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THE INVENTION OF NEW RADICAL CHAIN REACTIONS. PART VIII. RADICAL CHEMISTRY OF THIOHYDROXAMIC ESTERS; A NEW METHOD FOR THE GENERATION OF CARBON RADICALS FROM CARBOXYLIC ACIDS.

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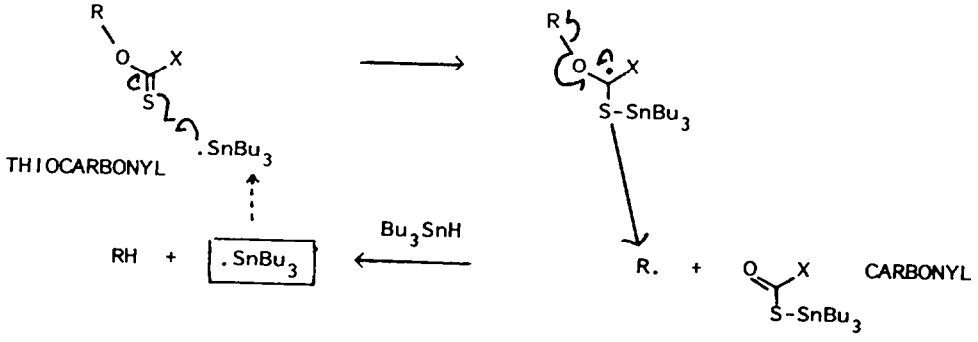
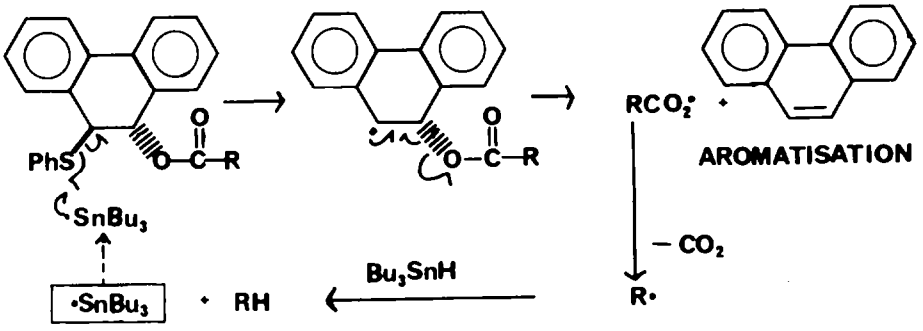
Abstract - The aliphatic and alicyclic esters of N-hydroxypyridine-2-thione are readily reduced by tributylstannane in a radical chain reaction to furnish nor-alkanes.[1] In the absence of the stannane a smooth decarboxylative rearrangement occurs to give 2-substituted thiopyridines.[1] The radicals present in this reaction provoke with t-butylthiol an efficient radical reaction with formation of nor-alkane and 2-pyridyl-t-butyl disulphide.[1] Similarly these carbon radicals can be captured by halogen atom transfer to give noralkyl chlorides, bromides and iodides.[2] With oxygen in the presence of t-butylthiol the corresponding noralkyl hydroperoxides are formed in another radical chain reaction.[3]

The overall yields of free radical chain reactions are determined by the efficiency of the various propagation steps involved. In the invention of new radical reactions, and faced with the, at present, impossible task of calculating the relative rates of all the desired propagation steps and of possible side reactions, the incorporation of suitable thermodynamic driving forces is a proven and fundamental concept. In practice this concept requires the incorporation of a relatively weak bond into the substrate and the formation of a relatively stable strong bond in either the product or a secondary product. Part I[4] of this series dealt with the tributylstannane reduction of various thiocarbonyl esters of secondary alcohols and introduced the thiocarbonyl to carbonyl change as a useful thermodynamic driving force (Scheme 1).



Scheme 1

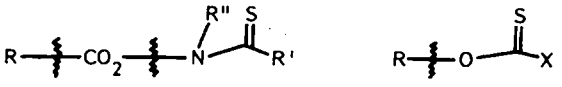
Parts II[5], III[6], V[7], VI[8], VII[9] of this series applied this concept to the radical, stannane induced fragmentation of cyclic thiocarbonates[5], 1,2-dixanthates[6], α-epoxyxanthates[7], primary xanthates[8] and tertiary thioformates.[9] More recently, and prompted by the proposition of a mechanism for xanthate reduction not involving this driving force by Beckwith and Barker[10], we have sought and provided[11] further evidence for the validity of the mechanism of Scheme 1. In our reductive decarboxylation of carboxylic acids[12] (Part IV of this series), the necessary thermodynamic driving force was provided by the aromatisation of the phenanthrene B ring upon fragmentation (Scheme 2).



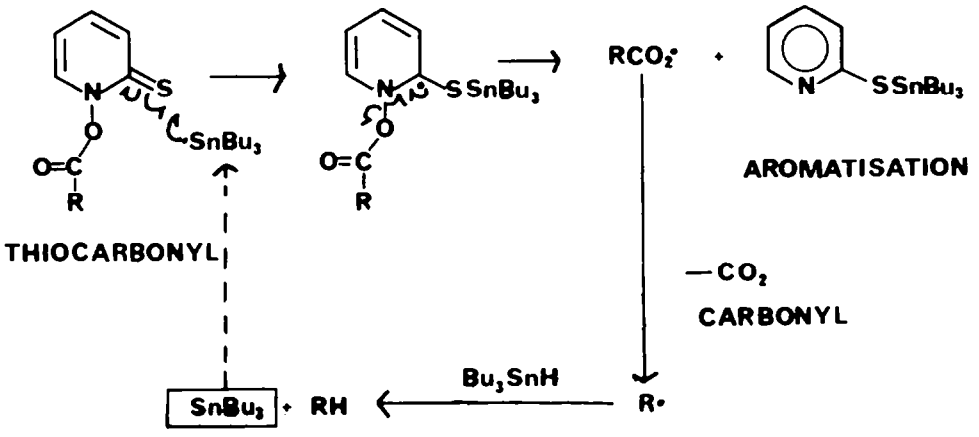
Scheme 2

The formation of three product molecules from two reactant molecules in the decarboxylation of carboxylic esters also renders such reactions favourable from an entropy standpoint.

Variable yields in the esterfication step of this decarboxylation sequence prompted us to search for a more efficient series of reactions. Recognition of the similarity between thiocarbonyl esters of alcohols and O-esters of thiohydroxamic acids (Scheme 3) led us to propose the stannane induced reductive decarboxylation reaction outlined in Scheme 4.

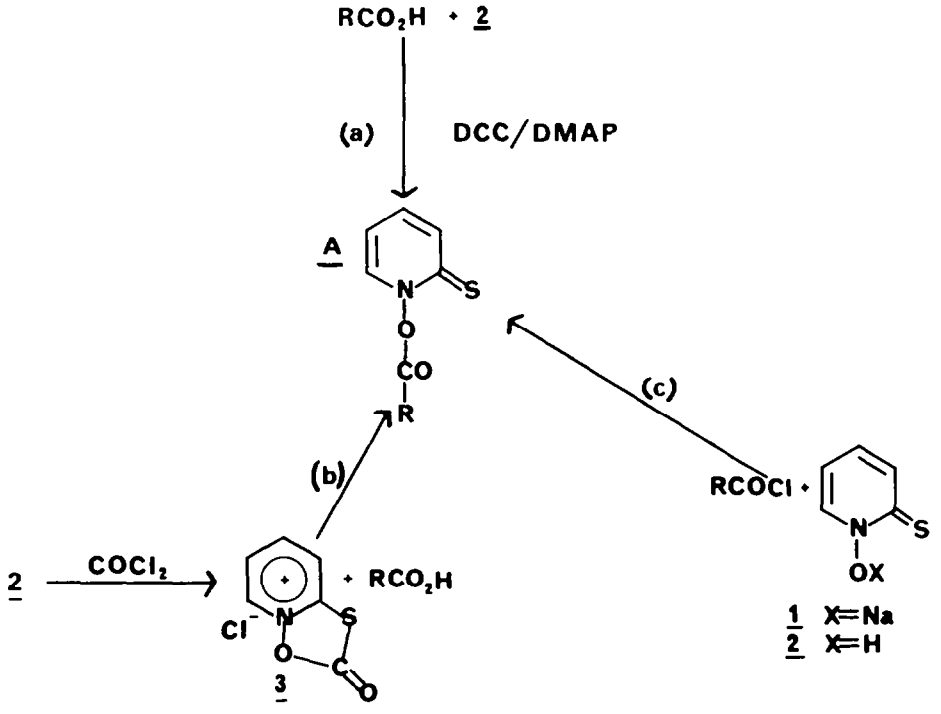


Scheme 3



Scheme 4

Use of the unsaturated cyclic thiohydroxamic acid 2, readily obtained from its commercially available salt 1, enabled us to incorporate into this reaction both driving forces outlined above (thiocarbonyl → carbonyl, aromatisation) and retain the favourable overall increase in entropy inherent in such systems. There is literature precedent for the facile homolytic cleavage of nitrogen oxygen single bonds.[13] Nevertheless no examples of such cleavage are to be found in a recent review of thiohydroxamic acid chemistry.[14] Connaissance of the use of O-esters of thiohydroxamic acids as so called "activated esters" in peptide synthesis[15] led to the supposition that these same esters might be somewhat unstable. It was desirable therefore from a practical as well as an aesthetic point of view to design a one pot synthesis and reduction of these derivatives. In the case of the primary acids 4 and 10 (Table 1) esterification with DCC/DMAP (Scheme 5 (a)) in benzene followed by AIBN initiated reduction with tri-n-butyl-stannane gave the nor-hydrocarbons 5 and 11 in high yields by a one pot procedure.



Scheme 5

Application of this method to the secondary acid 18 (Table 1) was however dissappointing (44% optimised yield). The N-acylurea 20 was a major by-product of this reaction and it was obvious that, at least in the case of secondary acids, the well known intramolecular rearrangement[16] of the intermediate O-acylisoureas was a serious competing reaction with attack by external nucleophiles (DMAP or 2). Reaction of the acid with the cyclic pyridinium salt 3, itself readily available by the action of phosgene on 2, and subsequent reduction with stannane provided a second "one pot" method (Table 1, entries 2, 10, Scheme 5, path (b)). This method however suffers from the disadvantage of prolonged esterification times. Fischer-Speier esterification with a variety of acid catalysts proved ineffective as did the application of various methods for carboxyl group activation (Mukaiyama's salt, triphenylphosphine/diethylazodi-

carboxylate, etc.). Eventually the reaction of derived acid chlorides with the sodium salt 1 of the thiohydroxamic acid 2 proved to be, and remains, the most effective overall proceedure (Scheme 5, path c). Thus brief treatment of the acid in benzene with an excess of oxalylchloride and a catalytic amount of DMF followed by evaporation to dryness furnished the acid chloride, which was taken up in the reaction solvent and allowed to react with a slight excess of salt 1 in the presence of a catalytic amount of p-dimethylaminopyridine, a well proven catalyst for nucleophilic displacements.[17] After reduction of the ester "in situ" with tri-n-butylstannane the nor-hydrocarbons could be isolated in good to excellent yields (Table 1, entries 5-8, 11-16). Inverse, dropwise, addition of the preformed ester to tri-n-butylstannane in benzene at reflux also proved to be effective (Table 1, entry 3).

