329. *The Chemistry of Hop Constituents. Part XV.*[1] *Tetrahydrocohulupone.*

By R. Stevens and D. Wright.

Colupulone has been converted by two routes into 3-isobutyryl-5,5-di-isopentylcyclopentane-1,2,4-trione which has light absorption and other properties in agreement with its being tetrahydrocohulupone and thus confirms the structure (II) assigned to the hulupones.

Considerable oxidation of the principal resins of the hop cone (*Humulus lupulus* L.) occurs during storage before the hops are used for brewing. The lupulones (I; R' = $CH_2{\cdot}CH{:}CMe_2$) are oxidized more rapidly than the humulones[2] (I; R' = OH) (each of these groups of resins consists of the parent compound, R = Bu^i, together with analogues including those distinguished by the prefixes co-, R = Pr^i, and ad-, R = Bu^s). No general picture of these oxidative changes has yet emerged but application of reversed-phase chromatography to hop resins yielded a mixture of compounds called hulupones.[3] This consisted of three analogues for which, mainly on the basis of mass spectrometry,

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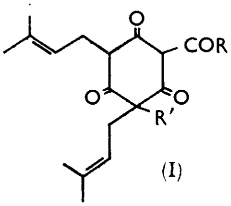
[1] Part XIV, Brown and Howard, *J.*, 1960, 164.

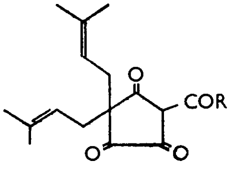
[2] See, *e.g.*, Owades, Gimbel, and Schwartz, *Amer. Brewer*, 1958, Nov., 49.

[3] Spetsig, Steninger, and Brohult, Proc. Eur. Brewing Conv., Copenhagen, 1957, Elsevier, p. 22.

the structure (II) was proposed.[4] The work described in this paper, of which a preliminary report has already appeared,[5] relates the lupulones and their oxidation products to the hulupones.



(I)



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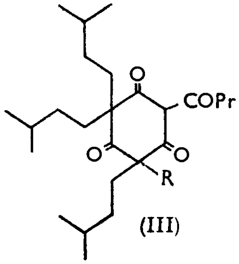

(III)

Initial experience, some of which is discussed more fully in the following paper,[6] demonstrated that the autoxidation of colupulone was complex. Attention was therefore directed to the oxidation of hexahydrocolupulone (III; R = H) to avoid the possible complicating effect of the dimethylallyl side chains. When a solution of this substance in cyclohexane was shaken in oxygen, 1 mol. was slowly absorbed, giving a hydroperoxide; this is formulated as (III; R = O·OH) in agreement with experience on the introduction of hydroperoxy-groups [7] and because attack at the carbon atom carrying the acyl group, the only other possible position, can be excluded since none of the subsequent degradation products resembles either lupuloxinic acid or lupulenol.[8] Light-absorption properties of the hydroperoxide both in the ultraviolet ($\lambda_{\max.}$ 240, 280 mμ in ethanol, $\lambda_{\max.}$ 280 mμ in alkaline ethanol) and in the infrared region ($\nu_{\max.}$ 1727, 1669, and 1550 cm.$^{-1}$) are reminiscent of leptospermone [9] (6-isovaleryl-2,2,4,4-tetramethylcyclohexane-1,3,5-trione) and other tetrasubstituted acyl phloroglucinols,[10] in support of the assigned structure. Hydrogenation reduced the hydroperoxide (III; R = O·OH) but the product retained similar light-absorption properties in neutral solution and is accordingly formulated as 2-hydroxy-6-isobutyryl-2,4,4-tri-isopentylcyclohexane-1,3,5-trione (III; R = OH). This compound, which may be regarded as a tetrahydroisopentylcohumulone, failed to give an insoluble lead salt with methanolic lead acetate but was rearranged in an analogous manner to humulone on distillation or treatment with mild alkali, giving the isomerized product (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe_2$). This compound, which was readily isolated as its insoluble sodium salt, had light absorption reminiscent of oxyhumulinic acid, in agreement with the assigned structure.

