The Chemistry of Santonene. Part VII.[1] The Action of Phosphorus Trihalides on the Santonins, Santonene, and Related Compounds

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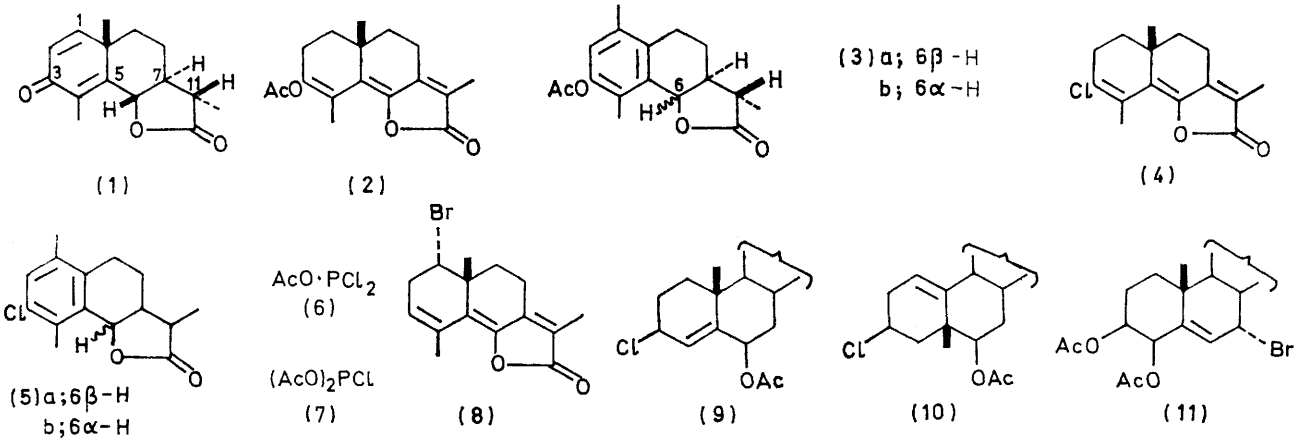
Treatment of santonin with acetyl chloride–acetic anhydride–hydrogen chloride gives 3-acetoxyeudesma-3,5,7(11)-trien-6,13-olide and also *cis*- and/or *trans*-desmotroposantonin acetates, the corresponding compounds with AcO replaced by Cl. The same chloro-compounds can be obtained in greater yield by using phosphorus trichloride in acetic acid. The action of both phosphorus trichloride and the tribromide in acetic acid on β-santonin, pyrosantonin, santonene, β-santonenic acid, 8-oxosantonin and other derivatives of santonin is reported: either the eudesma-3,5,7-trien-6,13-olide or the eudesma-3,5-dien-6,13-olide chromophoric group with 1α- or 1β-halogen substituents is formed. In no other case apart from that of the two santonins is halogen found in the 3-position.

SOME years ago, we investigated the action of acetic anhydride–acetyl chloride on santonin (1).[2] The products were identified as the enol acetate (2) and the *trans*- and/or *cis*-desmotroposantonin acetates (3a) and (3b). We subsequently confirmed the structure of the enol acetate.[3] We now report a reinvestigation of the reaction by which (2) and (3) are formed.

We have found that, in addition to the acetates (2), (3a), and (3b), other products can be obtained in low yield. These were the chloro-analogues (4), (5a), and (5b). The spectral properties of (4) are very similar to those of the enol acetate (2). The *trans*-lactone (5a) shows a u.v. spectrum characteristic of a substituted benzene and three methyl signals and an aromatic proton singlet in the n.m.r. spectrum (see Experimental section). The *trans* nature of the lactone ring fusion follows from the coupling constant of 9 Hz for the 6-proton doublet at τ 4·99.

As these compounds were obtained in poor yield, we



[1] Part VI, T. B. H. McMurry and D. F. Rane, *J. Chem. Soc.* (*C*), 1971, 1389.
[2] W. Cocker and T. B. H. McMurry, *J. Chem. Soc.*, 1955, 4430.
[3] T. B. H. McMurry and R. C. Mollan, *J. Chem. Soc.* (*C*), 1967, 1813.

sought a method for preparing them in higher yield. Phosphorus trichloride in acetic acid, in which either (6) or (7) may be the active species,[4] has been used to convert steroidal 4-en-3-ones into 3-chloro-3,5-dienes.[5] Treatment of santonin (1) with this reagent afforded the enol acetate (2), the chloro-triene (4), the chlorobenzene with the *cis*-fused lactone ring (5b), and the desmotroposantonin acetate (3b). The chloro-compounds were obtained in much better yields.

