Some Reactions of Unsaturated Sulphur–Nitrogen Heterocycles with Nucleophilic Substrates

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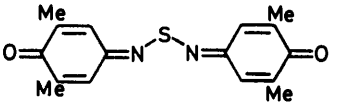
The reactivity of unsaturated sulphur–nitrogen heterocycles towards a variety of nucleophilic organic substrates has been studied. Tetrasulphur tetranitride (S_4N_4) is a relatively poor electrophile, but thiotrithiazyl chloride (S_4N_3Cl) and especially trithiazyl trichloride ($S_3N_3Cl_3$) react readily with electron-rich molecules. However, the diversity of mechanistic pathways followed by these reagents imposes limitations on their synthetic utility.

COMPOUNDS containing sulphur–nitrogen bonds are of considerable theoretical and practical interest. They have been traditionally prepared by reactions of separate sulphur- and nitrogen-bearing components.[1] Recent investigations have shown that substituted sulphur–nitrogen derivatives such as sulphenamides [2] and imide analogues of sulphur dioxide [3] may be employed usefully in organic synthesis.

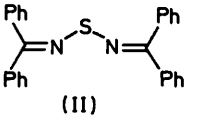
We considered that several members of the family of sulphur–nitrogen heterocycles, whose potential synthetic utility has been little investigated,[4] offered attractive possibilities for the direct introduction of the sulphur–nitrogen moiety unencumbered by additional substituents. We here describe the results of an investigation of the reactivity of tetrasulphur tetranitride (S_4N_4), thiotrithiazyl chloride (S_4N_3Cl), trithiazyl trichloride ($S_3N_3Cl_3$) (and the derived monomer NSCl), and tetrasulphur dinitride (S_4N_2) towards electron-rich organic substrates.

2,6-Xylenol reacted slowly with S_4N_4, more readily with S_4N_3Cl, and much more rapidly with $S_3N_3Cl_3$ to give *NN'*-thiobis-(2,6-dimethyl-1,4-benzoquinone imine) (I), in yields proportional to the order of reactivity. As S_4N_3Cl is insoluble in inert organic solvents, we carried out a reaction between 2,6-xylenol and S_4N_3Cl in trifluoroacetic acid, in which case the reaction mixture was initially homogeneous. However, the sole isolated product was 4-chloro-2,6-xylenol.

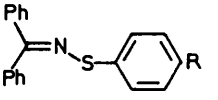
The low to moderate yields of compound (I) may in



(I)



(II)



(III)

a ; R = H

b ; R = NO_2

part be attributed to competitive reaction at the phenolic oxygen, for alcohols are known to react with S_4N_4,[5] S_4N_3Cl,[6] and $S_3N_3Cl_3$,[7] although in no case has full

[1] F. A. Davis, *Internat. J. Sulphur Chem.*, 1973, **8**, 71.

[2] J. Almog, D. H. R. Barton, P. D. Magnus, and R. K. Norris, *J.C.S. Perkin I*, 1974, 853, and previous papers in the series.

[3] G. Kresze and W. Wucherpfennig, *Angew. Chem. Internat. Edn.*, 1967, **6**, 149; N. Schönberger and G. Kresze, *Annalen*, 1975, 1725, and previous papers in the series; K. B. Sharpless and T. Hori, *J. Org. Chem.*, 1976, **41**, 176; W. L. Mock and R. M. Nugent, *J. Amer. Chem. Soc.*, 1975, **97**, 6521.

[4] A. J. Banister, 'M.T.P. International Reviews of Science: Inorganic Chemistry Series Two,' 1975, vol. 3, p. 41, and references therein; H. W. Roesky, *Chem.-Ztg.*, 1974, **98**, 121.

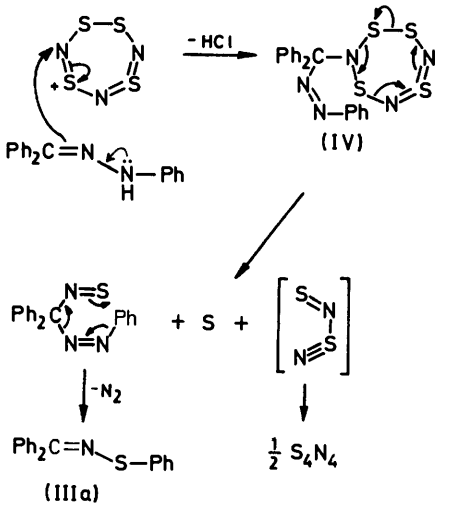
[5] W. Gesierich, Diplomarbeit, Heidelberg, 1954, quoted in M. Goehring, *Quart. Rev.*, 1956, **10**, 437.

[6] H. Wölbling, *Z. anorg. Chem.*, 1908, **57**, 281.

[7] A. Meuwsen, Colloquium of the Inorganic Chemistry Section, I.U.P.A.C., Münster, September 2—6, 1954, p. 130.

characterisation of the products been reported. In our hands cholestan-3β-ol reacted readily with $S_3N_3Cl_3$ to give, after chromatography on silica gel, cholestan-3β-yl sulphite.

We found S_4N_4 relatively unreactive towards electron-rich derivatives of benzophenone.* Thus, benzophenone



SCHEME 1

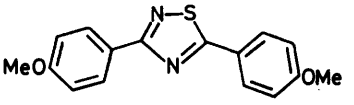
oxime reacted very slowly with S_4N_4 to give *NN'*-thiobis(diphenylmethyleneamine) (II) in low yield, and benzophenone hydrazone did not react in benzene solution during 27 h at reflux.

In contrast, benzophenone hydrazone reacted readily with S_4N_3Cl to give benzophenone azine in moderate yield, and benzophenone phenylhydrazone with S_4N_3Cl gave, albeit in low yield, *N*-(phenylthio)diphenylmethyleneamine (IIIa).[8] We attributed the formation of (IIIa) to intramolecular trapping of a thionitroso[9] intermediate (Scheme 1). As S_4N_3Cl is known[10] to undergo ring expansion on heating in benzene, the first step in this and other reactions under similar conditions, may involve attack of an intermediate in the ring expansion, rather than of $(S_4N_3)^+$. We substantiated our proposed mechanism by isolation of *N*-(*p*-nitrophenylthio)-diphenylmethyleneamine (IIIb) as the major product from reaction of benzophenone *p*-nitrophenylhydrazone with S_4N_3Cl. The formation in the same reaction of the imine (II) [attack on the intermediate corresponding to (IV) by a second substrate molecule] and 4-nitrobiphenyl [capture by the solvent of the 4-nitrophenyl radical, derived from loss of nitrogen by the thionitroso intermediate or the intermediate corresponding to (IV)] is consistent with this mechanism. The same products were obtained from the reaction of benzophenone *p*-nitrophenylhydrazone with $S_3N_3Cl_3$ in benzene at ambient temperature or in slightly different proportions at reflux.

