Radical-induced Ring Opening of Epoxides. A Convenient Alternative to the Wharton Rearrangement

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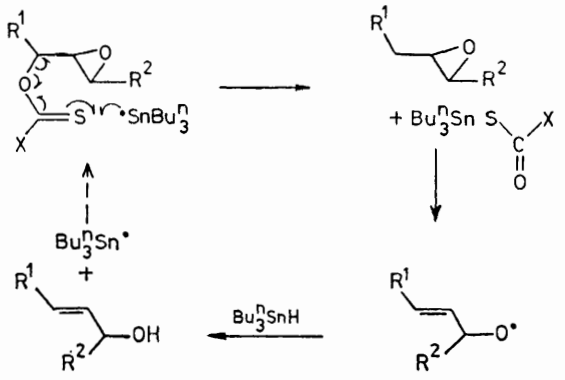
Tri-n-butyltin hydride reduction of an αβ-epoxy-*O*-thiocarbonylimidazolide derivative of an alcohol leads *via* oxiran ring-opening to the formation of an allylic alkoxyl radical. By a suitable choice of experimental conditions, this radical can either be quenched by hydrogen-atom transfer from the stannane or allowed to undergo further rearrangement.

THE deoxygenation of secondary alcohols by reaction of the derived thioxoesters, dithiocarbonates, or thiocarbonylimidazolides with tri-n-butyltin hydride [1] is an efficient radical-chain process which has subsequently found wide application in natural product chemistry.[2] The fate of the intermediate alkyl radical is however determined to some extent, by the nature of vicinal functional groups. Thus we have shown that 1,2-bis-dithiocarbonates [3] and 1-isocyano-2-dithiocarbonates [4] undergo smooth fragmentation to give olefins.

It seemed reasonable to hypothesize that the generation of a carbon radical by this kind of reduction α to an epoxide function would lead to radical fission of the latter (Scheme 1). Such a sequence would therefore constitute a useful alternative to the Wharton reaction [5] (treatment of the epoxide of an αβ-unsaturated ketone by hydrazine). Examination of the literature showed that

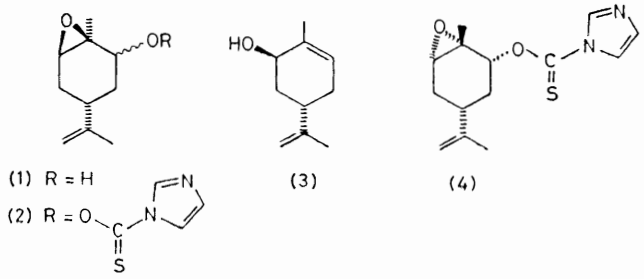


SCHEME 1

decomposition of di-t-butyl peroxide in the presence of cyclohexene oxide leads, in an indiscriminate reaction, to the formation of some cyclohex-2-enol, among other products.[6a] Such a reaction has also been postulated in biosynthetic studies [6b] and has been observed in radicals generated by ketone photolysis.[6c]

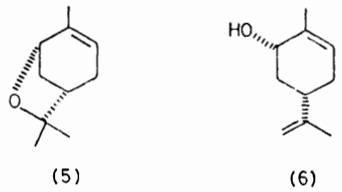
The monoterpene alcohol, carveol, was chosen for preliminary study. Base-catalysed epoxidation of (−)-carvone and subsequent borohydride reduction yielded the known [7] stereoisomeric mixture of epoxy-alcohols (1), which was transformed in essentially quantitative yield to the required thiocarbonyl imidazolide derivatives (2) by reaction with *NN'*-thiocarbonyldi-imidazole. Addition of tri-n-butylstannane to a refluxing benzene solution of (2) led very smoothly to the formation of optically pure (+)-*trans*-carveol (3) which was isolated in the form of its crystalline 3,5-dinitrobenzoate ester [8] in 65% yield. The principle features of the desired reaction were therefore clearly established.

