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ON THE MECHANISM OF THE DEOXYGENATION OF SECONDARY ALCOHOLS BY THE REDUCTION OF THEIR METHYL XANTHATES BY TIN HYDRIDES

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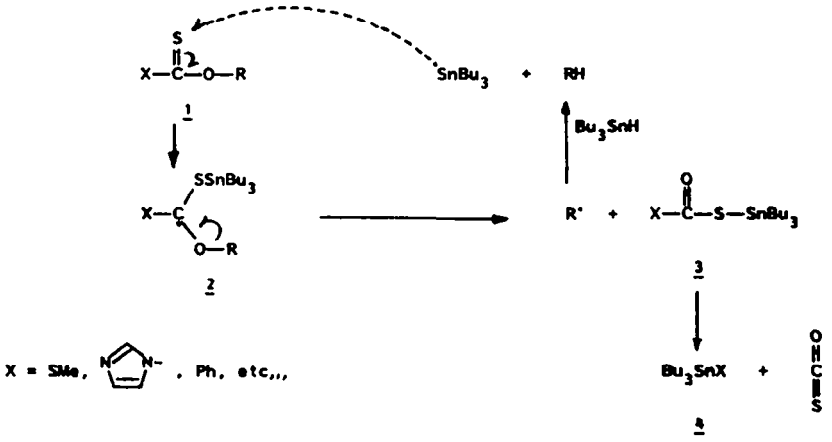
Abstract - Two alternate proposals for the mechanism of reduction of xanthates by tributylstannane have been examined. Evidence has been secured that under normal reduction conditions the thiocarbonyl group is attacked reversibly. At a high enough temperature the carbon radical fragments to give eventually the reduction product. Under modified conditions, where no reducing agent (Sn-H) is present, the radical formed eliminates methylthiotributylstanne and affords the thiocarbonyloxy radical observed in the e.s.r. spectrum.

The reduction of thionoesters 1 and especially xanthates 1 (X = CH_3S-), with tri-n-butylstannane is a mild and general method for the deoxygenation of alcohols.[1,2] The reaction works best with secondary alcohols and has found widespread use, particularly in the area of carbohydrates and aminoglycosides for which it was primarily designed.



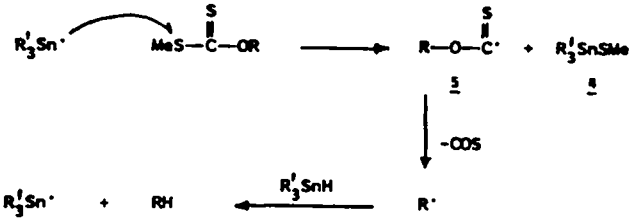
Scheme 1

The mechanism that was first conceived is outlined in Scheme 1. Tri-butylstannyl radical, initially generated by small amounts of AIBN (azo-bis-isobutyronitrile) attacks the

thiolcarbonyl sulphur to produce a radical intermediate 2 which undergoes β scission to thiolcarbonate 3 and an alkyl radical. Hydrogen abstraction from the stannane gives the alkane (RH) and tri-n-butylstannyl radical, thus completing the cycle of this simple chain reaction. The absence of a carbonyl absorption in the infra-red spectrum of crude reaction mixtures, in the case of S-methylxanthates led to the suggestion that 3 (X = SMe) was unstable and extruded carbonyl sulphide (COS) yielding ultimately methylthio tri-n-butylstannane 4 (X = MeS-). This supposition is supported by the similar behaviour observed in related systems.[3]

Recently, however, a different mechanism for the deoxygenation via xanthates was proposed by Barker and Beckwith[4] involving a direct S_H2 attack of the stannyl radical on the sulphide sulphur (Scheme 2). This leads to an alkoxythiocarbonyl radical 5 which looses a molecule of carbonyl sulphide to give an alkyl radical. Reduction of the latter with the stannane completes the cycle. Compound 4 in this case is produced directly. Evidence for this mechanism is primarily spectroscopic. When a mixture of the xanthate, hexamethyldistannane (Me_3Sn-$SnMe_3$) and di-t-butylperoxide was irradiated at -30°C, an e.p.r. signal was observed and attributed unambiguously to the alkoxythiocarbonyl radical 5.

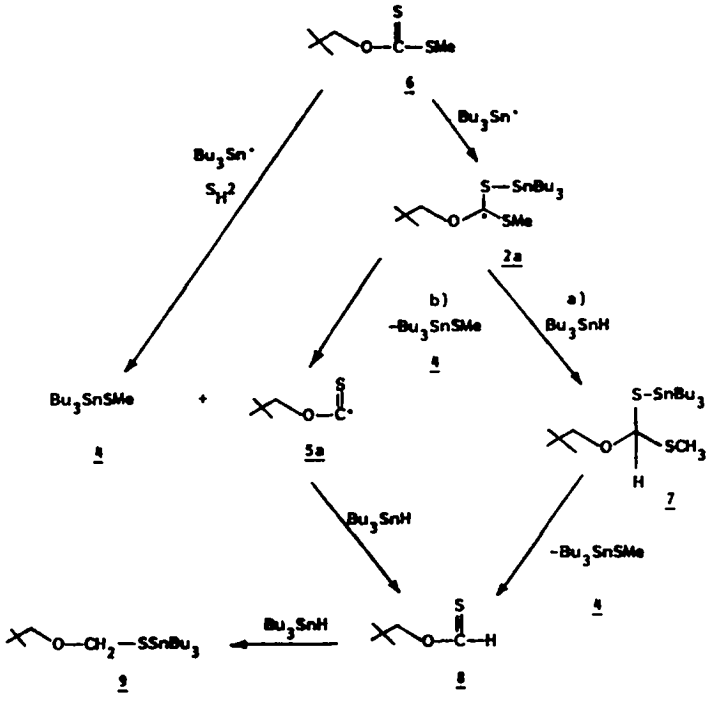
In view of the relevance of the proposals to our own research, we have designed a series of experiments to determine the actual mechanism involved. Part of this work has appeared as a preliminary communication.[5]



