Reactions of Relevance to the Chemistry of Aminoglycoside Antibiotics. Part 14.† A Useful Radical-deamination Reaction

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Primary, secondary, and tertiary aliphatic or alicyclic isocyanides are smoothly reduced under radical conditions using tri-n-butylstannane to the corresponding hydrocarbons. The relative ease of reduction is tertiary > secondary > primary. Aromatic isocyanides are not reduced under these conditions. The reduction of isothiocyanates (or isoselenocyanates) by tri-n-butylstannane also affords hydrocarbons, but here the isocyanides have been shown to be intermediates. The reduction of a compound with isocyanide and xanthate functions in a 1,2-relationship gives a smooth radical fragmentation to furnish an olefin. An efficient synthesis of 2-deoxy-D-glucose starting with glucosamine is described.

THE selective replacement of a primary amino-function by a hydrogen atom is a desirable reaction for the modification of natural products, particularly aminoglycoside antibiotics. We now describe, in some detail,[1] the realisation of this objective.

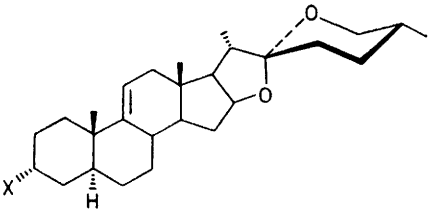
Although deamination reactions involving ionic intermediates have been described,[2,3] we sought to design a radical reaction which could be carried out under neutral conditions without the possibility of rearrangement. We envisaged that homolysis of the carbon–nitrogen bond in a suitable derivative of the amine, followed by quenching of the resultant carbon radical by hydrogen-atom transfer, would satisfy these requirements. In this respect, the reaction is conceptually similar to our method for the deoxygenation of secondary alcohols.[4]

From initial observations by Saegusa,[5] it was apparent that tri-n-butylstannane reduction of the isocyanide function led to the corresponding hydrocarbon. Yields, however, were low, and isocyanides bearing an unactivated primary alkyl chain were considered to be inert. The strong affinity of the tri-n-butylstannyl radical for the thionocarbonyl group led us to propose that the corresponding isothiocyanate or isoselenocyanate might lead to more efficient radical fragmentation reactions.

Initially, we chose to use as model the steroidal amine (1) derived from Δ^9-tigogenin. Formylation with formyl acetic anhydride and dehydration with toluene-*p*-sulphonyl chloride in pyridine yielded the desired isocyanide (2) in good yield. Subsequent reaction with elemental selenium gave the corresponding isoselenocyanate (3). The isothiocyanate (4) was prepared by reaction of the amine with carbon disulphide and dicyclohexylcarbodi-imide (DCC). Reaction of each of these derivatives, (2), (3), and (4), in refluxing benzene with tri-n-butyltin hydride in the presence of azobisisobutyronitrile (AIBN) as initiator, led smoothly, and in virtually identical yield, to the deaminated hydrocarbon (5) (*ca.* 89%). Thus, it did not appear that the isothiocyanate or isoselenocyanate groupings offered any significant advantage over the isocyanide. Moreover, careful monitoring of the reduction of (3) and (4) indicated the intermediacy of the isocyanide. 3α-Isocyano- and 3α-isothiocyanato-cholestane were also readily reduced under standard conditions to give cholestane.

An anticipated, the isocyanide derived from 2-methyl-2-aminononadecane, by virtue of bearing a tertiary α carbon atom, gave ready fragmentation in refluxing benzene solution; even at 50 °C, 2-methylnonadecane was isolated in excellent yield (91%).

We have successfully extended this deamination reaction to amines which possess a primary alkyl chain. Although the activation energy for the homolysis of the carbon–nitrogen bond is considerably higher, a good yield of n-octadecane was obtained from the isocyanide and the isothiocyanate by refluxing in xylene solution



(1) X = NH_2

(2) X = N=C:

(3) X = N=C=Se

(4) X = N=C=S

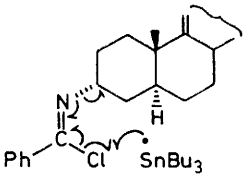
(5) X = H

with periodic additions of initiator (80%). It was of interest to note that, by working at a lower temperature, it was possible to isolate the isocyanide as the primary intermediate from reduction of the isothiocyanate, thus confirming the spectroscopic observations made in the spirostane series. In an effort to obtain fragmentation at a lower temperature we studied the reaction of n-octadecyl isocyanide with tri-n-hexylsilane and tri-n-butylgermane. The silane was completely unreactive towards the isocyanide function. The germane re-

† Part 13, A. G. M. Barrett, R. W. Read, and D. H. R. Barton, *J.C.S. Perkin I*, 1980, 2194.

duction led to a comparable yield of hydrocarbon as obtained with tri-n-butylstannane at a similar temperature.

The deamination reaction cannot be extended to aromatic isocyanides. Thus anisole was not detected



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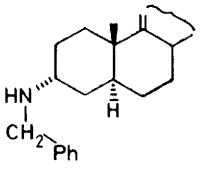
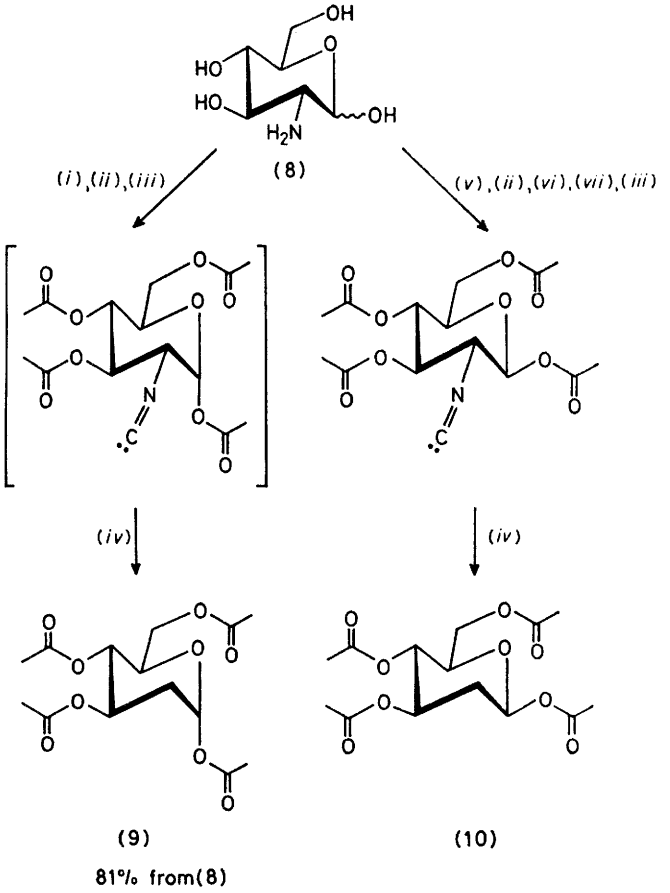


(7)

in the reduction of *p*-methoxyisocyanobenzene. Aryl isothiocyanates are reported to react with stannanes to give, either the product of addition across the thiocarbonyl group,[6] or a mixture of the corresponding isocyanide and aniline.[7]

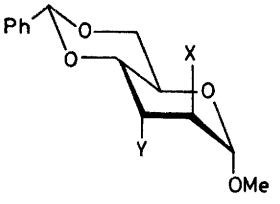
It is important to note that the isocyanide grouping occupies a key role as the leaving group for radical



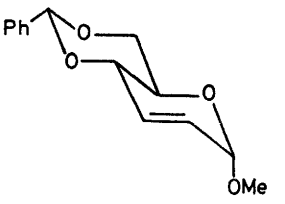
SCHEME 1 *Reagents:* (*i*) *p*-nitrophenyl formate; (*ii*) Ac_2O–py; (*iii*) $POCl_3$–Et_3N; (*iv*) Bu^n_3SnH; (*v*) *p*-methoxybenzaldehyde; (*vi*) HCl, hydrolysis; (*vii*) acetic formic anhydride

deamination. Carbon–nitrogen bond cleavage was not observed in the reactions of n-octadecyl isocyanate or DCC with tri-n-butylstannane. Similarly, fragmentation [arrows in formula (6)] of the imidoyl halide derivative of Δ^9-tigogenin was found to be energetically unfavourable. Reduction with tri-n-butylstannane afforded the benzylamine derivative (7) (64%).

