323. *The Triterpene Group. Part III. The Double Bond of β-Boswellic Acid.*

By JAMES C. E. SIMPSON and NORMAN E. WILLIAMS.

β-Boswellic acid contains a double bond which is resistant to catalytic hydrogenation. Methyl *O*-acetyl-β-boswellate, unlike the amyrins and several other triterpenes, is recovered unchanged after attempted partial dehydrogenation with sulphur, but, in common with these compounds, contains the system $>C{=}CH{-}CH_2-$ (a).

Nor-β-boswellanedione, previously erroneously formulated as $C_{26}H_{42}O_2$ (Simpson and Williams, this vol., p. 687), is now shown to have the formula $C_{29}H_{46}O_2$ and to be formed from nor-β-boswellenone, $C_{29}H_{46}O$, by conversion of system (a) into $>CH{\cdot}CO{\cdot}CH_2-$ (b).

Two types of oxidation involving the ethylenic linkage of β-boswellic acid derivatives have been encountered: (i) (a) ⟶ $>C{=}CH{-}CO-$, and (ii) (a) ⟶ (b). In any given ethylenic oxidation either (i) or (ii) occurs, *but not both*, the controlling factor being the degree of substitution of C_1 [see (VII) for numbering]. When C_1 carries a methyl and a carbomethoxyl group, reaction (i) takes place, (ii) proceeding if C_1 carries a methyl group and a hydrogen atom.

Reduction of the C_2-carbonyl group also proceeds selectively, the resultant steric configuration on C_2 depending on which of the two groupings (a) and (b) is present in the compound reduced.

These selective oxidations suggest close association of C_1—C_2 with (a) and (b), such as would result from the presence of the double bond of β-boswellic acid at C_6—C_7 or C_8—C_9.

IN continuation of our preliminary work (Simpson and Williams, this vol., p. 686) on the structure of β-boswellic acid we have had as our objective the characterisation of its double bond. [It was shown by Winterstein and Stein (*Z. physiol. Chem.*, 1932, **208**, 9) that β-boswellic acid is isomeric with oleanolic acid, and by Beaucourt (*Monatsh.*, 1930, **55**, 185) that it yields on dehydrogenation with selenium a hydrocarbon which is probably identical with 1 : 8-dimethylpicene (Ruzicka *et al.*, *Helv. Chim. Acta*, 1932, **15**, 431; 1937, **20**, 1155), from which it follows that the acid is in all probability pentacyclic and therefore contains one ethylenic linkage.]

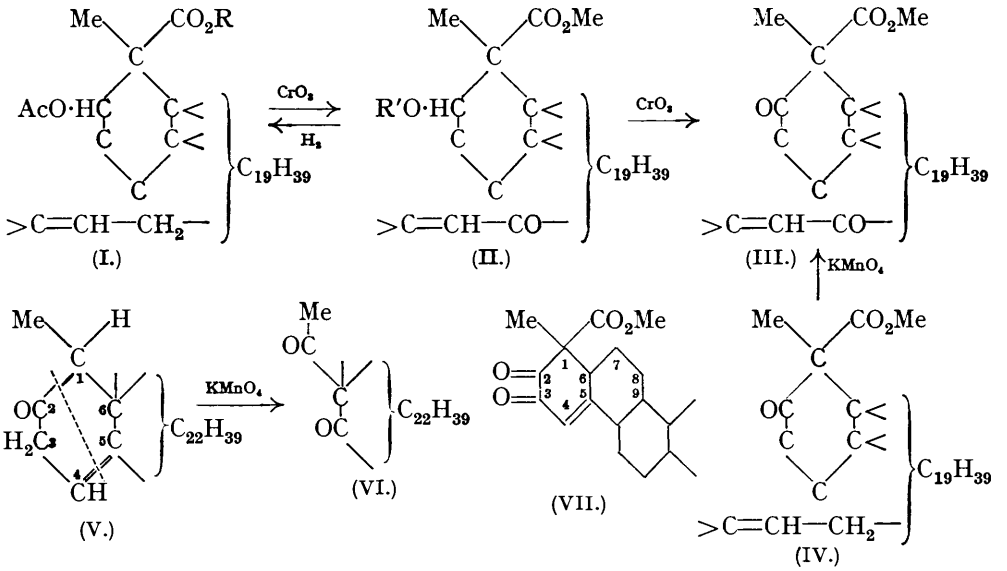
The unsaturated nature of the acid is shown by the strong positive reactions which we have found that it gives with the Liebermann–Burchard reagent and with tetranitromethane. Titrations of *O*-acetyl-β-boswellic acid with perbenzoic acid (0·16—0·18 atom of oxygen absorbed after 96 hours) carried out by Trost (*Ann. Chim. Appl.*, 1937, **27**, 178) indicate that the double bond is of the inert type characteristic of both α- and β-amyrin, and our own experiments have confirmed this, for, although acetyl-β-boswellic acid, in our hands, slowly absorbed oxygen from perbenzoic acid (0·75 atom of oxygen after 10 days) (compare perbenzoic acid titrations in the α-amyrin series; Ruzicka, Silbermann, and Furter, *Helv. Chim. Acta*, 1932, **15**, 482), we have found that methyl acetyl-β-boswellate is resistant to catalytic hydrogenation under ordinary conditions.