Prolonged alkaline hydrolysis of the sodium salt of the product (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe_2$) afforded γ-methylvaleric acid and the analogue (IV; R = H) of humulinic acid; the latter had similar light absorption to the unhydrolysed product. Attempts to prepare crystalline derivatives of the last product (IV; R = H) were unsuccessful but on oxidation with bismuth oxide [11a] it gave 5-isobutyryl-3,3-di-isopentylcyclopentane-1,2,4-trione (V). This had ultraviolet-light absorption in alkaline solution and infrared absorption between 2·5 and 7·0 μ in complete agreement with those published for hulupone [4] and is therefore tetrahydrocohulupone, substantiating the structure proposed for the hulupones.

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[4] (*a*) Brohult, Ryhage, Spetsig, and Stenhagen, Proc. Eur. Brewing Conv., Rome, 1959, Elsevier, p. 121; (*b*) Spetsig and Steninger, *J. Inst. Brewing*, 1960, **65**, 413.

[5] Stevens and Wright, *Proc. Chem. Soc.*, 1960, 417.

[6] Wright, following paper.

[7] (*a*) Waters, *Ann. Reports*, 1954, **51**, 132; (*b*) Davies, "Organic Peroxides," Butterworths Scientific Publns., London, 1961, p. 22.

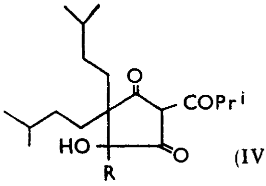
[8] (*a*) Howard and Pollock, *J.*, 1952, 1902; (*b*) Howard, Pollock, and Tatchell, *J.*, 1955, 174.

[9] (*a*) Briggs, Hassall, and Short, *J.*, 1945, 706; (*b*) Chan and Hassall, *J.*, 1956, 3495.

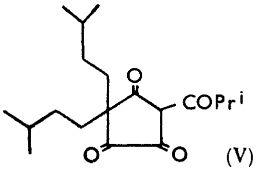
[10] Riedl, Nickl, Risse, and Mitteldorf, *Chem. Ber.*, 1956, **89**, 1849.

[11] Howard and Slater, *J.*, (*a*) 1957, 1924, (*b*) 1958, 1460.

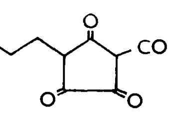
The trione (V) was characterized further by the preparation of an insoluble sodium salt, which, even after drying in a high vacuum at 110° for several hours, retained half a molecule of water. In this connection it may be recalled that both calythrone (2-isovaleryl-4,5-dimethylcyclopent-4-ene-1,3-dione) and valone (2-isovalerylindane-1,3-dione) form sodium salts which tenaciously retain a molecule of water,[12] in contrast to the sodium salts of humulinone [13] and the analogue (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe_2$) which are not hydrated. With *o*-phenylenediamine the triketone (V) only gave an oil but with 2,3-diaminonaphthalene a quinoxaline was formed. Oxidation of the triketone (V) by alkaline hydrogen peroxide afforded ultimately di-isopentylmalonic and isobutyric acid, in agreement with the assigned structure. An intermediate product was also isolated which, by analogy with the oxidation of isohumulinic acid (VI),[14] might have been the deacylated triketone (VII) but analyses and the ultraviolet-light absorption were not in agreement with this, so that its structure remains unknown.



(IV)



(V)

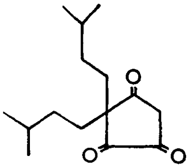


(VI)

As would be expected from analogy with the isohumulone series,[15] the analogue (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe_2$) was oxidised directly to tetrahydrocohulupone (V) in 18% yield, but the structure of the major product of this reaction remains unknown.

Thermal decomposition of the hydroperoxide (III; R = O·OH) gave tetrahydrocohulupone directly, and this route may be related to the mechanism of the formation of hulupones in the hop cone.