Table 1. Decarboxylation by tributylstannane

Entry	Substrate	Solvent	Type	Esterification Temp.(°C)	Esterification Time (h)	Reduction Temp.(°C)	Reduction Time (h)	Products (% Yields)
1	4	benzene	A	80	0.75	80	6	5 (95)
2	4	benzene	B	80	4	80	3	5 (70)
3	6	benzene	C	80[i]	0.5	80	2	7 (72)
4	10	toluene	A	80	4	110	6	11 (68)
5	10	benzene	C	80	0.25	80	6	11 (91)
6	12	toluene	C	110	1.5	110	24	13 (46)
7	12	benzene	C	80	0.5	80	4.5	13 (77) + 14 (20)
8	15	benzene	C	80	0.25	80	6	16 (92)
9	18	benzene	A	80	0.5	80	4	19 (44) + 20 (32)
10	18	benzene	B	80	15	80	24	19 (62)
11	18	toluene	C	110	1.5	110	17	19 (79)
12	18	benzene	C	60	0.75	60	3	19 (48) + 21 (39)
13	18	benzene	C	20[i]	0.75	40	6	19 (72) + 21 (15)
14	22	toluene	C	110	2	110	0.3	23 (73)
15	25	benzene	C	80	4	80	4	26 (65)
16	28	benzene	C	80	2	80	2	29 (86)

A: DCC/DMAP. B: Salt 3. C: Acid chloride. i: Inverse addition.

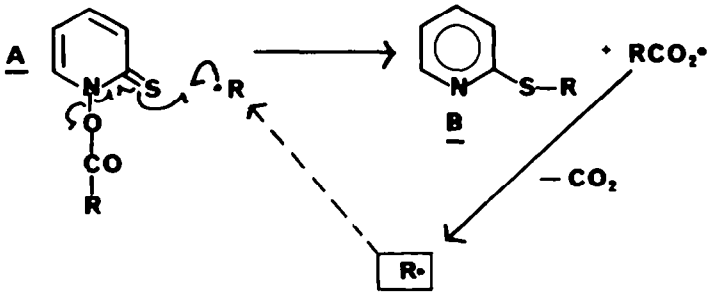
$CH_3(CH_2)_nX$

4 n = 16, X = CO_2H
5 n = 16, X = H
6 n = 14, X = COCl
7 n = 14, X = H
8 n = 16, X = 2'-pyridylthio
9 n = 14, X = 2'-pyridylthio

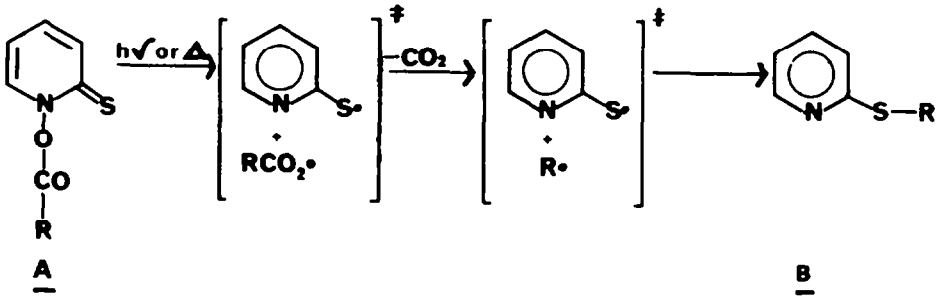
46 n = 14, X = Cl
50 n = 14, X = Br
55 n = 14, X = I
58 n = 14, X = OH
66bn = 14, X = OOH
70 n = 13, X = OH

It became obvious during the course of yield optimisation studies that i) the primary acids 10 and 12 were reduced more effectively and cleanly to 11 and 13 at the reflux temperature of benzene than at that of toluene (Table 1, entries

4-7); that ii) a lowering of the esterification temperature for the secondary acid 18 resulted in a cleaner overall reaction (Table 1, entries 11-13); and finally that iii) the nor-alkyl-2-pyridylsulphides 20 and 21 were formed as significant by-products in the reductions of 12 and 18 (Table 1). On the basis of these observations we concluded that esters A were undergoing a decarboxylative rearrangement to the nor-alkylpyridyl sulphides B and that this rearrangement in certain structures occurs at a similar rate to the desired stannane reduction. It followed that in the absence of reducing agent decarboxylative rearrangement to nor-alkylpyridyl sulphides should be the major reaction pathway. This is indeed the case and Table 2 summarises the yields of alkylpyridyl sulphides obtained on reaction of an acid chloride with 1 in benzene or toluene at reflux. We consider that this unimolecular rearrangement takes place via a free radical chain mechanism as outlined in Scheme 6 but are unable at this point to rule out completely a "leaky" radical cage mechanism (Scheme 7).

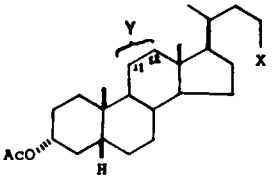


Scheme 6



Scheme 7

Irradiation of the reaction mixture with a simple 300 W tungsten lamp causes a considerable increase in reaction rate (Table 2, entry 18) and even permits the reaction to be carried out at room temperature (Table 2, entry 19).



10 Y = 12 oxo, X = CO_2H
11 Y = 12 oxo, X = H
12 Y = 11 oxo, X = CO_2H
13 Y = 11 oxo, X = H
18 Y = 11 oxo, X = 2-pyridylthio
15 Y = 12$^{\alpha}$AcO, X = CO_2H
16 Y = 12$^{\alpha}$AcO, X = H
17 Y = 12$^{\alpha}$AcO, X = 2-pyridylthio

48 Y = 12$^{\alpha}$AcO, X = Cl
52 Y = 11 oxo, X = Br
62 Y = 12$^{\alpha}$AcO, X = OH
66a Y = 12 oxo, X = I

Table 2. Formation of alkyl pyridyl sulphides

Entry	Substrate	Solvent	Esterification Type	Temperature (°C)	Time (h)	Products (% Yields)
1	4	toluene	A	110	1.5	8 (68)
2	4	toluene	B	110	2	8 (74)
3	6	cyclohexane	B	81	2	9 (92)
4	12	toluene	B	110	2	14 (77)
5	15	toluene	B	110	2.5	17 (74)
6	18	toluene	B	110	1.5	21 (98)
7	22	toluene	B	110	2	24 (72)
8	25	benzene	B	80	3	27 (71)
9	28	benzene	B	80	1	30 (74)
10	31	benzene	B	80	1	32 (58)
11	31	toluene	B	110	24	33 (30)
12	31	chlorobenzene	B	133	15	33 (55)
13	34	toluene	B	110	1.5	35 (60)
14	38	cyclohexane	B	81	1.5	39 (71)
15	40	cyclohexane	B	81	2,5	41 (78)
16	42	chlorobenzene	B	133	1.5	43 (78)
17	36	chlorobenzene	B	133	2.5	37 (88)
18	6	cyclohexane	B	80[1]	0.1	9 (70)
19	6	benzene	C	20[1]	0.75	9 (50) + 7 (23)

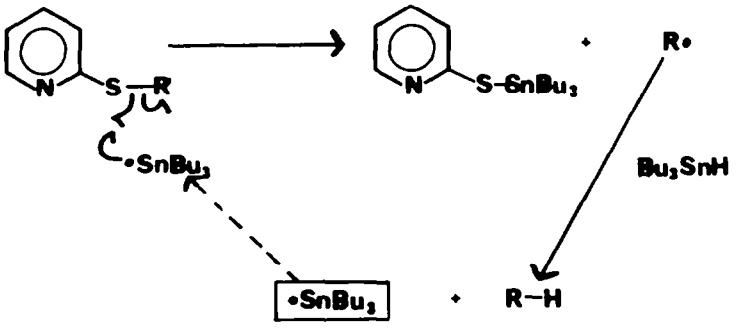
A: DCC/DMAP. B: RCOCl + 1. C: RCOCl + 2 + pyridine. 1: irradiation (300W tungsten).

With the exception of 1-adamantane-carboxylic acid all the primary secondary and tertiary aliphatic and alicyclic acids we studied underwent rearrangement in high yield in a few hours at 110°C. The adamantane derivative (32) was stable in benzene at reflux and was the only ester A to be isolated and characterised in this study (see experimental part). Derivative 32 could however be caused to undergo rearrangement to 33 on prolonged heating in chlorobenzene at reflux (Table 2, entry 12). t-Butylacetyl chloride 42 reacted smoothly with 1 to give neopentylpyridylsulphide in 78% yield (Table 2, entry 16), no trace of 2-methyl-isobutylpyridylsulphide was found in this experiment thus eliminating the possibility of cationic reaction intermediates. Alkyl pyridylsulphides, prepared by other methods, have already found various applications in organic synthesis[18] and thus we limited ourselves to a simple demonstration of their ease of reductive desulphurisation. Treatment of an ethanolic solution of 14 with "nickel boride" prepared *in situ* from sodium borohydride and hexaaquanickel (II) chloride in the presence of boric acid[19] yielded the desulphurised product 13 in 70% yield. Mukaiyama and co-workers have published a similar proceedure which uses a mixture of lithium aluminium hydride and cupric chloride.[20] Secure in the knowledge that esters A undergo an efficient decarboxylative rearrangement to alkylpyridyl-sulphides in the absence of radical trapping agents we were able to explain in full the apparent anomalies outlined above. Esters A derived from primary acids are stable in benzene at reflux and undergo the proposed reduction with tri-n-butylstannane outlined in Scheme 4. In toluene at reflux these same primary esters A first suffer rearrangement to the alkylpyridylsulphides B which are themselves reduced with the stannane in a radical chain manner (Scheme 8), but at a much slower rate. Secondary esters A are rearranged to sulphides B even

at 80°C in benzene. However, on lowering the reaction temperature sufficiently this rearrangement could be suppressed in favour of the desired reduction of the ester with the stannane. In the case of tertiary esters A it would seem that the rearrangement is almost always faster than the reduction, but that the tertiary alkylpyridylsulphides B are reduced much more readily with tri-n-butylstannane than their primary and secondary counterparts. As a final verification of this hypothesis, we carried out the tri-n-butylstannane reduction of several alkylpyridylsulphides. As indicated in Table 3 the primary sulphide 8 and the secondary sulphide 21 were reduced slowly in toluene at 110°C, whereas the secondary-α-acetoxy-sulphide 24 was rapidly reduced to 23 in toluene and the tertiary sulphide 30 was reduced effectively in benzene at 80°C to 29.

Table 3. Reduction of alkylpyridylsulphides with tributylstannane

Entry	Substrate	Solvent	Temperature (°C)	Time (h)	Equivalents of stannane	Products (% Yields)
1	8	toluene	110	6	3	5 (26) + 8 (55)
2	21	toluene	110	24	1,5	19 (55) + 21 (45)
3	24	toluene	110	1	3	23 (57)
4	30	benzene	80	2	3	29 (76)



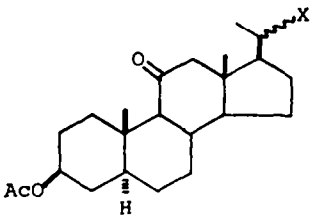
Scheme 8

Consideration of the radical chain mechanism proposed (Scheme 6) for the rearrangement of esters A to alkylpyridylsulphides B resulted in the concept that esters A should be a new, facile, source of carbon radicals in the design of new radical chain reactions. One of the main disadvantages of organostannane reductions is the sometimes tedious removal of organostannane residues from the product. A good proceedure (see experimental part) consists of the transformation of organostannanes into insoluble polymeric tin fluorides. Other literature proceedures involve the partitioning of the crude reaction mixture between pentane and acetonitrile[21] and the use of a catalytic quantity of tri-n-butylstannane generated *in situ* by borohydride reduction of the corresponding tin chloride.[22] The ideal solution is to completely avoid the use of tri-n-butylstannane. We were able to achieve this, at least in the reduction of esters A, by adding the acid chloride to a suspension of 1, of DMAP and of the poorly nucleophilic t-butylmercaptan in benzene or toluene at reflux (Table 4). The decomposition of esters A serves as an initiator for the reaction which proceeds via a radical chain

Table 4. Decarboxylation by tertiobutylmercaptan

Entry	Substrate	Method	Solvent	Temperature (°C)	Time (h)	Products (% Yields)
1	6	A	toluene	110	3	7 (95)
2	6	B	toluene	110	3	7 (72) + 44 (87)
3	12	B	toluene	110	4	13 (62)
4	15	B	toluene	110	3,5	16 (74)
5	18	A	toluene	110	2	19 (77)
6	18	B	toluene	110	1	19 (82)
7	28	B[1]	benzene	80	3	29 (85)

A: RCOCl + 2 + pyridine + inverse addition to the mercaptan.
B: addition of RCOCl to the mixture of 1 and of t-butylmercaptan.
C: esterification by DCC/DMAP.
1: addition to the mercaptan after 5 mins.

