The Invention of New Radical Chain Reactions. Part 12.† Improved Methods for the Addition of Carbon Radicals to Substituted Allylic Groups

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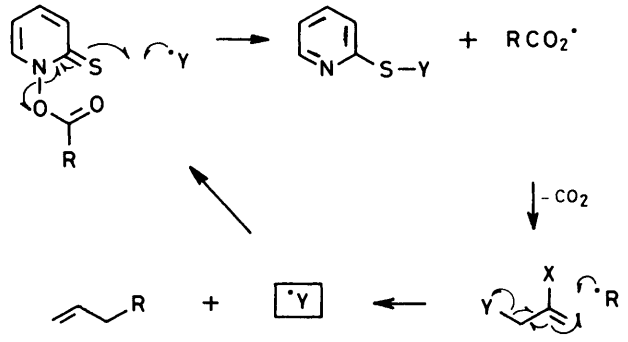
Reagents for the allylation of carbon radicals derived from the esters (mixed anydrides) of *N*-hydroxy-2-thiopyridone have been investigated. Because of competition between the background reaction of decarboxylative rearrangement and the desired allylation process, conventional allylation reagents give moderate yields of the desired adducts. Improved yields are secured if the β-position bears an electron withdrawing group. A concerted addition and elimination process can be postulated.

The formation of new carbon–carbon single bonds by an S_H2' mechanism involving the attack of a carbon radical onto a double bond with concomitant displacement of a radical from the allylic position is a useful synthetic process. Based on preliminary studies by Japanese[1] and French[2] groups Keck and Yates[3] developed a method for the free-radical allylation of halides and pseudohalides, using allyltributylstannane, and employed it in their elegant synthesis of perhydrohistrionicotoxin.[4] Webb and Danishefsky[5] adapted the method to the allylation of phenyl selenides and Keck *et al.*[6] used it in substitution at the anomeric position of a carbohydrate. More recently Smith and Whitham[7] and Keck and Enholm[8] have developed free radical-cyclisations in which the key step was an S_H2' reaction.

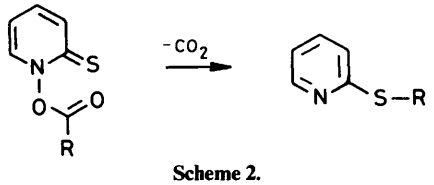


Scheme 1.

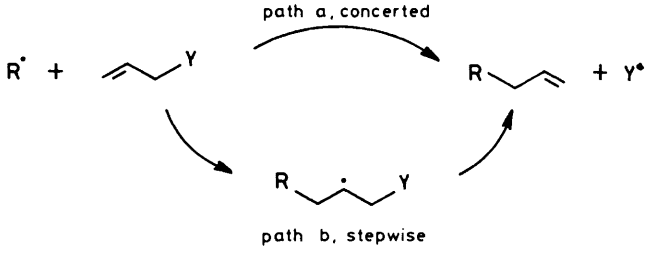
We wish to report here in full[9] the results of our own experiments on free radical allylation reactions which complement our previous free radical carbon–carbon bond forming procedures.[10] Essentially we were of the opinion that radicals generated from carboxylic acids *via* their mixed anhydrides with the thiohydroxamic acid (**1**) ought to undergo an S_H2' reaction with alkenes such as allyl t-butyl sulphide and that the expelled t-butylthio radical would serve, as previously,[11] to propagate the free radical chain (Scheme 1, X = H, Y = Bu^{t}S•).

From the outset we were aware that the rearrangement of the mixed anhydrides to alkyl pyridyl sulphides could be a serious competing reaction[11,12] (Scheme 2).

Our early experiments using allyl t-butyl sulphide as a trap proved this to be the case, for although we were able to isolate the desired allylation product the major product in the reaction mixture was the rearrangement product (Table 1, entries 1 and 2). By using the sulphide as the solvent we obtained a yield of 47% of octadec-1-ene from palmitoyl chloride (Table 1, entry 3).



Scheme 2.

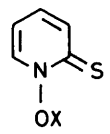


Scheme 3.

There are however two possible mechanisms for the S_H2' process, one in which the addition of the radical is concerted with the loss of the leaving radical (Scheme 3, path a) and a second stepwise mechanism in which the adduct radical has a definite existence (Scheme 3, path b).

If the stepwise mechanism is correct then the nature of Y• will have little or no effect on the rate of addition of R• to the double bond. But if mechanism a is operative, then by changing the stability of Y as a radical and so varying the strength of the allylic carbon–Y bond, we might change the rate of addition of R• onto the double bond. Thus the more stable Y• the faster the addition of R• would be. On this basis we synthesized a range of allylic compounds [(**4**)—(**12**)] and tested their affinity for alkyl radicals generated from thiohydroxamic–carboxylic mixed anhydrides. In going from Y = SBu^t (**3**) to the much more sterically hindered Y = $SCEt_3$ (**4**) little change was apparent (Table 1, entry 5). Ueno *et al.*[13] have carried out a series of experiments in which tributylstannane was allowed to react with acetophenones substituted at the methyl group with two different leaving groups. Ueno considered this reaction as an S_H2' reaction in which the stannyl radical attacked the carbonyl oxygen with subsequent expulsion of the leaving radical and was able to formulate an order of leaving group priorities for this type of reaction (PhSO• > PhS• > $PhSO_2$•). In our opinion however Uneo's results are better interpreted in terms of a direct S_H2 attack of the stannyl radical on the sulphur moiety. The

† Part II, preceding paper.