Scheme 2

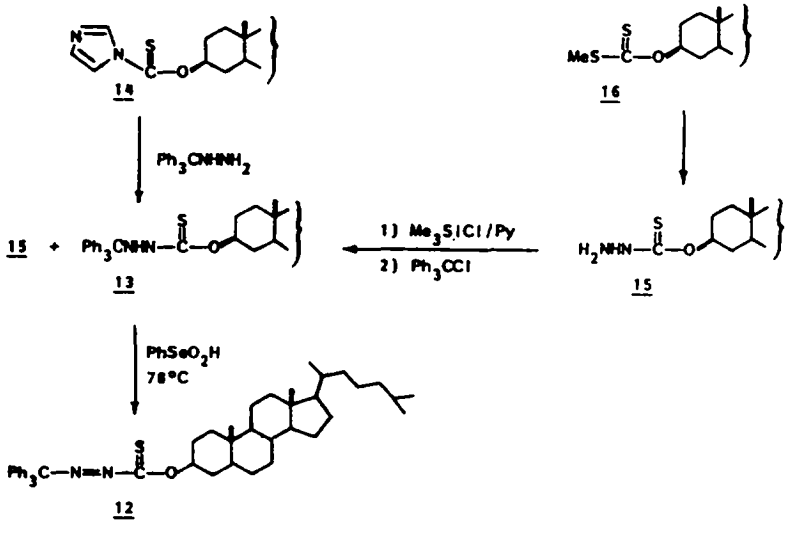
Xanthates of primary alcohols require a fairly high temperature (ca. 130°C) for the deoxygenation to occur efficiently.[6] By conducting the reaction at a lower temperature, it might be possible to detect one or more of the intermediates by NMR, and hence obtain information about the preferred site of attack by the stannyl radical.

The xanthate 6 of neopentyl alcohol was selected because of its simple NMR spectrum and the possibility that its steric bulk might render the presumed intermediates (Scheme 3) more persistent. Xanthate 6 was therefore exposed to tri-n-butylstannane and a trace of AIBN in deuterobenzene at 80°C and the reaction monitored by ^{1}H-NMR spectroscopy. A new methyl signal appeared at δ 2.1 attributed to methylthiotributylstannane 4. The methylene signal of the xanthate was shifted from δ 4.35 to 3.25 and a singlet (2H) appeared at δ 5.1. Furthermore, two equivalents of the hydride were required to complete the reaction. These observations are compatible with structure 9.[7] No intermediate could be detected. As outlined in Scheme 3, thioacetal 9 may be produced by either pathway and so no unambiguous conclusions may be drawn. Any intermediate, therefore, is reduced much faster than the starting xanthate 6. We have checked this for the thionoformate and indeed found that ethyl thionoformate 10[9] (EtOCHS) is very rapidly reduced to give the corresponding thioacetal 11, Et-OCH_2SSnBu_3 (methylene singlet at δ 5.0).



Scheme 3

A crucial assumption in the mechanism proposed by Barker and Beckwith concerns the extrusion of carbonyl sulphide from the alkoxythiocarbonyl radical 5 (Scheme 2). Almost nothing is known about the thermal behaviour of such radicals in contrast to their oxygen analogs. Alkoxy carbonyl radicals R-O-CO· are more familiar and those derived from secondary alcohols do not loose carbon dioxide at 80-110°C[8], the typical temperature range for the deoxygenation of secondary alcohols. One source of alkoxy thiocarbonyl radicals appeared to be the thermal decomposition of azo compound 12, in principle obtainable by oxidation of thiocarbazate 13 (Scheme 4).



Scheme 4

The latter was prepared in 30% yield by treating imidazolide 14 with tritylhydrazine. Carbazate 15 is also produced in this reaction. A better route to 13 was via carbazate 15, isolated in nearly quantitative yield by exposure of xanthate 16 to hydrazine. Sequential treatment of 15 with trimethylsilyl chloride-pyridine then with tritylchloride gave 13 in 43% overall yield. Oxidation to the yellow crystalline azo derivative 12 was accomplished with phenylseleninic acid at -78°C in tetrahydrofuran in 35% yield.