However, attempted repetition of the sequence under



(1) R = H
(2) R = O–C(=S)–N

(3) (4)

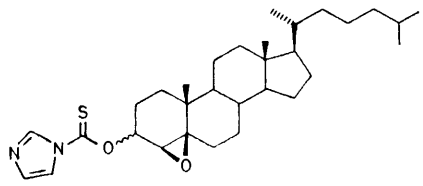


(5) (6)

essentially identical conditions using the derivative (4) prepared from optically pure (−)-*cis*-carveol led to an entirely different result. In this instance, careful g.l.c. and n.m.r. analysis of the complex reaction mixture revealed that carveol was formed in only 16% yield. Pinol [9] (5) was also detected by comparison with an authentic sample, thus indicating that intramolecular addition of the intermediate allylic alkoxyl radical to the isopropenyl double bond was an efficient competing reaction. In an effort to minimize secondary cyclisation, dropwise addition of the thiocarbonylimidazolide (4) to a ten fold excess of tri-n-butylstannane (inverse addition) was attempted. The desired (+)-*cis*-carveol (6) was isolated from this reaction as the 3,5-dinitrobenzoate ester in 47% yield.

The importance of the mode of addition was reinforced by a study of the cholestanol derivative (7). 'Inverse addition' led to effective quenching of the alkoxyl radical and formation of the tertiary allylic alcohol (8) (58%) whose structure was confirmed by comparison with an authentic sample derived by Wharton rearrangement of 4β,5β-epoxycholestan-3-one.[5] A

secondary product formed in this reaction (13%) proved however to be the major product (47%) when the 'normal' mode of addition was employed. Mass-spectral and elemental analysis indicated that the rearranged



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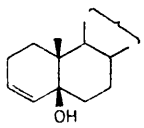

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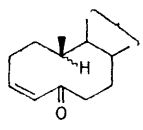

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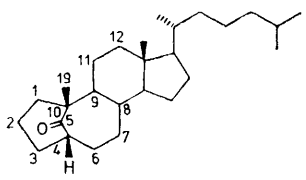

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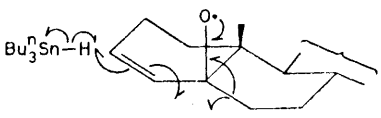


(11)

product was an isomer of the tertiary allylic alcohol (8), and the infrared spectrum displayed carbonyl absorption at 1 680 cm^{-1}. The ultraviolet and proton n.m.r. spectra confirmed the absence of an enone chromophore, thus ruling out the plausible structure (9). Detailed analysis of the ^{13}C and 90 MHz ^1H n.m.r. spectra of the ketone and its derived alcohol and acetate proved to be most informative (Table). In particular, the two α-carbon

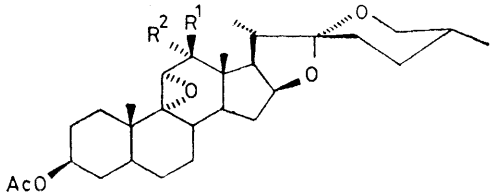
Significant ^{13}C chemical shifts of the bicyclic ketone (10) and its derived alcohol and acetate [a]

Carbon atom	Ketone (10)	Alcohol	Acetate
1	32 *	33.8 *	34.0 *
2	22.9	30.4	29.9
3	30.3 *	31.3 *	31.3 *
4	46.8 (d)	36.1	33.2 (d)
5	220	85.3	86.0
6	30.1 *	32.7 *	32.0 *
7	32.4 *	34.6 *	34.1 *
8	35.8 [b]	42.0	43.2
9	53.9	48.7	49.6 (d)
10	51.2	42.9	41.0 (s)
19	26.0	24.1	24.1

[a] In p.p.m. relative to $SiMe_4$: adjacent peaks marked * may be interchanged; s = singlet, d = doublet. [b] Tentative assignment, signal obscured by adjacent peaks.

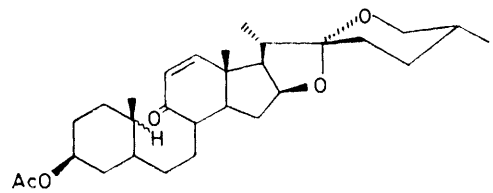
atoms flanking the carbonyl group were shown to possess only a single C–H bond ($R_3C{\cdot}CO{\cdot}CHR_2$), and the large changes observed in the chemical shifts for the α-, β-, and γ-carbon atoms on reduction of the ketone were strongly indicative of a rigid polycyclic structure.[10] In the light of this evidence, the bridged bicyclic ketone (10) is considered to be a plausible structure, thus inferring that fragmentation of the tertiary allylic alkoxyl radical (11) occurrs with preferential migration of the *trans*-allylic carbon–carbon bond as shown.