(1) X = H
(2) X = Na

$CH_2=CHCH_2X$

(3) X = $SCMe_3$
(4) X = $SCEt_3$
(5) X = SPh
(6) X = $SC_6H_2Me_3$-2,4,6
(7) X = $SC_6H_4NO_2$-*p*
(8) X = $S(O)CMe_3$
(9) X = $SO_2C_6H_4Me$-*p*
(10) X = SePh
(11) X = $SnPh_3$
(12) X = $CoDMG_2Py$.
DMG = dimethylglyoximato

better leaving groups in S_H2' reactions. We first tested the allylic aryl sulphides (**5**), (**6**), and (**7**) (Table 1, entries 6, 7, and 8) but were unable to obtain any significant improvement in the yield. Surprisingly, the use of the allyl sulphoxide (**8**) (Table 1, entry 9) led to a complex reaction mixture from which only the product (**15**) was isolated in low yield. Use of the sulphone (**9**) gave a clean reaction but the rearrangement product (**14**) still predominated (Table 1, entry 10). We next replaced sulphur by selenium in the hope that the weaker carbon–selenium bond would encourage the concerted mechanism. The use of allyl phenyl selenide (**10**) in toluene at reflux gave octadec-1-ene in 55% yield (Table 1, entry 11). However, when we employed molten allyl phenyl selenide as the reaction solvent the major product, from the acid chloride (**20**), was the selenide (**23**) (Table 1, entry 12). This product probably arises from radical addition to the selenium moiety of compound (**10**) as opposed to the alkene and is undoubtedly facilitated by the expulsion of the allyl radical (Scheme 4). Carbon radicals add readily to seleno carbonyls[15] and to diselenides.[16] The use of allyltriphenyl-

Table 1. Allylation

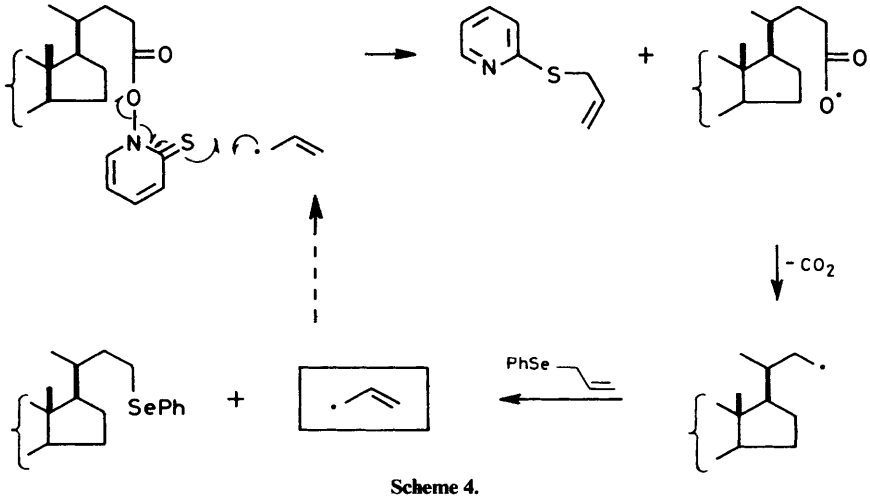
Entry	Substrate	Alkene (mmol)	Solvent	Temp. (°C)	Time (h)	Products (% Yield)
1	(**13**)	(**3**)(9)	Toluene	110	2.5	(**15**)(23) + (**19**)11) + (**14**)(62)
2	(**13**)	(**3**)(9)	Xylene	142	1	(**15**)(35) + (**14**)(60)
3	(**13**)	(**3**)(solvent)	(**3**)	140	0.5	(**15**)(47) + (**14**)(30)
4	(**13**)	(**3**)(solvent)	(**3**)	20 + *hν*	1	(**15**)(35) + (**14**)(17)
5	(**20**)[a]	(**4**)(7)	Chlorobenzene	133	2	(**21**)(28) + (**22**)(44)
6	(**13**)	(**5**)(7)	Toluene	110	1.5	(**15**)(20) + (**14**)(22)
7	(**13**)	(**6**)(7)	Toluene	110	2	(**15**)(25) + (**14**)(45)
8	(**13**)	(**7**)(3.5)	Toluene	110	1.5	(**15**)(12) + (**14**)(27)
9	(**13**)	(**8**)(7)	Toluene	110	1	(**15**)(7)
10	(**13**)	(**9**)(5)	Toluene	110	2	(**15**)(21) + (**14**)(55)
11	(**13**)	(**10**)(7)	Toluene	110	1.5	(**15**)(55) + (**14**)(37)
12	(**20**)[a]	(**10**)(solvent)	(**10**)	110	2	(**23**)(58)
13	(**13**)	(**11**)(2)	Xylene	142	1	(**16**)(50) + (**14**)(30)
14	(**13**)	(**12**)(2)	Toluene	20 + *hν*	0.25	
15	(**13**)	(**12**)(2)	Toluene	20 (Darkness)	16	(**15**)(3)

[a] Use of compound (**20**) to facilitate product separation.

order of priority then becomes the order of rates of participation in an S_H2 reaction. Nevertheless there is a considerable amount of experimental evidence[14] which seems to suggest that sulphinyl radicals are considerably more stable than either sulphonyl or thio radicals and therefore that these ought to be

stannane (**11**) gave a 50% yield of octadecene (Table 1, entry 13).

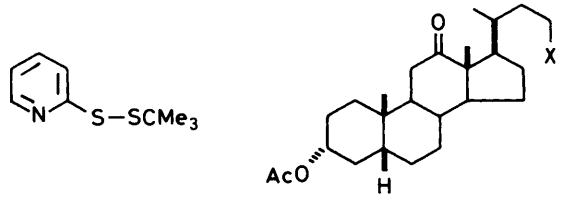
Finally we attempted the use of allylbis(dimethylglyoximato)cobalt(III) (**12**) as an allylating reagent. This reagent has previously been used for the allylation of electrophilic



Scheme 4.

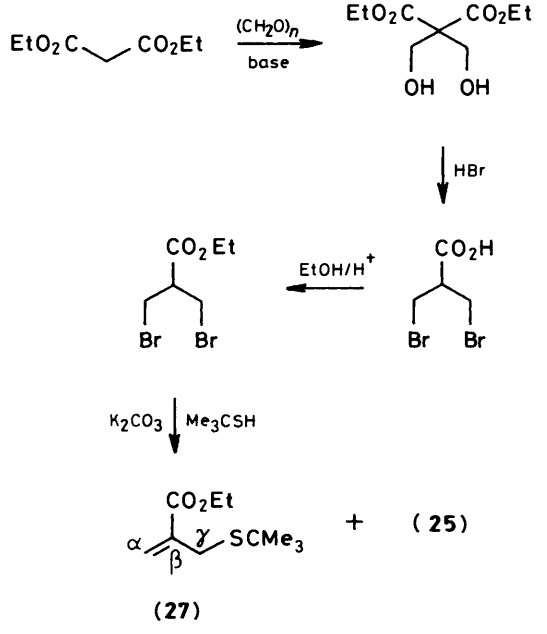
$Me(CH_2)_{14}X$

(13) X = COCl
(14) X = 2-pyridylthio
(15) X = $CH_2CH{=}CH_2$
(16) X = H
(17) X = $CH_2C(=CH_2)CO_2Et$
(18) X = $CH_2C(=CH_2)CO_2CH_2CH{=}CH_2$