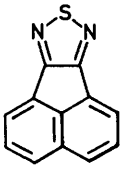
Benzophenone 2,4-dinitrophenylhydrazone did not react with S_4N_3Cl in benzene, and was recovered (94%) after 42 h at reflux.

p-Anisaldehyde *p*-nitrophenylhydrazone reacted readily with S_4N_3Cl in benzene at reflux to give 4-nitrobiphenyl and, in low yield, *p*-methoxybenzonitrile and 3,5-bis-(*p*-methoxyphenyl)-1,2,4-thiadiazole (V), the formation of each of which can be rationalised by invoking initial formation of a thionitroso intermediate (Scheme 2). However, whether the thiadazole (V) arises from the known[11] trapping of nitrile sulphide by nitrile [path (a)], or by a radical reaction with subsequent oxidation [path (b)] is uncertain. Similarly, *p*-methoxybenzonitrile may be derived from rearrangement analogous to that in Scheme 1 and subsequent elimination [path (c)] or by loss of sulphur from the nitrile sulphide [paths (a), (a')].

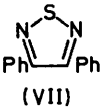
Earlier claims[12] that S_4N_4 effects 1,3-dipolar addition of nitrogen to strained olefins were, during this work, shown to be incorrect; the reaction in fact leads to carbon–sulphur bond formation,[12] so that vicinal diamination of olefins remains a challenging synthetic



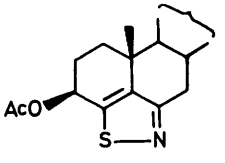
(V)



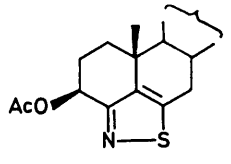
(VI)



(VII)



(VIIIa)



(VIIIb)

objective.[13] Nevertheless, we were encouraged by our initial observations that $S_3N_3Cl_3$ appeared to be a good

* We frequently recovered benzophenone from reactions of benzophenone derivatives with sulphur–nitrogen heterocycles and attribute its formation to hydrolysis of products during chromatography, as benzophenone was invariably obtained when 'streaking' on preparative t.l.c. plates was observed.

[8] D. H. R. Barton, I. A. Blair, P. D. Magnus, and R. K. Norris, *J.C.S. Perkin I*, 1973, 1037.

[9] F. A. Davis and E. B. Skibo, *J. Org. Chem.*, 1976, **41**, 1333, and references therein.

[10] M. Goehring, 'Ergebnisse und Probleme der Chemie der Schwefelstickstoffverbindungen,' Akademische Verlag, Berlin, 1957, quoted by I. Haiduc in 'The Chemistry of Inorganic Ring Systems,' Wiley–Interscience, London, 1970, part 2, p. 938.

[11] R. K. Howe and J. E. Franz, *J. Org. Chem.*, 1974, **39**, 962.

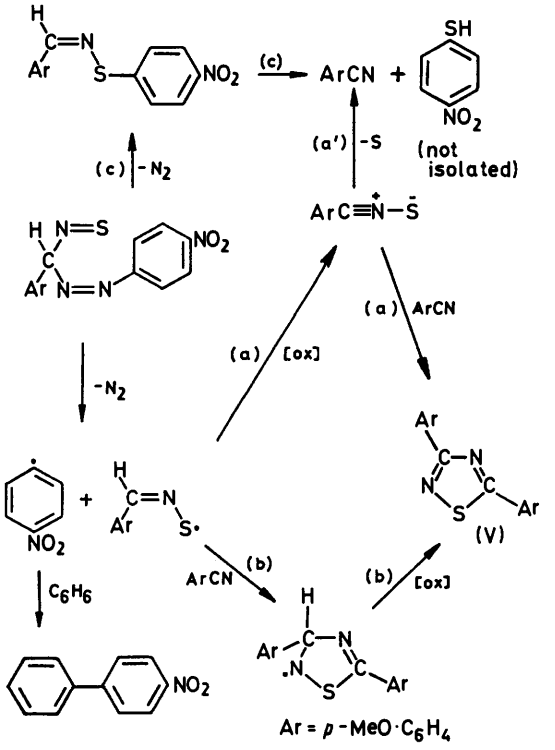
[12] W. L. Mock and I. Mehrotra, *J.C.S. Chem. Comm.*, 1976, 123, and references therein.

[13] *Cf.* K. B. Sharpless, D. W. Patrick, L. K. Truesdale, and S. A. Biller, *J. Amer. Chem. Soc.*, 1975, **97**, 2305; K. B. Sharpless, A. O. Chong, and K. Oshima, *J. Org. Chem.*, 1976, **41**, 177.

source of electrophilic nitrogen and much more reactive than S_4N_4. We examined a series of reactions of $S_3N_3Cl_3$ with olefinic substrates.

Acenaphthylene reacted readily with $S_3N_3Cl_3$ to give the 1,2,5-thiadiazole (VI) in moderate yield together with, in low yields, *cis*- and *trans*-1,2-dichloroacenaphthene. *trans*-Stilbene and $S_3N_3Cl_3$ afforded 3,4-diphenyl-1,2,5-thiadiazole (VII), which has been reduced stereoselectivity to *meso*-1,2-diphenylethylenediamine,[14] thus achieving vicinal diamination of an olefin in two steps.

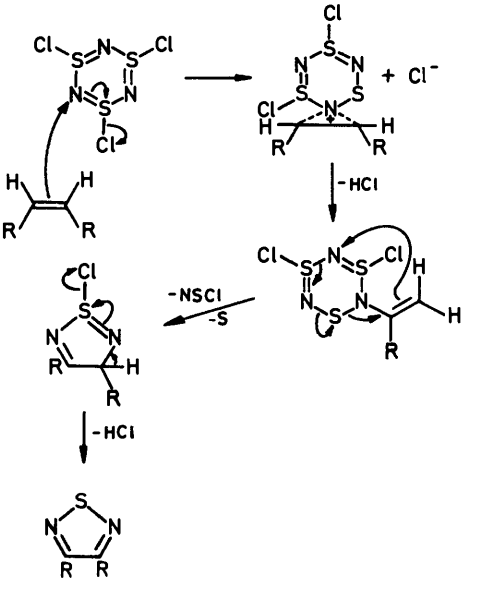
The formation of a 1,2,5-thiadiazole from an olefin with $S_3N_3Cl_3$ can be envisaged to proceed *via* initial



