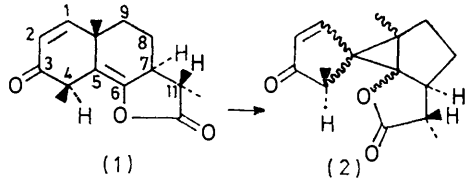
Chemistry of Santonene. Part IX.[1] Photolysis Products of Santonene, and Their Chemical Transformations

By D. Stuart R. East, Kiyoyasu Ishikawa, and T. Brian H. McMurry,* Chemistry Department, Trinity College, Dublin 2, Ireland

Irradiation of santonene [3-oxo-4α*H*-eudesma-1,5,7(11)-trien-12,6-olactone] (3) affords photosantonenes A and B [(4) and (5)] which both possess a spiro(bicyclo[3.1.0]hexane)-6,1'-cyclopentane skeleton, and are in thermal equilibrium. Both give 1,2-dihydro-derivatives, (6) and (7). These in turn can be equilibrated (at 110°) with their 6,10-isomers, (11) and (12) respectively.

Treatment of dihydro-A (6) with acetic acid–hydrogen chloride affords the cyclopentenone (13a). This can also be obtained from the keto-acid (14), which itself is derived from the known photopyrosantonins A and D. The cyclopentenone (13a) and an isomer (13b) can also be prepared from photosantonene A by reduction with zinc. Treatment of (13b) with base affords (13a). Over-reduction of photosantonene A affords a hexahydro-derivative (16a) with opening of the cyclopropane ring. The photo-isomer A also undergoes acid catalysed methanolysis to the methoxy-lactone (17b). This equilibrates with the isomer (17a) in trifluoroacetic acid–benzene. Pyrolysis of photosantonene A affords partially racemised santonene.

In Part VIII,[1] we reported that 4α*H*-pyrosantonin (1), like an analogous steroid system,[2,3] underwent a photochemical transformation to four products of general formula (2). Two of these isomers were formed in a



(1) (2)

symmetry allowed process,[4] and two by a secondary photochemical process. Schaffner *et al.* have also investigated the photolysis of a 4,4-dimethyl-1,5-dien-3,7-dione system.[5] We have available santonene (3),[6] an analogue of pyrosantonin in which there is a 5,7(11)-dienelactone chromophore. In our hands, irradiation of santonene affords only two products, photosantonenes A and B, (4) and (5) respectively.

The photosantonene isomers show physical properties expected for the gross structure [as in (4)]. Thus, they show n.m.r. signals attributable to angular methyl, 11-methyl, 4-methyl, and cyclopentenone vinyl hydrogens. The u.v. spectrum of isomer-A is somewhat unusual in that it shows a plateau between 240 and 257 nm. This can be attributed to overlapping chromophores, due to an αβ-unsaturated ketone and an αβ-unsaturated lactone both conjugated with the cyclopropane ring. The u.v. spectrum of isomer-B (5) showed only a peak at 255 nm. The i.r. spectra support the presence of cyclopentenone and butenolide systems. Reduction of (4) and (5) afford dihydro-derivatives (6) and (7) which show u.v. peaks at *ca.* 255 nm. The c.d. spectra of photosantonenes A and B both show negative $n \longrightarrow \pi^*$ peaks at *ca.* 330 nm., indicating that they have the same stereochemistry at the 4-position, and that it is identical with that of the photopyrosantonins.[1]

We first wished to assign the stereochemistry at the 10- and hence the 6-position in both isomers. This assignment was complicated by the fact that the isomers (4) and (5) equilibrate in non-polar solvents even at room temperature. This easy thermal transformation also prevents us from determining whether or not the process is promoted photochemically. The thermal transformation (4) $\rightleftharpoons$ (5), like the corresponding photochemical process in the photopyrosantonins,[1] probably proceeds through the 5,6-diradical (8) or equivalent species. Conjugation would be expected to stabilise both diradicals, thus explaining the ease with which the reaction occurs. With the corresponding photopyrosantonins, rearrangement is only induced photochemically or under acidic conditions.[1]