Attempts to synthesize tetrahydrohulupone by alkylation of isohumulinic acid (VI) with isopentyl bromide, in an analogous manner to the preparation of hulupone reported in the following paper,[6] have so far been unsuccessful. Under more vigorous conditions the acyl side chain of the isohumulinic acid was removed.[14]



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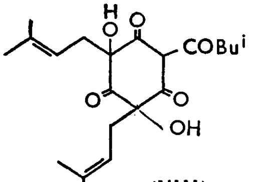
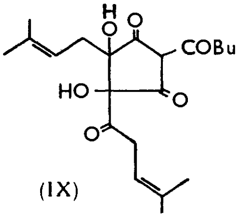


(VIII)



(IX)

In a preliminary communication,[5] the reduction product of hexahydrohydroxycolupulone (III; R = OH) and its isomerized product (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe_2$) were termed hexahydrocolupulinone and hexahydroisocolupulinone, respectively, by analogy with humulinone for which the structure (VIII) had been advanced.[16] These names are now inappropriate as the alternative structure (IX) for humulinone has been established by nuclear magnetic resonance measurements [17] and is in agreement with light-absorption data. If humulinone had the structure (VIII) its light absorption should resemble that of (III; R = OH) and other tetrasubstituted phloroglucinols, whereas it

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[12] Birch, *J.*, 1951, 3026.
[13] Cook and Harris, *J.*, 1950, 1873.
[14] Harris, Howard, and Pollock, *J.*, 1952, 1906.
[15] Brown, Howard, and Tatchell, *J.*, 1959, 545.
[16] Cook, Howard, and Slater, *J. Inst. Brewing*, 1955, **61**, 321.
[17] Shoolery, Verzele, and Alderweireldt, *Tetrahedron*, 1960, **9**, 271.

resembles much more closely that of isohumulone, humulinic acid, and oxyhumulinic acid, compounds in which the five-membered ring is well established.[18]

Additional evidence for the structure of humulinone as (IX) comes from hydrogenation studies. In the presence of palladium chloride, hydrogenolysis of both humulone and lupulone leads to the elimination of an isopentenyl side chain,[19] and, on the basis of the structure (VIII), a similar cleavage would be expected in humulinone. However, under the same conditions humulinone affords only the corresponding tetrahydro-derivative. The fact that humulinone has been isolated in all cases as its insoluble sodium salt after the treatment with mild alkali and the ease with which the hydroxide (III; R = OH) is converted into compound (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe_2$) by similar treatment suggests that structure (VIII) cannot be excluded as an intermediate in the oxidation of humulone to humulinone and that this compound may thus be present in old hops.

EXPERIMENTAL

Hexahydrocolupulone (III; R = H) was prepared from colupulone (from Pacific Coast lupulin; E Clemens Horst Co., San Francisco) by Riedl and Nickl's method.[20] It had m. p. 139—140° and $\nu_{max.}$ (in Nujol) 1653 and 1587 cm.$^{-1}$ similar to that reported for (co)lupulone.[8a]

Autoxidation of Hexahydrocolupulone.—Hexahydrocolupulone (0·86 g.), suspended in cyclohexane (50 ml.), was shaken in oxygen until the resin had dissolved and 1 mol. of gas had been absorbed (1—2 days). At this time the mixture had negligible light absorption at 340 mμ. Removal of the solvent by rotary evaporation in a vacuum afforded the *hydroperoxide* (III; R = O·OH) as a colourless oil which liberated iodine from an acidified solution of potassum iodide (Found: hydroperoxide, 6·3. $C_{25}H_{41}O_4{\cdot}O{\cdot}OH$ requires O·OH, 7·5%) and had $\lambda_{max.}$ 245 ($E_{1\,cm.}^{1\%}$ 182) and 280 mμ ($E_{1\,cm.}^{1\%}$ 214) in ethanol, and $\lambda_{min.}$ 235 ($E_{1\,cm.}^{1\%}$ 165) and $\lambda_{max.}$ 278 mμ ($E_{1\,cm.}^{1\%}$ 282) in alkaline ethanol, and $\nu_{max.}$ 3448 (OH), 1727 (unconjugated C=O), 1669 (conjugated C=O), 1550 (chelated C=O) cm.$^{-1}$. Chan and Hassall [9b] report for leptospermone $\lambda_{max.}$ 279 mμ, $\nu_{max.}$ 1715, 1660, 1550 cm.$^{-1}$.

