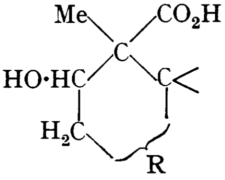
# 123. *The Triterpene Group. Part I. β-Boswellic Acid.*

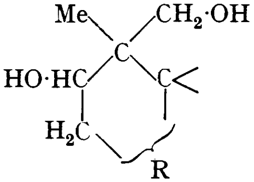
By James C. E. Simpson and Norman E. Williams.

Derivatives of the triterpene acid β-boswellic acid are described which demonstrate that it is a β-hydroxy-acid, in contrast to the statement of Trost (*Ann. Chim. Appl.*, 1937, **27**, 178) that it is an α-hydroxy-acid.

β-Boswellic acid, one of the principal triterpenoid constituents of frankincense, was first isolated in the pure state by Winterstein and Stein (*Z. physiol. Chem.*, 1932, **208**, 9) and characterised by them as a monobasic monohydroxy-acid, $C_{30}H_{48}O_3$. Although no work on the detailed structure of this acid has yet been published, the results obtained by Beaucourt (*Monatsh.*, 1930, **55**, 185) from selenium dehydrogenation of the (impure) acid indicate that it belongs to the important group represented by hederagenin, oleanolic acid, gypsogenin, the amyrins, and sia- and suma-resinolic acids; in particular, the hydrocarbon, m. p. 305°, isolated by Beaucourt (*loc. cit.*) is probably identical (see Ruzicka *et al.*, *Helv. Chim. Acta*, 1932, **15**, 431) with 1 : 8-dimethylpicene (Ruzicka and Hofmann, *ibid.*, 1937, **20**, 1155).

It was recently found in this laboratory that β-boswellic acid is converted by fairly mild oxidation with chromic anhydride into a ketone, $C_{29}H_{46}O$, for which the name *nor-β-boswellenone* is suggested. On the other hand, methyl β-boswellate, $C_{31}H_{50}O_3$, is oxidised under similar conditions to the corresponding *keto-ester*, $C_{31}H_{48}O_3$. These results indicate, as pointed out by one of us (Simpson, *Nature*, 1937, **140**, 467), that β-boswellic acid is a β-hydroxy-acid (I, $R = C_{24}H_{40}$), which on oxidation passes into nor-β-boswellenone (IV, $R = C_{24}H_{40}$) *via* the intermediate keto-acid (III, $R = C_{24}H_{40}$). The ketonic nature of the oxygen atom in nor-β-boswellenone has been diagnosed by the formation of an *oxime* and also by the facile conversion of the ketone into the corresponding hydrocarbon, *nor-β-boswellene*, on Clemmensen reduction. The partial structure (I, $R = C_{24}H_{40}$) for β-boswellic acid is supported by the striking analogy between the oxidation already referred to and that of hederagenin methyl ester (II, $R = C_{25}H_{40}O_2$) previously studied by Jacobs and Gustus (*J. Biol. Chem.*, 1926, **69**, 641), which undergoes a parallel transformation to the corresponding ketone (IV, $R = C_{25}H_{40}O_2$) by way of the intermediate (III, $R = C_{25}H_{40}O_2$).


(I.)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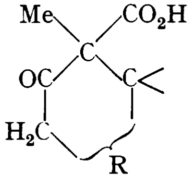
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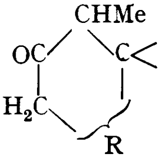
(IV.)

Nor-β-boswellenone and the methyl ester of the acid (III, $R = C_{24}H_{40}$) have also been prepared by Trost (*Ann. Chim. Appl.*, 1937, **27**, 178) by oxidation of β-boswellic acid and its ester respectively. This author, however, states that the acid is an α-hydroxy-acid (V) and that nor-β-boswellenone is an aldehyde (VII) formed from (V) *via* the keto-acid (VI). Trost's conclusions must be regarded as unjustified for the following reasons: (i) The group $CH(OH)\cdot CO_2H$ does not account for the fact, observed both by Trost and by Winterstein and Stein (*loc. cit.*), that methyl β-boswellate is highly resistant to saponification; (ii) nor-β-boswellenone was not shown by Trost to possess aldehydic properties (we have in fact found that it has no such properties); (iii) the isolation of an aldehyde in quantity is improbable under the conditions obtaining in Trost's experiment (chromic anhydride–acetic acid at 90°); (iv) the significance of the analogous oxidation of hederagenin methyl ester is entirely disregarded.

$$C_{28}H_{45}\cdot CH(OH)\cdot CO_2H \quad \text{(V.)} \qquad C_{28}H_{45}\cdot CO\cdot CO_2H \quad \text{(VI.)} \qquad C_{28}H_{45}\cdot CHO \quad \text{(VII.)}$$

Definite proof that Trost's hypothesis is indeed untenable has been furnished by the results of the further degradation of nor-β-boswellenone now in progress. The ketone is smoothly oxidised by permanganate in acetic acid to a new *ketone*, for which analytical data indicate the formula $C_{26}H_{42}O_2$. Acid products, which would be expected to predominate were nor-β-boswellenone an aldehyde, are formed only in traces. This ketone differs markedly in its colour reactions from its precursor and from β-boswellic acid; its structure will be discussed in a future communication.

## EXPERIMENTAL.

(Melting points uncorrected; specific rotations in chloroform.)

β-Boswellic acid was prepared by the method of Winterstein and Stein (*loc. cit.*), a 2% yield of the pure acid, m. p. 233—234°, being obtained.