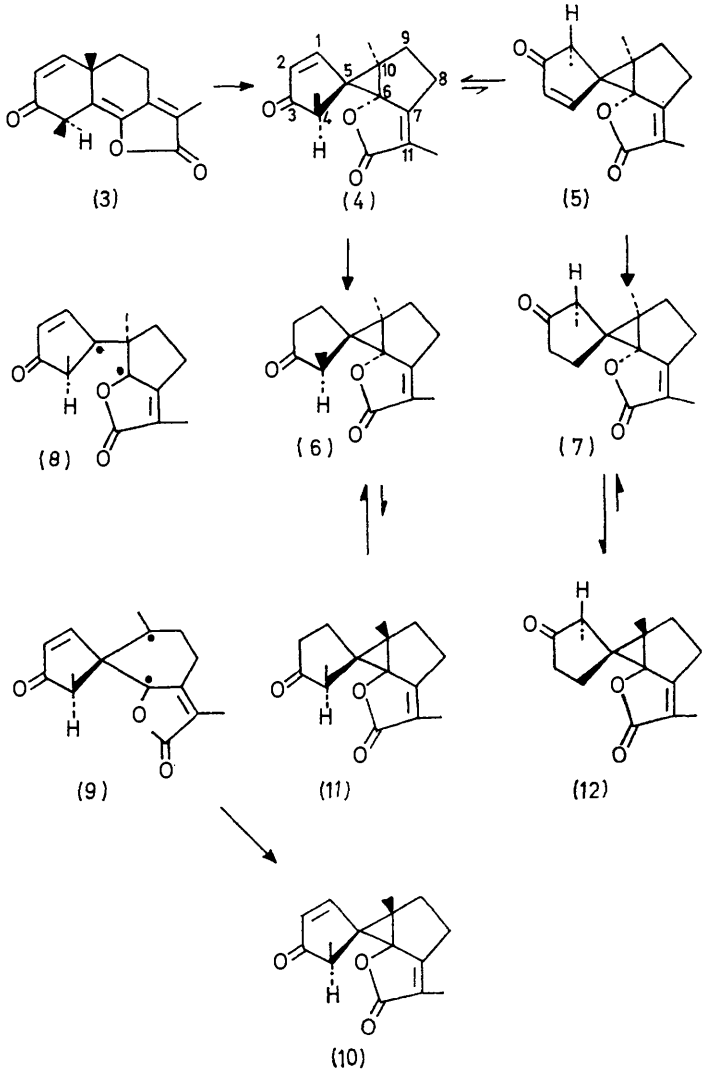
We cannot exclude, however, the possibility that the equilibrium is set up *via* a 6,10-diradical (9). This would lead to a structure (10) for photosantonene B which differed from that of the isomer-A at the 6- and 10-positions. This implies that we cannot use evidence derived from experiments during which the equilibrium can be achieved, to deduce the stereochemistry at the 10-position of either isomer.

However, we can prove the stereochemistry of the two photoproducts as follows. Compounds (4) and (5) give the dihydro-derivatives (6) and (7) respectively, and these are not identical. Dihydrophotosantonene-A (6) on pyrolysis in toluene is in equilibrium with an isomer, isodihydro-A (11), the equilibrium lying largely on the side of (6). Dihydro-B (7) under the same conditions is in equilibrium with isodihydro-B (12), the equilibrium lying on the side of isodihydro-B (12). The iso-compounds are not identical with the dihydro-derivatives, or with each other.

The c.d. spectra of (6) and (7) show negative peaks at 231—236 nm attributable to the $\pi \longrightarrow \pi^*$ transition

[1] Part VIII, K. Ishikawa and T. B. H. McMurry, *J.C.S. Perkin I*, 1973, 914.
[2] B. Nann, D. Gravel, P. Shorta, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, 1963, **46**, 2473.
[3] B. Nann, H. Wehrli, K. Schaffner, and O. Jeger, *Helv. Chim. Acta*, 1965, **48**, 1680.
[4] R. B. Woodward and R. Hoffmann, *Angew. Chem. Internat. Edn.*, 1969, **8**, 781.
[5] S. Domb and K. Schaffner, *Helv. Chim. Acta*, 1970, **53**, 1765.
[6] T. B. H. McMurry and R. C. Mollan, *J. Chem. Soc.* (*C*), 1967, 1813.

of the butenolide chromophore. The corresponding peaks in the c.d. spectra of (11) and (12) are positive. As the sign of these peaks must be linked with the stereochemistry at the 6-position,* it follows that dihydro-A and -B have identical stereochemistry at the 6- and 10-positions, and that the equilibria mentioned above are achieved by rupture and reformation of the 6,10-bond.[1] The ease with which the reaction occurs compared with the analogous rearrangement with photopyrosantonin can be attributed to the greater stability of the transition states involved in the former case.



Examination of models of (6), (7), (11), and (12) shows that in (12) the 4-methyl group lies over and within the shielding zone of the 7(11)-double bond, and that in (6), the 4-hydrogen is similarly placed. The 4-methyl signal in the n.m.r. spectrum of isodihydrosantonene B (12) lies at high field (see Table 1) and the 4-hydrogen signal of dihydrophotosantonene A (6) also lies at high field. The 4-hydrogen signal in (6) is at τ 7·86 (decoupling experiment) and in (7), (11), and (12) is at *ca.* τ 7·5. This leads to the assignment of structure (6) to dihydrophotosantonene A and of (12) to isodihydrophotosantonene B. The structures (4) and (5) follow for photosantonene A and B respectively.

