579. *The Photochemistry of Verbenone.*[1]

By J. J. HURST and G. H. WHITHAM.

When verbenone (I) in cyclohexane is irradiated with ultraviolet light it is converted into the isomeric ketone chrysanthenone (II). In ethanol, wet ether, or ethereal ammonia there are obtained, in addition, the esters (XI) and (XII; X = OEt), the acid (XII; X = OH), and the amide (XII; $X = NH_2$) respectively.

A STUDY of the photochemistry of verbenone (I) was initiated in the expectation that rearrangements would occur owing to the presence of an αβ-unsaturated ketone chromophore in a fused-ring system with the β-position adjacent to a tertiary centre. In particular it was hoped that one of the transformation products would be the terpene ketone chrysanthenone (II),[2] * thereby providing a relatively simple synthesis of this otherwise inaccessible compound.

* The identity of chrysanthenone with " car-3-ene 5,6-epoxide " [3] has been suggested by Blanchard [4] and confirmed by Kotake and Nonaka.[5]

[1] Preliminary communication: Hurst and Whitham, *Proc. Chem. Soc.*, 1959, 160.

[2] Kotake and Nonaka, *Annalen*, 1957, **607**, 153.

[3] Penfold, Ramage, and Simonsen, *J.*, 1939, 1496.

[4] Blanchard, *Chem. and Ind.*, 1958, 293.

[5] Nonaka, personal communication.

Preliminary experiments involved the irradiation of verbenone in ethanol with ultraviolet light. The crude product showed infrared bands at 1780 (cyclobutanone?), 1720—1740 (ester C=O), and 1675 cm.$^{-1}$ (C=O of verbenone). Evidently esters were being produced by the interaction of ethanol with the system and further irradiations were carried out, at this stage, in cyclohexane. In this way crude material was obtained which had infrared bands at 1780 and 1675 cm.$^{-1}$ only, in the carbonyl region. The substance responsible for the former band was obtained pure by chromatography. Analysis, together with the boiling point, indicated that it was an isomer of verbenone and the spectral properties [infrared bands at 3030 and 1660 (isolated C=C) and 1780 cm.$^{-1}$ (cyclobutanone), $\lambda_{\text{max.}}$ 290 mμ (ε 120)] are consistent with structure (II), that of chrysanthenone. In particular the abnormally high value of the extinction coefficient of the band at 290 mμ is characteristic of a $\beta\gamma$-unsaturated ketone in which interaction of the double bond and carbonyl group can occur.[6]

Structure (II) for the photo-isomer of verbenone was confirmed as follows. Reduction with lithium aluminium hydride gave an unsaturated alcohol, reoxidisable to the starting ketone with pyridine–chromium trioxide. The unsaturated alcohol was characterised as its crystalline 3,5-dinitrobenzoate and the latter was shown to be identical, by direct comparison, with the corresponding derivative similarly obtained from natural chrysanthenone.[2] * The stereochemistry of the unsaturated alcohol, chrysanthenol (III), is assigned as shown on the basis of preferred attack by hydride from the side remote from the *gem*-dimethyl group, *i.e.*, (V $\longrightarrow$ VI). Kotake and Nonaka's proof of the structure of chrysanthenone excludes formula (IV), which would be produced by migration of the methylene bridge, for the photo-isomer.

During the attempted hydrolysis of the 3,5-dinitrobenzoate of chrysanthenol with methanolic alkali, the isomeric aldehyde[7] (VIII), characterised as its 2,4-dinitrophenylhydrazone, was obtained. This easy ring opening presumably proceeds as shown (VII) and is facilitated by the release of strain associated with the fused ring system. Chrysanthenol was readily regenerated from its 3,5-dinitrobenzoate by cleavage with lithium aluminium hydride.