It was important to assess the compatibility of neighbouring functional groups towards isocyanide formation and deamination within the carbohydrate framework. The reduction of 2-amino-2-deoxy-D-glucose (8) was selected for study since the conventional synthesis of this antibiotic component requires six steps from glucose.[8] As indicated (Scheme 1), formation of the isocyanide and deamination with tri-n-butyl stannane proceeded smoothly, resulting in a short and



(11) X = NC:, Y = OH
(12) X = NH_2, Y = OH
(13) X = H, Y = OH
(14) X = NC:, Y = OSO_2Me
(15) X = H, Y = OSO_2Me
(16) X = NC:, Y = 



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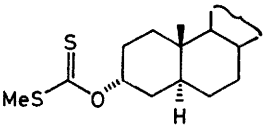


(18)

efficient synthesis of either anomer (9) or (10) of 1,3,4,6-tetra-*O*-acetyl-2-deoxy-D-glucose.

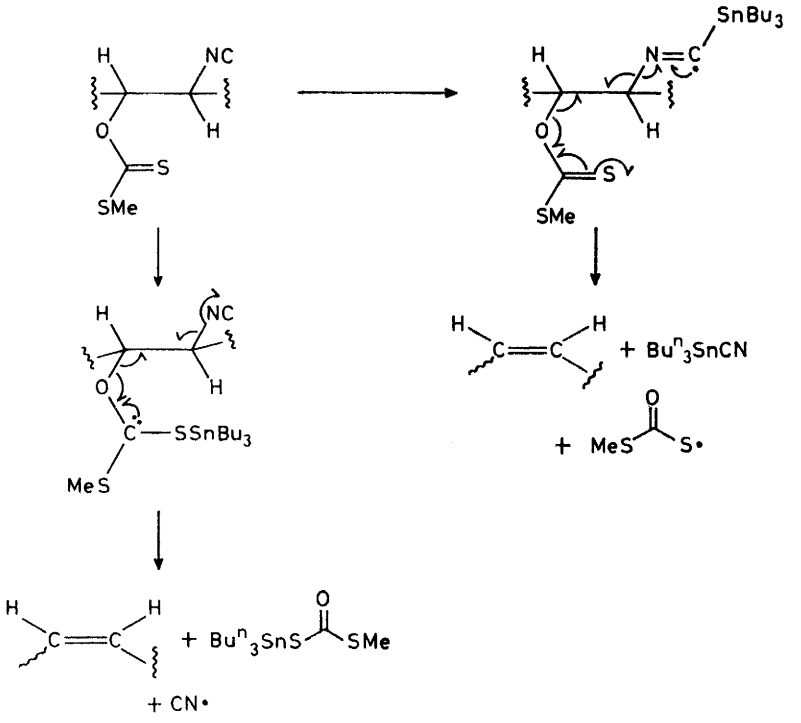
The isocyanide (11) from methyl 2-amino-4,6-*O*-benzylidene-2-deoxy-α-D-altroside[9] (12) was also prepared in high overall yield by the usual formylation–dehydration sequence. Radical-induced deamination with tri-n-butylstannane gave the corresponding deoxy-alcohol (13) (92%).

The course of the reaction was not affected by the presence of a neighbouring mesyloxy-group in the isocyano-mesylate (14). The resultant deoxy-mesylate (15) (77%) was also independently prepared by mesylation of the deoxy-alcohol (13).

In view of our reported conversion of vicinal diols into olefins by radical elimation *via* the derived bis-dithiocarbonates,[10] the dithiocarbonate (16) was a derivative of particular interest. Treatment with tri-n-butylstannane led to a virtually quantitative yield of the olefin (17). This transformation involves two alternative mechanisms (Scheme 2) and deserves some comment. By allowing a 1 : 1 mixture of 3α-isocyano-Δ^9-tigogenin (2) and cholestan-3α-yl *S*-methyl dithiocarbonate (18) to compete for a deficiency of tri-n-butylstannane, it was shown, from the resultant ratios of isolated hydrocarbons and starting materials, that the reduction of the isocyanide and the deoxygenation of the dithiocarbonate were proceeding at a comparable rate. Repetition of the experiment with cholestan-3β-yl *S*-methyl dithiocarbonate led to essentially the same result. Thus it is

not possible from these experiments to define which group induces the radical elimination of the other.

We have also examined the deamination of (±)- and *meso*-1,2-di-isocyano-1,2-diphenylethanes to give bibenzyl (55%) and toluene (14%). Stilbene was not detected in these reactions. Since the formation of the conjugated double bond in stilbene provides an additional driving force for radical elimination,[10] it would seem probable that the formation of the olefin (17) requires that in the dithiocarbonate (16) it is the isocyano-group which is attacked first followed by concerted fragmentation.



SCHEME 2

The tri-n-butylstannane reduction of isocyanides is a general method of value for the modification of natural products. The reaction is compatible with the common functional groups found in carbohydrate chemistry. In addition, we have also shown that deamination of amino-acid esters can be achieved in high yield.[11] Others [12] have demonstrated the value of the reaction in β-lactam chemistry. We are currently examining the selective deamination of aminoglycoside antibiotics by this technique.

EXPERIMENTAL

M.p.s were determined with a Kofler hot-stage apparatus. N.m.r. spectra were determined for solutions in deuteriochloroform with tetramethylsilane as internal standard. I.r. spectra were recorded on a Perkin-Elmer 257 instrument. Optical rotations were measured on a Perkin-Elmer 141 polarimeter in chloroform (unless stated to the contrary). Mass spectra were recorded with an AEI MS9 instrument. All solvents and reagents were purified and dried by standard techniques.

3β-*Tosyloxy*-(25R)-5α-*spirost*-9(11)-*ene*.—To an ice-cold solution of Δ^9-tigogenin (5.0 g) in pyridine (80 ml) was added, in portions, toluene-*p*-sulphonyl chloride (5.0 g). After the addition was complete the reaction mixture was allowed to warm to room temperature and stirred for a further 7 h. Water (75 ml) was added and the mixture was allowed to stand overnight. The precipitated solid was filtered off, washed with dilute HCl and water, and dried *in vacuo*. Recrystallisation from acetone gave the 3β-*tosylate* (6.86 g, 87%) as plates, m.p. 167—169 °C, $[\alpha]_D^{20}$ −57.2°, $\nu_{max.}$ (CCl_4) 1 180, 1 055, and 940 cm^{-1}, δ ($CDCl_3$) 7.71 and 7.23 (4 H, AA'BB' q), 5.25 (1 H, m), 4.6—4.2 (2 H, m), 3.47 (2 H, m), and 2.43 (3 H, s), *m/e* 568 (Found: C, 71.6; H, 8.4; S, 5.7. $C_{34}H_{48}O_5S$ requires C, 71.79; H, 8.51; S, 5.64%).