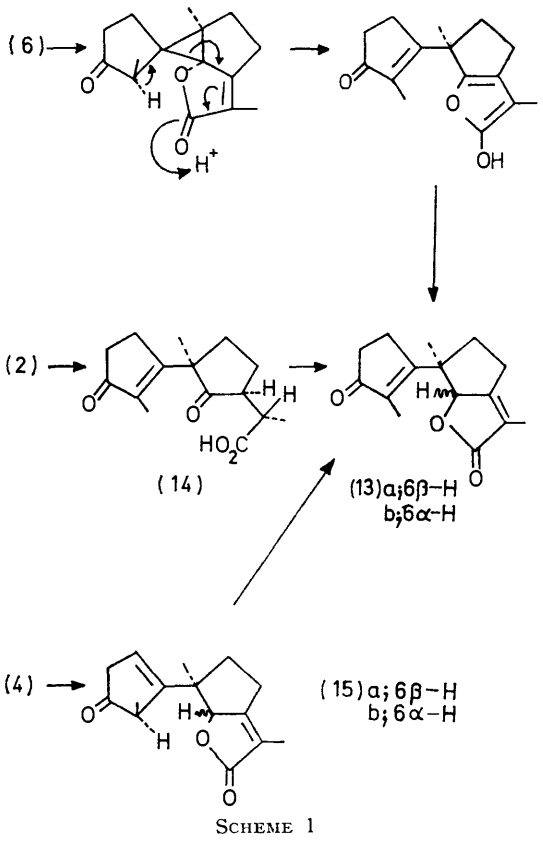
In each case, (4) $\rightleftharpoons$ (5), (6) $\rightleftharpoons$ (11), and (7) $\rightleftharpoons$ (12), the equilibrium lies on the side of the compound in which the 1-carbon and lactone 6-oxygen are *cis* with respect to the cyclopropane ring. The interactions between the 4-methyl and 10-methyl or 6-oxygen may be responsible for the instability of the less favoured isomer.

These assignments were confirmed by further experiments. Dihydrophotosantonene A (6) on treatment

* The sign of a second lactone $\pi \longrightarrow \pi^*$ band at *ca.* 260 nm cannot be correlated with the stereochemistry at position 6 but this peak appears in several cases only as an inflection of the side of the larger $\pi \longrightarrow \pi^*$ peak, and the true sign of the peak may not be apparent. The u.v. maxima for the dihydro-compounds lies between the two $\pi \longrightarrow \pi^*$ bands in the c.d. spectrum.

with acetic acid–hydrogen chloride at 60° affords the cyclopentenone (13a) by the mechanism depicted in Scheme 1. It is unlikely that acidic catalysis can effect the isomerisation (6) ⇌ (11), prior to the opening of the cyclopropane ring. The cyclopentenone (13a) can be derived from the diketo-carboxylic acid (14), which itself can be derived from photopyrosantonin A or D, which possess a 10α-methyl group.[1] The ring closure of the keto-acid (14) is best achieved by using trifluoroacetic anhydride, followed by treating the resulting mixture (4 spots on t.l.c., and not investigated further) with triethylamine.

N.O.e. measurements on photosantonene-A (4) show that the 10-methyl and 1-hydrogen are in close proximity



SCHEME 1

to one another. There is a 14% enhancement of the 1-proton signal when the 10-methyl group is irradiated. Further, the 1-proton signal in the simple n.m.r. spectrum is at lower field with photosantonene A than with B (*cf.* reference 1).

The keto-lactones (13a) and (13b) can also be prepared, in a stereochemically more ambiguous experiment, by reduction of photosantonene A (4) with zinc–acetic acid to afford the βγ-unsaturated ketones (15a) and (15b) which were not isolated, but were recognised from their n.m.r. spectra. Acidic treatment rearranges the βγ-enones to the αβ-enones (13a) and (13b).[1,7]

The two enones (13a) and (13b) can be distinguished by the position of the 10-methyl peaks in the n.m.r. spectra. In the 6β*H*-isomer (13a), the 10-methyl lies close to the shielding zone of the 7(11)-double bond and the lactone carbonyl group, and hence lies at higher field (τ 9·08) than the corresponding peak in the 6α*H*-isomer (13b) (τ 8·40). Parallel behaviour is found in the βγ-enones (15a) and (15b). Analogues for this assignment are found in the n.m.r. spectra of the 6-hydroxy- and 6-acetoxy-santonenes.[8]

The assignment above is confirmed by n.O.e. measurements. Irradiation of the 10-methyl signal in (13a) and (13b) causes a 9—10% increase in the 6-hydrogen signal in the latter, but not the former. C.d. measurements of (13a) and (13b) are not conclusive, as the $\pi \longrightarrow \pi^*$ peaks of the αβ-unsaturated lactone and ketone chromophores appear to overlap, and no satisfactory deduction can be made, even though the relevant peaks are of opposite sign.

The two enones are stable under acidic conditions, but with base, and in the presence of a proton donor (13b) is converted into (13a). In (13b), there are steric interactions between the bulky cyclopentenyl group and the 6-oxygen. This accounts for the single product (13a) formed in the preparation from the ketoacid (14) using base.

