); Experientia, **16**, 424 (1960); Endeavour, **77**, 5 (1961).
4. J. Kennedy, N. J. McCorkindale, and R. A. Raphael. J. Chem. Soc. 3813 (1961).
5. E. J. Lease and S. M. McElvain. J. Am. Chem. Soc. **55**, 807 (1933).
6. M. Barbier and M.-F. Hügel. Bull. soc. chim. France, 951 (1961).
7. C. G. Butler and D. A. Gibbons. J. Insect Physiol. **2**, 61 (1958).
8. J. Pain. Institute National de la Recherche Agr. Serie A. No. 3674. 1961.
9. G. F. Townsend, W. H. Brown, E. E. Felauer, and B. Hazlett. Can. J. Biochem. Physiol. **39**, 1765 (1961).

Received January 19, 1962.
Departments of Chemistry and Apiculture,
Ontario Agricultural College,
Guelph, Ontario.