Action of Beckmann's mixture on some monocyclic terpenes. Pt. 2, Terpinolene and "origanene" / by T.A. Henry and H. Paget.

Henry, Thomas Anderson, 1873-1958.
Paget, Humphrey.
Wellcome Chemical Research Laboratories.

London : Wellcome Chemical Research Laboratories, [1931.]

No. 225

THE ACTION OF BECKMANN'S MIXTURE ON SOME MONOCYCLIC TERPENES

PART II

TERPINOLENE AND "ORIGANENE"

BY

T. A. HENRY AND H. PAGET

(From the Transactions of the Chemical Society, 1931)

* * *

THE WELLCOME CHEMICAL RESEARCH LABORATORIES
(The Wellcome Foundation Ltd.)
T. A. HENRY, D.SC., *Director*
6, King Street, Snow Hill
LONDON, E.C.1

Reprinted from the Journal of the Chemical Society, 1931.

III.—*The Action of Beckmann's Mixture on Some Monocyclic Terpenes. Part II. Terpinolene and "Origanene."*

By Thomas Anderson Henry and Humphrey Paget.

An examination of the action of Beckmann's mixture on α-terpinene, α-phellandrene, and limonene (Henry and Paget, J., 1928, 70) showed that oxidation of the first two was probably preceded by the addition of a molecule of water at each of the double linkages, whereas limonene underwent hydration at the extra-cyclic linkage only, a hydroxyl group being added at each end of the cyclic linkage.

Each of these hydrocarbons contains one ethylenic linkage in the 1 : 2-position, and it is of interest to examine the behaviour of terpinolene, $\Delta^{1:4(8)}$-*p*-menthadiene, under the same conditions, in view of its close relationship to α-terpinene and limonene, $\Delta^{1:3}$- and $\Delta^{1:8(9)}$-*p*-menthadienes respectively.

It is doubtful whether terpinolene occurs in nature, and the methods by which it is prepared, from turpentine oil or from terpineol, give rise to considerable proportions of terpinene and dipentene; of two commercial samples examined, one contained about 8% of terpinolene, and the other apparently none. Attempts to prepare it from the pinene fraction of American turpentine oil by heating with formic or sulphuric acid gave poor results, but it was obtained with more success by shaking *dl*-α-pinene, for which the authors are indebted to Professor J. L. Simonsen, with cold alcoholic sulphuric acid, or from commercial terpineol by treatment with hot aqueous oxalic acid solution or with cold alcoholic sulphuric acid.

FIG. 1.

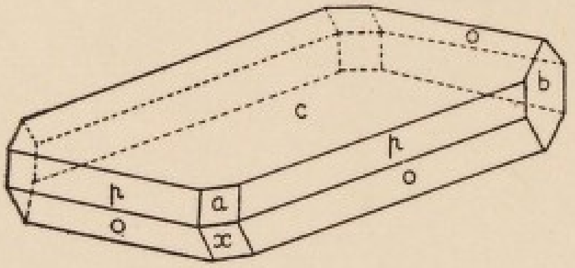
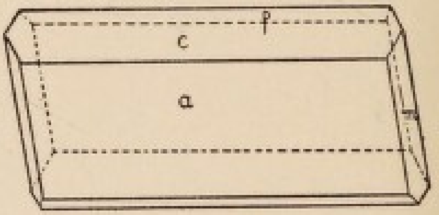


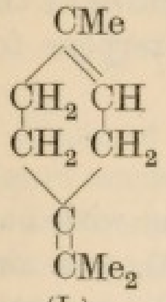
FIG. 2.

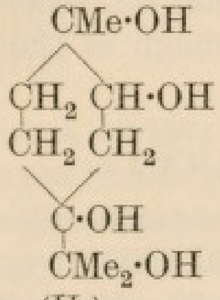


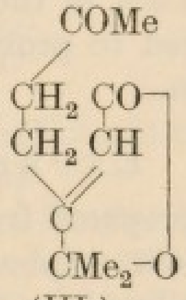
The terpinolene used for oxidation was regenerated from the recrystallised tetrabromide. When first prepared, terpinolene tetrabromide separates in irregular clusters of crystals (A), melting at 122°. On slow recrystallisation, square-ended tablets appear (B), which are more stable than (A) and melt at 119°. Both forms on debromination yield the same terpene. The authors are indebted to Mr. H. M. Powell, of the Department of Mineralogy of Oxford University, who kindly undertook to examine these crystals: his measurements show that (A) (Fig. 1) is identical with the specimen of terpinolene tetrabromide described by Hintze (*Z. Kryst.*, 1885, **10**, 258), whilst (B) (Fig. 2) has not been described previously.