Attempts to prepare a crystalline derivative from the hydroperoxide with 2-ethoxy-1,2-dihydro-1-methyl-6,8-dinitroquinoline were unsuccessful.[21]

2-*Hydroxy*-6-*isobutyryl*-2,4,4-*tri-isopentylcyclohexane*-1,3,5-*trione*.—The hydroperoxide (0·9 g.) in methanol (40 ml.) was hydrogenated in the presence of 5% palladium–charcoal (175 mg.) at atmospheric pressure, hydrogen absorption (0·9 mol.) being complete in 20 min. After removal of the catalyst and solvent the *hydroxide* (III; R = OH) remained as an oil which failed to liberate iodine from an acidified solution of potassium iodide. It had $\lambda_{max.}$ 245 ($E_{1\,cm.}^{1\%}$ 179), 280 ($E_{1\,cm.}^{1\%}$ 252) in ethanol and $\lambda_{max.}$ 255 ($E_{1\,cm.}^{1\%}$ 329) and 270 sh ($E_{1\,cm.}^{1\%}$ 291) mμ in alkaline ethanol, and $\nu_{max.}$ (as a film) 3448, 1725, 1670, and 1550 cm.$^{-1}$.

The hydroxide (III; R = OH) failed to give a precipitate with 4% methanolic lead acetate but with cupric acetate gave an amorphous copper salt which was soluble in most organic solvents including light petroleum. In the usual conditions it failed to give a crystalline phenylurethane.

4-*Hydroxy*-2-*isobutyryl*-4-*γ-methylvaleryl*-5,5-*di-isopentylcyclopentane*-1,3-*dione* (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe_2$).—(i) Distillation of the hydroxide (III; R = OH), b. p. 130—140° (bath)/10^{-3} mm., afforded the isomerized *compound* (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe_2$) (Found: C, 71·3; H, 9·9. $C_{25}H_{42}O_5$ requires C, 71·1; H, 9·9%), $\lambda_{max.}$ 250 ($E_{1\,cm.}^{1\%}$ 176), 280 ($E_{1\,cm.}^{1\%}$ 239) in ethanol, $\lambda_{max.}$ 255 ($E_{1\,cm.}^{1\%}$ 375), 270 sh ($E_{1\,cm.}^{1\%}$ 286) mμ in alkaline ethanol, $\nu_{max.}$ 3534, 1701, 1631, and 1585 cm.$^{-1}$. (ii) The hydroxide (III; R = OH) (3·35 g.) was stirred with N-sodium hydroxide (80 ml.), to give a sticky *sodium salt* which was washed with water and after recrystallization from ethanol–hexane had m. p. 240° (Found: C, 67·6; H, 9·6. $C_{25}H_{41}O_5Na$ requires C, 67·6; H, 9·3%), $\lambda_{max.}$ 250 ($E_{1\,cm.}^{1\%}$ 322) and 275 ($E_{1\,cm.}^{1\%}$ 307) mμ, $\nu_{max.}$ (in Nujol) 3333 (OH), 1715 (unconjugated C=O), 1669 (conjugated C=O), 1626 (conjugated C=C), and 1558 (chelated C=O) cm.$^{-1}$. The

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[18] Alderweireldt and Verzele, *Bull. Soc. chim. belges*, 1957, **66**, 391.

[19] (*a*) Wollmer, *Ber.*, 1916, **49**, 780; 1925, **58**, 672; (*b*) Wieland, *Ber.*, 1925, **58**, 102.

[20] Riedl and Nickl, *Chem. Ber.*, 1956, **89**, 1863.

[21] Rieche, Schmitz, and Dietrich, *Chem. Ber.*, 1959, **92**, 2239.

free acid was regenerated by shaking the sodium salt with 2N-sulphuric acid and light petroleum. The organic layer was washed with water, dried, and evaporated in a vacuum, to give the compound (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CHMe_2$), with the above absorption. The infrared spectrum could be superimposed upon that of the distilled product. The product did not crystallize and gave a copper salt soluble in all the usual organic solvents including light petroleum.