(19)

(20) X = COCl
(21) X = $CH_2CH{=}CH_2$
(22) X = 2-pyridylthio
(23) X = SePh
(24) X = $CH_2C(=CH_2)CO_2Et$



Scheme 5.

radicals.[17] On reaction at room temperature and with tungsten photolysis we were unable to isolate any allylation product from the palmitoyl derivative (Table 1, entry 14). The sulphide (**14**) was not formed in this reaction. On carrying out the same reaction in the dark octadecene was obtained in 5% yield (Table 1, entry 15).

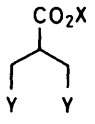
It was evident on the basis of the above results that either free radical allylation is not concerted or that if it is concerted the leaving group has little effect on the alkene L.U.M.O. Clearly, in order to direct the course of the reaction away from rearrangement and towards allylation it was necessary to further activate the alkene towards nucleophilic radicals. In the course of a general discussion on this problem of improved allylation, we suggested that if the intermediate radical were stabilised by appropriate substitution in the β-position, the chain might be carried by a thiol group originally bonded at the α-position (to avoid alkene polymerisation). Our colleague Dr. S. Z. Zard, whom we thank warmly, then suggested that the chain-carrying group would be better placed in the γ-position. This suggestion was then examined. The alkene (**27**) was synthesised in four easy steps from diethylmalonate (Scheme 5).

The decarboxylation of palmitic acid in the presence of compound (**27**) at reflux in chlorobenzene resulted in a 69% yield of the ethoxycarbonylallylation product (**17**) (Table 2, entry 1). This proceeds *via* a radical chain mechanism (Scheme 1; X = CO_2Et, Y = SBu^t), analogous to that proposed for allylation. This is supported by the isolation of the disulphide (**19**) in yields comparable to those of the desired product. We have carried out a series of experiments at different temperatures (Table 2, entries 1—3) and find that although the reaction goes in benzene or toluene at reflux the best yields were obtained in refluxing chlorobenzene. The reaction can be carried out at room temperature with tungsten photolysis but the yield is lower (Table 2, entry 4). We have also studied the effect of alkene concentration (Table 2, entries 5—7) and have found that 2 mole equivalents give optimum yields. The reaction has been applied to several functionalised primary, secondary, and tertiary carboxylic acids and yields of the order of 70% were obtained in chlorobenzene at reflux. This demonstrates, once again, the tolerance of such free radical chain reactions towards many frequently encountered functional groups as well as their diminished sensitivity towards steric hindrance. As in the case of the primary acid (**13**) we noted lowered yields in benzene at reflux when the reaction was applied to cyclohexane carboxylic acid (**29**) (Table 2, entry 9) and to adamantane-1-carboxylic acid (**37**) (Table 2, entry 14). Mixtures of diastereoisomers were obtained from the secondary acids (**31**) and (**33**). However the tertiary triterpenoid acid derivative (**39**) gave a single diastereoisomer. This was also the case when (**39**) was subjected to the reductive decarboxylation procedure[11] and to the decarboxylative oxygenation procedure.[11] We had previously concluded,[11] on the basis of a 2-dimensional ^1H n.m.r. study, that the reductive decarboxylation of (**39**) had taken place with retention of configuration. We chose here to determine the configuration at position 17 of the product (**40**) by chemical methods. Thus product (**40**) was oxidised with chromic anhydride in acetic acid to give, after methylation with methyl iodide and a highly hindered guanidine base,[18] the hederagenin derivative (**41**) in 23% overall yield. This product was identical to an authentic sample of (**41**), prepared in 40% yield by chromic acid oxidation and subsequent methylation of hederagenin diacetate. We conclude, in accord with our earlier spectroscopic study, that reactions involving free radicals at position 17 of the olean-12-ene series of pentacyclic triterpenoids proceed with retention of configuration.

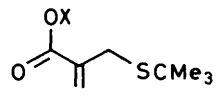
Having now set up an efficient S_H2' reaction we returned to the question of mechanism. If the stepwise mechanism is operating then conceivably the use of the allyl ester (**28**), [prepared analogously to compound (**27**)], in the reaction sequence might allow for the intramolecular trapping of the adduct radical to give either or both of the cyclisation products (**42**) and (**43**). In the event this was not the case. Free radical addition to (**28**) both in benzene at reflux and at room temperature with tungsten photolysis yielded only one major product (**18**), resulting from an S_H2' reaction (Table 2, entries 16 and 17). These results suggest that the S_H2' reaction with expulsion of stabilised radicals may be concerted, as we hoped. Alternatively it could be a stepwise process in which the second step is extremely fast. It is, in fact, already known that β-elimination for a BuS$^\bullet$ radical can be three times faster than the standard Ingold clock reaction of the hex-5-enyl radical cyclisation.[19]