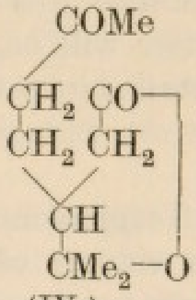
Terpinolene (I) is not very readily attacked by Beckmann's mixture. The principal products of oxidation are lævulic (VII) and acetic acids. The intermediate product (II) has not been isolated, but a small amount of an unsaturated keto-lactone has been obtained, to which the formula of β-*thujaketo-lactone* (III) is assigned, since on catalytic reduction it yields homoterpenyl methyl ketone (IV) by the addition of two atoms of hydrogen. It is readily oxidised by permanganate to lævulic acid (VII), and on prolonged treatment with Beckmann's mixture at 60° it breaks somewhat unexpectedly between the two methylene groups, giving a quantitative yield of terebilic acid (VIII), the identity of which was confirmed by catalytic reduction to terebic acid (IX).

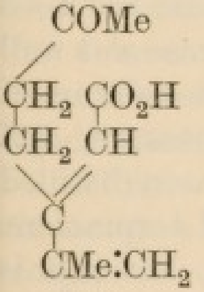
Hydrolysis of the keto-lactone (III) takes place only on warming with alkali. The product is not the corresponding hydroxy-acid, but an unsaturated *acid*, which is represented by formula (V), since on reduction it absorbs four atoms of hydrogen with great rapidity, giving ε-keto-β-*iso*propylheptoic acid (VI). This unsaturated acid is presumably formed from β-thujaketo-lactone (III) by loss of water between the hydroxyl group on what was the 8-carbon atom of terpinolene and an adjacent hydrogen atom attached to carbon 9.

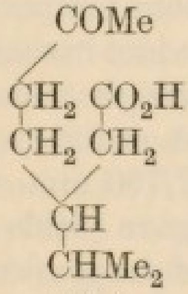

(I.)

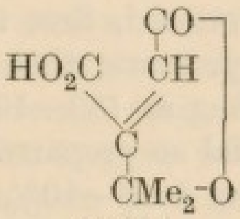

(II.)

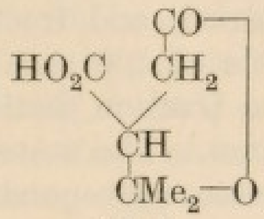

(III.)

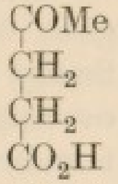

(IV.)


(V.)


(VI.)


(VIII.)


(IX.)


(VII.)

This sequence of reactions is best explained by the assumption that the first step in the oxidation is the formation of the tetrahydric alcohol (II). The formation of β-thujaketo-lactone (III) provides direct evidence of the addition of hydroxyl groups at carbon atoms 4 and 8 and the addition of hydroxyl groups at 1 and 2 is in harmony with what takes place in the case of limonene, where the trihydric alcohol, 1 : 2 : 8-trihydroxyterpan, was isolated as an intermediate product.

"*Origanene.*"—It was suggested (*Ann. Reports*, 1908, **5**, 100) that this terpene, which Pickles (J., 1908, **93**, 866) regarded as $\Delta^{1:3}$-*p*-menthadiene, is α-terpinene, for which this formula is now generally accepted. That suggestion ignores the fact that "origanene" yields a nitrosyl chloride, m. p. 91—94°, a nitrolpiperidide,

m. p. 198°, and a nitrolbenzylamine, m. p. 104—105°, all well-defined crystalline substances, which have not been recorded as obtainable from α-terpinene. As the authors have had at their disposal a small quantity of residues left from the preparation of carvacrol from Cyprus origanum oil, the only known source of "origanene," they have taken the opportunity of examining this material and have shown that α-terpinene is present by the preparation of the characteristic nitrosite of this terpene and by the identification of dimethylacetonylacetone among the chromic acid oxidation products (Henry and Paget, *loc. cit.*). There is, however, also present, along with *p*-cymene, a terpene giving the three characteristic crystalline derivatives referred to above, as described by Pickles, and for this terpene the name "origanene" should be provisionally retained, until the terpene can be definitely identified. As the yield of the fraction rich in "origanene" in the present instance was only 1·4% of the original oil, large quantities of the latter will be required to provide enough of the pure terpene for detailed investigation.

