cis- and *trans*-Tetrahydroisohumulones

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Repeated acylation of phloroglucinol followed by intermediate reduction gave 4-deoxytetrahydrohumulone (VI), which was, by procedures of known type, converted into a mixture of (±)-*cis*- and (±)-*trans*-tetrahydroisohumulones [racemates of (XIX) and (XX) respectively]. The isomers were separated by chromatography and differentiated by their u.v. and 220 MHz n.m.r. spectra.

Several by-products were isolated and identified in the synthesis, including isobutyl 2',3,4',5,6'-pentahydroxybiphenyl-4-yl ketone (X) and 3,4-dihydroxy-2-isopentyl-4-(4-methylvaleryl)cyclopent-2-en-1-one (XVI).

Hydrogenation of a mixture of *cis*- (III) and *trans*- (IV) isohumulones obtained from (−)-humulone (II) gave, after separation, (−)-*cis*- (XIX) and (+)-*trans*- (XX) tetrahydroisohumulones, which, apart from their optical activities, were spectroscopically identical with the synthetic specimens.

THE structure (I) of isohumulone, the principal bittering substance of beer, obtained by the isomerisation of humulone (II),† was first proposed by Wieland [2] in 1925 and (I) was subsequently (1927) isolated by Windisch, Kolbach, and Schleicher.[3] Indications were later found [4] that both the isohumulone in beer and that obtained by direct isomerisation of humulone, were heterogeneous and in 1964 Spetsig first succeeded in separating [5] (I) into the (—)-*cis*- (III) and (+)-*trans*- (IV) forms, whose existence and relative proportions (40% *cis*, 60% *trans*) had been predicted [6] (*cf*. ref. 7) by n.m.r. analysis of the mixture. It was claimed [5] that a difference in bittering power of the two isomers existed. Slight differences in the u.v. spectra were recorded and the expected [6] differences in the chemical shifts and in the spin–spin splittings of the 5-protons were observed when a subsequent [7] separation of (III) and (IV) was achieved by counter-current distribution.

If the proposed configuration of natural (—)-humulone (II), and its stereospecific [8] rearrangement to the isohumulones are assumed, the structural formulae for (—)-*cis*- and (+)-*trans*-isohumulones would be expected to differ at the centre of chirality introduced at C-5.[9] When the rearrangement occurs in the presence of deuterium oxide, deuterium is introduced into the 5-position.[6] The configuration of the chiral centre at C-4 must be the same in both isomers, but if the (—)-humulone rearrangement is not completely stereospecific, but stereoselective, then some diastereoisomeric forms of (III) and (IV), epimeric at C-4, would be produced.

Models show that the 4β-hydroxy-configuration would be expected to result from a possible conformer (A) (see Scheme) of humulone (II) in which hydrogen-bonding occurred between the 4-hydroxy-group and the 3-oxygen atom (*cf*. ref. 8). However, in the absence of this hydrogen-bonding, the conformer (B) with an equatorial 4-isopentenyl group would be expected to give the opposite configuration at C-4 in the isohumulone.

The related tetrahydroisohumulones have also received

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† The D-configuration for natural (—)-humulone is assumed.[1]

[1] G. A. Howard, *Chem. and Ind.*, 1956, 1504.

[2] H. Wieland, *Ber.*, 1925, **58**, 2012.

[3] W. Windisch, P. Kolbach, and R. Schleicher, *Wochschr. Brau.*, 1927, **44**, 453.

[4] G. A. Howard, C. A. Slater, and A. R. Tatchell, *J. Inst. Brewing*, 1957, **63**, 237.

[5] L. O. Spetsig, *J. Inst. Brewing*, 1964, **70**, 440.

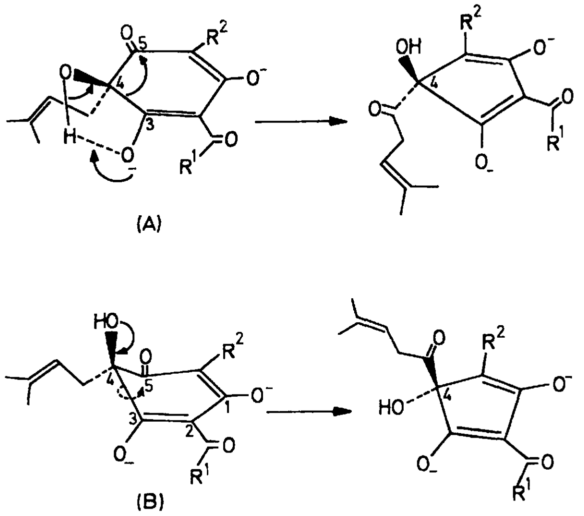
[6] J. S. Burton, R. Stevens, and J. A. Elvidge, *J. Inst. Brewing*, 1964, **70**, 345.

[7] F. Alderweireldt, M. Verzele, M. Anteunis, and J. Dierckens, *Bull. Soc. chim. belges*, 1965, **74**, 29.

[8] M. Anteunis and M. Verzele, *Bull. Soc. chim. belges.*, 1959, **68**, 102.

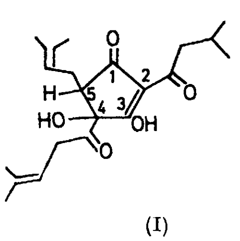
[9] B. J. Clarke and R. P. Hildebrand, *J. Inst. Brewing.*, 1965, **71**, 26.

considerable attention, but their differentiation and separation have so far not been achieved. Verzele and Govaert[10] reported a tetrahydroisohumulone, m.p. 43°, prepared by hydrogenation of impure isohumulone (I), and Brown, Howard, and Tatchell[11] obtained a tetrahydroisohumulone, m.p. 32—34°, by hydrogenation of an isohumulone preparation later shown[5] to be a mixture of (III) and (IV). The latter authors also described material, m.p. 49—53°, derived by isomerisation of tetrahydrohumulone (V) which had been obtained by oxidation of the optically inactive 4-deoxytetrahydrohumulone (VI), itself prepared by hydrogenolysis[12] of lupulone (VII). This sample of tetrahydroisohumulone showed, however, some optical activity—presumably because the starting material contained some optically active contaminants.

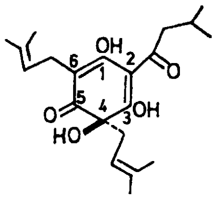


SCHEME

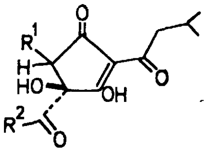
It was suggested[11] that the differences in reported m.p.s of the various samples of tetrahydroisohumulone might be due to the racemic or optically active nature of the compounds, but at this time there was no mention of the presence of *cis*- or *trans*-isomers. We decided to obtain unambiguously optically inactive tetrahydroisohumulone by synthesis from phloroglucinol *via* 4-deoxytetrahydrohumulone (VI) and to examine the product carefully for the presence of individual *cis*- or *trans*-isomers. This synthetic route was selected because it was of interest to compare the stability to oxygen of the incompletely alkylated and acylated synthetic intermediates.



