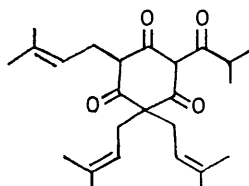


The Chemistry of Hop Constituents. Part XL.¹ Structure of a Five-membered-ring Oxidation Product of Colupulone

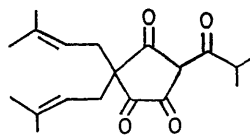
By (Mrs.) Jean Coates and Derek R. J. Laws, Brewing Industry Research Foundation, Nutfield, Surrey RH1 4HY
John A. Elvidge,* University of Surrey, Guildford GU2 5XH

Oxygen acts on colupulone in petroleum at 60° to give 5-hydroxy-5-isobutyryl-3,3-bis-(3-methylbut-2-enyl)-cyclopentane-1,2,4-trione, which we find present in old hops. Cohulupone is evidently an intermediate, but the new product appears not to be an intermediate in the oxidation of cohulupone to hulupinic acid.

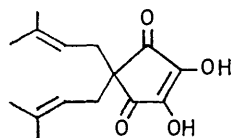
THE hop resin constituent colupulone (I) is rapidly oxidised in stored hops and when oxygen is passed through its solutions. Whilst there may be cyclisation of a side chain onto an oxygen substituent of the ring, loss of a side chain, and introduction of hydroxy-groups, the six-membered carbocyclic ring either persists or contracts to a five-membered ring. Products of the first type include benzodipyran,² dihydrobenzopyran,³ and dihydrobenzofurans.³ Ring-contraction products include cohulupone⁴ (II) and hulupinic acid⁵ (III) (both minor constituents of hop resin^{6,7}), and a cyclopentafuran and a cyclopentapyran.⁸



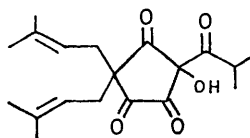
(I)



(II)



(III)



(IV)

We now describe the isolation and characterisation of a new oxidation product (IV), obtained by passing oxygen through a solution of colupulone (I) in light petroleum at 60°. It forms yellow prisms, has the composition C₁₉H₂₆O₅, and gives a u.v. spectrum like

¹ Part XXXIX, M. Collins and D. R. J. Laws, *J.C.S. Perkin I*, 1973, 2013.

² D. M. Cahill and P. V. R. Shannon, *J. Chem. Soc. (C)*, 1969, 938.

³ E. Byrne, D. M. Cahill, and P. V. R. Shannon, *J. Chem. Soc. (C)*, 1970, 1637.

⁴ D. Wright, *J. Chem. Soc.*, 1963, 1769.

⁵ J. S. Burton, R. Stevens, and J. A. Elvidge, *J. Chem. Soc.*, 1964, 952.

that of cohulupone⁴ (II) except that the maxima do not shift when alkali is added to the solution. Evidently the new product has a five-membered ring and a β-tricarbonyl system, similar to cohulupone, but is incapable of enolisation. In contrast to cohulupone, which shows enol hydroxy-absorption at 3450 cm⁻¹,¹⁰ the new product shows a reasonably sharp hydroxy-band at 3350 cm⁻¹. These observations suggest the structure (IV) in which enolisation is blocked by a hydroxy-group. Strong support comes from the ¹H n.m.r. spectrum. In the τ 9.0—5.0 region, the spectrum closely resembles that of cohulupone¹¹ (II) but at low field there is no sharp signal from a chelated enolic proton, only a very broad one-proton signal centred at τ 0.3. When the solution is shaken with water, separated, and re-examined, the last signal has moved upfield to τ 3.4 and is less broad, behaviour typical of a non-chelated hydroxy-group.

We conclude that the new oxidation product of colupulone (I) is 5-hydroxy-5-isobutyryl-3,3-bis-(3-methylbut-2-enyl)cyclopentane-1,2,4-trione (IV).

In agreement with this constitution, the compound is obtained from cohulupone (II) by oxygenation in petroleum. Although the yield is low, it is much higher than from colupulone (I), suggesting that in the oxidation of the latter to the new product (IV), cohulupone (II) is an intermediate. Attempts to oxidise the new product (IV) further to hulupinic acid (III), by oxygen in boiling ethanol,⁵ failed, compound (IV) being recovered (68%). Thus the new compound (IV) appears not to be an intermediate in the oxidation of cohulupone (II) to hulupinic acid (III) but is presumably a parallel oxidation product.

The new compound (IV) is present in old hops, as found by extraction, trimethylsilylation, and separation by g.l.c. The complex chromatogram shows a peak

⁶ R. Stevens and D. Wright, *J. Inst. Brewing*, 1961, 67, 496.

⁷ J. S. Burton and R. Stevens, *J. Inst. Brewing*, 1965, 71, 51.

⁸ R. Van den Bossche, M. Anteuinis, M. Vandewalle, and M. Verzele, *J.C.S. Perkin I*, 1972, 1599.

⁹ Cf. P. R. Ashurst and J. A. Elvidge, *J. Chem. Soc. (C)*, 1966, 675; B. E. Connett and J. A. Elvidge, *ibid.*, 1968, 1193.

¹⁰ L. O. Spetsig and M. Steninger, *J. Inst. Brewing*, 1960, 66, 413.