When we substituted phosphorus tribromide for the trichloride, the reaction proceeded in a slightly different manner; we isolated the enol acetate (2) and the desmotroposantonin acetate (3b), but no bromo-compounds corresponding to (4) or (5a). Instead, we obtained two compounds, one of which was the monobromo-compound (8). The u.v. spectrum of (8) shows the presence of the triene-lactone chromophore and its n.m.r. spectrum showed that the 4- and 11-methyl groups were attached to the double bond system, and that there was in addition a CHBr group [τ 5·85 (q)] and an olefinic proton (τ 4·33). The width of the CHBr signal (7 Hz) indicated that this proton is equatorial.

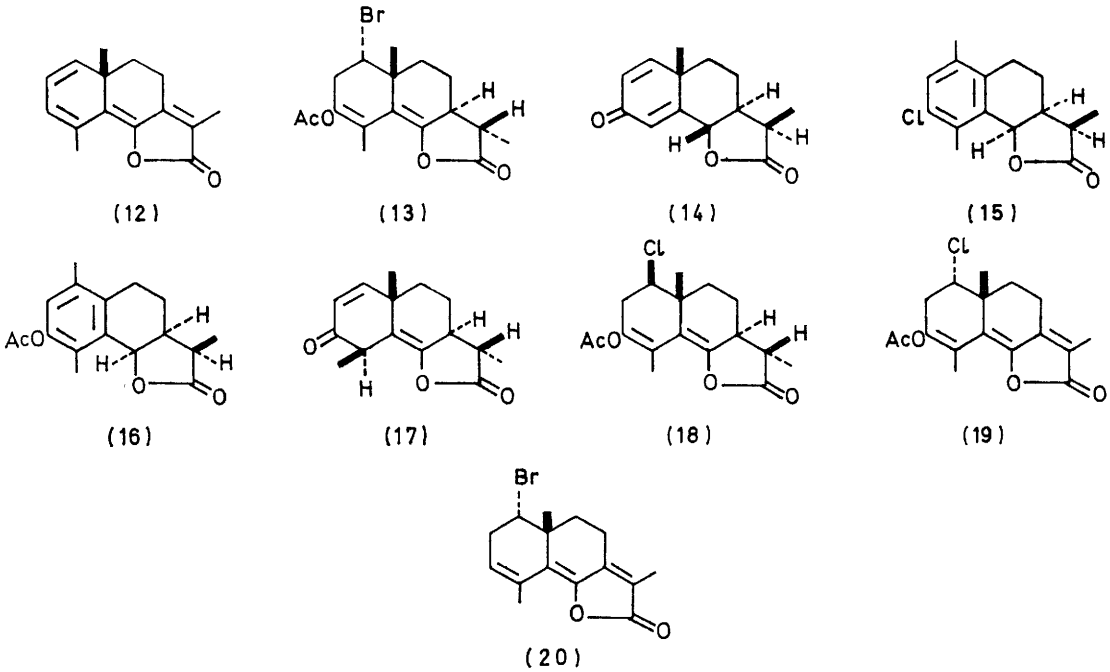
We were faced, here and later, with the problem of the location of the halogen atom. Plausible mechanisms can be advanced for halogen substitution in either the 1- or the 2-position. Where the substituent is bromine, the CHX signal occurs within the narrow range τ 5·80—5·86; with a chloro-substituent the range is greater, τ 5·94—6·03. The narrow range implies that the location of the halogen substituent was identical in all cases. There seems to be little variation between axial and equatorial protons.

The literature on the n.m.r. spectra of cyclic allylic and homoallylic halides is slight. However, the allylic chloride (9) shows a CHCl signal at τ 5·80 while the homoallylic chloride (10) has the analogous signal at τ 5·99;[6] the allylic bromide (11) shows a peak at τ 5·40.[7] These results suggest that the halogen substituents in the compounds described here are located in the homoallylic 1-position.

This view is supported by n.m.r. data. The n.m.r. spectrum of the enol acetate (2) shows a methylene signal at *ca.* τ 8·4 and another at *ca.* 7·2—7·45, each integrating for four protons. The former can be attributed to the C(1) and C(9) methylene protons, the latter to the C(2) and C(8) methylene protons. In the halogenated derivatives the ratio of the areas of the two envelopes is never greater than 2 : 4, and is often less, perhaps because of the 1,3-diaxial or the equivalent 1,3-diequatorial relationship between the C(1) halogen atom and the 9α- and 9β-protons. This would have the effect of moving the appropriate 9-H signal downfield[8] and under, perhaps beyond, the 4- and 11-methyl signals.