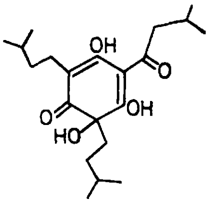
(I)



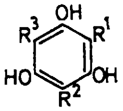
(II)



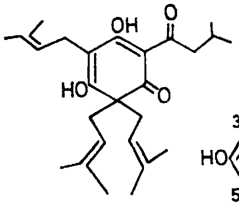
(III) $R^1 = \alpha\text{-}CH_2\cdot CH{=}CMe_2$, $R^2 = CH_2\cdot CH{=}CMe_2$
(IV) $R^1 = \beta\text{-}CH_2\cdot CH{=}CMe_2$, $R^2 = CH_2\cdot CH{=}CMe_2$
(XIX) $R^1 = \alpha\text{-}[CH_2]_2\cdot CMe_2$, $R^2 = [CH_2]_2\cdot CMe_2$
(XX) $R^1 = \beta\text{-}[CH_2]_2\cdot CMe_2$, $R^2 = [CH_2]_2\cdot CMe_2$



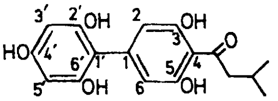
(V)



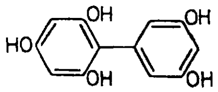
(VI) $R^1 = CO\cdot CH_2\cdot CHMe_2$, $R^2 = R^3 = [CH_2]_2\cdot CHMe_2$
(VIII) $R^1 = CO\cdot CH_2\cdot CHMe_2$, $R^2 = R^3 = H$
(IX) $R^1 = R^3 = CO\cdot CH_2\cdot CHMe_2$, $R^2 = H$
(XII) $R^1 = [CH_2]_2\cdot CHMe_2$, $R^2 = R^3 = H$
(XIII) $R^1 = CO\cdot CH_2\cdot CHMe_2$, $R^2 = [CH_2]_2\cdot CHMe_2$, $R^3 = H$
(XIV) $R^1 = R^3 = CO\cdot CH_2\cdot CHMe_2$, $R^2 = [CH_2]_2\cdot CHMe_2$
(XV) $R^1 = R^3 = [CH_2]_2\cdot CHMe_2$, $R^2 = H$



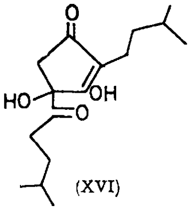
(VII)



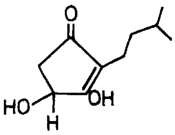
(X)



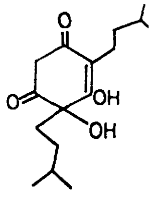
(XI)



(XVI)



(XVII)



(XVIII)

Phloroglucinol was converted into 2′,4′,6′-trihydroxyisovalerophenone[13] (VIII). Small amounts (*ca.* 10%) of di-isovalerylphloroglucinol (IX) were also isolated by chromatography and identified spectroscopically after crystallisation. In addition, smaller amounts of the substituted biphenyl (X) were formed. This compound, after recrystallisation, showed a molecular ion at 318 in its mass spectrum and gave a satisfactory analysis for

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[10] F. Govaert and M. Verzele, *Congr. Internat. Industr. Ferm.*, 1947, 297.

[11] P. M. Brown, G. A. Howard, and A. R. Tatchell, *J. Chem. Soc.*, 1959, 545.

[12] W. Wöllmer, *Ber.*, 1925, **58**, 672.

[13] T. S. Kenny, A. Robertson, and S. W. George, *J. Chem. Soc.*, 1939, 1601.

the monohydrate $C_{17}H_{18}O_6,H_2O$. The presence of five hydroxy-groups was confirmed by the mass spectrum of the trimethylsilyl derivative, which when submitted to combined mass spectrometry–g.l.c. showed a molecular ion at 678 a.m.u. Its n.m.r. spectrum (solution in deuterioacetone) displayed the expected signals from the isovaleryl side chain, and the aromatic proton signals were separated into two singlets, at τ 3·50 (2H, 2- and 6-H) and 3·96 (2H, 3′- and 5′-H). The 2′- and 6′-hydroxy-protons appeared as a broad singlet at τ 2·1 (2H), and the remaining, non-hydrogen bonded 4′-hydroxy-resonance appeared at τ 1·75 (1H). The 3- and 5-hydrogen-bonded hydroxy-protons appeared, as expected, as a singlet at τ −1·36 (2H). It seemed likely that the biphenyl was formed either by aluminium chloride-catalysed condensation of phloroglucinol and (VIII), or by self-condensation of phloroglucinol followed by monoacylation. This was confirmed as follows: g.l.c. of the trimethylsilylated reaction mixture showed that dry 2′,4′,6′-trihydroxyisovalerophenone, dry phloroglucinol, and aluminium chloride in nitrobenzene gave the biphenyl (X) and a second compound considered to be the biphenyl (XI). This was identical (g.l.c.) with the sole product obtained from phloroglucinol and aluminium chloride in nitrobenzene.

Clemmensen reduction of the acylphloroglucinol (VIII) gave isopentylphloroglucinol (XII) and further acylation afforded 2′,4′,6-trihydroxy-3′-isopentylisovalerophenone [14] (XIII) together with small quantities of di-isovalerylisopentylphloroglucinol (XIV), the structure of which was confirmed by its n.m.r. and mass spectra. Clemmensen reduction of (XIII) gave di-isopentylphloroglucinol (XV) which was isolated with difficulty, by chromatography, as an oil, unstable in air, which was characterised as its crystalline triacetate.[15]

This reaction also afforded a minor product, isolable in crystalline form by column chromatography, which showed a molecular ion at 282 a.m.u.; its unusual u.v. spectrum [16] [$\lambda_{\text{max.}}$ (EtOH) 272; $\lambda_{\text{max.}}$ (acid EtOH) 254 nm.] and its i.r. spectrum [$\nu_{\text{max.}}$ 3450 (OH) and 1695 (C=O) cm.$^{-1}$], elemental analysis, and n.m.r. spectrum supported the identification as the cyclopentenone (XVI). Hydrolysis with alkali afforded 4-methylvaleric acid (g.l.c.) and small amounts of a further crystalline solid, m.p. 142·5—143°, $C_{10}H_{16}O_3$ (mass spectrometry), to which is assigned structure (XVII). This compound, with similar u.v. maxima to those we observed, has been described previously (lit.,[16] m.p. 135—137°). We considered the original cyclopentenone (XVI) to be an artifact of the Clemmensen reaction formed by competitive oxidation of the di-isopentylphloroglucinol (XV) to give a humulone-type intermediate (XVIII) which would then rearrange to (XVI) under the acid conditions used. Indeed when purified di-isopentylphloroglucinol (XV) was kept in oxygen, partial conversion occurred into a more polar substance, the properties of which were in keeping with structure (XVIII). This slowly changed into (XVI) on treatment with acid, or more rapidly when treated with hot sodium carbonate solution. It was also possible to convert the purified di-isopentyl compound (XV) directly into (XVI) under the simulated conditions of the Clemmensen reduction.