3α-*Azido*-(25R)-5α-*spirost*-9(11)-*ene*.—To a slurry of sodium azide (8 g) in dry dimethyl sulphoxide (60 ml) was added 3β-tosyloxy-(25*R*)-5α-spirost-9(11)-ene (2.36 g), and the mixture was stirred for 6 h at 84 °C. After cooling to room temperature, ice–water was added and the mixture was allowed to stand overnight in a refrigerator. The resultant precipitate was filtered off, washed with water, and crystallised from acetone to yield the 3α-*azide* (1.6 g, 88%), m.p. 201—203 °C (sublimes), $[\alpha]_D^{20}$ −80.1° (*c*, 0.6), $\nu_{max.}$ (CCl_4) 2 105 cm^{-1}, δ ($CDCl_3$) 5.30 (1 H, m), 4.6—4.3 (1 H, m), and 3.6—3.4 (2 H, m), *m/e* 439 (Found: C, 73.8; H, 9.35; N, 9.7. $C_{27}H_{41}N_3O_2$ requires C, 73.76; H, 9.40; N, 9.56%).

3α-*Isothiocyanato*-(25R)-5α-*spirost*-9(11)-*ene*.— To a solution of the azide (9.13 g) in dry ether (200 ml) at 0 °C was added lithium aluminium hydride (3.6 g). The mixture was stirred for 8 h at room temperature, cooled to 0 °C, and

carefully treated with ice during 1 h. The resultant precipitate was filtered off and washed with ether. The combined ethereal phases were dried and evaporated to yield the steroidal amine (1) as a foam in quantitative yield. To a solution of dicyclohexylcarbodi-imide (DCC) (0.43 g) and carbon disulphide (1 ml) in dry ether (50 ml) at −10 °C was added a saturated solution of the crude amine (0.86 g) in dry ether. The reaction mixture was slowly warmed to room temperature and filtered. The solvent was removed under reduced pressure and the residual solid redissolved in CCl_4. Filtration and preparative t.l.c. (SiO_2–ether : pentane) followed by crystallisation from acetone gave the *isothiocyanate* (4) (0.61 g, 64%), m.p. 187—188 °C (decomp.), $[\alpha]_D^{20}$ −31.8° (*c*, 1.2), $\nu_{max.}$ (CCl_4) 2 122 and 2 060 cm^{-1}, δ ($CDCl_3$) 3.20 (1 H, m), 4.6—4.3 (1 H, m), 4.2—4.0 (1 H, m), and 3.5—3.25 (2 H, m), *m/e* 455 (Found: C, 73.95; H, 9.3; N, 3.0; S, 6.8. $C_{28}H_{41}NO_2S$ requires C, 73.8; H, 9.05; N, 3.05; S, 7.05%).

3α-*Formamido*-(25R)-5α-*spirost*-9(11)-*ene*.—To a saturated solution of the amine (1) (4.71 g) in ether at 0 °C was added dropwise acetic formic anhydride (1.3 g). After stirring for 3 h at 0 °C the mixture was cooled to −20 °C and the crystalline precipitate filtered off and washed with hexane. Addition of hexane to the mother-liquor resulted in the precipitation of a second crop of the formamide. Recrystalisation of the combined crops from acetone gave the pure *formamide* (4.57 g, 91%) as needles, m.p. 255—256 °C (decomp.), $[\alpha]_D^{20}$ −34.9° (*c*, 1.1), $\nu_{max.}$ ($CHCl_3$) 3 455 and 1 700 cm^{-1}, δ ($CDCl_3$) 8.04 (1 H, d), 5.89 (1 H, br), 5.32 (1 H, m), 4.6—4.1 (2 H, m), and 3.5—3.3 (2 H, m), *m/e* 441 (Found: 74.8; H, 9.9; N, 2.9. $C_{28}H_{43}O_3N{\cdot}0.5H_2O$ requires C, 74.63; H, 9.84; N, 3.11%).

3α-*Isocyano*-(25R)-5α-*spirost*-9(11)-*ene*.—To a suspension of the formamide (2.12 g) in dry pyridine (40 ml) at 0 °C was added toluene-*p*-sulphonyl chloride (1.5 g). After being stirred for 2 h at room temperature the mixture was poured onto ice–water and allowed to stand overnight. The precipitate was filtered off, washed thoroughly with water, dried, and recrystallised from acetone to give the *isocyanide* (2) (1.73 g, 85%) as needles, m.p. 232—233 °C (sublimes), $[\alpha]_D^{20}$ −45.2° (*c*, 1.2), $\nu_{max.}$ (CCl_4) 2 140 cm^{-1}, δ ($CDCl_3$) 5.12 (1 H, m), 4.6—4.2 (1 H, m), 4.0—3.8 (1 H, m), and 3.5—3.25 (2 H, m), *m/e* 423 (Found: C, 79.1; H, 9.8; N, 3.2. $C_{28}H_{41}O_2N$ requires C, 79.39; H, 9.76; N, 3.31%).

3α-*Isoselenocyanato*-(25R)-5α-*spirost*-9(11)-*ene* (3).—A mixture of the isocyanide (2) (0.127 g) and selenium (0.27 g) heptane (10 ml) was heated at reflux under nitrogen for 2 h. The mixture was cooled to room temperature and the excess of selenium was removed by filtration. The filtrate was evaporated under reduced pressure. Recrystallisation from acetone–water gave the *isoselenocyanate* (3) (0.123 g, 82%) as needles, m.p. 196—198 °C (decomp.), $[\alpha]_D^{20}$ −19.9° (*c*, 1.8), $\nu_{max.}$ (CCl_4) 2 115 cm^{-1}, δ ($CDCl_3$), 5.25 (1 H, m), 4.6—4.3 (1 H, m), 4.3—4.0 (1 H, m), and 3.5—3.25 (2 H, m), *m/e* 501 and 503 (Found: C, 66.75; H, 8.1; N, 2.76; Se, 14.8. $C_{28}H_{41}O_2NSe{\cdot}0.5Me_2CO$ requires C, 66.64; H, 8.34; N, 2.63; Se, 14.85%).

3α-*Benzamido*-(25R)-5α-*spirost*-9(11)-*ene*.—To a solution of 3α-amino-(25*R*)-5α-spirost-9(11)-ene (0.413 g) in dry pyridine (20 ml) at 0 °C was added benzoyl chloride (0.155 g). The mixture was maintained at room temperature for 2 h and then poured onto ice–water. The crude product was filtered off and recrystallised from acetone to give the *benzamide* (0.377 g, 69%) as needles, m.p. 273—275 °C (decomp.), $[\alpha]_D^{20}$ −27.9° (*c*, 1.5), $\nu_{max.}$ ($CHCl_3$) 3 450 and 1 672 cm^{-1}, δ ($CDCl_3$) 7.7—7.15 (5 H, m), 6.4 (1 H, br), 5.17 (1 H, m), 4.4—4.1 (1 H, m), and 3.45—3.3 (2 H, m), *m/e* 517 [Found: C, 78.15; H, 9.1; N, 2.45. $C_{34}H_{47}O_3N{\cdot}0.5(CH_3)_2CO$] requires C, 77.98; H, 9.22; N, 2.56%).