Dehydrobromination of the triene (8) afforded the tetraene (12) as a gum, which did not give good analytical data, but whose i.r., u.v., and n.m.r. spectra were in accord with the suggested structure.

The second new compound from the action of phos-



[4] *Cf.* M. Ya. Kraft and V. V. Katyshkina, *Zhur. obshchei Khim.*, 1959, **29**, 59 (*Chem. Abs.*, 1959, **53**, 21,632), but see J. A. Cade and W. Gerrard, *J. Chem. Soc.*, 1954, 2030; 1960, 1249.

[5] J. A. Ross and M. D. Martz, *J. Org. Chem.*, 1964, **29**, 2784.

[6] A. Fischer, M. J. Hardman, M. P. Hartshorn, D. N. Kirk, and A. R. Thawley, *Tetrahedron*, 1967, **23**, 159.

[7] C. Rufer, H. Hoffmeister, H. Schairer, and M. Traut, *Chem. Ber.*, 1965, **98**, 2383.

[8] L. M. Jackman and S. Sternhell, 'Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, Oxford, 2nd edn., 1969, p. 237.

phorus tribromide on santonin also showed a CHBr signal in its n.m.r. spectrum, in the same position and with the same width as the corresponding signal for compound (8). The spectral data obtained were consistent with structure (13) (see Experimental section). The chromophores in the bromides (8) and (13) have already been met in other compounds.[9]

Treatment of β-santonin (14) with phosphorus trichloride gave the chloro-triene (5), the enol acetate (2), the chlorobenzene (*cis*-fused lactone) (15), and the desmotroposantonin acetate (16). With phosphorus tribromide, β-santonin afforded the enol acetate (2), the 1α-bromo-3,5,7(11)-triene (8), and the acetate (16).

We have already reported the action of phosphorus trichloride and acetic acid on γ-metasantonin.[6]

Treatment of pyrosantonin [1,10] (17) with the trichloride afforded the enol acetate (2), the acetate (3b), and two chloro-compounds. One of these (18) was the chloro-analogue of (13). The 1-chloro-substituent must be equatorial, from the shape of the 1-H signal in the n.m.r. We were unable to obtain the axial 1α-chloro-compound, but instead we obtained a triene (19), in which both the 4- and 11-methyl groups are attached to double bonds, there is an acetyl group, and the 1α-chloro-group is axial. The assignment of structure was confirmed by the u.v. spectrum. The formation of this compound involves oxidation, but we are unable to determine whether this occurs by disproportionation during the reaction (we were unable to find any traces of reduced compounds) or by autoxidation during the work-up.

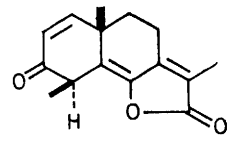
With phosphorus tribromide, pyrosantonin afforded the enol acetate (2), the desmotroposantonin acetate (3b), and two bromo-compounds. One of these was the triene (8) and the other the 1β-bromo-isomer (20) in which the configuration of the halogen substituent follows from the width of the 1-H signal ($J_{AX} + J_{BX}$ 18 Hz).

[9] T. B. H. McMurry and D. F. Rane, *J. Chem. Soc.* (*C*), 1970, 2012.

Treatment of santonene [3] (21) with phosphorus trichloride in acetic acid afforded the enol acetate (22), the chloro-compound (19), and the 1β-chloro-compound (23). The width of the 1-H signal (16·5 Hz) in the n.m.r. spectrum of the chloro-compound (23) indicates that the proton is axial. Both chlorides can be dehydrochlorinated by diazabicyclo-octane in benzene to give the enol acetate (19).

Santonenic acid (24) [3] would be expected to lactonise to santonene under the conditions of the experiment, and indeed with the trichloride it affords the same products as santonene itself. With the tribromide it gives the dibromides (25) and (26), characterised by the width of the 1-proton signals.

8-Oxosantonin (27),[11] with either trihalide in acetic acid, gave the rearrangement product (28), characterised by its n.m.r. spectra (see Experimental section). The assignment of aromatic protons is based on the assumption that the β-protons absorb at a higher field than α-protons,[12] and that the 2- and 6-protons would be broadened by benzylic coupling with adjacent alkyl groups. The naphthalene skeleton is also suggested by the i.r. and u.v. spectra (see Experimental section).