We have also prepared the pure isomers (12) and (13) derived from the hecogenin skeleton. Each isomer gave the same fragmentation product (14) on normal addition reaction with tri-n-butylstannane, thus confirming the result suggested in the carveol series that there is no stereoelectronic requirement for alkyl–oxygen cleavage of the epoxide ring. The product formed under inverse addition reaction conditions was not the anticipated tertiary allylic alcohol, but the saturated analogue of the ketone (14). The products derived by catalytic hydrogenation of the enone (14) or by separate reaction with an excess of tri-n-butylstannane proved to be identical.



(12) $R^1 = OCS-N$, $R^2 = H$

(13) $R^1 = H$, $R^2 = OCSN$



(14)

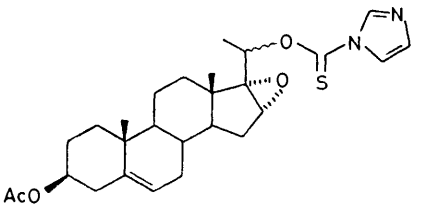
Tri-n-butyltin hydride reduction of enones is known to occur with saturation of the carbon–carbon double bond.[11] In this case, secondary rearrangement of the allylic alkoxyl radical to give a tertiary carbon radical occurs in preference to the sterically more demanding approach of the hydride from the α-face.

The epoxypregnenolone derivative (15), prepared from the known 2 : 1 mixture of epimeric alcohols,[12] was of interest in as much as Wharton rearrangement of the corresponding ketone has reportedly led, under certain conditions, to unwanted pyrazoline formation.[13] Reduction of (15) under inverse addition conditions led smoothly to the 16α-allylic alcohols (16) in 60% yield. N.m.r. analysis of the allylic alcohols showed that the reaction product was a 2 : 1 mixture of the *Z*- and *E*-isomers.[14]

An attempt was also made to extend the utility of this approach to the carbohydrate area. Although the preparation of the required thiocarbonyl derivatives from the sugars (17) and (18) was occasioned without

difficulty, subsequent reaction with tri-n-butylstannane under a wide variety of conditions led to very complex product mixtures. Evidently, the plethora of oxygen atoms adorning the carbohydrate skeleton provides an unparalleled opportunity for further extended fragmentations of alkoxyl radicals [*e.g.* arrows in (19)].

Although the influence of substrate structure can play an important role, it is therefore apparent that the fate



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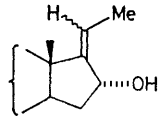

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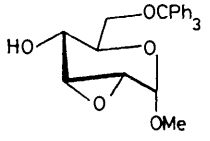

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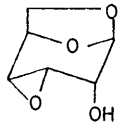

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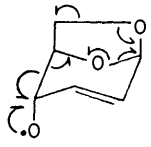

or

(19)

of the intermediate allylic alkoxyl radical can, in many cases, be controlled by a suitable choice of reaction conditions. We do not, however, foresee that this radical Wharton reaction will be useful in carbohydrate chemistry.

From the mechanistic point of view it is of interest that alkoxyl radicals may, under the appropriate conditions, have time to fragment or rearrange before being quenched by tin hydride. This phenomenon merits kinetic investigation.

