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### Some Reactions of Isoaleuritic Acid

J. N. CHATTERJEA, S. C. SENGUPTA\*, R. N. MAJEE &  
S. N. MUKHERJEE

Indian Lac Research Institute, Namkum, Ranchi 834010

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**threo-7,8,16-Trihydroxyhexadecanoic acid (iso-aleuritic acid, I)** has been converted into its **erythro-isomer (VI)** and vice versa. Several other reactions of **I** have also been studied.

**I**SOALEURITIC acid (7,8,16-trihydroxyhexadecanoic acid, I) was prepared by Sabnis *et al.*<sup>1</sup> from *threo*-aleuritic acid (9,10,16-tri-hydroxyhexadecanoic acid) in several steps, the last stage involving Bouveault-Blanc reduction of the half-ester (II). Although lithium borohydride reduction of this half-ester failed to give I, controlled LAH reduction afforded I along with the expected tetrol (III). Periodate oxidation of I gave  $\omega$ -hydroxynonanal<sup>2</sup> (IV)<sup>2</sup>, thus confirming its structure.

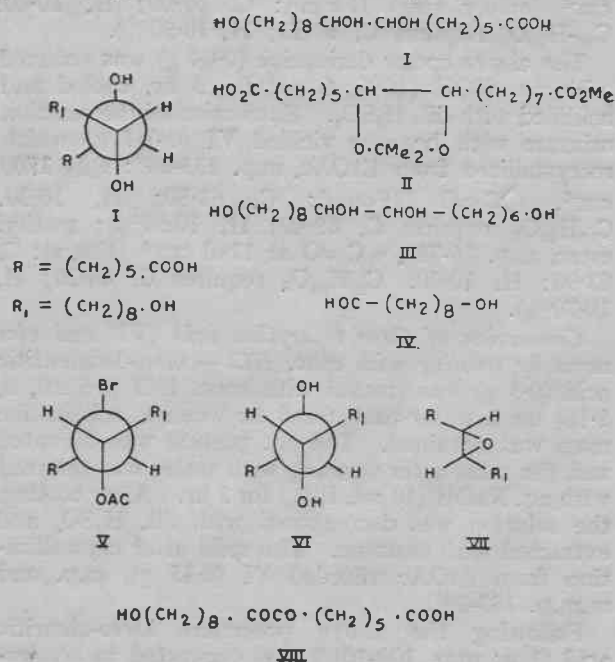
Action of hydrobromic acid-acetic acid<sup>3</sup> on I gave the *erythro*-bromoacetate (V) which on hydrolysis with aq. alkali gave *erythro*-isoaleuritic acid (VI). As in the case of aleuritic acid<sup>3</sup> this conversion may be carried out in two stages: (i) treatment of V with ethanolic alkali to the *trans*-epoxide (VII), and (ii) fission of the epoxide with dilute alkali. Prior cleavage of epoxide ring of VII with acetic acid followed by hydrolysis is sometimes advantageous in the preparation of VI. It was observed that treatment of I with conc. HCl on a boiling water-bath for a few hours afforded a polymeric rubber like chlorohydroxy derivative, obviously an inter-ester which on boiling with aq. alkali afforded VI in almost quantitative yields. Treatment of the polymeric material with ethanolic alkali afforded the pure *trans*-epoxide (VII). The conversion of *erythro*→*threo* was also carried out using HCl although the yield was not satisfactory.

\*To whom all enquiries should be addressed.

(+)-*threo*-aleuritic acid<sup>4,5</sup> on similar treatment gave ( $\pm$ )-*erythro*-isomer. This indicates that the mechanism of conversion of V to VI proceeds through the intermediacy of epoxide (VII) where both the chiral centres are attacked by water (OH<sup>-</sup>).

The epoxide (VII) when hydrogenated in acetic acid over Pd/C gave 7(8),16-dihydroxyhexadecanoic acid as an oil which was characterized as *p*-phenylphenacyl derivative. The ring cleavage of VII with HBr afforded a crystalline bromohydrin, *cis*-7(8)-bromo-8(7)-hydroxy-16-hydroxyhexadecanoic acid. The bromohydrin was converted back to the epoxide on treatment with ethanolic alkali.

The *erythro*-isomer may easily be distinguished from the *threo*-isomer from the IR spectra (*vide* Experimental) and by its behaviour on TLC (silica gel impregnated with boric acid). Oxidation of



the vicinal dihydroxy group with N-bromosuccinimide<sup>6</sup> in water produced 16-hydroxy-7,8-dioxohexadecanoic acid (VIII) which was characterized through the preparation of its bis-2,4-DNP derivative.