EXPERIMENTAL.

Terpinolene was prepared from *dl*-α-pinene by shaking with half its volume of alcoholic sulphuric acid (50% by weight), and also from terpineol by boiling it gently for 30 minutes with 40% aqueous oxalic acid solution or by keeping it at room temperature for 2—3 days with alcoholic sulphuric acid. The product in each case was well washed, dried, and fractionated, first through a short column of glass beads at 100 mm. pressure, then at ordinary pressure, and finally the fraction distilling at 180—190°/760 mm. was redistilled over sodium. The material so prepared gave yields of terpinolene tetrabromide corresponding to 3—10% of terpinolene, but this is a doubtful guide to the actual amount of terpinolene present.

In the preparation of terpinolene tetrabromide, which is somewhat unstable, ether was found preferable to chloroform or glacial acetic acid as a diluent, since it is readily removed, and allows of the maintenance of a lower temperature. The redistilled terpene (25 c.c.), dissolved in 100 c.c. of ether and well cooled in ice and salt, was treated with 12·3 c.c. of bromine, added very slowly. The solvent was then removed by aspiration, and the crystalline residue filtered from oil and washed with acetic acid. After crystallisation once, from two volumes of alcohol, acetone, or ethyl acetate, irregular clusters of crystals (Fig. 1) separated (A), m. p. 122°. By slow recrystallisation from ten volumes of acetone, square-ended rectangular plates (Fig. 2) were obtained (B), m. p. 119°. A marked depression of melting point was observed with mixtures of A and

B, or on addition to either of dipentene or *iso*limonene tetrabromide (J., 1921, **119**, 1718), from which they differ also in crystalline form. Both A and B belong to the monoclinic system. The measurements of the two crystal forms furnished by Mr. H. M. Powell are given below.

A. Monoclinic, $a:b:c = 0·7804:1:0·9668$; $\beta = 114° 15'$.
Hintze (*loc. cit.*) records $a:b:c = 0·79678:1:0·98522$; $\beta = 114° 37'$.

c a	(001) : (100)	(Powell) 64° 45′	(Hintze) 65° 25′
c p	(001) : (110)	70° 27′	70° 17′
c o	(001) : $(\bar{1}11)$	71° 5′	71° 21′
p o	(110) : $(11\bar{1})$	38° 38′	38° 22′

B. Monoclinic, showing *a* 100, *m* 110, *c* 001, *ρ* $\bar{1}01$, elongated parallel to the *b* axis. $a:b:c = 2·5995:1:2·0333$; $\beta = 118° 8\tfrac{1}{2}'$.

a m	(100) : (110)	observed 70° 9′	calculated —
m m′	(110) : $(\bar{1}10)$	39° 26′	39° 42′
a c	(100) : (001)	61° 51½′	—
c m	(001) : (110)	98° 59½′	99° 13′
c ρ	(001) : $(\bar{1}01)$	70° 36′	—
ρ a	$(\bar{1}01)$: $(\bar{1}00)$	47° 34′	47° 32½′
ρ m	$(\bar{1}01)$: (110)	103° 12′	103° 16′

Plane of optic axis *b*(010); one optic axis of a negative biaxial figure emerges perpendicular to *a*(100).

Debromination of the Tetrabromide.—To the A form of terpinolene tetrabromide (35 g.), dissolved in dry ether (250 c.c.) and dry alcohol (100 c.c.), zinc dust (40 g.) was added in small amounts. When the vigorous action had subsided, the mixture was boiled gently for 1 hour and set aside for 24 hours. The ethereal solution was then filtered, washed with water, and dried, and the solvent removed by distillation. The residual oil was free from bromine; it distilled at 72°/10 mm., 121°/112 mm., and had $d_{15°}^{15°}$ 0·8633, $n_D^{20°}$ 1·4883; in acetic anhydride solution it gave with a drop of concentrated sulphuric acid a transient pale pink colour. On bromination it yielded 86% of tetrabromide A.

The debromination of tetrabromide B proceeded exactly in the same way. The recovered terpene had b. p. 121°/111 mm., 186°/764 mm., $d_{15°}^{17°}$ 0·8632, $n_D^{20°}$ 1·4886; on bromination it yielded 88% of tetrabromide A.