EXPERIMENTAL

Melting points were determined with a Kofler hot-stage apparatus. Proton n.m.r. spectra were recorded on a Varian T-60 instrument using [^{2}H]chloroform as solvent and tetramethylsilane as internal standard. ^{13}C N.m.r. spectra were determined on a Bruker WP 60 instrument. Infrared spectra were recorded on a Perkin-Elmer 257 instrument. Optical rotations were measured on a Perkin-Elmer 141 polarimeter in chloroform solution unless stated to the contrary. Mass spectra were recorded on an AEI MS 9 instrument. Analytical g.l.c. employed a Perkin-Elmer F 11 gas chromatograph. All solvents and reagents were purified and dried by standard techniques. The standard work-up involved addition of dichloromethane, sequential washing with water, 1M-hydrochloric acid, 5% aqueous sodium hydrogencarbonate solution, water, and finally brine. The organic extract was then dried over sodium sulphate. All thiocarbonylimidazolide derivatives of alcohols were prepared immediately before use, characterised spectroscopically, and used without further purification. Each derivative was also independently verified to be thermally stable in the refluxing solvent chosen for the reduction, for at least the time required for reaction with the stannane.

(+)-trans-*Carveol* (3) *from* (−)-*Carvone by Tri-n-butylstannane Reduction of the Derived Thioimidazolides* (2).—Sodium borohydride reduction of (−)-carvone oxide furnished a 2 : 1 mixture of epimeric alcohols.[7] The mixture of alcohols (309 mg, 1.8 mmol) and *NN'*-thiocarbonyldiimidazole (620 mg, 3.6 mmol) were refluxed in dry dichloromethane until reaction was complete (t.l.c.). Work-up and removal of solvent afforded the required product (463 mg, 91%) as a viscous liquid, $\nu_{max.}$ ($CHCl_3$) 1 450, 1 385, 1 310, 1 265, 1 080, 980, 960, and 890 cm^{-1}; δ 8.05 ($\frac{1}{3}$ H, s), 8.0 ($\frac{2}{3}$ H, s), 7.4 (1 H, m), 6.78 (1 H, s), 5.65 (1 H, m), 4.62 (2 H, s), 3.05 (1 H, s), 1.65 (3 H, s), and 1.15 (3 H, s). To a solution of the above derivative (99.5 mg, 0.36 mmol) in dry benzene (1.5 ml) was added dropwise a solution of tri-n-butylstannane (221 mg, 0.76 mmol) in benzene (2 ml) containing azobisisobutyronitrile (AIBN) (6 mg, 0.04 mmol) as initiator at reflux under nitrogen. T.l.c. after addition showed the reaction to be complete and the mixture was allowed to cool. Pyridine (0.5 ml) and 3,5-dinitrobenzoyl chloride (301 mg, 1.3 mmol) were then added with vigorous stirring. When reaction was complete (t.l.c.), water (1 ml) and sodium hydrogencarbonate solution (5 ml; 5%) were added and the organic phase was separated. The aqueous phase was thoroughly extracted with dichloromethane and the combined organic extracts were washed with brine and dried. Removal of solvent *in vacuo* and chromatography on silica gel yielded the desired 3,5-dinitrobenzoate ester of (+)-*trans*-carveol (81 mg, 65%), m.p. 110—110.5 °C (from ethanol), $[\alpha]_D^{20}$ +229° (*c*, 1.9) (lit.[8] m.p. 111.5 °C, $[\alpha]_D^{20}$ +232°).

Tri-n-butylstannane Reduction of (4). *Normal Addition.*—A pure sample of (−)-*cis*-carveol was prepared by lithium aluminium hydride reduction of (−)-carvone at −78 °C,[9] formation and recrystallisation of the derived 3,5-dinitrobenzoate ester,[15] and base hydrolysis of the ester. Controlled *meta*-chloroperbenzoic acid epoxidation (<5 °C) gave the required stereochemically pure mono-epoxy-alcohol, $[\alpha]_D^{20}$ −27.3° (*c*, 5.42 in acetone), (lit.,[7] $[\alpha]_D$ −29°). The epoxy-alcohol (1.04 g, 6.2 mmol) was heated under reflux with *NN'*-thiocarbonyldi-imidazole (2.20 g, 12.4 mmol) in dry dichloromethane (50 ml) under nitrogen until reaction was complete (t.l.c.). Work-up and removal of solvent gave the required thiocarbonylimidazolide (4) (1.48 g, 86%) as a viscous oil, $\nu_{max.}$ ($CHCl_3$) 1 450, 1 370, 1 320, 1 265, 1 080, 980, 960, and 890 cm^{-1}; δ 8.4 (1 H, s), 7.7 (1 H, s), 7.07 (1 H, s), 5.8 (1 H, dd), 4.72 (2 H, s), 3.2 (1 H, d), 1.7 (3 H, s), and 1.4 (3 H, s); *m/e* 278(M^+). A solution of tri-n-butylstannane (908 mg, 3.1 mmol) containing AIBN (27 mg, 0.16 mmol) in dry benzene (28 ml) was added dropwise to a refluxing solution of (4) (433 mg, 1.56 mmol) in benzene (28 ml) under nitrogen. T.l.c. immediately after addition showed the reaction to be complete. G.l.c. of the reaction mixture (200 cm Carbowax column, 85 °C) using napthalene as a calibrated internal standard revealed a complex mixture of products comprising carveol (16%) and pinol (18%). An authentic sample of

