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CHEMISTRY OF LAC RESIN—VIII†‡

SYNTHESIS OF JALARIC ESTER-I, POSSIBLE KEY COMPOUND IN THE ELABORATION OF LAC RESIN BY *LACCIFER LACCA* KERR

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Abstract—Preparation of (*E*)- and (*Z*)-16-hydroxy-9-hexadecenoic acids and *erythro*-aleuritic acid starting from naturally occurring aleuritic acid, is described. 16-Hydroxy-(*Z*)-9-hexadecenoic acid and jalaric acid have been selectively condensed to furnish the naturally occurring jalaric ester-I. The possible importance of this compound in the elaboration of lac resin by the insect is pointed out.

We have already described[1] the isolation and structure elucidation of laccijalaric ester-I **1**, jalaric ester-I **2**, laccijalaric ester-II **3** and jalaric ester-II **4**, which together constitute bulk of the "soft resin" from lac, a versatile resin, secreted by a tiny insect *Laccifer lacca* Kerr (family: Lacciferidae Cockerell).[2] Similarly, we have also reported[3] the structure **5** for the so-called "pure lac resin", the chief component of the "hard resin" of lac. From data to be reported later, it is also clear that the neutral fraction[4] of lac resin contains as the major constituent, compound **6**. An analysis of structures **1–6** revealed that jalaric ester-I **2**[5] may be playing a key role in the elaboration of these compounds by the insect. Conceptually, jalaric ester-I on epoxidation[6] should furnish **7**, which on hydrolysis[6] would give jalaric ester-II **4** in which aleuritic acid moiety will have the required[7] *threo* configuration or, it can undergo intramolecular epoxide opening by the carboxyl function to generate **6** or, it can lead to polyesters of type **5** resulting from intermolecular oxirane ring-cleavage. These considerations prompted us to investigate a preparative route to jalaric ester-I **2**, so that we could later investigate the transformations, delineated above, in the laboratory.

Synthesis of jalaric ester-I was patterned after our earlier method[1] for the synthesis of jalaric ester-II **4**. The first requirement was an easy access to 16 - hydroxy - (*Z*) - 9 - hexadecenoic acid **8**, which has been synthesised earlier[7] via 16 - hydroxyhexadec - 9 - ynoic acid, a route considered as less convenient. With the availability[8–11] of some highly stereospecific methods for the conversion of vicinal diols into geometrically well-defined olefins, it appeared worthwhile to start[12] with the commercially available aleuritic acid **10**. This acid has *threo* configuration **10**,[7] whereas for the preparation of (*Z*)-olefin **8** by any of these methods, one would need *erthyro*-aleuritic acid **11**. Conversion of natural *threo*-aleuritic acid into the *erythro*-isomer has been carried out[7] in yields of 19–59% by the action of HBr–AcOH, followed by alkali hydrolysis. We have preferred to develop a two-step sequence involving *trans*-hydroxylation of the *trans*-acid **12**, which should be readily accessible from the natural aleuritic acid **10** by the application of any one of the various elimination reactions, mentioned earlier. We have preferred to utilise the method of Eastwood *et al.*[9] for the elimination step, because of its extreme simplicity of operation. Heating aleuritic acid and ethyl orthoformate in the presence of benzoic acid, followed by pyrolysis of the resulting 2 - ethoxy - 1,3 - dioxolan yielded the known,[13] 16 - hydroxy - (*E*) - 9 - hexadecenoic acid **12** in yields of over 92%. *Trans*-hydroxylation of **12** with performic acid, followed by mild hydrolysis furnished the required *erythro* acid **11** in 92% yield.

The above *erythro* acid **11** was subjected to the same elimination reaction to give this time the required 16 - hydroxy (*Z*) - 9 - hexadecenoic acid **8**[7] in 95% yield.

†Part VII: *Tetrahedron* **30**, 3689 (1974).