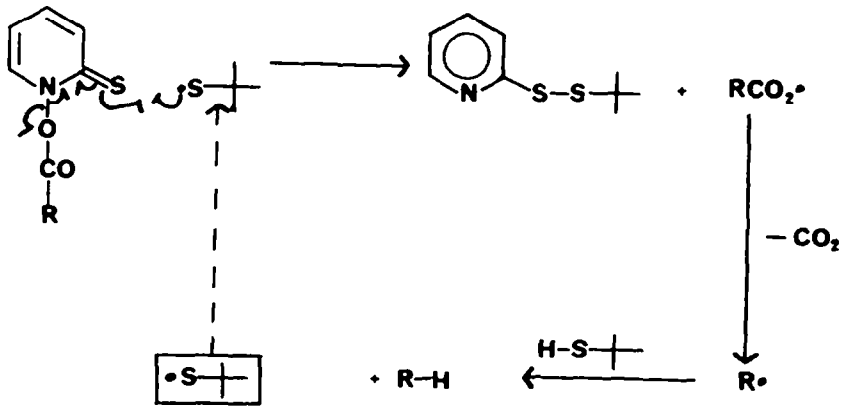


18 X = CO_2H (20R)
19 X = H
20 X = $CON(C_6H_{11})CONH(C_6H_{11})$ (20R)
21 X = 2-pyridylthio (20 RS)

$R^1R^2R^3CX$

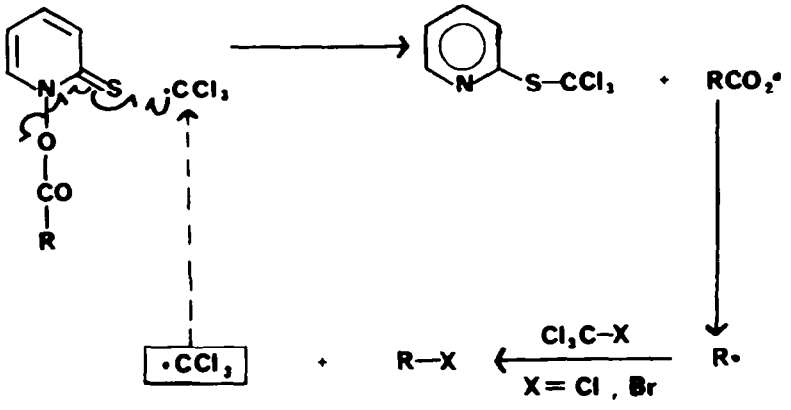
38 $R^1 = R^2 = R^3 = CH_3$, X = COCl
39 $R^1 = R^2 = R^3 = CH_3$, X = 2-pyridylthio
40 R^1 = H, $R^2 = R^3 = CH_3$, X = COCl
41 R^1 = H, $R^2 = R^3 = CH_3$, X = 2-pyridylthio
42 $R^1 = R^2$ = H, $R^3 = {}^tBu$, X = COCl
43 $R^1 = R^2$ = H, $R^3 = {}^tBu$, X = 2-pyridylthio
44 $R^1 = R^2 = R^3 = CH_3$, X = S-S-2-pyridyl
45 $R^1 = R^2 = R^3$ = Cl, X = 2-pyridylthio
54 $R^1 = R^2 = R^3 = CH_3$, X = Cl

mechanism (Scheme 9). The fact that the esters A are generated *in situ* in the presence of the hydrogen source completely eliminates the rearrangement reaction that was in competition with the stannane reduction. Similar overall yields were obtained for the stannane and mercaptan reductions, the latter having the distinct advantage that a simple aqueous extraction and flash chromatography gave pure products in a minimum of time.

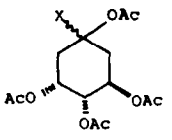


Scheme 9

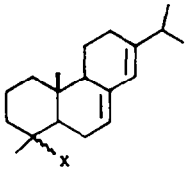
We next turned our attention to the Hunsdiecker reaction. With the exception of the tertiary "butylhypoiodite" method[23] all currently used modifications of this reaction[24] use heavy metal salts such as those of lead[23,25], mercury[26] and thallium[27] and the disadvantages of such proceedures are obvious. We conceived that the decomposition of esters A in bromotrichloromethane as solvent and halogen atom source would result in the formation of nor-alkylbromides in a radical chain reaction (Scheme 10).



Scheme 10



22 X = β-CO_2H
23 X = H
24 X = 2-pyridylthio



25 X = α-CO_2H
26 X = H
27 X = β-2-pyridylthio

$PhCH_2X$

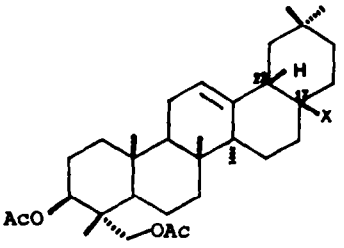
34 X = CO_2H
35 X = 2-pyridylthio

This was readily proven to be the case. Addition of a derived acid chloride to a slight excess of 1 and a catalytic amount of DMAP suspended in either bromotrichloromethane or tetrachloromethane at reflux resulted in the efficient formation of nor-bromides or chlorides in good to excellent yields (Table 5, entries 1-9). The fact that trichloromethyl-2-pyridylsulphide 45 was formed in each of these reactions and was isolated in two cases (Table 5, entries 3 and 9) in yields very close to those of the main product strongly supports the proposed radical chain mechanism. The adamantane-1-carboxylic acid derivative 32, formed *in situ*, underwent smooth decarboxylative halogenation (Table 5, entries 3 and 8) in good yield and in contrast to the elevated temperatures neccessary to bring about its rearrangement to the pyridylsulphide 33. Having established a mild method for the decarboxylative chlorination and bromination of carboxylic acids, without having recourse to strongly electrophilic reagents, we sought to extend the method to iodination. Molecular iodine is beyond doubt the most facile source of iodine atoms and we originally attempted the decomposition of esters A in benzene at reflux and in the presence of iodine. The isolated yield of 26% of n-pentadecyliodide 55 from palmitoyl chloride 6 (Table 5, entry 10) was however far from satisfactory. We assume the low yield to be the result of electrophilic attack by iodine on the thiocarbonyl sulphur and subsequent decomposition. The use of tetraiodomethane in benzene at reflux was unsatisfactory, presumably due to the known[28] decomposition of the reagent *in situ* to iodine and tetraiodoethylene.

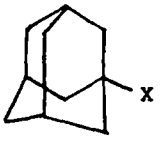
Iodoform in benzene at reflux gave reasonable results (Table 5, entries 11 and 12), however the reactions tended to become strongly coloured after a certain time. We reasoned that iodine was being generated *in situ*. We therefore decided to work with iodoform in solution in cyclohexene so that any iodine liberated, presumably by decomposition of the diiodomethyl-2-pyridylsulphide formed as a by product, would be rapidly trapped and thus be prevented from undergoing electrophilic attack at the thiocarbonylsulphur. Indeed the use of cyclohexene as reaction solvent led to much cleaner reactions (Table 5, entries 13-15) and in one case a marked increase in yield (Table 5, entry 13).

Table 5. Decarboxylation with Halogenation

Entry	Substrate	Solvent	Temperature (°C)	Time (h)	Products (% Yields)
1	6	CCl_4	76	1,5	46 (70)
2	15	CCl_4	76	2	48 (95)
3	31	CCl_4	76	1	49 (88) + 45 (95)
4	38	CCl_4	76	2	54 (82)
5	36	CCl_4	76	2	47 (72)
6	6	$BrCCl_3$	105	1,5	50 (95)
7	12	$BrCCl_3$	105	1,5	52 (77)
8	31	$BrCCl_3$	105	0,5	53 (98)
9	36	$BrCCl_3$	105	1	51 (90) + 45 (87)
10	6	benzene + I_2	80	1	55 (26)
11	6	benzene + CHI_3	80	1,5	55 (74)
12	36	benzene + CHI_3	80	1,5	56 (60)
13	6	cyclohexene + CHI_3	83	4	55 (97)
14	36	cyclohexene + CHI_3	83	2	56 (66)
15	10	cyclohexene + CHI_3	83	2,5	66a (65)



28 X = CO_2H
29 X = H
30 X = 2-pyridylthio
60 X = OH
61 X = OOH



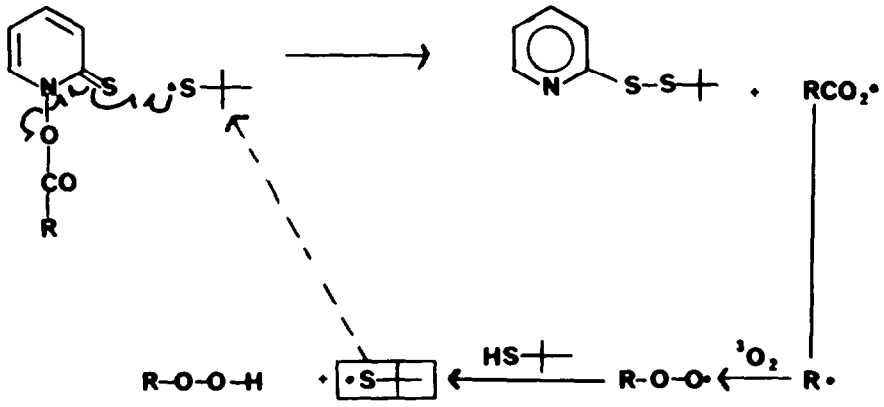
31 X = CO_2H
32 X = CO-O-
33 X = 2 pyridylthio
49 X = Cl
53 X = Br

$(PhCH_2)_2CHX$

36 X = COCl
37 X = 2-pyridylthic
47 X = Cl
51 X = Br
56 X = I
59 X = OH
69 X = OOH

The functional group transformation $R\text{-}CO_2H \longrightarrow R\text{-}OH$ is normally a multistep proceedure (e.g. $R\text{-}CO_2H \rightarrow R\text{-}Br \rightarrow R\text{-}OCOR' \rightarrow ROH$). It is well known that carbon radicals are rapidly and efficiently trapped by triplet oxygen giving hydroperoxyl radicals. We considered that the thermal or photolytic decomposition of esters A in the presence of oxygen would lead to nor-alkylhydroperoxides which could then either be reduced to alcohols or eliminated to aldehydes or ketones. There exist very few efficient general syntheses of non-tertiary aliphatic and alicyclic hydroperoxides. The well known method of Walling and Buckler[29] involves the action of oxygen on alkylmagnesium halides. Whitesides and Hill reduced alkylmercuryhalides with sodium borohydride in the presence of oxygen and obtained the corresponding alcohols.[30] Bartlett and collaborators carried out the decomposition of tertiary peracids under an oxygen atmosphere and reduced the hydroperoxides formed with lithium aluminium hydride.[31]

When we carried out the decomposition of esters of type A at 80°C in toluene saturated with oxygen, only low yields of the desired hydroperoxides and alcohols could be isolated from the complex reaction mixtures. One possible source of side products was the intra and/or intermolecular abstraction of hydrogen atoms from the carbon skeleton by the intermediate hydroperoxyl radicals. On the basis of this assumption we added t-butylmercaptan, as a hydrogen donor, to the reaction mixture and subsequently obtained much cleaner reactions, which gave high yields of alcohols after reduction with either dimethylsulphide or trimethylphosphite. We consider that this reaction occurs by a free radical chain mechanism in which the t-butylmercaptan not only acts as an efficient trap for alkylhydroperoxyl radicals but also provides the t-butylthiyl radical neccessary for efficient chain propagation (Scheme 11).