2-*Formamido*-2-*methylnonadecane*.—To a suspension of potassium cyanide (5 g) and 2-methylnonadecan-2-ol (2 g) in dibutyl ether (20 ml) was added dropwise concentrated sulphuric acid (10 ml) at 40—45 °C. After the addition was complete, the mixture was stirred for 4 h at room temperature and then poured onto ice–water (100 ml). The aqueous mixture was cautiously treated with aqueous KOH until strongly alkaline. The ether was dried and evaporated off to yield the formamide as a solid, which crystallised from CH_2Cl_2–MeOH to yield the *formamide* (1.8 g, 82%), m.p. 58 °C, $\nu_{max.}$ ($CHCl_3$) 3 445 and 1 701 cm^{-1}, δ ($CDCl_3$) 8.05 (d, *J* 16 Hz) and 7.86 (d, *J* 2 Hz) (total 1 H), 5.2 (1 H, br), and 1.33 (6 H, s), *m/e* 325 (Found: C, 77.5; H, 13.2; N, 4.1. $C_{21}H_{41}NO$ requires C, 77.47; H, 13.31; N, 4.30%).

2-*Isocyano*-2-*methylnonadecane*.—2-Formamido-2-methylnonadecane (1.3 g) in dry pyridine (35 ml) was treated with toluene-*p*-sulphonyl chloride (1.3 g) during 1 5 h at room temperature. The reaction mixture was poured onto ice–water and cooled in a refrigerator for 2 h. The solid precipitate was filtered off and thoroughly washed with water, dried, and crystallised from CH_2Cl_2–MeOH to yield the *isocyanide* (1.14 g, 93%), m.p. 41 °C, $\nu_{max.}$ ($CHCl_3$) 2 136 cm^{-1}, δ ($CDCl_3$) 1.8—0.8 (m), *m/e* 307 (Found: C, 82.0; H, 13.25; N, 4.35. $C_{21}H_{42}N$ requires C, 82.01; H, 13.44; N, 4.55%).

1-*Formamido-octadecane*.—*Method A*. A mixture of formic acid (16 ml), acetic anhydride (10 ml), and n-octadecylamine (2.04 g) was heated under reflux for 12 h. The mixture was then cooled and diluted with water and dichloromethane. The organic phase was washed with saturated sodium hydrogencarbonate solution, and then 0.5M-HCl was added. The resulting precipitate was filtered off and dried to yield n-octadecylamine hydrochloride (0.205 g, 9%). The organic phase was washed with water, dried, applied to a column of silica and eluted with ether to yield the *bisformylamide* (0.47 g, 10%) as a microcrystalline solid, m.p. 73 °C, $\nu_{max.}$ (CCl_4) 1 695 cm^{-1}, δ ($CDCl_3$) 8.79 (2 H, s) and 3.53 (2 H, t, *J* 6 Hz), *m/e* 325 (Found: C, 73.95; H, 12.1; N, 4.1. $C_{20}H_{39}NO_2$ requires C, 73.72; H, 12.08; N, 4.12%). Later fractions contained the desired *monoformamide* which crystallised from methanol as needles (1.26 g, 56%), m.p. 66 °C, $\nu_{max.}$ ($CHCl_3$) 3 460 and 1 705 cm^{-1}; δ ($CDCl_3$) 8.15 (1 H, s), 5.55 (1 H, br), and 3.25 (2 H, t, *J* 6.1 Hz), *m/e* 297 (Found: C, 76.4; H, 13.05; N, 4.6. $C_{19}H_{39}NO$ requires C, 76.70; H, 13.21; N, 4.71%).

Method B. To a saturated solution of octadecylamine (2 g) in ether–pentane was added acetic formic anhydride (0.8 g) dropwise at 0 °C. After 1 h pentane was added until the mixture became turbid when it was cooled to −20 °C. The precipitated formamide was filtered off and recrystallised from methanol to yield the formamide (2.0 g, 91%), identical to the product described under Method A.

1-*Isocyano-octadecane*.—*Method A*. To the formamide (0.712 g) in dry pyridine (30 ml) was added toluene-*p*-sulphonyl chloride (0.77 g). The mixture was stirred for 2 h at room temperature and poured onto ice–water. The precipitated solid was filtered off, washed with water, and recrystallised from chloroform–methanol to yield the *isocyanide* (0.635 g, 95%), m.p. 35 °C, $\nu_{max.}$ (CCl_4) 2 140 cm^{-1}, δ ($CDCl_3$) 3.56 (2 H, t, *J* 6 Hz), *m/e* 279 (Found: C, 81.7; H, 13.45; N, 4.7. $C_{19}H_{37}N$ requires C, 81.65; H, 13.34; N, 5.01%).

Method B. 1-Isocyanato-octadecane (1.5 g) and triethylphosphite (0.85 g) were heated at 180 °C for 6 h under N_2. After cooling, the mixture was applied to a column of silica and eluted with ether–pentane (1 : 10). Recrystallisation of the crude product gave the isocyanide (0.51 g, 36%) as a microcrystalline solid, identical to that described above.

1-*Isothiocyanato-octadecane.*—1-Amino-octadecane (0.43 g) in dry ether (50 ml) was added to a solution of DCC (0.34 g) and CS_2 (0.8 ml) in dry ether (40 ml) at −10 °C. The mixture was allowed to warm to room temperature and stirred for 5 h. After removal of the precipitated thiourea, preparative t.l.c. (SiO_2; pentane) gave the *isothiocyanate* (0.304 g, 61%) as an oil which crystallised from CH_2Cl_2–MeOH, m.p. 32 °C, $\nu_{max.}$ (film) 2 190 and 2 090 cm^{-1}, δ (CCl_4) 3.49 (2 H, t, *J* 6 Hz), *m/e* 311.

3α-*Isothiocyanatocholestane.*— 3α-Aminocholestane [13] (357.7 mg) in diethyl ether (1 ml) was added slowly to a stirred solution of DCC (190.3 mg) and carbon disulphide (0.5 ml) in diethyl ether (1 ml) with cooling in an ice-salt-bath (−10 °C). The reaction mixture was allowed to warm and stirred at room temperature for 18 h. The precipitated urea was filtered off and washed with ether. The combined filtrate and ethereal washings were concentrated and the residue was recrystallised twice from acetone to give the *isothiocyanate* (250 mg, 49%), m.p. 103 °C, $[\alpha]_D^{20}$ +15.5 (*c*, 1.37, CH_2Cl_2), $\nu_{max.}$ (CCl_4) 2 120 and 2 010 cm^{-1}, *m/e* 429 (Found: C, 78.4; H, 10.75; N, 3.5; S, 7.25. $C_{28}H_{47}NS$ requires C, 78.27; H, 11.03; N, 3.26; S, 7.45%).

Reduction of 1-*Isocyano-octadecane. with Tri-n-buiyl-stannane.*—A solution of the isocyanide (0.279 g) and azobisisobutyronitrile (AIBN) (0.1 g) in dry xylene (50 ml) was added dropwise to a solution of tri-n-butylstannane (0.64 g, 2.2 mol equiv.) in refluxing xylene (50 ml), under nitrogen, over 2 h. A solution of AIBN (0.1 g) in xylene (50 ml) was slowly added over 5 h. The solvent was removed under reduced pressure and the residue dissolved in pentane. Iodine in pentane solution was added until the colour of iodine persisted. The solvent was removed and the octadecane was isolated by preparative t.l.c. (SiO_2; pentane) and sublimation *in vacuo* (0.205 g, 81%), m.p. 29 °C, with spectral characteristics identical with those of an authentic specimen.