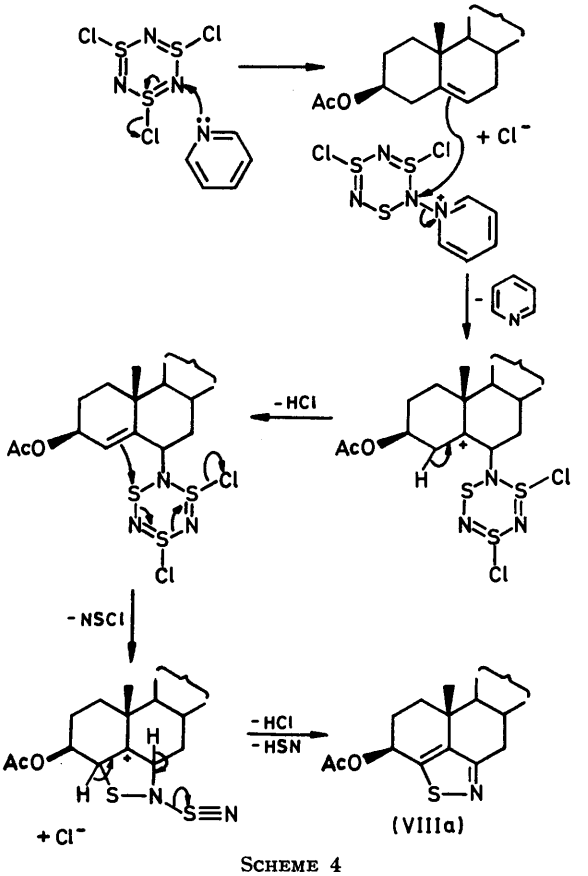
SCHEME 2

amination, followed by loss of HCl to give an enamine which reacts intramolecularly (Scheme 3). However, when we sought to extend this reaction to less reactive olefins bearing allylic hydrogens, different products were obtained.

Thus, cholesteryl acetate reacted readily with $S_3N_3Cl_3$ in the presence of pyridine to give a substance for which either of the structures (VIIIa and b) can be inferred from the molecular formula and the u.v. spectrum, which is in accord with that expected for an isothiazole with alkyl substituents.[15] As the reaction took an entirely different course in the absence of pyridine (see below), we consider that $S_3N_3Cl_3$ and pyridine rapidly give rise to an electrophile other than $S_3N_3Cl_3$ itself. Electrophilic addition followed by intramolecular trapping of the intermediate (Scheme 4) leads to the product; this favours structure (VIIIa). There is a possible mechanism leading to (VIIIb) if attack on electrophilic S is accepted (see below).



SCHEME 3



SCHEME 4

The reaction of cholesteryl acetate with the monomeric species NSCl (readily generated by pyrolysis of S_3N_3-

[14] V. Bertini and A. De Munno, *Gazzetta*, 1967, **97**, 1614.
[15] R. Slack and K. R. H. Wooldridge, *Adv. Heterocyclic Chem.*, 1965, **4**, 107.

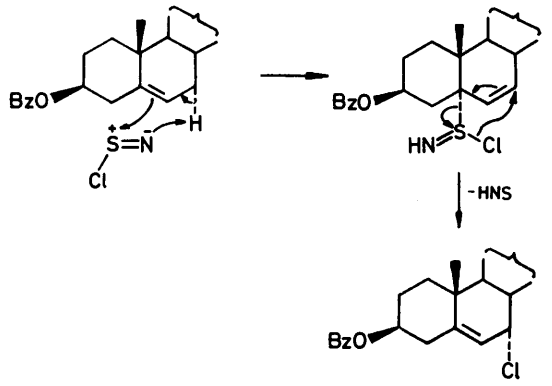
Cl_3[16]) gave, after chromatography, 7α- and 7β-hydroxycholesteryl acetate together with 4β-acetoxycholesterol, identified by conversion into the known acetoxybenzoates.

In the expectation that reaction at the 4-position would be minimised, the same reaction was investigated with cholesteryl benzoate: 7α-hydroxycholesteryl benzoate was the sole allylic alcohol obtained. If the highly crystalline S_4N_4 was initially removed from the crude product by washing a solution in ether–benzene with cold aqueous alkali, 7α-chlorocholesteryl benzoate could be obtained by direct crystallisation. The latter substance is presumably another crystal form of that obtained by treatment of 7α-hydroxycholesteryl benzoate with thionyl chloride; the two samples were identical except for their m.p.s, and the mixture m.p. was sharp (at the lower value).

The method of isolation suggested that 7α-hydroxycholesteryl benzoate was formed by hydrolysis of the chloride during chromatography, and this was readily confirmed by isolation of 7α-hydroxycholesteryl benzoate from preparative t.l.c. of crystalline 7α-chlorocholesteryl benzoate. It can be assumed reasonably that the allylic alcohols obtained from cholesteryl acetate were formed similarly.

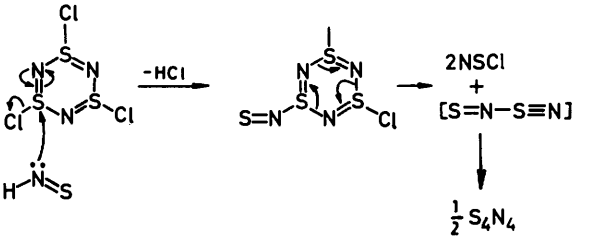
7α-Chlorocholesteryl benzoate was also obtained from the reaction of cholesteryl benzoate with $S_3N_3Cl_3$, but in this case the reaction displayed an induction period. Characteristically, no reaction between cholesteryl benzoate and $S_3N_3Cl_3$ in benzene solution was observed (t.l.c. analysis) after 1 h, but during a further 1 h the substrate was entirely consumed. Induction periods of up to 3 h were observed, to be compared with complete reaction of the substrate at a lower temperature after 1 h when NSCl was used as the reagent.

It is unlikely that the induction period is associated with a radical reaction, because 7α-chlorocholesteryl



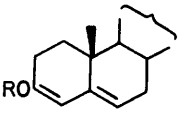
SCHEME 5

benzoate was obtained in similar yield from reactions of cholesteryl benzoate with $S_3N_3Cl_3$ in benzene or xylene and in the latter case chlorination of the solvent would be expected efficiently to consume the reagent if a radical process were operative. Rather, a mechanism involving two ene reactions (Scheme 5) appears more likely, in which case the reaction with $S_3N_3Cl_3$ in solution would be slow initially because of the low concentration of NSCl at ambient temperature; however, once reaction had commenced rapid consumption of the substrate would be expected because the by-product, HNS, can react with $S_3N_3Cl_3$ to produce two equivalents of NSCl and the stable S_4N_4 (Scheme 6).