4-Hydroxy-2-isobutyryl-5,5-di-isopentylcyclopentane-1,3-dione (IV; R = H).—The sodium salt of the ketone (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CMe_2$) (201 mg.) was heated under reflux with 2N-sodium hydroxide (3 ml.) and ethanol (3 ml.) for 5 hr. After removal of the ethanol, the solution was extracted 4 times with ether and ethereal extracts were dried and evaporated to give the sodium salt of compound (IV; R = H) (150 mg.) which did not crystallize. The free *compound* had b. p. 180° (bath)/10^{-3} mm. (Found: C, 70·8; H, 10·1. $C_{19}H_{32}O_4$ requires C, 70·4; H, 9·9%), $\lambda_{\text{max.}}$ 265 ($E_{1\,\text{cm.}}^{1\%}$ 324), $\lambda_{\text{min.}}$ 240 mμ in ethanol, $\lambda_{\text{max.}}$ 255 ($E_{1\,\text{cm.}}^{1\%}$ 595), 265 infl. ($E_{1\,\text{cm.}}^{1\%}$ 500) mμ in alkaline ethanol, $\nu_{\text{max.}}$ (film) 3472, 1700, 1620, and 1580 cm.^{-1}. This material failed to yield a crystalline oxime or dichloroanil.

The residue from the hydrolysis, after extraction with ether, was acidified and distilled in steam to give γ-methylvaleric acid in 85% yield, identified as 4-bromophenacyl ester that after chromatography on silica gel,[22] elution with 1 : 9 ether–light petroleum (b. p. 40—60°), and recrystallization had m. p. and mixed m. p. 75—76°.

5-Isobutyryl-3,3-di-isopentylcyclopentane-1,2,4-trione (*Tetrahydrocohulupone*) (V).—(i) The sodium salt of compound (IV; R = H) (250 mg.) was heated under reflux with bismuth oxide (500 mg.) and glacial acetic acid (4 ml.) for 5 hr., cooled, diluted with 2N-hydrochloric acid, and extracted with ether. The extract was washed, dried ($MgSO_4$), and evaporated to give *tetrahydrocohulupone* (V), b. p. 90—100° (bath)/10^{-4} mm., n_D^{18} 1·4902 (70%) (Found: C, 71·0; H, 9·6. $C_{19}H_{30}O_4$ requires C, 70·8; H, 9·3%), $\lambda_{\text{max.}}$ 285 ($E_{1\,\text{cm.}}^{1\%}$ 282) in acidified ethanol, $\lambda_{\text{max.}}$ 255 ($E_{1\,\text{cm.}}^{1\%}$ 488), 325 ($E_{1\,\text{cm.}}^{1\%}$ 336) mμ in alkaline ethanol, $\nu_{\text{max.}}$ (film) 1755, 1710, 1650, and 1585 cm.^{-1}. Spetsig and Steninger [4] report that hulupone has $\lambda_{\text{max.}}$ 255 ($E_{1\,\text{cm.}}^{1\%}$ 410), 325 ($E_{1\,\text{cm.}}^{1\%}$ 280) mμ in alkaline methanol and give infrared absorption spectra for hulupone in the region 2—10 μ identical with that found for tetrahydrocohulupone. When a solution of tetrahydrocohulupone in light petroleum was triturated with saturated aqueous sodium hydrogen carbonate a pale yellow *sodium salt*, m. p. 227°, was obtained. This salt, which was only slightly soluble in water, fairly soluble in ether, and readily soluble in ethanol and chloroform, crystallized from ethanol–hexane with 0·5 mol. of water and had m. p. 228° (Found: C, 64·8, 64·7; H, 8·9, 8·4. $C_{19}H_{29}NaO_4,0{\cdot}5H_2O$ requires C, 64·5; H, 8·5%), $\lambda_{\text{max.}}$ 255 ($E_{1\,\text{cm.}}^{1\%}$ 349), 325 ($E_{1\,\text{cm.}}^{1\%}$ 263), $\lambda_{\text{min.}}$ 280 mμ in ethanol, $\lambda_{\text{max.}}$ 285 and $\lambda_{\text{min.}}$ 240 mμ in acidified ethanol, and $\nu_{\text{max.}}$ (in KBr) 1740, 1680, 1620, and 1570 cm.^{-1}. Tetrahydrocohulupone gave an orange colour with ethanolic ferric chloride, but no crystalline derivative with phenylhydrazine. During conductometric titration of tetrahydrocohulupone with 4% methanolic lead acetate a point of minimum conductance corresponding to the formation of $(C_{19}H_{29}O_4)_2Pb$ was observed although no precipitate was formed.