A promising method of approach to the problem appeared to be offered by the experi-

ments of Jacobs and Fleck (*J. Biol. Chem.*, 1930, **88**, 137, 153; 1931, **92**, 487; 1932, **96**, 341) on the partial dehydrogenation of triterpene alcohols and acids with sulphur. Whereas thio-compounds containing an aromatic nucleus (Simpson, this vol., p. 1313) are produced from β-amyrin, oleanolic acid, and hederagenin, sulphur-free dehydro-compounds, on the other hand, result from ursolic acid and α-amyrin. The diagnostic value of this reaction, so far as concerns these two groups of triterpenes, has been experimentally confirmed by the conversion of gypsogenin into hederagenin and oleanolic acid (Ruzicka and Giacomello, *Helv. Chim. Acta*, 1936, **19**, 1136; 1937, **20**, 299), of the latter into β-amyrin (Ruzicka and Schellenberg, *ibid.*, 1937, **20**, 1553), and of ursolic acid into α-amyrin (Goodson, this vol., p. 999).

When, however, the Jacobs–Fleck reaction was applied to methyl *O*-acetyl-β-boswellate (I, R = Me), the ester was recovered unchanged; under more severe conditions a tendency for general dehydrogenation to occur was manifest.

We therefore turned our attention to the action of oxidising agents on various derivatives of β-boswellic acid. Treatment of methyl acetyl-β-boswellate, $C_{33}H_{52}O_4$ (I, R = Me), with chromic anhydride produces a compound $C_{33}H_{50}O_5$, m. p. 204° (II, R′ = Ac); we have also obtained this compound, which we designate *methyl* O-*acetyl-β-boswellenonolate*, by a similar oxidation of acetyl-β-boswellic acid (I, R = H), followed by methylation of the resultant acid fraction.



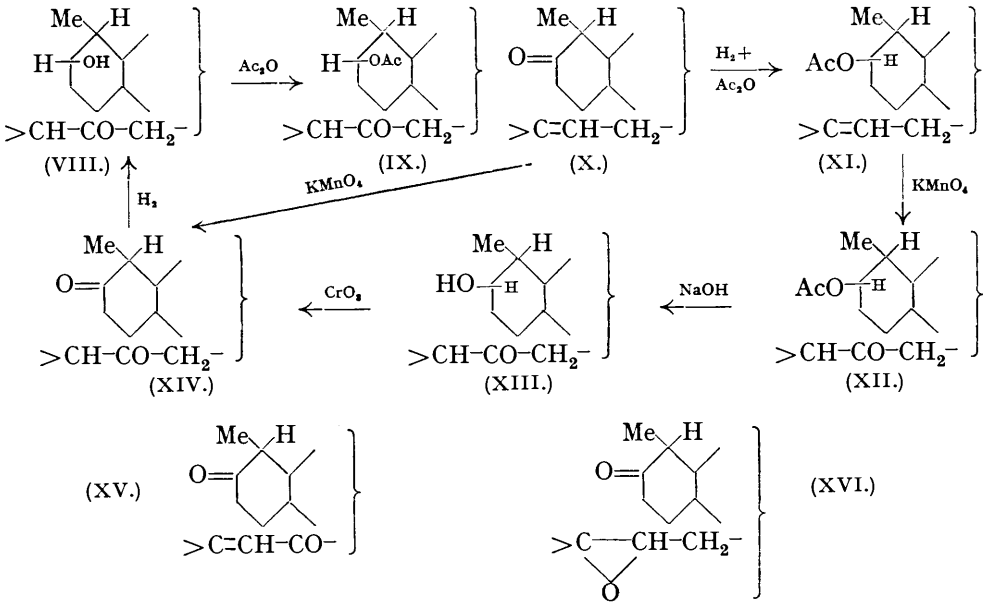
Although the compound (II, R′ = Ac) does not form an oximé, and is recovered unchanged after treatment with aluminium *iso*propoxide, a study of its properties has shown that it is unquestionably an αβ-unsaturated ketone. It exhibits the ultra-violet absorption spectrum characteristic of such ketones, and also, in common with these compounds (compare Ostromisslensky, *J. pr. Chem.*, 1911, **84**, 489; Spring and Vickerstaff, J., 1937, 249; Ruzicka, Leuenberger, and Schellenberg, *Helv. Chim. Acta*, 1937, **20**, 1271), fails to give a coloration with tetranitromethane, in contrast to its precursor (I, R = Me). Furthermore, it is converted by catalytic hydrogenation into methyl acetyl-β-boswellate (I, R = Me), in entire analogy with the conversion of the αβ-unsaturated ketones, methyl glycyrrhetate and α-amyrenonyl acetate, into the corresponding deoxy-methyl ester and α-amyrin acetate respectively (Ruzicka, Leuenberger, and Schellenberg, *loc. cit.*).