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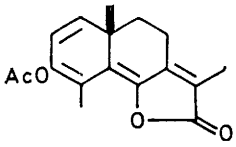

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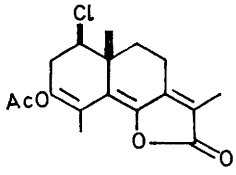

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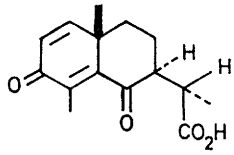

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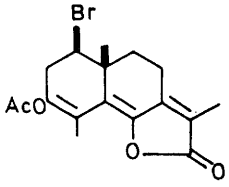

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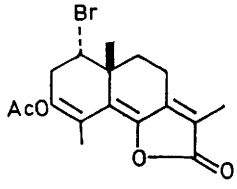

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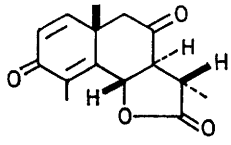

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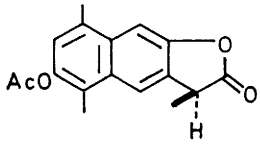


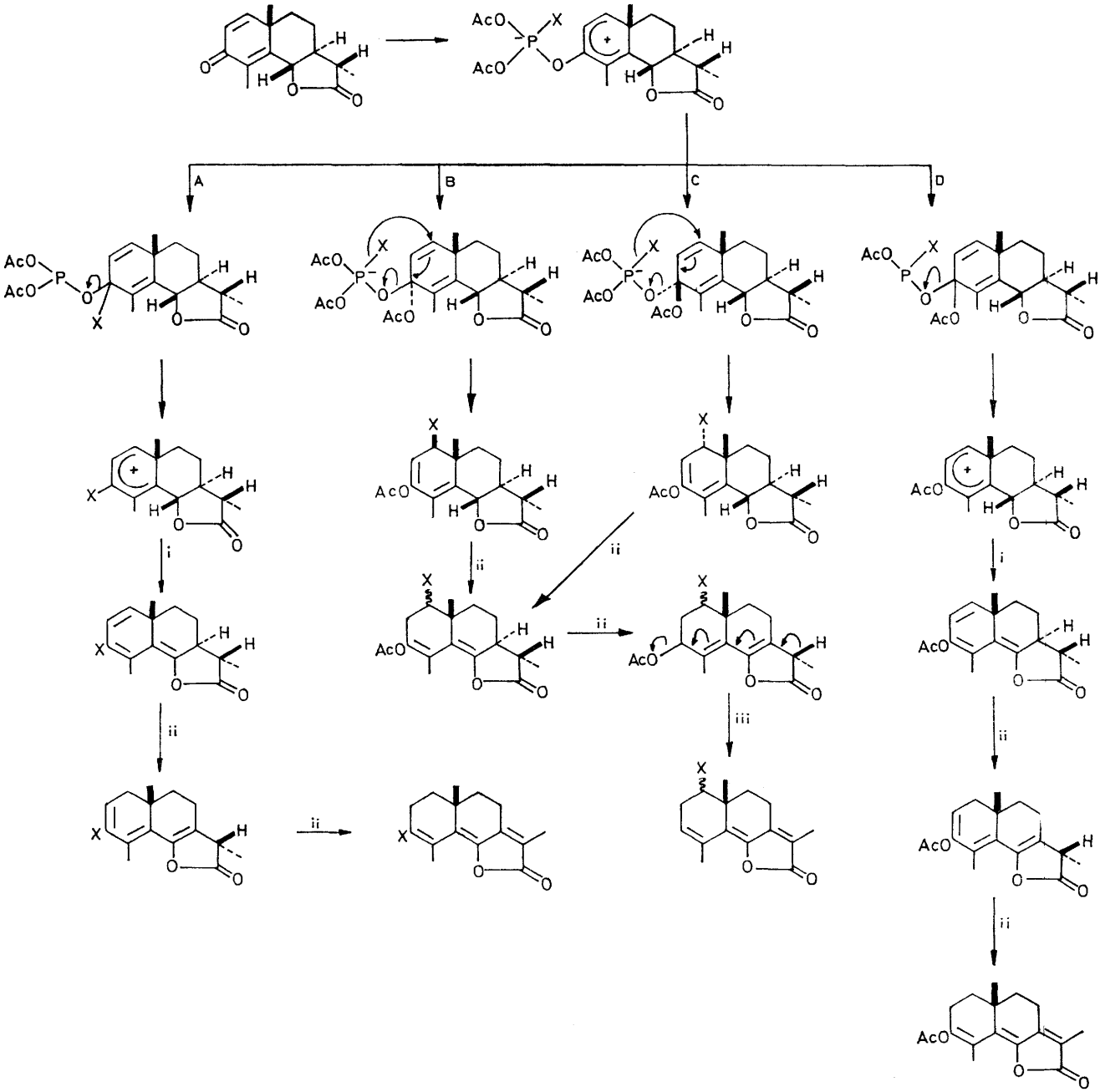
(28)