Acylation of the di-isopentylphloroglucinol (XV) afforded a mixture of compounds which on chromatography gave the expected 4-deoxytetrahydrohumulone (VI), characterised as its crystalline tribenzoate.[17] The phloroglucinol (VI), which has not been synthesised previously by this route, underwent spontaneous oxidation in air to (±)-tetrahydrohumulone (V), which was incidentally obtained continuously from the chromatographic column. Further small amounts of the cyclopentenone (XVI) were also obtained, presumably derived by oxidation–ring contraction of the starting material (XV).

Controlled oxidation [17] of the 4-deoxy-compound (VI) in the presence of lead(II) acetate gave the lead salt of (±)-tetrahydrohumulone (V), from which the parent compound was regenerated by treatment with acid, chromatography on silicic acid, and low temperature crystallisation; m.p. 82—84° [lit.,[17] 82—83° for a sample prepared *via* hydrogenolysis of lupulone (VII) and oxidation of the resultant 4-deoxytetrahydrohumulone (VI)]. Smooth rearrangement of (V) with sodium carbonate then gave an oily mixture of (±)-*cis*- and (±)-*trans*-tetrahydroisohumulones [racemates of (XIX) and (XX) respectively].

In view of the uncertainty of previous tetrahydroisohumulone preparations, we examined methods for isomer separation. After preliminary purification by counter-current distribution [11] the mixture was chromatographed on silicic acid; this separated the racemate of (XIX) from that of (XX). Repeated chromatography of each fraction afforded pure crystalline (±)-*cis*-tetrahydroisohumulone [racemate of (XIX)] and (±)-*trans*-tetrahydroisohumulone [racemate of (XX)]. The ratio of *cis*- to *trans*-isomer in the original mixture was 2 : 3, in keeping with the expected relative stabilities of the two compounds. Small but significant differences in the i.r. spectra were paralleled by differences in the u.v. spectra which were analogous to those described for the *cis*- (III) and *trans*- (IV) isohumulones.[7] For these isomers, the chemical shifts of the 5-methine protons are resolved in the n.m.r. spectrum at 60 MHz and the signal from the *cis*- (III) isomer appears at higher field than that from the *trans* (IV).[6] In the spectra of the tetrahydroisohumulones (XIX) and (XX), the resonances of the low-field methylene protons in the 4-methylvaleryl chains obscure the 5-methine proton signals with which they partially overlap at 60 MHz. However at 220 MHz there is a complete separation of the 5-methine, isovaleryl methylene, and 4-methylvaleryl methylene signals and the 5-methine signal from the *cis*-isomer (XIX)

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[14] W. Riedl and E. Leucht, *Chem. Ber.*, 1958, **91**, 2784.

[15] R. A. Finnegan, B. Gilbert, E. J. Eisenbraun, and C. Djerassi, *J. Org. Chem.*, 1960, **25**, 2169.

[16] J. S. Burton, J. A. Elvidge, and R. Stevens, *J. Chem. Soc.*, 1965, 1276.

[17] W. Riedl and H. Hubner, *Chem. Ber.*, 1957, **90**, 2870.

appears at a higher field (τ 7·15) than that from the *trans*-isomer (XX) (τ 6·95) in accord with the spectra and configurations of both *cis*- and *trans*-isohumulones[6] [(III) and (IV)] and the humulinic acids.[18]

Natural (−)-humulone (II), purified by counter-current distribution from its homologues, was isomerised with sodium carbonate under the same conditions as for the synthetic (±)-tetrahydrohumulone. The resultant isohumulones after counter-current distribution were hydrogenated over palladised charcoal to give a mixture of tetrahydroisohumulones which were purified by counter-current distribution and separated by repeated chromatography to give (−)-*cis*- (XIX) and (+)-*trans*- (XX) tetrahydrisohumulones in the approximate ratio 3 : 1. The naturally derived compounds were identical in i.r., u.v., and n.m.r. spectra with the synthetic isomers, although their m.p.s were different and covered a greater range. Careful low-temperature crystallisation was found to raise the m.p.s considerably and to decrease the range to 2—3°.

Our results show that the *cis*- and *trans*-forms of the tetrahydroisohumulones are present in different proportions when obtained (*a*) from isohumulones, derived by isomerisation of (−)-humulone, and (*b*) from isomerisation of (±)-tetrahydrohumulone. Since the *cis*- and *trans*-isomers have different m.p.s and u.v. spectra, it is not surprising that previous preparations, in which separation of isomers was not described, have shown different m.p.s and spectroscopic properties. An additional factor to be considered is that the optically active or racemic nature of the product will give rise to differences[11] in m.p. This has been borne out in our own preparations. The degree of stereoselectivity in the rearrangement of humulone is uncertain and may well lead to *cis*- and *trans*-forms of varying optical purity.

Since the preparation of this paper, an account has appeared[19] of the isolation of *cis*- and *trans*-forms of 'tetrahydroisohumulone.' Although these preparations appear to be derived from mixtures of homologues and analogues the m.p.s recorded are different and for the *cis*-isomer higher than our value. The rearrangement conditions (pH 5·6) were, however, different and may account for the apparent anomaly, *e.g.* if the degree of stereoselectivity is a function of pH.

The present work shows that the facility with which substituted phloroglucinols undergo oxidation followed by ring contraction is not confined to the precursors of the natural humulones. Such reactions may offer a convenient synthetic route to certain complex cyclopentenones.

EXPERIMENTAL

M.p.s are corrected. I.r. spectra were measured, unless stated otherwise, for solutions in chloroform with a Unicam SP 200 spectrophotometer and u.v. spectra with a Beckman DB spectrophotometer. N.m.r. spectra were measured, unless stated otherwise, for solutions in deuteriochloroform (*ca.* 10% w/v) with a Perkin-Elmer R10 spectrometer at 60 MHz, with tetramethylsilane as internal standard. G.l.c. was carried out with a Pye series 104 chromatograph [silylated glass column (1·5 m.) packed with 1% D.C. 560 (formerly called F.60) on Gas Chrom. P (mesh size 100—120) which had previously been acid-washed and silylated]. The column was temperature programmed from 150 to 250° at 3° per min.; nitrogen flow rate 45 c.c./min. Trimethylsilylation was performed by dissolving the compound (*ca.* 1 mg.) in dimethylformamide (0·5 c.c.). Hexamethyldisilazane (0·5 c.c.) was added and the solution was kept at 50° for 30 min. Silica gel for t.l.c. was Merck Kieselgel G. Silicic acid for column chromatography was Mallinckrodt 100 mesh. Light petroleum refers to the fraction b.p. 40—50°, obtained by redistillation of petroleum, b.p. 40—60°.