Reduction of 1-*Isothiocyanato-octadecane.*—Using the conditions described above the isothiocyanate (0.311 g) was treated with tri-n-butylstannane (1.25 g) to yield octadecane (0.202 g, 80%). Repetition of this experiment using toluene as solvent for 2 h, and following the disappearance of starting material by t.l.c. (SiO_2; pentane–ether, 4 : 1) led to the isolation of 1-isocyano-octadecane (0.138 g, 50%) and octadecane (0.013 5 g, 5%).

Reduction of 1-*Isocyano-octadecane with Tri-n-butyl-germane.*—To a refluxing solution of tri-n-butylgermane (0.12 g) in dry xylene (10 ml) under N_2 was added a solution of 1-isocyano-octadecane (0.078 g) and AIBN (0.02 g) in xylene (20 ml) over 2 h. A further quantity of AIBN (0.040 g) in xylene (40 ml) was added dropwise during 5 h. The reaction mixture was cooled and the solvent was removed under reduced pressure. The residue was dissolved in hexane and treated with iodine as previously described. The octadecane (0.052 g, 73%) was isolated by preparative t.l.c. followed by sublimation *in vacuo.*

(25R)-5α-*Spirost*-9(11)-*ene* (5).—(i) *From the isocyanide* (2). A solution of the isocyanide (2) (0.178 g) and AIBN (0.006 5 g) in benzene (20 ml) was added during 1.5 h to a refluxing solution of tri-n-butylstannane (0.79 g, 22 mol equiv.) in dry benzene (10 ml) under nitrogen. AIBN (0.005 g) in benzene (20 ml) was then added over 2 h. Preparative t.l.c. (SiO_2; pentane–Et_2O, 5 : 1) followed by sublimation *in vacuo* (0.5 Torr at 110 °C) yielded the *deaminated steroid* (5) (0.149 g, 89%), m.p. 148—150 °C (sublimes), $[\alpha]_D^{20}$ −65.6° (*c*, 1.1), $\nu_{max.}$ ($CHCl_3$) 2 960, 2 935, 2 880, 2 863, 1 453, and 1 377 cm^{-1}, δ ($CDCl_3$) 5.27 (1 H, m), 4.6—4.2 (1 H, m), and 3.5—3.3 (2 H, m), *m/e* 398 (Found: C, 81.15; H, 10.55. $C_{27}H_{42}O_2$ requires C, 81.35; H, 10.62%).

(ii) *From the isothiocyanate* (4). The isothiocyanate (0.2 g) was treated with tri-n-butylstannane (0.64 g, 5 mol equiv.) and AIBN (13 mg) as described above to yield the deaminated steroid (0.146 g, 90%).

(iii) *From the isoselenocyanate* (3). By the same method the isoselenocyanate (0.098 g) was reduced with tri-n-butylstannane (0.26 g, 4.6 equiv.) in the presence of AIBN (0.008g) to yield the deaminated steroid (0.068 g, 55%).

3α-*Benzylamino*-(25R)-5α-*spirost*-9(11)-*ene* (7).—(*i*) To a mixture of 3α-benzamido-(25*R*)-5α-spirost-9(11)-ene (0.126 g) in dry chloroform (1 ml) and pyridine (0.12 ml) was added thionyl chloride (53 μl) at 0 °C. After stirring for 2 h at 35 °C the solvent was evaporated off and dry benzene was added and removed under reduced pressure. Addition of benzene and evaporation was repeated twice to ensure complete removal of traces of thionyl chloride. The imidoyl chloride (6) thus obtained had δ ($CDCl_3$) 8.0—7.8 (2 H, m), 7.6—7.2 (3 H, m), 5.27 (1 H, m), 4.6—4.35 (1 H, m), 4.35—4.15 (1 H, m), and 3.55—3.25 (2 H, m). A suspension of the imidoyl halide in toluene (20 ml) and AIBN (0.010 g) was added at 85 °C to a solution of tri-n-butylstannane (0.355 g) in toluene (10 ml) under nitrogen over 1 h. A further quantity of AIBN (0.01 g) in toluene was added over 2 h. The mixture was cooled and after evaporation of the solvent under reduced pressure purified by preparative t.l.c. (SiO_2; $CHCl_3$–MeOH, 9 : 1). The benzamide (0.0375 g, 30%) and the *N*-benzylamine (7) (0.0787 g, 64%) were isolated. No deaminated steroid was detected. The benzylamine (7) was identical in all respects to an authentic specimen (see below).

(*ii*) 3β-Tosyloxy-(25*R*)-5α-spirost-9(11)-ene (0.57 g) was heated under reflux for 2 h in benzylamine (5 ml) under nitrogen. After cooling to room temperature the reaction mixture was poured into ice–water and the *N*-benzylamino-steroid (7) was filtered off and purified by preparative t.l.c. (SiO_2; $CHCl_3$–methanol–pyridine, 35 : 4 : 1). Recrystallisation from wet hexane gave the *benzylamine* (7) (0.311 g, 62%), m.p. 151 °C, $[\alpha]_D^{20}$ −38.9 (*c*, 0.95), $\nu_{max.}$ ($CHCl_3$) 3 300, 1 642, and 1 605 cm^{-1}, δ ($CDCl_3$) 7.19 (5 H, s), 5.25 (1 H, m), 4.6—4.2 (1 H, m), 3.70 (2 H, s), 3.5—3.3 (2 H, m), and 2.87 (1 H, m), *m/e* 503 (Found: C, 80.8; H, 9.7; N, 2.65. $C_{34}H_{49}O_2N$ requires C, 81.06; H, 9.80; N, 2.78%).

2-*Methylnonadecane.*—To a refluxing solution of tri-n-butylstannane (0.32 g, 1.7 mol equiv.) in benzene (20 ml) was added a solution of 2-isocyano-2-methylnonadecane (0.2 g) and AIBN (0.005 g) in benzene (20 ml). After 20 min the mixture was cooled and the solvent evaporated off. The residual product was treated with iodine as previously described and purified by preparative t.l.c. (SiO_2; pentane) followed by sublimation *in vacuo* to yield 2-*methylnonadecane* (0.167 g, 91%), m.p. 20 °C, $\nu_{max.}$ (film) 2 960, 2 930, 2 863, 1 471, 1 369, and 722 cm^{-1}, δ (CCl_4) 1.24 (33 H, br s) and 1.05—0.8 (9 H, m), *m/e* 292 (Found: C, 84.8; H, 15.0. $C_{20}H_{42}$ requires C, 85.02; H, 14.98%).

Cholestane.—Method A. From 3α-*isocyanocholestane.*[13] 3α-Isocyanocholestane (86.2 mg) in toluene (3 ml) containing

AIBN was added dropwise to a refluxing solution of tri-n-butylstannane (94.4 mg) in toluene (2 ml) under nitrogen. Reflux was continued until all starting material had been consumed (i.r.). The solvent was removed *in vacuo* and the residue purified by column chromatography on alumina to give cholestane (44.9 mg, 56%), m.p. 80—81 °C and mixed m.p. 80—81 °C, identical with an authentic sample.

Method B. From 3-Isothiocyanatocholestane. 3α-Isothiocyanatocholestane (205 mg) in toluene (10 ml) containing AIBN was added slowly to a refluxing solution of tri-n-butylstannane (695 mg) in toluene (20 ml) and the reaction mixture was heated under nitrogen at reflux for 24 h. Work-up and purification as described above afforded cholestane (148.3 mg, 83%), m.p. and mixed m.p. 80—81 °C.