The mass spectra of both keto-lactones show a molecular ion peak, and three other major peaks in each case, at *m/e* 110, 82, and 53. These correspond to the fragmentation pattern shown in Scheme 2. This pattern is confirmed by mass spectrum of the 6-deuterio-keto-lactone (as 13a) which shows peaks at *m/e* 111, 83, and 53. The molecular ion peaks are at *m/e* 248 and 249, corresponding to the introduction of two or three deuterium atoms at the 1- or 2- and 6-positions. In the undeuteriated compounds (13a) and (13b) there is a metastable peak at *m/e* 61, corresponding to the fragmentation *m/e* 110 ⟶ 82.

We have described the reduction of photosantonene-A to its dihydro-derivative. Over-reduction leads to the formation of the hexahydro-derivative (16a). Neither photosantonene B nor the photopyrosantonins[1] undergo this reaction. The reduction removes both the cyclopropane ring and the 7(11)-double bond. We suggest that in dihydrophotosantonene-A (6), the geometry of the molecule is such that the β-face (cyclopropane and B-rings) is absorbed onto the catalyst surface, and hydrogenolysis of the cyclopropane ring thereby achieved. The dihydrophotopyrosantonins lack the 7(11)-double bond, and therefore are not held on the catalyst surface. In dihydrophotosantonene B, the geometry of the A-ring is such that the 4-methyl group might prevent absorption.

We have carried out the experiments which suggest that the hexahydro-compound has the stereochemistry (16a). The 5-hydrogen must be β-oriented (*trans*

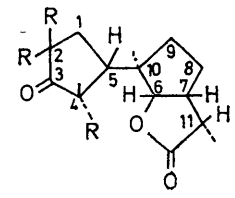
[7] D. S. R. East, T. B. H. McMurry, and R. C. Mollan, *J. Chem. Soc.* (*C*), 1970, 2008.
[8] C. Ouannes and J. Jacques, *Bull. Soc. chim. France*, 1965, 3601.

to the 4-hydrogen [9]) as deuterium exchange replaces three hydrogens in the 2- and 4-positions (16b) (n.m.r. and mass spectrum) *without* inversion.

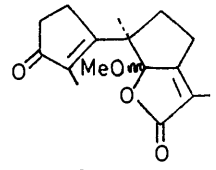
The 6-hydrogen appears to be β-oriented, as the 6-hydrogen shows no n.O.e. when the 10α-methyl is irradiated. We assume that the 6-, 7-, and 11-hydrogens are all *cis*.

The rupture of the 5,6-bond during hydrogenolysis thus proceeds with retention of configuration at the 6-position, but with inversion at the 5-position. However, the stereochemistry of the hydrogenolysis merits further investigation.

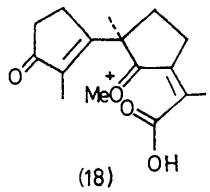
The hexahydro-compound shows mass spectral peaks at *m/e* 250 (molecular ion), 125, 112, 97, and 55. The



(16) a; R = H
b; R = D



(17) a; 6β—OMe
b; 6α—OMe



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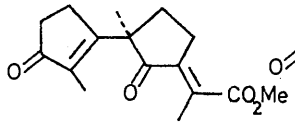

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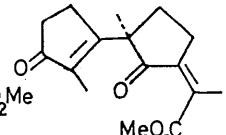

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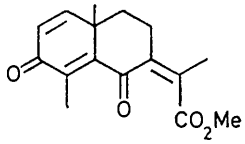
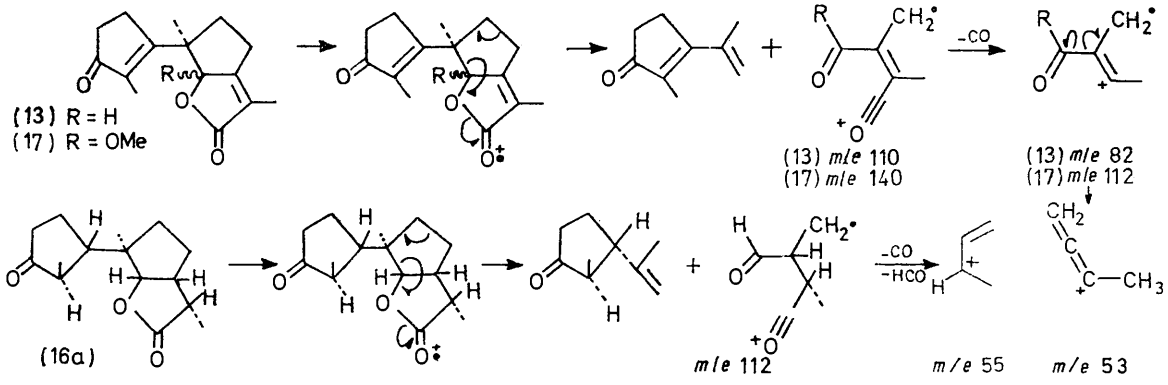


(21)

The cyclopropane ring is also cleaved by acid. Treatment of photosantonene A with methanolic hydrogen chloride affords as the primary product the 6α-methoxy-keto-lactone (17b). If the reaction is worked up by pouring the mixture into sodium hydrogen carbonate solution, (17b) is the only product detected. If the reaction is carried out under more acidic conditions and worked up by removing the solvent under reduced pressure, then two products can be isolated, (17b) and the 6α-methoxy-isomer (17a). The two methoxy-lactones can be separated by preparative thin layer chromatography (p.l.c.), and both show methoxy-methyl signals at *ca.* τ 6·8 in their n.m.r. spectra.