Scheme 11

We eventually developed three proceedures for the formation of nor-alkylhydroperoxides (Table 6, see experimental part). Method A involves the addition of the acid chloride and of the mercaptan simultaneously to a suspension of 1 in toluene saturated with oxygen at 80°C. Method B involves the addition of preformed ester A to the mercaptan and 1 in toluene saturated with oxygen at 80°C. Method C involves the room temperature photolysis (tungsten) of a solution of ester A in toluene saturated with oxygen. In all cases, after complete consumption of starting ester (decolourisation of the bright yellow solution and t.l.c. analysis) the hydroperoxides were reduced *in situ* with either dimethylsulphide or better trimethylphosphite (see Table 6). In almost all cases it was possible to isolate, by flash chromatography, the mixed disulphide 44, required by the

proposed chain mechanism (Scheme 11), with yields close to those of the alcohol. We were able to obtain moderate to good yields of aliphatic and alicyclic primary, secondary and tertiary alcohols by this very straight-forward and readily applicable proceedure (Table 6). We previously stated[3] that acid 28 led to an undetermined mixture of two diastereoisomeric alcohols; 60 and its 17α-hydroxy counterpart. We have subsequently been able to separate the two components and find that the less polar one is the expected 17β-hydroxy-nor-alkane 60 (56%) and that the second more polar compound is not in fact the 17α alcohol but the 17β-hydroperoxy derivative 61 (33%). This finding is in agreement with the observation that the same acid 28 furnishes only one hydrocarbon 29 on reduction and only one pyridylsulphide 30 on rearrangement. This selectivity surely reflects the conformational preference of the C_{17} radical.

That reduction of acid 28 proceeds with retention of configuration at position 17 was verified by a 2 dimensional NMR study of the product 29 by which method the coupling constant of the 17β and 22β hydrogens was found to be of the order of 5-6 Hz.

Table 6. Formation of Nor Alcohols

Entry	Substrate	Method	Reaction Time (mn) with O_2	^tBuSH (mmol)	$^iMe_2S$ (ml)	$(MeO)_3P$ (ml)	Time (mn) with $Me_2S/(MeO)_3P$	Products (% Yields)
1	6	A	10	9	1	0	60	67 (14) + 58 (51) + 44 (80)
2	6	A	10	27	1	0	60	7 (41) + 58 (35) + 44 (67)
3	6	A	10	4.5	1	0	60	67 (15) + 58 (41) + 44 (42)
4	6	C	10	9	2	0	60	67 (17) + 58 (57) + 44 (47)
5	6	A	10	9	0	0.25	30	7 (26) + 58 (75) + 44 (68)
6	6	C	20	9	0	0.25	120	7 (23) + 58 (67) + 44 (56)
7	6	C	15	9	0	0.25	120	66b (77)[11] + 7 (13) + 44 (25)
8	15	A	20	9	0	0.25	120	62 (69) + 44 (65)
9	28	A	20	9	0	0	0	60 (56) + 63 (39)
10	36	B	60	9	0	0.25	120	59 (82)

A: Simultaneous addition of RCOCl and ^tBuSH to a suspension of 1 in toluene saturated with oxygen at 80°C. B: Addition of the ester to ^tBuSH in toluene saturated with oxygen at 80°C. C: Photolysis (tungsten 300W) at room temperature. i: Reduction with dimethylsulphide was carried out at 80°C. ii: Estimated by NMR before treatment with $(MeO)_3P$.

The use of oxidation method C, permitted determination of the yield of hydroperoxide formed; after disappearance of the ester A, the reaction mixture was subject to an aqueous work up, to remove excess mercaptan. After drying and evaporation to dryness the ^1H NMR spectrum of the crude extracts showed them to be an almost 1/1 mixture of hydroperoxide and of disulphide 44 and thus allowed estimation of the hydroperoxide yield (Table 7). At the same time it was established that no alcohol was present in the reaction mixture[32], prior to treatment with Me_2S or $(MeO)_3P$. The mixtures of hydroperoxides and of 44 obtained in this manner were taken up in pyridine and treated with toluene sulphonylchloride for

several hours at room temperature in order to affect their transformation into oxo derivatives (Scheme 12). We were able to isolate the oxo derivatives in reasonable overall yields from the corresponding carboxylic acids. (Table 7)

Table 7. Formation of nor-hydroperoxides and nor-oxo derivatives.

Entry	Substrate	Method	Reaction Time with O_2 (mn)	tBuSH (mmol)	Hydroperoxides[1] (% Yields)	Products (% Yields)
1	7	C	10	9	66b (89)	67 (53)-> 65 (37)
2	15	C	15	9	68 (80)	64b (57)
3	15	C	10	9	68 (74)	63 (56)
4	36	C	10	9	69 (85)	64a (62)
5	7	C	15	9	66b (84)	65 (18) + 66b (45) + 44 (84) + 70 (9)

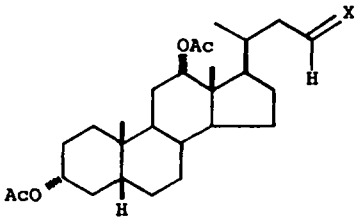
1: Estimated by NMR

$CH_3(CH_2)_{13}CH=X$

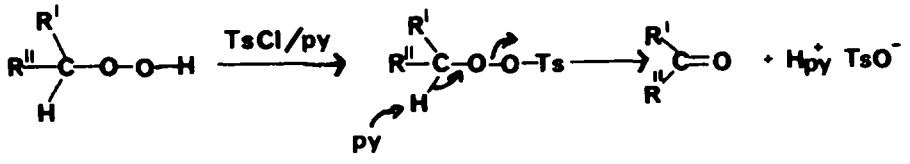
57 X = O
65 X = N-NH-$C_6H_3(NO_2)_2$
67 X = O (polymer)

$(PhCH_2)_2C=O$

64a



63 X = O
64b X = N-NH-$C_6H_3(NO_2)_2$



Scheme 12

Originally the concept of stannane reduction of O-esters of N-hydroxy-2-thiopyridone (2-mercaptopyridine-N-oxide) was constructed around three thermodynamic driving forces : i) the passage from thiocarbonyl to carbonyl, ii) aromatisation of the pyridine nucleus and iii) the overall increase in entropy upon fragmentation. We have since demonstrated elsewhere[33] that esters of thiohydroxamic acids which do not undergo aromatisation on fragmentation only undergo

reaction under much more forcing conditions, thus reinforcing the viability of our original approach.

The wide variety of functional groups, encountered and tolerated in the course of this study serve to emphasize the mildness and selectivity of the reactions developped. Several of the reactions outlined above include as many as four chain propagation steps, and given that typical overall yields are between 70 and 90%, then the yield of an average progagation step is around 95%.

EXPERIMENTAL SECTION

Melting points were taken on a Reichert hot stage apparatus and are uncorrected. Optial rotations were measured for chloroform solutions with a Perkin Elmer 141 MC apparatus. UV spectra were obtained with a Jobin Yvon Duospac 203 spectrophotometer and IR spectra with a Perkin Elmer 297 spectrophotometer. Mass spectra were recorded at 70 eV with either an AEI MS-9 or an AEI MS-50 mass spectrometer. ^{1}H NMR spectra were recorded at 60 MHz unless otherwise stated and on the following instruments 60 MHz : Varian T60 or Varian EM 360; 80 MHz : Brucker WP 80; and 400 MHz Brucker WM 400. Chemical shifts are given in ppm downfield from tetramethylsilane as internal standard. Reaction solvents were dried and distilled according to standard proceedures. All reactions with the exception of oxygenations were carried out under a nitrogen atmosphere. N-Hydroxypyridine-2-thione sodium salt 1, sold as 2-Mercaptopyridine-N-oxide Sodium Salt was commerial (Fluka) and used as such without further purification. N-Hydroxypyridine-2-thione 2 was precipitated from an aqueous solution of its sodium salt with 6M hydrochloric acid and recrystallised from aqueous ethanol according to the literature proceedure.[34]

Preparation of Acid Chlorides.

Unless otherwise stated acid chlorides were prepared immediately prior to use by treatment of the acid (1 mmol) in benzene (5 ml) with oxalylchloride (0.5 ml) and DMF (1 drop) at room temperature under magnetic stirring for 2 hrs. The reaction mixture was evaporated to dryness, redissolved in benzene (5 ml) and evaporated to dryness again yielding the crude acid chloride which was used as such.

Reductive Decarboxylation with Tri-n-butylstannane. General Procedure.

The acid chloride (1 mmol) in the appropriate solvent (Table 1) (5 ml) was added to a stirred, dried (Dean-Stark apparatus) suspension of 1 (1.2 mmol) and of DMAP (0.1 mmol) in the same solvent (10 ml) at reflux. After 10-15 minutes at reflux tri-n-butylstannane[35] (3 mmol) and AIBN (10-20 mg) in the appropriate solvent (5 ml) were added dropwise over 15 mins. The progress of the reaction was monitored by t.l.c. and more stannane and initiator added as neccessary. After completion the reaction was coolad to 80°C and treated with tetrachloromethane (10 ml) for 1 hr. Subsequently the reaction mixture was evaporated to dryness and the residues vigourously stirred overnight in a two phase system comprising a saturated solution of iodine in dichloromethane (20 ml) and a saturated aqueous solution of potassium fluoride (20 ml). The white, polymeric, precipitate was filtered on celite and washed with dichloromethane. The washings were combined with the reaction mixture and after decantation the aqueous phase was further extracted with dichloromethane (3x15 ml). The combined organic phases were washed with sodium thiosulphate (20 ml 2M), water (20 ml) and saturated sodium chloride (20 ml), dried on sodium sulphate, filtered and evaporated to dryness yielding the crude reaction product. Pure products were isolated by flash chromatography over silica gel and either recrystallised or distilled (Kugelrohr) as appropriate.

n-Pentadecane 7 (use of redistilled commercial palmitoyl chloride) was isolated chromatographically (eluant n-pentane) and its identity established by mass spectrometry. m/z 212 ($M^{+\cdot}$).

n-Heptadecane 5 was isolated as for n-pentadecane, mp 22°C (pentane) lit.[36], 22°C.

3α-Acetoxy-24-nor-5βH-cholan-12-one 11 (eluant: pentane/ether 1/1) had mp 155°C (MeOH/H_2O) lit.[37] 158.5-159° $[\alpha]_D^{16}$ = 91° (c=1).

3α-Acetoxy-24-nor-5βH-cholan-11-one 14 (eluant: pentane/ether 1/1) was a non crystaline resin $[\alpha]_D^{18}$ + 71° (c=0.6): ν(CH_2Cl_2): 1720, 1700 cm^{-1}, δ(80 MHz): 0.6 (3H, s); 0.9 (3H, s); 2.00 (3H, s); 4.65 (1H, m), m/z : 388 ($M^{+\cdot}$); 328 (M-$HOAc^{+\cdot}$) (Found: C, 77.27; H, 10.37%. Calc. for $C_{25}H_{40}O_3$: C, 77.23; H, 10.30%).

3α,12α-Diacetoxy-24-nor-5βH-cholane 17 (eluant: dichloromethane/ethylacetate 4/1) had mp 116-117°C, lit.[37] 116.5-117.5°C.