Alkaline hydrolysis of (II, R′ = Ac) yielded *methyl* β-*boswellenonolate*, m. p. 212° (II, R′ = H), which on mild oxidation with chromic anhydride gave in good yield *methyl* β-*boswellendionate*, m. p. 264° (III). This diketo-ester was also easily obtained by permanganate oxidation of methyl β-boswellenonate (IV), which in turn arises by oxidation (Simpson and Williams, *loc. cit.*) of methyl β-boswellate.

It was previously shown (Simpson and Williams, *loc. cit.*) that oxidation of nor-β-boswellenone (X) with permanganate gives rise to a ketone, m. p. 218°, for which analytical data indicated the formula $C_{26}H_{42}O_2$. The only feasible explanation for the production of a compound of this formula, on the assumption that β-boswellic acid contains the 1 : 8-dimethylperhydropicene skeleton, would be the location of the unsaturated centre in nor-β-boswellenone at C_4—C_5, as in (V); oxidation as indicated by the dotted line could then give a diketone $C_{26}H_{42}O_2$ of structure (VI). If this hypothesis is correct, it follows that the diketo-ester (III) must have the partial structure (VII) (it is assumed that no migration of the double bond occurs during the formation of nor-β-boswellenone from β-boswellic acid), and should therefore condense with *o*-phenylenediamine. No condensation, however, occurs with this reagent under a variety of conditions, and the 4 : 5-position is therefore definitely eliminated.

Further investigation showed that the formula $C_{26}H_{42}O_2$ for the ketone, m. p. 218°, was derived from inaccurate analytical data. Fresh analyses (Schoeller) on samples of the compound having the same physical constants and prepared under identical conditions gave results in excellent agreement with the formula $C_{29}H_{46}O_2$, which was confirmed by the preparation of the corresponding monohydric *alcohol*, $C_{29}H_{48}O_2$, m. p. 232° (VIII), readily obtained by reduction of the ketone with aluminium *iso*propoxide; this alcohol was converted into its *monoacetate*, m. p. 237° (IX), analysis of which indicated the formula $C_{31}H_{50}O_3$.

Definite proof that the ketone, m. p. 218°, contains the carbonyl group originally present in nor-β-boswellenone, and therefore that its formation from the latter involves merely the addition of one atom of oxygen, is provided by the following series of experiments. Nor-β-boswellenone (X) was reduced by means of aluminium *iso*propoxide to the corresponding alcohol, *nor-β-boswellenol*, m. p. 190°, acetylation of which yielded *nor-β-boswellenyl acetate*, $C_{31}H_{50}O_2$, m. p. 166° (XI). This acetate on oxidation with permanganate furnished an *acetate*, $C_{31}H_{50}O_3$, m. p. 233° (XII), isomeric with the acetate (IX). Careful hydrolysis of the acetate (XII) yielded the *alcohol*, m. p. 183° (XIII), which was then oxidised with chromic anhydride at room temperature. The product (XIV) from this oxidation was identical with the ketone $C_{29}H_{46}O_2$ obtained directly from nor-β-boswellenone by permanganate oxidation. The precise relationship between the latter compound and the ketone, m. p. 218° (XIV), is thus established, and it also follows that the two acetates (IX) and (XII) differ merely in their steric configurations around C_2.



The assignment of the structure (XIV) to the ketone $C_{29}H_{46}O_2$ (which we now designate as *nor-β-boswellanedione*) necessarily implies that the nature of the oxidation effected by permanganate depends on the groups attached to C_1, for it has already been shown that oxidation of methyl β-boswellenonate (IV), in which C_1 carries a methyl group and a carbomethoxyl group, produces an αβ-unsaturated ketone. Consideration of the following facts establishes beyond doubt that the latter type of oxidation does not occur in the formation of the ketone $C_{29}H_{46}O_2$ from nor-β-boswellenone. First, a comparison of the stability towards alkali of nor-β-boswellanedione with that of the αβ-unsaturated ketone (II, R′ = H) demonstrates the presence of different groupings in these two compounds, for whereas the substance (II, R′ = H) is stable to boiling 3% alcoholic potash, nor-β-boswellanedione is completely resinified under the same conditions. [It was previously observed (this vol., p. 688) that the latter compound is recoverable only in small yield after treatment with boiling 1% alcoholic potash.] Furthermore, nor-β-boswellanedione does not show the absorption spectrum of an αβ-unsaturated ketone, and also the analytical data both of this compound and of its related alcohol and acetate (VIII and IX) are in markedly better agreement with the formula $C_{29}H_{46}O_2$ than with $C_{29}H_{44}O_2$. Finally, if nor-β-boswellanedione were an αβ-unsaturated ketone (XV), it should be derivable by the alternative method of saponification of the acid (II, R′ = Ac; CO_2H instead of CO_2Me), followed by oxidation with chromic anhydride, in analogy with the conversion of β-boswellic acid into nor-β-boswellenone; actually, however, no trace of nor-β-boswellanedione could be isolated by this procedure.

