Photochemical Transformations. Part XXX.† Photolysis of Thiobenzoic Acid *O*-Esters. Part I. Photolysis of *O*-Cholesteryl Thiobenzoate

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O-Cholesteryl thiobenzoate (I; Ar = Ph) is smoothly photolysed to give cholesta-3,5-diene (II) and thiobenzoic acid in high yield.

We have previously shown [1] that *S*-acyl xanthates are smoothly converted into xanthate and acyl radicals on irradiation. This photochemical reaction occurs because of the presence of the chromophoric thione grouping (n–π^* transition). Although it is known that thiobenzoic acid *O*-esters, unlike their *S*-ester and benzoate analogues, absorb in the visible region, no irradiation studies of these *O*-esters have been reported.[2] To date, work on thiobenzoic acid *O*-esters has been largely concerned with their thermal rearrangement to thiobenzoic acid *S*-esters.[3a-d]

O-Cholesteryl thiobenzoate (I; Ar = Ph),[4] $\lambda_{max.}$ 256, 288, and 420 nm (ε 7100, 8000, and 140) was irradiated in cyclohexane through Pyrex with a medium-pressure mercury vapour lamp. The starting material (250 mg) was consumed in 12 min (disappearance of u.v. absorption at 256 and 288 and appearance of new maxima at 228 and 235 nm). After oxidation (see Experimental section) of the resulting thiobenzoic acid, dibenzoyl disulphide and cholesta-3,5-diene (II) [5] were isolated in quantitative yield. *O*-Cholesteryl thioanisoate (I; Ar = C_6H_4·OMe-*p*) similarly gave cholesta-3,5-diene on irradiation, but the yield was only 56%, owing to a rapid readdition of the thioanisic acid to the newly generated diene system. A similar readdition of thiobenzoic acid

† Part XXIX, D. H. R. Barton, P. G. Sammes, and G. G. Weingarten, *J. Chem. Soc.* (*C*), 1971, 729.

[1] D. H. R. Barton, M. V. George, and M. Tomoeda, *J. Chem. Soc.*, 1962, 1967; see also R. H. Bell, D. Horton, and D. M. Williams, *Chem. Comm.*, 1968, 323.

[2] Preliminary communication, S. Achmatowicz, D. H. R. Barton, P. D. Magnus, G. A. Poulton, and P. J. West, *Chem. Comm.*, 1971, 1014.

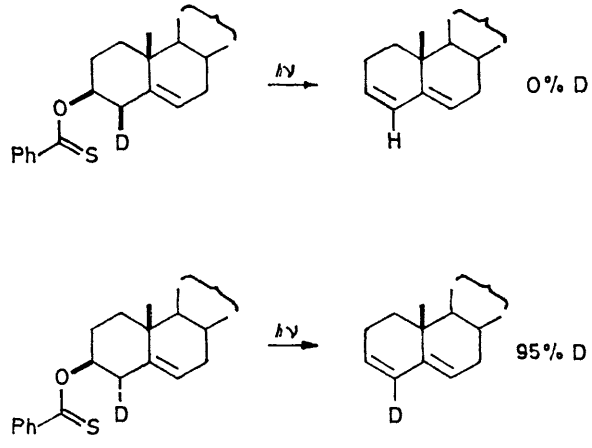
[3] (*a*) S. G. Smith, *J. Amer. Chem. Soc.*, 1961, **63**, 4285; (*b*) S. Braverman and Y. Stabinskey, *Israel J. Chem.*, 1967, **5**, 125; (*c*) S. G. Smith, *Tetrahedron Letters*, 1962, **21**, 979; (*d*) S. G. Smith and J. P. Retrowich, *J. Org. Chem.*, 1965, **30**, 2882.

[4] D. H. R. Barton, C. Chavis, M. K. Kaloustian, P. D. Magnus, G. A. Poulton, and P. J. West, following paper.