Since (+)-verbenone is derived from (+)-α-pinene it has the absolute configuration shown in formula (I).[8] The photochemical conversion of a sample of verbenone ($[\alpha]_D$ +222°) into chrysanthenone gave optically active material, $[\alpha]_D$ +37°. Regardless of the precise mechanism of the change it seems highly unlikely that specific inversion of configuration at $C_{(5)}$ † would occur, though, as shown below, the chrysanthenone has a lower optical purity than the verbenone from which it is derived. The transformation thus relates the configuration of verbenone to that of chrysanthenone, the (+)-enantiomer of which is to be represented as in (II), *i.e.*, a derivative of (—)-α-pinene.

This photochemical route to chrysanthenone may be of biogenetic significance. Mechanistically it is probably best represented as a redistribution of electrons in the excited state (IX) involving cleavage of the weakest bond (1,6) and migration of the *gem*-dimethyl bridge to $C_{(3)}$. There is no evidence for the reversibility of this step.

The products obtained from irradiation of verbenone in ethanol were then re-investigated. Chromatography of the crude product gave two esters besides chrysanthenone and unchanged verbenone. One, which predominated, was an $\alpha\beta$-unsaturated ester since it had infrared bands at 1720 (conjugated ester C=O) and 1650 cm.$^{-1}$ (conjugated C=C), and its ultraviolet absorption showed $\lambda_{\text{max.}}$ 215 mμ (ε 9800). The other was a non-conjugated

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* We are indebted to Dr. H. Nonaka, Osaka City University, for the authentic sample.

† Numbering as for pinane.[9]

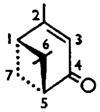
[6] Cookson and Wariyar, *J.*, 1956, 2302.

[7] Jitkow and Bogert, *J. Amer. Chem. Soc.*, 1941, **63**, 1979.

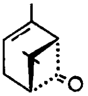
[8] Birch, *Ann. Reports*, 1950, **47**, 191.

[9] "I.U.P.A.C. Nomenclature of Organic Chemistry, 1957," Butterworths, London, 1958, rule A–72.1.

ester as shown by the infrared spectrum (band at 1745 cm.$^{-1}$) and the lack of selective ultraviolet absorption.



(I)



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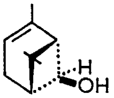

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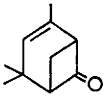

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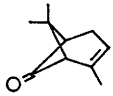

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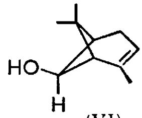

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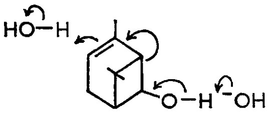
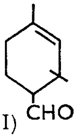
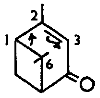


(VII)



(VIII)



(IX)

The structure of the αβ-unsaturated ester was assigned as follows. Analysis, the absorption of two mol. of hydrogen on hydrogenation, and the spectral data indicated an acyclic structure. Hydrolysis of the hydrogenation product gave tetrahydrogeranic acid, thus giving partial formula (X), with an additional double bond, for the parent ester. That it is ethyl geranate (XI) followed from the absence of methylenic infrared absorption and from the fact that treatment with sodium methoxide followed by hydrolysis gave no conjugated diene acid. Authentic ethyl geranate, prepared from citral,[10] had an infrared spectrum similar to but not identical with that of the above conjugated ester. That the two samples differed in geometrical isomer content was shown by their nuclear magnetic resonance spectra[11] which indicated that the ethyl geranate from citral contained a preponderance of the *trans*-isomer (ethoxycarbonyl *trans* to main chain) while the ethyl geranate from verbenone contained more of the *cis*-isomer.

The non-conjugated ester from the irradiation of verbenone in ethanol was shown to be the unconjugated isomer (XII; X = OEt) of ethyl geranate by hydrogenation to ethyl tetrahydrogeranate and by its identity with the ethyl ester obtained from the acid (XII; X = OH) (see below).