Nor-β-boswellanedione contains only one reactive carbonyl group; this is illustrated both by its behaviour on reduction with aluminium *iso*propoxide and also by its conversion into a mono-oxime, monosemicarbazone (Simpson and Williams, *loc. cit.*), *azine*, m. p. 211°, and *mono-α-methyloxime*, m. p. 200°. The alternative representation of the compound as a keto-oxide (XVI), while affording adequate interpretation of these reactions, is incompatible with its instability towards alkali, for it is well established that ethylene oxide rings in polycyclic hydroaromatic compounds are stable towards this reagent [compare α- and β-stigmasteryl oxides (Fernholz, *Annalen*, 1934, **508**, 215); α-dihydrofucosteryl oxide (Coffey, Heilbron, and Spring, J., 1936, 738); α-spinasteryl oxide (Simpson, J., 1937, 730)]. Further, nor-β-boswellanedione is not formed by the action of perbenzoic acid on nor-β-boswellenone (X). We therefore consider, having regard to the fact that inert carbonyl groups are frequently encountered in triterpene derivatives, that (XIV) is the only possible structure for nor-β-boswellanedione; the production of the grouping $>CH\cdot CO\cdot CH_2-$ by oxidation at an ethylenic linkage may be assumed to occur by the mechanism:

$$>C{=}CH{-}CH_2- \longrightarrow \underset{(a.)}{} \overset{*}{} >\underset{OH}{C}{-}\underset{OH}{CH}{-}CH_2- \longrightarrow >C{=}\underset{OH}{C}{-}CH_2- \longrightarrow >CH{-}CO{-}CH_2- \underset{(b.)}{}$$

The reactions discussed in this paper demonstrate that β-boswellic acid contains the grouping (a), and also disclose two further points of interest. First, the groupings attached to C_1 control the course of the oxidising action of permanganate [(IV) ⟶ (III); (X) ⟶ (XIV)]; secondly, the steric configuration produced by reduction of a carbonyl group on C_2 to $>CH\cdot OH$ depends on whether grouping (a) or (b) is present in the compound reduced, C_1 carrying the same groups in each case [(XIV ⟶ (VIII); (X) ⟶ (XI, H instead of Ac)]. Both these points are suggestive of a close association of C_1—C_2 with systems (a) and (b), such as would be provided by the location of the double bond of β-boswellic acid at C_6—C_7 (or, less probably, at C_8—C_9). Our investigation is being continued from this point of view.

Experimental.

(All analyses are by Schoeller. Melting points are uncorrected, and specific rotations are in chloroform.)

Nor-β-boswellenone.—A slightly improved yield of this compound was obtained by the

* The dehydration of this glycol in acid solution to the ketone (b) is reminiscent of the semihydrobenzoinic dehydrations (without group migration) studied by McKenzie and co-workers (J., 1924, **125**, 847; 1932, 2597; *Ber.*, 1929, **62**, 272).

following procedure: A solution of chromic anhydride (3 g.) in acetic acid (130 c.c. of 90%) was added during 75 minutes to a stirred solution of β-boswellic acid (10 g.) in acetic acid (440 c.c. of 90%) at room temperature. After 16 hours the product was worked up as previously described (this vol., p. 687), crystallisation of the neutral fraction (7 g.) from absolute alcohol giving 2·9 g. of pure nor-β-boswellenone. The acid fraction (2 g.) was decarboxylated by refluxing for 1½ hours with glacial acetic acid (150 c.c.), after which the solution was concentrated under reduced pressure. The residue was dissolved in ether and shaken with 3% sodium hydroxide solution; the neutral fraction thus obtained (1 g.) was crystallised from alcohol and yielded a further 240 mg. of the pure ketone. The total yield was thus 35% of the theoretical amount, the average yield from the procedure previously described being 28%.