Table 2. Ethoxycarbonylallylation

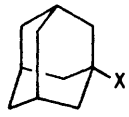
Entry	Substrate	Alkene (mmol)	Solvent	Temp. (°C)	Time (h)	Products (% Yield)
1	(**13**)	(**27**) (2)	Chlorobenzene	133	1	(**17**)(69) + (**19**)(73)
2	(**13**)	(**27**) (2)	Toluene	110	1.5	(**17**)(62) + (**19**)(67)
3	(**13**)	(**27**) (2)	Benzene	80	4.5	(**17**)(53) + (**14**)(17) + (**19**)(75)
4	(**13**)	(**27**) (2)	Ether	20 + *hν*	1	(**17**)(38) + (**19**)(40)
5	(**20**)	(**27**) (5)	Chlorobenzene	133	1.5	(**24**)(49)
6	(**20**)	(**27**) (1.2)	Chlorobenzene	133	1.5	(**24**)(60)
7	(**20**)	(**27**) (2)	Chlorobenzene	133	1.5	(**24**)(76) + (**19**)(90)
8	(**29**)	(**27**) (1.5)	Chlorobenzene	133	0.75	(**30**)(74) + (**19**)(83)
9	(**29**)	(**27**) (2)	Benzene	80		(**30**)(46) + (**19**)(55)
10	(**31**)	(**27**) (2)	Chlorobenzene	133	0.75	(**32**)(74) + (**19**)(80)
11	(**33**)	(**27**) (2)	Chlorobenzene	133	0.5	(**34**)(56) + (**19**)(56)
12	(**35**)	(**27**) (1.5)	Chlorobenzene	133	0.75	(**36**)(60) + (**19**)(78)
13	(**37**)	(**27**) (1.5)	Chlorobenzene	133	1	(**38**)(71) + (**19**)(85)
14	(**37**)	(**27**) (2)	Benzene	80	2.5	(**38**)(52) + (**19**)(68)
15	(**39**)	(**27**) (2)	Chlorobenzene	133	0.5	(**40**)(74) + (**19**)(64)
16	(**13**)	(**28**) (3)	Benzene	80	3	(**18**)(55) + (**14**)(8) + (**19**)(34)
17	(**13**)	(**28**) (3)	Ether	20 + *hν*	0.5	(**18**)(36)



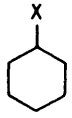
(**25**) X = Et, Y = $SCMe_3$
(**26**) X = $CH_2CH{=}CH_2$, Y = Br



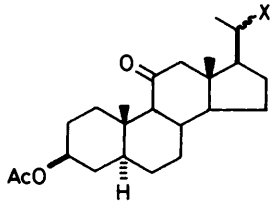
(**27**) X = Et
(**28**) X = $CH_2CH{=}CH_2$



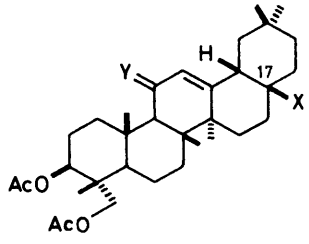
(**37**) X = COCl
(**38**) X = $CH_2C(=CH_2)CO_2Et$



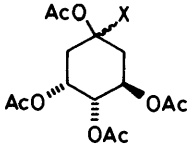
(**29**) X = COCl
(**30**) X = $CH_2C(=CH)CO_2Et$



(**31**) X = COCl (20*R*)
(**32**) X = $CH_2C(=CH_2)CO_2Et$



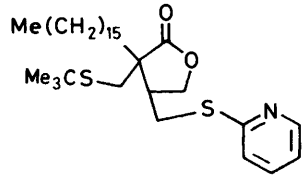
(**39**) X = COCl, Y = H_2
(**40**) X = $CH_2C(=CH_2)CO_2Et$, Y = H_2
(**41**) X = CO_2Me, Y = O



(**33**) X = β-COCl
(**34**) X = $CH_2C(=CH_2)CO_2Et$

$(PhCH_2)_2CHX$

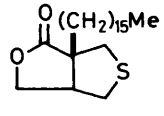
(**35**) X = COCl
(**36**) X = $CH_2C(=CH_2)CO_2Et$



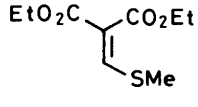
(**42**)

Finally we attempted an addition–elimination type radical carbon–carbon bond forming reaction. This type of process (Scheme 6) requires the addition of a radical to the substituted end of an alkene, which is normally an inefficient reaction except for highly activated double bonds. This being the case the doubly activated methylene malonate (**44**) was synthesized by sequential addition of ethyl thioformate and methyl iodide to sodium diethyl malonate.

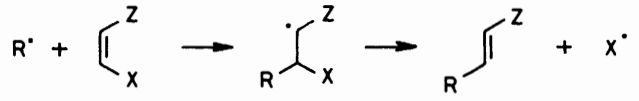
The decarboxylation of palmitic acid, *via* its *O*-ester with compound (**1**) in the presence of alkene (**44**) led only to high yields of the sulphide (**14**). This type of 'proximal' radical carbon–carbon forming reaction is evidently only applicable



(**43**)



(**44**)



Z = electron withdrawing group
X = free radical leaving group

Scheme 6.

when there exists no easier path for the radical to take, as was the case with the recent work of Baldwin *et al.*[20]

Experimental

Melting points, taken with a Reichert hot stage apparatus are uncorrected. Optical rotations for chloroform solutions, were taken with a Perkin-Elmer 141 polarimeter. Unless otherwise stated n.m.r. spectra were measured at 60 MHz for solutions in deuteriochloroform. Chemical shifts are in p.p.m. downfield from tetramethylsilane as the internal standard. 60 MHz N.m.r. spectra were recorded with either a Varian T 60 or EM 360L Spectrometer. 80, 200, and 400 MHz N.m.r. were recorded with Bruker WP 80, WM 200, and WM 400 instruments respectively. Mass spectra were recorded on either an AEI MS9 or an AEI MS50 instrument. I.r. spectra were measured with a Perkin-Elmer 297 spectrophotometer and u.v. spectra with a Jobin Yvon Duospec 203 Spectrophotometer. All solvents were dried and distilled according to standard techniques.

The allyl sulphides (**3**),[21] (**5**),[22] (**6**),[23] (**7**),[24] (**8**),[25] (**9**),[26] (**11**),[27] and (**12**)[28] were prepared according to literature procedures.

Allyl 3-Ethylpentan-3-yl Sulphide (**4**).—3-Ethylpentan-3-yl thiol (5 g, 38 mmol) was added dropwise under nitrogen to a stirred solution of sodium hydroxide (1.51 g, 38 mmol) in absolute ethanol (10 ml) at reflux. After 10 min allyl bromide (4.80 g, 40 mmol) was added over 10 min to the stirred solution at reflux and the reaction maintained at reflux for a further 3 h. The reaction was then diluted with water (100 ml), extracted with ether (3 × 50 ml), and the extracts were dried (Na_2SO_4), filtered, and evaporated to dryness. The residue was purified by Kugelrohr distillation (120 °C/15 mmHg) to give the *title sulphide* (4.77 g, 73%) as a colourless oil, δ 0.9 (9 H, t, *J* 7 Hz), 1.55 (6 H, q, *J*, 7 Hz), 3.15 (2 H, d, *J* 6 Hz), 5.10 (2 H, m), and 5.7—6.4 (1 H, m); *m/z* 172 (M^+); $\nu_{max.}$(film) 2 950, 2 900, 1 630, 1 450, 990, 920, and 850 cm^{-1} (Found: C, 69.75; H, 11.85; S, 18.5. $C_{10}H_{20}S$ requires C, 69.70; H, 11.70; S, 18.61%).

