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SOME REGIOSELECTIVE REACTIONS OF PHOTOALDRIN AND PHOTODIELDRIN

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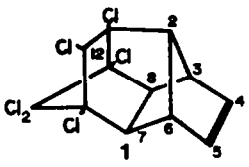
Abstract—A study has been made of the regioselectivities of some typical addition reactions of photoaldrin and epoxide ring-opening reactions of photodieldrin. The structures of the resulting products have been established by appropriate interconversions and syntheses. The factors responsible for the observed regioselectivities are discussed.

Surprisingly little is known about the chemical reactions of photoaldrin (1) and photodieldrin (2), although appreciable amounts of these compounds appear to have entered the environment as a result of photochemical[1] modification of the widely used insecticides aldrin and dieldrin. In this paper we report on the regioselective reactions of these compounds with some typical electrophiles.

The addition of acetic acid to photoaldrin (1), catalysed by sulphuric acid, provided the three acetates (3a, 4 and 5a) in the approximate ratio of 5:3:2. The acetate 3a was partially isomerised to its *endo* isomer 4 on treatment with sulphuric-acetic acids under similar conditions, whereas the *exo*-acetate 5a was recovered essentially unchanged. The identities of these compounds were established by the following transformations. Photocyclisation of the known[2] *exo*-dihydroaldrinyl acetate (7), in the presence of benzophenone, provided the two *exo*-acetates (3a and 5a), whose orientations were demonstrated by conversion via the alcohols (3b, 5b) to the known[3] ketones (8, 9a). Reduction of these ketones with sodium borohydride[4] and subsequent acetylation yielded the corresponding *endo*-acetates (4 and 6). Alternatively, hydroboration of photoaldrin also provided a mixture of the acetates (3a and 5a), but the latter isomer was then the predominant one.

Treatment of photodieldrin (2) with hydrobromic acid gave only one bromohydrin, formulated as 10 on the basis of the following evidence. Oxidation of 10 with Jones reagent, provided a bromoketone. As this compound resisted debromination and attempted epimerisation it was brominated further to the dibromoketone which was identical with the compound 9d obtained from dibromination of ketone 9a. As the product of monobromination of ketone 9a can reasonably be expected[6] to yield the *exo*-bromoketone 9c and as this was different to the bromoketone derived from the bromohydrin, the latter ketone must have the *endo* configuration (9b). Hence the bromohydrin has the *trans* orientation (10a). By analogy, the corresponding structure 10b can be assigned to the chlorohydrin obtained[7] either by irradiation of dieldrin or by treatment of photodieldrin with hydrochloric acid.

Treatment of dieldrin (11) with acetic anhydride containing sulphuric acid provided as the major product a compound assigned a dihydrophotoaldrindiol structure[8] prior to reformulation[9] as 13. Consideration of the proposed pathway for its formation suggested that appropriate epoxide ring-opening of photodieldrin would also lead via 12 to 13. However, none of the anticipated



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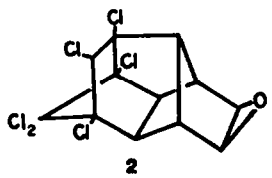

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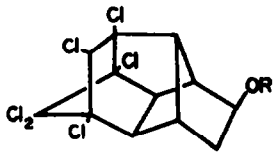
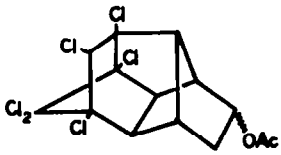


3a: R = Ac
b: R = H
c: R = Ms



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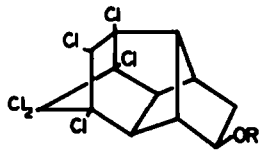
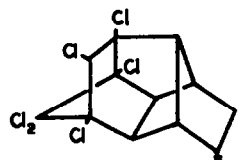


5a: R = Ac
b: R = H
c: R = Ms



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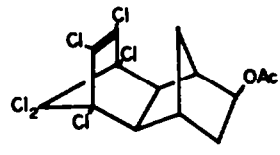