(X) $CHMe_2{\cdot}CH_2{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{=}CH{\cdot}CO_2Et$ $CMe_2{=}CH{\cdot}CH_2{\cdot}CH_2{\cdot}CMe{=}CH{\cdot}CO_2Et$ (XI)

$CMe_2{=}CH{\cdot}CH_2{\cdot}CH{=}CMe{\cdot}CH_2{\cdot}CO{\cdot}X$ (XII)

The irradiation of verbenone in the presence of other nucleophiles was also investigated. In aqueous ether the unconjugated acid (XII; X = OH) was the sole acidic product, while ethereal ammonia led to the formation of the amide (XII; X = NH_2). These structures were assigned on the basis of hydrogenation and spectral data.

The formation of these products and the ethyl geranates is regarded as proceeding *via* the keten(s) (XIV, XV) produced by isomerisation of chrysanthenone (XIII), the reaction being initiated by cleavage of the weakest bond $C_{(1)}$–$C_{(6)}$. In agreement with this, irradiation of chrysanthenone in the presence of nucleophiles gave the same products as were obtained from verbenone. Apparently, however, yields are higher when starting from verbenone, so there may be a route whereby an excited state of verbenone can collapse directly to the keten. That keten formation can proceed either photochemically or thermally from chrysanthenone is indicated by the isolation of the same acid (differences in geometrical isomer content being neglected) from both types of reaction with water.

The formation of unconjugated products on reaction of the keten with water and ammonia can be interpreted as involving 1,2-addition (XVI), while formation of a preponderance of the conjugated ester with ethanol is explained by competing 1,4-addition

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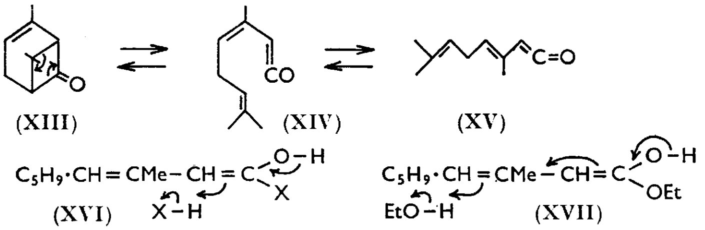
[10] Bernhauer and Forster, *J. prakt. Chem.*, 1936, **147**, 199; Kappeler, Grütter, and Schinz, *Helv. Chim. Acta*, 1953, **36**, 1862.

[11] Burrell, Jackman, and Weedon, *Proc. Chem. Soc.* 1959, 263.

(XVII). The latter may be due to a greater stabilisation of the transition state for 1,4-addition in line with the greater conjugative power of the ester group than of carboxyl or amide groups. An alternative explanation involving isomerisation of previously formed unconjugated ester (XII; X = OEt) was rendered untenable by the finding that pure unconjugated ester, obtained from the corresponding acid, was unaffected either by the conditions of the reaction or by prolonged contact with neutral alumina.


(XIII) (XIV) (XV)

(XVI) (XVII)

Additional evidence in favour of a keten intermediate was obtained from the observation that the optical rotation of isolated chrysanthenone was lower the longer the period of irradiation in cyclohexane. In the absence of nucleophiles, keten formation from chrysanthenone would still be expected to occur, the only reactions available to it being either polymerisation or recyclisation to chrysanthenone. In the latter case racemic material would result, thereby explaining the fall in the rotation of chrysanthenone.

Ketens have previously been postulated as intermediates in a number of cases where carboxylic acids or their derivatives are produced in photochemical transformations of ketones.[12]

EXPERIMENTAL

Ultraviolet and infrared spectra were determined for EtOH and CCl_4 solutions respectively. Light petroleum refers to the fraction of b. p. 40—60°. Unless otherwise stated alumina for chromatography is of activity III.

Verbenone.—*trans*-Verbenol (12 g.) in light petroleum (300 c.c.) was treated with neutral active manganese dioxide[13] (120 g.), and the mixture was stirred until heat was no longer evolved and then shaken at 20° during 1 hr. After filtration the liquid was evaporated and distilled to give verbenone (8 g., 65%), b. p. 102—105°/12 mm., n_D^{18} 1·4957, $\lambda_{max.}$ 253 mμ (ε 6730). Moore and Fisher[14] report n_D^{20} 1·4961, $\lambda_{max.}$ 253 mμ (ε 6840), for verbenone obtained by autoxidation of α-pinene and purified through the semicarbazone.