(+)-pinol was prepared by intramolecular oxymercuriation of (−)-*cis*-carveol and subsequent borohydride reduction.[9]

Tri-n-butylstannane Reduction of (4). *Inverse Addition.*—A solution of the thiocarbonylimidazolide (4) (397 mg, 1.44 mmol) containing AIBN (22 mg, 0.14 mmol) in benzene (8.5 ml) was added dropwise to a refluxing solution of tri-n-butyltin hydride (4.2 g, 14.4 mmol) in benzene (8.5 ml) containing naphthalene (128 mg, 1 mmol) as internal g.l.c. standard under nitrogen. After addition, the reaction was found to be complete (t.l.c.). G.l.c. of the crude reaction product indicated the formation of carveol (42%) and pinol (6%). The reaction mixture was cooled, carbon tetrachloride (10 ml) was added, and stirring was continued until the Sn–H stretch at 1 800 cm^{-1} was absent in the infrared spectrum. The mixture was then titrated with a dilute solution of iodine in ether until the iodine colour persisted in order to cleave the tin–tin bond. After dilution with an equal volume of ether, the reaction mixture was washed with aqueous potassium fluoride [16] (10%) until no further precipitation of polymeric stannane was observed. Ether was removed by distillation at atmospheric pressure and the 3,5-dinitrobenzoate ester of (+)-*cis*-carveol was prepared as described above using pyridine (2.5 ml) and 3,5-dinitrobenzoyl chloride (1.5 g). Column chromatography and recrystallisation from ethanol gave (+)-*cis*-carveol 3,5-dinitrobenzoate (234 mg, 47%), m.p. 90—91 °C $[\alpha]_D^{20}$ −44.6° (*c*, 1.23) (lit.,[8] m.p. 92—95 °C, $[\alpha]_D$ −43.8°).

N-(4β,5-*Epoxy*-5β-*cholestan*-3α- *and* -3β-*yloxythiocarbonyl*)-*imidazole* (7).—Sodium borohydride reduction of purified 4β,5-epoxy-5β-cholestan-3-one [17] gave a 3 : 2 mixture of the derived 3α- and 3β-alcohols respectively.[18] A mixture of the epoxy-alcohols (363 mg, 0.9 mmol) and *NN'*-thiocarbonyldi-imidazole (326 mg, 1.8 mmol) in dry benzene (16 ml) was heated to reflux under nitrogen until reaction was complete (t.l.c.). Benzene was removed *in vacuo* and replaced by dichloromethane. Work-up and removal of solvent gave the required derivative (427 mg, 93%) as a foam which was used directly for reduction, $\nu_{max.}$ ($CHCl_3$) 1 450, 1 380, 1 320, and 1 280 cm^{-1}; δ 8.2 (1 H, s), 7.5 (1 H, s), 6.88 (1 H, s), 5.6 (1 H, complex), 3.28 ($\frac{2}{5}$ H, d, *J* 4 Hz, H-4), 2.98 ($\frac{3}{5}$ H, s, H-4), and 0.7 (3 H, s); *m/e* 512 (M^+).