SCHEME 2

fragmentation path is suggested in Scheme 2. The trideuteriated compound (16b) in addition to the molecular ion mentioned above shows peaks at *m/e* 127, 126, 112, 99, and 98. Peaks at 125 and 97 from the undeuteriated compound (16a) are unaccounted for in Scheme 2. This parallel between the fragmentation patterns of (13a), (13b), (16a), (17a), and (17b) (see below) suggests that all these compounds possess very similar ring skeletons.

The two methoxy-lactones can be distinguished in the same way as the two lactones (13a) and (13b). The 10-methyl group in (17a) lies close to the shielding zone of the 7(11)-double bond and the lactone carbonyl group, and its n.m.r. signal is at high field (τ 9·04). The c.d. spectra are not informative. Incidentally,

[9] G. Stork, G. L. Nelson, F. Rouessac, and O. Gringore, *J. Amer. Chem. Soc.*, 1971, **93**, 3091; R. E. Ireland and R. H. Mueller, *ibid.*, 1972, **94**, 5898.

precedent [1,7] is available for the isomerisation of the 1,2-double bond in photosantonene A (14) to the 4,5-double bond in (17a) and (17b).

The methoxy-lactone (17b) on treatment with trifluoroacetic acid in benzene affords an equilibrium mixture of (17a) and (17b) in which the 6β-methoxy-compound (17a) predominates (approximate ratio 10 : 1). The intermediate is presumably the methoxonium ion (18).

The mass spectra of the two methoxy-lactones (17a) and (17b) show peaks at *m/e* 276, 140, 112, and 53. The fragmentation pattern is similar to that of the keto-lactones (13a) and (13b) (Scheme 2). In these cases, metastable peaks occur at *m/e* 90 and 71, corresponding to the fragmentation 140 ⟶ 112 and 276 ⟶ 140 respectively, indicating concerted processes.

Besides the two methoxy-lactones (17a) and (17b), two other products are formed by the action of methanolic hydrogen chloride on photosantonene A. Also treatment of either methoxy-lactone with methanolic hydrogen chloride affords a mixture containing these compounds. They can be separated from the methoxy-lactones, but not from each other, by p.l.c., but any attempt at purification leads to decomposition. However, their presence, and probable structure, is indicated by the n.m.r. spectrum of the equilibrium mixture. The main product appears to be the keto-ester (19), with peaks at τ 8·65 (10-Me), 8·36 (4-Me), 7·65 (11-Me), and 6·22 (OMe). The minor product is the geometrical isomer (20) with peaks at τ 8·75 (10-Me), 8·0 (4- and 11-Me), and 6·22 (OMe). The known keto-ester [8] (21) shows n.m.r. peaks at τ 8·75 (10-Me), 7·98 (4- and 11-Me), and 6·20 (OMe).

Photosantonene A (4) on pyrolysis in diphenyl ether at 252° affords santonene which is *partially racemic*. This implies some breaking and reforming of both the 5,10- and the 6,10-bonds. In the experimental section we describe an easier method for the production of (−)santonene.

EXPERIMENTAL

For general experimental details, see Part VIII.[1]

Santonene (3).—(a) A solution of santonenic acid [6] (10 g) in benzene (200 ml) was evaporated to 100 ml. The solution was cooled, and trifluoroacetic anhydride (9 ml) was added dropwise with stirring. The mixture was heated at 70° for 1 h. The solution was concentrated under reduced pressure and the residue triturated with ethanol (10 ml) to give santonene [3-oxo-4α*H*-eudesma-1,5,7(11)-trien-12,6-olactone] (5 g), m.p. 145°. The residue on chromatography on silica (150 g) gave a further sample of santonene (1·6 g).

(b) Use of oxalyl chloride (5 ml) instead of trifluoroacetic anhydride afforded santonene (5 g).