Methyl O-*Acetyl*-β-*boswellenonolate* (II, R′ = Ac).—A solution of chromic anhydride (320 mg.) in acetic acid (10 c.c.) was added during 55 minutes to a solution of methyl acetyl-β-boswellate (400 mg.) in glacial acetic acid (40 c.c.) at 40°. The solution was kept at this temperature for a further hour; the excess of chromic anhydride was then removed with methyl alcohol, the solution concentrated under reduced pressure, and the residue separated in the usual manner into acid and neutral fractions with 5% sodium carbonate solution. A solution of the neutral material (95% of the whole) in aqueous methyl alcohol deposited *methyl* O-*acetyl*-β-*boswellenonolate* in fine prismatic needles, m. p. 203—204° (constant) after five crystallisations, $[\alpha]_D^{23°}$ + 51·7° (l = 1, c = 0·895) (Found: C, 75·0; H, 9·4. $C_{33}H_{50}O_5$ requires C, 75·2; H, 9·6%). *Light absorption in hexane*: maximum at 2400 A., log ε = 4·16. The keto-ester gave a negative tetranitromethane reaction in chloroform and a bright red colour with the Liebermann–Burchard reagent; it was recovered unchanged in quantitative yield after refluxing with (a) aluminium *iso*propoxide in absolute *iso*propyl alcohol for 18 hours, and (b) hydroxylamine acetate in ethyl alcohol for 2½ hours.

Reduction of Methyl β-*Boswellenonolate*.—A solution of the keto-ester (280 mg.) in glacial acetic acid (50 c.c.) was shaken with Adams's platinum oxide (208 mg., previously reduced) in an atmosphere of hydrogen, 27·5 c.c. (1·86 mols.) being slowly absorbed; after 18 hours all absorption had ceased. The product, isolated by precipitation with water, crystallised from methyl alcohol in fine prismatic needles, m. p. 189—190° either alone or on admixture with authentic methyl acetyl-β-boswellate. $[\alpha]_D^{23°}$ + 70·6°, + 71·3° (l = 1, c = 1·015, 2·155) (Found: C, 77·2; H, 10·2. Calc. for $C_{33}H_{52}O_4$: C, 77·3; H, 10·2%). A solution of the ester in chloroform gave an immediate yellow coloration with tetranitromethane. Its identity was confirmed by heating it under reflux (100 mg.) with alcoholic potassium hydroxide (20 c.c. of 3%) for 2 hours; the free hydroxy-ester separated from methyl alcohol in prismatic needles, m. p. 195—196°, $[\alpha]_D^{20°}$ + 166°, + 166° (l = 1, c = 1·21, 1·03), and gave no depression in m. p. when mixed with * authentic methyl β-boswellate of m. p. 194—195° and $[\alpha]_D^{19°}$ + 169° (l = 1, c = 1·495).

Methyl β-*Boswellenonolate* (II, R′ = H).—The acetate (II, R′ = Ac) (130 mg.) was refluxed with 0·1N-alcoholic potassium hydroxide (10 c.c.) for 1½ hours. The *keto-alcohol*, isolated by precipitation with water, separated from aqueous methanol in sheaves of short prismatic needles, m. p. 211—212°, $[\alpha]_D^{20°}$ + 120° (l = 1, c = 0·665) (Found: C, 76·75; H, 10·0. $C_{31}H_{48}O_4$ requires C, 76·9; H, 10·0%). This compound was also obtained in the same yield (80% of pure product) when hydrolysis was effected with 3% alcoholic potash under reflux.

Methyl β-*Boswellendionate* (III).—(a) A solution of chromic anhydride (15 mg.) in acetic acid (2·5 c.c.) was added at room temperature during 70 minutes to a stirred solution of the above keto-alcohol (70 mg.) in glacial acetic acid (7 c.c.). The *diketone*, precipitated with water, separated from aqueous acetone in clusters of fine long needles, m. p. 263·5—264°, $[\alpha]_D^{20°}$ + 117° (l = 1, c = 2·36) (Found: C, 76·95; H, 9·6. $C_{31}H_{46}O_4$ requires C, 77·1; H, 9·6%). The tetranitromethane test with this compound was negative, but the Liebermann–Burchard reagent produced an immediate bright red colour.

(b) Methyl β-boswellenonate (IV) (2 g.) in glacial acetic acid (200 c.c.) was treated at 45° with N-potassium permanganate (50 c.c. ≡ 5O), added during 70 minutes with stirring. After a further ½ hour at 45°, the solution was clarified with sodium bisulphite, diluted with water, and extracted with ether; the extract was washed with water and 3% sodium hydroxide solution, dried, and evaporated. The residue crystallised from aqueous acetone in long needles, m. p. 262—263° either alone or when mixed with the diketone prepared by method (a) (Found: C, 77·05; H, 9·3%).

* On numerous occasions we have obtained specimens of methyl β-boswellate which melted at 185—187° after comparatively rapid crystallisation; such samples, of apparently constant m. p., melted at 195° when allowed to crystallise slowly. This behaviour is possibly attributable to polymorphism.

The *monosemicarbazone* was prepared by heating a solution of the diketone (100 mg.) in methanol (25 c.c.) with semicarbazide hydrochloride (500 mg.) and anhydrous sodium acetate (800 mg.) under reflux for 4 hours. After precipitation with water and crystallisation from methanol it separated in fine needles, m. p. 280—281° (decomp.) (Found : C, 71·0; H, 9·05; N, 7·5. $C_{32}H_{49}O_4N_3$ requires C, 71·2; H, 9·2; N, 7·8%).