Allyl Phenyl Selenide (**10**).—Diphenyl diselenide (10 g) in ethanol (100 ml) was treated under nitrogen at room temperature with sodium borohydride (2.6 g) to give an almost colourless solution of sodium phenyl selenide (7 mmol). To this stirred solution was added allyl bromide (4 g) over 10 min at room temperature. After the reaction had been stirred for a further 18 h at room temperature, under nitrogen, the reaction mixture was diluted with water (250 ml) and extracted with ether (3 × 50 ml). The extracts were washed with water (2 × 100 ml), dried (Na_2SO_4), evaporated, and the residue was distilled to give allyl phenyl selenide as pale yellow oil (9.6 g, 70%), b.p. 50 °C/0.5 mmHg (lit.,[29] 82—83 °C/3 mmHg).

Allylation: General Method.—The acid chloride (1 mmol) in the appropriate solvent (10 ml) was added dropwise over 30 min to a stirred suspension of reagent (**1**) (165 mg, 1.1 mmol), *p*-dimethylaminopyridine (12 mg, 0.1 mmol), and the alkene (see Table 1) in the reaction solvent (10 ml) at reflux under nitrogen. At the end of the reaction (decolourisation, t.l.c.) the cooled solution was filtered and evaporated to dryness. Further purification depended on the individual alkene.

(*a*) *Allyl t-butyl sulphide and allyl phenyl sulphide.* The excess of the alkene was removed on the rotary evaporator together with the solvent and the crude product was then chromatographed on silica gel.

(*b*) *Allyl* p-*nitrophenyl sulphide and allyl* p-*tolyl sulphone.* After filtration the crude reaction mixture was concentrated until crystallisation began. The sulphide was then allowed to crystallise and after filtration the filtrate was purified by chromatography on silica gel.

(*c*) *Allyl 3-ethylpentan-3-yl sulphide, allyl mesityl sulphide, allyl t-butyl sulphoxide, allyl phenyl selenide, allyltriphenylstannane, and allyl(pyridyl)bis(dimethylglyoximato)cobalt*(III). These were removed by careful, and where necessary, repeated chromatography on silica gel.

Octadec-1-ene (**15**). This colourless oil was eluted with pentane and had δ 0.85 (3 H, t), 1.30 (28 H), 2.0 (2 H, m), 4.8 (1 H, m), 5.1 (1 H, m), and 5.5—6.0 (1 H, m). It was further characterised as its crystalline dibromide, m.p. 24 °C (EtOH) (lit.,[30] 24 °C).

Pentadecyl 2-pyridyl sulphide (**14**) *and 2-pyridyl t-butyl disulphide* (**19**). These compounds, eluted with mixtures of pentane and dichloromethane were identical to authentic samples.

3α-Acetoxy-27-nor-12-oxo-5βH-cholest-25-ene (**21**). This crystalline compound was eluted with pentane–ether (1:1) and had m.p. 95—98 °C (Et_2O), $[\alpha]_D^{20}$ +58° (*c* 3); δ (200 MHz) 0.83 (3 H, d, *J* 6.7 Hz, 21-H_3), 0.99 (6 H, s, 18, 19-H_3), 1.99 (3 H, s, $MeCO_2$), 2.43 (1 H, m, 11β-H), 4.66 (1 H, m, 3β-H), 4.66 (1 H, m, 3β H), 4.90 (2 H, m, 26-H), and 5.8 (1 H, m, 25 H); *m/z* 429 (M^+ + 1); $\nu_{max.}$(CH_2Cl_2) 1 720, 1 700, 1 025, and 820 cm^{-1} (Found: M^+, 428.3290. $C_{28}H_{44}O_3$ requires *M*, 428.3288).

3α-Acetoxy-23-(2-pyridylthio)-24-nor-12-oxo-5β-cholane (**22**). This compound eluted with pentane–ether (1:1) and was a glass with $[\alpha]_D^{20}$ +30° (*c* 0.4); δ (200 MHz) 0.85 (3 H, d, *J* 6.7 Hz, 21-H_3), 0.99 (6 H, s, 18, 19-H_3), 1.99 (3 H, s, $MeCO_2$), 2.43 (1 H, m, 11β-H), 3.00 + 3.27 (2 × 1 H, m, 23-H_2), 4.66 (1 H, m, 3β-H), 6.93 (1 H, m), 7.10 (1 H, m), 7.43 (1 H, m), and 8.45 (1 H, m); *m/z* 497 (M^+); $\nu_{max.}$(CH_2Cl_2) 1 720, 1 700, 1 580, 900, and 825 cm^{-1} (Found: C, 72.15; H, 8.8; N, 2.7; S, 6.5. $C_{30}H_{43}NO_3S$ requires C, 72.39; H, 8.71; N, 2.81; S, 6.44).

3α-Acetoxy-24-nor-12-oxo-23-phenylseleno-5βH-cholane (**23**). This *crystalline selenide* was eluted with dichloromethane and had m.p. 172—174 °C (benzene–hexane); $[\alpha]_D^{20}$ +106° (*c* 0.3); δ (200 MHz) 0.86 (3 H, d, *J* 6.7 Hz), 1.0 (6 H, s, 18- + 19-H_3), 2.0 (3 H, s, $MeCO_2$); 2.43 (1 H, m, 11β-N), 2.83 + 3.0 (2 × 1 H, m, 23-H_3), 4.70 (1 H, m, 3β-H), 7.28 (3 H, m), and 7.50 (2 H, m); *m/z* 543, 545 (M^+), 388 (M^+ − PhSe), and 328 (388 − AcOH)$^+$; $\nu_{max.}$(CH_2Cl_2) 1 720, 1 700, 1 575, 1 360, and 1 025 cm^{-1} (Found: C, 68.8; H, 8.3. $C_{31}H_{44}O_3Se$ requires C, 68.49; H, 8.19).