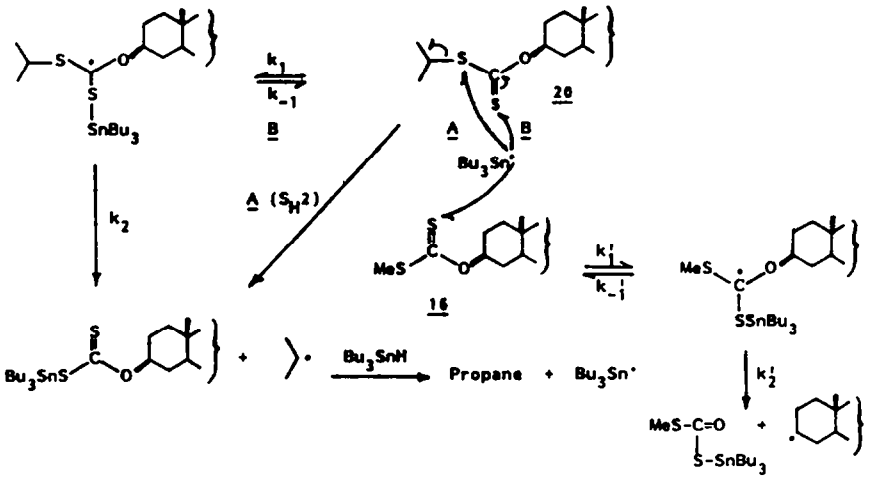
When heated alone in toluene for 1 hour, compound 12 was completely decomposed giving as major products cholest-2- and 3-ene. In the presence of t-butyl mercaptan, however, the major product was cholestane 17 (49%). Cholestanyl thioformate 18 was not observed. Although these results may be construed as evidence for the fragmentation of the corresponding alkoxy thiocarbonyl radical, an alternative chain reaction analogous to that in Scheme 1, where X = -N=N-CPh_3 and $Bu_3Sn^{\cdot}$ is replaced by t-BuS $^{\cdot}$, may be formulated. The Δ^2- and Δ^3-cholestene produced in the absence of a thiol arise almost certainly from the non-radical Chugaev elimination. Any thermal decomposition of 12 proceeding by way of alkoxythiocarbonyl radicals 5 (R = 3β-cholestanyl) is perforce a minor process. If the cholestane 17 obtained in the second experiment is formed by fragmentation of 5 (R = 3β-cholestanyl) to give the 3-cholestanyl radical which then abstracts a hydrogen from the thiol, then substaintial amounts of Δ^2 and Δ^3 cholestene should have also been observed, since the Chugaev elimination is operating independently of the radical processes. It is more plausible that in the presence of the thiol a fast chain reaction, such as the one proposed, sets in which overtakes the Chugaev elimination. Further work on the extrusion of carbonyl sulphide from alkoxythiocarbonyl radicals 5 is needed.

Another inconclusive experiment involved a competition reaction between the S-methyl xanthate 16 and its oxygen counterpart, thiolcarbonate 19, prepared in excellent yield by mild oxidation of 16 with dianisyltelluroxide.[9] This thiolcarbonate can only be reduced by an S_H2 mechanism. In the event, cholestane 17 was produced in 96% yield, whereas thiol carbonate 19 remained practically intact and could be recovered in 92% yield (Table 1, entry 1). Even if, intuitively, such a result suggests a dominant role for the thiocarbonyl group, the large variance in reactivity may still be ascribed to the differing nature of the leaving groups, i.e. alkoxy thiocarbonyl versus alkoxy carbonyl, in a direct radical substitution (S_H2). However, had the thiolcarbonate 19 reacted faster, strong support for the S_H2 process would have been secured.

An alternative and in retrospect more rewarding approach was the study of the influence on the rate of steric factors. By analogy with other S_H2 reactions,[10] direct substitution on the sulphide sulphur, as proposed by Barker and Beckwith, should be significantly retarded if, for example, the methyl group in 16 is replaced by the bulkier isopropyl as in xanthate 20. In contrast, addition of the stannyl radical onto the thiocarbonyl is expected to be relatively insensitive to such a change.

A competition experiment was therefore performed between the methyl xanthate 16 and its isopropyl analog 20 in deuterobenzene at 80°C with only one equivalent of tributylstannane. The result was at first quite surprising. The isopropyl derivative 20 reacted faster than 16, which could be recovered in 78% yield by thin layer chromatographic purification (Table 1, entry 1). Furthermore, no cholestane 17 was formed and the NMR signals due to the isopropyl group had disappeared. Clearly, C-S(sulphide) rather than C-O bond fission had taken place with the consequent absence of deoxygenation, the products of the reaction being the labile S-tributylstannyl-O-(3β-cholestanyl)dithiocarbonate 22 and propane (Table 1, Entry 3). The structure of 22 was deduced from its NMR and U.V. ($\lambda_{max.}$ 235 nm, ε ~ 3000 and 292 nm, ε = 5800; typical of xanthates) spectra and further confirmed by the following chemical transformations of the crude product: i) exposure to methyl iodide gave S-methyl xanthate 16 in 62% overall yield; ii) treatment with tributylstannane produced cholestane 17 (67%).

Although the nature of the products may be explained by an S_H2 route (Scheme 5, path A), the surprising rapidity of the reaction is more difficult to rationalise. This is especially true in view of the relative inertness of the corresponding S-isopropylthiolcarbonate 21 (Table 1, entry 2). A more plausible mechanism would appear to be path B (Scheme 5) involving a reversible addition of the stannyl radical on the thiocarbonyl groups, followed by -scission of the C-S(sulphide) bond. The reversibility of the first step is necessary in order to explain the high recovery of the S-methylxanthate 16. If this step was not reversible, at least 50% of 16 would have been consumed since, for steric reasons, attack of the thiocarbonyl is very probably less favoured in the case of the isopropyl derivative 20 (i.e. $k'_1 > k_1$), other factors being more or less the same. It is obvious that the reverse reaction and the loss of isopropyl radical (mechanistically, these two processes are very similar) must be faster than the breaking of the C-O bond (k_2 and $k'_{-1} >> k'_2$).