Condensation of the diketone with its own weight of *o*-phenylenediamine was attempted (i) in alcoholic solution under reflux for 1 hour; (ii) in glacial acetic acid under reflux for 1 hour; (iii) by fusion at 150—160° for 40 minutes. In each case the diketone was recovered in almost quantitative yield.

Oxidation of O-*Acetyl-β-boswellic Acid.*—A stirred solution of the acetyl acid (3 g.) in glacial acetic acid (240 c.c.) was treated with a solution of chromic anhydride (2·4 g.) in acetic acid (70 c.c.), added drop by drop during 70 minutes. After a further 70 minutes (temperature 41° throughout) methyl alcohol was added, the solvent removed under reduced pressure, and the residue dissolved in ether. The acid fraction (90% of the whole), isolated by means of 3% sodium hydroxide solution, could not be obtained in crystalline form; a portion was therefore treated with diazomethane, and the product dissolved in methyl alcohol, from which methyl β-boswellenonolate separated on cooling in prismatic needles, m. p. 198—199°, which gave no depression when mixed with an authentic specimen of m. p. 203—204°.

The remainder of the acid fraction (1·8 g.) was refluxed for 3 hours with methyl-alcoholic potassium hydroxide (60 c.c. of 5%). The product, isolated by acidification and ether-extraction, was dissolved in glacial acetic acid (90 c.c.) and treated with a solution of chromic anhydride (0·77 g.) in acetic acid (26 c.c.), added during 45 minutes at 56°. The product was isolated in the usual manner and separated into an acid and a neutral fraction. Attempts to crystallise the latter fraction (340 mg.) from a small quantity of methyl alcohol were unsuccessful (in which solvent nor-β-boswellanedione is sparingly soluble), nor could any crystalline material be obtained when the solution was seeded with crystals of nor-β-boswellanedione.

Nor-β-boswellanonol (VIII).—A solution of nor-β-boswellanedione (200 mg.) in dry *iso*propyl alcohol (30 c.c.) was refluxed for 3½ hours with aluminium *iso*propoxide (1 g.). Excess of dilute sulphuric acid was then added, and the product extracted with ether. The extract was washed with water, dried, and evaporated, and the residue dissolved in slightly aqueous methanol, from which *nor-β-boswellanonol* separated in fine needles, m. p. 231—232°, $[\alpha]_D^{19°}$ + 137° (l = 1, c = 1·135) (Found : C, 81·2; H, 11·3. $C_{29}H_{48}O_2$ requires C, 81·2; H, 11·3%). A solution of the keto-alcohol in chloroform gave a negative tetranitromethane test and a purple-red Liebermann–Burchard reaction.

Nor-β-boswellanonyl acetate (IX), obtained by heating (VIII) with acetic anhydride in pyridine at 90°, crystallised from aqueous methanol in clusters of needles, m. p. 236·5—238°, $[\alpha]_D^{18°}$ + 111° (l = 1, c = 0·940) (Found : C, 78·8; H, 10·65. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%). It was recovered unchanged after treatment with semicarbazide acetate in alcohol under reflux for 3½ hours.

Nor-β-boswellenol.—Nor-β-boswellenone (1 g.) was refluxed for 3½ hours in dry *iso*propyl alcohol (70 c.c.) with aluminium *iso*propoxide (5·5 g.). The product was worked up as in the reduction of nor-β-boswellanedione, *nor-β-boswellenol* separating from acetone in sheaves of long silky needles, m. p. 190—191°, $[\alpha]_D^{20°}$ + 112° (l = 1, c = 1·140) (Found : C, 84·1; H, 11·5. $C_{29}H_{48}O$ requires C, 84·4; H, 11·7%).

Nor-β-boswellenyl acetate (XI), prepared by heating a solution of nor-β-boswellenol in pyridine with acetic anhydride on the water-bath, crystallised from aqueous methyl alcohol in stout prismatic needles, m. p. 165—166°, $[\alpha]_D^{20°}$ + 109° (l = 1, c = 1·025), and from aqueous acetone in leaflets, m. p. 151·5—152° (Found : C, 81·7; H, 11·0. $C_{31}H_{50}O_2$ requires C, 81·8; H, 11·1%).

Oxidation of Nor-β-boswellenyl Acetate.—The acetate (120 mg.) was dissolved in glacial acetic acid (22 c.c.) and treated at 45° with N-potassium permanganate (3 c.c.), added drop by drop during 35 minutes. After a further ½ hour at 45°, sodium bisulphite was added, and the oxidation product precipitated by addition of water. The new *keto-acetate* (XII) crystallised from aqueous methyl alcohol in narrow rectangular plates, m. p. 233—233·5°, giving a depression of 30° when mixed with the isomeric acetate (IX). $[\alpha]_D^{18°}$ + 163° (l = 1, c = 0·735) (Found : C, 79·1; H, 10·6. $C_{31}H_{50}O_3$ requires C, 79·1; H, 10·7%).