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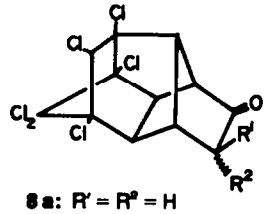
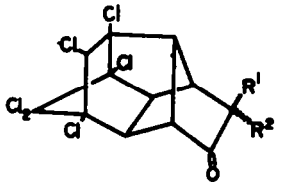


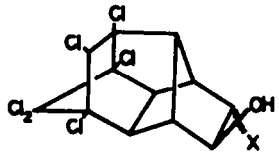
8a: R' = R² = H
b: R' = Br, R² = H
c: R' = R² = Br

13 resulted from similar treatment of photodieldrin, instead two other isomeric diacetates were formed. One of these was readily identified as the *cis*-diacetate (14a) as it was obtained also from *cis*-hydroxylation of photoaldrin with osmium tetroxide and subsequent acetylation. The other diacetate is believed to be the *trans* isomer (15).

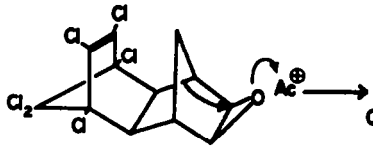
Earlier studies[2] have revealed the much decreased reactivity of these polychlorocompounds relative to their hydrocarbon analogues. This may be attributed to the strong electron withdrawing effect of the chlorines which



9a: R' = R² = H
b: R' = H, R² = Br
c: R' = Br, R² = H
d: R' = R² = Br



10a: X = Br
b: X = Cl



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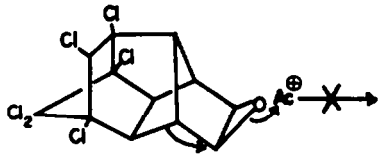

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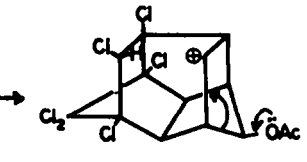

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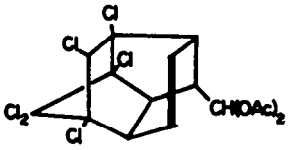

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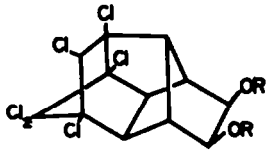
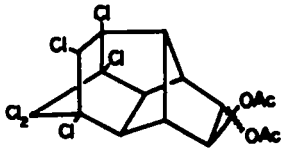


14 a: R = Ac
b: R = H



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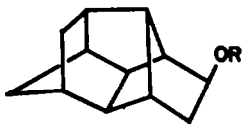
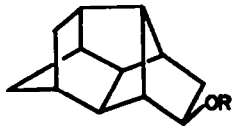
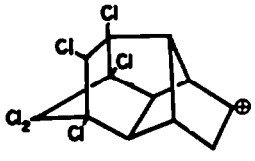


16 a: R = Bs
b: R = Ac



17 a: R = Bs
b: R = Ac



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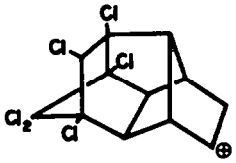

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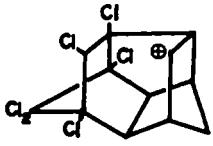

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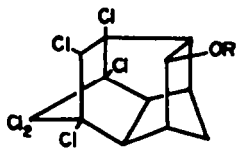
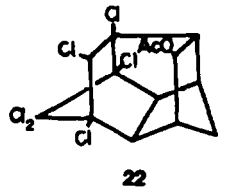