Scheme 5

Additional evidence against an S_H2 mechanism was obtained by examining the relative behaviour of xanthates 16, 23 and 24 under the usual conditions. The last two derivatives were prepared by the action of thiophenol or mesitylenethiol on imidazolide 14 with catalysis by DBU (diazabicycloundecene) in 72% and 82% yield respectively. These xanthates, in contrast to the isopropyl derivative 20 have a stronger aryl sulphide bond and do not undergo C-S(sulphide) bond fission. They also possess different steric and electronic properties.

A series of competition experiments performed in refluxing toluene (Table 1, entries 4-6) indicated that the reactivity is in the order 23 > 24 > 16 and that the relative rates were very approximately 4.5:1.5:1. At this temperature (110°C) moreover, only cholestane 17 is produced. These findings are compatible with either mechanism since alkyl aryl sulphides are known to react faster with Bu_3SnH than dialkyl sulphide.[11] However, when the three reductions were conducted simultaneously in benzene at 80°C under as identical conditions as possible (same oil bath, same concentration of reactants, etc...), the results were different (Table 2): i) the order of reactivity changed becoming 24 > 23 > 16, i.e. the mesityl derivative reacts fastest; and ii) varying amounts of the hemithioacetal 26 are produced in addition to cholestane. Similar results were obtained from two separate runs. Thiohemiacetal 26 is, in all likelihood, the hydrolysis product of 25, itself produced by the reduction of thioformate 18 as was shown for neopentyl xanthate 6 (Scheme 3).

According to the mechanism proposed by Barker and Beckwith (Scheme 2), the substitution to give the alkoxythiocarbonyl radical 5, which, incidentally is the same for all three xanthates involved in this study (R = 3β-cholestanyl), is essentially irreversible. This step, therefore controls the relative rate of consumption of starting materials. Since the activation energy for this S_H2 reaction for each of 16, 23 and 24 is not expected to change over such a small temperature range (cf. Arrhenius equation) increasing the temperature would perhaps reduce the difference but not change the order of the reactivity, under otherwise identical reaction conditions. This is clearly not in keeping with the experimental observations where reducing the temperature now favours the more hindered xanthate 24 !

Moreover, as just noted above, if such a mechanism is actually operating, the fragmenting species, the alkoxythiocarbonyl 5, is identical for all three xanthates. Therefore, the ratio of cholestane 17 produced (by fragmentation of 5) to hemithioacetal 26 (quenching of 5 by the tributylstannane) should be very similar. Inspection of Table 2 reveals that this is not the case, the ratios being roughly 0.8, 1 and 6 for 16, 23 and 24 respectivly.

The original mechanism conceived by Barton and McCombie (Scheme 1), modified with respect to the reversibility of the first propagation step as outlined in Scheme 5, appears to be more consonant with the experimental data. Thus, addition of the stannyl radical to the thiocarbonyl to give 2 is fast[12] and reversible whereas the fragmentation is slow and rate determining.[12b]. At the lower temperature of 80°C, quenching of the radical 2 by tributylstannane (e.g. Path a, Scheme 3) competes with the fragmentation. Steric factors in the case of the mesityl derivative promote the fragmentation (relief of non bonded interactions) and reduce the rate of quenching of radical 2 (hindered by the two o-methyl groups). Consequently, in comparison to xanthates 16 and 23, the reaction is faster and less hemithioacetal 26 is produced. At the higher temperature of 110°C, collapse of 2 is more rapid than its quenching hence only cholestane 17 is obtained. At this temperature, the fragmentation rate has probably increased sufficiently to be comparable to the addition of stannyl radical to the thiocarbonyl group. Both steps, therefore, become consequential in determining the overall rate, in contrast to lower temperature reactions where the fragmentation is rate determining. The resulting change in the order of reactivity is a reflection of the interplay of the various factors involved. Steric factors, for example, promote the fragmentation but retard the addition.

We have obtained further corroborating evidence for the reversibility of the first step by conducting a competition experiment at 110°C between the xanthate 16 and the mesitol derived xanthate 27. At 80° the latter does not undergo deoxygenation but is reduced to give hemithioacetal 28 (which is hydrolysed on work up to mesitol 29) at a rate comparable to the reduction of 16. In the presence of a limited quantity of stannane, however, 16 was reduced significantly faster at 110° (Table 1, Entry 7). Again, if the addition of stannyl radicals to the thiocarbonyl is irreversible, both 16 and 27 should have been consumed to a similar extent.

The e.p.r. experiments reported by Barker and Beckwith were conducted under conditions very different from the usual deoxygenation procedure. At the low temperature of -30°C and in the absence of hydrogen atom donor, neither fragmentation of 2 nor its reduction can take place. It collapes therefore to the more persistent alkoxythiocarbonyl radical 5 (cf. 2a in Scheme 3, path b).

Professor Beckwith with whom we have had a friendly exchange of information, has kindly informed us that under the normal conditions of xanthate reduction he agrees that the original mechanism[2] does not require modification (except for the reversibility of the first step).