3β-Acetoxy-5αH-pregnan-11-one 20 (eluant: pentane/ether 2/1) had mp 160-162°C (MeOH), lit.[38], mp 160-163°C; $[\alpha]_D^{20}$ + 38° (c=1), lit.[38], $[\alpha]_D$ = +40°.

1β,2β,3α,5αβ-Tetraacetoxycyclohexane 24 (eluant: pentane/ether 4/1) was a glass, $[\alpha]_D^{18}$ -19° (c=1) ν(CH_2Cl_2) 1730-1720 cm^{-1} broad absorption. δ(400 Mhz) 1.96-2.08 (6 singulets total integration 12H); 4.90 (0.5H, m); 5.1 (3H, m); 5.41 (0.5H, m); (Found: C, 53.52; H, 6.53%. Calc. for $C_{14}H_{20}O_8$ C, 53.16; H, 6.37%).

3β,24-Diacetoxy-28-nor-olean-12-ene 30 (eluant: pentane/ether 3/1) had mp 114-115°C; (MeOH) $[\alpha]_D^{16}$ +80° (c=1). ν(nujol): 1740, 1730 cm^{-1}. δ(400 MHz): 0.89 (3H, s); 0.925 (6H, s); 0.95 (3H, s); 1.05 (3H, s); 1.09 (3H, s); 2.08 (3H, s); 2.13 (3H, s); 2.40 (1H, m, 22βH); 3.73 (1H, d, J=8Hz, 24H); 3.91 (1H, d, J=8Hz, 24H); 4.81 (1H, m, 3αH); 5.13 (1H, s, 12H), m/z: 512 ($M^{+\cdot}$); 452 (M-$HOAc^{+\cdot}$); 512 -> 452 m^* 399.0 (Found: C, 77.38; H, 10.11%. Calc. for $C_{33}H_{52}O_4$: C, 77.30; H, 10.23%).

By the method of 2 dimensional ^1H NMR spectroscopy at 400 MHz (COSY 45° 2D NMR)[39] the coupling constant between the 22βH and the 17H was found to be of the order of 5-6Hz; this and the very weak allylic coupling between 22βH and 12H strongly suggest that the D/E ring junction is cis fused and that the hydrogen on position 17 is β.

n-Heptadecane 5 *by the DCC/DMAP Method.*

A solution of stearic acid (286 mg; 1mmol); N-hydroxypyridin-2-thione (151 mg; 1.2 mmol), DMAP (183 mg; 1.5 mmol) and DCC (310 mg; 1.5 mmol) in benzene (10 ml) was brought to reflux for 0.75 hr. This solution was then reduced with tributylstannane as in the general method. n-Heptadecane was isolated by chromatography on silica gel (228 mg) 95% mp 22°C (pentane), idential in all respects to the product described above.

3α-Acetoxy-24-nor-5βH-cholan-12-one 11 *by the DCC/DMAP Method.*

Acetyl-12-ketolithocholic acid 10 (432 mg; 1 mmol), N-hydroxy-pyridin-2-thione (151 mg; 1.2 mmol), DMAP (183 mg, 1.5 mmol) and DCC (310 mg, 1.5 mmol) were dissolved with stirring in toluene at 80°C. After 4 hrs at 80°C the reaction mixture was subject to reduction by tributylstannane according to the general method. Standard work up and chromatography gave 3α-acetoxy-24-nor-5βH-cholan-12-one 11 (264 mg) 68%, mp 155-156 (MeOH) $[\alpha]_D^{16}$ +91° (c=1) which was identical to the sample described above.

3β-Acetoxy-5αH-pregnan-11-one 19 *and N-(3β-acetoxy-5αH-pregnan-11-one-20-carbonyl)-N,N'-dicyclohexylurea* 20 *DCC/DMAP Method.*

DCC (310 mg, 1.5 mmol) in benzene (5 ml) was added over 15 mins to a solution of 3β-acetoxy-11-ketobisnorallocholanic acid 18 (404 mg; 1 mmol), N-hydroxypyridin-2-thione (252 mg; 2 mmol) and DMAP (183 mg; 1.5 mmol) in benzene (10 ml) at reflux. After 30 mins at reflux the standard stannane reduction proceedure and work up was applied. Chromatography on silica gel of the crude reaction mixture gave first 3β-acetoxy-5αH-pregnan-11-one 19 (160 mg) 44%, mp 160-162°

(MeOH), identical to the sample described above and then the N-acylurea 20 (196 mg) 32% (eluant: pentane/ether 1/2), mp 141-143°C (ether); $[\alpha]_D^{18}$ +29° (c=1). ν(nujol): 3425, 1720, 1700, 1650 cm^{-1}. δ(400 MHz): 0.63 (3H, s, 18 $\underline{CH_3}$); 1.05 (3H, s, 19 $\underline{CH_3}$); 1.15 (3H, d, J=6.6 Hz, 21 $\underline{CH_3}$); 2.05 (3H, s, $\underline{CH_3}CO_2$-); 2.35 (1H, d, J= 13 Hz, 9α$\underline{H}$); 2.45 (2H, m, 12α$\underline{H}$ + 12β$\underline{H}$); 3.70 (1H, m, CONH-$\underline{CH}$); 4.66 (1$\underline{H}$, m, 3α$\underline{H}$); 5.37 (1H, m, $(RCO)_2\underline{NCH}$). m/z 485/M-$C_6H_{11}N$=C=O$^{+\cdot}$); 470 (485-15$^+$); 457 (485-28$^+$) 155 ($C_6H_{11}NHCOEt^+$). (Found: C, 72.75; H, 9.53; N, 4.40%. Calc. for $C_{37}H_{58}N_2O_5$: C, 72.75; H, 9.57; N, 4.59%).

The Hydrocarbon 26.

Abietic acid 25 (302 mg; 1 mmol) was dissolved in a saturated solution of phosgene in benzene (5 ml) and 1 drop of DMF added. After 30 mins the phosgene was removed in vacuo at room temperature and the resultant red solution added to a stirred, azeotropically dried, suspension of 2 (165 mg; 1.1 mmol) and DMAP (12 mg; 0.1 mmol) in benzene (10 ml) at reflux. After 4 hrs at 80°C the reaction mixture was subject to reduction with tributylstannane and worked up as above. Chromatography of the crude product gave the hydrocarbon 26 as a colourless oil (167 mg, 65%) (eluant: pentane), $[\alpha]_D^{18}$ -108° (c=0.7). By 400 MHz NMR the product was a 1/1.3 mixture of diastereoisomers at position 4. δ(400 MHz) major diastereoisomer: 0.71 (3H, S, 15 $\underline{CH_3}$); 0.81 (3H, d, J = 6 Hz, 14 $\underline{CH_3}$); 5.40 (1H, d, J=13 Hz vinylic $\underline{H}$ at 7); 5.77 (1H, s, vinylic $\underline{H}$ at 14). Minor diastereoisomer: 0.81 (3H, s, 15 $\underline{CH_3}$); 0.97 (3H, d, J=7 Hz, 14 $\underline{CH_3}$); 5.40 (1H, d, J=13 Hz, vinyl $\underline{H}$); 5.77 (1H, s, vinyl H), lit.[40], δ 0.71 + 0.77 (2x3H s); 0.82 + 0.96 (2x3H, d, J=6Hz and 7Hz respectively). m/z 258 ($M^{+\cdot}$) λ_{max} (cyclohexane) 236 (ε 18,200).

n-Pentadecane 7; Inverse Addition.

Redistilled commercial palmitoylchloride (274 mg; 1 mmol) in benzene (2 ml) was added to a stirred solution of 2 (139 mg; 1.1 mmol), pyridine (79 mg; 1 mmol) and DMAP (12 mg; 0.1 mmol) in benzene (10 ml) at reflux. After 30 mins the reaction was cooled to room temperature filtered through a glass wool plug and the resultant, clear, yellow solution, to which had been added AIBN (10 mg), was added over 30 mins to a solution of tri-n-butylstannane (3 mmol) in benzene at reflux. All subsequent steps are identical to those described in the general proceedure for stannane reductions. After chromatography (eluant: pentane) pure n-pentadecane 7 was obtained (152 mg) 72%, identical to the above isolated product.

1-Oxa-2-oxo-3-thia-indolizinium Chloride 3.

A solution of 2 (3,15 g; 25 mmol) in benzene (10 ml) was added dropwise, at room temperature, to a stirred, saturated, solution of phosgene in benzene (10 ml). The resultant white precipitate was filtered, washed with a little benzene and dried under vacuum at 50°C for 6 hrs giving the salt 3 (4.40 g), 93%, mp 108-110°C. ν(nujol) 1770 cm^{-1}, (Found: C, 38.26; H, 2.26; Cl, 18.95; N, 7.48; S, 17.00%. Calc. for $C_6H_4ClN_2OS$: C, 38.01; H, 2.13; Cl, 18.70; N, 7.39; S, 16.91%).

n-Heptadecane 5; Use of salt 3.

Stearic acid (286 mg, 1 mmol) and dry pyridine (0.5 ml) were added to a stirred suspension of the salt 3 (208 mg; 1.1 mmol) in benzene (5 ml) and the reaction brought to reflux for 4 hrs. The reaction mixture was then reduced with tri-n-butyl-stannane and the products isolated as described above to yield, after chromatography, n-heptadecane 5 (168 mg, 70%).

3β-Acetoxy-5αH-pregnan-11-one 19; Use of salt 3.

A mixture of 3β-acetoxy-11-ketobisnorallocholanic acid 18 (404 mg, 1 mmol), triethylamine (0.14 ml, 1 mmol) and salt 3 (208 mg, 1.1 mmol) was stirred at room temperature in benzene (20 ml) for 2 hrs after which more of the salt 3 (400 mg, 2 mmol) was added and the reaction brought to reflux for 15 hrs. Reduction was then affected with tri-n-butylstannane as described above (a total of 7 mmol of Bu_3SnH added over 15 hrs). Chromatography on silica yielded 3β-acetoxy-5αH-pregnan-11-one 19 (223 mg, 62%).

General Method for The Decarboxylative Rearrangement to Alkylpyridylsulphides.

The acid chloride (1 mmol) in toluene (5 ml) was added to a stirred, azeotropically dried suspension of N-hydroxypyridin-2-thione-Na salt (1.2 mmol) and DMAP (0.1 mmol) at reflux in toluene. At the end of the reaction (t.l.c.) the mixture was cooled to room temperature, filtered on celite and evaporated to dryness. Chromatography on silica gel gave the pure product, n-heptadecyl-2'-pyridylsulphide 8 (eluant: CH_2Cl_2), mp 31-33°C (pentane), $\nu(CH_2Cl_2)$ 1575 cm^{-1}, δ:0.90 (3H, t); 1.30 (30, m); 3.15 (2H, t, J=8 Hz); 6.90 (2H, m); 7.35 (1H, m); 8.35 (1H, d, J=5 Hz), m/z 349 ($M^{+\cdot}$), (Found: C, 75.75; H, 11.16%. Calc. for $C_{22}H_{39}NS$: C, 75.58; H, 11.24%). Similarly obtained n-pentadecyl-2'-pyridylsulphide 9 had mp 52-54°C (pentane), $\nu(CHCl_2)$: 1570, 1550, 1320 cm^{-1}. δ: 0.9 (3H, t), 3.10 (2H, t, J=7Hz), 6.70-7.40 (3H, m), 8.30 (1H, d, J=5 Hz), m/z: 321 ($M^{+\cdot}$), (Found: C, 74.41, H, 11.04; N, 4.19; S, 9.19%. Calc. for $C_{20}H_{35}NS$: C, 74.70; H, 10.97; N, 4.36; S, 9.97%).