Chrysanthenone.—Verbenone (1·25 g.) in cyclohexane (125 c.c.) was irradiated under reflux in a quartz flask with ultraviolet light from a Hanovia U.V. S. 500 mercury-arc lamp during 3 hr. (in preliminary runs the course of the reaction was followed by the disappearance of the characteristic ultraviolet absorption peak of verbenone). After evaporation of the cyclohexane the residue was taken up in light petroleum, filtered from a small amount of polymer, and adsorbed on a column of alumina. Elution with light petroleum gave chrysanthenone (0·58 g., 47%) sufficiently pure for further transformations. Further elution of the column with light petroleum–ether (4 : 1) gave unchanged verbenone (0·41 g.).

Further purification of the chrysanthenone was effected by chromatography in light petroleum on a column of activated charcoal–Celite (1 : 1). Material obtained from verbenone of $[\alpha]_D$ +222°, when purified in this way, had b. p. 88—89°/12 mm. n_D^{22} 1·4720, $[\alpha]_D$ +37° (*c* 2·1 in $CHCl_3$), $\lambda_{max.}$ 290 mμ (ε 120) (Found: C, 79·7; H, 9·25. Calc. for $C_{10}H_{14}O$: C, 79·95; H, 9·4%). After irradiation for 9 hr. the chrysanthenone obtained had $[\alpha]_D$ +14°.

Irradiation in dry ether gave similar results.

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[12] Barton and Quinkert, *J.*, 1960, 1; Van Tamelen, Levin, Brenner, Wolinsky, and Aldrich, *J. Amer. Chem. Soc.*, 1959, **81**, 1666.

[13] Henbest, Jones, and Owen, *J.*, 1957, 4909.

[14] Moore and Fisher, *J. Amer. Chem. Soc.*, 1956, **78**, 4362.

Chrysanthenol.—Chrysanthenone (0·5 g.) was reduced with lithium aluminium hydride (0·13 g.) in ether (20 c.c.) in the usual way. The crude product was adsorbed from light petroleum on a short column of alumina; elution with light petroleum gave a trace of unchanged chrysanthenone, and further elution with light petroleum–ether (98 : 2) gave chrysanthenol (0·31 g., 62%). The 3,5-dinitrobenzoate (needles from ethanol) had m. p. 114—116° undepressed on admixture with a sample of the 3,5-dinitrobenzoate of chrysanthenol derived from natural chrysanthenone. The highly characteristic infrared spectra of the two samples were identical (Found: C, 59·25; H, 5·1; N, 8·25. Calc. for $C_{17}H_{18}N_2O_6$: C, 58·95; H, 5·25; N, 8·1%).

Oxidation of Chrysanthenol.—Chrysanthenol (0·1 g.) in pyridine (2 c.c.) was added to pyridine–chromium trioxide complex [from chromium trioxide (0·2 g.)]. After 16 hr. water was added and the product was isolated with ether; its infrared spectrum was essentially the same as that of pure chrysanthenone.

Alkaline Cleavage of the 3,5-*Dinitrobenzoate of Chrysanthenol.*—The 3,5-dinitrobenzoate (0·33 g.) was heated under reflux with 5% methanolic potassium hydroxide (5 c.c.) during 2 hr. After addition of water the product was isolated with ether as an oil (0·1 g.), the infrared spectrum of which had bands at 2700 (C–H of aldehyde) and 1722 cm.$^{-1}$ (CO of aldehyde). This was converted into the 2,4-dinitrophenylhydrazone in the usual way. Chromatography on alumina and elution with chloroform gave 4-formyl-1,3,3-trimethylcyclohexene 2,4-dinitrophenylhydrazone, needles (from ethanol), m. p. 161—162°. Jitkow and Bogert [7] give m. p. 164—165°.