In the Scheme, we suggest some possible pathways to the product types obtained, with santonin as a typical reactant, and assuming that the diacetoxyphosphorus chloride (7) is the effective reagent. Similar pathways can be written for the other reactants, and with acetoxyphosphorus dichloride (6) as the reagent. Halide can only be transferred from anionic phosphorus (paths A, B, and C). This accounts for the occurrence of 3-acetoxy-1-halogeno-derivatives, and the absence of dihalogeno-derivatives. Path C is not followed where X = Br, possibly because the longer P–Br bond leads to a preference for paths A and B.

[10] K. Shaffner-Sabba, *Helv. Chim. Acta*, 1969, **52**, 1237.
[11] M. Sumi, *J. Amer. Chem. Soc.*, 1958, **80**, 4869.
[12] M. J. S. Dewar and R. C. Fahey, *J. Amer. Chem. Soc.*, 1963, **85**, 2704; C. MacLean and E. L. Mackor, *Mol. Phys.*, 1960, **3**, 223.

EXPERIMENTAL

For general details, see Part VI.[1] The phosphorus trihalides were carefully distilled before use. Acetyl chloride was heated under reflux over sodium acetate for 3 h, and then distilled. Acetic anhydride was distilled from calcium carbide.



SCHEME (i) $-H^+$, (ii) $+H^+$, $-H^+$, (iii) $-H^+$, $-OAc^-$

Treatment of Santonin with Acetic Anhydride–Acetyl Chloride.—Santonin (10 g), acetic anhydride (20 ml), acetyl chloride (100 ml), and water (2·5 ml) were heated under reflux for 2·5 h. The mixture was poured into water, and the aqueous solution extracted with dichloromethane (3 × 100 ml). The extracts were washed with sodium hydrogen carbonate solution and water, and were then dried ($MgSO_4$). Removal of solvent afforded a gum which was dissolved in dichloromethane (50 ml) and chromatographed on silica (200 g). Elution with light petroleum containing increasing proportions of ether gave, in order, the *chlorotriene* (4) (600 mg) as yellow needles, m.p. 105° (from light petroleum), $[\alpha]_D^{20}$ −376° (*c* 0·07) (Found: C, 68·3; H, 6·3; Cl, 13·1. $C_{15}H_{17}ClO_2$ requires C, 68·2; H, 6·4; Cl, 13·3%), $\nu_{max.}$ 1775, 1650, and 1600 cm^{-1}, $\lambda_{max.}$ 332, 234, and 227 nm (log ε 4·40, 3·51, and 3·52), τ 8·90 (10-Me), 8·12 (br s, 11-Me), and 7·73 (d, *J* 1·5 Hz, 4-Me).

Further elution afforded the *chlorobenzene* (**5a**) (20 mg) as

plates, m.p. 160—162° (from dichloromethane–light petroleum), $[\alpha]_D^{23}$ +112° (*c* 0·07) (Found: C, 67·9; H, 6·4; Cl, 13·1%), $\lambda_{max.}$ 284, 276, and 222 nm (log ε 3·02, 3·00, and 3·94), $\nu_{max.}$ 1780 and 1650 cm^{-1}, τ 8·71 (d, *J* 7·0 Hz, 11-Me), 7·84 (s, 1-Me), 7·53 (s, 4-Me), 4·99 (d, *J* 9 Hz, 6-H), and 2·85 (s, 2-H).

Later fractions afforded the enol acetate [2] (2) (5·5 g), m.p. and mixed m.p. 133°, the *trans*-desmotroposantonin acetate [2] (3a) (1·2 g), m.p. and mixed m.p. 180°, and (—)-α-desmotroposantonin acetate [2] (3b) (800 mg), m.p. and mixed m.p. 155°.

Phosphorus Trihalide Reactions.—General procedure. The santonin derivative (5 g), acetic acid (25 ml), and phosphorus trihalide (3 ml) were stirred at room temperature overnight. The red mixture was poured into water, and was extracted with ether (3 × 50 ml). The extracts were washed with sodium hydrogen carbonate solution and water, and were dried ($MgSO_4$). Removal of the solvent usually gave a gum, which was dissolved in the minimum quantity of dichloromethane, and chromatographed on silica (150 g). The column was eluted with light petroleum containing increasing proportions of ether.