3α-Acetoxy-23(2'-pyridylthio)-24-nor-cholan-11-one 14 was a resin (eluant: CH_2Cl_2), $[\alpha]_D^{18}$ + 60° (c=0.9), δ(400 MHz): 0.65 (3H, s, 18$\underline{CH_3}$); 1.00 (3H, d, J=7 Hz, 21$\underline{CH_3}$), 1.18 (3H, s, 19$\underline{CH_3}$), 2.03 (3H, s, $CH_3\underline{CO_2}$), 2.28 (1H, d, J=10Hz, 8β$\underline{H}$), 2.40 (1H, d, J=10Hz, 9α$\underline{H}$), 2.55 (2H, m, 12α$\underline{H}$+, 12β$\underline{H}$); 3.05 (1H, m, 23$\underline{H}$); 3.30 (1H, m, 23$\underline{H}$), 4.72 (1H, m, 3β$\underline{H}$), 6.95 (1H, dd, J_1=9Hz, J_2=6Hz), 7.15 (1H, d, J_3=10Hz), 7.37 (1H, dd, J_3=10Hz, J_1=9Hz), 8.40 (1H, d, J_2=6Hz), m/z: 497 ($M^{+\cdot}$), λ_{max} (EtOH): 253 nm (ε 7900), 292 nm (ε 2900) (Found: C, 72.02; H, 8.58; N, 2.58; S, 5.89%. Calc. for $C_{32}H_{43}NO_3S$: C, 72.39; H, 8.71; N, 2.81; S, 6.44%).

Neopentyl-2'-pyridylsulphide 43 was a yellow oil (eluant: CH_2Cl_2), $\nu(CH_2Cl_2)$: 1570, 1550, 1120 cm^{-1}. δ: 1.1 (9H, s), 3.2 (2H, s), 6.9 (1H, dd, J_1=6Hz, J_2=2Hz), 7.2 (2H, m), 8.3 (1H, d, J_3=5Hz); m/z: 181 ($M^{+\cdot}$); λ_{max} (EtOH): 255 nm (ε 11000); 292 nm (ε 5300). (Found: C, 66.45; H, 8.47. Calc. for $C_{10}H_{15}NS$: C, 66.25; H, 8.34%).

Benzyl-2'-pyridylsulphide 35 was an oil (eluant: CH_2Cl_2). δ: 4.4 (2H, s); 6.8 (1H, dd, J_1=6Hz, J_2=2Hz); 7.2 (7H, m); 8.3 (1H, d, J=5Hz); λ_{max} (EtOH): 254 nm (ε 8700), 288 (ε 5000), lit.[41], λ_{max} (H_2O) 248 nm (ε 8300), 290 (ε 5500).

3β-Acetoxy-20RS(-2'-pyridylthio)-5αH-pregnan-11-one 21 was an oil. It was a 3/1 mixture of diastereoisomers at position 20 by NMR (eluant: CH_2Cl_2). After 1 crystalisation in methanol an 88/12 mixture was obtained, mp 181-183°C; $\nu(CH_2Cl_2)$: 1720, 1700 cm^{-1}; δ (400 MHz) major product: 0.78 (3H, s, 18$\underline{CH_3}$); 1.07 (3H, s, 19$\underline{CH_3}$); 1.45 (3H, d, J=7Hz, 21$\underline{CH_3}$), minor product: 0.73 (3H, s, 18$\underline{CH_3}$); 1.04 (3H, s, 19$\underline{CH_3}$); 1.40 (3H, d, J=10Hz, 21$\underline{CH_3}$). Common signals: 3.88 (1H, m, 20$\underline{H}$), 4.67 (1H, m, 3α$\underline{H}$); 6.95 (1H, dd, J_1=9Hz, J_2=6Hz); 7.10 (1H, d, J_3=10Hz), 7.41 (1H, dd, J_3=10Hz, J_1=9Hz); 8.38 (1H, d, J_2=6Hz); m/z: 469 ($M^{+\cdot}$); 436 ($M-33^{+}$). λ_{max} (EtOH): 256 nm (ε 6400), 298 nm (ε 2600) (Found: C, 71.34; H, 8.17; N, 3.15; S, 6.89%. Calc. for $C_{28}H_{39}NO_3S$: C, 71.60; H, 8.37; N, 2.98; S, 6.83%).

1αβ,3β,4β,5α-Tetraacetoxy-1αβ(2'-pyridylthio)-cyclohexane 24 was a resin (eluant: EtOAc/pentane 4/1), $[\alpha]_D^{18}$ -100° (c=1). This product is an approximately 60/40 mixture by NMR. $\nu(CH_2Cl_2)$: 1740-1720 broad absorption, 1700, 1575, 1360, 1210 cm^{-1}. δ(400 MHz): 2.00-2.13 (8 singlets), 2.30 (1H, m), 2.41 (2H, m), 2.50 (2H, m), 2.80 (1H, m), 3.22 (1H, m), 3.40 (1H, m), 5.00 (1H, m), 5.18 (1H, m), 5.25 (1H, m), 5.28 (1H, m), 5.36 (1H, m), 5.57 (1H, m), 7.25 (2H, m), 7.43 (2H, m), 7.62 (2H, m), 8.55 (2H, m); m/z: 425 ($M^{+\cdot}$); λ_{max} (EtOH): 250 nm (ε 4300), 284 nm (ε 3600) (Found: C, 53.89; H, 5.71; N, 3.15; S, 7.41%. Calc. for $C_{19}H_{23}NO_8S$: C, 53.64; H, 5.44; N, 3.29; S, 7.54%).

Isopropyl-2'-pyridylsulphide 41 was an oil (eluant: CH_2Cl_2). δ: 1.40 (6H, d, J=7Hz), 3.99 (1H, sept. J=7Hz), 6.70-7.50 (3H, m), 8.40 (1H, d, J=5Hz), Lit.[42] ($DMSOd_6$), 8.45 (1H, d, J=9Hz); m/z: 153 ($M^{+\cdot}$).

The 2'-pyridylsulphide 27 was a colourless oil (eluant: CH_2Cl_2). It was a 9/1 mixture of diastereoisomers at position 4 by NMR. $[\alpha]_D^{18}$ -61° (c=1.25). $\nu(CH_2Cl_2)$: 1570, 1550, 1200, 900, 850 cm^{-1}. δ(400 MHz): major diastereoisomer only, 0.85 (3H, s, 15$\underline{CH_3}$), 1.00 (6H, m, ($\underline{CH_3}$)$_2$CH-), 1.47 (3H, s, 14CH_3); 5.37 (1H, m, vinylic $\underline{H}$ at 7), 5.78 (1H, s, vinylic $\underline{H}$ at 14), 7.10 (1H, m), 7.32 (1H, d, J=10Hz), 7.50 (1H, m), 8.50 (1H, d, J=6Hz). Double irradiation of the methyl signal at δ 0.85 ppm caused no significant enhancement or diminution in the intensity of the methyl signal at δ 1.47; m/z: 367 ($M^{+\cdot}$). λ_{max} (EtOH): 236 nm (ε 12 200); 243 nm (ε 13 000), 252 nm (ε 10 500), 291 nm (ε 4900). (Found: C, 78.70; H, 9.10%. Calc. for $C_{24}H_{33}NS$: C, 78.42; H, 9.05%).

3β,24-Diacetoxy-28-nor-17β(-2'-pyridylthio)-olean-12-ene 30 was a resin (eluant: CH_2Cl_2), $[\alpha]_D^{19}$ +36° (c=1); $\nu(CH_2Cl_2)$: 1725, 1720, 1570 cm^{-1}. δ(400 MHz): 0.86 (3H, s), 0.89 (3H, s), 0.93 (3H, s), 1.02 (3H, s), 1.14 (3H, s), 1.16 (3H, s), 2.03 (3H, s), 2.07 (3H, s), 2.60 (1H, m), 3.70 (1H, d, J=10Hz), 3.90 (1H, d, J=10Hz), 4.83 (1H, m), 5.23 (1H, m), 7.07 (1H, m), 7.30 (1H, m), 7.50 (1H, m), 8.50 (1H, d, J=5Hz); m/z 622 ($M^{+\cdot}$). λ_{max} (cyclohexane): 263 nm (ε 11 800), 303 (ε 5800). (Found: C, 73.10; H, 8.91; N, 1.91%. Calc. for $C_{38}H_{55}NO_4S$: C, 73.39; H, 8.91; N, 2.25%).
1,1-Dimethylethyl-2'-pyridylsulphide 39 was an oil (eluant: CH_2Cl_2). δ: 1.55 (9H, s), 6.70–7.50 (3H, m), 8.45 (1H, d, J=5Hz), lit.[43], δ: 1.53, 7.03, 7.28, 7.52, 8.53; m/z: 167 ($M^{+\cdot}$).

1-(Adamantane-1'-carboxyl)-1H-pyridine-2-thione 32

The acid chloride derived from 1-adamantane-carboxylic acid (1 mmol) in benzene (5 ml) was added to 1 (180 mg, 1.2 mmol) and DMAP (12 mg, 0.1 mmol) in benzene (10 ml), with stirring at reflux. After 1 hr at reflux the reaction mixture was cooled to room temperature and filtered on celite. Trituration of the clear yellow filtrate with hexane caused the precipitation of the "ester" 32. P.l.c. of the mother liquors on silica (eluant: CH_2Cl_2) enabled isolation of a further amount of "ester" (total yield 167 mg, 58%), mp 163–164° (benzene/hexane). $\nu(CH_2Cl_2)$: 1780, 1605, 1525, 1460, 1450, 1010, 960, 930 cm^{-1}. δ(80MHz): 1.75 (6H, m), 2.18 (9H, m), 6.50 (1H, ddd, J_1=2Hz, J_2=6Hz, J_3=8Hz); 7.08 (1H, ddd, J_2=6Hz, J_4=8Hz, J_5=2Hz), 7.35 (1H, dd, J_3=8Hz, J_5=2Hz); 7.50 (1H, dd, J_4=8H_4, J_1=2Hz); m/z: 289 ($M^{+\cdot}$), 276 (M-CH^{+}), 244 (M-CO_2-H^{+}). λ_{max} (EtOH): 286 nm (ε 14000), 364 (ε 4400). (Found: C, 66.80; H, 6.80; N, 4.98; S, 10.74%. Calc. for $C_{16}H_{19}NO_2S$: C, 66.41; H, 6.62; N, 4.84; S, 11.08%).

1-Adamantanyl-2'-pyridylsulphide 33 was a yellow solid (eluant: CH_2Cl_2), mp 78–80°C; $\nu(CH_2Cl_2)$: 2875, 2840, 1570, 1555 cm^{-1}; δ(80MHz): 1.75 (6H, m), 2.12 (9H, m), 7.05 (1H, m), 7.40 (2H, m), 8.50 (1H, d, J=4Hz); m/z: 244 (M-$1^{+\cdot}$); λ_{max} (EtOH): 257 nm (ε 7800), 291 nm (ε 3800). (Found: C, 73.21; H, 7.71; N, 5.73; S, 12.87%. Calc. for $C_{15}H_{19}NS$: C, 73.42; H, 7.80; N, 5.71; S, 13.07%).

3α,12α-Diacetoxy-24-nor-23(-2'-pyridylthio)-5αH-cholane 17 (eluant: CH_2Cl_2/EtOAc 9/1) had mp 153–155°C (EtOAc); $[\alpha]_D^{20}$ +89° (c=1). $\nu(CH_2Cl_2)$: 1720, 1575 cm^{-1}; δ: 0.75 (3H, s, 18$\underline{CH_3}$), 0.90 (6H, s, 19 + 21$\underline{CH_3}$), 2.00 (3H, s), 2.10 (3H, s), 3.20 (2H, m, 23$\underline{H}$), 4.60 (1H, m, 12$\underline{\beta H}$), 5.02 (1H, m, 3$\underline{\beta H}$), 6.90 (2H, m), 7.35 (1H, m), 8.35 (1H, d, J=5Hz); m/z: 542 ($M^{+\cdot}$); λ_{max} (EtOH): 254 nm (ε 7100); 297 nm (ε 2600). (Found: C, 70.57; H, 8.94; N, 2.64; S, 5.70%. Calc. for $C_{33}H_{47}NO_6S$: C, 70.94; H, 8.74; N, 2.59; S, 5.92%).