[5] W. Bergmann and F. Hirschmann, *J. Org. Chem.*, 1939, **4**, 40.

could be observed with *O*-cholesteryl thiobenzoate (I; Ar = Ph) if the irradiation was prolonged after the elimination reaction was complete. When the photolysis of (I; Ar = Ph) was carried out in ethanol it was found that the readdition of thiobenzoic acid took place rapidly. From the reaction mixture the 3,5-diene (II) and *S*-(cholest-5-en-3α- and -3β-yl) thiobenzoates (III; 3α and 3β) could be isolated. The structure of compound (III; 3β) was confirmed by comparison with an authentic sample, formed by displacement of cholesteryl 3β-tosylate with potassium thiobenzoate in acetone.[6] When cholesta-3,5-diene (II) was irradiated in the presence of thiobenzoic acid the products (III; 3α and 3β) were formed in the same ratio. When the irradiation was carried out in the presence of triethylamine no readdition of thiobenzoic acid took place. Similarly, irradiation in the presence of bis-*p*-nitrobenzoyl peroxide oxidised the liberated thiobenzoic acid to dibenzoyl disulphide, thus preventing readdition.

To determine whether the photoelimination was proceeding in a stereospecific manner *O*-(4α- and 4β-deuteriocholesteryl) thiobenzoates were prepared by the following route. Cholesteryl benzoate was oxidised with selenium dioxide to the 4β-alcohol (IV).[7,8] Treatment of the alcohol (IV) with thionyl chloride in ether at 0° gave the chloride (V).[9] Reaction with lithium aluminium deuteride then gave 4β-deuteriocholesterol.[9] Oxidation of compound (IV) with chromium trioxide in pyridine gave 4-oxocholesteryl benzoate [10] which was reduced with sodium borodeuteride to give the deuterio-alcohol (VI). Treatment of (VI) with thionyl chloride in ether, followed by reduction with lithium aluminium hydride, gave 4α-deuteriocholesterol. The mass spectra of the trimethylsilyl ethers of the products showed 85 (4β-) and 87% (4α-) deuterium incorporation, respectively. Irradiation of *O*-(4β-deuteriocholesteryl) thiobenzoate gave the 3,5-diene with complete loss of deuterium (n.m.r. and mass spectral analysis), whereas irradiation of the 4α-isomer gave the 3,5-diene with complete retention of deuterium (see Scheme). The $k_H : k_D$ ratio, determined by direct observation of the photolysis rates, was 1·4 : 1.



SCHEME

O-Cholestanyl thiobenzoate (VII) was photolysed slowly (1/70th of the rate of cholesteryl thiobenzoate; tungsten lamp) in ethanol to give two products in 21 and 17% yield, respectively. These were characterised as the 3α- and 3β-*S*-esters [(VIII) and (IX)] by comparison with authentic samples.[11]

Similarly, *O*-(4,4-dimethylcholesteryl) thiobenzoate and *O*-(5,6-dihydroergosteryl) thiobenzoate were photo-

[6] R. Bourdon *Bull. Soc. chim. France* 1962, 844.
[7] O. Rosenheim and W. W. Starling, *J. Chem. Soc.*, 1937, 377.
[8] V. A. Petrov, O. Rosenheim, and W. W. Starling, *J. Chem. Soc.*, 1943, 135.
[9] R. E. Ireland, T. I. Wrigley, and W. G. Young, *J. Amer. Chem. Soc.*, 1959, **81**, 2818.
[10] L. F. Fieser and R. Stevenson, *J. Amer. Chem. Soc.*, 1954, **76**, 1728.
[11] J. H. Turnbull, *Chem. and Ind.*, 1959. 515; R. Bourdon, *Bull. Soc. chim. France*, 1962, 844.

lysed slowly and did not produce any characterisable elimination products. For the ready elimination of thiobenzoate the transition state should provide some conjugative stabilisation of the newly forming double bond.