Table 1. Competing Reductions of Xanthates with Tri-n-butylstannane

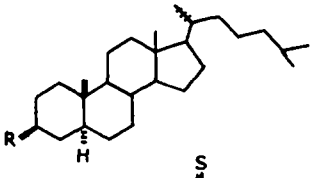
Entry	Xanthates (mmol)	Bu_3SnH (mmol)	Temperature (°C)	Products (% Yields)
1	16 (0.3) + 19 (0.3)	0.32	110	4 (94) + 17 (96) + 19 (92)
2	20 (0.1) + 21 (0.1)	0.1	80	20 (24) + 21 (96)
3	16 (0.036) + 20 (0.034)	0.045	80	16 (78) + 22 (~75%)
4	16 (0.1) + 23 (0.1)	0.15	110	16 (52) + 23 (8)
5	16 (0.05) + 24 (0.05)	0.15	110	16 (34) + 24 (20)
6	23 (0.05) + 24 (0.05)	0.05	110	ratio 23/24 = 1/2.5[a]
7	16 (0.2) + 27 (0.2)	0.22	110	16 (27) + 27 (69)

a) In this case the xanthates 23 and 24 could not be separated by t.l.c. and the ratio of unchanged product was determined by 400 MHz ^1H NMR.

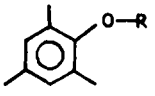
Table 2. Reduction of Xanthates 16, 23 and 24 at 80°C.

Entry	Substrate	Time (hrs)	Products (% Yields)	Ratio 17/26
1	16	8[a]	17 (40 5) + 26 (35 5)	1
2	23	6[a]	17 (29 9) + 26 (35 3)	0.8
3	24	2.5	17 (75 5) + 26 (13 2)	6

a) Extra AIBN (2.5 mg) was added after 5 hrs at reflux.



16, R = O-C(=S)-SMe
17, R = H
18, R = -O-C(=S)-H
19, R = -O-C(=O)-S-Me
20, R = -O-C(=S)-SCH(CH$_3$)$_2$



21, R = -O-C(=O)-SCH(CH$_3$)$_2$
22, R = -O-C(=S)-SSnBu$_3$
23, R = -O-C(=S)-SPh
24, R = -O-C(=S)-S- 
25, R = -O-CH$_2$SSnBu$_3$
26, R = -O-CH$_2$SH

27, R = -C(=S)-SMe
28, R = -CH$_2$SSnBu$_3$
29, R = H

General Experimental

Melting points were taken on a Reichert Hot Stage apparatus and are uncorrected. Infra red spectra were measured with a Perkin Elmer 297 spectrophotometer and UV spectra with a Jobin Yvon Duospec 203 spectrophotometer. NMR spectra of chloroform solutions were recorded at 60 MHz unless otherwise stated with either a Varian T-60 or EM 360-L spectrometer. 400 MHz NMR spectra were measured with a Brucker WH 400 spectrometer. Chemical shifts (δ) are in ppm downfield from tetramethylsilane as internal standard. 70eV, E.I. mass spectra were recorded with either an AEI MS-9 or an AEI MS-50 apparatus. All solvents were dried and distilled by standard procedures.

Reduction of Neopentylxanthate with Tri-n-butylstannane.- i) O-Neopentyl-S-methyldithiocarbonate 6 (36 mg, 0.2 mmol), tri-n-butylstannane (72 mg, 0.2 mmol) and AIBN (5 mg) were dissolved in deuterobenzene (0.5 ml) in an NMR tube and the ^{1}H NMR spectrum of the mixture taken. The tube was then immersed in an oil bath preheated to 80°C. The course of the reaction was monitored by ^{1}H NMR spectroscopy. ii) The above experiment was repeated with the exception that tri-n-butylstannane was used in two fold excess (130 mg, 0.4 mmol).

Synthesis of Methylthiotri-n-butylstannane 4.- Tri-n-butylstannane (7.6 g, 20 mmol) and a trace of AIBN was added to a solution of dimethyldisulphide (2 g, 21 mmol) in toluene (10 ml) and the mixture heated to reflux under nitrogen for 1 hr causing a vigorous evolution of methyl mercaptan which was passed into a sodium hypochlorite trap. The solvent was then removed in vacuo and the residue subjected to Kugelrohr distillation (110°C/0.1 mm) to give methylthiotri-n-butylstannane 4 (6.01 g, 89%) as a colourless oil [13] δ2.10 (3H,s, SCH_3) (lit. bp 104°C/0.22 mm).

Reduction of O-Ethylthioformate 10 with tri-n-butylstannane.- O-Ethylthioformate 10 (20 mg, 0.2 mmol) was treated with tri-n-butylstannane (87 mg, 0.3 mmol) and AIBN (5 mg) in deuterobenzene (0.5 ml) at 80°C in an NMR tube and the reaction monitored by ^{1}H NMR spectroscopy.

Reaction of Triphenylmethylhydrazine with 3β-Cholestanyloxythiocarbonyl imidazole 14.- Triphenylmethylhydrazine hydrochloride (204 mg, 0.66 mmol) was added to a stirred solution of the thiocarbonylimidazolide 14 (246 mg, 0.5 mmol) and triethylamine (0.25 ml) in benzene (5 ml) (5 ml) at room temperature and under nitrogen. After stirring for 4 hrs at room temperature the reaction was diluted with ether (5 ml), filtered and evaporated to dryness. Chromatography of the crude reaction mixture on silica gel gave the triphenylmethylthiocarbazate 13 (105 mg, 30%) (eluant: pentane-dichloromethane 1:1) as a colourless oil with ν_{max} (CH_2Cl_2): 3350, 1360, 1190, 1030 cm^{-1}; δ: 0.65 (3H, s, $18CH_3$), 0.80 (3H, s, $19CH_3$), 5.15 (1H, m, $3\alpha H$), 7.5 (15H, m) (Found: C, 80.34; H, 8.96; N, 3.80; S, 4.28. $C_{47}H_{64}N_2OS$ requires: C, 80.06; H, 9.15; N, 3.97; S, 4.55%).