Tetrahydrocohulupone (100 mg.) and 2,3-diaminonaphthalene (55 mg., 1·1 mol.) were heated in ethanol (0·6 ml.) and acetic acid (0·3 ml.) on the steam-bath for 1 hr., diluted with water, and extracted with ether. After removal of the solvent, the residue was chromatographed on silica gel (15 g.). The *quinoxaline* was eluted with 1 : 9 ether–light petroleum and formed orange prisms, m. p. 148—150° (42 mg.), from methanol (Found: C, 77·8; H, 7·9; N, 6·5. $C_{29}H_{36}N_2O_2$ requires C, 78·5; H, 8·1, N, 6·3%).

(ii) 4-Hydroxy-2-isobutyryl-4-γ-methylvaleryl-5,5-di-isopentylcyclopentane-1,3-dione (IV; R = $CO{\cdot}CH_2{\cdot}CH_2{\cdot}CMe_2$) (1·31 g.) was heated under reflux for 24 hr. in acetic acid (25 ml.) with bismuth oxide (2·59 g.). The solution did not blacken but on dilution with 2N-hydrochloric acid, extraction in ether, and distillation afforded fractions, (i) b. p. 90—110° (bath)/5 × 10^{-4} mm. (178 mg., 18%), having infrared absorption identical with that of tetrahydrocohulupone, and (ii) b. p. 110—180° (bath)/5 × 10^{-4} mm. (1·63 g.), $\lambda_{\text{max.}}$ 230 ($E_{1\,\text{cm.}}^{1\%}$ 216) and 300 ($E_{1\,\text{cm.}}^{1\%}$ 197), $\lambda_{\text{min.}}$ 265 ($E_{1\,\text{cm.}}^{1\%}$ 106), in ethanol, $\lambda_{\text{max.}}$ 250, ($E_{1\,\text{cm.}}^{1\%}$ 272) and 325 ($E_{1\,\text{cm.}}^{1\%}$ 181) $\lambda_{\text{min.}}$ 290 ($E_{1\,\text{cm.}}^{1\%}$ 142) in alkaline ethanol, $\nu_{\text{max.}}$ (film) 1754, 1706, 1647, 1618, and 1585 cm.^{-1} (Found: C, 73·4, 73·2; H, 10·0, 9·95%).

Degradation of Tetrahydrocohulupone.—(i) The sodium salt of tetrahydrocohulupone was set aside in a mixture of 30% hydrogen peroxide (1 ml.) and water (3 ml.). After 2 days

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[22] Wright and Howard, *J. Inst. Brewing*, 1961, **67**, 236.

2N-sodium hydroxide (1 ml.) was added which brought the suspended matter into solution, and after addition of more hydrogen peroxide (2 ml.) the mixture was left for a further 18 hr. Acidification then afforded di-isopentylmalonic acid, m. p. 149° (decomp.) (57 mg., 92%), m. p. 159° (from benzene–hexane) (Found: C, 63·8; H, 9·4. Calc. for $C_{13}H_{24}O_4$: C, 63·9; H, 9·85%). On admixture with a synthetic sample, m. p. 152—154° (lit.,[23] m. p. 147—148°, 152·5—154°), the m. p. was 155—157°. The infrared spectra of the two samples were identical.

The remaining acidic filtrate was extracted with light petroleum, the extract was shaken with 0·1N-sodium hydroxide (1·1 ml.), and the sodium salt was converted into the 4-bromophenacyl ester which, after chromatography on silica gel and recrystallization from aqueous methanol, had m. p. 72° undepressed on admixture with authentic 4-bromophenacyl isobutyrate (m. p. 74—75°) but depressed to m. p. 58° on admixture with 4-bromophenacyl γ-methylvalerate (m. p. 75—76°).