21 a: R = Ms
b: R = Ac

militates against anchimeric interactions. This effect was further exemplified by the behaviour of the *exo*-mesylates (3c and 5c) on acetolysis. In both cases the only products observed were photoaldrin (1) and the respective *endo* acetates (4 and 6). In contrast the corresponding *exo*-brosylates (16a and 17a) are reported[10] to give predominantly the respective *exo*-acetates (16b and 17b), in keeping with the incidence of anchimeric assistance in these acetolyses. The cation 19 derivable from the *exo*-mesylate (5c) would have been expected to interconvert with the half-cage cation (20). Lest the failure to observe any products derived from 20 in the solvolysis of 5c was a consequence of appreciably differing cation stabilities the acetolysis of the half-cage *exo*-mesylate (21a) was re-examined. Only the previously reported[2] products namely 21b, 22 and a saturated chlorohydrocarbon were obtained and none of the anticipated acetate (5a) was detected. The tentative structure 23 originally suggested[2] for this chlorohydrocarbon was excluded by comparison of the fully decoupled and off-resonance decoupled ^{13}C NMR spectra. This revealed the presence of eight methine groups (δ 18.7, 22.1, 23.9, 42.4, 53.6, 56.1, 62.3, 67.3), of which the three at highest field can be provisionally assigned to a cyclopropyl group by comparison with reported[11] values. The dichloromethylene carbon was observed at δ 99.9 and the three remaining chlorine bearing carbons δ 88.45, 76.9 and 74.2. In the light of this evidence and its ready conversion into the half-cage *exo*-acetate (21b) on treatment with sulphuric and acetic acids the chlorohydrocarbon would seem to be more appropriately formulated as 24.[12]



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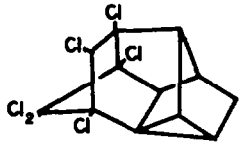

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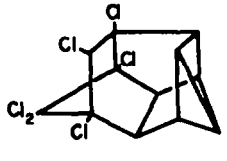

24

The regioselectivities observed for the reactions of photoaldrin and photodieldrin with electrophiles are attributable to an enhanced stability of one of the potential intermediary cations (e.g. 18) relative to the other (e.g. 19). Examination of molecular models shows that *exo* and *endo* substituents at C4 of the dihydrophotoaldrin nucleus will be subject to greater steric repulsions by hydrogens at C2 and, C7 and C8 respectively than when the same substituents are placed at C5. This is borne out by the preferential hydroboration of photoaldrin at C5. It should be noted that there would seem to be little scope for any helpful anchimeric contribution here, since any such interaction in the cation (18) would introduce additional molecular distortions.

EXPERIMENTAL

^1H NMR spectra were recorded at 90 MHz by the U.L.I.R.S. at King's College and the ^{13}C NMR spectra by the P.C.M.U. Harwell. In both cases spectra were recorded for $CDCl_3$ solutions with internal TMS. IR spectra were recorded for Nujol mulls on a Unicam SP 200 spectrophotometer.

Photocyclisation of exo-*dihydroaldrinol acetate* (8). The *exo*-acetate 7[2] (16 g) and benzophenone (6.8 g) dissolved in benzene (300 ml) were irradiated under N_2 in a Rayonet Photochemical Reactor (300 nm) until all of 7 was consumed (IR). The resulting soln was evaporated and the residue chromatographed on silica gel in CCl_4. Elution with CCl_4 gave successively benzophenone (6.2 g), the *exo*-acetate 8a (1.2 g), a mixture of 8a and 3a (7.3 g) and the *exo*-acetate 3a (5.9 g). Rechromatography of the mixed fractions provided additional amounts of 8a (2.1 g) and 3a (1.2 g), as well as mixed fractions. The acetate 3a had m.p. 176–177° from EtOH (Found: C, 39.6; H, 3 d.p. $C_{14}H_{12}Cl_6O_2$ requires: C, 39.5; H, 2.8%) ν_{max} 1710, 1260 cm^{-1}; NMR δ 1.56–2.1 (m, 5H, includes singlet for CH_3 at 2.05), 2.49 (dd, 1H, J=6, J=3), 2.73–3.1 (m, 4H), 4.92 (s, H 12), 4.94 (dd, H4, J=6, J=4). Basic hydrolysis provided the alcohol (3b) m.p. 165–167° from aq.MeOH (Found: C, 37.6; H, 2.7. $C_{12}H_{10}Cl_6O$ requires: C, 37.5; H, 2.7%) ν_{max} 3320, 1050 cm^{-1}. The acetate (5a) had m.p. 123–125° from MeOH (Found: C, 40.1; H, 3.1. $C_{14}H_{12}Cl_6O_2$ requires: C, 39.5; H. 2.8%) ν_{max} 1710, 1240 cm^{-1}; NMR δ 1.53–1.7 (m, 1H), 1.8 (dd, 1H, J=5, J=3), 1.9–2.13 (m, 4H, including singlet for CH_3 at 2.04), 2.56 (dd, 1H, J=6, J=2), 2.67–2.9 (m, 2H), 2.99 (dd, 1H, J=4, J=2), 4.71 (dd, H5, J=7, J=3), 4.86 (s, H12). Basic hydrolysis gave the alcohol (5b) m.p. 149–151° from aq.MeOH (Found: C, 37.6; H, 2.6. $C_{12}H_{10}Cl_6O$ requires: C, 37.5; H, 2.7%) ν_{max} 3350, 1070 cm^{-1}.