Oxidation of Terpinolene.—The terpene (24 c.c.) was oxidised by consecutive quantities of 200 c.c. of Beckmann's mixture. Oxidation proceeded slowly and after three repetitions 10·5 c.c. of oil remained, distilling at 75°/26 mm. and yielding 80% of tetrabromide A. After continued oxidation, 0·5 c.c. of residual oil was obtained, which gave a trace of *p*-tolyl methyl ketone semicarbazone and in which dipentene was identified by its tetrabromide to the extent of about 1% of the total terpene taken. This amount may have been present as impurity in the form of its tetrabromide with the terpinolene tetrabromide used, but it is not unlikely that it arose from conversion of terpinolene during debromination or distillation. The oxidation liquors were extracted thoroughly with ether and with chloroform and the extracts were washed with dilute sodium carbonate solution and so divided into neutral extract (5·7 g.) and acids (15·7 g.).

The neutral extract on treatment with an alcoholic solution of semicarbazide gave a colourless crystalline *semicarbazone*, m. p. 222—223° (corr.; decomp.), which was sparingly soluble in boiling alcohol (Found: C, 55·3; H, 6·9; N, 17·8. $C_{11}H_{17}O_3N_3$ requires C, 55·2; H, 7·1; N, 17·6%). On shaking the semicarbazone, in suspension in ether, with an excess of 10% hydrochloric acid until no material remained undissolved, the ketone was obtained; it crystallised in nodular masses, m. p. 48—50°, from a little water (Found: C, 65·8; H, 8·1. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·7%). The aqueous solution was neutral to litmus and did not neutralise alkali on standing with it in the cold; but when the mixture was heated on the water-bath for 15 minutes alkali equivalent to 5·5 c.c. of *N*-sodium hydroxide for 1 g. of substance was absorbed (calc. for 1 g. of $C_{10}H_{14}O_3$, 5·5 c.c.). On hydrogenation in aqueous solution with palladium catalyst this keto-lactone absorbed the equivalent of two atoms of hydrogen (Found: 1 g. required 137·3 c.c. of hydrogen. Calc. for $C_{10}H_{14}O_3 \longrightarrow C_{10}H_{16}O_3$, 123·0 c.c. at *N.T.P.*). The reduced product was identified as homoterpenyl methyl ketone by conversion into the semicarbazone, m. p. 209° (Found: C, 54·7; H, 8·1. Calc. for $C_{11}H_{19}O_3N_3$: C, 54·8; H, 7·9%), which showed no depression of melting point on admixture with an authentic specimen. The keto-lactone $C_{10}H_{14}O_3$ is therefore regarded as β-*thujaketo-lactone*(ε-*keto*-β-*hydroxy*iso*propyl*-Δ^{α}-*heptenolactone*) (III), and the following observations confirm this view.

When the keto-lactone is dissolved in warm alkali, as stated above, the solution obtained does not on acidification yield the corresponding hydroxy-acid or regenerate the keto-lactone unchanged, but furnishes instead an acid, crystallising in slender rods, m. p. 130°, which is isomeric with the keto-lactone and can be titrated in the cold (Found: by micro-analysis, C, 65·8; H, 7·7; 1 g. required 5·5 c.c. of *N*-NaOH. $C_{10}H_{14}O_3$ requires C, 65·9; H, 7·7%; 1 g. = 5·5 c.c. of *N*-NaOH). This acid we propose to represent by formula (V). On hydrogenation in presence of palladium catalyst 1 g. absorbed 228 c.c. of hydrogen (Calc. for $C_{10}H_{14}O_3 \longrightarrow C_{10}H_{18}O_3$, 246·2 c.c.), yielding an oily acid which readily furnished a semicarbazone, m. p. 140—143° after recrystallisation from alcohol (Found: C, 54·3; H, 8·5; N, 17·2. Calc. for $C_{11}H_{21}O_3N_3$: C, 54·3; H, 8·6; N, 17·3%). This substance is undoubtedly the semicarbazone of *dl*-ε-keto-β-*iso*propylheptoic acid (VI). This acid has been prepared from various sources: Wallach obtained it by the reduction of thujaketonic acid and prepared the semicarbazone, m. p. 140° (*Annalen*, 1911, **381**, 83). Higher melting points have been recorded for the semicarbazone, *e.g.* 158—159° in the case of acid prepared from carvotanacetone, but these always relate to the optically active acid as pointed out by Wallach (*ibid.*, 1917, **414**, 285).

The keto-lactone was very readily oxidised by a 2% aqueous solution of potassium permanganate at 0°, yielding a mixture of acids, smelling strongly of acetic acid, in which lævulic acid was identified by conversion into its semicarbazone, m. p. 188° (alone or mixed with an authentic specimen).