*LAH reduction of threo-16-methyl hydrogen 7,8-isopropylidenedioxyhexadecanedioate (II)*—The half-ester<sup>1</sup> (II, 0.5 g) in THF (25 ml) was reduced with LAH (0.1 g) under agitation and left overnight. The excess LAH was destroyed with a few drops of water, treated with cold dil. HCl and the reaction mixture extracted with ether. The ether extract was then extracted with NaHCO<sub>3</sub> solution (5%) which after acidification and extraction with EtOAc afforded the expected isoacid (I) (0.1 g). It recrystallized from EtOAc, m.p. 95-96°;  $\nu_{\text{C=O}}$  at 1720 and 1690 cm<sup>-1</sup>; *p*-phenylphenacyl derivative, m.p. 124-26°; methyl ester, m.p. 45-47° (EtOAc),  $\nu_{\text{C=O}}$  at 1740 cm<sup>-1</sup> (Found: C, 63.90; H, 10.50. Calc. for C<sub>17</sub>H<sub>34</sub>O<sub>5</sub>: C, 64.20; H, 10.70%).

The residual ether extract, which contained the related tetrol and the unchanged half-ester, was extracted with NaOH solution (5%). The ether solution after washing with water and drying (Na<sub>2</sub>SO<sub>4</sub>) afforded the tetrol as a liquid (0.28 g), IR showed the absence of carbonyl absorption. From the alkaline extract the half-ester was recovered (0.09 g).

*erythro-Isoaleuritic acid (VI)*—*threo*-Isoaleuritic acid (0.05 g) was treated with HBr in gl. AcOH (5 ml; *d*, 1.3) and the solution kept overnight at room temperature. The reaction mixture was poured on ice and extracted exhaustively with EtOAc. Removal of the solvent gave an oily bromo compound (0.07 g) which was refluxed with 0.5N ethanolic KOH (3 ml) for 1 hr, cooled and acidified with aq. AcOH (50%). The solution was then extracted with benzene, and the extract washed with water and dried (Na<sub>2</sub>SO<sub>4</sub>). Removal of benzene gave the *trans*-epoxide (VII, 0.04 g) which recrystallized from EtOAc pet. ether at 0°, m.p. 80-81°;  $\nu_{\text{max}}$  890 cm<sup>-1</sup> (epoxy ring) (Found: C, 67.00; H, 10.40. C<sub>16</sub>H<sub>30</sub>O<sub>4</sub> requires C, 67.13; H, 10.50%).

The above epoxy derivative (0.04 g) was refluxed with aq. KOH (10%, 6 ml) for 3 hr, cooled and acidified with dil. H<sub>2</sub>SO<sub>4</sub>. Extraction of the reaction mixture with benzene yielded VI (0.047 g) which recrystallized from EtOAc, m.p. 133-34°;  $\nu_{\text{max}}$  1700 cm<sup>-1</sup>. ( $\nu_{\text{C=O}}$ ) (Found: C, 63.50; H, 10.30. C<sub>16</sub>H<sub>32</sub>O<sub>5</sub> requires C, 63.40; H, 10.50%); methyl ester, m.p. 76-78°,  $\nu_{\text{C=O}}$  at 1740 cm<sup>-1</sup> (Found: C, 63.90; H, 10.60. C<sub>17</sub>H<sub>34</sub>O<sub>5</sub> requires C, 64.20; H, 10.70%).

*Conversion of threo to erythro acid (VI) and vice versa by treating with conc. HCl*—*threo*-Isoaleuritic acid (0.5 g) was treated with conc. HCl (2.5 ml, *d*, 1.16) on a water-bath for 6 hr when a rubber-like mass was obtained. The aq. portion was decanted and the mass after washing with water was refluxed with aq. NaOH (10 ml, 10%) for 3 hr. After cooling, the solution was decomposed with dil. H<sub>2</sub>SO<sub>4</sub> and extracted with benzene. The solid after crystallization from EtOAc afforded VI (0.45 g), m.p. and m.m.p. 133-34°.

Following the above procedure *threo*-aleuritic acid (1 g; m.p. 100-101°) was converted to *erythro*-

isomer (0.9 g; m.p. 126-28°); *erythro*-isoaleuritic acid (0.5 g) to the *threo*-isomer (0.3 g; m.p. 95-96°); and *erythro*-aleuritic acid (1 g) to the *threo*-isomer (0.7 g; m.p. 102-3°).