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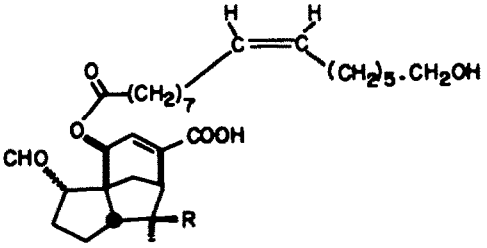
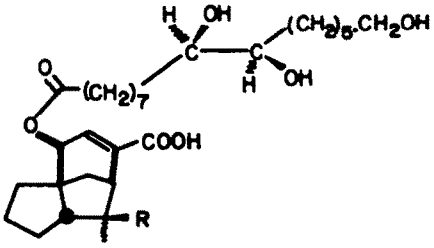


1: R = Me
2: R = CH_2OH



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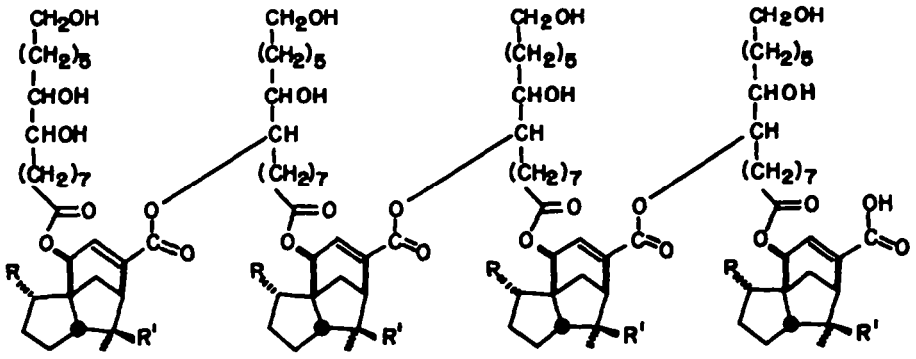
4: R = CH_2OH



R = CHO/COOH; R' = CH_2OH/Me

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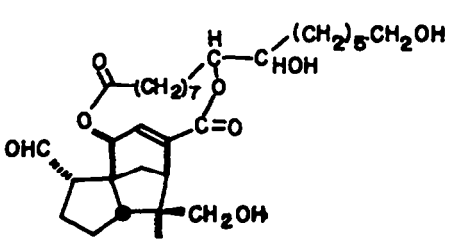

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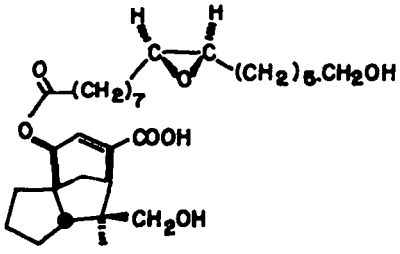

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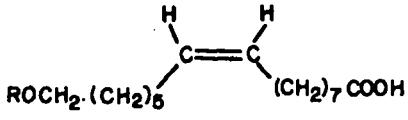
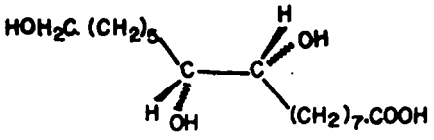


8 : R = H

9 : R = HCO



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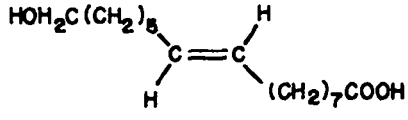

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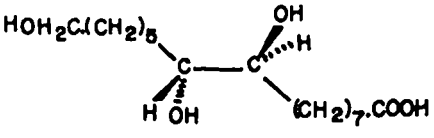

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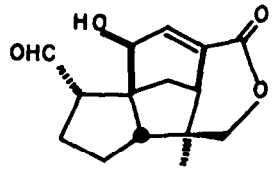

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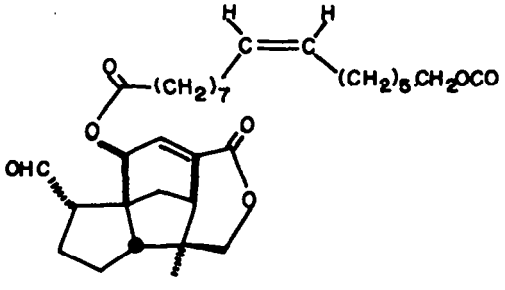