2′,4′,6′-*Trihydroxyisovalerophenone* (VIII).—Phloroglucinol (16 g.) was treated with isovaleryl chloride (b.p. 42—43°/7 mm.; 13 c.c.) according to Robertson's procedure,[13] with vigorous stirring throughout the reaction. After steam distillation, the crude product (11·5 g.) was chromatographed in two portions on a short column of silicic acid (15 × 5 cm.) and eluted in ether–light petroleum (3 : 2) to give 2′,4′,6′-trihydroxyisovalerophenone (VIII) (10 g., 45%), m.p. 142° [m.p. 145° (from water) (lit.,[2] 145°)], $\lambda_{max.}$ (EtOH) 325sh, 288 (ε 15,870), and 226 (12,020) nm., $\lambda_{max.}$ (alkaline EtOH) 321 (22,500) nm., $\nu_{max.}$ 3300 (OH) and 1630 and 1605 (C=O) cm.$^{-1}$, τ [$(CD_3)_2CO$] 9·05 (6H, d, *J* 6·5 Hz, $HC\mathit{Me}_2$), 7·75 (m, *J* 6·5 Hz, $\mathit{H}CMe_2$), 7·04 (2H, d, *J* 7·5 Hz, $C\mathit{H}_2{\cdot}CHMe_2$), 4·08 (2H, s, ArH), and −1·3br (s, OH).

2′,4′,6′-*Trihydroxy-3′-isovalerylisovalerophenone* (IX). The early fractions from the column [material eluted in ether–light petroleum (1 : 9)] afforded an oil contaminated with nitrobenzene, giving a high R_F spot on t.l.c. Nitrobenzene was removed by steam distillation and the residual solid was crystallised from light petroleum to give crude (IX) (1·0 g.; m.p. 112—114·5°). The mother liquors deposited a further 200 mg. Recrystallisation from light petroleum gave pure 2′,4′,6′-trihydroxy-3-isovaleryliso-valerophenone (IX), m.p. 114—115° (lit.,[20] 113—114°], $\lambda_{max.}$ (EtOH) 275 (ε 35,570) nm., $\lambda_{max.}$ (alkaline EtOH) 293 (ε 37,780) nm., $\lambda_{max.}$ (acid EtOH) 273 (45,200) nm., τ ($CDCl_3$) 9·02 (d, *J* 6 Hz, 2 × $CH_2{\cdot}CH\mathit{Me}$), 7·74 (septet, *J* 6 Hz, $CH_2{\cdot}C\mathit{H}Me_2$), 7·02 (d, *J* 7 Hz, $CO{\cdot}C\mathit{H}_2{\cdot}CHMe_2$), and 4·10 (s, ArH), *m/e* 294 (M^+), 279 (M − Me), 237 (100%, $M - C_4H_9$), and 219 [$M - (C_4H_9 + H_2O)$] (Found: C, 65·5; H, 7·1. Calc. for $C_{16}H_{22}O_5$: C, 65·3; H, 7·5%).

Isobutyl 2′,3,4′,5,6′-*Pentahydroxybiphenyl-4-yl Ketone* (X) (*Monohydrate*).—Fractions eluted in ether–light petroleum (9 : 1) afforded an amorphous yellow solid (*ca.* 300 mg.). Recrystallisation from methanol–light petroleum gave the *ketone* (X) as pale yellow crystals of the monohydrate, m.p. 256° (decomp.), $\lambda_{max.}$ (EtOH) 317 (ε 10,300), 264sh (6660), and 224sh (19,980) nm., $\lambda_{max.}$ (alkaline EtOH) 357 and 258 nm., τ [$(CD_3)_2CO$] 9·04 (6H, d, *J* 6 Hz, $HC\mathit{Me}_2$), 7·7 (1H, m, *J* 6 Hz, $\mathit{H}CMe_2$), 6·95 (2H, d, *J* 7 Hz, $C\mathit{H}_2{\cdot}CHMe_2$), 3·96 (2H, s, 3′- and 5′-H), 3·5 (2H, s, 2- and 6-H), 2·1 (2H, s, 2′- and 6′-OH), 1·75 (1H, s, 4′-OH), and −1·36 (2H, s, 3- and 5-OH) (Found: C, 60·6; H, 6·1. $C_{18}H_{18}O_6,H_2O$ requires C, 60·7; H, 6·0%).

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[18] J. S. Burton, J. A. Elvidge, and R. Stevens, *J. Chem. Soc.*, 1964, 3816.

[19] E. Kokubu and Y. Kuroiwa, *Reports Res. Lab. Kiririn Brewery Co.*, 1968, No. 11, 33.

[20] Belg.P. 649,240/1964 (*Chem. Abs.*, 1966, **64**, 8088b).

Rigorously dried phloroglucinol (60 mg.), 2′,4′,6′-trihydroxyisovalerophenone (VIII) (100 mg.), and aluminium chloride (150 mg.) were stirred in nitrobenzene (1·5 c.c.). After 4 days, the mixture was acidified and extracted with ether. A small sample of the dried extract, on trimethylsilylation and g.l.c., gave two peaks corresponding to the starting materials, a third which was not resolved from the *authentic biphenyl* (X), and a fourth which was not resolved from the sole product obtained from a similar procedure with phloroglucinol (120 mg.) and aluminium chloride (150 mg.). G.l.c. indicated that both the phloroglucinol and 2′,4′,6′-trihydroxyisovalerophenone were pure before use.

Isopentylphloroglucinol (XII).— 2′,4′,6′-Trihydroxyisovalerophenone (VIII) (9·0 g.) was reduced by the Clemmensen method, according to the procedure of ref. 13. The isopentylphloroglucinol (XII) had m.p. 125—126° (lit.,[13] 126°) (6·0 g., 71%), $\lambda_{max.}$ (EtOH) 278 (ε 760) and 272 (768) nm., $\lambda_{max.}$ (alkaline EtOH) 354 (ε 6500), 256 (17,000), and 226 (16,700) nm. $\nu_{max.}$ (KBr disc) 3300 (OH), 1612, and 1528 cm.$^{-1}$, τ [$(CD_3)_2CO$] 9·1 (6H, d, *J* 5·5 Hz, CH*Me*$_2$), 8·6 (m, *J* 7 Hz, C*H*$_2$·CHMe$_2$), 7·4 (2H, t, *J* 7·5 Hz, =C·C*H*$_2$), 4·06 (2H, s, ArH), 2·32 (1H, s, OH *para* to isopentyl), and 2·26 (2H, s, OH *ortho* to isopentyl) (Found: C, 67·2; H, 8·1. Calc. for $C_{11}H_{16}O_3$: C, 67·3; H, 8·25%).