(a) *Santonin.* (i) *With phosphorus trichloride.* Santonin (5 g) under the conditions described afforded the enol chloride (4) (1·0 g), m.p. and mixed m.p. 105°, the chlorobenzene with *trans*-fused lactone ring (5a) (35 mg), m.p. and mixed m.p. 162°, and the *chlorobenzene* with a *cis*-fused lactone ring (5b) (700 mg) as needles, m.p. 130° (from ether–light petroleum), $[\alpha]_D^{22}$ —165° (*c* 0·08) (Found: C, 68·5; H, 6·4; Cl, 13·2%), $\lambda_{max.}$ 285, 277, and 223 nm (log ε 3·01, 2·98, and 3·91), $\nu_{max.}$ 1761 cm^{-1}, τ 8·61 (d, *J* 7·0 Hz, 11-Me), 7·57 (4-Me), 7·80 (1-Me), 4·42 (d, *J* 5·9 Hz, 6-H), and 2·84 (2-H). Further elution afforded the enol acetate (2) (600 mg), the *trans*-desmotroposantonin acetate (3a) (250 mg), and (—)-α-desmotroposantonin acetate (3b) (475 mg).

(ii) *With phosphorus tribromide.* Santonin (5 g) with phosphorus tribromide afforded 1α-*bromoeudesma*-3,5,7(11)-*trien*-6,13-*olide* (8) (230 mg) as yellow needles, m.p. 158—159° (from ether–light petroleum), $[\alpha]_D^{25}$ —17·4° (*c* 0·16) (Found: C, 58·2; H, 5·4; Br, 25·3. $C_{15}H_{17}BrO_2$ requires C, 58·2; H, 5·5; Br, 25·9%), $\lambda_{max.}$ 327 and 220 nm (log ε 4·17 and 3·55), $\nu_{max.}$ 1755 and 1620 cm^{-1}, τ 8·81 (10-Me), 8·10 (d, *J* 1·5 Hz, 11-Me), 7·81 (t, *J* 1·5 Hz, 4-Me), 5·85 (q, $J_{AX} + J_{BX}$ 7 Hz, 1-H), and 4·33 (3-H).

Further elution afforded 3-*acetoxy*-1α-*bromoeudesma*-3,5-*dien*-6,13-*olide* (13) (25 mg) as needles, m.p. 123—124° (from ether–light petroleum), $[\alpha]_D^{24}$ —24·6° (*c* 0·09) (Found: C, 55·5; H, 5·9; Br, 21·2. $C_{17}H_{21}BrO_4$ requires C, 55·3; H, 5·7; Br, 21·7%), $\lambda_{max.}$ 245 nm (log ε 3·32), $\nu_{max.}$ 1792, 1730, 1672, and 1642 cm^{-1}, τ 8·72 (s, 10-Me), 8·71 (d, *J* 7 Hz, 11-Me), 8·08 (br s, 4-Me), 7·82 (s, OAc), and 5·85 (q, $J_{AX} + J_{BX}$ 7 Hz, 1-H).

Further fractions afforded the enol acetate (2) (2·0 g) and (—)-α-desmotroposantonin acetate (3b) (200 mg).

(b) β-*Santonin.* (i) *With phosphorus trichloride.* β-Santonin (5 g) afforded the chloro-triene (4) (200 mg), m.p. and mixed m.p. 105°, and the *chlorobenzene* with a *cis*-fused lactone ring (15) (1·5 g), as needles, m.p. 175° (from ether–light petroleum), $[\alpha]_D^{22}$ —116° (*c* 0·1) (Found: C, 68·3; H, 6·5; Cl, 13·4%), $\lambda_{max.}$ 285, 277, and 224 nm (log ε 3·02, 3·00, and 3·99), $\nu_{max.}$ 1750 cm^{-1}, τ 8·73 (d, *J* 7 Hz, 11-Me), 7·81 (1-Me), 7·59 (4-Me), 4·68 (d, *J* 6 Hz, 6-H), and 2·81 (2-H).

Further elution afforded the enol acetate (2) (50 mg) and (—)-β-desmotroposantonin acetate (16) (1·2 g), m.p. and mixed m.p. 156°.

(ii) *With phosphorus tribromide.* β-Santonin (5 g) afforded the 1α-bromo-triene (8) (150 mg), the enol acetate (2) (45 mg), and (—)-β-desmotroposantonin acetate (16) (2·30 g).