Reduction of p-Methoxyphenyl Isocyanide with Tri-n-butylstannane.—The aromatic isocyanide [14] (280 mg, 2.1 mmol) in toluene (3 ml) containing AIBN as initiator was added dropwise to a refluxing solution of tri-n-butylstannane (873 mg, 3 mmol) in toluene (3 ml) under nitrogen. After 6 h i.r. and t.l.c. failed to detect the presence of anisole in the reaction mixture. Repetition of the reaction without solvent at 150 °C led to a similar result. Slow decomposition of the isonitrile to more polar products was observed.

2-Deoxy-2-formamido-β-D-glucose 1,3,4,6-Tetra-acetate.—A suspension of glucosamine tetra-acetate hydrochloride [15] (1 g) and Amberlite IR 4B(OH) ion-exchange resin (5 ml) in chloroform (100 ml) was stirred for *ca.* 0.5 h until all the sugar had dissolved. The resin was filtered off and the filtrate was evaporated to yield the free base as a crystalline solid in quantitative yield, m.p. 142 °C, δ ($CDCl_3$), 4.53 (1 H, d, *J* 8 Hz), 2.95 (1 H, dd, *J* 8 Hz), and 1.39 (2 H, br). A saturated solution of the free amine in ether–THF was cooled to 0 °C, and acetic formic anhydride (0.5 g) was added dropwise. After 1 h the mixture was cooled to −78 °C, filtered, and the precipitate washed with pentane and dried to yield the *formamide* (0.92 g, 94%), m.p. 168—169 °C, $[\alpha]_D^{26}$ +5.8 (*c*, 0.8), $\nu_{max.}$ ($CHCl_3$) 3 425, 1 762, and 1 704 cm^{-1}, δ ([$^2H_6$]DMSO; 90 °C), 7.86 (1 H, d, *J* 12 Hz), 7.5 (1 H, br), 5.62 (1 H, d, *J* 8.5 Hz), 3.80 (1 H, dd, *J* 8.59 Hz), *m/e* 376 (Found: C, 47.7; H, 5.6; N, 3.6. $C_{15}H_{21}NO_{10}$ requires C, 48.00; H, 5.64; N, 3.73%).

1,3,4,6-Tetra-O-acetyl-2-deoxy-2-isocyano-β-D-glucose.—*Method A.* To *N*-formylglucosamine tetra-acetate (1.35 g) in dry pyridine (30 ml) was added toluene-*p*-sulphonyl chloride (1.2 g) at 0 °C. The mixture was stirred for 12 h at 25 °C and the reaction monitored by i.r. spectroscopy. After 12 h the mixture was poured into ice–water and the resulting mixture was neutralised with sodium hydrogencarbonate solution and extracted several times with chloroform. The combined extracts were washed with water, dried, and evaporated to yield the crude isocyanide (1.09 g, 85%). Chromatography on a short column (SiO_2; $CHCl_3$–MeOH, 9 : 1) followed by crystallisation from ether–hexane and recrystallisation from ethanol gave the pure *isocyanide* (0.77 g, 60%), m.p. 131—132 °C, $[\alpha]_D^{20}$ +48.7° (*c*, 2.5), $\nu_{max.}$ ($CHCl_3$) 2 155 and 1 763 cm^{-1}, δ ($CDCl_3$) 5.77 (1 H, d, *J* 8 Hz) and 3.76 (1 H, dd, *J* 8 Hz), *m/e* 357 (Found: C, 50.25; H, 5.3; N, 4.1. $C_{15}H_{19}NO_9$ requires C, 50.42; H, 5.36; N, 3.92%).

Method B. To the formamide (0.101 g) in dry dichloromethane (5 ml) was added triethylamine (0.3 ml) and the mixture was cooled to −30 °C. Phosphorus oxychloride (0.48 μl) was added and the mixture was allowed to warm to room temperature and stirred for a further 30 min until reaction was complete (t.l.c.). The mixture was transferred directly onto a column (SiO_2; benzene–tetrahydrofuran, 22 : 3) and rapidly eluted. The resultant product was crystallised from dichloromethane–hexane to yield the isocyanide (0.08 g, 86%), identical to that described above.

1,3,4,6-Tetra-O-acetyl-2-deoxy-β-D-glucose (10).—To a solution of tri-n-butylstannane(0.291 g, 2 mol equiv) in dry benzene (10 ml) was added a solution of AIBN (0.004 g) and the sugar isocyanide (0.178 g) in dry benzene (20 ml) over 45 min under nitrogen. After 15 min the mixture was cooled and the solvent removed under reduced pressure. Addition of wet methanol and repeated extraction with pentane removed most of the tin residues. Further purification was acheived by preparative t.l.c. (SiO_2; $CHCl_3$, triple development) and crystallisation from hexane–ether to give the *tetra-acetate* (10) (0.12 g, 72%), m.p. 92—93 °C (lit.,[16] 91—93 °C), $[\alpha]_D^{20}$ −5.2° (*c*, 1.0 in methanol) (lit.,[16] −9°), $\nu_{max.}$ ($CHCl_3$) 1 757 cm^{-1}, δ ($CDCl_3$) 5.49 (1 H, dd, *J* 2.5 and 9 Hz), *m/e* 332.

1,3,4,6-Tetra-O-acetyl-2-deoxy-α-D-glucose (9).—Glucosamine hydrochloride (35 g) was dissolved in water (50 ml) and sodium hydrogencarbonate (1.42 g) was added. A solution of *p*-nitrophenyl formate (5.42 g, 2 equiv.) in dioxan (50 ml) was added and the mixture was stirred for 48 h at room temperature. The dioxan was removed under reduced pressure and the residual aqueous phase was extracted with ether (2 × 50 ml) and then concentrated to dryness. Acetic anhydride (50 ml) and pyridine (5 ml) were added and the mixture was stirred at room temperature for 2 days, concentrated to dryness, and the residue dissolved in chloroform. The inorganic residues were filtered off and the filtrate was evaporated to yield the *N*-formylamino-sugar as a foam in quantitative yield, $\nu_{max.}$ ($CHCl_3$) 3 415, 1 740, and 1 690 cm^{-1}, δ 7.1 (1 H, br s), 6.2 (1 H, d, *J* 5 Hz), 3.5—6.0 br m), and 1.9—2.2 (12 H, overlapping acetyl signals).

Without further purification this product in CH_2Cl_2 (200 ml) was cooled to −30 °C and Et_3N (15 ml) was added. $POCl_3$ (2.5 g) was added dropwise over 10 min. The mixture was stirred and allowed to warm to room temperature. After 2 h, t.l.c. (SiO_2; toluene–tetrahydrofuran, 22 : 3) indicated that the reaction was incomplete. Further $POCl_3$ (2.5 g) and Et_3N (15 ml) were then added. After 6 h no starting material could be detected and the reaction mixture was concentrated to 25 ml and loaded onto a silica column (5 × 20 cm) packed in toluene. (An exothermic reaction took place on the column but this in no way affected the separation.) Elution with toluene–tetrahydrofuran 22 : 3 gave the isocyanide (5.17 g, 89%) which was chromatographically homogenous, $\nu_{max.}$ ($CHCl_3$) 2 140 and 1 735 cm^{-1}, δ 6.3 (1 H, d, *J* 3 Hz), 3.5—6.0 (6 H, m), 1.9—2.3 (12 H, overlapping acetate signals).