Coprost-3-*en*-5β-*ol* (8) *by Tri-n-butylstannane Reduction of* (7). *Inverse Addition.*—A solution of the thiocarbonylimidazolide (7) (222 mg, 0.45 mmol) and AIBN (7.6 mg, 0.05 mmol) in toluene (2 ml) was added dropwise over 10 min to a refluxing solution of tri-n-butylstannane (1.154 g, 4 mmol) in toluene (2 ml) under nitrogen. After addition, when the reaction was complete (t.l.c.), the solvent was removed *in vacuo*. The residue was chromatographed on silica gel to yield the bridged ketone of possible structure (10) (22.4 mg, 13.4%) and the title compound (8) (97 mg, 58%), m.p. 90—92 °C (lit.,[5] 93.5—94.5 °C). The spectral (i.r., n.m.r., and mass) and chromatographic properties of the tertiary allylic alcohol were identical with those of the substance obtained by treatment of 4β,5-epoxy-5β-cholestanone with hydrazine.[5]

5,6-*Seco*-4,6-*cyclo*-4β-*cholestan*-5-*one* (10) *by Tri-n-butylstannane Reduction of* (7). *Normal Addition.*—A solution of tri-n-butylstannane (493 mg, 1.7 mmol) and AIBN (14 mg, 0.09 mmol) in dry toluene (9 ml) was added dropwise over 20 min to a refluxing solution of the thiocarbonylimidazolide (7) (427 mg, 0.83 mmol) under nitrogen. Solvent was removed *in vacuo* and the residue chromatographed on silica gel to give the allylic alcohol (8) (78.5 mg, 24%) and the *title derivative* (10) (150 mg, 47%) as a viscous glass, $[\alpha]_D^{20}$ −10.2° (*c*, 1.1), $\nu_{max.}$ ($CHCl_3$) 1 680 cm^{-1}; $\lambda_{max.}$ (cyclohexane) 276 nm (ε 38), *m/e* 386 (M^+) (Found: C, 83.95; H, 11.85; O, 4.35. $C_{27}H_{46}O$ requires C, 83.87; H, 11.99; O, 4.14%). Samples of the derived alcohol and acetate were also prepared for ^{13}C n.m.r. analysis by reduction with sodium borohydride (methanol–THF) and acetylation (acetic anhydride–pyridine at 100 °C).

(25R)-3β-*Acetoxy*-9,11α-*epoxy*-12β-[*imidazol*-1-*yl*(*thiocarbonyl*)*oxy*]-5α-*spirostan* (12).—(25*R*)-9,11α-epoxy-3β,12β-5α-dihydroxy-5α-spirostan-3-yl acetate [19] (244 mg, 0.5 mmol) and *NN'*-thiocarbonyldi-imidazole (178 mg, 1 mmol) were refluxed in dry benzene (10 ml) under argon. When the reaction was complete (t.l.c.), the solvent was removed, water was added, and the residue was taken up in dichloromethane. Work-up and removal of solvent gave the title derivative (12) (279 mg, 95%) as a foam, $\nu_{max.}$ (CCl_4) 1 730, 1 450, 1 390, 1 320, 1 280, 1 220, and 980 cm^{-1}; δ 8.0 (1 H, s), 7.4 (1 H, s), 6.8 (1 H, s), 5.3 (1 H, s), 2.95 (1 H, s), 1.9 (3 H, s), and 1.13 (3 H, s); *m/e* 598 (M^+).

(25R)-3β-*Acetoxy*-9,11α-*epoxy*-12α-[*imidazol*-1-*yl*(*thiocarbonyl*)*oxy*]-5α-*spirostan* (13).—This was prepared in an analogous manner from the corresponding 12α-alcohol,[19] and had δ 8.3 (1 H, s), 7.6 (1 H, s), 7.0 (1 H, s), 5.44 (1 H, d, *J* 4 Hz, H-12β), 3.55 (1 H, d, J 4 Hz), 1.97 (3 H, s), and 1.10 (3 H, s); *m/e* 598 (M^+).