(c) *Pyrosantonin.* (i) *With phosphorus trichloride.* Pyrosantonin (1·5 g) afforded 3-*acetoxy*-1β-*chloroeudesma*-3,5-*dien*-6,13-*olide* (18) (650 mg) as needles, m.p. 118—120°, $[\alpha]_D^{18}$ —312° (*c* 0·14) (Found: C, 62·5; H, 6·9; Cl, 11·0. $C_{17}H_{21}ClO_4$ requires C, 62·8; H, 6·5; Cl, 10·9%), $\lambda_{max.}$ 243 (log ε 4·34), $\nu_{max.}$ 1810, 1765, 1680, and 1650 cm^{-1}, τ 8·84 (10-Me), 8·69 (d, *J* 6 Hz, 11-Me), 8·16 (t, *J* 1·5 Hz, 4-Me), 7·85 (OAc), and 6·03 (q, $J_{AX} + J_{BX}$ 16·5 Hz, 1-H).

Further elution afforded 3-*acetoxy*-1α-*chloroeudesma*-3,5,7(11)-*trien*-6,13-*olide* (19) (60 mg), as pale yellow needles, m.p. 181—183° (from ethyl acetate–light petroleum), $[\alpha]_D^{22}$ +103·5° (*c* 0·08) (Found: C, 63·7; H, 6·0; Cl, 11·6. $C_{17}H_{19}ClO_4$ requires C, 63·4; H, 5·8; Cl, 11·0%), $\lambda_{max.}$ 327 and 223 nm (log ε 4·45 and 3·54), $\nu_{max.}$ 1775 and 1640 cm^{-1}, τ 8·71 (10-Me), 8·08 (br s, 11-Me), 7·92 (t, *J* 1·5 Hz, 4-Me), 7·79 (OAc), and 5·94 (q, $J_{AX} + J_{BX}$ 7 Hz, 1β-H).

Further fractions afforded the enol acetate (2) (20 mg), and (—)-α-desmotroposantonin acetate (3b) (150 mg).

(ii) *With phosphorus tribromide.* Pyrosantonin (1·5 g) afforded 1β-*bromoeudesma*-3,5,7(11)-*trien*-6,13-*olide* (20) (190 mg) as yellow cubes, m.p. 85° (from ether–light petroleum), $[\alpha]_D^{20}$ —341° (*c* 0·17) (Found: C, 58·9; H, 5·6; Br, 25·2%), $\lambda_{max.}$ 342, 323, and 263 nm (log ε 4·35, 4·48, and 3·65), $\nu_{max.}$ 1760, 1648, and 1628 cm^{-1}, τ 8·84 (10-Me), 8·10 (br s, 11-Me), 7·88 (br s, 4-Me), 5·86 (q, $J_{AX} + J_{BX}$ 18 Hz, 1-H), and 4·38 (3-H).

Further elution afforded the 1α-bromo-triene (8) (85 mg), m.p. and mixed m.p. 133°, santonin enol acetate (2) (400 mg), and (—)-α-desmotroposantonin acetate (3b) (120 mg).

(d) *Santonene with phosphorus trichloride.* Santonene (300 mg) afforded 3-*acetoxy*-1β-*chloroeudesma*-3,5,7(11)-*trien*-6,13-*olide* (23) (98 mg), as yellow cubes, m.p. 141—143° (from ethanol), $[\alpha]_D$ —289·5° (*c* 0·1) (Found: C, 63·1; H, 5·8; Cl, 11·4%), $\lambda_{max.}$ 327 and 223 nm (log ε 4·51 and 3·62), $\nu_{max.}$ 1775 and 1640 cm^{-1}, τ 8·81 (10-Me), 8·08 (t, *J* 1 Hz, 11-Me), 7·98 (t, *J* 1·5 Hz, 4-Me), 7·79 (OAc), and 5·96 (q, $J_{AX} + J_{XB}$ 16·5 Hz, 1-H).

Further elution afforded santonene enol acetate (22) [3] (20 mg) as orange needles, m.p. and mixed m.p. 114°, and the 1α-chloro-enol acetate (19) (20 mg), m.p. and mixed m.p. 181—183°.

(e) *Santonenic acid.* (i) *With phosphorus trichloride.* Santonenic acid (5 g) gave the 1β-chloro-compound (23) (1·5 g), santonene enol acetate (22) (300 mg), and the 1α-chloro-compound (19) (1·0 g).