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Formylation[14] of **8** gave the formate **9**, which was converted into the acid chloride with oxalyl chloride. This was condensed with jalaric acid δ-lactone **13** in benzene containing some pyridine to give the required ester **14**. Selective hydrolysis of **14** with $NaHCO_3$ in aq. dioxane at ~100° for 0.5 h furnished, besides small amounts of jalaric acid and 16 - hydroxy - hexadecenoic acid **8**, the required inter-ester **2** as the major product. This was found to be completely identical (TLC, IR, PMR) with jalaric ester-I isolated[1] from "soft resin".

EXPERIMENTAL

All m.ps and b.ps are uncorrected. Light petroleum refers to the fraction b.p. 40–60°. Silica gel for column chromatography was −100/+200 mesh, and was washed with hot distilled water till sulphate-free, dried, activated at 125–130° (6–8 h) and standardised.[15] TLC was carried out on silica gel layers (0.3 mm) containing 15% gypsum; visualization agent: conc. H_2SO_4 or iodine vapours. Mixed solvent composition is by volume. The following instruments were used for spectral/analytical data: Perkin–Elmer Infracord, 137E (IR); Varian Associates A-60 spectrometer (PMR; TMS as internal standard).

16-Hydroxy-(Z)-9-hexadecenoic acid **12**

Threo-aleuritic acid (natural, m.p. 100–101°; 4.0 g), ethyl orthoformate (7 ml) and benzoic acid (0.2 g) were mixed and heated in a flask carrying a thermometer dipping in the liquid and arranged for distillation. Bath temp was slowly raised so that EtOH started slowly distilling (inside temp 70–80°); it was maintained at this temp. till no more EtOH distilled (45 min). The internal temp. was, next, slowly raised to 170°, when CO_2 evolution started. After 3.5 to 4 h at this temp. the evolution of gases had practically ceased. Excess ethyl orthoformate was removed under suction and the residue (4.3 g) diluted with alcoholic alkali (1.5 g KOH in 15 ml H_2O + 15 ml EtOH) and refluxed for 5 h. Most of the alcohol was distilled off, the residue diluted with water (25 ml) and acidified with 10% H_2SO_4 aqueous. The product was isolated by extraction with EtOAc (40 ml × 3) and recrystallization of the crude product from CCl_4: 3.35 g (94%), m.p. 69–70° (lit.[7] m.p. 66–68°). IR (Nujol): COOH 2532, 1690 cm^{-1}; OH 3175, 1060 cm^{-1}; *trans* CH=CH 970 cm^{-1}. PMR (CCl_4): CH_2COOH (2H, *t*, 2.28 ppm, J = 6 Hz), CH_2OH (2H, *t*, 3.55 ppm, J = 6.5 Hz), CH=CH (2H, *m*, 5.3 ppm).

Erythro-aleuritic acid **11**

To a mixture of H_2O_2 aqueous (30%, 2 ml) and formic acid (90%, 10 ml), the above olefin (2.0 g) was added and stirred at room temp. (25–30°) for 24 h. Excess of formic acid etc were removed at ~55°/20 mm and the residue treated with 5% KOH aqueous (30 ml) on a steam bath for 1 h. The reaction mixture was cooled, acidified with H_2SO_4 aqueous, when a white solid separated and was collected by filtration. The solid was washed with water, air-dried and crystallised from EtOH to give the required compound **11** (2.1 g, 92%), m.p. 125–126° (lit.[7] m.p. 126–127°). IR (Nujol): COOH 2650, 1690 cm^{-1}; OH 3300, 1070 cm^{-1}.

16-Hydroxy-(E)-hexadecenoic acid **8**

By following exactly the procedure outlined for **12** above, 1.8 g of *erythro* acid furnished crude **8** as a thick liquid, which was passed through a column of SiO_2 gel/IIA (15 cm × 11 cm) using C_6H_6. 25% EtOAc in C_6H_6 (50 ml × 4) gave pure **8** (1.45 g) as a thick oil, m.p. 20–21° (lit.[7] m.p. 20–22°). IR (liq.): COOH 2620, 1710 cm^{-1}; OH 3330, 1060 cm^{-1}; *cis* CH=CH 720 cm^{-1}. PMR (CCl_4): CH_2COOH (2H, *t*, 2.27 ppm, J = 6.5 Hz), CH_2OH (2H, *t*, 3.57 ppm, J = 6 Hz), CH=CH (2H, *t*, 5.27 ppm, J = 5 Hz).