Photosantonenes A *and* B (4) *and* (5).—(a) *Photolysis in benzene.* Santonene (500 mg) in dry benzene (45 ml) was irradiated for 6 h under the conditions described previously. Evaporation under reduced pressure, and chromatography of the residue on silica gel (100 g) using ether–light petroleum (60 : 40 to 80 : 20) as eluant afforded *photosantonene* A (4) (374 mg) as rhombs, m.p. 138—139° (from ethyl acetate–light petroleum), $[\alpha]_D^{20}$ +370° (*c* 3·8) (Found: C, 73·95; H, 6·6. $C_{15}H_{16}O_3$ requires C, 73·75; H, 6·6%), *m/e* 244 (M^+), $\nu_{max.}$ 1755, 1708, 1670, and 1570 cm^{-1}, $\lambda_{max.}$ 257—247 nm (log ε 4·26), c.d. (methanol) 335, 264, and 234 nm (Δε − 1·51, +41·95, and −54·0), τ 8·68 (d, *J* 8 Hz, 4-Me), 8·45 (10-Me), 8·11br (s, 11-Me) 3·79 (d, *J* 6 Hz, 2-H), and 2·42 (d, *J* 6 Hz, 1-H). From later fractions, *photosantonene* B (5) (73 mg) was isolated as needles, m.p. 105—106° (from ethyl acetate–light petroleum), $[\alpha]_D^{21}$ −330° (*c* 0·14 in ethanol) (Found: M^+, 244·1121. $C_{15}H_{16}O_3$ requires *M*, 244·1099), $\nu_{max.}$ 1757, 1705, 1675, and 1570 cm^{-1}, $\lambda_{max.}$ 255 nm (log ε 4·52), c.d. (methanol) 328, 276, and 226 nm (Δε −2·43, −6·39, and −11·4), τ 8·62 (d, *J* 8 Hz, 4-Me), 8·56 (10-Me), 8·05br (s, 11-Me), 3·77 (d, *J* 6Hz, 2-H), and 2·52 (d, *J* 6 Hz, 1-H).

(b) *Photolysis in ether.* Santonene (3) (250 mg) was irradiated in dry ether (45 ml) for 3·5 h. Chromatography over silica gel gave photosantonene A (4) (210 mg). Traces of isomer-B were detected by t.l.c.

1,2-*Dihydrophotosantonene* A (6).—Photosantonene A (200 mg), 5% palladium–charcoal (100 mg), and ethyl acetate (50 ml) were stirred in an atmosphere of hydrogen until 1 mol. of hydrogen was absorbed (10 min). Chromatography over silica (30 g) afforded 1,2-*dihydrophotosantonene* A (6) (180 mg). The physical constants and spectral data are recorded in Table 1.

1,2-*Dihydrophotosantonene* B (7).—Photosantonene B (50 mg) and palladium–charcoal (50 mg) in ethyl acetate (50 ml) was hydrogenated as above for 1 h to give *dihydrophotosantonene* B (7) (11 mg). The physical properties of the compound are recorded in Table 1.

Equilibration of Photosantonenes A *and* B [(4) ⇌ (5)].—(a) Photosantonene A (860 mg) in benzene (50 ml) was refluxed for 2 h. The mixture (ratio 9 : 1 by n.m.r.) was chromatographed over silica (200 g) to give photosantonenes *A* (590 mg) and *B* (48 mg) (from ethyl acetate–light petroleum). The compounds were identified by their i.r. and n.m.r. spectra.

(b) Photosantonene *B* (10 mg) in deuteriochloroform (0·3 ml) was set aside at 33° for 48 h, monitoring the reaction by n.m.r. The mixture consisted of photosantonenes A and B in the ratio 9 : 1. Photosantonene A was isolated after crystallisation, and identified by i.r. and n.m.r. spectra.

Equilibration of 1,2-*Dihydrophotosantonene* A (6) *and Iso*-1,2-*dihydrophotosantonene A* (11).—1,2-Dihydrophotosantonene A (6) (200 mg) and toluene (50 ml) were refluxed for 5 h. The solvent was removed, and the residue chromatographed over silica (100 g) to give starting material (166 mg) and *iso*-1,2-*dihydrophotosantonene* A (11) (16 mg). Physical constants are recorded in Table 1.

Equilibration of 1,2-*Dihydrophotosantonene* B (7) *and Iso*-1,2-*dihydrophotosantonene* B (12).—1,2-Dihydrophotosantonene B (7) (50 mg) and toluene (50 ml) were refluxed for 5 h. P.l.c. gave *iso*-1,2-*dihydrophotosantonene* B (12) (26 mg). Traces of dihydrophotosantonene B were detected by t.l.c. Physical constants are recorded in Table 1.

The Keto-lactones (13a) *and* (13b).—(a) 1,2-Dihydrophotosantonene A (6) (50 mg), and 0·5N-acetic acid–hydrogen chloride (20 ml) were heated to 55—60° for 2 h. Removal of the solvent and purification by p.l.c. (ethyl acetate–ether–light petroleum, 1 : 1 : 1) afforded the *keto-lactone* (13a) (39 mg). The physical properties are recorded in Table 2.

(b) The diketo-carboxylic acid (14) as its hydrate (45 mg) in benzene (50 ml) was azeotropically distilled to 25 ml. Trifluoroacetic anhydride (60 mg) was added, and the mixture refluxed for 2 h. T.l.c. showed four spots. Triethylamine (1 ml) was added, and the solution was refluxed for 30 min. Ethyl acetate and dilute hydrochloric acid were added, and the organic layer was washed with sodium hydrogen carbonate solution, and saturated sodium chloride solution. The solution was dried (Na_2SO_4), and evaporated under reduced pressure. The resulting oil was purified by p.l.c. to give the keto-lactone (13a) (19 mg) identical (m.p., mixed m.p., and $[\alpha]_D$) with the keto-lactone prepared as in (a).