To a stirred solution of tri-n-butylstannane (4.63 g) in dry toluene (50 ml) at 85 °C, was added dropwise over 15 min the crude isocyanide and AIBN (0.1 g) in dry toluene (50 ml). After 2 h, t.l.c. indicated that some unchanged isocyanide was still present and a further quantity of tri-n-butylstannane (1 g) and AIBN (0.1 g) was added. After a further 2 h, the i.r. spectrum showed no $-\overset{+}{N}\equiv\overset{-}{C}$ stretch and the mixture was cooled, reduced in volume, and treated with a solution of iodine in toluene until the iodine colour persisted. The solution was filtered through a short silica column and concentrated to dryness. The colourless product was dissolved in acetonitrile (25 ml) and the solution washed with pentane (2 × 25 ml), concentrated to dryness and the residual solid dissolved in ether (50 ml). The

ethereal solution was washed with aqueous KF (2 × 25 ml, 10% w/v), dried ($MgSO_4$), filtered, and evaporated to yield the *tetra-acetate* (9) (4.35 g, 81% based on glucosamine HCl), m.p. 105—107 °C (lit.,[14] 106 °C), $\nu_{max.}$ ($CHCl_3$) 1 740 cm^{-1}, δ 6.2 (1 H, m), 4.8—5.5 (2 H, m), 3.9—4.5 (3 H, m), and 1.9—2.1 (14 H, m), $[\alpha]_D^{20}$ +104° (*c*, 0.24 in EtOH) [lit.,[16] +117° (MeOH)]. Although m.p. and spectroscopic properties indicated the product to be pure, it was possible to detect the smell of organotin residues. Repeated recrystallisation from ethanol removed this odour the melting point increasing to 109—110 °C, and $[\alpha]_D^{20}$ to 107°.

Methyl 4,6-O-*Benzylidene*-2-*deoxy*-2-*formamido*-α-D-*altropyranoside*.—To a stirred solution of the amino-alcohol [9] (12) (281 mg, 1 mmol) in tetrahydrofuran, cooled in an ice-bath, was added *p*-nitrophenyl formate (184 mg, 1.1 mmol). The mixture was allowed to attain room temperature and was then stirred for 6 h. The solvent was evaporated off and ether was added. The insoluble residue was filtered off, and washed with ether to give the desired *formamido-alcohol* (238 mg, 77%), m.p. 226.6—228.5 °C, $\nu_{max.}$ (Nujol) 3 300 (NH), 1 672, and 1 658 (N–CHO) cm^{-1}, δ (pyridine) 9.3 (1 H, br d, NH), 8.3 (1 H, s, CHO), 5.7 (1 H, s, PhCH), 3.35 (3 H s, OMe) (Found: C, 58.0; H, 6.2; N, 4.6; O, 30.8. $C_{15}H_{19}NO_6$ requires C, 58.25; H, 6.19; N, 4.53; O, 31.03%).

Methyl 4,6-O-*Benzylidene*-2-*deoxy*-2-*isocyano*-α-D-*altropyranoside* (11).—To a stirred suspension of the formamide (1.57 g, 5.1 mmol) and triethylamine (1.43 ml, 10.2 mmol) in dichloromethane (15 ml), cooled in an ice-bath, was added phosgene (1.01 g, 10.2 mmol) in dichloromethane (10 ml). The rate of addition was such that the temperature of the reaction mixture remained between 10 and 20 °C. When reaction was complete (t.l.c.), ammonia gas was bubbled through the solution until the mixture was alkaline, the precipitated ammonium chloride was filtered off, and the filtrate was evaporated. Filtration of the residue through a short column of silica gel yielded the *isocyanide* (11) (0.9 g, 60%), m.p. 158—159 °C (from ether), $[\alpha]_D^{20}$ +66.6° (*c*, 0.6 in $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 3 560 (OH) and 2 150 (–N=C:) cm^{-1}, δ 7.27 (5 H, br s, Ph), 5.6 (1 H, s, PhC*H*), 4.8 (1 H, br s, br C*H*OMe), and 3.4 (3 H, s, OMe) (Found: C, 61.9; H, 5.85; N, 4.8; O, 27.7. $C_{15}H_{17}NO_5$ requires C, 61.85; H, 5.88; N, 4.81; O, 27.46%).

Methyl 4,6-O-*Benzylidene*-2-*deoxy*-2-α-D-*altropyranoside* (13).—The isocyano-alcohol (11) (218 mg, 0.75 mmol) in toluene (10 ml) containing AIBN (12 mg) was added dropwise during 15 min to a solution of tri-n-butylstannane (447 mg, 1.5 mmol) in toluene (5 ml) with refluxing under nitrogen. After 20 min the mixture was cooled and the solvent was removed *in vacuo*. Trituration of the residue yielded the deoxy-alcohol (13) (181 mg, 92%), m.p. 117—119 °C (lit.,[17] 117—119 °C), $[\alpha]_D^{20}$ +138° (*c*, 1.35 in $CHCl_3$) [lit.,[18] +140° (*c*, 2.82 in $CHCl_3$)].

Methyl 4,6-O-*Benzylidene*-2-*deoxy*-2-*isocyano*-3-O-*mesyl*-α-D-*altropyranoside* (14).—To the isocyano-alcohol (11) (142 mg, 0.48 mmol) in pyridine (5 ml) was added methanesulphonyl chloride (114.6 mg, 0.96 mmol) and the mixture was allowed to stir at room temperature overnight. The mixture was then treated with water and extracted with ether. The combined extracts were washed with 5% sodium carbonate solution and water, and then dried. Chromatography on silica gel yielded the *methanesulphonate* (14) as a foam (82 mg, 45%) which was used without further purification, $[\alpha]_D^{20}$ +31.5° (*c*, 0.41, $CHCl_3$), $\nu_{max.}$ ($CHCl_3$) 2 130 (N=C:) cm^{-1}, δ 1.25 (5 H, s, Ph), 5.5 (1 H, s, PhC*H*), 3.35 (3 H, s, OMe), and 2.9 (3 H, s, SO_2Me).

Methyl 4,6-O-*Benzylidene*-2-*deoxy*-3-O-*mesyl*-α-D-*altropyranoside* (15).—The methanesulphonate (14) (45 mg, 0.12 mmol) in toluene (2 ml) containing AIBN (1 mg) was added dropwise to a refluxing solution of tri-n-butylstannane (139.6 mg, 4.8 mmol) in toluene (3 ml) under nitrogen. The mixture was refluxed for a further 2 h. Removal of solvent and column chromatography on silica gel gave the deoxy-derivative (15) (32 mg, 77%), m.p 125—125.5 °C (decomp.) [lit.,[9] 118—119 °C (decomp.)], $[\alpha]_D^{20}$ +124.5° (*c*, 0.935) [lit.,[9] +134° (*c* 1.28)], identical to a sample prepared by treatment of the deaminated alcohol (13) with methanesulphonyl chloride in pyridine.

Methyl 4,6-O-*Benzylidene*-2-*deoxy*-2-*isocyano*-α-D-*altropyranoside* 3-(S-*Methyl Dithiocarbonate*) (16).—The isocyano-alcohol (11) (94 mg, 0.3 mmol) and potassium hydride (26 mg, 0.6 mmol) in tetrahydrofuran (7 ml) were stirred under nitrogen for 2 h. Carbon disulphide (0.1 ml) was added and stirring was continued for a further 2 h, when methyl iodide (0.1 ml) was added. When reaction was complete (t.l.c.), water was added and the tetrahydrofuran was removed *in vacuo*. The residue was extracted several times with ether and the combined extracts were dried (Na_2SO_4). Removal of solvent and chromatography of the product on silica gel [ether–pentane (4 : 6) as eluant] gave the desired *derivative* (16) as a foam (81.3 mg, 64%), $[\alpha]_D^{20}$ +31.2 (*c*, 0.97), $\nu_{max.}$ ($CHCl_3$) 2 130 (–N=C:) cm^{-1}, δ 7.25 (5 H, br s, Ph), 5.45 (1 H, s, PhC*H*), 3.35 (3 H, s, OMe), and 2.5 (3 H, s, SMe), *m/e* 381 (Found: C, 53.35; H, 5.15; N, 3.4; S, 16.75; $C_{17}H_{19}NO_5S_2$ requires C, 53.53; H, 5.02; N, 3.67; S, 16.81%).