SCHEME 6

We considered that the dienol ether (IXa) or acetate (IXb) might trap the pyridinium electrophile postulated



(IX)
a; R = Et
b: R = Ac

(Scheme 4) more efficiently than cholesteryl acetate. Indeed (IXa) reacted with $S_3N_3Cl_3$ in the presence of pyridine at −78 °C while (IXb) reacted rapidly at ambient temperature, but the major product in each case was that expected[17] from electrophilic chlorination of the substrate, namely 6β-chlorocholest-4-en-3-one. The presence of pyridine is not essential to the chlorination reaction: (IXb) gave the same product under similar conditions without pyridine.

Clearly $S_3N_3Cl_3$ (and the electrophile proposed in Scheme 4) can act as a source of electrophilic chlorine, but the chlorinations of (IXa) and (IXb) were the only examples encountered in this work where this was the *predominant* reaction pathway.

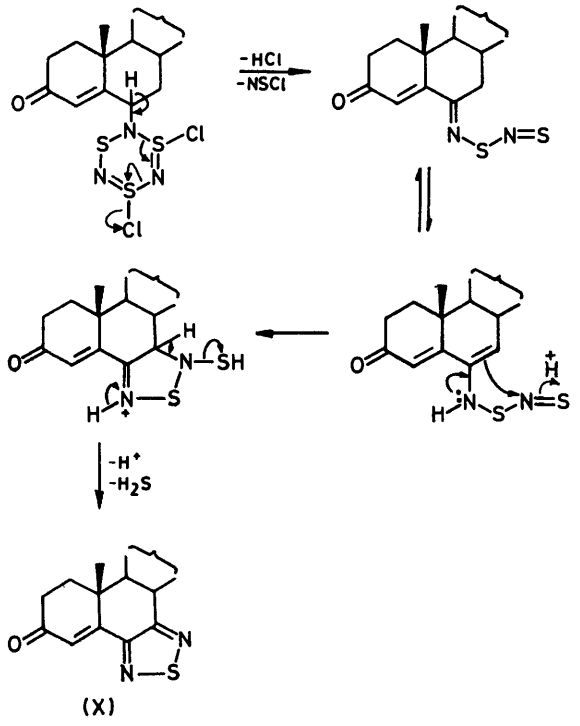
Cholest-5-en-3-one reacted readily with $S_3N_3Cl_3$ in the presence of pyridine to give the thiadiazole (X). Conjugation of the double bond with the 3-ketone function, which favours the initial electrophilic addition in this case, once achieved, renders the second electrophilic attack at C-4 less likely so that intramolecular reaction at C-7 is preferred (Scheme 7).

In principle the thiadiazole (X) is accessible *via* the reaction of $S_3N_3Cl_3$ with cholesta-4,6-dien-3-one, by analogy with the reactions of acenaphthylene and *trans*-stilbene. However, cholesta-4,6-dien-3-one and cholest-1-en-3-one did not react with $S_3N_3Cl_3$ in benzene

[16] R. L. Patton and W. L. Jolly, *Inorg. Chem.*, 1970, **9**, 1079.
[17] S. K. Malhotra and H. J. Ringold, *J. Amer. Chem. Soc.*, 1963, **85**, 1538.

at reflux after 6.5 and 9 h, respectively, and cholest-4-en-3-one did not react with $S_3N_3Cl_3$ in the presence of pyridine during 21 h in benzene solution at room temperature. Conjugation with a carbonyl group is clearly sufficient to prevent reaction between an olefin and $S_3N_3Cl_3$, and the reagent is presumably ultimately consumed by chlorination of the benzene solvent or of pyridine, accompanied by formation of S_4N_4, which was noted in each case.

That nitrogen is added to cholest-5-en-3-one before or during isomerisation of the double bond is apparent



SCHEME 7

because of the lack of reaction of cholest-4-en-3-one with $S_3N_3Cl_3$ under more forcing conditions.

Finally S_4N_2, reported to be a relatively unstable substance,[18] did not react in benzene at reflux with cholesteryl acetate or cyclohexene, but produced S_4N_4 and, presumably, sulphur.

In conclusion, S_4N_3Cl and $S_3N_3Cl_3$ lead to a variety of interesting products in reactions with electron-rich organic substrates. However, the crude product is usually a complex mixture and yields of pure substances are generally low. The multiplicity of pathways by which these reagents can react, although mechanistically fascinating, imposes limitations on their synthetic utility.*

EXPERIMENTAL

The reagents S_4N_4,[19] S_4N_3Cl,[20] $S_3N_3Cl_3$,[20] and S_4N_2 [21] were prepared by literature methods.

Except for the reaction of 2,6-xylenol with S_4N_3Cl in trifluoroacetic acid, all reactions were carried out in predried solvents in an inert atmosphere (purified nitrogen or argon). Extracts were routinely dried over anhydrous sodium sulphate. S_4N_4, S_4N_3Cl, and benzophenone were identified by comparison of i.r. spectra with those of authentic samples; other substances for which authentic samples were available were identified by m.p., mixed m.p., and comparison of i.r. spectra. Unless otherwise indicated, m.p.s were determined with a Kofler hot-stage apparatus. N.m.r. spectra were recorded for solutions in [^{2}H]chloroform with tetramethylsilane as internal standard (Varian T60 instrument). I.r. spectra were measured for Nujol mulls, u.v. spectra for solutions in dioxan, and, unless otherwise indicated, optical rotations for solutions in chloroform. Light petroleum refers to the fraction of b.p. 60—80 °C. Kieselgel GF_{254} (Merck) was used for t.l.c. and 100—200 mesh silica gel (Hopkin and Williams) for column chromatography.