(25R)-9,10-*Seco*-3β-*acetoxy*-5α-*spirost*-11-*en*-9-*one* (14) *from* (12) *and* (13) *by Tri-n-butylstannane Reduction. Normal Addition.*—Tri-n-butylstannane (587 mg, 0.98 mmol) in toluene (26 ml) with AIBN (16 mg, 0.01 mmol) was added dropwise over 45 min to a solution of (12) (593 mg, 2.04 mmol) in toluene (26 ml) at reflux under nitrogen. The reaction was found to be complete after addition (t.l.c.). Removal of solvent *in vacuo* and chromatography on silica gel yielded the *title enone* (14) as a glass (463 mg, 82%), $[\alpha]_D^{20}$ − 73.4° (*c*, 0.9), $\nu_{max.}$ ($CHCl_3$) 1 710 and 1 660 cm^{-1}, $\lambda_{max.}$ (cyclohexane) 225 nm (ε 6 400), δ 6.8 (1 H, d, $J_{11,12}$ 10 Hz, H-12), 5.7 (1 H, d, $J_{11,12}$ 10 Hz, H-11), and 1.9 (3 H, s, OAc). 400 MHz N.m.r. spectra confirmed the loss of the C-19 methyl singlet and the formation of an ill-resolved doublet (3 H, d, broad) at δ 0.90. ^{13}C F.T. n.m.r. spectra displayed signals for the enone chromophore at 201.4 (C-9), 128.2 (C-11) and 157.5 (C-12) p.p.m., and the loss of one quaternary carbon atom. By analogy with the known spectra of sapogenin derivatives,[20] methyl resonances were assigned as follows, 17.1 (C-18), 17.3 (C-25), 14.4 (C-21), and 19.3 (C-19), *m/e* 472 (M^+) (Found: C, 73.3; H, 9.2; O, 16.5. $C_{29}H_{44}O_5$ requires C, 73.69 ; H, 9.38; O, 16.92%). Reduction of (13) (90 mg, 0.15 mmol) in toluene (4.1 ml) with AIBN (2.9 mg, 0.01 mmol) and tri-n-butylstannane (87.7 mg, 0.3 mmol) in toluene (4.1 ml) and purification as above yielded the same enone (14) (50 mg, 70%) as evidenced by spectral (i.r., n.m.r., and mass) and chromatographic properties.

(25R)-9,10-*Seco*-3β-*acetoxy*-5α-*spirostan*-9-*one from* (12) by *Tri-n-butylstannane Reduction. Inverse Addition.*—A solution of (12) (199 mg, 0.33 mmol) in toluene (2 ml) containing AIBN (5 mg, 0.03 mmol) was added dropwise over 10 min to a solution of tri-n-butylstannane (0.978 g, 3.34 mmol) in toluene (2 ml) at reflux under nitrogen. The reaction was complete immediately after addition (t.l.c.). Removal of solvent and chromatography on silica gel yielded the title compound (120 mg, 75%), $\nu_{max.}$ ($CHCl_3$) 1 700 cm^{-1} (removal of the 3β-acetoxy-group by base hydrolysis gave $\nu_{max.}$ 1 690 cm^{-1}); *m/e* 474 (M^+). The spectral and chromatographic characteristics of this compound were identical

with the compound obtained by catalytic hydrogenation of the enone (14) in ethanol over 10% palladium–charcoal, thus confirming the proposed structure.

Tri-n-Butylstannane Reduction of (14). *Inverse Addition.*—Addition of a solution of enone (14) (27 mg, 0.06 mmol) with AIBN (1 mg, 0.006 mmol) in toluene (1 ml) to a refluxing solution of tri-n-butylstannane (171 mg, 0.58 mmol) in toluene (1.5 ml) under nitrogen resulted in immediate product formation. Removal of solvent and chromatography on silica gel gave the reduced enone (19.2 mg, 71%) whose spectral (i.r., n.m.r., and mass) and chromatographic properties were identical to those above.