(ii) *With phosphorus tribromide.* Santonenic acid (5 g) afforded 3-*acetoxy*-1β-*bromoeudesma*-3,5,7(11)-*trien*-6,13-*olide* (25) (3·0 g), as yellow cubes, m.p. 134—135° (from ether–light petroleum), $[\alpha]_D^{20}$ —272° (*c* 0·2) (Found: C, 55·8; H, 5·3; Br, 21·8. $C_{17}H_{19}BrO_4$ requires C, 55·6; H, 5·2; Br, 21·8%), $\lambda_{max.}$ 323 and 222 nm (log ε 4·15 and 3·63), $\nu_{max.}$ 1757 and 1630 cm^{-1}, τ 8·79 (10-Me), 8·09 (t, *J* 1 Hz, 11-Me), 8·00 (t, *J* 1·5 Hz, 4-Me), 7·80 (OAc), and 5·81 (q, $J_{AX} + J_{BX}$ 17 Hz, 1-H).

Further elution afforded santonene enol acetate (22) (200 mg) and 3-*acetoxy*-1α-*bromoeudesma*-3,5,7(11)-*trien*-6,13-*olide* (26) (1·25 g) as yellow cubes, m.p. 158° (from ether–light petroleum), $[\alpha]_D^{22}$ +98·7° (*c* 0·4) (Found: C, 55·9; H, 5·1; Br, 21·6%), $\lambda_{max.}$ 323 and 223 nm (log ε 4·18

and 3·75), $\nu_{max.}$ 1760 and 1633 cm^{-1}, τ 8·72 (10-Me), 8·10 (br s, 11-Me), 7·94 (t, J 1·5 Hz, 4-Me), and 7·80 (q, $J_{AX} + J_{BX}$ 7 Hz, 1-H).

(f) 8-*Oxosantonin* (27).[11] *With either trihalide.* 8-Oxosantonin (1 g) with either phosphorus trihalide afforded (2S)-2-(7-*acetoxy*-3-*hydroxy*-5,8-*dimethyl*-2-*naphthyl*)-*propionic acid lactone* (28) (500 mg), as needles, m.p. 180—183° (from dichloromethane–light petroleum), $[\alpha]_D^{21}$ −47·8° (c 0·18) (Found: C, 71·3; H, 5·3. $C_{17}H_{16}O_4$ requires C, 71·8; H, 5·6%), $\lambda_{max.}$ 332, 312, 290, 280, 270, 242, and 237 nm (log ε 3·32, 3·25, 3·42, 3·51, 3·45, 4·64, and 4·69), $\nu_{max.}$ 1800, 1745, 1645, and 1615 cm^{-1}, τ 8·38 (d, J 7 Hz, CH_3·CH), 7·63 (OAc), 7·57 (5-Me), 7·42 (8-Me), 2·98 (br s, 6-H), 2·48 (1H, 4-H), and 2·16 (br d, J 1 Hz, 1-H).

Dehydrohalogenation Experiments.—(a) *Eudesma*-1,3,5,7(11)-*tetraen*-6,13-*olide.* 1α-Bromoeudesma-3,5,7(11)-trien-6,13-olide (8) (150 mg), lithium carbonate (400 mg), and dimethylformamide (20 ml) were heated on a water bath for 4 h. The mixture was poured into water, and the aqueous solution was extracted with ether. The extracts were washed with dilute hydrochloric acid and water, and were dried ($MgSO_4$). Removal of the solvent gave a gum which was chromatographed on silica (10 g) to afford the tetraene (12) as an orange oil (110 mg), $[\alpha]_D^{21}$ −912° (c 0·17), $\lambda_{max.}$ 382, 339, 268, and 262 nm (log ε 3·99, 4·02, 3·82, and 3·80), $\nu_{max.}$ 1765 and 1650 cm^{-1}, τ 8·82 (10-Me), 8·12 (br s, 11-Me), 7·82 (br s, 4-Me), and 4·17 (m, 1-, 2-, and 3-H).

(b) *Santonene enol acetate.* (i) 3-Acetoxy-1β-chloroeudesma-3,5,7(11)-trien-6,13-olide (23) (300 mg), diazabicyclo-octane (150 mg), and benzene (25 ml) were heated under reflux for 36 h. The mixture was cooled, and the diazabicyclo-octane hydrochloride was collected. Removal of the benzene from the filtrate afforded the 3-acetoxy-1,3,5,7(11)-tetraen-6,13-olide (22) (120 mg) as orange needles, m.p. and mixed m.p. 115°.

(ii) 3-Acetoxy-1α-chloroeudesma-3,5,7(11)-trien-6,13-olide (19) (300 mg) under the same conditions gave the enol acetate (22) (180 mg) as orange needles, m.p. and mixed m.p. 115°.

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