Regeneration of Chrysanthenol from the 3,5-*Dinitrobenzoate.*—The 3,5-dinitrobenzoate (0·93 g.) in dry ether was heated under reflux with lithium aluminium hydride (1·5 g.) during 2 hr. The product (0·43 g.), isolated in the usual way, was chromatographed on alumina. Elution with light petroleum gave some hydrocarbon; further elution with light petroleum–ether (20 : 1) gave chrysanthenol (0·3 g.), identified by its infrared spectrum.

Irradiation of Verbenone in Ethanol.—A solution of verbenone (2·5 g.) in absolute ethanol (200 c.c.) in a silica flask was irradiated with ultraviolet light under reflux during 4 hr. After evaporation, the residue, which had a broad infrared band at 1720—1740 cm.$^{-1}$, was dissolved in light petroleum (10 c.c.). Polymeric material was filtered off and the solution was chromatographed on alumina, fractions being identified by their infrared spectra. Elution with light petroleum gave (i) (0·11 g.) ethyl geranate, (ii) (0·68 g.) a mixture of ethyl geranate and ethyl 3,7-dimethylocta-3,6-dienoate, (iii) (0·23 g.) a mixture of ethyl 3,7-dimethylocta-3,6-dienoate and chrysanthenone, and (iv) (0·26 g.) chrysanthenone. Further elution of the column with light petroleum–ether gave a mixture (0·84 g.) of chrysanthenone and verbenone.

Mixed esters from a number of runs (4·6 g.) were rechromatographed on neutral alumina (activity I), giving fractions (i) eluted with light petroleum–ether (9 : 1), 1·27 g. of ethyl geranate, b. p. 114—116°/10 mm., $\lambda_{max.}$ 215 mμ (ε 9800) (Found: C, 73·6; H, 10·2. Calc. for $C_{12}H_{20}O_2$: C, 73·4; H, 10·3%), (ii) eluted with light petroleum–ether (8 : 2), 0·75 g. of an ester mixture, and (iii) 0·16 g. of ethyl 3,7-dimethylocta-3,6-dienoate.

Characterisation of the Ethyl Geranate.—Hydrogenation of the ester (165 mg.) over prereduced Adams platinum catalyst (100 mg.) in glacial acetic acid (25 c.c.) resulted in the uptake of 42 c.c. of hydrogen (Calc.: $2H_2$ = 42 c.c.); after filtration and evaporation the residue had an infrared spectrum identical with that of authentic ethyl tetrahydrogeranate. Hydrolysis with 10% ethanolic potassium hydroxide was followed by conversion into the amide, m. p. 101—103·5° [from light petroleum (b. p. 60—80°)] undepressed on admixture with authentic tetrahydrogeranamide (prepared in a similar way from authentic ethyl geranate [10]); the infrared spectra of the two samples were identical. The *S*-benzylisothiouronium salt had m. p. 149—151° (from aqueous ethanol), mixed m. p. with an authentic sample (see below) 151—154°.

Attempted Isomerisation of the Ethyl Geranate.—The ester (100 mg.) was heated under reflux with sodium methoxide (from sodium, 0·5 g.) in methanol (10 c.c.) during 1 hr. Water was added and heating continued for 30 min. The acid fraction (90 mg.) showed no selective absorption above 225 mμ.

S-*Benzylisothiouronium Salt of Tetrahydrogeranic Acid.*—Prepared in the usual way from tetrahydrogeranic acid the *derivative* had m. p. 154—155° (from aqueous ethanol) (Found: C, 64·1; H, 9·0. $C_{18}H_{30}N_2O_2S$ requires C, 63·9; H, 8·9%).

Characterisation of the Ethyl 3,7-*Dimethylocta*-3,6-*dienoate.*—The undistilled ester (0·2 g.) was hydrogenated in acetic acid over Adams platinum catalyst, 1·60 mol. of hydrogen being absorbed. The product was identified as ethyl tetrahydrogeranate by its infrared spectrum and by hydrolysis to tetrahydrogeranic acid identified as its *S*-benzylisothiouronium salt.