The (+)-*threo*-isomer was also converted to the *erythro*-isomer through the chlorohydroxy derivative as above. The *erythro*-isomer on recrystallization from EtOAc, had m.p. 120-21° and showed no optical activity (CD measurement).

The *threo* and *erythro* acids had R<sub>f</sub> values of 0.75 and 0.61 respectively on boric acid impregnated plates using chloroform-methanol-acetic acid (90:10:2) as solvent.

*trans-7,8-Epoxy-16-hydroxyhexadecanoic acid*—The chlorohydroxy rubbery mass obtained by the above procedure from *threo*-isoaleuritic acid (0.5 g) was refluxed with ethanolic KOH (20 ml, 0.5N) for 1 hr. The solution after cooling was acidified with aq. AcOH (50%) and worked up as described earlier. The epoxide (0.3 g), m.p. 80-81°, was identical (m.m.p., IR) with the specimen obtained from the bromohydrin.

In a similar manner *trans*-9,10-epoxy-16-hydroxyhexadecanoic acid, m.p. 72-73°, was readily prepared from *threo*-aleuritic acid in good yield (~60%).

*cis-7(8)-Bromo-8(7), 16-dihydroxyhexadecanoic acid*—*trans*-7,8-Epoxy-16-hydroxyhexadecanoic acid (0.05 g) was dissolved in ether (5 ml) and aq. HBr (*d*, 1.4, 0.08 ml) added under agitation. After 5 min the solution was extracted with ether and the bromohydrin isolated as a solid (0.054 g). It crystallized from ether-pet. ether at 0° in prisms, m.p. 84-86° (Found: C, 52.20; H, 8.30. C<sub>16</sub>H<sub>31</sub>O<sub>4</sub>Br requires C, 52.31; H, 8.44%). *trans*-7,8-Epoxy-16-hydroxyhexadecanoic acid was obtained back on treatment of the bromohydrin with aq. alkali.

*7(8),16-Dihydroxyhexadecanoic acid*—*trans*-7,8-Epoxy-16-hydroxyhexadecanoic acid (0.05 g) was dissolved in gl. AcOH (1 ml) and hydrogenated over Pd/C (10%, 25 mg). The product was obtained as an oil (0.045 g) and all attempts to crystallize it were unsuccessful; on IR band at 890 cm<sup>-1</sup> (epoxy group); *p*-phenylphenacyl derivative, m.p. 152-54°,  $\nu_{\text{C=O}}$  at 1690 and 1740 cm<sup>-1</sup> (Found: C, 74.42; H, 8.52. C<sub>30</sub>H<sub>42</sub>O<sub>5</sub> requires C, 74.70; H, 8.71%).

*16-Hydroxy-7,8-dioxohexadecanoic acid (VIII)*—*threo*-Isoaleuritic acid (0.1 g) was oxidized by the method of McGhie *et al.*<sup>6</sup> with NBS (0.22 g) in EtOAc (4.2 ml) and water (3 ml) under reflux. The diketone (VIII, 0.08 g) was obtained as a solid which on treatment with ethanolic 2,4-dinitrophenylhydrazine (H<sub>2</sub>SO<sub>4</sub>) afforded bis-hydrazone, m.p. 136-38° (chloroform-EtOH) (Found: N, 16.70. C<sub>28</sub>H<sub>36</sub>O<sub>11</sub>N<sub>8</sub> requires N, 17.00%).

#### References

- SABNIS, S. D., MATHUR, H. H. & BHATTACHARYA, S. C., *J. chem. Soc.*, (1963), 2477.
- HELFERICH, B. & SCHÄFER, W., *Ber. deut. chem. Ges.*, **57** (1924), 1913.
- MADHAV, R., Ph.D. thesis, *A chemical study of lac resin and lac-host* (Delhi University), 1965.
- ESWARAN, S. V., SESHADRI, T. R., SRIRAM, N. & SUBRAMANIAN, G. B. V., *Indian J. Chem.*, **9** (1971), 196.
- MCGHIE, J. F., ROSS, W. A., SPENCE, J. W. & JAMES, F. J., *Chem. Ind. (London)*, **38** (1971), 1074.
- AMES, D. E., GOODBURN, T. G., JEVANS, A. W. & MCGHIE, J. F., *J. chem. Soc. (C)*, (1968), 268.