(c) Photosantonene A (4) (100 mg), powdered zinc (1·0 g), and acetic acid (40 ml) were stirred at 25° for 18 h. Removal of the zinc and solvent, and extraction of the residue with chloroform afford an oily mixture of the keto-lactones (15a), τ 9·16 (10-Me), 8·58 (d, *J* 8 Hz, 4-Me), 8·16 (m, 11-Me) 7·07 (m, 2- and 4-H), 5·05 (m, 6-H), and 4·06 (m, 1-H) and (15b), τ 8·75 (10-Me), 8·77 (d, *J* 8 Hz, 4-Me), 8·16 (m, 11-Me), 7·17 (m, 2-H and 4-H), 5·23 (m, 6-H) and 4·36 (m, 1-H). The two products occur in the approximate ratio of 2 : 1.

The crude mixture was treated directly with trifluoroacetic acid (0·5 ml) in benzene (5 ml) at 55—60° for 2 h. The solvent was removed under reduced pressure, and the resulting mixture was separated by p.l.c. to give (13a) (50 mg) and (13b) (22 mg). The lactone (13a) was identical with that prepared in (a). Physical properties are recorded in Table 2.

Isomerisation of the Keto-lactone (13b).—The keto-lactone (13b) (35 mg) and triethylamine (1 ml) in methanol (10 ml) were refluxed for 1 h (the solution being monitored by t.l.c.). Removal of base and solvent and purification by p.l.c. afforded the keto-lactone (13a) (17 mg) identical (m.p., mixed m.p., and n.m.r.) with a sample prepared as above. Neither trifluoroacetic acid nor triethylamine alone in benzene caused the isomerization.

Deuteriated Keto-lactone (13a).—The keto-lactone (13a) (17 mg), [$^2H_4$]methanol (5 ml) and triethylamine (0·7 ml) were refluxed for 2 h. The n.m.r. spectrum of the residue was identical with that of (13a) except for the absence of the 6-hydrogen peak (τ 4·94) and changes in the region τ 7·1—7·8, *m/e* 249, 248, 111, 83, and 53.

Hexahydrophotosantonene A (16a).—Photosantonene A (200 mg) and 5% palladium–charcoal (100 mg) in ethyl acetate (50 ml) were stirred in an atmosphere of hydrogen for 40 min to give *hexahydrophotosantonene* A (16a) (150

TABLE 1

Physical properties of dihydro- and isodihydro-photosantonenes

		Dihydro-A (6)	Isodihydro-A (11)	Dihydro-B (7)	Isodihydro-B (12)
M.p. (form) [a]		167—168° (rhombs)	144—146° (needles)	144—146° (needles)	165—166° (needles)
$[\alpha]_D^{21}$ (*c*)		+ 140° (2·7 in chloroform)	+ 320° (0·08 in ethanol)	+ 52° (0·065 in ethanol)	+ 109° (0·10 in ethanol)
Analysis (%)	Found [b] C	73·5	73·6	73·5	73·0
	H	7·3	7·2	7·3	7·5
	M+	246	246	246	246
$\lambda_{max.}$/nm (log ε)		258 (4·23)	261 (3·95)	255 (4·01)	257 (3·50)
$\nu_{max.}$/cm^{-1}		1740	1745	1735	1735
		1660	1670	1670	1670
C.d. $\lambda_{max.}$/nm (Δε) in methanol		300 (+3·10)	289 (+3·61)	298 (+7·02)	298 (+9·0)
		264 (+3·26)			263 (−3·54)
		231 (−12·00)	236 (+16·2)	235 (−16·75)	232 (+16·00)
τ (*J*/Hz)	4-Me	8·8 (d,8)	8·81 (d, 8)	8·76 (d, 8)	9·01 (d,8)
	10-Me	8·65	8·65	8·73	8·64
	11-Me	8·15	8·16	8·15	8·14

[a] From ethyl acetate–light petroleum. [b] $C_{15}H_{18}O_3$ requires C, 73·2; H, 7·4%, *M*, 246.

TABLE 2

Physical properties of keto-lactones (13a) and (13b) and 6-methoxy-lactones (17a) and (17b)