Reactions of 2,6-Xylenol.—(i) *With* S_4N_3Cl *in benzene.* A mixture of S_4N_3Cl (0.206 g) and 2,6-xylenol (0.061 g), in benzene (5 ml) was heated at reflux, with stirring, for 1.25 h. After cooling, and dilution with benzene, the crude mixture was adsorbed onto silica gel (1 g) and chromatographed on silica gel (12 g). Elution with ether–benzene (1 : 49) gave an oily solid (0.079 g) which after preparative t.l.c., with ether–benzene (1 : 19) as developing solvent, gave NN′-*thiobis*-(2,6-*dimethyl*-1,4-*benzoquinone imine*) (I) (0.026 g), δ 2.07 (12 H, s, 4 × Me) and 7.00 (4 H, s, 4 × vinylic H). Recrystallisation from methylene chloride methanol gave red needles, m.p. 198—199°, $\nu_{max.}$ 1 635, 1 605, 1 320, 900, 805, and 780 cm^{-1}, $\lambda_{max.}$ (ε 45 000) and 260 nm (14 000) (Found: C, 63.8; H, 5.2; N, 9.2; S, 10.7. $C_{16}H_{16}N_2O_2S$ requires C, 64.0; H, 5.3; N, 9.3; S, 10.7%), *m/e* 300 (M^+), 166, and 135.

(ii) *With* S_4N_4. A solution of 2,6-xylenol (0.061 g) and S_4N_4 (0.092 g) in benzene (15 ml) containing pyridine (2 ml) was heated under reflux for 40 h. Concentration, followed by preparative t.l.c. with ether–benzene (1 : 9) as developing solvent, gave compound (I) (0.013 g), identical with that obtained from S_4N_3Cl.

(iii) *With* $S_3N_3Cl_3$. $S_3N_3Cl_3$ (0.110 g) in carbon tetrachloride (5 ml) was added, during 0.25 h, to a stirred solution of 2,6-xylenol (0.055 g) and pyridine (0.075 g) in carbon tetrachloride (5 ml) at ambient temperature. The mixture was stirred for a further 0.2 h and diluted with chloroform, and the solution was washed with water, dried, filtered, and

* A referee kindly commented that attack of a nucleophile on $S_3N_3Cl_3$ and related structures should take place at S rather than N. The formation of cholestanol sulphite from cholestanol and $S_3N_3Cl_3$ demonstrates this. We agree that the primary site of nucleophilic attack may be the sulphur, but argue that this is reversible and leads to subsequent reaction at nitrogen with reduction of sulphur(IV) to sulphur(II). Schemes 1, 2, and 3 and 7 explain the products better by attack on nitrogen than on sulphur. Scheme 4 could be rewritten with initial attack on sulphur. This would furnish structure (VIIb) and not (VIIIa) which we favour. Also in Scheme 4 it might be better to postulate attack of pyridine upon sulphur rather than nitrogen followed by electron displacements as before.

[18] H. G. Heal, *Adv. Inorg. Chem. Radiochem.*, 1972, **15**, 375; I. Haiduc in ' The Chemistry of Inorganic Ring Systems,' Wiley–Interscience, London, 1970, part 2, p. 964.

[19] M. Villena-Blanco and W. L. Jolly, *Inorg. Synth.*, 1967, **9**, 98.

[20] W. L. Jolly and K. D. Maguire, *Inorg. Synth.*, 1967, **9**, 102.

[21] M. Becke-Goehring, *Inorg. Synth.*, 1960, **6**, 123.

concentrated to give a brown oil which on preparative t.l.c. [ether–benzene (1 : 19)] gave compound (I) (0.034 g), identical with that obtained from S_4N_3Cl.

(iv) *With* S_4N_3Cl *in trifluoroacetic acid.* 2,6-Xylenol (0.061 g) was added to S_4N_3Cl (0.113 g) in trifluoroacetic acid (5 ml). The mixture was stirred for 3 h at ambient temperature, then diluted with chloroform, and the solution was washed with water. The washings were re-extracted with chloroform, the extracts were again washed with water, and the combined extracts were dried, filtered, and concentrated to give a brown solid (0.080 g) which was chromatographed on silica gel (12 g). Sublimation of the product from the benzene eluate gave 4-chloro-2,6-xylenol (0.036 g), m.p. 75—83°, δ 2.17 (6 H, s, 2 × Me), 4.54br (1 H, s, OH), and 6.84 (2 H, s, ArH). A second sublimation raised the m.p. to 83—84° (lit.,[22] 83°), *m/e* 158/156 (M^+).

Reaction of Cholestan-3β-ol with $S_3N_3Cl_3$.—A solution of cholestan-3β-ol (0.248 g) in benzene (10 ml) was added dropwise during 0.25 h to a stirred solution of $S_3N_3Cl_3$ (0.052 g) in benzene (2 ml). The mixture was stirred for 5 h at ambient temperature, diluted with benzene (10 ml), and heated under reflux for 1 h. The cooled solution was concentrated and the residue filtered through silica gel (25 g) in benzene to give cholestan-3β-yl sulphite (0.169 g), m.p. (from acetone) 198—199° (lit.,[23] 196—197.5°), $[\alpha]_D^{23}$ +10° (*c* 0.66) (lit.,[23] $[\alpha]_D^{31}$ +5.2 ± 2.5°), $\nu_{max.}$ 1 210 cm^{-1} (Found: C, 78.6; H, 11.1. Calc. for $C_{54}H_{94}O_3S$: C, 78.8; H, 11.5%).

Reaction of Benzophenone Oxime with S_4N_4.—A solution of benzophenone oxime (0.098 g) and S_4N_4 (0.092 g) in benzene (10 ml) was heated under reflux for 27 h. More S_4N_4 (0.092 g) was added and the solution was heated at reflux for an additional 43 h, then cooled. The excess of S_4N_4 was filtered off. Preparative t.l.c., of the mother liquor with benzene as developing solvent afforded *NN'*-thiobis-(diphenylmethyleneamine) (II) (0.008 g), identical with an authentic sample,[24] and, from two other bands, benzophenone (0.047 g). Development of the base-line with ether–benzene (1 : 9) yielded further benzophenone (0.015 g).

Reaction of Benzophenone Hydrazone with S_4N_3Cl.—A solution of benzophenone hydrazone (0.100 g) in benzene (10 ml) containing S_4N_3Cl (0.103 g) was heated under reflux, with stirring, for 0.5 h, cooled, and concentrated. The residue was redissolved in hot chloroform and the solution was filtered to remove an intractable yellow solid (0.013 g) and cooled to give S_4N_4 (0.012 g). Preparative t.l.c. of the mother liquor, with benzene–light petroleum (1 : 1) as developing solvent, gave more S_4N_4 (0.016 g) and benzophenone azine (0.047 g).

Reaction of Benzophenone Phenylhydrazone with S_4N_3Cl.—A solution of benzophenone phenylhydrazone (0.272 g) in benzene (15 ml), containing S_4N_3Cl (0.206 g) was heated under reflux, with stirring, for 0.3 h, and then cooled and concentrated. Preparative t.l.c. of the residue, with benzene–light petroleum (1 : 4) as developing solvent, afforded *N*-(phenylthio)diphenylmethyleneamine (IIIa) (0.029 g), identical with an authentic sample.[8] A very broad band yielded benzophenone (0.067 g).