Since it appeared probable that the photolysis was proceeding *via* a triplet state radical mechanism, several reagents were studied in attempts to intercept any radical intermediate. Irradiation of *O*-cholesteryl thiobenzoate (I; Ar = Ph) in the presence of ethyl vinyl ether, iodine, nitric oxide, bis-*p*-nitrophenyl nitroxide, methyl acrylate, or oxygen gave either the 3,5-diene (II) or an intractable mixture. Since the lifetimes of the reactive states obtained from Stern–Volmer plots were very small it is not surprising that the intermediate diradicals could not be intercepted.[12] Chemical evidence for a diradical intermediate will be presented later.[13]

Since thiobenzoic acid *S*-esters undergo ready photoelimination reactions other thiocarbonyl derivatives were examined. Cholesteryl *S*-methyl xanthate[14] (X; X = C·SMe) was photostable, as were compounds (X; X = CNPhMe) and (X; X = PPh_2), whereas the thiocarbonate[15] (X; X = C·O·C_6H_4Cl-*p*), on irradiation in cyclohexane, slowly gave the 3,5-diene (II) in 90% yield (time for 50% photolysis, 150 min).

EXPERIMENTAL

M.p.s were taken with a Kofler hot-stage apparatus. Unless otherwise stated, u.v. spectra were measured for solutions in ethanol and i.r. spectra for Nujol mulls. N.m.r. spectra were taken for solutions in deuteriochloroform at 20°, with tetramethylsilane as internal standard. All solvents were dried by standard techniques. Irradiations were carried out in Pyrex apparatus. The lamps used for the photolyses were: a Philips MBW/U 125 W medium-pressure blacklight lamp with the dark outer glass cover removed and a Philips MBL 125, W high-pressure lamp. A tungsten lamp was also used where indicated.

Light petroleum refers to the fraction of b.p. 40—60°. Chromatography was carried out on acid-washed silica gel. The thermal stability of all thiobenzoic acid *O*-esters under the irradiation conditions was checked by appropriate blank experiments. All preparations and purifications of *O*-esters were carried out with exclusion of light.

O-*Cholesteryl Thiobenzoate* (I; Ar = Ph).—Dry cholesterol (7·8 g) in pyridine (50 ml) was treated at 0° with thiobenzoyl chloride (5 ml); the mixture was left overnight at room temperature, poured into 2N-hydrochloric acid (50 ml), and extracted with ether. The extract was washed with water and dried to yield the crude thiobenzoate (I; Ar = Ph). Chromatography (elution with light petroleum) gave *material* (8·60 g, 85%) of m.p. 164—166° (from light petroleum), $[\alpha]_D^{20}$ −5° (*c* 1·0 in CCl_4), $\nu_{max.}$ (CCl_4) 1226 cm^{-1}, $\lambda_{max.}$ (C_6H_{12}) 256, 288, and 420 nm (ε, 7100, 8000, and 140) (Found: S, 6·3. $C_{34}H_{50}OS$ requires S, 6·3%).

Photolysis of O-*Cholesteryl Thiobenzoate* (I; Ar = Ph).—The thiobenzoate (250 mg) in cyclohexane (150 ml) under nitrogen was cooled externally in a water-bath (fitted with a cooling coil) and irradiated with a medium-pressure mercury vapour lamp placed directly beneath the flask and bath. The reaction was followed by measurement of the u.v. maxima at 252 and 288 nm. After 12 min the mixture was extracted with 4N-sodium hydroxide. The basic solution was treated with hydrogen peroxide (10 vol; 5 ml), left for 10 min, then extracted with ether. The extract was dried (Na_2SO_4) and evaporated to give dibenzoyl disulphide (60 mg), m.p. 129—130° (from methanol). The cyclohexane solution was evaporated and the residue was chromatographed on alumina (G3) (50 g). Elution with light petroleum gave cholesta-3,5-diene (II) (0·167 g), m.p. 78—80° (from methanol–acetone), identified by comparison (m.p. and mixed m.p.) with an authentic sample.[5]