		(13a)	(13b)	(17a)	(17b)
M.p. (form)		136° (needles) [a]	152—153° (leaflets) [a]	87—88° (needles) [b]	114—115° (rhombs) [a]
$[\alpha]_D^{20}$ (*c*)		+62° (0·090 in ethanol)	−20° (0·080 in ethanol)	+10° (0·070 in ethanol)	+4·7° (2·15 in chloroform)
Analysis (%)	Found [c] C	73·4	73·6	68·9	70·1
	H	7·2	7·3	7·3	7·6
	M+	246	246	276	276
$\lambda_{max.}$/nm (log ε)		233 (4·29)	222 (4·15)	236 (4·16)	235 (4·08)
			237sh (4·06)		
$\nu_{max.}$/cm^{-1}		1740	1745	1755	1760
		1685	1685	1698	1695
		1625	1615	1627	1615
C.d. $\lambda_{max.}$/nm (Δε) in methanol		242 (+15·3)	248 (−3·38)	242 (+6·65)	237 (+6·37)
		217 (−24·4)	220 (+8·74)	213 (−18·81)	222 (−4·01)
					206 (+8·61)
		9·08 (10-Me)	8·40 (10-Me)	9·04 (10-Me)	8·53 (10-Me)
		8·14 (m,4- and 11-Me)	8·21 (m, 4-Me)	8·22 (m,4-Me)	8·20 (br, 4- and 11-Me)
		4·94 (m,6-H)	8·15 (m,11-Me)	8·10 (br, 11-Me)	
			5·15 (m,6-H)	6·88 (OMe)	6·80 (OMe)

[a] From ethyl acetate–light petroleum. [b] From ether–light petroleum. [c] $C_{15}H_{18}O_3$ requires, C, 73·1; H, 7·4%, *M*, 246; $C_{16}H_{20}O_4$ requires, C, 69·5; H, 7·3%, *M*, 276.

mg) as needles (from ethyl acetate–light petroleum), m.p. 81—82°, $[\alpha]_D^{20}$ +5·0° (*c* 2·5) (Found: C, 72·0; H, 8·9. $C_{15}H_{22}O_3$ requires C, 72·0; H, 8·9%), *m/e* 250 (M^+), $\lambda_{max.}$ 280 nm (log ε 1·44), $\nu_{max.}$ 1770 and 1735 cm^{-1}, τ 9·00 (10-Me), 8·82 (d, *J* 6 Hz, 4-Me), 8·78 (d, *J* 7 Hz, 11-Me) and 5·48 (d, *J* 7 Hz, 6-H). The 4- and 11-signals were distinguished by decoupling experiments.

Attempted Isomerisation of Hexahydrophotosantonene A (16a).—(a) The keto-lactone (16a) (30 mg), and trifluoroacetic acid (0·5 ml) were heated at 70° for 2 h. Removal of the solvent gave starting material (n.m.r. and mixed m.p.).

(b) The keto-lactone (16a) and [^{2}H]trifluoroacetic acid (0·5 ml) were heated as above. The n.m.r. spectrum was identical with that of the starting material, except that the 4-methyl signal was a singlet (τ 8·83) and the methylene multiplet centred at τ 7·75 disappeared, *m/e* 253 (M^+).

The 6α-*Methoxy-keto-lactone* (17b).—(a) Photosantonene A (150 mg) and 0·1N-methanolic hydrogen chloride (10 ml) were set aside at room temperature for 16 h. The mixture was poured into 5% sodium hydrogen carbonate solution, and extracted with chloroform. Removal of the solvent gave the 6α-*methoxy-lactone* (17b) (80 mg). Physical constants are recorded in Table 2.

(b) Photosantonene A (100 mg) and 0·5N-methanolic hydrogen chloride (20 ml) were set aside at room temperature for 24 h. The solvent was removed under reduced pressure to give a gum. Separation by p.l.c. afforded the 6β-methoxy-lactone (17a) (28 mg), the 6α-methoxy-lactone (17b) (45 mg), and a mixture of (19) and (20) (18 mg).

Equilibration of 6α- *and* 6β-*Methoxy-keto-lactones* [(17b) ⇌ (17a)].—(a) The 6α-methoxy-lactone (17b) (50 mg), trifluoroacetic acid (0·5 ml), and benzene (30 ml) were refluxed for 6 h. Removal of the solvent under reduced pressure gave a mixture of (17b) and (17a), in the ratio of 1 : 10 (n.m.r.). Separation of the mixture by p.l.c. afforded the 6β-methoxy-lactone (17a) (43 mg). Physical constants are recorded in Table 2.

(b) The 6β-methoxy-lactone (17a) (20 mg), and N-methanolic hydrogen chloride (15 ml) were refluxed for 3 h. The solvent was removed to give a mixture of (17a), (19), and (20) recognised by their n.m.r. spectra and t.l.c.

(c) The 6α-methoxy-lactone (17b) (30 mg) under the same conditions afforded a mixture of (17a), (19), and (20).

Pyrolysis of Photosantonene A (4).—Photosantonene A (100 mg) and diphenyl ether (5 ml) were heated at 252° for 15 min. Chromatography and crystallisation from ethyl acetate–light petroleum gave partially racemised santonene (33 mg) as rhombs, m.p. 127—130°, $[\alpha]_D^{24}$ +100° (*c* 0·065) (optically active santonene shows [6] m.p. 142—146°, $[\alpha]_D^{21}$ +196°) (Found: C, 73·6; H, 6·5. Calc. for $C_{15}H_{16}O_3$: C, 73·75; H, 6·6%). The i.r. spectrum was identical with that of optically active santonene.

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