Further elution with dichloromethane gave the thiocarbazate 15 (150 mg, 65%) which was a colourless crystalline substance with m.p. 230-232°C (MeOH-CH_2Cl_2); ν_{max} (nujol): 3280, 1225, 1020 cm^{-1}; δ: 0.65 (3H, s), 3.70 (2H, large, NH_2), 5.25 (1H, m, $3\alpha H$), 7.50 (1H, large CSNH), m/z: 464 (M^+), 402 (M-COS) (Found: C, 72.82; H, 10.97; N, 5.99; S, 6.84. $C_{28}H_{50}N_2OS$ requires: C, 72.67; H, 10.89; N, 6.05; S, 6.93%).

Carbazate 13 from Xanthate 16.- Hydrazine hydrate (2 ml) was added to a stirred solution of the xanthate 14 (478 mg, 1 mmol) in dichloromethane (10 ml) under nitrogen at room temperature. After stirring for 30 mins at room temperature the reaction was poured into water (50 ml) and the organic phase separated. The aqueous phase was extracted with dichloromethane (10 ml) and the combined organic phases washed with water (3 x 20 ml), dried on sodium sulphate, filtered and evaporated to dryness yielding the crude carbazate 15. The product taken up in THF (10 ml) was cooled to 0°C under nitrogen and treated with pyridine (0.2 ml) and then chlorotrimethylsilane (0.15 ml), 1.1 mmol). The reaction mixture was stirred at 0°C for 1.5 hrs before triphenylmethyl chloride (417 mg, 1.5 mmol) was added as a suspension in THF (10 ml). The reaction was stirred for a further 30 mins at 0°C and then 30 mins at room temperature and finally poured into water (100 ml) and extracted with dichloromethane (3 x 25 ml). The extracts were washed with water (3 x 25 ml), dried on sodium sulphate, filtered and evaporated to dryness. Chromatography of the crude product on silica gel gave the pure carbazate 13 (304 mg, 43%) which was identical to the sample isolated above.

3β-Cholestanyloxy-triphenylmethylazothioformate 12.- Phenylseleninic acid (28 mg, 0.15 mmol) in THF (10 ml) was added to a stirred solution of the thiocarbazate 13 (223 mg, 0.3 mmol) in ether (10 ml) under nitrogen at -78°C. The reaction was then allowed to warm to room temperature over 2 hrs before the solvent was removed in vacuo and the crude mixture subjected to prepared t.l.c. (silica gel eluant: pentane-dichloromethane 9:1) to give the yellow crystalline azothioformate 12 (70 mg, 31%) which had m.p. 104-105°C decomp. (ether-hexane); λ_{max} (cyclohexane): 255 nm (ε 7440); ν_{max} (CH_2Cl_2): 1300, 1140 cm^{-1}. δ: 0.65 (3H, s, $18CH_3$), 0.8 (3H, s, $19CH_3$), 5.30 (1H, m, $3\alpha H$), 7.4 (15H, m) (Found: C, 80.35; H, 8.79; N, 4.03; S, 4.54. $C_{47}H_{62}N_2OS$ requires: C, 80.29; H, 8.89; N, 3.98; S, 4.56%).

Decomposition of the Azothioformate 12.- The azothioformate 10 (58 mg) in toluene (2 ml) was added to a solution of t-butylmercaptan (0.25 ml) in toluene (2 ml) at reflux under nitrogen. After 1 hr at reflux the reaction was evaporated to dryness and the ^{1}H-NMR of the crude product recorded (total absence of thioformate HCSO-R). The crude mixture was then filtered on silica gel (eluant: pentane) to yield cholestane 17 (15 mg, 49%), m.p. and mixed m.p. 79-81°C (acetone).

Treatment of a Mixture of Xanthate 16 and Thiolcarbonate 19 with Tri-n-butylstannane.- Tri-n-butylstannane (116 mg of 80%, 0.32 mmol) and AIBN (10 mg) in toluene (5 ml) were added dropwise over 10 mins to a solution of xanthate 16 (143 mg, 0.3 mmol) and of thiolcarbonate 19 (139 mg, 0.3 mmol) in toluene (5 ml) at reflux under nitrogen. After 1 hr at reflux the solution was cooled to room temperature and the toluene evaporated in vacuo. The crude reaction mixture was then subjected to Kugelrohr distillation (130°C/0.2 mm) giving methylthiotri-n-butylstannane 2 (95 mg, 94%) which was identical with an authentic sample. The distillation residues were then chromatographed on silica gel to give 5αH-cholestane 17

(107 mg, 96%) (eluant: pentane), m.p. and mixed m.p. 81°C (acetone) and then the recovered thiolcarbonate 19 (129 mg, 92%) (eluant: pentane).