2′,4′,6′-*Trihydroxy*-3′-*isopentylisovalerophenone* (XIII).— Isopentylphloroglucinol (XII) (7·4 g.) was acylated with isovaleryl chloride (3·84 c.c.) and aluminium chloride (6·0 g.) as described for phloroglucinol (reaction time was 4 days). After steam distillation the crude brown oily product was taken up in benzene, dried (Na_2SO_4), and then chromatographed on silicic acid (20 × 3·5 cm.). Elution with ether–light petroleum (9 : 11) gave a yellow crystalline product (3·6 g., 41%). Starting material (0·34 g.) was eluted by ether–light petroleum (3 : 2). The crude product afforded 2′,4′,6′-trihydroxy-3′-isopentylisovalerophenone (XIII), m.p. 173—175° (from hexane) (lit.,[14] 167—168°), $\lambda_{max.}$ (EtOH) 292 (ε 17,280) and 240sh nm., $\lambda_{max.}$ (alkaline EtOH) 329 (ε 25,270) and 240sh nm., $\nu_{max.}$ (KBr) 3400, 1628, 1600, and 1577 cm.$^{-1}$, τ [$(CD_3)_2CO$] 9·04 (12H, d, *J* 6 Hz, CH$_2$·CH$_2$·CH*Me*$_2$ and CO·CH$_2$·CH*Me*$_2$), 8·52 (m, CH$_2$·C*H*$_2$·CHMe$_2$), 7·41 (2H, m, C*H*$_2$·CH$_2$·CHMe$_2$), 7·03 (2H, d, *J* 6·5 Hz, CO·C*H*$_2$·CH), 4·0 (1H, s, ArH), and 2·67 (2H, s, non-hydrogen-bonded OH) (Found: C, 68·8; H, 8·8. Calc. for $C_{16}H_{24}O_4$: C, 68·5; H, 8·65%)

2′,4′,6′-*Trihydroxy*-3′-*isopentyl*-5′-*isovalerylisovalerophenone* (XIV). The fraction eluted in ether–light petroleum (3 : 22) afforded a red oil (230 mg.) which solidified when stored at −20° in the absence of air. T.l.c. indicated that this was a single main product, and crystallisation from chloroform–light petroleum at −30° gave a brown solid (140 mg.; mp. 106·5—108·5°). Further recrystallisation afforded colourless crystals of the *ketone* (XIV) (92 mg., m.p. 109·5—111°), M^+ 364, $\lambda_{max.}$ (EtOH) 385 (ε 5690) and 296 (20,290) nm., $\lambda_{max.}$ (acid EtOH) 342 (ε 3190) and 274 (25,940) nm., $\lambda_{max.}$ (alkaline EtOH) 387 (ε 6550) and 297 (20,980) nm., τ 9·0 (18H, d, *J* 6·5 Hz, 2 × CO·CH$_2$·CH*Me*$_2$ and CH$_2$·CH$_2$·CH*Me*$_2$), 8·55 (m, CH$_2$·C*H*$_2$·C*H*Me$_2$), 7·73 (m, *J* 6·5 Hz, CO·CH$_2$·C*H*Me$_2$), 7·46 (m, =C·C*H*$_2$), 7·03 (4H, d, *J* 6·5 Hz, 2 × CO·C*H*$_2$·CHMe$_2$), and −6·70 (2H, s, hydrogen-bonded OH) (Found: C, 69·15; H, 8·6. $C_{21}H_{32}O_5$ requires C, 69·2; H, 8·85%).

Di-isopentylphloroglucinol (XV).—2′,4′,6′-Trihydroxy-3′-isopentylisovalerophenone (XIII) (7·4 g.) was reduced by Robertson's [13] method, but with an increased quantity (200 c.c.) of methanol. T.l.c. then showed that no starting material was present. The product was collected in ether and after removal of solvent the residual gum (7·0 g.) was chromatographed on silicic acid (25 × 5 cm.). The crude product (XV) (4·8 g., 68%) was eluted in ether–light petroleum (1 : 1) as a brown oil which showed a minor (10%) additional peak on g.l.c. of its trimethylsilyl derivative. Rechromatography of the oil did not affect the g.l.c. trace of the trimethylsilyl derivative, but the product (4·5 g.) showed a single spot on t.l.c. and its n.m.r. spectrum indicated that it was pure. The compound was unstable (a sample decomposed completely in 7 days); it was therefore used immediately. Freshly prepared material showed $\lambda_{max.}$ (EtOH) 277 nm., τ [$(CD_3)_2CO$] 9·07 (d, *J* 6 Hz, CH$_2$·CH*Me*$_2$), 8·32—8·92 (m, C*H*$_2$·CHMe$_2$), 7·37 (4H, t, *J* 7·5 Hz, =C·C*H*$_2$), 4·0 (s, ArH), and 2·2—3·3 (s, OH). The triacetate (204 mg.) [from (XV) (250 mg.) and acetic anhydride (0·66 c.c.) in pyridine (3·5 c.c.)] after chromatography on silicic acid had m.p. 107·5° (from hexane) (lit.,[15] 104·5—105°) (Found: C, 67·05; H, 8·4. Calc. for $C_{22}H_{32}O_6$: C, 67·3; H, 8·2%).

3,4-*Dihydroxy*-2-*isopentyl*-4-(4-*methylvaleryl*)*cyclopent*-2-*en*-1-*one* (XVI). Also eluted in ether–light petroleum (9 : 1) was a colourless crystalline solid (725 mg.), m.p. 152°. Recrystallisation from chloroform–light petroleum gave the pure *cyclopentenone* (XVI), m.p. 156°, *M* 276 (Rast), M^+ 282 a.m.u., $\lambda_{max.}$ (EtOH) 272 (ε 19,960) nm., $\lambda_{max.}$ (acid EtOH) 254 nm., $\nu_{max.}$ (KBr) 3450 (OH), 1695 (C=O), and 1140 (C–OH) cm.$^{-1}$, τ [$(CD_3)_2CO$] 9·18 and 9·16 (12H, each d, *J* 5 Hz, CH$_2$·CH*Me*$_2$), 8·66 (6H, m, 2 × C*H*$_2$·C*H*Me$_2$), 7·85 (2H, m, partially obscured, =C·C*H*$_2$), 7·54 (2H, m, CH$_2$·C*H*$_2$·CO), and 7·32 (m, HO·C·C*H*$_2$·CO) (Found: C, 68·2; H, 9·0. $C_{16}H_{26}O_4$ requires C, 68·05; H, 9·3%).