Jalaric ester-I **2**

The above acid **8** (3.1 g) was mixed with acetic-formic anhydride (8 ml) and left aside at room temp. (25–30°), under anhydrous conditions for 24 h, after which the excess of reagent etc were flashed off at room temp. under vacuum (~1 mm) to furnish the crude formate **9** (3.33 g). PMR (CCl_4): CH_2COOH (2H, *t*, 2.3 ppm, J = 6 Hz), CH_2OCOH (2H, *t*, 4.1 ppm, J = 6.5 Hz), CH=CH (2H, *t*, 5.29 ppm, J = 5 Hz), CH_2OCOH (1H, *s*, 7.91 ppm).

The above formate (3.0 g) was dissolved in dry C_6H_6 containing pyridine (0.5 ml), cooled to 10° and oxalyl chloride (1.5 ml) added. The reaction mixture was left overnight (16 h) at room temp. (25–30°) and the refluxed for 10 min. The excess reagent was flashed off under reduced pressure. To the residual crude acid chloride at room temp., a soln of jalaric acid δ-lactone[1] (13, 2.62 g) in benzene (35 ml) and pyridine (0.2 ml), was added. The reaction mixture was refluxed for 5 h, solvent flashed off and the residue treated with water (50 ml) and acidified with HCl aqueous and the product extracted with EtOAc (50 ml × 4). EtOAc removal gave a gum (5.4 g), which was taken up in 50% dioxane aqueous (35 ml), $NaHCO_3$ (2.5 g) added and the mixture heated on a steam bath, with occasional swirling, for 0.5 h. Solvent was rapidly (2 min) removed under suction (30 mm) from the steam-bath and the residue immediately treated with ice-water (50 ml) and acidified at ~0° with H_2SO_4 aq. Usual work up by extraction with EtOAc (60 ml × 4) gave a product (5.25 g), showing three spots on TLC (solvent: 40% EtOAc in C_6H_6 containing a trace of AcOH) and having R_f 0.5 (olefinic acid **8**), 0.3 (major, required compound) and 0.2 (jalaric acid). This product (5.0 g) was chromatographed over silica gel/IIA (100 g) with TLC monitoring:

Fraction	Solvent	Volume	Products
1	15% EtOAc in C_6H_6	100 ml × 10	1.0 g, R_f 0.5
2	15% EtOAc in C_6H_6	100 ml × 7	0.8 g, mixture, R_f 0.3, 0.5
3	25% EtOAc in C_6H_6	100 ml × 3	0.2 g, mixture
4	25% EtOAc in C_6H_6	100 ml × 30	2.0 g, R_f 0.3
5	40% EtOAc in C_6H_6	100 ml × 8	0.4 g, mostly with R_f 0.3
6	40% EtOAc in C_6H_6	100 ml × 8	0.4 g, mixture, R_f 0.3, 0.2

Fraction 4 (gum) was pure by TLC and was identical (TLC, IR, PMR) with the natural jalaric ester-I **2**.

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[5]The same remarks would apply to the laccijalaric ester-I **1** for the compounds/part structure based on laccijalaric acid.

[6]Biological equivalents of these reactions are well-known, see e.g.: W. Charney and H. L. Herzog, *Microbial Transformation of Steroids*, pp. 43, 66. Academic Press, New York (1967).

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[12]During the course of this work preparation of **8** from *erythro*-aleuritic acid, using Corey-Winter extrusion has been reported: L. Hevesi, J. Hontoy, A. Krief, J. Lubochinsky and B. Lubochinsky, *Bull. Soc. Chim. Belg.* **84**, 709 (1975). However, the method described in the present communication is far more convenient.

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