Reactions of Benzophenone p-*Nitrophenylhydrazone.*—(i) *With* S_4N_3Cl. A solution of benzophenone *p*-nitrophenylhydrazone (0.159 g) in benzene (10 ml) containing S_4N_3Cl (0.103 g) was heated under reflux, with stirring, for 3 h, with further additions of S_4N_3Cl (0.103 g each time) after 1 and 2 h. The mixture was cooled and concentrated and the residue redissolved in chloroform. The precipitated mixture (i.r. analysis) of S_4N_4 and S_4N_3Cl was filtered off. Preparative t.l.c. of the filtrate with 25—100% benzene–light petroleum as developing solvent yielded 4-nitrobiphenyl (0.019 g), m.p. (from ether–light petroleum) 112—114° (lit.,[25] 113°), *m/e* 199 (M^+) and 152; *NN'*-thiobis-(diphenylmethyleneamine) (II) (0.018 g), identical with an authentic sample; benzophenone (0.031 g); and N-(p-*nitrophenylthio)diphenylmethyleneamine* (IIIb) (0.055 g), δ 7.17—7.94 (12 H, m, 2 Ph and protons *meta* to NO_2) and 8.07—8.44 (2 H, m, protons *ortho* to NO_2), m.p. (from methylene chloride–methanol) 128—130°, $\nu_{max.}$ 1 580, 1 500, 1 335, 860, 840, 780, 745, and 700 cm^{-1}, $\lambda_{max.}$ 367 nm (ε 26 000) (Found: C, 68.3; H, 4.4; N, 8.5; S, 9.6. $C_{19}H_{14}N_2O_2S$ requires C, 68.3; H, 4.2; N, 8.4; S, 9.6%), *m/e* 334 (M^+), 211, and 180.

(ii) *With* $S_3N_3Cl_3$ *at ambient temperature.* A solution of benzophenone *p*-nitrophenylhydrazone (0.130 g), $S_3N_3Cl_3$ (0.100 g), and pyridine (0.130 g) in benzene (10 ml) was stirred at ambient temperature for 15 h. The precipitated pyridine hydrochloride was filtered off and the filtrate concentrated. Preparative t.l.c. of the residue yielded 4-nitrobiphenyl (0.014 g) and compounds (II) (0.037 g) and (IIIb) (0.032 g), all identical with samples obtained from the corresponding reaction with S_4N_3Cl.

(iii) *With* $S_3N_3Cl_3$ *in benzene at reflux.* $S_3N_3Cl_3$ (0.100 g) in benzene (10 ml) was added during 0.3 h to benzophenone *p*-nitrophenylhydrazone (0.389 g) and pyridine (0.096 g) in benzene (8 ml) at reflux. After 1.5 h, more $S_3N_3Cl_3$ (0.100 g) in benzene (4 ml) was added and the mixture was heated under reflux for an additional 1.5 h. Work-up as above gave 4-nitrobiphenyl (0.114 g) and compounds (II) (0.092 g) and (IIIb) (0.095 g).

Reaction of p-*Anisaldehyde* p-*Nitrophenylhydrazone with* S_4N_3Cl.—A solution of *p*-anisaldehyde *p*-nitrophenylhydrazone (0.135 g) in benzene (10 ml) containing S_4N_3Cl (0.103 g) was heated under reflux, with stirring, for 0.75 h. More S_4N_3Cl (0.050 g) was added and the mixture was heated at reflux for an additional 0.5 h, cooled, and concentrated. Preparative t.l.c. of the residue with 25—100% benzene–light petroleum as developing solvent gave 4-nitrobiphenyl (0.044 g), identical with that obtained from benzophenone *p*-nitrophenylhydrazone, *p*-methoxybenzonitrile (0.004 g), and 3,5-bis-(*p*-methoxyphenyl)-1,2,4-thiadiazole (V) (0.005 g), m.p. (from methylene chloride–light petroleum) 138—140° (lit.,[26] 139—140°), δ 3.90 (6 H, s, 2 × OCH_3), 6.84—7.24 (4 H, AA'XX', C_6H_4), and 7.90—8.50 (4 H, AA'XX', C_6H_4), *m/e* 298 (M^+), 165, and 133.

Reaction of Acenaphthylene with $S_3N_3Cl_3$.—A solution of acenaphthylene (0.165 g) and $S_3N_3Cl_3$ (0.265 g) in benzene (13 ml) was warmed during 0.2 h and heated under reflux for 0.1 h. The solution was cooled, concentrated, and filtered and the filtrate was poured into aqueous sodium hydrogen carbonate and extracted with methylene chloride. Potassium hydroxide was added to the aqueous phase, which was further extracted with methylene chloride. The combined

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extracts were washed with water, dried, filtered, and concentrated to give a red oil which after preparative t.l.c. with 0—50% benzene–light petroleum as developing solvent gave S_4N_4 (0.032 g); acenaphtho[1,2-*c*][1,2,5]thiadiazole (VI) (0.071 g), δ 7.40—8.30 (m), m.p. (from ether–light petroleum) 136—137° (lit.,[27] 132—133°) (Found: C, 68.4; H, 3.0; N, 13.5; S, 15.3. Calc. for $C_{12}H_6N_2S$: C, 68.6; H, 2.9; N, 13.3; S, 15.2%), *m/e* 210 (M^+), 178, and 151; *cis*-1,2-dichloroacenaphthene (0.007 g), m.p. (from ether–light petroleum) 116—118° (lit.,[28] 116°), δ 5.94 (2 H, s, ArC*H*Cl·C*H*ClAr) and 7.42—8.09 (6 H. m, ArH), *m/e* 224/222 (M^+), 189/187 (M^+ − Cl), and 152 (M^+ − 2 Cl); and *trans*-1,2-dichloroacenaphthene (0.003 g), m.p. (from ether–light petroleum) 67—68° (lit.,[28] 67—68°), δ 5.75 (2 H, s, ArC*H*Cl·C*H*ClAr) and 7.45—8.15 (6 H, m, ArH), *m/e* 224/222 (M^+), 189/187 (M^+ − Cl), and 152 (M^+ − 2 Cl).