Ethyl 2-Methylene-3-t-butylthiopropanoate (**27**) *and Ethyl* 1,3-*Di-t-butylthiopropane-2-carboxylate* (**25**).—1,1-Dimethylethanethiol (0.4 ml) was added at room temperature to a vigorously stirred suspension of potassium carbonate (0.5 g) and ethyl 1,3-dibromopropane-2-carboxylate[31] (1 g) in absolute ethanol (5 ml). Stirring was maintained for 18 h before the reaction mixture was poured into water (100 ml) and ether extracted (3 × 20 ml). The extracts were dried (Na_2SO_4), filtered, and evaporated to dryness. Distillation of the crude product through a short Vigreux column gave *ethyl 2-methylene-3-t-butylthiopropanoate* (**27**) (510 mg, 69%) as a colourless oil with b.p. 54 °C/0.3 mmHg; δ 1.33 (3 H, t, *J* 7 Hz), 1.40 (9 H, s), 3.50 (2 H, s), 4.30 (2 H, q, *J* 7 Hz), 5.90 (1 H, s), and 6.33 (1 H, s); *m/z* 202 (M^+); $\nu_{max.}$(film) 1 720 and 1 625 cm^{-1} (Found: C, 59.25; H, 9.15. $C_{10}H_{18}O_2S$ requires C, 59.37; H, 8.9%).

Further distillation gave the *by-product* (**25**) (100 mg, 9%)

which was also a colourless oil and had b.p. 130—135 °C/0.2 mmHg; δ 1.33 (21 H, m), 2.85 (5 H, m), and 4.25 (2 H, q, *J* 7 Hz); *m/z* 292 (M^+); $\nu_{max.}$(film) 1 730 cm^{-1} (Found: C, 57.6; H, 9.75; S, 21.8. $C_{14}H_{28}O_2S_2$ requires C, 57.49; H, 9.65; S, 21.92%).

Ethoxycarbonylallylation: General Method.—The acid chloride (1 mmol) in the appropriate solvent (5 ml) was added over 10 min to a stirred suspension of the reagent (**2**) (180 mg, 1.2 mmol) and the alkene (**27**) in the appropriate solvent (5 ml) at reflux under nitrogen. After completion (t.l.c.) the reaction mixture was cooled to room temperature, filtered and the filtrate evaporated to give the crude reaction mixture, chromatography of which on silica gel gave the pure products and the disulphide (**19**).

Ethyl 2-methylenestearate (**17**). This *white crystalline ester* was eluted with dichloromethane–hexane (1:1) and had m.p. 24—25 °C (pentane); δ 0.9 (3 H, t), 1.3 (31 H, m), 2.25 (2 H, t, *J* 6 Hz), 4.3 (2 H, q, *J* 7 Hz), 5.65 (1 H, s), and 6.25 (1 H, s); *m/z* 324 (M^+); $\nu_{max.}$(film) 1 710 and 1 625 cm^{-1} (Found: C, 77.95; H, 12.65. $C_{21}H_{40}O_2$ requires C, 77.72; H, 12.42%).

Ethyl 3α-acetoxy-12-oxo-5βH-cholest-25-en-27-oate (**24**). This *crystalline ester*, eluted with dichloromethane–ethyl acetate (95:5) had m.p. 169—171 °C (MeOH); $[\alpha]_D^{20}$ +94° (*c* 1.5); δ (200 MHz) 0.83 (3 H, d, *J* 6 Hz, 21-H_3), 0.97 (6 H, s, 18- + 19-H_3), 1.23 (3 H, t, *J* 7 Hz), 2.0 (3 H, s), 4.16 (2 H, q, *J* 7 Hz), 4.66 (1 H, m, 3β-H), 5.50 (1 H, s), and 6.12 (1 H, s); *m/z* 500 (M^+); $\nu_{max.}$(CH_2Cl_2) 1 720, 1 700, 1 620, and 1 100 cm^{-1} (Found: C, 74.4; H, 9.85. $C_{31}H_{48}O_5$ requires C, 74.36; H, 9.66%).

Ethyl 3-cyclohexyl-2-methylenepropionate (**30**). This compound, a *colourless oil*, was eluted with dichloromethane–hexane (1:1) and had b.p. 80 °C/4 mmHg (Kugelrohr); δ 1.00—1.8 (14 m), 2.25 (2 H, d, *J* 7.Hz), 4.20 (2 H, q, *J* 7 Hz), 5.55 (1 H, s), and 6.25 (1 H, s); *m/z* 195 ($M^+ - 1$); $\nu_{max.}$(film) 1 715, 1 625, 1 180, and 1 160 cm^{-1} (Found: C, 73.15; H, 10.3. $C_{12}H_{20}O_2$ requires C, 73.43; H, 10.27%).

Ethyl 3β-acetoxy-23-methylene-11-oxo-5αH-cholan-24-oate (**32**) (20*R* + 20*S*). This compound was a mixture of diastereoisomers at position 20 and had m.p. 91—92 °C (MeOH); $[\alpha]_D^{20}$ +23° (*c* 0.9); δ (200 MHz) 0.64 (3 H, s, 18-H_3), 0.83 (3 H, m, 2 × 21-H_3), 1.03 (3 H, s, 19-H_3), 1.29 (3 H, t, *J* 7 Hz), 2.02 (3 H, s), 2.27 (1 H, d, *J* 12 Hz, 12β-H), 2.53 (3 H, m, 12α-H), 4.20 (2 H, 2 superimposed q's), 4.70 (1 H, m, 3α-H), 5.50 (1 H, s), and 6.20 (1 H, s); *m/z* 472 (M^+); $\nu_{max.}$(CH_2Cl_2) 1 720, 1 700, 1 620, and 1 025 cm^{-1} (Found: C, 73.5; H, 9.55. Calc. for $C_{29}H_{44}O_5$: C, 73.69; H, 9.38%).