S-Isopropyl-O-3β-cholestanyldithiocarbonate 20.- Sodium hydride (0.5 g of 50% dispersion) and imidazole (10 mg) were added to a solution of 3β-cholestanol (3.88 g, 10 mmol) in THF (50 ml) at room temperature under nitrogen and the reaction brought to reflux for 3 hrs. Carbon disulphide (0.5 ml) was added and after a further 30 mins at reflux isopropyliodide (0.5 ml) was added. The reaction was maintained at reflux for a further 30 mins and then quenched with glacial acetic acid (3 ml) after cooling to room temperature. The reaction was then poured into water (100 ml) and extracted with ether (3 x 50 ml). The combined extracts were washed with dilute hydrochloric acid (50 ml) and water (2 x 50 ml), dried on sodium sulphate filtered and evaporated to dryness. Filtration on silica gel (eluant: pentane) and recrystallisation from acetone gave the xanthate 20 as a white crystalline substance (4.9 g, 97%) which had m.p. 94.5-95.5°C; ν_{max} (nujol): 1220, 1045 cm^{-1}; δ: 0.7 (3H, s, 18CH_3), 0.85 (3H, s, 19CH_3), 1.45 (6H, d, J = 7 Hz, $(CH_3)_2CHS$), 3.90 (1H, sept J = 7 Hz, S$CH(CH_3)_2$), 5.7 (1H, m, 3αH); m/z: 506 (M^+), 371 (M-OCSS-$CH(CH_3)_2$), 370 (M-HSCOSCH$(CH_3)_2$) (Found: C, 73.67; H, 10.62; S, 12.81. $C_{31}H_{54}OS_2$ requires: C, 73.45; H, 10.74; S, 12.65%).

Treatment of a Mixture of Xanthates 16 and 20 with Tri-n-butylstannane.- The ^{1}H-NMR spectrum of a mixture of the xanthates 16 (17 mg, 0.036 mmol) and 20 (17 mg) and of tri-n-butylstannane (13 mg) in deuterobenzene (0.5 ml) was recorded. AIBN (trace) was then added to the mixture and the tube immersed in an oil bath preheated to 80°C. The reaction was followed by NMR spectroscopy until no further change was observed. The solvent was removed under vacuum and the crude reation mixture subjected to preparative t.l.c. on silica gel (eluant: pentane) to give unchanged S-methylxanthate 16 (13.3 mg, 78%). No 5αH-cholestane 17 was found.

Reduction of Xanthate 20 with Tri-n-butylstannane.- (i) One equivalent of stannane : A mixture of xanthate 20 (17 mg) and of tributylstannane (13 mg) in deuterobenzene (0.5 ml) with a trace of AIBN was heated quickly to 80°C. The reaction was followed by ^{1}H-NMR spectroscopy. When no further change was observed the solvent was evaporated and crude S-tri-n-butylstannyl-O-3β-cholestanylxanthate 22 was characterised spectroscopically. It had λ_{max} (cyclohexane): 235 nm (ε 3035), 292 (5800); ν_{max} (benzene): 1218, 1040 cm^{-1}; δ (benzene D_6): 5.5 (1H, m, 3αH). The crude reaction mixture was then dissolved in methyliodide (1 ml) and after standing for 18 hrs at room temperature and removal of solvent was purified by filtration on silica gel (eluant: pentane) to give S-methyl-O-3β-cholestanyldithiocarbonate 16 (10 mg, 62%) which was identical (t.L.c. and NMR) to an authentic sample.
(ii) Two equivalents of stannane : Xanthate 20 (17 mg) was reduced with tri-n-butylstannane (30 mg) in deuterobenzene (10 ml) and the reaction followed by ^{1}-H nmr spectroscopy. At the end of the reaction the solvent was removed under vacuum and the crude mixture filtered on silica gel (eluant: pentane) to give cholestane 17 (9 mg, 67%) which was identical to an authentic sample.

Reduction of Xanthate 16 with tri-n-butylstannane.- The S-methylxanthate 16 (17 mg) was reduced with one equivalent of tri-n-butylstannane (15 mg) in deuterobenzene (0.5 ml) at 80°C. The reaction was followed by ^{1}H-NMR spectroscopy. Chromatography of the crude reaction mixture yielded cholestane 17 (8 mg, 61%) identical to an authentic sample.

S-Isopropyl-O-3β-cholestanylthiolcarbonate 21.- A solution of xanthate 20 (507 mg, 1 mmol) and of dianisyltelluroxide (465 mg, 1.3 mmol) was stirred in dichloromethane (50 ml) at room temperature under nitrogen for 48 hrs. Removal of solvent and chromatography of the crude reaction mixture on silica gel (eluant: hexane-ether 50:1) and crystallisation from acetone gave the thiolcarbonate 21 (354 mg, 72%) which had m.p. 102.5°C; ν_{max} ($CHCl_3$): 1700, 1150 cm^{-1}; δ: 1.35 (6H, d, J = 7 Hz $(CH_3)_2CH$-S), 3.50 (1H, sept J = 7 Hz, S-$CH(CH_3)_2$), 4.9 (1H, m, 3αH) (Found: C, 75.66; H, 11.19; S, 6.56. $C_{31}H_{54}O_2S$ requires: C, 75.86; H, 11.09; S, 6.53%).

Reduction of a Mixture of Xanthate 20 and Thiolcarbonate 21.- A 1:1 mixture (0.1 mmol of each) of the xanthate 20 and the thiolcarbonate 21 was treated with tri-n-butylstannane (0.1 mmol) and a trace of AIBN in toluene at reflux. After evaporation of the solvent the xanthate 20 and thiolcarbonate 21 were recovered in 24% and 96% yield after preparative t.l.c. on silica gel.