Oxidation of alcohols (3b *and* 5b). The alcohol 3b (1.15 g) was dissolved in acetone (15 ml) and a soln of CrO_3 (0.23 g) in water (1 ml) plus H_2SO_4 (0.2 ml) added. The mixture was allowed to stand for 2 hr then diluted with water and the product isolated by $CHCl_3$ extraction. The ketone 8a (1 g) had m.p. 235–237° from EtOH (lit.[3] m.p. 243–245°) ν_{max} 1750, 1400 cm^{-1}. Similar oxidation of 5b yielded 9a (78%) m.p. 201–203° (lit.[3] m.p. 210–212°).

Reduction of ketones (8a *and* 9a). The ketone 8a (0.5 g) and $NaBH_4$ (0.5 g) were allowed to react in EtOH (50 ml) at room temp for 20 hr. The resulting soln was diluted with water and acidified with dil HCl. The crude alcohol was isolated by $CHCl_3$ extraction and acetylated with Ac_2O in pyridine, to give the *endo*-acetate 4 (0.3 g) m.p. 167–169° from MeOH (Found: C, 39.7, H, 2.9. $C_{14}H_{12}Cl_6O_2$ requires: C, 39.5; H, 2.8%). ν_{max} 1720, 1240 cm^{-1} NMR δ 1.29 (dd, 1H, J=15, J=4), 2.07 (s, CH_3), 2.3 (ddd, 1H, J=15, J=10, J=4), 2.6–2.9 (m, 3H), 3.0–3.29 (m, 2H), 4.9 (s, H12), 5.16 (ddd, H4, J=10, J=5, J=4). Similarly reduction and acetylation of 9a gave the *endo*-acetate 6 m.p. 145–147° from MeOH (Found: C, 39.4; H, 2.8%) ν_{max} 1735, 1235 cm^{-1}. NMR δ 1.4 (dd, 1H, J=15, J=4), 2.08 (s, CH_3), 2.24 (ddd, 1H, J=15, J=10, J=4), 2.7–3.07 (m, 5H), 4.88 (s, H12), 5.12 (ddd, H5, J=10, J=4, J=4).

Addition of acetic acid to photoaldrin. Photoaldrin[13] (9.4 g) was refluxed for 1 hr in AcOH (120 ml) and H_2SO_4 (24 ml). The cooled soln was diluted with water and the products extracted with $CHCl_3$. The crude product mixture was crystallised from EtOH to give the *exo*-acetate 3a (3.6 g). The mother liquors were evaporated and the residue chromatographed on SiO_2 in CCl_4. Elution with CCl_4-benzene (9:1) gave successively the *exo*-acetate 5a (0.8 g), a mixture (1.2 g) of 5a and 4 and finally the *endo*-acetate 4 (1.6 g).

Acid treatment of the acetates (3a *and* 5a). The acetate 3a (0.6 g) was refluxed for 1 hr in AcOH (10 ml) containing H_2SO_4 (2 ml). The products were isolated by diluting the mixture with

water and subsequent $CHCl_3$ extraction. Crystallisation of the crude product from MeOH gave **3a** (0.3 g) and the mother liquor provided the *endo* isomer **4** (0.14 g). The isomeric acetate **5a** was recovered unchanged after subjection to similar treatment.

Hydroboration of photoaldrin. BF_3 etherate (1.65 ml) was added dropwise to a stirred soln of photoaldrin (3.65 g) in diglyme (50 ml) containing $NaBH_4$ (0.4 g) under N_2. After stirring for 1 hr water (2 ml) was cautiously added and then a soln of NaOH (0.45 g) in water (4 ml) followed by 30% H_2O_2 (4 ml). The mixture was stirred overnight, then diluted with water and $CHCl_3$ extracted. The mixture of alcohols was dissolved in pyridine (10 ml), Ac_2O (3 ml) added and allowed to stand until the next day. The mixture of acetates was isolated by addition of water and $CHCl_3$ extraction. Chromatography on SiO_2 in CCl_4 and elution with CCl_4-benzene (4:1) provided the *exo*-acetate **5a** (1.1 g), a mixture of **5a** and **3a** (0.4 g) and the isomeric acetate **3a** (0.5 g).