Irradiation of Verbenone in Aqueous Ether.—Verbenone (1 g.) in ether saturated with water (150 c.c.) was irradiated under reflux during 3 hr. The neutral fraction (0·41 g.) was a mixture of verbenone and chrysanthenone. Distillation of the acid fraction gave 3,7-*dimethylocta*-3,6-*dienoic acid* (0·27 g.), b. p. 100—102°/0·4 mm. (Found: C, 71·35; H, 9·85. $C_{10}H_{16}O_2$ requires C, 71·4; H, 9·6%). The latter was converted, by successive treatment with oxalyl chloride and ammonia, into the amide (0·17 g.) [plates from light petroleum (b. p. 60—80°)], m. p. 87—97°. The amide was unstable and is presumed to be a mixture of stereoisomers owing to the wide m. p. range. Hydrogenation of a portion (125 mg.) in acetic acid proceeded with the uptake of 2·10 mol. of hydrogen and gave tetrahydrogeranamide (123 mg.), having m. p. and mixed m. p. 103—105° after crystallisation from light petroleum (b. p. 60—80°).

The 3,7-dimethylocta-3,6-dienoic acid obtained as above was esterified by dry ethanol (5 c.c.) containing sulphuric acid (1%). The infrared spectrum of the ester was identical with that of ethyl 3,7-dimethylocta-3,6-dienoate obtained by irradiation of verbenone in ethanol. It was unchanged after irradiation in ethanol during 4 hr. or after being adsorbed on a column of alumina for 16 hr.

Irradiation of Verbenone in Ethereal Ammonia.—Verbenone (1·3 g.) in dry ether saturated with ammonia (150 c.c.) was irradiated at 30° during 4 hr. After evaporation the residue was chromatographed on alumina. Elution with light petroleum–ether (4 : 1) gave (0·48 g.) a mixture of chrysanthenone and verbenone. Further elution with ether–ethanol (1 : 1) gave 3,7-*dimethylocta*-3,6-*dienamide* (0·27 g.), m. p. 100—104·5° [from light petroleum (b. p. 60—80°)] (Found: N, 8·25. $C_{10}H_{17}ON$ requires N, 8·4%). On hydrogenation in acetic acid (PtO_2) 2·10 mol. of hydrogen were absorbed, giving tetrahydrogeranamide identified by m. p. and mixed m. p.

Reactions of Chrysanthenone with Water.—(i) Chrysanthenone (150 mg.) was irradiated in ether saturated with water (25 c.c.) during 2 hr. The acidic fraction of the product (15 mg.) had an infrared spectrum identical with that of 3,7-dimethylocta-3,6-dienoic acid obtained as above; the neutral fraction (114 mg.) was unchanged chrysanthenone.

In a similar run verbenone (150 mg.) gave 3,7-dimethylocta-3,6-dienoic acid (50 mg.) and a neutral fraction (80 mg.; chrysanthenone and verbenone).

A control reaction in which chrysanthenone was heated under reflux with aqueous ether in the dark gave no acidic material.

(ii) Chrysanthenone (173 mg.) in dioxan (15 c.c.) and water (6 c.c.) was heated under reflux for 2 hr. The acidic fraction (61 mg.) was 3,7-dimethylocta-3,6-dienoic acid.

Reactions of Chrysanthenone with Alcohols.—The reaction of chrysanthenone with ethanol and methanol was examined, both under irradiation and in the dark, and the products were estimated from a qualitative examination of the infrared spectra of the crude product.

(i) Chrysanthenone in ethanol, irradiated under reflux gave a mixture of ethyl geranate and ethyl 3,7-dimethylocta-3,6-dienoate.

(ii) Chrysanthenone in ethanol, heated under reflux in the dark, gave a similar ester mixture.

(iii) Chrysanthenone in methanol, irradiated at 30—35°, gave a similar mixture of methyl esters on removal of solvent at a low temperature. A control dark reaction produced a smaller amount of esters.

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CHEMISTRY DEPARTMENT, THE UNIVERSITY,
BIRMINGHAM, 15.

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