Keto-alcohol (XIII).—In analogy with nor-β-boswellanedione, the keto-acetate (XII) is resinified by treatment with hot alcoholic alkali. We have, however, observed that 2-acetyl derivatives of β-boswellic acid are hydrolysed by 0·1N-alcoholic sodium hydroxide at room temperature, provided a free carboxyl group is not attached to C_1 (in which case an acetyl group

on C_2 can be removed only by refluxing with N-alcoholic alkali). Hydrolysis of (XII) was satisfactorily effected by allowing a solution of the acetate (350 mg.) in methyl alcohol (30 c.c.) and 4N-sodium hydroxide (3 c.c.) to stand for 18 hours at 10°. Water was then added, and the resultant suspension extracted with ether. The extract was washed, dried, and evaporated; a solution of the residue in methyl alcohol deposited fine needles (200 mg.) of the *keto-alcohol* (XIII), m. p. 182—183°, $[\alpha]_D^{20°}$ + 159° (l = 1, c = 0·975) (Found: C, 80·9; H, 11·3. $C_{29}H_{48}O_2$ requires C, 81·2; H, 11·3%). A small quantity of the keto-alcohol was heated on the water-bath with acetic anhydride in pyridine; the product after crystallisation from aqueous methyl alcohol melted at 232—233° both alone and when mixed with the keto-acetate (XII), thus showing that cold hydrolysis of the latter produces no effect beyond removal of the acetyl group.

Nor-β-boswellanedione from the Keto-alcohol (XIII).—The foregoing keto-alcohol (60 mg.) in glacial acetic acid (7 c.c.) was treated at 20° with a solution of chromic anhydride (20 mg.) in acetic acid (2 c.c.), added during 35 minutes. After a further 1¼ hours methyl alcohol was added, the solution concentrated under reduced pressure, dilute sulphuric acid then added, and the mixture extracted with ether. Evaporation of the washed and dried extract gave a crystalline residue, which after one crystallisation from methyl alcohol had m. p. 217—218°, both alone and when mixed with authentic *nor-β-boswellanedione*. $[\alpha]_D^{21°}$ + 159° (l = 1, c = 0·86) (Found: C, 81·5; H, 11·1. $C_{29}H_{46}O_2$ requires C, 81·6; H, 10·9%). *Light absorption in alcohol*: maximum at 2735 A., log ε = 1·753.

The diketone, prepared by permanganate oxidation of nor-β-boswellenone (Found: C, 81·6; H, 10·6%), was converted into the following derivatives: (i) The oxime, as previously described (Simpson and Williams, *loc. cit.*), crystallised from aqueous methanol in soft fine needles, m. p. 197—198°, unchanged by crystallisation from aqueous acetone (Found: C, 78·8, 79·0; H, 10·7, 10·8; N, 3·1. $C_{29}H_{47}O_2N$ requires C, 78·8; H, 10·8; N, 3·2%).

(ii) Several preparations of the semicarbazone, obtained by refluxing the diketone with semicarbazide acetate in alcohol, had m. p. 251—253° (decomp.) (Found: C, 74·3, 74·4, 74·5; H, 10·1, 10·4, 10·2; N, 8·5, 8·6. $C_{30}H_{49}O_2N_3$ requires C, 74·45; H, 10·2; N, 8·7%).

(iii) The diketone (450 mg.) was refluxed for 4 hours with 50% hydrazine hydrate (0·3 c.c.) in absolute alcohol (30 c.c.). On dilution with water an emulsion was formed, which was coagulated, by the addition of a drop of dilute hydrochloric acid, to a granular precipitate; this was repeatedly crystallised from methyl alcohol, from which the *azine* finally separated in long prismatic needles, m. p. 210—211° [Found: C, 81·4; H, 10·7; N, 3·5; *M* (Rast), 815, 863, 925. $C_{58}H_{92}O_2N_2$ requires C, 82·0; H, 10·9; N, 3·3%; *M*, 849].

(iv) The diketone (100 mg.) was refluxed for 3 hours with α-methylhydroxylamine (0·4 c.c.) in alcohol (10 c.c.). The *α-methyloxime*, obtained by precipitation with water, crystallised from methyl alcohol in fine feathery needles, m. p. 199—200° after five crystallisations (Found: C, 78·95; H, 10·8; N, 3·1. $C_{30}H_{49}O_2N$ requires C, 79·1; H, 10·85; N, 3·1%).