Reaction of photodieldrin with hydrobromic acid. A soln of photodieldrin[13] (3.8 g) in $CHCl_3$ (40 ml) was stirred for 20 hr with HBr (48%, 15 ml). Water was then added and the chloroform layer separated, washed with water and dried (Na_2SO_4). Evaporation and crystallisation of the residue from aq.MeOH gave **10a** (3.85 g) m.p. 196–197° (Found: C, 31.5; H, 2.0. $C_{12}H_9BrCl_6O$ requires: C, 31.2; H, 1.95%) ν_{max} 3550, 1050 cm^{-1} NMR δ 2.29 (s, OH), 2.6–2.8 (m, 3H), 3.04–3.20 (m, 2H), 3.29 (d,d, 1H, J=6, J=2), 4.03 (br s, 2H, H4 & H5), 4.83 (s, H12).

Oxidation of bromohydrin (**10a**). A soln of CrO_3 (0.7 g) in water (3 ml) and H_2SO_4 (0.6 ml) was added to a stirred soln of **10a** (3.2 g) in acetone (30 ml). Next day the mixture was diluted with water and the precipitated **9b** (2.6 g) crystallised from aq.MeOH m.p. 198–201° (Found: C, 31.6; H, 1.8. $C_{12}H_7BrCl_6O$ requires: C, 31.3; H, 1.5%) ν_{max} 1750 cm^{-1}; NMR δ 2.93 (dd, 1H, J = 6, J = 2), 3.1–3.3 (m, 3H), 3.4–3.6 (m, 2H), 4.47 (d, H4, J = 4), 4.67 (s, H12).

Bromination of bromoketone (**9b**). The ketone (0.3 g) and Br_2 (0.15 g) were heated at 100° for 2 days in AcOH (5 ml) containing 3 drops of an acetic acid soln of HBr (45% w/v). **9d** (0.3 g) crystallised out and was recrystallised from AcOH m.p. 257–259°. (Found: C, 27.2; H, 1.1. $C_{12}H_6Br_2Cl_6O$ requires: C, 26.8; H, 1.1%) ν_{max} 1755 cm^{-1} NMR δ 2.84–3.0 (m, 1H), 3.3–3.6 (m, 3H), 3.8–3.9 (m, 1H), 4.65 (s, H12).

Bromination of ketones (**8a** *and* **9a**). The ketone **9a** (0.4 g) was treated with 2 equivs Br_2 in AcOH (10 ml) containing 3 drops HBr/AcOH at room temp for 7 days. Dilution with water gave **9c** (0.43 g) m.p. 206–208° from aq.MeOH (Found: C, 31.3; H, 1.5. $C_{12}H_7BrCl_6O$ requires: C, 31.3; H, 1.5%) ν_{max} 1760 cm^{-1}; NMR δ 2.81 (dd, 1H, J = 6, J = 3), 3.1–3.3 (m, 2H), 3.3–3.43 (m, 1H), 3.5 (dd, 1H, J = 4, J = 2), 4.18 (s, H4), 4.68 (s, H12).

Repetition of this experiment at a reaction temp of 100° resulted in the slow separation of **9d** (0.13 g in 2 days).

Similarly, bromination **8a** at room temp gave **8b** m.p. 222–5° from aq.MeOH (Found: C, 31.1; H, 1.5. $C_{12}H_7BrCl_6O$ requires: C, 31.3; H, 1.5%) ν_{max} 1760 cm^{-1}. NMR δ 2.81 (dd, 1H, J = 3, J = 6), 3.05–3.3 (m, 2H), 3.3–3.4 (m, 1H), 3.4–3.6 (m, 1H), 3.98 (s, H5), 4.93 (s, H12). Attempted bromination of **8a** at 100° to give **8c** proceeded with reluctance and only inseparable mixtures of **8b** and **8c** were obtained as indicated by NMR.