*Methyl β-Boswellate.*—Esterification of the acid with ethereal diazomethane yielded the ester as prisms (from chloroform–methanol), m. p. 195—195·5°, $[\alpha]_D^{14°}$ +161°, +160° ($l = 1$, $c = 0·96$, 2·55). Winterstein and Stein give m. p. 189—190° (corr.), $[\alpha]_D^{19°}$ +116°; Trost records m. p. 198—200° (corr.), $[\alpha]_D^{20°}$ +145° [Found (all analyses by Weiler): C, 78·85; H, 10·5; OMe, 6·3. Calc. for $C_{31}H_{50}O_3$: C, 79·1; H, 10·7; OMe, 6·6%].

*Oxidation of Methyl β-Boswellate.*—A solution of the ester (0·5 g.) in glacial acetic acid (100 c.c.) and water (10 c.c.) was stirred at 50° while chromic anhydride (0·2 g. in 2 c.c. of water and 10 c.c. of acetic acid) was run in during 20 minutes; the temperature was slowly raised and maintained at 70° for a further hour. Methyl alcohol was then added, the solvent removed under reduced pressure, and the residue, after addition of very dilute sulphuric acid and extraction with ether, separated into acid and neutral fractions with 3% sodium hydroxide solution. The latter fraction separated from methyl alcohol in long, brittle, needle-like rods of the *keto-ester*, m. p. 159—160° after several crystallisations [Trost gives m. p. 155—157° (corr.)] (Found: C, 79·1; H, 10·2. $C_{31}H_{48}O_3$ requires C, 79·4; H, 10·3%).

The *oxime* crystallised from aqueous alcohol in soft slender needles; it melted at 202° to a turbid liquid which cleared at 210° [Trost, m. p. 194—196° (corr.)] (Found: N, 3·3. $C_{31}H_{49}O_3N$ requires N, 2·9%).

*Nor-β-boswellenone.*—A solution of β-boswellic acid (10 g.) in glacial acetic acid (500 c.c.) and water (50 c.c.) was stirred mechanically while a solution of chromic anhydride (4 g. in 150 c.c. of acetic acid and 30 c.c. of water) was added during 1 hour at 55°. After a further 1½ hours at this temperature the product was worked up as in the oxidation of methyl β-boswellate; the ketone separated in needles from an alcoholic solution of the neutral fraction, and had m. p. 195—196° [Trost gives 200—202° (corr.)] after recrystallisation (yield, 35%). In our hands the conditions employed by Trost for the preparation of this compound gave a much inferior yield of pure material, although Trost states that the (presumably crude) product was isolated in 90% yield (Found: C, 84·8; H, 11·1. $C_{29}H_{46}O$ requires C, 84·8; H, 11·3%). *Nor-β-boswellenone* gives a yellow coloration with tetranitromethane in chloroform, and a wine-red colour with the Liebermann–Burchard reagent. Negative reactions were obtained with the Schiff and the Tollens reagent. $[\alpha]_D^{12°}$ +128° ($l = 1$, $c = 1·065$).

The *oxime* crystallised from methanol in clusters of minute needles, m. p. 164—167° [Trost, m. p. 196—197° (corr.)] (Found: C, 81·3; H, 10·7; N, 3·4. $C_{29}H_{47}ON$ requires C, 81·8; H, 11·1; N, 3·3%).

*Nor-β-boswellene.*—Nor-β-boswellenone (0·1 g.) in glacial acetic acid (12 c.c.) was refluxed for 3 hours with amalgamated zinc (1·2 g.) and concentrated hydrochloric acid (6 c.c.). The *hydrocarbon* was obtained by dilution of the filtered solution and was recrystallised from chloroform–methanol and finally from acetone; it formed clusters of needles, m. p. 168—169° (yield, 80%) (Found: C, 87·7; H, 12·4. $C_{29}H_{48}$ requires C, 87·8; H, 12·2%). It gave a yellow colour with tetranitromethane in chloroform, and a crimson-mauve Liebermann–Burchard reaction. $[\alpha]_D^{12°}$ +143° ($l = 1$, $c = 0·99$).

*Further Oxidation of Nor-β-boswellenone.*—The ketone (2 g.) was dissolved in glacial acetic acid (200 c.c.) and treated with 50 c.c. of N-potassium permanganate (≡ *ca.* 5 O), added drop by drop with stirring during 1 hour at 48°. After a further ½ hour the solution was clarified with sodium bisulphite, diluted with water, and extracted with ether. The extract was shaken with 3% sodium hydroxide solution, washed, dried, and evaporated. A methyl-alcoholic solution of the residue (1·8 g.) deposited the new *ketone* in colourless needles, m. p. 217—218° after recrystallisation (yield, 45%); $[\alpha]_D^{11°}$ +157° ($l = 1$, $c = 0·90$) (Found: C, 80·7, 81·0; H, 10·5, 10·6. $C_{26}H_{42}O_2$ requires C, 80·8; H, 11·0%). The substance gave no coloration with tetranitromethane in chloroform, and only a yellowish-brown colour with the Liebermann–Burchard reagent. It was recovered unchanged, although in rather small yield, after refluxing for 2 hours with 1% alcoholic potash.

On treatment with hydroxylamine acetate under the usual conditions a *product* was formed which crystallised from aqueous methanol in small needles, m. p. 197—198° (Found: C, 78·85, 79·4; H, 10·3, 10·5; N, 4·0, 3·6, 4·0%).

The *semicarbazone*, prepared by refluxing for 3 hours a solution of the ketone in methyl alcohol with semicarbazide acetate, was crystallised from aqueous methanol and finally from benzene–ligroin, from which it separated in clusters of needles, m. p. 238—239° (Found: C, 73·5; H, 9·95; N, 8·7. $C_{27}H_{45}O_2N_3$ requires C, 73·1; H, 10·2; N, 9·5%).

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