O-*Cholesteryl Thioanisoate* (I; Ar = C_6H_4·OMe-*p*).—Cholesterol (1·0 g) in dry pyridine (20 ml) at 0° was treated with thioanisoyl chloride (1·0 g). After 15 h at room temperature, work-up as before gave the *thioanisoate* (I; Ar = C_6H_4·OMe-*p*) (640 mg) as yellow needles, m.p. 184—185° (from methanol–dichloromethane), $\nu_{max.}$ 1210, 1247, and 1268 cm^{-1}, $\lambda_{max.}$ 228, 234, 266, 312·5, and 419 nm (ε 11,600, 11,300, 7700, 16,400, and 160), τ 9·31 (3H, s), 9·19 (3H, s), 9·10 (6H, s), 8·90 (3H, s), 7·44 (2H, d), 6·16 (3H, s), 4·56 (2H, m), 3·14 (2H, d, *J* 9 Hz), and 1·80 (2H, d, *J* 9 Hz) (other signals constituted the methylene envelope) (Found: C, 78·2; H, 9·6; S, 6·2. $C_{35}H_{52}O_2S$ requires C, 78·3; H, 9·8; S, 6·0%).

Photolysis of O-*Cholesteryl Thioanisoate* (I; Ar = C_6H_4·OMe-*p*).—The thioanisoate (120 mg) in cyclohexane (100 ml) was irradiated in the usual way to give, after work-up, dianisoyl disulphide (23 mg, 59%) and cholesta-3,5-diene (49·3 mg, 58%), both identified by comparisons with authentic samples (m.p. and mixed m.p.).

Photolysis of O-*Cholesteryl Thiobenzoate* (I; Ar = Ph) *in Ethanol.*—The thiobenzoate (200 mg) in ethanol (100 ml) was irradiated in the usual way. When the photolysis was complete (u.v.) the ethanol was evaporated off and the residue chromatographed on silica gel GF 254. Elution with light petroleum–dichloromethane (4 : 1) gave *S*-cholest-5-en-3α-yl thiobenzoate (III; 3α) (17%), m.p. 156—157° (from acetone) and *S*-cholesteryl thiobenzoate (III; 3β) (13%), m.p. 147—148° (from acetone).

The 3β-thiobenzoate was identified by comparison with an authentic sample.[6] The 3α-thiobenzoate (III; 3α) was reduced with lithium aluminium hydride in ether to the thiol, m.p. 100—101° (from acetone), identical with an authentic sample.[6]

Irradiation of Cholesta-3,5-diene (II) *in the Presence of Thiobenzoic Acid.*—Cholesta-3,5-diene (II) (500 mg) and thiobenzoic acid (1·0 g) were irradiated together in ethanol (100 ml). Work-up in the usual way gave a mixture of 3α- and 3β-*S*-esters (III; 3α and 3β) in the same ratio (n.m.r.) as before. Mass spectrometry indicated that only monothiobenzoate (M^+ 508) were present.

4β-*Hydroxycholest-5-en-3β-yl Benzoate* (IV).[7,8]—Selenium dioxide (2 g) in water (1 ml) and acetic acid (100 ml) was added to cholesteryl benzoate (10 g) in glacial acetic acid (100 ml). The mixture was heated at reflux for 5 min and sodium acetate (7·5 g) was added. The hot solution was filtered; on cooling, the benzoate (IV) (3·10 g) separated; m.p. 206—207° (from methanol–ethyl acetate), $[\alpha]_D^{20}$ −56°.

6β-*Chlorocholest-4-en-3β-yl Benzoate* (V).[9]—Thionyl

[12] D. H. R. Barton, M. Bolton, P. D. Magnus, G. Porter, P. West, and J. Wirz, *J.C.S. Chem. Comm.*, 1973, 632.

[13] D. H. R. Barton, M Bolton, P. D. Magnus, and P. West, *J.C.S.* Perkin I, 1973, 1580.

[14] G. L. O'Connor and H. R. Nace, *J. Amer. Chem. Soc.*, 1953, **75**, 2118.

[15] D. L. Garmaise, A. Uchiyama, and A. F. McKay, *J. Amer. Chem. Soc.*, 1962, **27**, 4509.

chloride (0·1 ml) was added to the benzoate (IV) (200 mg) in ether (10 ml) at 0°. After 2 h the mixture was evaporated to give the 6β-chloro-compound (V) (162 mg), m.p. 124—126° (from acetone).