Hydrolysis. The cyclopentenone (XVI) (50 mg.) in methanol (2 c.c.) was added to 2N-sodium hydroxide heated under reflux in a nitrogen atmosphere, and refluxing was continued for 7 hr. The mixture was then added to ice (8 g.) and concentrated hydrochloric acid (2·2 c.c.), and extracted into ether (6 × 15 c.c.). The ether layers were combined, washed with water, dried, and evaporated to leave a brown oil (30 mg.). Crystallisation from chloroform–light petroleum afforded an amorphous white solid (7 mg.; m.p. 133·5—135°). Two further similar preparations gave material (13 mg.), m.p. 131·5—133·5°. The combined solids, on recrystallisation, deposited 3,4-dihydroxy-2-isopentylcyclopent-2-en-1-one (XVII) (9·5 mg.), m.p. 142·5—143° (lit.,[16] 135—137°), $\lambda_{max.}$ (acid EtOH) 249 (ε 15,800) [lit.,[16] 250 (12,600)] nm., $\lambda_{max.}$ (alkaline EtOH) 273 (ε 27,100) [lit.,[16] 275 (20,700)] nm., $\nu_{max.}$ (KBr) 3380, 2940, 2650, 1560, 1440, 1380, 1315, 1286, 1257, 1200, 1124, 1091, 1055, 996, 922, and 888 cm.$^{-1}$ (Found: M^+, 184·1092. Calc. for $C_{10}H_{16}O_3$: M^+, 184·1099).

G.l.c. of the mother liquors from the first crystallisation on a Trimer acid column at 160°, with formic acid in the carrier gas gave a single peak (r.t. 44 min.) unresolved from authentic 4-methylvaleric acid.

Treatment of (XV) *with Acid in Air*.—A sample of (XV) (40 mg.), previously purified by column chromatography, which gave only one spot on t.l.c., was kept in a boiling mixture of methanol (1 c.c.) and 15% hydrochloric acid (2 c.c.) for 4·5 hr. The mixture was cooled and extracted into ether; the extract washed, dried, and evaporated, and the residue (33 mg.) was chromatographed on a small column of silicic acid. The cyclopentenone (XVI) (5·4 mg.) was eluted [ether–light petroleum (4 : 1)] and showed i.r. and t.l.c. properties indistinguishable from those of the specimen just described.

Decomposition of (XV) *in Air*.—A sample of (XV) (310 mg.) was kept at $-30°$ for several weeks; t.l.c. then indicated that a new component had formed, R_F 0·48 in hexane–ethyl formate–formic acid (12 : 8 : 1). Chromatography on a column of silicic acid afforded unchanged (XV) (240 mg.) and a yellow oil (XVIII) (44 mg.), of much higher polarity, $\lambda_{\text{max.}}$ (EtOH) 290 nm., τ 9·14 and 9·10 (each d, *J* 5·5 Hz, $\mathrm{CH}\mathit{Me}_2$), 8·64 (m, $\mathit{CH}_2\cdot\mathrm{C}\mathit{H}\mathrm{Me}_2$), 8·10 [m, $\mathrm{C(OH)}\cdot\mathrm{C}\mathit{H}_2\cdot\mathrm{CH}_2\cdot\mathrm{CHMe}_2$], 7·65 (t, *J* 7 Hz, $=\mathrm{C}\cdot\mathrm{C}\mathit{H}_2$), 6·47 (m, $\mathrm{CO}\cdot\mathrm{C}\mathit{H}_2\cdot\mathrm{CO}$). A sample of the material kept in acidic methanol at 20° gradually changed into a component indistinguishable from (XVI) by t.l.c.

The major part of the oil (28 mg.) in methanol (1 c.c.) was added to boiling aqueous 0·1M-sodium carbonate solution (4·5 c.c.). After 20 min. the mixture was added to ice and treated with hydrochloric acid; the product was isolated with ether as a colourless solid (22 mg.). Chromatography on silicic acid column gave the cyclopentenone (XVI) (10·7 mg.), m.p. 150—153°, $\lambda_{\text{max.}}$ (EtOH) 272 nm., $\lambda_{\text{max.}}$ (acid EtOH) 254 nm. Recrystallisation from chloroform–light petroleum gave the pure compound (4·5 mg.), m.p. 157·5—158°, mixed m.p. 156—156·5° (with authentic material, m.p. 157—157·5°). The i.r. spectrum was identical with that of authentic material.

4-*Deoxytetrahydrohumulone* (VI).—Di-isopentylphloroglucinol (4·5 g.) in nitrobenzene (40 c.c.) was added dropwise to nitrobenzene (20 c.c.). During the addition (45 min.) aluminium chloride (freshly ground; 2·7 g.) was added in portions with continuous stirring. The nitrobenzene had previously been de-gassed with nitrogen, and the entire reaction was carried out under nitrogen. Isovaleryl chloride (1·8 c.c.) was then added dropwise at 0°. After 66 hr. stirring at 20°, a sample of the mixture was treated with dilute hydrochloric acid and extracted into ether; t.l.c. [ethyl acetate–light petroleum (3 : 2)] then showed a new spot of higher R_F value than the starting material. The mixture was added to excess of iced hydrochloric acid and extracted into ether. The extracts were washed with sodium hydrogen carbonate solution and water. The ether was evaporated off, then most of the nitrobenzene was removed by distillation at 43°/1 mm.

The residue, which still contained nitrobenzene (*ca.* 3 c.c.), was taken up in ether (100 c.c.) and repeatedly extracted with 0·2M-sodium hydroxide (8 × 100 c.c.). The alkaline extracts were acidified and the products were re-extracted into ether. The dried ($\mathrm{Na_2SO_4}$) extract yielded a crude product (4·7 g.; contaminated with nitrobenzene), which was chromatographed on silicic acid (23 × 3·5 cm.) in two equal portions.