The keto-lactone was not readily attacked by Beckmann's mixture, but, after standing with an excess of this reagent at 60° for 2 days, 0·9 g. yielded 0·3 g. of unchanged material and 0·6 g. of an acid, which crystallised well from water, sublimed slightly at about 120°, and melted at 168° (Found: by micro-analysis, C, 53·8; H, 5·3; 1 g. required 6·35 c.c. of *N*-NaOH. Calc. for $C_7H_8O_4$: C, 53·85; H, 5·1%; 1 g. = 6·4 c.c. of *N*-NaOH). The barium salt, which was very soluble in water, was obtained crystalline by slow evaporation of its aqueous solution [Found: Ba, 29·6. Calc. for $(C_7H_7O_4)_2Ba$: Ba, 30·6%]. These characters are those of terebilic acid (VIII) (Roser, *Ber.*, 1882, **15**, 295), and confirmation of the identity was obtained by reduction of the acid to terebic acid (IX). When the acid in aqueous solution was shaken with palladium catalyst in an atmosphere of hydrogen, the equivalent of two atoms of hydrogen was absorbed (Found for 1 g., 150·3 c.c. Calc. for $C_7H_8O_4 \longrightarrow C_7H_{10}O_4$, 143·5 c.c. at *N.T.P.*), and thereafter, by extraction with ether, an acid was obtained which crystallised well from water; alone or mixed with authentic terebic acid, it melted at 174°, but the m. p. of a mixture with the acid $C_7H_8O_4$ was 155—160°.

The acid fraction from the original oxidation of terpinolene did not crystallise. Volatile acids were removed in three fractions by partial neutralisation and distillation with steam; each fractional distillate was neutralised with baryta and evaporated to dryness [Found: Ba, (i) 53·5, (ii) 53·8, (iii) 46·6. Calc. for barium acetate: Ba, 53·8%]. From the last fraction a little lævulic acid was isolated as the semicarbazone. The acid remaining in the flask was extracted with chloroform, and was oily. It reacted readily with semicarbazide solution, giving an 88% yield of lævulic acid semicarbazone, m. p. 188° (from water). It was also identified by the semicarbazone, m. p. 149°, of its methyl ester (Found: C, 44·7; H, 7·0; N, 22·6. Calc. for $C_7H_{13}O_3N_3$: C, 44·9; H, 6·9; N, 22·5%).

"*Origanene.*"—From 500 g. of the non-phenolic portion of Cyprus origanum oil, by repeated fractional distillation, finally over sodium, two hydrocarbon fractions, (*a*) b. p. 167—172° (38 g.) and (*b*) b. p. 172—186° (88 g.), were prepared. Fraction (*b*) yielded per c.c. 0·0138 g. of a crystalline nitrosite, m. p. 158° (alone or mixed with authentic α-terpinene nitrosite). On oxidation with Beckmann's chromic acid mixture, as described above, 25 c.c. of the same fraction yielded a small amount of neutral oil, which on treatment with an alcoholic solution of semicarbazide furnished 0·18 g. of a crystalline substance, m. p. 203° (alone or mixed with authentic dimethylacetonylacetone semicarbazone) (Found: C, 59·6; H, 8·5; N, 22·95. Calc. for $C_9H_{15}ON_3$: C, 59·7; H, 8·3; N, 23·2%).

A portion of the same fraction on appropriate treatment furnished per c.c. 0·0109 g. of a crystalline nitrosochloride, m. p. 101° (decomp.), falling to 98° after recrystallisation from chloroform by addition of methyl alcohol (compare Pickles, *loc. cit.*). From fraction (*a*) the same nitrosochloride was obtained in larger yield (0·0433 g. per c.c.) (Found: N, 7·2. Calc. for $C_{10}H_{16}ONCl$: N, 6·9%). On suspension in alcohol and treatment with piperidine, the nitrosochloride furnished a nitrolpiperidide, m. p. 198° after recrystallisation from hot alcohol.

The authors are indebted to Mr. E. M. Gibbs for much assistance in the experimental work and to Mr. A. Bennett for a number of microanalyses.

WELLCOME CHEMICAL RESEARCH LABORATORIES.

[*Received, November 27th,* 1930.]

PRINTED IN GREAT BRITAIN BY RICHARD CLAY & SONS, LIMITED,
BUNGAY, SUFFOLK.