4β-Deuteriocholesterol.[9]—Lithium aluminium deuteride (100 mg) was added to the 6β-chloro-compound (V) (900 mg) in dry ether (100 ml). After 2 h at reflux, saturated aqueous ammonium chloride solution (10 ml) was added at 0°. The ether layer was dried (Na_2SO_4) and evaporated to give 4β-deuteriocholesterol (67·0 mg), m.p. 145—146° (from acetone). Mass spectral analysis of the trimethylsilyl ether indicated a deuterium content of 85%.

4-Oxocholest-5-en-3β-yl Benzoate.[10]—Chromium trioxide–pyridine reagent (5 ml) [from chromium trioxide (5 g), water (5 ml), and pyridine (50 ml)] was added to the benzoate (IV) (100 mg) in dry pyridine (0·1 ml). After 4 h at 50—55° the mixture was poured into water (50 ml) and extracted with ether. The extract was washed with N-hydrochloric acid, saturated aqueous sodium hydrogen carbonate, and finally water. Evaporation of the dried (Na_2SO_4) extract and chromatography of the residue on a thick-layer plate (silica gel) gave the 4-ketone [10] (40 mg), m.p. 152—153° (from acetone), $\nu_{max.}$ 1720, 1700, and 1277 cm^{-1}.

4α-Deuterio-4β-hydroxycholest-5-en-3β-yl Benzoate (VI).—Sodium borodeuteride (6 mg) was added to the foregoing ketone (50 mg) in dry dioxan (5 ml). The mixture was stirred overnight, poured into water, and extracted with ether. The dried (Na_2SO_4) extract was evaporated to give the hydroxy-benzoate (VI) [9] (40 mg), m.p. 209—210° (from acetone), $[\alpha]_D$ −56·5° (*c* 1·0 in $CHCl_3$).

6β-Chloro-4-deuteriocholest-4-en-3β-yl Benzoate.—Thionyl chloride (0·05 ml) was added to the hydroxy-benzoate (VI) (40 mg) in dry ether (5 ml) at 0°. After 2 min the mixture was evaporated to give the 6β-chloro-derivative (29 mg), m.p. 123—125° (from acetone).

4α-Deuteriocholesterol.—Lithium aluminium hydride (10 mg) was added to the foregoing 6β-chloro-compound (30 mg) in dry ether (10 ml). After 2 h at reflux the mixture was cooled to 0° and saturated aqueous ammonium chloride solution (1 ml) was added. The ether layer was dried (Na_2SO_4) and evaporated to give 4α-deuteriocholesterol (19 mg), m.p. 142—144° (from acetone). The deuterium content, calculated from the mass spectrum of the trimethylsilyl ether, was 87%.

O-(*4β-Deuteriocholesteryl*) *Thiobenzoate.*—Thiobenzoyl chloride (0·15 ml) was added to 4β-deuteriocholesterol (50 mg) in pyridine (2 ml) at 0°. Work-up in the usual way gave *O*-(4β-deuteriocholesteryl) thiobenzoate (36 mg), m.p. 161—163° (from methanol), $[\alpha]_D$ −5° (*c* 1·0 in $CHCl_3$). Similarly prepared, *O*-(4α-deuteriocholesteryl) thiobenzoate had m.p. 162—163° (from methanol), $[\alpha]_D$ −5° (*c* 1·0 in $CHCl_3$).

Photolysis of O-(*4α- and 4β-Deuteriocholesteryl*) *Thiobenzoates.*—The thiobenzoates (25 mg) in cyclohexane (75 ml) were photolysed in the usual way. Cholesta-3,5-diene (II), m.p. 77—78°, from the 4β-deuteriocholesteryl thiobenzoate had M^+ 368 (% deuterium = 0). Cholesta-3,5-diene (II), m.p. 78—79°, from the 4α-deuteriocholesteryl thiobenzoate had M^+ 369·35158 (Calc. for $C_{27}H_{43}D$, 369·35056), *i.e.* % deuterium = 82·6% (98% retention).