The combined chromatogram fractions afforded (*a*) nitrobenzene, eluted with light petroleum; (*b*) crude 4-deoxytetrahydrohumulone (VI) (1·2 g.), eluted with ether–light petroleum (1 : 3); (*c*) crude starting material (XV) (1·3 g.), eluted with ether–light petroleum (9 : 11); and (*d*) a solid, m.p. 156° (143 mg.), eluted with ether–light petroleum (1 : 1), shown by its u.v. spectrum and mixed m.p. (156°) to be 3,4-dihydroxy-2-isopentyl-4-(4-methylvaleryl)cyclopent-2-en-1-one (XVI). Material (550 mg.) which corresponded to tetrahydrohumulone (V) (t.l.c.) was eluted continuously in the chromatogram after the 4-deoxytetrahydrohumulone. The freshly prepared, but unstable, 4-deoxytetrahydrohumulone (VI) showed $\lambda_{\text{max.}}$ (EtOH) 293 nm., $\lambda_{\text{max.}}$ (alkaline EtOH) 349 nm., τ 9·02 (18H, d, *J* 6 Hz, 3 × $\mathrm{CH_2}\cdot\mathrm{CH}\mathit{Me}_2$), 8·26—8·86 (7H, m, 2 × $\mathrm{CH_2}\cdot\mathrm{C}\mathit{H}_2\cdot\mathrm{C}\mathit{H}\mathrm{Me}_2$ and $\mathrm{CO}\cdot\mathrm{CH}_2\cdot\mathrm{C}\mathit{H}\mathrm{Me}_2$), 7·20—7·70 (4H, m, 2 × $=\mathrm{C}\cdot\mathrm{C}\mathit{H}_2\cdot\mathrm{CH}_2\cdot\mathrm{CHMe}_2$), 7·00 (d, *J* 7 Hz, $\mathrm{CO}\cdot\mathrm{C}\mathit{H}_2\cdot\mathrm{CHMe}_2$), 4·62br (1H, s, non-hydrogen-bonded OH), and 0·25br (2H, s, hydrogen-bonded OH).

The tribenzoate from benzoyl chloride (redistilled; 280 mg.) and 4-deoxytetrahydrohumulone (VI) (142 mg.) in dry pyridine (2 c.c.) was chromatographed on silicic acid and gave, after several recrystallisations from methanol, colourless crystals, m.p. 167—168° (softens 158°) (lit.,[17] 165—166°), $\lambda_{\text{max.}}$ (EtOH) 235 (ε 59,950) nm., $\lambda_{\text{max.}}$ (alkaline EtOH) 235 nm. (Found: C, 76·2; H, 6·85. Calc. for $\mathrm{C_{42}H_{46}O_7}$: C, 76·1; H, 7·0%).

(±)-*Tetrahydrohumulone* (V).—4-Deoxytetrahydrohumulone (VI) (700 mg.) was dissolved in methanol (10 c.c.). Lead(II) acetate trihydrate (530 mg.) was added and the mixture treated with a slow stream of oxygen at 20° for 48 hr. The precipitate was collected by centrifugation, washed with methanol, and dried at 20° overnight under reduced pressure to give the lead salt of tetrahydrohumulone (712 mg.).

The salt (700 mg.) in ether (200 c.c.) was shaken with 6N-sulphuric acid (200 c.c.) and the ether layer was separated, washed with saturated sodium chloride solution, and dried ($\mathrm{Na_2SO_4}$). Evaporation under reduced pressure gave crude (±)-tetrahydrohumulone (400 mg.) as a pale yellow solid, m.p. 71—73°. Chromatography on silicic acid (21 × 2·5 cm.) and elution with ethyl acetate–light petroleum (1 : 24) gave a product (m.p. 81—83°; 372 mg.) which yielded pure (±)-tetrahydrohumulone (V), m.p. 82—84° (from iso-octane at 25°) (lit.,[17] 82—83° lit.,[21] 85—85·5°), M^+ 366, $\lambda_{\text{max.}}$ (EtOH) 357sh (ε 10,870), 328 (12·860), and 230 (13,970) nm., $\lambda_{\text{max.}}$ (alkaline EtOH) 357sh (ε 8,208), 328 (10,640), and 230 (10,200) nm., $\lambda_{\text{max.}}$ (acid EtOH) 356sh (ε 6212), 324 (7450), 289 (7550), 246 (9190), and 233 (9530) nm., τ 9·18 and 9·07 (each d, *J* 6 Hz, $\mathrm{CH_2}\cdot\mathrm{CH_2}\cdot\mathrm{CH}\mathit{Me}_2$), 9·00 and 9·04 (each d, *J* 6·5 Hz, $\mathrm{CO}\cdot\mathrm{CH_2}\cdot\mathrm{CH}\mathit{Me}_2$) (a similar splitting of the acyl methyls is evident in spectra of other humulones), 8·0—8·85 (m, $\mathrm{CH_2C}\mathit{H}_2\mathrm{C}\mathit{H}\mathrm{Me}_2$ and $\mathrm{COCH_2C}\mathit{H}\mathrm{Me}_2$) 7·59 (t, *J* 7·5 Hz, $\mathrm{C}\cdot\mathrm{C}\mathit{H}_2\cdot\mathrm{CH_2}\cdot\mathrm{CHMe_2}$), 7·21 (d, *J* 7·5 Hz, $\mathrm{CO}\cdot\mathrm{C}\mathit{H}_2\cdot\mathrm{CHMe_2}$), and $-10·3$ (s, H-bonded chelated OH). The compound gave a single spot on t.l.c. (blue-black with $\mathrm{FeCl_3}$), R_F 0·6 in hexane–ethyl formate–formic acid (12 : 8 : 1).

(±)-*Tetrahydroisohumulones*.—(±)-Tetrahydrohumulone (V) (200 mg.) was added in methanol (1·5 c.c.) to boiling aqueous sodium carbonate solution (0·1M; 40 c.c.) under nitrogen.[22] The mixture was boiled for 20 min., then added to ice (20 g.) and hydrochloric acid (1·2 c.c.) and extracted with light petroleum (4 × 60 c.c.). The recovered oil (175 mg.) was distributed on a twenty-tube Craig-type counter-current apparatus (upper phase 0·5M-potassium phosphate buffer adjusted to pH 6·5 with phosphoric acid; lower phase iso-octane).[11] After twenty transfers, acidification with N-sulphuric acid (20 c.c.) and u.v. assay indicated a single symmetrical peak centered on tube 11. The combined top layers of tubes 7—16 were washed with water (× 2), dried ($\mathrm{Na_2SO_4}$), and evaporated to give a yellow oil (150 mg.). The oil [$\lambda_{\text{max.}}$ (EtOH) 274sh and 253 nm.] was chromatographed on a column (21 × 2·5 cm.) of

[21] M. Anteunis and M. Verzele, *Bull. Soc. chim. belges.*, 1959, **68**, 705.