1,3-Diphenyl-2-(2'-pyridylthio)-propane 37 was an oil (eluant: CH_2Cl_2), bp 200°/0.2 nm (Kugelrohr). ν(film): 3000, 2900, 1600, 1575, 1490, 1450, 1410, 1120, 950, 900 cm^{-1}; δ: 3.00 (4h, d, J=6Hz), 4.40 (1H, q, J=6Hz), 6.8–7.8 (13H), 8.35 (1H, d, J=5Hz).

n-Heptadecyl-2'-pyridylsulphide 8 *by the DCC/DMAP Method.*- A mixture of stearic acid (286 mg, 1 mmol), 2 (151 mg, 1.2 mmol), DCC (310 mg, 1.5 mmol) and DMAP (181 mg, 1.2 mmol) was brought to reflux with stirring in toluene (20 ml) for 1.5 hrs, after which the reaction was cooled to room temperature and the precipitate of dicyclohexylurea filtered off. The filtrate was evaporated to dryness and the residue subject to chromatographic purification to yield n-heptadecyl-2'-pyridylsulphide 8 (449 mg) 65%, identical to the sample obtained above.

n-Pentadecyl-2'-pyridylsulphide 9 by Photolysis.- Palmiloyl chloride (274 mg, 1 mmol) in benzene (1 ml) was added to a solution of 2 (140 mg, 1.1 mmol) and pyridine (0.01 ml) in benzene (5 ml) with stirring at room temperature. After 20 mins at room temperature the white precipitate of pyridinium hydrochloride was filtered off and the clear yellow filtrate irradiated at room temperature, with a 300 W tungsten lamp, for 45 mins. Evaporation of the solvent followed by chromatography on silica gel gave first n-pentadecane (49 mg, 23%) and then n-pentadecyl-2'-pyridylsulphide 9 (159 mg, 50%), identical to the sample prepared above.

Reduction of Alkyl-2'-pyridylsulphides with Tri-n-butylstannane.- Tri-n-butylstannane (3 mmol) and AIBN (10 mg) in the appropriate solvent (Table 3) (5 ml) were added dropwise over 15 mins to a solution of the substrate (1 mmol) at reflux in the appropriate solvent. The reaction was monitored by t.l.c. and more stannane and initiator added as required. The reaction was worked up analogously to the reductions of acids described earlier and the products, which were isolated by column chromatography wer identical to those obtained above.

3α-Acetoxy-24-nor-5βH-cholan-11-one 13 by "Nickel Boride" Reduction.- The derived acid chloride of acetyl-11-ketolithocholic acid 12 (1 mmol) in toluene (5 ml) was added to a stirred, azeotropically dried, suspension of 1 (180 mg, 1.2 mmol) and DMAP (12 mg, 0.1 mmol) in toluene (10 ml) at reflux. After 2 hrs at reflux the solvent was removed under vacuum and the residues taken up in abs. ethanol (100 ml). To this solution were added hexaaquanickel(II) chloride (11.85 g, 50 mmol) and boric acid (3.1 g, 50 mmol) and finally, after purging with nitrogen for 5 mins, a solution of sodium borohydride (3,8 g, 100 mmol) in a mixture of ethanol/water (50 ml 1/1) was cautiously added to bring about the copious precipitation of black "nickel boride". After heating to reflux for 24 hrs, the precipitate was filtered off on celite and the filtrate concentrated to 100 ml and poured into 2M sodium bicarbonate (50 ml). Extraction with dichloromethane (3x50 ml) gave the crude product which after chromatography on silica (eluant: CH_2Cl_2) gave 3α-acetoxy-24-nor-5βH-cholan-11-one 13 (205 mg, 70%) which was indistinguishable from the sample prepared above.

General Method for the Reductive Decarboxylation of Acids (t-Butylthiol Method - Normal Addition.- The acid chloride (1 mmol) in toluene (5 ml) was added dropwise (15 mins) to a dried, stirred suspension of N-hydroxypyridin-2-thione-Na salt (1.2 mmol) and DMAP (0.1 mmol) at reflux (efficient condensor) in toluene. After completion the reaction was cooled to room temperature and thoroughly washed with water, then with a saturated solution of sodium chloride. After drying on sodium sulphate, filtration and evaporation to dryness the products were purified by chromatography on silica. All reduction products were identical to those isolated above.

Reduction with t-Butylthiol - Inverse Addition.- The acid chloride (1 mmol) in toluene (1 ml) was added at room temperature to a stirred, solution of 2 (140 mg, 1.1 mmol) and pyridine (0.1 ml) in toluene (10 ml) at room temperature. After 10 mins the precipitate was filtered off and the filtrate added dropwise over 30 mins to a solution of t-butylthiol (0.5 ml) in toluene (20 ml) at reflux (efficient condensor). After completion of the reaction (t.l.c.) the products were isolated as described immediately above.

t-Butyl-2'-pyridyldisulphide 44 .- This compound is a by product in the reduction with t_butyl-mercaptan; it can be removed either by extraction with 6M hydrochloric acid or by chromatography on silica gel (eluant: CH_2Cl_2); δ: 1.35 (9H, s), 7.00 (1H, m), 7.7 (2H, m), 8.40 (1H, d, J=5Hz); ν(CH_2Cl_2): 2850, 1560, 1360, 1140, 1110, 900 cm^{-1}; m/z: 199 ($M^{\overline{1}+\cdot}$), 143 ($M-CH_2=C(CH_3)_2^{\overline{1}+}$), lit.[44], bp 91-92°C/0.01mm.

Decarboxylative Chlorination (and Bromination) : General Method.- The acid chloride (1 mmol) in tetrachloromethane (or bromotrichloromethane) (5 ml) was added over 15 mins to a stirred, dried suspension of 1 (180 mg, 1.2 mmol) and DMAP (12 mg, 0.1 mmol) in tetrachloromethane (or bromo-

trichloromethane) (10 ml) at reflux. The reaction is monitored by t.l.c. and after completion is cooled to room temperature, filtered on celite and evaporated to dryness. The crude product thus obtained was purified by chromatography on silica gel to yield the nor-chloride (or bromide) and 2-pyridyl-trichloromethylsulphide.

2-Pyridyl-trichloromethylsulphide (45) was a viscous yellow oil (eluant: CH_2Cl_2). δ: 7.30 (2H, m), 7.75 (1H, d, J=4Hz), 8.65 (1H, d, J=4Hz); m/z: 227, 229, 231 ($M^{+\cdot}$); 193, 195, 197 ($M-HCl^{+}$). Lit.[45], bp 76°/0.05 torr.

n-Pentadecylchloride (46) was a colourless oil (eluant: pentane), bp 200°/15 mm (Kugelrohr). Lit.[46], bp 168-171/10mm.

2-Chloro-1,3-Diphenylpropane (47) was a colourless oil (eluant: pentane); ν(film): 3010, 2900, 1600, 1490, 1445, 740, 700 cm^{-1}; δ: 3.00 (4H, d, J=7Hz), 4.20 (1H, q, J=7Hz), 7.20 (10H, m). (Found: C, 78.14; H, 6.50; Cl, 15.41%. Calc. for $C_{15}H_{15}Cl$: C, 78.08; H, 6.55; Cl, 15.35%).

3α,12α-Diacetoxy-23-chloro-24-nor-5βH-Cholane 48 (eluant: CH_2Cl_2/EtOAc 95/5) had mp 133-134°C (hexane), $[\alpha]_D^{20}$ +100° (c=0.3); ν(CH_2Cl_2): 2850, 1710, 1560, 1360, 1020, 900 cm^{-1}; δ(80 MHz): 0.75 (3H, s, 18$\underline{CH_3}$), 0.90 (3H, s, 19$\underline{CH_3}$), 2.00 (3H, s, $\underline{CH_3}$COO-), 2.09 (3H, s, $\underline{CH_3}$COO-), 3.50 (2H, m, 23$\underline{CH_2}$), 4.60 (1H, m, 3βH), 5.02 (1H, m, 12βH); m/z: 407 ($M-AcO^{+}$), 409 ($M_{Cl^{37}}-AcO^{+}$); 345 + 347 ($M-AcO-AcOH^{+\cdot}$). (Found: C, 69.46; H, 9.34; Cl, 7.62%. Calc. for $C_{27}H_{43}ClO_4$: C, 69.43; H, 9.28; Cl, 7.59%).

1-Chloroadamantane 49 (eluant: pentane) had mp 165°C (sealed tube after sublimation at 110°C/-15mm). Lit.[47], mp 165°C (sealed tube).

1-Bromopentadecane 50 was a colourless oil (eluant: pentane); δ(80 MHz): 0.9 (3H, t); 1.3 (26H, m), 3.45 (2H, t, J=7Hz). Lit.[48], bp 159-160°C/5mm.

2-Bromo-1,3-diphenylpropane 51 was an oil (eluant: pentane); δ: 3.19 (4H, d, J-7Hz), 4.40 (1H, q, J-7Hz), 7.20 (10H, m); m/z: 275 + 277 ($M^{+\cdot}$). (Found: C, 65.48; H, 5.51; Br, 29.31%. Calc. for $C_{15}H_{15}Br$: C, 65.47; H, 5.49; Br, 29.04).

3α-Acetoxy-23-bromo-24-nor-5βH-Cholan-11-one 52 (eluant: CH_2Cl_2) had mp 164.5-165°C (hexane), $[\alpha]_D^{20}$ +81° (c=0.3); ν(CH_2Cl_2): 1720, 1700 cm^{-1}; δ: 0.66 (3H, s, 18$\underline{CH_3}$), 0.9 (3H, d, J=4Hz, 21$\underline{CH_3}$), 1.20 (3H, s, 19$\underline{CH_3}$), 2.00 (3H, s, $\underline{CH_3}CO_2$-), 3.40 (2H, m, 23CH_2), 4.70 (1H, m, 3β$\underline{H}$); m/z: 466 + 468 ($M^{+\cdot}$). (Found: C, 63.97; H, 8.35; Br, 17.34%. Calc. for $C_{25}H_{39}BrO_3$: C, 64.23; H, 8.41; Br, 17.09%).

1-Bromoadamantane 53 (eluant: pentane) had mp 118°C (sealed tube after sublimation at 100°/15 mm). Lit.[47], mp 118°C (sealed tube: MeOH).

1,1-Dimethylethylchloride 54.- This product was distilled directly from the reaction mixture together with tetrachloromethane (10 ml). The distillate was then subject to fractional distillation through a 10cm vigreux column, bp 50-54°C, lit.[49] 52°C.

Decarboxylative Iodination. General Method.- The acid chloride (1 mmol) in the appropriate solvent (Table 5) (1 ml) was added to a dried, stirred suspension of 1 (165 mg, 1.1 mmol), DMAP (12 mg) and iodoform (433 mg, 1.1. mmol) [or iodine (170 mg, 1.5 mmol)] at reflux in the appropriate solvent (10 ml). At the end of the reaction (t.l.c), the reaction mixture was cooled to room temperature, filtered on celite and concentrated to dryness. The pure products were isolated by chromatography on silica gel.

1-Iodopentadecane 55 (eluant: pentane) had mp 22-24°C (pentane). Lit.[50], mp 20-22°C.

2-Iodo-1,3-diphenylpropane 56 was an oil (eluant: pentane), δ: 3.20 (4H, d, J=7Hz), 4.35 (1H, q, J=7Hz), m/z: 321 ($M-1^+$); 194 ($M-HI^+$). (Found: C, 56.03; H, 4.76%. Calc. for $C_{15}H_{15}I$: C, 55.92; H, 4.69%).