Thermal Decomposition of the Hydroperoxide (III; R = O·OH).—The crude hydroperoxide (400 mg.) was heated slowly at 10^{-4} mm. to 100° and held at that temperature for 2 hr.; a pale yellow oil (171 mg.) distilled. The product was triturated with a saturated solution of sodium hydrogen carbonate, giving the pale yellow sodium salt of tetrahydrocohulupone (74 mg.), m. p. and mixed m. p. 228° (from ethanol–hexane), $\lambda_{\text{max.}}$ 255 ($E^{1\%}_{1\,\text{cm.}}$ 360) and 325 ($E^{1\%}_{1\,\text{cm.}}$ 271) mμ.

Attempted Synthesis of Tetrahydrocohulupone.—(i) In attempts to alkylate isohumulinic acid with isopentyl bromide (cf. ref. 6) starting material was recovered. (ii) Isohumulinic acid (500 mg.) was heated with a solution from potassium (158 mg.) in methanol (5 ml.) for 30 min. Isopentyl iodide (0·6 ml.) was added and the heating continued overnight. The mixture was then diluted, acidified, and extracted with ether, and the extract distilled, having b. p. 90—100° (bath)/10^{-4} mm. Part of the distillate crystallized and after recrystallization from light petroleum gave 3-isopentylcyclopentane-1,2,4-trione, m. p. 93—95° (Found: C, 65·7; H, 7·8. Calc. for $C_{10}H_{14}O_3$: C, 66·0; H, 7·7%), $\lambda_{\text{max.}}$ 275 (ε 11,047) mμ in ethanol and 330 (ε 11,157), 235 sh (ε 11,921) mμ in alkaline ethanol. Harris, Howard, and Pollock[14] report m. p. 102° and similar $\lambda_{\text{max.}}$.

Hydrogenolysis of Humulinone.—Humulinone (652 mg.) in methanol (20 ml.) was shaken in hydrogen in the presence of palladium chloride (40 mg.) in water (2 ml.): hydrogen absorption (85 ml. 2 Mol. = 83 ml.) was complete in 6 hr. After removal of catalyst and solvent the residue was set aside in ether overnight in contact with a saturated solution of sodium hydrogen carbonate. The sodium salt of tetrahydrohumulinone recovered by filtration was washed with ether and dried and had m. p. 209—211° (Found: C, 61·9; H, 8·1. $C_{21}H_{31}NaO_6$ requires C, 62·1; H, 8·2%), $\lambda_{\text{max.}}$ 260 ($E^{1\%}_{1\,\text{cm.}}$ 420) and 275 sh ($E^{1\%}_{1\,\text{cm.}}$ 382) mμ. Cook and Harris[13] report $\lambda_{\text{max.}}$ 259 ($E^{1\%}_{1\,\text{cm.}}$ 500) for the sodium salt of humulinone. Tetrahydrohumulinone had m. p. 79—83° but could not be recrystallized (cf. tetrahydrocohumulinone[11b]); it had $\lambda_{\text{max.}}$ 230 ($E^{1\%}_{1\,\text{cm.}}$ 251) and 277·5 ($E^{1\%}_{1\,\text{cm.}}$ 280) in ethanol, 255 ($E^{1\%}_{1\,\text{cm.}}$ 482) and 270 sh ($E^{1\%}_{1\,\text{cm.}}$ 442) mμ in alkaline ethanol, and $\nu_{\text{max.}}$ (in Nujol) 3500, 1710, 1650, and 1590 cm.$^{-1}$ in agreement with data for humulinone.[13, 16, 18]

The authors thank Dr. A. H. Cook, F.R.S., and Dr. G. Harris for their interest and encouragement and Dr. A. G. Davies for a sample of 2-ethoxy-1,2-dihydro-1-methyl-6,8-dinitroquinoline.

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[*Received, September* 14*th*, 1962.]

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[23] (*a*) Fournier, *Compt. rend.*, 1899, **128**, 1288; (*b*) Asano, Kameda, and Wada, *J. Pharm. Soc. Japan*, 1943, **63**, 540.