Reaction of trans-Stilbene with $S_3N_3Cl_3$.—A solution of *trans*-stilbene (0.101 g) and $S_3N_3Cl_3$ (0.137 g) in benzene (11 ml) was stirred at ambient temperature. After 1.5 h no reaction was indicated (t.l.c.) and the solution was heated under reflux for 4.5 h, cooled, and concentrated. Preparative t.l.c. of the residue with benzene–light petroleum (1 : 9) as developing solvent afforded *trans*-stilbene (0.026 g), S_4N_4 (0.003 g), and 3,4-diphenyl-1,2,5-thiadiazole (VII) (0.019 g), m.p. (from methylene chloride–methanol) 84—85° (lit.,[29] 85—86°), *m/e* 238 (M^+), 135, and 103.

Reaction of Cholesteryl Acetate with $S_3N_3Cl_3$ *in the Presence of Pyridine*.—A solution of $S_3N_3Cl_3$ (0.261 g) in benzene (10 ml) was added dropwise, during 0.1 h, to a stirred solution of cholesteryl acetate (0.228 g) in benzene (5 ml) containing pyridine (0.253 g). After 1 h, pyridine hydrochloride was filtered off and the filtrate was concentrated and chromatographed on silica gel (25 g). Elution with benzene gave S_4N_4 (0.097 g); elution with ether–benzene (1 : 99 and 1 : 49) afforded an orange oil (0.093 g) which after preparative t.l.c., with ether–benzene (1 : 19) as developing solvent, yielded 3β-*acetoxycholest*-4-*eno*[6,5,4-cd]*isothiazole* (VIIIa) (0.034 g), δ 0.75 (s), 1.23 (s), 2.12 (s, OAc), and 5.70—6.07 (1 H. m, H-3α). Recrystallisation from methylene chloride–methanol gave a sample with m.p. 152—154°, $[\alpha]_D^{17}$ −178° (*c* 0.45), $\nu_{max.}$ 1 730, 1 255, and 1 040 cm^{-1}, $\lambda_{max.}$ 254 nm (ε 6 900) (Found: C, 73.9; H, 9.6; N, 2.9; S, 6.9. $C_{29}H_{45}NO_2S$ requires C, 73.8; H, 9.6; N, 3.0; S, 6.9%), *m/e* 481 (M^+), 456, 412, and 396.

Reaction of Cholesteryl Acetate with NSCl.—A stirred solution of cholesteryl acetate (0.58 g) in ether (25 ml) containing potassium carbonate (1 g) was treated with NSCl vapour (from pyrolysis of $S_3N_3Cl_3$ at 70—80 °C) by using a short-path nitrogen stream until complete consumption of the substrate was indicated by t.l.c. Ether was added and the solution was washed with brine, dried, filtered, and concentrated to give a brown foam which was chromatographed on silica gel (40 g). Elution with benzene gave an oily solid (0.202 g) which in ether yielded S_4N_4 (0.030 g). Preparative t.l.c. of the mother liquor did not yield any pure substance. Elution with ether afforded an orange foam (0.277 g) which after preparative t.l.c. with ether–benzene (1 : 4—1 : 19) gave 7β-hydroxycholesteryl acetate (0.010 g), m.p. (from aqueous methanol) 106—110° (lit.,[30] 110—111°), $[\alpha]_D^{23}$ −9° (*c* 0.10) (lit.,[30] $[\alpha]_D^{16}$ −5°) {treatment with benzoyl chloride–pyridine gave 7β-benzoyloxycholesteryl acetate, m.p. (from methanol) 167—170° (lit.,[30] 166°), $[\alpha]_D^{23}$ +82° (*c* 0.15) (lit.,[30] $[\alpha]_D^{17}$ +82°)}; 7α-hydroxycholesteryl acetate (0.008 g), m.p. (from aqueous methanol) 137—140° (lit.,[30] 139°), $[\alpha]_D^{23}$ −85° (*c* 0.24) (lit.,[30] $[\alpha]_D^{20}$ −87.5°) {treatment with benzoyl chloride–pyridine gave 7α-benzoyloxycholesteryl acetate, m.p. (from methanol) 115—117° (lit.,[30] 113°), $[\alpha]_D^{22}$ −167° (*c* 0.21) (lit.,[30] $[\alpha]_D^{20}$ −176°)}; and 4β-acetoxycholesterol (0.015 g), m.p. (from methanol) 156—159° (lit.,[31] 159—161°; lit.,[32] 164—165°), $[\alpha]_D^{23}$ −95° (*c* 0.16) (lit.,[32] $[\alpha]_D^{24}$ −88.8°) {treatment with benzoyl chloride–pyridine gave 4β-acetoxycholesteryl benzoate, m.p. (from methanol) 167—170° (lit.,[33] 166—167°), $[\alpha]_D^{23}$ −54° (*c* 0.19) (lit.,[33] $[\alpha]_D^{20}$ −55.9°)}.

Reactions of Cholesteryl Benzoate with $S_3N_3Cl_3$.—(i) 7α-*Chlorocholesteryl benzoate*. A solution of cholesteryl benzoate (0.186 g) and $S_3N_3Cl_3$ (0.186 g) in benzene (20 ml) was stirred at room temperature for 2 h. Ether was added and the solution was washed in turn with cold aqueous sodium hydroxide (1N) and brine, dried, filtered, and concentrated to give a straw-coloured foam (0.193 g) which deposited a brown solid (0.053 g) from acetone. Further crystallisation of this solid from acetone (charcoal) afforded 7α-chlorocholesteryl benzoate, m.p. and mixed m.p. (sealed capillary) 137—138° (decomp.) (lit.,[34] 149—150°), $[\alpha]_D^{21}$ −118° (*c* 0.05) (lit.,[34] $[\alpha]_D^{18}$ −119°) (Found: C, 77.9; H, 9.3. Calc. for $C_{34}H_{49}ClO_2$: C, 77.8; H, 9.4%).

In a companion experiment with xylene as solvent, cholesteryl benzoate (0.125 g) afforded, from the initial crystallisation, a brown solid (0.038 g), m.p. 130—132°, and after further purification as above, 7α-chlorocholesteryl benzoate, m.p. (sealed capillary) 135—137° (decomp.), $[\alpha]_D^{25}$ −117° (*c* 0.41).

(ii) 7α-*Hydroxycholesteryl benzoate*. Cholesteryl benzoate (0.184 g) and $S_3N_3Cl_3$ (0.184 g) were stirred together in benzene (15 ml) for 3 h. After removal of the solvent under reduced pressure, preparative t.l.c. with ether–benzene (1 : 19) afforded 7α-hydroxycholesteryl benzoate (0.040 g), m.p. (from acetone; sealed capillary) 166—168° (lit.,[30] 167—168°), $[\alpha]_D^{23}$ −50° (*c* 0.77) (lit.,[30] $[\alpha]_D^{18}$ −50.5°).