Reaction of photodieldrin with acetic anhydride. A soln of photodieldrin[13] (5 g) in Ac_2O (200 ml) containing H_2SO_4 (2 ml) was refluxed 1 hr, then poured into ice-water and stirred until hydrolysis of Ac_2O was complete. Filtration gave a black residue which was dissolved in $CHCl_3$. The soln was washed with water, dried (Na_2SO_4), and evaporated. The resulting black solid was extracted with benzene and the extract chromatographed on silica gel. Elution with benzene-EtOAc (9:1) gave a mixture of the diacetates, which were separated by extraction with MeOH which left the insoluble *cis*-diacetate **14a** (1.1 g) m.p. 276–279° from $CHCl_3$-MeOH. (Found: C, 39.5; H, 2.9. $C_{16}H_{14}Cl_6O_4$ requires: C, 39.6; H, 2.9%) ν_{max} 1740, 1720, 1260, 1230 cm^{-1}; NMR δ 2.06 (2×CH_3), 2.61 (dd, H7, J = 6, J = 3), 2.76 (br, H6), 2.88 (br, H3), 2.93 (ddd, H8, J = 6, J = 3, J ≈ 1), 3.25 (dd, H2, J ≈ 2 J ≈ 2), 4.82 (s, H12), 4.91 (d, H5, J = 6.2), 5.08 (d, H4, J = 6.2). Evaporation of the MeOH extract provided the *trans*-diacetate **15** m.p. 151–154 from aq.MeOH (Found: C, 39.9; H, 2.9. $C_{16}H_{14}Cl_6O_4$ requires: C, 39.6; H, 2.9%) ν_{max} 1720, 1240 cm^{-1}; NMR δ 2.09 & 2.10 (2×s, 6H, 2×CH_3), 2.69–2.85 (m, 2H), 3.09 (s, 2H), 3.14 (s, 1H), 4.60 (d, 1H, J = 1.5 Hz), 4.81 (s, H12), 5.0–5.2 (m, 1H).

Dihydroxylation of photoaldrin. Osmium tetroxide (0.5 g) was added to a soln of photoaldrin (0.73 g) in pyridine (10 ml) and the reaction was allowed to stand for 3 days at room temp. Sodium metabisulphite (0.9 g) dissolved in water (15 ml) and pyridine (10 ml) was added and the mixture stirred for 2 hr. The product was isolated by dilution with water and chloroform extraction. Crystallisation from aq.MeOH gave the *cis*-diol **14b** (0.58 g) m.p. 181–182° (Found: C, 36.4; H, 3.3. $C_{12}H_{10}Cl_6O_2.CH_4O$ requires C, 36.2: H, 3.25%) ν_{max} 3300, 3150, 1050, 1020 cm^{-1}. Acetylation with Ac_2O in pyridine yielded the *cis*-diacetate (**14a**).

Solvolysis of mesylates (**3c** *and* **5c**). The alcohol **3b** (3.8 g) was dissolved in pyridine (10ml) and methanesulphonyl chloride (3 g) added. The soln was allowed to stand for 6 days and then diluted with water. The ppt was filtered off, dried and crystallised from $CHCl_3$ to give **3c** (3.4 g) m.p. 199–200° (Found: C, 34.0; H, 2.6. $C_{13}H_{12}Cl_6O_3S$ requires: C, 33.8; H, 2.6%) ν_{max} 1325, 1165 cm^{-1}. The mesylate **5c** was similarly prepared, m.p. 195–196° from $CHCl_3$ (Found: C, 33.8; H, 2.6%). ν_{max} 1355, 1175 cm^{-1}.

The mesylate **3c** (3 g) in AcOH (50 ml) containing NaOAc (2.5 g) was refluxed 20 hr. The cooled soln was poured into water and chloroform extracted. The extract was washed with water, dried (Na_2SO_4), evaporated and the residue chromatographed on silica gel in CCl_4. Elution with CCl_4 provided **1** (0.36 g) and CCl_4-benzene (3:2) eluted the *endo*-acetate **4** (1.3 g).

Similar acetolysis of **5c** (1.2 g) gave photoaldrin (0.2 g), the *endo*-acetate **6** (0.28 g) and unchanged mesylate (0.4 g).

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