3β-*Acetoxy*-16α,17α-*epoxy*-20α- *and* -20β-[*imidazol*-1-*yl*-(*thiocarbonyl*)*oxy*]*pregn*-5-*ene* (15).—A 2 : 1 mixture of the 20β- and 20α-alcohols [12] (as evidenced by n.m.r.) was prepared from 3β-acetoxy-16α,17α-epoxypregn-5-en-20-one by reduction with sodium borohydride in methanol–tetrahydrofuran. The alcohols (310 mg, 0.8 mmol) and *NN'*-thiocarbonyldi-imidazole (296 mg, 1.7 mmol) were refluxed in dry benzene (20 ml) under nitrogen until reaction was complete (t.l.c.). Removal of solvent and work-up gave the derivatives (15) (402 mg, quantitative), δ 8.08 ($\frac{2}{3}$ H, s), 7.95 ($\frac{1}{3}$ H, s), 7.39 (1 H, s), 6.78 (1 H, s), 6.2 ($\frac{2}{3}$ H, q, *J* 6 Hz), 6.0 ($\frac{1}{3}$ H, q, *J* 6 Hz), 5.18 (1 H, m), 3.24 ($\frac{1}{3}$ H, s), 3.14 ($\frac{2}{3}$ H, s), and 1.90 (3 H, s).

3β-*Acetoxypregna*-5,17-*dien*-16α-*ol* (16) *from Tri-n-Butylstannane Reduction of* (15). *Inverse Addition.*—A solution of the thiocarbonylimidazolide (15) (187 mg, 0.4 mmol) with AIBN (9 mg, 0.06 mmol) in toluene (2 ml) was added dropwise to a solution of tri-n-butylstannane (1.21 g, 4.1 mmol) in toluene (2 ml) at reflux temperature under nitrogen. Reaction was complete (t.l.c.) when the addition was finished. The reaction mixture was cooled and treated sequentially with carbon tetrachloride, iodine, and potassium fluoride as described above. Chromatography on silica gel yielded a crystalline mixture of allylic alcohols (16) (80 mg, 60%), m.p. 177—179 °C (from hexane–dichloromethane), $\nu_{max.}$ ($CHCl_3$) 3 600, 3 450, and 1 720 cm^{-1}; δ 5.25 (2 H, m), 4.65—4.4br (2 H, m), and 2.0 (3 H, s) (Found: C, 76.85; H, 9.6; O, 13.15. Calc. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56; O, 13.39%). The composition of the mixture of isomeric allylic alcohols (16) was shown to be *E* : *Z* = 1 : 2 on the basis of 90 MHz n.m.r. spectra: [14] δ (*E*-isomer) 0.89 (3 H, s, H-18); δ (*Z*-isomer) 0.73 (3 H, s, H-18).

Methyl 2,3-*Anhydro*-4-O-(*imidazol*-1-*ylthiocarbonyl*)-6-O-*trityl*-α-D-*allopyranoside*.—Methyl 2,3-anhydro-6-*O*-trityl-α-D-allopyranoside [21] (209 mg, 0.5 mmol) and *NN'*-thiocarbonyldi-imidazole (184 mg, 1.03 mmol) were refluxed in dry benzene (10 ml) under nitrogen until reaction was complete. Removal of solvent and work-up furnished the desired title derivative (284 mg, 91%), δ 7.85 (1 H, s), 7.1 (16 H, m), 6.85 (1 H, s), 5.2 (1 H, d, *J* 9 Hz), 4.9 (1 H, d, *J* 3 Hz), and 3.4 (3 H, s), *m/e* 243 ($M^+ - CPh_3$).

1,6 : 3,4-*Dianhydro*-2-O-(S-*methyldithiocarbonato*)-β-D-*Allopyranose*.—1,6 : 3,4-Dianhydro-β-D-allopyranose (18) [22] (90.7 mg, 0.63 mmol), sodium hydride (50% dispersion; 30.3 mg, 1.2 mmol), and imidazole (0.8 mg) were stirred at room temperature under nitrogen in tetrahydrofuran (2 ml) for 50 min. Carbon disulphide (0.28 ml) was added and the reaction mixture was stirred for a further 1 h, followed by addition of methyl iodide (0.28 ml). After 1 h, the reaction mixture was diluted with water and extracted with dichloromethane. Work-up and removal of solvent gave the title xanthate (147 mg, 100%), $\nu_{max.}$ ($CHCl_3$) 1 140, 1 060, and 990 cm^{-1}, δ ($CDCl_3$–CCl_4) 5.2 (2 H, m), 4.65 (1 H, d, *J* 4 Hz), 3.65br (3 H, m), 3.05 (1 H, m), and 2.5 (3 H, s).

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