Action of Sulphur on Methyl O-Acetyl-β-boswellate.—An intimate mixture of the acetyl ester (1 g.) and sulphur (1 g.) was heated in a stream of nitrogen at 210—220° (compare Jacobs and Fleck, *loc. cit.*) for 5¾ hours, during which time a very slow evolution of hydrogen sulphide occurred. The reaction-mass was thoroughly extracted with ether, and the extract dried and evaporated; repeated crystallisation of the residue from aqueous ethanol yielded needles (450 mg.), m. p. 177—178°, and 183—184° when mixed with methyl *O*-acetyl-β-boswellate.

More drastic conditions were then employed, the mixture of sulphur and the acetyl ester being heated at 230—240° for 2 hours and then at 250° for a further hour. In spite of a more vigorous evolution of hydrogen sulphide the only crystalline product isolated was impure starting material (m. p. 176—177°, 440 mg.).

The identity of both these specimens was confirmed by refluxing with 5% alcoholic potash; the product, after three crystallisations from methyl alcohol, had m. p. 187—188° (190° when mixed with authentic methyl β-boswellate of m. p. 194—195°).

Specific Rotations of β-Boswellic Acid Derivatives.—The specific rotation of the β-boswellic acid used in this, and also in our earlier, work was considerably higher than the values given by Winterstein and Stein (*loc. cit.*) and by Trost (*loc. cit.*). Our acid was prepared by the method of Winterstein and Stein, which involves precipitation of the mixture of α- and β-boswellic acids as barium salts, followed by decomposition of the latter with acetic anhydride. This is a strongly exothermic reaction, and we have observed that the time for which it is allowed to proceed determines the rotation of the product. Thus, following our usual procedure of refluxing the mixture for approximately 1 hour after the initial reaction, we obtained an acid of high rotation; when, however, no external heat was applied, the rotations of the resultant acid and its derivatives agreed closely with those of Winterstein and Stein and of Trost. In

Table I, column A includes derivatives of the " high rotation series " arising from the β-acetyl acid obtained by refluxing the barium salts with acetic anhydride; in B are given rotations of derivatives of the β-acetyl acid obtained from the barium salts without subsequent refluxing; and in C and D are given the values of Winterstein and Stein and of Trost.

TABLE I.

	A.		B.		C.		D.	
	M. p.	$[\alpha]_D$.	M. p.	$[\alpha]_D$.	M. p.*	$[\alpha]_D$.	M. p.*	$[\alpha]_D$.
O-Acetyl-β-boswellic acid	273—275°	136°	273—275°	74·3°	271—273°	69°	273—275°	71·5°
β-Boswellic acid	234	215 (a) 208 (b)	—	—	238—240	119	238—239	118
Methyl *O*-acetyl-β-boswellate	189—190	131 (c) 132 (d) 134 (e) 135 (e)	193—194	70·0 (c)	197·5—198·5	73·8	—	—
Methyl β-boswellate	195—196 and 184—185	190 (f) 194 (f)	195—196 and 184—185	111 (g)	189—190	116	198—200	145
Nor-β-boswellenone	195—196	128	—	—	—	—	198—200	127

* M. p.'s corrected. (a) Recrystallised twice. (b) Recrystallised seven times. (c) By methylation of *O*-acetyl-β-boswellic acid. (d) From methyl β-boswellate *ex* seven times recrystallised β-boswellic acid. (e) From methyl β-boswellate *ex* twice recrystallised β-boswellic acid. (f) *Ex* β-boswellic acid seven times recrystallised. (g) *Ex* methyl *O*-acetyl-β-boswellate.

The similarity between corresponding m. p.'s in columns A and B is of interest in view of the widely divergent rotations. On only one occasion have we obtained a low-rotation derivative from one of high rotation, namely, methyl *O*-acetyl-β-boswellate by the reduction of methyl *O*-acetyl-β-boswellenonolate (from high-rotation methyl *O*-acetyl-β-boswellate); hydrolysis of the acetyl group in this case immediately caused reversion to the " high-rotation series " (p. 1716).

The changes in steric configuration involved in the two modifications of β-boswellic acid derivatives would seem to be confined to C_1—C_2, inasmuch as the physical constants of nor-β-boswellenone, in which C_2 is no longer asymmetric and decarboxylation has occurred at C_1, are independent of those of the β-boswellic acid used in its preparation.

Perbenzoic Acid Titrations.—Solutions of (a) acetyl-β-boswellic acid and (b) nor-β-boswellenone in excess of approximately 0·3N-perbenzoic acid in chloroform were kept at 5°, and the oxygen consumption determined at various times in the usual manner :

(a) Acetyl-β-boswellic acid.

Time (hours)	17	24	42	48	68	113	238
Oxygen consumption (atoms)	0·385	0·49	0·63	0·61	0·60	0·68	0·75

(b) Nor-β-boswellenone.

Time (hours)	19	42	100	173
Oxygen consumption (atoms)	0·16	0·36	0·40	0·45

KING'S COLLEGE, UNIVERSITY OF LONDON.

[*Received, July 29th,* 1938.]