O-*Cholestan-3β-yl Thiobenzoate* (VII).—Thiobenzoyl chloride (3·0 ml) was added to cholestan-3β-ol (7·76 g) in pyridine (100 ml) at 0°. Work-up in the usual way gave the *thiobenzoate* (VII) (7·0 g), m.p. 141—142° (from light petroleum), $[\alpha]_D$ +3° (*c* 1·0 in $CHCl_3$), $\nu_{max.}$ (CCl_4) 1220 and 1235 cm^{-1}, $\lambda_{max.}$ 251 and 289 nm (ε 7000 and 7600) (Found: S, 6·1. $C_{34}H_{52}OS$ requires S, 6·3%).

Photolysis of O-*Cholestan-3-yl Thiobenzoate* (VII).—The thiobenzoate (VII) (200 mg) in ethanol (100 ml) was irradiated in the usual way. When the reaction was complete the ethanol was evaporated off and the residue was chromatographed on silica gel GF_{254}. Elution with light petroleum–dichloromethane (4 : 1) gave *S*-cholestan-3α-yl thiobenzoate (VIII) (21%), m.p. 149—151° (from acetone), and *S*-cholestan-3β-yl thiobenzoate (IX) (17%), m.p. 140—141° (from acetone), identified by comparison with authentic samples.[11]

O-(*4,4-Dimethylcholesteryl*) *Thiobenzoate.*—Thiobenzoylation of 4,4-dimethylcholesterol in the usual way gave the thiobenzoate, m.p. 159—161° (from dichloromethane–methanol), $[\alpha]_D$ −37° (*c* 1·0 in $CHCl_3$), $\lambda_{max.}$ 253 and 290 nm (ε 10,500 and 10,500), $\nu_{max.}$ (CCl_4) 1240 cm^{-1} (Found: C, 80·8; H, 10·0; S, 6·0. $C_{36}H_{54}OS$ requires C, 80·9; H, 10·2; S, 6·0%). Photolysis proceeded slowly to give at least eight products (t.l.c.).

O-*Cholesteryl* O-p-*Chlorophenyl Thiocarbonate* (X; X = $C{\cdot}O{\cdot}C_6H_4Cl$-*p*).—*p*-Chlorophenol (320 mg) in N-sodium hydroxide (2·5 ml) was added during 40 min with stirring to thiophosgene (290 mg) in dichloromethane (2 ml). After 2 h the dichloromethane layer was separated, washed with water, dried (Na_2SO_4), and evaporated. The residue, in ether (5 ml), was added to cholesterol (940 mg) in ether (15 ml). The mixture was stirred for 15 h, then evaporated, and the residue was chromatographed on silica gel. Elution with dichloromethane gave the *thiocarbonate* (X; X = $C{\cdot}O{\cdot}C_6H_4Cl$-*p*) (300 mg), m.p. 191—192° (from acetone), $\nu_{max.}$ 1595, 1300, 1195, 1018, and 892 cm^{-1}, $\lambda_{max.}$ (CH_2Cl_2) 308, 277, and 240 nm (ε 80, 1000, and 7800), τ 9·30 (3H, s), 9·26 (3H, s), 9·08 (6H, s), 8·92 (3H, s), 7·40 (2H, d), 4·83br (1H, s), 4·51 (1H, d), 2·92 (2H, d, J_{AB} 9 Hz), and 2·57 (2H, d, J_{AB} 9 Hz), M^+ 556 ($C_{34}H_{49}ClO_2S$ requires *M*, 556).

Photolysis of the Thiocarbonate (X; X = $C{\cdot}O{\cdot}C_6H_4Cl$-*p*).—The thiocarbonate (277 mg) in dichloromethane (100 ml) containing triethylamine (0·5 ml) was irradiated in the usual way. After 300 min work-up in the usual way gave cholesta-3,5-diene (II) (168 mg).

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