[22] G. A. Howard, *J. Inst. Brewing*, 1959, **65**, 414.

silicicic acid, which was eluted with ethyl acetate–light petroleum (1 : 24). Isomer A, m.p. 50—58° (62 mg.), was eluted between 120 and 180 c.c. and isomer B, m.p. 47—52° (40·7 mg.), between 190 and 270 c.c. T.l.c. in hexane–ethyl formate–formic acid (12 : 8 : 1) gave separate spots, R_F 0·59 (A) and 0·54 (B). Rechromatography of each isomer under the same conditions afforded, after careful drying under reduced pressure in the dark, isomer A, (±)-trans-*tetrahydroisohumulone* [racemate of (XX)], m.p. 59—62·5°, $\lambda_{max.}$ (EtOH) 273sh (ε 13,730) and 254 (17,690) nm., $\lambda_{max.}$ (acid EtOH) 267 (9150) and 228 (9760) nm., $\lambda_{max.}$ (alkaline EtOH) 269sh (ε 14,640) and 249 (18,300) nm., $\nu_{max.}$ 3450, 2960, 1698, 1625, 1580, 1472, 1390, 1372, 1328, 1275, 1234, 1168, and 1135 cm.$^{-1}$, τ (220 MHz) 9·13 (d, *J* 6·5 Hz, $CH_2\cdot CH_2\cdot CH\mathit{Me}_2$), 9·03 (m, $CO\cdot CH_2\cdot CH\mathit{Me}_2$), 8·81 (m, $CH\cdot CH_2\cdot C\mathit{H}_2\cdot CHMe_2$), 8·53 (m, $CH\cdot C\mathit{H}_2\cdot CH_2\cdot CHMe_2$ and $CO\cdot CH_2\cdot C\mathit{H}_2\cdot CHMe_2$), 8·30 (m, $CH_2\cdot CH_2\cdot C\mathit{H}Me_2$), 7·83 (m, $CO\cdot CH_2\cdot C\mathit{H}Me_2$), 7·46 (t, *J* 6 Hz, $CO\cdot C\mathit{H}_2\cdot CH_2\cdot CHMe_2$), 7·26 (d, *J* 7 Hz, $CO\cdot C\mathit{H}_2\cdot CHMe_2$), and 6·95 (t, *J* 7 Hz, $C\mathit{H}\cdot CH_2\cdot CH_2\cdot CHMe_2$) (Found: M^+, 366·2363. $C_{21}H_{34}O_5$ requires *M*, 366·2410).

Isomer B, (±)-cis-*tetrahydroisohumulone* [racemate of (XIX)], had m.p. 51—53° (lit.,[11] 49—53° for tetrahydroisohumulone), $\lambda_{max.}$ (EtOH) 272sh (ε 12,480) and 253 (16,490) nm., $\lambda_{max.}$ (acid EtOH) 278 (9830) (lit.,[11] ε 9700 at 275 nm. for tetrahydroisohumulone) and 224 (ε 8130) nm., $\lambda_{max.}$ (alkaline EtOH) 271sh (11,530) and 252 (14,230) nm., $\nu_{max.}$ 3500, 2960, 1698, 1632, 1583, 1472, 1390, 1374, 1280, 1158, 1133, and 1074 cm.$^{-1}$, τ (220 MHz) 9·14 (m, $CH_2\cdot CH_2\cdot CH\mathit{Me}_2$), 9·02 (m, $CO\cdot CH_2\cdot CH\mathit{Me}_2$), 8·84 (m, $CH\cdot CH_2\cdot C\mathit{H}_2\cdot CHMe_2$), 8·58 (m, $CH\cdot C\mathit{H}_2\cdot CH_2\cdot CHMe_2$, $CO\cdot CH_2\cdot C\mathit{H}_2\cdot CHMe_2$, and $CH_2\cdot CH_2\cdot C\mathit{H}Me_2$), 8·07 (m, $CH_2\cdot CH_2\cdot C\mathit{H}Me_2$), 7·86 (m, $CO\cdot CH_2\cdot C\mathit{H}Me_2$), 7·50 (m, $CO\cdot C\mathit{H}_2\cdot CH_2\cdot CHMe_2$), 7·30 (d, *J* 7 Hz, $CO\cdot C\mathit{H}_2\cdot CHMe_2$), and 7·15 (m, $C\mathit{H}\cdot CH_2\cdot CH_2\cdot CHMe_2$) (Found: M^+, 366·2363. $C_{21}H_{34}O_5$ requires *M*, 366·2409).

Preparation of (—)-cis- (XIX) *and* (+)-trans- (XX) *Tetrahydrohumulones*.—Pure (—)-humulone (II) (400 mg.) was prepared by counter-current distribution as previously described.[23] Isomerisation [22] and further counter-current distribution [9] gave a mixture of (—)-*cis*- and (+)-*trans*-isohumulones ($[\alpha]_D$ +30·2°, *cf.*,[9] 27·8°). This mixture (210 mg.) was hydrogenated in methanol (9 c.c.) over palladised charcoal (5%; Johnson, Matthey, and Co.; 50 mg.) until the theoretical hydrogen uptake had occurred. The product (180 mg.) was first purified by counter-current distribution.[11] The resultant mixture of tetrahydroisohumulones (110 mg.) showed $\lambda_{max.}$ (EtOH) 270sh and 252 (ε 17,100) nm., $\lambda_{max.}$ (acid EtOH) 271 and 228 nm., $\lambda_{max.}$ (alkaline EtOH) 268sh and 251 (ε 16,100) nm. Chromatography on a column of silcicic acid as already described gave (—)-*cis*-tetrahydroisohumulone (XIX) (19·1 mg.; m.p. 59—69°) and (+)-*trans*-tetrahydroisohumulone (XX) (59 mg.; softens at 38° and melts up to 53°). Rechromatography of each isomer gave (XIX), m.p. 62—69°, $[\alpha]_D^{20}$ $-1·5° \pm 0·5°$ (*c* 0·6) and (XX), m.p. 47—53° (softens at 38°), $[\alpha]_D^{20}$ +21·6° (*c* 1·55). The u.v., i.r., and n.m.r. spectra of each isomer were at this stage identical with those of the synthetic compounds. Careful repeated low-temperature crystallisation from hexane at −30° gave crystalline specimens of (XIX), m.p. 75·5—78°, $\lambda_{max.}$ (EtOH) 272sh (ε 12,400) and 254 (16,500) nm., $\lambda_{max.}$ (alkaline EtOH) 271sh (ε 16,200) and 252 (20,200) nm., $\lambda_{max.}$ (acid EtOH) 279 (ε 8900) and 226 (6800) nm.; and (XX), m.p. 67·5—69°, $\lambda_{max.}$ (EtOH) 272sh (ε 11,300) and 254 (14,600) nm., $\lambda_{max.}$ (alkaline EtOH) 270sh (ε 13,000) and 251 (15,600) nm., $\lambda_{max.}$ (acid EtOH) 269 (7300) and 230 (7300) nm.

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[23] F. L. Rigby and J. L. Bethune, *J. Amer. Chem. Soc.*, 1955, **77**, 2828.