Tri-n-butylstannane Reduction of the Dithiocarbonate (16).—The dithiocarbonate (16) (63 mg, 0.17 mmol) in toluene (3 ml) containing AIBN (5 mgm) was added dropwise to a solution of tri-n-butylstannane (249 mg, 0.9 mmol) in toluene (3 ml) with refluxing under nitrogen. After 1 h, the mixture was cooled and the toluene was removed *in vacuo*. The residue was chromatographed on silica gel to yield the olefin (17) (36 mg, 90%), m.p. 117—120 °C (lit.,[19] 117—119 °C), whose spectroscopic properties were identical with those of an authentic sample.

Tri-n-butylstannane Reduction of 3α-*Isocyano*-Δ[9]-*tigogenin and* 5α-*Epicholestanyl* S-*Methyl Dithiocarbonate* (18). *Competition Experiment*.—3α-Isocyano-(25*R*)-5α-spirost-9(11)-ene (2) (57.6 mg, 0.14 mmol) and 5α-epicholestanyl *S*-methyl dithiocarbonate [20] (18) (62.4 mg, 0.13 mmol) in toluene (5 ml) containing AIBN (5 mg) was added dropwise to a refluxing solution of tri-n-butylstannane (44.2 mg, 0.15 mmol) in toluene (2 ml) under nitrogen. Refluxing was continued for 1 h and then the solvent was removed *in vacuo*. The following compounds, identified by comparison with authentic samples, were isolated by preparative t.l.c. on silica gel: cholestane (27 mg, 55.5%), epicholestanyl *S*-methyl dithiocarbonate (10.5 mg, 16.8%), (25*R*)-5α-spirost-9(11)-ene (19 mg, 35%), and 3α-isocyano-(25*R*)-5α-spirost-9(11)-ene (2) (28.2 mg, 49%).

Tri-n-butylstannane Reduction of 3α-*Isocyano*-Δ[9]-*tigogenin and Cholestan*-3β-*yl* S-*Methyl Dithiocarbonate*. *Competition Experiment*.—3α-Isocyano-(25*R*)-5α-spirost-9(11)-ene (50.5 mg, 0.12 mmol) and cholestan-3β-yl *S*-methyl dichiocarbonate (59.4 mg, 0.12 mmol) in toluene (5 ml) containing AIBN (4 mg) was added dropwise to a refluxing solution of tri-n-butylstannane (44.5 mg, 0.15 mmol) in toluene (2 ml) under nitrogen. Refluxing was continued for 1 h, and solvent was removed *in vacuo*. The following compounds, identified by comparison with authentic samples, were

isolated by preparative t.l.c. on silica gel: cholestane (23 mg, 50%), cholestan-3β-yl *S*-methyl dithiocarbonate (11.9 mg, 20%), (25*R*)-5α-spirost-9(11)-ene (4 mg, 8.5%), and 3α-isocyano-(25*R*)-5α-spirost-9(11)-ene (34.7 mg, 64.4%).

(±)-1,2-*Bisformamido*-1,2-*diphenylethane*.—The (±)-bisamine [21] (320 mg, 1.5 mmol) was stirred at room temperature in acetic formic anhydride (3 ml) as solvent until reaction was complete (3 h) (t.l.c.). Removal of solvent and recrystallisation of the resulting residue from methanol gave the *bisformamide* (225 mg, 62%), m.p. 212—214 °C, $\nu_{max.}$ (Nujol) 3 340 (NH) and 1 660 (amide) cm^{-1} (Found: C, 71.65; H, 5.95; N, 10.45; O, 12.1. $C_{16}H_{16}N_2O_2$ requires C, 71.62; H, 6.01; N, 10.44; O, 11.92%).

meso-1,2-*Bisformamido*-1,2-*diphenylethane*.—Reaction of the *meso*-diamine [21] as described above afforded the meso-*bisformamide* (57%) in an analytically pure form, crystalline change at 280 °C, sublimation and decomposition at 317—319 °C, $\nu_{max.}$ (Nujol) 3 340 (NH) and 1 660 (amide) cm^{-1} (Found: C, 71.45; H, 6.05; N, 10.55; O, 11.75. $C_{16}H_{11}N_2O_2$ requires C, 71.62; H, 6.01; N, 10.44; O, 11.92%).

(±)-1,2-*Di-isocyano*-1,2-*diphenylethane*.—To a stirred solution of the (±)-bisformamide (446 mg, 1.7 mmol) and triethylamine (1.15 ml, 8.1 mmol) in dichloromethane (10 ml), with cooling in an ice-bath, was added dropwise a solution of phosphorus oxychloride (512 mg, 3.3 mmol) in dichloromethane (8 ml). The temperature of the reaction mixture was maintained at 10—20 °C during the addition. The mixture was then allowed to attain, room temperature and stirred for a further 12 h. A solution of sodium hydrogencarbonate (5 g) in water (50 ml) was then added and the mixture was stirred for 1.5 h. The layers were separated and the aqueous phase was thoroughly extracted with dichloromethane. The combined organic extracts were dried (Na_2SO_4) and the solvent removed to give a crude product which was purified by filtration on a short silica gel column (ether as eluant) to give the (±)-di-isocyanide as a relatively unstable solid which was used without further purification (372 mg, 96%), $\nu_{max.}$ ($CHCl_3$) 2 140 (–N=C:) cm^{-1}, δ 4.84 (2 H, s, ArC*H*) and 7.1 (10 H, br s, Ph), *m/e* 233 and 116.

meso-1,2-*Di-isocyano*-1,2-*diphenylethane*.—This compound was prepared in an analogous manner (63%), $\nu_{max.}$ ($CHCl_3$) 2 140 (–N=C:) cm^{-1}, δ 4.85 (2 H, s, PhC*H*) and 7.1 (10 H, s, br., Ph).

Tri-n-butylstannane Reduction of (±)-1,2-*Di-isocyano*-1,2-*diphenylethane*.—The di-isocyanide (116 mg, 0.5 mmol) in benzene (3 ml) containing AIBN (10 mg) as initiator was added dropwise to a refluxing solution of tri-n-butylstannane (291 mg, 1 mmol) in benzene (2 ml) under nitrogen. The mixture was refluxed for a further 45 min. Removal of solvent and chromatography on silica gel gave bibenzyl (51 mg, 56%), m.p. 52 °C, δ 2.9 (4 H, s, CH_2) and 7.07 (10 H, s, aromatic).

Tri-n-butylstannane Reduction of meso-1,2-*Di-isocyano*-1,2-*diphenylethane*.—Reduction of the *meso*-di-isocyanide as described above afforded bibenzyl (53%). The yield of bibenzyl was unchanged by temperature when refluxing toluene or xylene was used as solvent. By using deuteriobenzene as solvent, the formation of toluene was detected by the appearance of a singlet at δ 2.14 in the n.m.r. spectrum (13%). Addition of toluene to the reaction mixture led to a relative increase in the intensity of this signal.

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