(iii) *Hydrolysis of* 7α-*chlorocholesteryl benzoate on silica gel*. 7α-Chlorocholesteryl benzoate (0.030 g) {m.p. 136—137° (decomp.), $[\alpha]_D^{26}$ −103° (*c* 0.48)}, obtained by direct crystallisation from the mixture formed by the reaction of cholesteryl benzoate with $S_3N_3Cl_3$ [see (i)], was subjected to preparative t.l.c. with ether–benzene (1 : 9) as developing solvent. Extraction of the polar band yielded 7α-hydroxycholesteryl benzoate (0.015 g), m.p. (from acetone; sealed capillary) 166—168°, $[\alpha]_D^{23}$ −49° (*c* 0.35).

Reactions of Cholesteryl Benzoate with NSCl.—(i) 7α-*Chlorocholesteryl benzoate*. A stirred, cold (ice-bath) solution of cholesteryl benzoate (0.268 g) in ether (30 ml) was treated with NSCl (from pyrolysis of $S_3N_3Cl_3$ at 60—70 °C) until complete consumption of the substrate was indicated by t.l.c. Ether was added and the solution was washed in

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turn with cold aqueous sodium hydroxide (1N) and brine, dried, filtered, and concentrated to give a brown foam which deposited a pale brown solid (0.040 g) from acetone. Further crystallisation from acetone afforded 7α-chlorocholesteryl benzoate, m.p. (sealed capillary) 134—135° (decomp.), mixed m.p. (sealed capillary) 135—136.5° (decomp.), $[\alpha]_D^{23}$ −119° (*c* 0.12).

(ii) *7α-Hydroxycholesteryl benzoate*. Cholesteryl benzoate (0.290 g) in ether (25 ml) was treated with NSCl as in (i). After 1 h the mixture was diluted with ether and the solution was washed with brine, dried, filtered, and concentrated to give an orange foam. Preparative t.l.c. with ether–benzene (1 : 9) afforded 7α-hydroxycholesteryl benzoate (0.094 g), m.p. (from ether–light petroleum) 167—169°, $[\alpha]_D^{24}$ −48° (*c* 0.54).

Treatment of an ethereal solution with thionyl chloride [34] gave 7α-chlorocholesteryl benzoate, m.p. (from acetone; sealed capillary) 148—150°, $[\alpha]_D^{22}$ −119° (*c* 0.41).

Reaction of 3-Ethoxycholesta-3,5-diene with $S_3N_3Cl_3$.—$S_3N_3Cl_3$ (0.040 g) in ether (7.5 ml) was added dropwise, during 0.3 h, to a stirred solution, at −78 °C, of 3-ethoxycholesta-3,5-diene [35] (0.067 g) in ether (12 ml) containing pyridine (0.077 g). After a further 0.25 h the mixture was diluted with ether and the solution was washed with brine, dried, filtered, and concentrated to a brown oil. Preparative t.l.c. with ether–benzene (1 : 19) as developing solvent, afforded 6β-chlorocholest-4-en-3-one (0.023 g) as a pale yellow oil, δ 4.74 (1 H, m, $W_{\frac{1}{2}}$ 8 Hz, H-6α) and 5.89 (1 H, s, H-4), which on trituration with methanol yielded light yellow crystals, m.p. 126—128° (lit.,[36] 129—130°), $[\alpha]_D^{30}$ +14° (*c* 0.19) {lit.,[36] $[\alpha]_D$ +14° (*c* 2.32); $[\alpha]_D$ +17°, (*c* 1.13)}, $\nu_{max.}$ 1 690 cm^{-1}, *m/e* 420/418 (M^+).

Reactions of 3-Acetoxycholesta-3,5-diene with $S_3N_3Cl_3$.—(i) *With pyridine*. 3-Acetoxycholesta-3,5-diene [37] (0.091 g) in benzene (10 ml) was added to a stirred solution, at ambient temperature, of $S_3N_3Cl_3$ (0.101 g) and pyridine (0.098 g) in benzene (10 ml). After 0.25 h the mixture was diluted with ether, washed with brine, dried, filtered, and concentrated. Preparative t.l.c. of the residue, with benzene as developing solvent, afforded 6β-chlorocholest-4-en-3-one (0.032 g), m.p. (from ethyl acetate–methanol) 128—129°, $[\alpha]_D^{22}$ +12° (*c* 0.39).

(ii) *Without pyridine*. 3-Acetoxycholesta-3,5-diene (0.070 g) and $S_3N_3Cl_3$ (0.077 g) were stirred together in benzene (20 ml) for 0.7 h. Work-up as above gave 6β-chlorocholest-4-en-3-one (0.024 g), m.p. (from ethyl acetate–methanol) 127—129°, $[\alpha]_D^{22}$ +13° (*c* 0.47).

Reaction of Cholest-5-en-3-one with $S_3N_3Cl_3$.—A solution of $S_3N_3Cl_3$ (0.300 g) in ether (25 ml) was added dropwise, during 1 h, to a stirred suspension, at −78 °C, of cholest-5-en-3-one (0.470 g) in ether (15 ml) containing pyridine (0.290 g). After a further 1 h at −78 °C, t.l.c. indicated the presence of only cholest-5-en-3-one, and the mixture was therefore allowed to warm to room temperature during 2.3 h, after which more $S_3N_3Cl_3$ (0.400 g) was added and stirring was continued for 0.2 h. The solution, after dilution with ether, was washed with brine, and the aqueous washings were extracted with methylene chloride. The organic solutions were combined, dried, filtered, and concentrated to give an oily brown solid, which was chromatographed on silica gel (20 g). Elution with ether gave a brown foam (0.370 g) which after preparative t.l.c. [with benzene and ether–benzene (1 : 19)] gave *cholest-4-eno*[6,7-c][1,2,5]*thiadiazol-3-one* (X) as a yellow oil (0.033 g), δ 6.77 (1 H, s, H-4). Two crystallisations from methylene chloride–methanol gave the methanol solvate as yellow needles, m.p. 147—150°, $[\alpha]_D^{23}$ +86° (*c* 0.12 in dioxan), $\nu_{max.}$ 1 670 cm^{-1}, $\lambda_{max.}$ 313 (ε 20 500) and 255 nm (18 000) (Found: C, 72.1; H, 8.3; N, 6.2; S, 7.2. $C_{27}H_{40}N_2OS,CH_3OH$ requires C, 71.8; H, 8.6; N, 6.0; S, 6.8%), *m/e* 440 (M^+), 384, 355, and 327.

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