¹¹ S. Forsen, M. Nilsson, J. A. Elvidge, J. S. Burton, and R. Stevens, *Acta Chem. Scand.*, 1964, 18, 513.

identical in retention time with that from the authentic trimethylsilyl derivative of compound (IV). Furthermore, separation of ethereal hop extract on a t.l.c. plate, elution of the appropriate zone, trimethylsilylation, and then g.l.c. separation, gives (apart from the solvent peak) a strong peak in the chromatogram, with the retention time for the derivative of compound (IV). This peak is enhanced by the prior addition of compound (IV) to the hop extract.

Having a somewhat bitter taste, the new compound possibly contributes to the bittering properties of hops.

EXPERIMENTAL

U.v. and i.r. spectra were measured with a Pye-Unicam SP 1800 and a Perkin-Elmer 157G spectrophotometer, respectively. ^1H N.m.r. spectra were recorded with a Perkin-Elmer R10 (60 MHz) spectrometer.

Oxidation of Colupulone.—Colupulone (I) (15 g) was suspended in light petroleum (800 ml; b.p. 60–80°) and placed in a jacketed tube (4 × 100 cm). The mixture was maintained at 60° by circulating water through the jacket while oxygen (6 l h⁻¹) was passed through the petroleum solution for 18 h. The mixture was cooled to 20° then filtered, and the filtrate was evaporated to leave a yellow oil (12.2 g). A portion of this oil (2.0 g) was chromatographed on a column of silicic acid (60 × 2.5 cm), and was eluted with hexane-ether (400 ml; 9 : 1) followed by hexane-ether (200 ml; 6 : 1); 50 ml fractions were collected. Fractions 8–10 gave a pale yellow oil (0.9 g) which crystallised at 0°. The yellow crystals were washed with light petroleum (b.p. 40–60°) and dried to give 5-hydroxy-5-isobutyryl-3,3-bis-(3-methylbut-2-enyl)cyclopentane-1,2,4-trione (IV) (40 mg), m.p. 107° (Found: C, 68.0; H, 7.7. C₁₉H₂₆O₅ requires C, 68.3; H, 7.8%), λ_{max} (acidic EtOH) 12 255 and 325 nm (ϵ 9160 and 6130), λ_{max} (alkaline EtOH) 12 253 and 324 nm (ϵ 12,660 and 8900), ν_{max} (Nujol) 3350 (OH), 2980 and 2940 (CH), 1755, 1710, 1695, and 1670 (CO), 1460s, 1380s, 1325w, 1270w, 1150w, 1115w, 1095w, 1080, 970w, and 850 cm⁻¹, τ (CDCl₃) 8.89 (d, J 6.7 Hz, Me₂ of acyl group), 8.44 (s, 2 × Me₂ of alkyl

¹² J. A. Elvidge and D. R. J. Laws, *J. Chem. Soc. (C)*, 1968, 1193.

groups), 7.59 (d, J 8 Hz, 2 × CH₂), 6.31 (septet, J 6.7 Hz, CH of acyl group), 5.17 (ca. t, 2 × CH= of alkyl groups), and 0.3 (1.8 p.p.m. broad, OH).

Oxidation of Cohulupone.—Freshly distilled cohulupone (200 mg) in light petroleum (10 ml; b.p. 60–80°) was oxidised as for colupulone. Evaporation of the solution left a pale yellow oil, which at 0° afforded yellow prisms of compound (IV) (15 mg), m.p. and mixed m.p. 107°.

Detection of Compound (IV) in Old Hops.—Northern Brewer hops (100 g) from 1965 growth were extracted with ether (4 l) for 18 h, and the extract was concentrated (to 500 ml), treated with charcoal (5 g), and filtered. A portion (0.25 ml) was streaked onto a t.l.c. plate (20 × 20 cm) coated with Kieselgel H (0.2 mm thick), and compound (IV) was used as a marker. After development with benzene-ether (16 : 1) the chromatogram was allowed to dry, and the marker chromatogram (only) was sprayed with 1% iron(III) chloride in methanol to reveal, as a yellow spot (R_F 0.8), the position of compound (IV). The corresponding zone in the hop-extract chromatogram was removed from the plate, eluted with methanol (20 ml) for 2 h; the extract was filtered and dried (MgSO₄). The combined extract from six plates was evaporated, and the residue shaken with *NO*-bis-(trimethylsilyl)acetamide (100 μ l) for 1 h. A portion (1 μ l) was then chromatographed in nitrogen (46 ml min⁻¹) on a column (9 ft × 0.25 in) packed with 3% methyl silicone gum on Diatomite CQ (100–120 mesh) (temperature programme 100–300° at 30° min⁻¹; flame ionisation detector). The chromatogram showed a peak with the same retention time (487 s) as the trimethylsilyl derivative of compound (IV). The former peak was appropriately enhanced when compound (IV) was added to the original ethereal hop extract and the procedure repeated.

A portion of the ethereal hop extract was treated with *NO*-bis-(trimethylsilyl)acetamide and the mixture was examined by g.l.c. as before. In the complex chromatogram there was a small peak with the same retention time (487 s) as the authentic trimethylsilyl derivative of compound (IV).

We thank Dr. C. E. Dalglish for his interest.

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