Compound (**34**). This non-crystalline mixture of diastereoisomers was eluted with dichloromethane–ethyl acetate (4:1) and had δ (200 MHz) 1.30 (3 H, t, *J* 7 Hz), 1.8 (4 H, m), 1.9—2.1 (total 12 H, 6 × s), 2.8—3.2 (2 H, m), 4.23 (2 H, 2 × q), 4.9—5.6 (3 H, m), 5.56 (1 H, s), and 6.23 (1 H, s); *m/z* 428 (M^+); $\nu_{max.}$(CH_2Cl_2) 1 735, 1 360, and 1 030 cm^{-1} (Found: C, 55.8; H, 6.4. Calc. for $C_{20}H_{28}O_{10}$: C, 56.08; H, 6.59%).

Ethyl 4-benzyl-2-methylene-5-phenylpentanoate (**36**). This *pale yellow oil* was eluted with dichloromethane and had b.p. 168 °C/2 mmHg (Kugelrohr); δ 1.2 (3 H, t, *J* 8 Hz), 2.30 (2 H, m), 2.55 (4 H, m), 3.0 (1 H, m), 4.2 (2 H, q, *J* 8 Hz), 5.5 (1 H, s), 6.25 (1 H, s), 7.3 (10 H, m); *m/z* 308 (M^+); $\nu_{max.}$(film) 1 710, 1 625, 1 600, and 1 190 cm^{-1} (Found: C, 81.65; H, 7.8. $C_{21}H_{24}O_2$ requires C, 81.78; H, 7.84%).

Ethyl 3-Adamantan-1-yl-2-methylenepropanoate (**38**). This *colourless oil* was eluted with dichloromethane–hexane (1:1) and had b.p. 150 °C/3 mmHg (Kugelrohr), δ 1.33 (3 H, t, *J* 8 Hz), 1.60 (6 H, m), 1.75 (6 H, m), 2.0 (3 H, m), 2.25 (2 H, s), 4.3 (2 H, q, *J* 8 Hz), 5.5 (1 H, s), and 6.35 (1 H, s); *m/z* 248 (M^+); $\nu_{max.}$(film) 1 710, 1 620, and 1 180 cm^{-1} (Found: C, 77.75; H, 9.9. $C_{16}H_{24}O_2$ requires C, 77.38; H, 9.74%).

Triterpenoid (**40**). Hederagenin diacetate acid chloride (**39**) yielded the *triterpenoid* (**40**) as resin after chromatography on silica gel [eluant: dichloromethane–ethyl acetate (4:1)]. It had $[\alpha]_D^{20}$ +61° (*c*, 1.2); δ (200 MHz) 0.83 (3 H, s), 0.85 (6 H, s), 1.0 (3 H, s), 1.05 (3 H, s), 1.15 (3 H, s), 1.28 (3 H, t, *J* 7 Hz), 3.70 (1 H, s, *J* 11 Hz), 3.90 (1 H, d, *J* 11 Hz), 4.20 (2 H, q, *J* 7 Hz), 4.83 (1 H, m), 5.23 (1 H, m), 5.46 (1 H, s), and 6.13 (1 H, s); *m/z* 624 (M^+); $\nu_{max.}$(CH_2Cl_2) 1 710, 1 620, and 1 020 cm^{-1} (Found: M^+, 624.4424. $C_{39}H_{60}O_6$ requires *M*, 624.4389).

The Ester (**17**) *by Photolysis at Room Temperature.*—Palmitoyl chloride (274 mg, 1 mmol) in dry ether (2 ml) was added to a stirred solution of the reagent (**1**) (140 mg, 1.1 mmol) and pyridine (87 μl) in dry ether (10 ml) under nitrogen in the dark at room temperature. After stirring for 1 h at room temperature in the absence of light, the yellow solution was filtered rapidly and after addition of the alkene (**27**) (404 mg, 2 mmol) was irradiated with two 100 W tungsten lamps under nitrogen at room temperature for 1 h. The reaction was then evaporated to dryness and filtered on silica gel [eluant: dichloromethane–hexane (1:1)] giving first the ester (**17**) (125 mg, 38%), identical to the above isolated product, then recovered alkene (**27**) (217 mg), and then the disulphide (**19**) (81 mg, 40%).

Allyl 1,3-Dibromopropane-2-carboxylate (**26**).—Crude 1,3-dibromopropane-2-carboxylic acid[31] (50 g) and allyl alcohol (75 ml) were heated to reflux with stirring in benzene (300 ml) with conc. sulphuric acid (1 ml) with continuous azeotropic distillation for 8 h. The cooled reaction mixture was washed with water (2 × 200 ml), shaken with charcoal (2 g), filter dried, and evaporated before distillation under vacuum to give the *title ester* (28.5 g, 45%) as a colourless oil with b.p. 140 °C/0.2 mmHg, δ 3.2 (1 H, m), 3.7 (4 H, d, *J* 5 Hz), 4.7 (2 H, d, *J* 5 Hz), 5.1—5.6 (2 H, m), and 5.9 (1 H, m); *m/z* 284 (M^+); $\nu_{max.}$(film) 1 745 and 1 175 cm^{-1} (Found: C, 29.65; H, 3.65; Br, 56.3. $C_7H_{10}Br_2O_2$ requires C, 29.40; H, 3.52; Br, 55.88%).

Allyl 2-Methylene-3-t-butylthiopropanoate (**28**).—1,1-Dimethylethanethiol (2.25 ml) was added to a stirred suspension of the dibromide (**26**) (5 g) and potassium carbonate (6.9 g) in absolute ethanol (20 ml). After the reaction had been stirred at room temperature for 18 h it was poured into water (150 ml) and extracted with ether (3 × 30 ml). The extracts were washed with water (2 × 100 ml), dried ($MgSO_4$), filtered, and evaporated to dryness. Kugelrohr distillation of the crude product yielded the *title ester* (2.5 g, 67%) as a colourless oil with b.p. 80 °C/0.5 mmHg (Kugelrohr), δ 1.3 (9 H, s), 3.5 (2 H, s), 4.65 (2 H, d, *J* 5 Hz), 5.1—5.6 (2 H, m), 5.7—6.2 (1 H, m), 5.9 (1 H, s), and 6.3 (1 H, s); *m/z* 214 (M^+); $\nu_{max.}$(film) 1 730 and 1 180 cm^{-1} (Found: C, 61.2; H, 8.65; S, 15.65. $C_{11}H_{18}O_2S$ requires C, 61.64; H, 8.47; S, 14.96%).