S-Phenyl-O-3β-cholestanyldithiocarbonate 23.- Thiophenol (3.2 g, 21 mmol), DBU (456 mg, 3 mmol) and the thiocarbonylimidazolide 14 (1.49 g, 3 mmol) were stirred under nitrogen at room temperature in toluene (6 ml). Pyridine (3.7 ml) was then added and the reaction mixture added dropwise to an ice cooled solution of oxalylchloride (2 ml) in dichloromethane (5 ml) (to remove excess thiophenol). After stirring for 30 mins at room temperature the reaction was diluted with water and extracted with dichloromethane. The extracts were washed with dilute sodium hydrogen carbonate solution, dilute hydrochloric acid and water, dried on magnesium sulphate, filtered and evaporated to dryness. Chromatography of the residue on silica gel (eluant: hexane-ether 200:1) gave the xanthate 23 (1.17 g, 72%) which had m.p. 84-85°C (acetone-MeOH); ν_{max} ($CHCl_3$): 1235, 1045 cm^{-1}; δ: 5.5 (1H, m, 3αH), 7.7 (5H, m) (Found: C, 74.13; H, 9.67; S, 11.74. $C_{34}H_{52}OS_2 \cdot 0.5\ H_2O$ requires: C, 74.26; H, 9.71; S, 11.66%).

S-(2,4,6-Trimethylphenyl)-O-3β-cholestanyldithiocarbonate 24.- The xanthate 24 was prepared in 82% yield in an analogous manner to xanthate 23 by treatment of the imidazolide 14 with mesitylmercaptan.[14] It was a colourless crystalline solid with m.p. 149°C (acetone); ν_{max} ($CHCl_3$): 1230, 1030 cm^{-1}; δ: 2.33 (3H, s, p-CH_3Ar-S), 2.40 (6H, s, o-CH_3Ar-S-), 5.6 (1H, m, 3αH), 7.13 (2H, s) (Found: C, 76.22; H, 10.00; S, 11.02. $C_{37}H_{58}OS_2$ requires: C, 76.23; H, 10.03; S, 11.00%).

O-2,4,6-Trimethylphenyl-S-Methyldithiocarbonate 27.- This xanthate was prepared in a manner exactly analogous to xanthate 20 in 87% yield. It was an oil with b.p. 100°C/0.1 mm (Kugelrohr); ν_{max} ($CHCl_3$): 1480, 1195, 1175, 1130, 1040 cm^{-1}; δ: 2.13 (6H, s), 2.28 (3H, s), 2.66 (3H, s), 6.68 (2H, s); m/z 226 (M^+) (Found: C, 58.02; H, 6.34; S, 28.79. $C_{11}H_{14}OS_2$ requires: C, 58.39; H, 6.24; S, 28.34%).

Competing Reductions of Pairs of Xanthates.- Equimolar mixture of the appropriate xanthates (0.1 mmol of each - see table 1) were brought to reflux in toluene under argon and an equimolar amount (0.1 mmol) of tri-n-butylstannane and a trace of AIBN added. After completion of the reaction the solvent was removed in vacuo and the products isolated by preparative t.l.c. on silica and shown by ^{1}H-NMR and t.l.c. to be identical to authentic samples. In the case of xanthates 23 and 24 it proved impossible to separate the mixture by t.l.c. and the ratio of recovered 23 to recovered 24 was estimated by 400 MHz ^{1}H-NMR spectroscopy.

Reduction of Xanthate 27 with Tri-n-butylstannane.- The xanthate 27 (113 mg, 0.5 mmol) and tri-n-butylstannane (291 mg, 1 mmol) in benzene (2 ml) were heated to reflux in the presence of AIBN for 1.5 hrs. The solvent was then evaporated under reduced pressure and the residue chromatographed on silica gel (eluant: hexane-ether 10:1) to yield 2,4,6-trimethylphenol (59 mg, 87%) which was identical to an authentic sample.

3β-Cholestanyloxy Methane Thiol 26.- Tri-n-butylstannane (873 mg, 3 mmol) and AIBN (8 mg) were added to a solution of xanthate 16 (479 mg, 1 mmol) at reflux under nitrogen in benzene (10 ml). After 30 mins at reflux the solvent was removed in vacuo and the crude reaction mixture fractionated on silica gel (eluant: pentane-ether 100:3) to give cholestane 15 (145 mg, 39%), m.p. and mixed m.p. 81°C (acetone) and then the hemithioacetal 26 which had m.p. 70-77°C decomp. (pentane); ν_{max} ($CHCl_3$): 2600 (br SH), 1055 cm^{-1}; δ: 3.6 (1H, m, 3αH), 4.9 (2H, d, J = 9 Hz, OCH_2SH); m/z: 434 (M^+) (Found: C, 74.19; H, 11.44; S, 6.51. $C_{28}H_{50}OS \cdot 1H_2O$ requires: C, 74.27; H, 11.58; S, 7.08%).

Reduction of Xanthates 16, 23 and 24 under Identical Conditions.- The three xanthates 16, 23 and 24 (0.3 mmol of each) were reduced side by side at the same time in the same oil bath in benzene (5 ml per experiment) with tri-n-butyl stannane (0.6 mmol) and AIBN (1.2 mg in each case, 2.5 mole %). After completion, the products were isolated by preparative t.l.c. on silica gel (eluant: pentane-ether 100:1).

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