3α-Acetoxy-23-iodo-24-nor-5βH-cholan-12-one 66a (eluant: CH_2Cl_2/EtOAc 95/5) had mp 228-230°C (benzene/hexane), $[\alpha]_D^{20}$ +102° (c=1); ν(nujol): 1720, 1710, 1260, 1025 cm^{-1}; δ: 1.00 (6H, 18+19 $\underline{CH_3}$), 2.00 (3H, s), 3.20 (2H, m, 23$\underline{CH_2}$), 4.70 (1H, m, 3βH); m/z: 514 ($M^{\dagger+}$), 454 ($M-AcOH^{\dagger+}$), 387 ($M-I^{\dagger+}$). (Found: C, 58.19; H, 7.57%. Calc. for $C_{25}H_{39}IO_3$: C, 58.36; H, 7.64%).

Formation of Nor-Hydroperoxides. Method A.- The acid chloride (1 mmol) and t-butylmercaptan (see Table 6) both in toluene (10 ml) were added simultaneously to a stirred, dried, suspension of 1 (180 mg, 1.2 mmol) and DMAP (12 mg, 0.1 mmol) in toluene (10 ml) at 80°C and through which oxygen was being passed via a sinter at a rate of approximately 0.33 l/min. Decolouration (and t.l.c. analysis) of the normally yellow solution indicated complete reaction.
Method B.- The acid chloride (1 mmol) in toluene (2 ml) was added at room temperature to a stirred solution of 2 (140 mg, 1.1 mmol) and of pyridine (0.25 ml) in toluene (10 ml) at room temperature. After 10-15 mins the precipitated pyridinium hydrochloride was removed by filtration and the yellow filtrate added dropwise over 15 mins to a solution of t-butylmercaptan (see Table 6) in toluene (10 ml) that was being continually saturated with oxygen as in Method A.
Method C. - A yellow solution of ester (1 mmol) in toluene (10 ml) was prepared according to method B and added dropwise under irradiation from a 300 W tungsten lamp over 15 mins to a stirred solution of t-butylmercaptan (see Table 6) in toluene (10 ml) that was being continually saturated with oxygen as in Method A at room temperature.

Reduction of Hydroperoxides to Alcohols. General Method.- After formation of the hydroperoxide by either of methods A, B, or C the crude reaction mixture was reduced either with dimethylsulphide (see Table 6) at 80°C for 1 hr or with trimethylphosphite (see Table 6) at room temperature. After complete reduction (t.l.c.) the reaction mixture was thoroughly washed with water (3x50 ml), dried on sodium sulphate, filtered and evaporated to dryness, yielding the crude reaction mixture which consisted of t-butyl-2-pyridyldisulphide 44 and the alcohol. Further purification was effected by chromatography on silica gel.

n-Pentadecanal 57 (eluant: CH_2Cl_2/pentane 1/1). This product is characterised by the presence of a 3H triplet in its NMR spectrum at δ 9.7 ppm. It undergoes polymerisation in a few hours at room temperature.

n-Pentadecanol 58 (eluant: CH_2Cl_2) had mp and mixed mp 45-46°C (pentane). Lit.[51], mp 45-46°C.

1,3-diphenylpropan-2-ol (59). (Eluant: CH_2Cl_2) had bp 190°C/15 mm (Kugelrohr). Lit.[50], bp 198°C/20 mm. δ: 2.80 (4H, d, J=8Hz); 4.05 (1H, q, J=8Hz), 7.27 (10H, m). (Found: C, 84.59; H, 7.75%. Calc. for $C_{15}H_{16}O$: C, 84.87; H, 7.60%).

3β,24-Diacetoxy-28-nor-olean-12-en-17β-ol (60) and 3β,24-Diacetoxy-17β-Hydroperoxy-28-nor-olean-12-ene (61).- In this experiment the treatment with dimethyl sulphide or trimethylphosphite was omitted. Chromatography on silica gel gave first the alcohol 60 (56%) (eluant: CH_2Cl_2/EtOAc 95/5), mp 191-192° (hexane/ether); $[\alpha]_D^{20}$ +82° (c=0.5); δ(400 MHz): 0.85 (3H, s), 0.91 (3H, s), 0.96 (3H, s), 0.97 (3H, s), 0.99 (3H, s), 1.25 (3H, s), 2.03 (3H, s), 2.08 (3H, s), 3.75 (1H, d, J=10Hz, 24$\underline{CH_2}$OAc), 3.93 (1H, d, J=10Hz, 24$\underline{CH_2}$OAc), 4.85 (1H, m, 3$\underline{\beta H}$), 5.36 (1H, m, vinylic $\underline{H}$ at 12); m/z: 528 ($M^{\dagger+}$), 510 ($M-18^{\dagger+}$). (Found: C, 74.94; H, 9.94%. Calc. for $C_{33}H_{52}O_5$:

C, 74.96; H, 9.91%). This product was closely followed by the 17β hydroperoxide 61 (39%) (eluant: CH_2Cl_2:EtOAc 95/5), mp 307-308°C (MeOH), $[\alpha]_D^{20}$ +55° (c=0.9); ν(CH_2Cl_2): 3500, 2500-3300 (broad), 1720, 1170, 1030 cm^{-1}; δ(200 MHz): 0.71 (3H, s), 0.77 (6H, s), 0.80 (6H, s), 0.88 (3H, s), 1.11 (3H, s), 1.95 (3H, s), 2.04 (3H, s), 2.08 (1H, m), 3.69 (1H, d, J=11Hz), 3.91 (1H, d, J=11Hz), 4.80 (1H, m), 5.34 (1H, m); m/z: 510 ($M-34^{\neg 1+}$), 451 ($510-AcO^{\neg 1+}$). (Found: C, 72.42; H, 9.14. Calc. for $C_{33}H_{52}O_6$: C, 72.76; H, 9.62%).

3α,12α-Diacetoxy-24-nor-5βH-cholan-23-ol 62 (eluant: CH_2Cl_2/EtOAc 9/1) had mp 147-149°C (MeOH), $[\alpha]_D^{20}$ +101° (c=0.6); ν(CH_2Cl_2): 1710, 1355, 1020 cm^{-1}; δ: 0.8 (3H, s, 18$\underline{CH_3}$), 0.99 (3H, s, 19$\underline{CH_3}$), 2.05 (3H, s), 2.1 (3H, s), 3.7 (2H, m, 23 $\underline{CH_2}$OH), 4.7 (1H, m, 12βH), 5.1 (1H, m, 3βH); m/z: 388 (M- $AcOH^{\neg 1+}$), 328 (388- $AcOH^{\neg 1+}$). (Found: C, 72.03; H, 9.88%. Calc. for $C_{27}H_{44}O_5$: C, 72.28; H, 9.89%).

Fragmentation of Hydroperoxides with Tosylchloride in Pyridine.- The hydroperoxide was prepared according to Method C. After aqueous work up the ^1H NMR of the crude reaction mixture showed it to be a mixture of t-butyl-2-pyridyldisulphide 44 and of hydroperoxide. No alcohol was present by NMR. This mixture was dissolved in pyridine (2 ml) and treated at room temperature with tosyl chloride (250 mg, 1.3 mmol) under magnetic stirring. After 3 hrs at room temperature the reaction mixture was diluted with 2M hydrochloric acid (20 ml) and extracted with dichloromethane (20 ml), water (20 ml) and saturated aqueous sodium chloride (20 ml), dried on sodium sulphate and evaporated to dryness. Further purification was carried out by chromatography on silica gel.

3α,12α-Diacetoxy-24-nor-5βH-cholan-23-al 63 (eluant: CH_2Cl_2/EtOAc 95/5) was a resin. δ: 0.8 (3H, s, 18$\underline{CH_3}$); 0.9 (3H, s, 19$\underline{CH_3}$); 2.05 (3H, s); 2.10 (3H, s); 4.60 (1H, m, 12β$\underline{H}$); 5.00 (1H, m, 3β$\underline{H}$); 9.55 (1H, m). This relatively unstable product was immediately transformed into its 2,4-dinitrophenylhydrazone 64b for further characterisation, mp 112-113°C (MeOH); $[\alpha]_D^{20}$ +63° (c=2,4); ν(CH_2Cl_2): 3295, 1720, 1615, 1590, 1510, 1500, 1325 cm^{-1}; δ: 0.70 (3H, s, 18 $\underline{CH_3}$); 0.90 (3H, s, 19 CH_3); 2.00 (3H, s); 2.10 (3H, s); 4.66 (1H, m, 12β$\underline{H}$); 5.05 (1H, m, 3β$\underline{H}$); 7.40 (1H, t, J_1=7Hz); 7.80 (1H, d, J_2=10Hz); 8.20 (1H, dd, J_2=10Hz, J_3=3Hz); 8.95 (1H, d, J_3=3Hz); 10.85 (1H, s); m/z: 625 ($M-I^{\neg 1+}$); 565 ($M-I-AcOH^{\neg 1+}$). (Found: C, 63.38; H, 7.62%. Calc. for $C_{33}H_{46}N_4O_8$: C, 63.24; H, 7.40%).

1,3-Diphenylacetone 64a was a yellow oil (eluant: CH_2Cl_2/pentane 1/1); δ: 3.70 (4H, s), 7.20 (10H, m), mp of DNP 110°C (MeOH), lit.[53] 110°C.

Pentadecanal-2,4-Dinitrophenylhydrazone 65.- Chromatography on silica (eluant: CH_2Cl_2) of the crude product mixture gave n-pentadecanal contaminated with a polymeric form. This mixture was taken up in methanol (3 ml) and treated with 2,4-dinitrophenylhydrazine (10 ml of 0.1M in 1/1 H_3PO_4/EtOH). After stirring for 1.5 hrs at room temperature the precipitated yellow solid was filtered and recrystallised from methanol, mp 106-107°C (MeOH), lit.[51], 107.5°C.

Pentadecanal-2,4-Dinitrophenylhydrazone 65 *by direct treatment of the hydroperoxide with 2,4-Dinitrophenylhydrazine.*- The crude reaction mixture of hydroperoxide and t-butyl-2-pyridyl-disulphide was taken up in methanol (10 ml) and treated with 2,4-dinitrophenylhydrazine (15 ml of 0.1 M in H_3PO_4/EtOH 1/1) for 2 hrs at room temperature. After dilution with water (30 ml), the reaction was extracted with dichloromethane (3x20 ml) and the combined extracts dried over sodium sulphate filtered and evaporated to dryness. Chromatography of the red oil thus obtained gave first n-pentadecanal-DNP 65 (73 mg), 18% (eluant CH_2Cl_2), mp and mixed mp 106-107 (MeOH), then a mixture of n-pentadecylhydroperoxide 66 and the disulphide 44 (280 mg) and finally n-tetradecanol 67 (20 mg, 9%) (eluant: CH_2Cl_2), mp 38-39°C (EtOH), Lit.[54], 39-39.5°C. Further chromatography of the mixture of hydroperoxide and disulphide on neutral alumina gave first of all the pure disulphide 44 (167 mg) 84% (eluant: CH_2Cl_2/pentane 3/1) identical with an authentic sample and then

the hydroperoxide 66b (109 mg, 45%) (eluant: CH_2Cl_2/pentane 3/1); mp 39-40°C (pentane); ν(film): 3350 (broad) cm^{-1}; δ: 0.9(3H, t), 1.4 (26H, m), 4.2 (2H, t, J=7Hz); m/z: 227 ($(M-17^{+})$). (Found: C, 73.52; H, 13.35%. Calc. for $C_{15}H_{32}O_2$: C, 73.71; H, 13.20%).

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