Allyl 2-Methylenestearate (**18**) *by Thermolysis in Benzene.*—Palmitoyl chloride (548 mg, 2 mmol) in benzene (5 ml) was added over 10 min to a stirred suspension of the reagent (**2**) (360 mg, 2.2 mmol) and the alkene (**27**) (1.3 g, 6 mmol) in benzene (10 ml) at reflux under nitrogen. After 3 h at reflux the reaction mixture was cooled to room temperature, filtered, and evaporated. The excess of alkene was removed by Kugelrohr distillation (100 °C/0.5 mmHg). Chromatography of the distillation residues gave the *title ester* [eluant: dichloromethane–hexane (1:1)] (369 mg, 55%) as a colourless oil; b.p. 190 °C/1 mmHg (Kugelrohr), δ (80 MHz) 0.9 (3 H, t), 1.3 (31 H, m), 2.3 [2 H, t, *J* 6 Hz, $CH_2C(=CH_2)CO_2R$], 4.65 (2 H, d, *J* 5 Hz, 5.1 to 5.5 (2 H, m), 5.55 (1 H, s), 5.75—6.2 (1 H, m), and 6.2 (1 H, s); *m/z* 336 (M^+); $\nu_{max.}$(film) 1 720 and 1 180 cm^{-1} (Found: C, 78.3; H, 11.8. $C_{22}H_{40}O_2$ requires C, 78.51; H, 11.98%). Further elution gave the rearrangement product (**14**) (50 mg, 8%) and eventually the disulphide (**19**) (136 mg, 34%).

Ester (**18**) *by Photolysis.*—Palmitoyl chloride (548 mg, 2 mmol) was allowed to react with the reagent (**1**) (280 mg, 2.2 mmol) and pyridine (176 μl) in ether (20 ml) in the dark at room temperature for 1 h. After filtration the alkene (**28**) (1.3 g, 6 mmol) was added and the mixture irradiated with two 100 W tungsten lamps for 30 min. The reaction mixture was evaporated prior to work-up exactly as above to give the ester (**18**) (242 mg, 36%).

Methyl 3β,23-*Diacetoxy*-11-*oxo*-*olean*-12-*en*-28-*oate* (**41**): *Preparation of an Authentic Sample.*—Chromic anhydride (0.5 g) in acetic acid (5 ml) was added over 30 min to a solution of hederagenin diacetate (0.5 g) in glacial acetic acid (25 ml) at 100 °C. The reaction was heated to reflux for a further 30 min and then diluted with warm water (25 ml) and extracted with dichloromethane (4 × 20 ml). The extracts were dried (Na_2SO_4), filtered, evaporated, taken up in DMF (5 ml), and treated under nitrogen at room temperature with *N,N,N′,N′*-tetramethyl-*N″*-t-butylguanidine[18] (0.25 g) and methyl iodide (1 ml). After the reaction had been stirred for 1 h at room temperature the reaction mixture was evaporated to dryness under reduced pressure and the residue taken up in dichloromethane (10 ml), washed with water (2 × 10 ml), dried (Na_2SO_4), filtered, and evaporated. Chromatography on silica gel [eluant: ether–dichloromethane (1:1)] gave the enone (**41**) (220 mg, 40%), m.p. 234—237 °C (hexane–ether), (lit.,[32] m.p. 236 °C); $[\alpha]_D^{20}$ +76° (*c*, 2) (lit.,[32] $[\alpha]_D$ +75.3°); δ (400 MHz) 0.85 (3 H, s), 0.92 (3 H, s), 0.94 (6 H, s), 1.06 (3 H, s), 1.35 (3 H, s), 2.03 (3 H, s), 2.08 (3 H, s), 2.38 (1 H, s, 9α-H), 2.85 (1 H, m, 17β-H), 3.02 (1 H, m), 3.65 (3 H, s, MeO), 3.70 (1 H, d, *J* 10 Hz, 24-H) + 3.87 (1 H, d, *J* 10 Hz, 24-H), 4.80 (1 H, m, 3α-H), and 5.80 (1 H, s, 12-H); *m/z* (*c.i.*) 585 (M^+ + 1).

The Triterpenoid (**41**) *by Oxidation of the Triterpenoid* (**40**).—The triterpenoid (**40**) (79 mg) was oxidised and methylated exactly analogously to hederagenin diacetate (above). After chromatography compound (**41**) was obtained (17 mg, 23%), m.p. and mixed m.p. 234—237 °C. The 400 MHz ^{1}H n.m.r. spectrum of (**41**) prepared from hederagenin diacetate and from (**40**) were superimposable and a mixture of the two samples was not resolved by h.p.l.c. on silica (2% ethyl acetate in dichloromethane).

Ethyl 2-*Ethoxycarbonyl*-3-*methylthioacrylate* (**44**).—Diethyl malonate (16 g) was added over 30 min at 0 °C to a stirred solution of sodium (2.3 g) in absolute ethanol (50 ml). After warming the reaction to room temperature *O*-ethyl thioformate[33] (6.1 ml) in absolute ethanol (10 ml) was added over 10 min to give a yellow suspension. The reaction mixture was stirred for 30 min at room temperature before methyl iodide (15 g) was added and the whole heated to reflux for 2 h. The reaction mixture was then diluted with water (250 ml) and extracted with ether (4 × 50 ml). The extracts were washed with water (2 × 50 ml), dried (Na_2SO_4), filtered and evaporated to dryness. Vacuum distillation of the residue through a short Vigreux column gave the *alkene* (**44**) (4 g, 19%) as a colourless oil, b.p. 128 °C/2.5 mmHg; δ 1.30 (6 H, 2 × q, *J* 7 Hz), 2.50 (3 H, s), 4.30 (4 H, 2 × t, *J* 7 Hz), and 8.50 (1 H, s); *m/z* 217 (M^+ − 1); $\nu_{max.}$(film) 1 710, 1 540, 1 250, 1 070, 1 025, 920, 840, and 800 cm^{-1} (Found: C, 49.6; H, 6.5. $C_9H_{14}O_4S$ requires C, 49.52; H, 6.4%).

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